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UTILIZATION OF EGGSHELL-DERIVED MATERIAL AS A SOLID BASE CATALYST FOR EFFICIENT SYNTHESIS OF SUBSTITUTED CHALCONES

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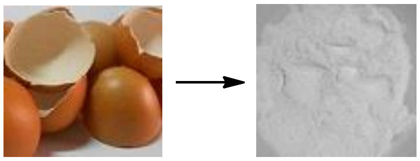
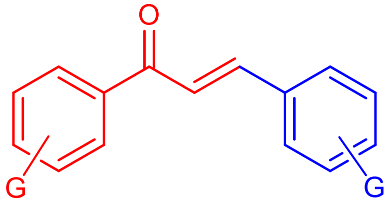
Graphical abstract



Simple Preparation of Eggshell-Derived catalyst



Green Synthesis of chalcones using Eggshell-Derived catalyst

Abstract

A simple preparation of sodium impregnated on activated chicken eggshells (Na-ACE) as a solid base material for substituted chalcones synthesis is presented. After characterization using FTIR, XRD, SEM, EDS and total basicity, the catalyst was applied in Aldol condensation to produce corresponding chalcones 3a-3j. Confirmation of products structure has been done by FTIR, UV-Vis and MS instruments. Reaction can be carried out in relative short time with ethanol as the best solvent and gave the highest yield of 95 %. This research presented a facile synthesis of chalcone derivatives, the prominent class of organic compounds with interesting biological activities.

Keywords: Activated chicken eggshells, chalcones, Aldol condensation

Abstrak

Pembuatan dengan cara yang mudah dari natrium yang terimpregnasi pada cengkerang telur ayam diaktifkan sebagai material basa padat untuk sintesis chalcone tersubstitusi telah dibentangkan. Setelah pencirian menggunakan FTIR, XRD, SEM, EDS dan pengiraan kebasaan total, pemangkin diaplikasikan dalam pemeluwapan Aldol untuk menghasilkan chalcone 3a-3j. Pengesahan struktur produk telah dilakukan menggunakan instrumen FTIR, UV-Vis dan MS. Reaksi dapat dilakukan dalam masa yang singkat dengan etanol sebagai pelarut terbaik yang akan menghasilkan peratus yield tertinggi 95%. Kajian ini membentangkan sintesis yang mudah dari chalcone, kelas penting dari sebatian organik dengan aktiviti biologi yang menarik.

Kata kunci: Cengkerang telur ayam teraktivasi, chalcone, pemeluwapan Aldol

1.0 INTRODUCTION

Chalcones are remarkably prominent class of natural products which have precious biological benefit in the field of medicine, such as exhibiting cytotoxic [1], antiamoebic [2], antimicrobial [3], antioxidant [4], and anticancer [5] activities. They also can act as an intermediate for the synthesis of various heterocyclic compounds like pyrazoles, isoxazoles, pyrimidines [6], 1,5-benzodiazepines [7,8], thiazines [9], and flavonoids [10]. Indeed, due to the wide application in pharmaceutical and biological sectors, techniques to synthesize chalcones have drawn tremendous attention over the past few years [11].

Chalcones are commonly synthesized via Claisen-Schmidt Aldol condensation using acids or bases homogeneous catalysts, such as NaOH [12,13], KOH [14], HCl, BF_3-Et_2O [15] and $TiCl_4$ [16]. Unfortunately, there are many drawbacks under these protocols such as catalyst recovery and waste-disposal problems [11]. In order to solve the problems, the use of solid catalysts provides several advantages like easy to handle and reusable. The catalysts such as modified activated carbon [17], hydrotalcites [18], bentonite, montmorillonite hectorite, and kaolin [19] have received great attention over the last decade. Generally, these catalysts can accomodate the production of chalcones in a medium to a high yield. But, some of previosly known catalysts suffer several limitation such as tedious work-up in catalyst preparation and also high cost catalyst materials. Thus, the demand for an eco-friendly, easy to prepare, and efficient catalyst is still highly required and motivated the present investigation.

Activated (or calcined) chicken eggshells, ACE is a simple, easy to obtain, and inexpensive material from the treatment of raw chicken eggshells waste [20]. Recently, various types of organic transformation using ACE have been reported, such as synthesis of 2-aminochromenes [21], esterification in biodiesel production [22,23], synthesis of dimethyl carbonate [24], partial oxidation of methane [25], and Schiff base formation [26]. The previous research shows that the main component present in ACE is calcium oxide [20], and its catalytic performance can be enhanced upon the active metal ion impregnation [27]. Herein, we will explore the catalytic ability of sodium impregnated on activated chicken eggshells (Na-ACE) in the synthesis of chalcone derivatives (the reaction scheme shown in Figure 1).

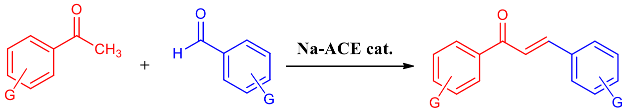


Figure 1 Reaction scheme of chalcones synthesis

2.0 METHODOLOGY

2.1 General and Instrumentation

All melting points were determined in Electrothermal-9100 melting point apparatus. The products purity was checked by analytical thin layer chromatography on TLC (0.5 mm thickness) using silica gel coated Al plates supplied from Merck, and visualized under UV light (254 nm). All chemicals were purchased from commercial suppliers. FTIR spectra were recorded on Shimadzu Prestige-21 spectrophotometer in KBr pellets. The maximum wavelength of compounds was determined using Shimadzu 2400 UV-Vis spectrophotometer. Structure elucidation was confirmed using mass spectrometer. XRD analysis was performed using Shimadzu XRD-7000 X-ray Diffractometer with the Cu-Kα (λ = 0.154 nm) radiation in the 2θ range of 10-80° at the 2°/min scanning rate. The morphological and elemental analyses were done using FESEM Hitachi S1460 tandem EDS instrument.

2.2 Catalyst Preparation

Na-ACE catalyst was prepared based on our previous work [20]. Briefly, the chicken eggshells were dried in an oven at 120°C for 2h and crushed into fine powder. The activated chicken eggshells (ACE) were obtained by calcination of the dried eggshells (30 g) at 900°C in air atmosphere with a heating rate of 10°C/min for 4h. To increase the basicity, sodium ion was impregnated on ACE by adding NaOH solution (2%) to ACE (4 g) in water (16 mL), stirred for 3h in sealed flask at room temperature until white slurry was observed. The sodium impregnated on the solid support, denoted as Na-ACE was obtained by heating the slurry at 700°C for 2h. Basicity of the catalyst was measured by titration method [28].

2.3 General Synthesis of Chalcone Derivatives

The catalytic chalcones synthesis was conducted in a 50 mL round-bottom flask connected with condenser. To explore the optimum protocol, a mixture of 2-hydroxybenzaldehyde 1a (2 mmol), 2-hydroxyacetophenone 2a (2 mmol), ethanol (5 mL), and catalyst (5-25% wt.) were stirred for varied time (1, 2, 3, and 4h) and temperature (30, 45, 60 and 75°C). During the reaction, the mixture turns yellow/orange color and later produced yellow/orange solid, and recrystallized from hot ethanol. The chalcones are also produced from other types of benzaldehydes and acetophenones with the same reaction condition referred to the optimum protocol obtained from the reaction of compound 1a and 2a. Most of chalcones obtained were in good purity, otherwise, the flash column chromatography was applied to get the pure products.

2.3.1 Data for compound 3a: (E)-1,3-bis(2-hydroxyphenyl)prop-2-en-1-one

Pale yellow solid, 85% yield; mp 122-124°C; IR (KBr, cm^{-1}) 3414 (OH stretching), 3140 (C-H aromatic stretching), 3030 (C-H olefinic stretching), 1658 (C=O stretching), 1460 (C=C stretching), UV-Vis (λ_{max}, nm) 326; MS (m/z) 241.25, 233.21, 219.18, 214.25, 191.16, 174.14.

2.3.2 Data for compound 3b: 1,3-diphenyl-2-propen-1-one

Yellow solid, 43% yield; mp 120-120°C; IR (KBr, cm^{-1}) 3059 (C-H aromatic stretching), 3026 (C-H olefinic stretching), 1660 (C=O stretching), 1602 (C=C stretching), UV-Vis (λ_{max}, nm) 309; MS (m/z) 208, 207.10, 179.10, 165.10, 131.10, 103.10, 89.10.

2.3.3 Data for compound 3c: (E)-3-(3-methoxyphenyl)-1-phenylprop-2-en-1-one

Yellow oil, 65% yield; IR (KBr, cm^{-1}) 3091 (C-H aromatic stretching), 3049 (C-H olefinic stretching), 2945 and 2848 (asymmetric and symmetric stretching of C-H sp^3), 1660 (C=O stretching), 1581 (C=C stretching), UV-Vis (λ_{max}, nm) 304; MS (m/z) 237.10, 207.10, 177.10, 133.10, 98.10, 69.10.

2.3.4 Data for compound 3d: (E)-3-(4-hydroxy-3-methoxyphenyl)-1-phenylprop-2-en-1-one

Orange brown solid, 95% yield; mp 226-228°C; IR (KBr, cm^{-1}) 3405 (OH stretching), 3105 (C-H aromatic stretching), 3029 (C-H olefinic stretching), 2967 and 2835 (asymmetric and symmetric stretching of C-H sp^3), 1647 (C=O stretching), 1581 (C=C stretching), 1125 (C-O stretching); UV-Vis (λ_{max}, nm) 309; MS (m/z) 254.10, 239.10, 131.10, 123.10, 77.10.

2.3.5 Data for compound 3e: (E)-1-(4-aminophenyl)-3-phenylprop-2-en-1-one

Yellow oil, 77% yield; IR (KBr, cm^{-1}) 3354 and 3340 (primary amine, NH_2 stretching), 3055 (C-H aromatic stretching), 3020 (C-H olefinic stretching), 1641 (C=O stretching), 1591 (C=C stretching), 1278 (C-N stretching); UV-Vis (λ_{max}, nm) 315; MS (m/z) 207.10 ($[M-NH_2]^+$), 177.20, 142.70, 138.00, 120.10, 107.00, 92.10, 79.00, 65.10.

2.3.6 Data for compound 3f: (E)-1-(4-aminophenyl)-3-(4-hydroxypnehyl)prop-2-en-1-one

Yellow solid, 83% yield; mp 230-231°C; IR (KBr, cm^{-1}) 3390 and 3329 (primary amine, NH_2 stretching), 3086 (C-H aromatic stretching), 3025 (C-H olefinic stretching), 1641 (C=O stretching), 1583 (C=C stretching), 1269 (C-N stretching), 1178 (C-O stretching); UV-Vis (λ_{max}, nm) 315, 294; MS (m/z) 207.10 ($[M-NH_2]^+$), 147.20, 138.00, 103.00, 92.10, 88.00, 65.10, 45.10.

2.3.7 Data for compound 3g: (E)-1-(4-aminophenyl)-3-(3-methoxyphenyl)prop-2-en-1-one

Yellow oil, 52% yield; IR (KBr, cm^{-1}) 3471 and 3354 (primary amine, NH_2 stretching), 3163 (C-H aromatic stretching), 3053 (C-H olefinic stretching), 2962 and 2835 (asymmetric and symmetric stretching of C-H sp^3) 1641 (C=O stretching), 1583 (C=C stretching), 1274 (C-N stretching), 1176 (C-O stretching); UV-Vis (λ_{max}, nm) 318; MS (m/z) 255.20, 207.00, 177.10, 147.10, 120.10, 104.00, 77.00, 65.10.

2.3.8 Data for compound 3h: (E)-1-(4-aminophenyl)-3-(4-hydroxy-3-methoxyphenyl) prop-2-en-1-one

Orange-brown solid, 86% yield; mp 236-237°C; IR (KBr, cm^{-1}) 3456 and 3363 (primary amine, NH_2 stretching), 3236 (C-H aromatic stretching), 3057 (C-H olefinic stretching), 2939 and 2835 (asymmetric and symmetric stretching of C-H sp^3) 1641 (C=O stretching), 1591 (C=C stretching), 1462 and 1357 (asymmetric and symmetric bending of C-H sp^3), 1280 (C-N stretching), 1176 (C-O stretching); UV-Vis (λ_{max}, nm) 313; MS (m/z) 268.10, 253.00, 221.00, 154.00, 55.20.

2.3.9 Data for compound 3i: (E)-3-(4-hydroxyphenyl)-1-(4-nytrophenyl)prop-2-en-1-one

Red-brown solid, 85% yield; mp 164-165°C; IR (KBr, cm^{-1}) 3200 (OH stretching), 3041 (C-H aromatic stretching), 3020 (C-H olefinic stretching), 1660 (C=O stretching), 1597 (C=C stretching), 1246 (C-N stretching), 1112 (C-O stretching); UV-Vis (λ_{max}, nm) 379; MS (m/z) 207.00, 133.10, 115.10, 89.10, 72.00, 59.10.

2.3.10 Data for compound 3j: (E)-3-(4-hydroxy-3-methoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one

Red-brown solid, 88% yield; mp 185-186°C; IR (KBr, cm^{-1}) 3493 (OH stretching), 3107 (C-H aromatic stretching), 3086 (C-H olefinic stretching), 2926 and 2837 (asymmetric and symmetric stretching of C-H sp^3), 1672 (C=O stretching), 1598 (C=C stretching), 1450 and 1398 (asymmetric and symmetric bending of C-H sp^3), 1199 (C-N stretching), 1022 (C-O stretching); UV-Vis (λ_{max}, nm) 381; MS (m/z) 297.10, 253.10, 225.10, 208.10, 180.10, 152.10, 115.20, 72.10.

3.0 RESULT AND DISCUSSION

3.1 Catalyst Characterization

Eggshells, such as chicken eggshells (CE) have been established to contain high level of calcium carbonate. The CE can be converted into activated chicken eggshells (ACE) which is potential material for base-catalyzed reaction [29]. The comparison of FTIR spectra between chicken eggshells (CE) and activated chicken eggshells were found in several absorption bands (Figure 2). In CE, the most intense band at 1760 cm^{-1} corresponds to stretching vibration of carbonyl group from carbonate ion (CO_3^{2-}). Meanwhile, the major absorption peak at the wavenumber of 1450 cm^{-1} and the minor absorption peaks at the wavenumber of 861 cm^{-1} and 750 cm^{-1} can be associated to the asymmetric stretching, out-of-plane vibrating and in-plane vibrating of carbonate group, respectively. The disappearance of these bands upon calcination signified the successful transformation of CE to ACE. The broad band appeared at 500-700 cm^{-1} was assigned to Ca-O group stretching vibration. The FTIR spectrum of Na-ACE is similar with ACE that indicates similar major chemical constituent present in both of ACE and Na-ACE. A very sharp band in ACE and Na-ACE at 3650 cm^{-1} is attributed to stretching vibration of OH group. This band was not suitable with ACE and might be associated with the presence of $Ca(OH)_2$ upon calcination of CE followed by its reaction with atmospheric water molecules. Similar observation was reported by Tan *et al.* [30] and Eletta *et al.* [31] in the preparation of calcined eggshells from ostrich and chicken eggshells waste.

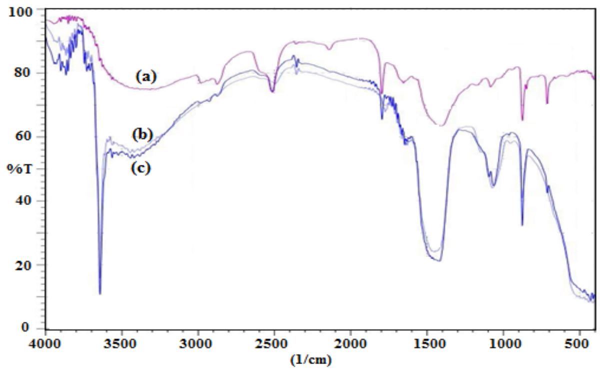


Figure 2 FTIR spectra of (a) CE (b) ACE (c) Na-ACE

XRD analyses were conducted to get information about the chemical identity of solid phase of the catalyst (Figure 3). Referred to the Joint Committee on Powder Diffraction Standards, the diffraction peaks observed at 29.47°, 36.06°, 39.46°, 43.20°, 47.51°, and 48.58° were attributed to the presence of calcite ($CaCO_3$) phase (JCPDS card No. 00-047-1743) in CE sample [30]. When it was calcined, no trace of these peaks could be detected in the ACE and Na-ACE, indicating that calcium carbonate has been perfectly converted. On the other hand, the main peaks attributed to the CaO phase (32.21°, 37.36°, 47.20°, 53.88°, 64.16° and 67.39°) were observed in the ACE and Na-ACE samples. From Figure 2, ACE and Na-ACE sample was observed to contain a mixture of CaO and $Ca(OH)_2$ phases (JCPDS card No. 00-004-0733). However, CaO is the main phase, and it was similar with previous investigation [30,32]. The major peaks of $Ca(OH)_2$ phase was observed at 18.14°, 47.24°, and 50.87°. It is in good agreement with catalyst characterization using FTIR that shows the OH absorption near 3600 cm^{-1}.

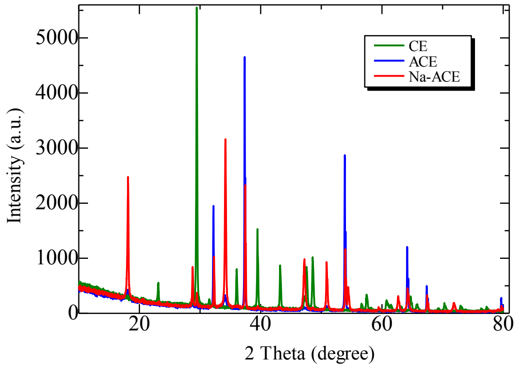


Figure 3 XRD spectra of eggshell-derived material

The morphology of ACE and Na-ACE was investigated and evaluated using SEM (5000× and 20,000× magnification). The ACE and Na-ACE materials display a macropore layered configuration (Figure 4) with aggregated and irregular shape of particles; in accordance with earlier research [33]. It is clearly observed that a huge section of the particle size distribution of ACE was within in the range of 1.0 – 2.3 µm, whereas another section was within 0.2 – 1.0 µm. The smaller size (0.10 – 1.5 µm) of the aggregates and grains was observed in Na-ACE.

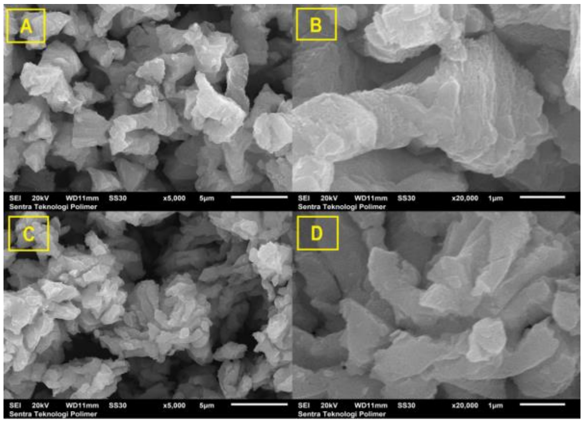
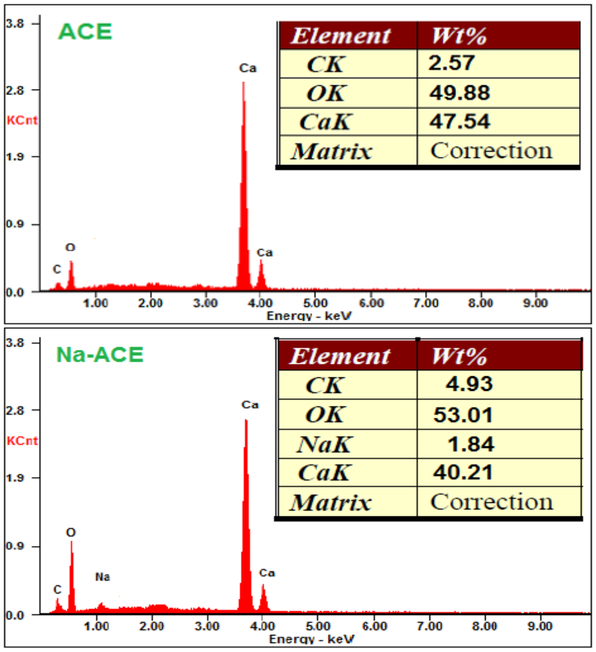


Figure 4 SEM micrographs of (A)-(B) ACE and (C)-(D) Na-ACE

Decreasing in particle size was supported by the data of crystallite size of the samples. Crystallite size of ACE and Na-ACE was measured using Debye-Scherer method from the most intense peak in XRD and found to be 107 and 50 nm, respectively. This result indicated that the samples have high degree of crystallinity.



Element	Wt%
CK	2.57
OK	49.88
CaK	47.54
Matrix	Correction

Element	Wt%
CK	4.93
OK	53.01
NaK	1.84
CaK	40.21
Matrix	Correction

Figure 5 EDS spectra of ACE and Na-ACE

The elemental analysis using EDS spectrometer is supported by the data obtained from XRD. The EDS analysis (Figure 5) revealed that the ACE contains Ca (47.54%) and O (49.88%) as major elements, consistent with previous work [24]. The amount of Na^+ ion incorporated into the ACE to yield Na-ACE that determined by EDS was found to be 1.84% wt. The incorporated sodium ion on ACE affected in the increase of its basic properties [27]. ACE has total basicity of 33.14 mmol/g, whereas for Na-ACE was 39.72 mmol/g. Total basicity value of Na-ACE catalyst is higher than commercial/pure CaO (33.93 mmol/g) [34]. It was known that basic property is a crucial factor affecting the catalytic activity of metal oxide-based materials [35].

3.2 Synthesis of Chalcone Derivatives

The observation of Na-ACE catalytic performance and to get optimum condition for substituted chalcones synthesis, we initially explored the Aldol condensation reaction between compound 1a (2 mmol) and compound 2a (2 mmol) in 5 mL of ethanol and stirred at variation of time and temperatures. First, this reaction was performed in the absence of catalyst at 60°C for 3h, and notwithstanding a prolonged time up to 8h, hence, no activity was observed. The effect of catalyst weight was observed using four different amounts of catalyst in four separated beaker glasses that contain two starting materials at the same condition (60°C and 3h in ethanol). The best yield of chalcone 3a obtained (85%) is by using 15% wt. of Na-ACE catalyst. However, using more than 15% wt. of Na-ACE has no significant effect in increasing the yield of product (Figure 6A).

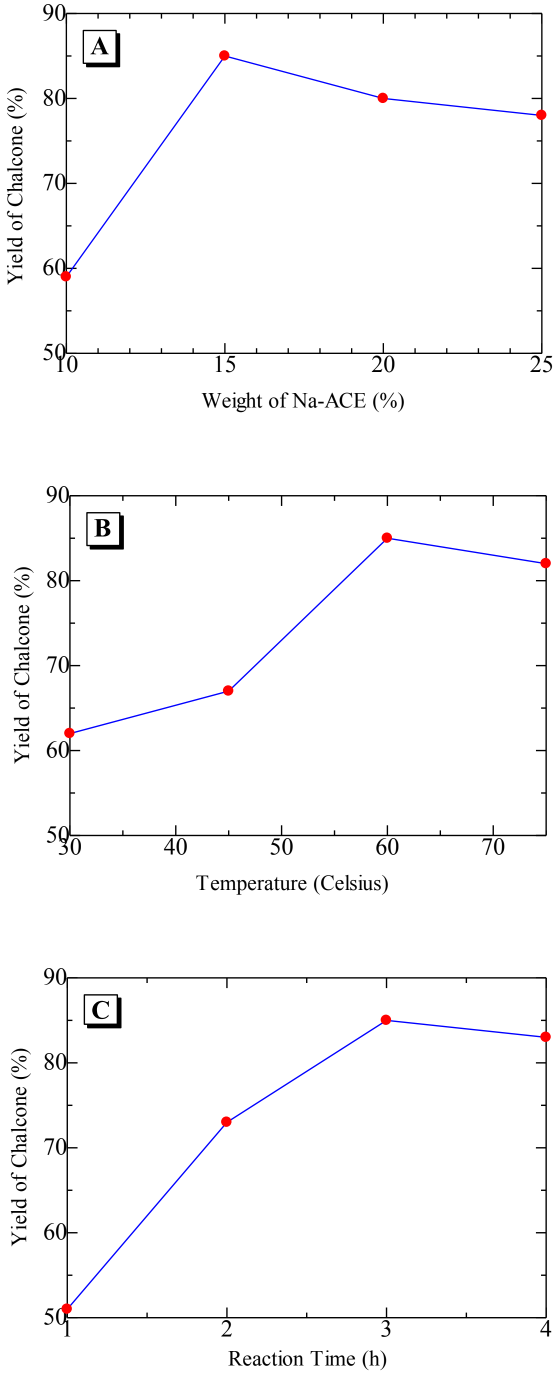


Figure 6 The effect of (A) catalyst weight, (B) temperature and (C) reaction time to produce the chalcone **3a**

The influence of temperature of reaction was detected by varying from 30 to 75°C, while the amount of catalyst and reaction time were kept constant (15% wt. and 3h). The yield of the product increased from 62% to 85% as the reaction temperature increased from 30° to 60°C (Figure 6B). It can be easily rationalized according to the increasing of kinetics energy of particles of the starting materials. However, increasing temperature of the reaction to 75°C will not affect the increasing of the chalcone yield. It may due to the evaporation of the solvent used that preventing the substrate-substrate and substrate-catalyst interaction.

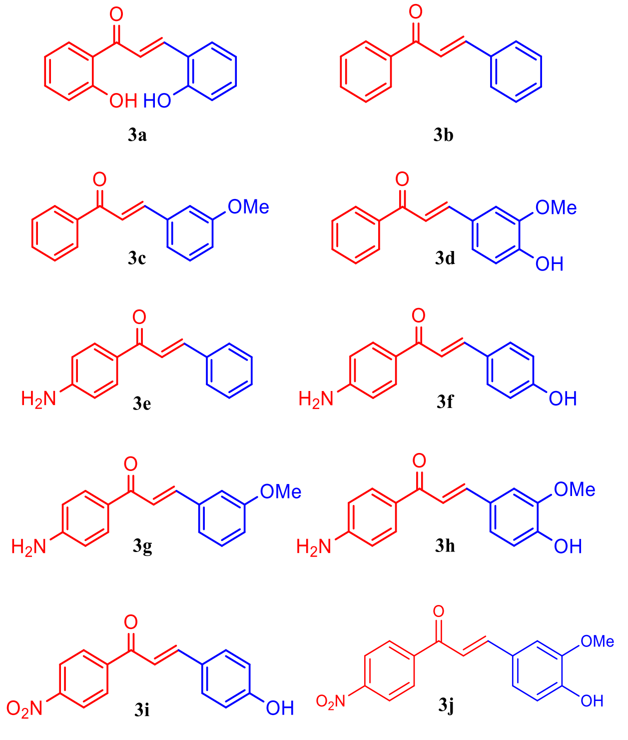


Figure 7 Structure of the synthesized chalcones

The relationship between reaction time and chalcone yield is directly and progressively proportional until the reaction time reached 3h (Figure 6C). At the reaction time of 1h, the desired chalcone, 3a obtained is only ~ 51% yield. This value increased to 73% and 85% yield when the reaction is prolonged to 2 and 3 h. As the reaction is carried out for 4h, the yield slightly decreased (83%), and it might be due to the dissociation of the product into its reactants. Until this stage, we have the optimum protocol to synthesize substituted chalcones is by using 15% wt. catalyst, at the reaction temperature of 60°C, and 3h reaction time.

Several substituted benzaldehydes were separately reacted with acetophenones by the catalytic of Na-ACE particles in the optimum condition that been determined previously except the reaction time. It can monitor the reactivity of each reacted substrate until completion. Un-substituted benzaldehyde and acetophenone produce chalcone in low yield, 43% (Table 1 Entry 2).

In general, electron withdrawing group (EWG) like nitro group attached to acetophenones ring leads to the higher yield of chalcones (Table 1 Entry 9 and 10). However, they need longer time for completion. When the electron donating group (EDG) like amino substituted acetophenones is used as reactant, chalcones is produced in high yield (Table 1 Entry 5-8) but still lower than when nitro acetophenones used. Surprisingly, chalcones that contain only a methoxy group in benzaldehyde skeleton (Table 1 Entry 3 and 7) are obtained in lower yield (65 and 52%) when they are compared to other products.

Table 1 yield and time consumption in chalcones synthesis

Entry	Product	Time (min)	Yield (%)
1	**3a**	60	85
2	**3b**	58	43
3	**3c**	76	65
4	**3d**	60	95
5	**3e**	65	77
6	**3f**	62	83
7	**3g**	69	52
8	**3h**	54	86
9	**3i**	90	85
10	**3j**	95	88

Reaction conditions: acetophenones (2 mmol), benzaldehydes (2 mmol), catalyst 15% wt., 60°C.

The presence of hydroxyl group in para position of benzaldehydes ring will cause the increasing yield of chalcones, such as in Entry 4, 6, 8, 9, and 10 (Table 1). Overall, based on the yields in Table 1, there is no significant effect of EWG and EDG substituted starting materials on the chalcones yield and the reaction time. But, as we have mentioned before, nitro substituted chalcones are obtained in relatively high yield. It can be associated with the electron withdrawing effect of $–NO_2$ which can polarize carbonyl group of acetophenones. It will lead to the ease of hydrogen abstraction in alpha position resulting enolate carbanion. As result, high yield of chalcones are obtained.

4.0 CONCLUSION

Na-ACE catalyst has been successfully prepared by simple wet impregnation method and fully characterized by some analytical instrumentation. To implement green chemistry principles in the organic transformation, especially for the synthesis of substituted chalcones, the simple and efficient solid base catalyst has been applied in the reaction of various benzaldehydes and acetophenones. Most of chalcones are obtained in good to excellent yield.

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