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RESEARCH ARTICLE

Effect of montmorillonite K-10 catalyst on the synthesis of (E)-1-phenyl-3-(2-methoxyphenyl)-2-propen-1-one using the microwave irradiation method

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Abstract

Background: A research investigation was conducted to examine how the utilisation of the montmorillonite K-10 catalyst impacts the production of *(E)*-1-phenyl-3-(2-methoxyphenyl)-2-propen-1-one (PMPP) using the microwave irradiation method since the conventional method has not been successful. **Objective:** The aim of this research was to investigate the impact of employing the montmorillonite K-10 catalyst in the synthesis of PMPP using the microwave irradiation method. **Method:** The compound was created using the Claisen-Schmidt condensation technique through a nucleophilic addition reaction. **Results:** The result of the synthesis was a yellowish powder. The percentage of synthesis of PMPP using the microwave irradiation method was 4.98%, with a melting point of 53-54°C. The synthesised compounds were identified by UV-Vis, Infrared and H-NMR spectroscopy. **Conclusion:** Synthesis of PMPP with montmorillonite K-10 catalyst can be carried out using microwave irradiation. The synthesis using the montmorillonite K-10 catalyst gave a relatively small yield of *(E)*-1-phenyl-3-(2-methoxyphenyl)-2-propen-1-one compared to a strong base catalyst.

Introduction

Drug development has undergone rapid advancement and stands as a crucial element within the pharmaceutical industry. Conventional methods have been utilised to develop drug compounds through organic reactions that often require high temperatures. Traditional heat sources include sand baths, oil baths, or heating mantles. These techniques demand prolonged reaction times and can lead to temperature discrepancies within the reacted samples. Moreover, the concentrated heat surface within the flask can result in localised overheating, leading to the degradation of products, substrates, and other reagents when exposed to prolonged heating. Consequently, alternative reaction methods are sought to achieve synthetic reactions with high yields and the desired quality. Synthesis reactions aided by microwave irradiation represent one of the innovative techniques for developing chemical compounds into new drugs (Hayes & Brittany, 2002; Stadler & Kremsner, 2014; Kappe, 2019).

The compound *(E)*-1-phenyl-3-(2-methoxyphenyl)-2-propen-1-one (PMPP) is a chalcone compound (2-methoxychalchone), chemically distinct from the class of antimalarial drugs that have become resistant. This compound holds potential for antimalarial (Nordina *et al,* 2020), antitubercular properties (Hans *et al*., 2010), antifungal (Dhaliwali, 2022), antioxidative effects (Venkates *et al*., 2016), anti-inflammatory (Mahapatra *et al.,* 2017), and anticancer activity (Wan *et al*., 2014). The synthesis of the compound PMPP can be accomplished through two synthetic routes: the

Knövenagel condensation followed by Friedel-Crafts acylation and the aldol Claisen Schmidt condensation (Solomons *et al.*, 2011a). The aldol Claisen Schmidt condensation represents a shorter, more practical pathway for synthesising substituted (*E*)-1,3-diphenyl-2-propen-1-one (substituted DPP) compounds. The aldol condensation can occur under both acidic and basic conditions and requires alpha hydrogen reagents. Catalysts are needed to expedite the reaction and can include acid or base catalysts, as well as other catalysts like Bentonite (Chlourou *et al.*, 2010), TiCl4 (Solomons *et al.,* 2011b), MgO (Ekanayake *et al.*, 2022), Potassium chloride (Kabalka *et al.,* 2001), and Alumina (Paul *et al.*, 2003). One extensively developed catalyst is montmorillonite K-10 (Bentonite), which possesses acidic properties. This catalyst offers several advantages and has been proven effective in various reactions (Habibi & Marvi, 2006a).

In this study, the synthesis of PMPP will be conducted using the reagents acetophenone and 2-methoxybenzaldehyde (Figure 1) using the Claisen Schmidt condensation with the assistance of montmorillonite K-10, an acidic catalyst and microwave irradiation. Previous attempts employing montmorillonite K-10 (an acidic catalyst) in conventional reactions have not yielded the substituted DPP (its derivative). Additionally, this method is chosen due to its utilisation of non-toxic solvents, relatively short reaction times, and mild heating conditions. Consequently, this method aligns with the principles of environmentally conscious chemistry, promoting reducing toxic solvent usage and resource conservation (Habibi & Marvi, 2006b).

Based on the aforementioned background, the research formulates the following problem: Can microwave irradiation with montmorillonite K-10 (acid) catalyst be utilised to synthesise PMPP? This study aims to synthesise the compound PMPP (the chalcone derivative) using a montmorillonite K-10 catalyst through the Claisen-Schmidt condensation reaction aided by microwave irradiation. This research can contribute novel insights into the Claisen-Schmidt condensation reaction method utilising montmorillonite K-10, an acidic catalyst, combined with microwave irradiation and PMPP synthesis (Figure 1).

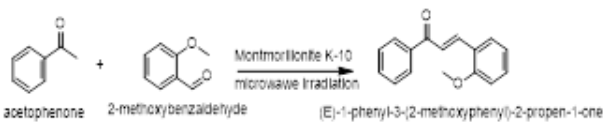

Figure 1: **Reaction of PMPP with montmorillonite K-10 catalyst**

Methods

Materials

Unless otherwise specified, all chemicals utilised in this research were of analytical grade purity (p.a.). The substances included acetophenone, benzaldehyde, 2-methoxybenzaldehyde, montmorillonite K-10 (p.g.), chloroform, silica gel GF254, tetrahydrofuran, 96% ethanol, hexane, ethyl acetate, dichloromethane, and silica gel for column chromatography.

Instrumentation

Common glassware employed in chemical synthesis laboratories, Sanyo EM-S800 Watt microwave, HEWLETT PACKARD 8452A UV-Vis spectrophotometer, Buck Scientific M 500 IR spectrophotometer, JEOL ECS-400 FT-NMR spectrometer.

Determination of optimal conditions for the synthesis of (E)-1-Phenyl-3-(2-methoxyphenyl)-2-propen-1-one (PMPP) with montmorillonite K-10 catalyst using microwave irradiation (Jain et al., 2007)

Before synthesising the PMPP compound, the reaction conditions were determined by orientation in synthesizing the DPP compound. Several series of syntheses of DPP were performed through the condensation reaction by combining the reactant materials. In a 100 ml glass beaker, 10 mmol of acetophenone, 20 mmol of 2-methoxybenzaldehyde, and 4.0 ml of tetrahydrofuran as the solvent were placed. Subsequently, 4.0 g of montmorillonite K-10 was added. The mixture was stirred using a magnetic stirrer until homogeneous. Then, it was evaporated to dryness. The concoction was transferred to a microwave oven, and conditions were set at 160, 320, 400, 480, 560, and 640 Watts for 3, 5, 8, 9, and 10 minutes. Each sample was extracted with chloroform three times at 5 ml each, and the extracted solution was evaporated until dry to obtain a solid product. The optimal conditions were determined based on the power and reaction time that produced the highest yield of the product.

Synthesis of (E)-1-Phenyl-3-(2-methoxyphenyl)-2-propen-1-one (PMPP) with microwave irradiation (Jain et al., 2007)

An equimolar mixture of acetophenone (10 mmol) and 2-methoxybenzaldehyde (20 mmol) was placed in Erlenmeyer flask, followed by adding 4.0 ml of tetrahydrofuran solvent and four grams of montmorillonite K-10. The mixture was stirred until homogeneous and then evaporated. Subsequently, microwave irradiation at 400 Watts for nine minutes (selected power) was applied. Following the process of

cooling to reach ambient temperature, the mixture was extracted with five millilitres of chloroform three times and then filtered. The obtained mixture was concentrated and purified through column chromatography. Purity was assessed through melting point analysis and thin layer chromatography, employing three distinct elements. Identification was carried out utilising UV-Vis spectrophotometry, Infrared (IR) spectrometry, and ^{1}H-NMR spectroscopy.

Results

The optimal condition for the synthesis of PMPP using microwave irradiation was found to be 400 Watts for nine minutes. The synthesised PMPP resulted in needle-shaped yellowish crystals. The synthesis yield percentage was 4.98%. The thin-layer chromatography outcomes using various elements exhibited several spots compared to the starting materials. The selected condition yielded the highest reaction output and low power and time requirements. Melting Point of PMPP using Fisher John Melting Point Apparatus was 53-54°C. The difference in melting points among replications of 1-2°C indicates the purity of the synthesised compound (Vogel, 1989). The results of the synthesis conditions with montmorillonite K-10 catalyst are presented in Table I. The selected condition was the one that yielded the highest reaction output, along with demanding low power and time requirements.

Table I: The results of determining the conditions for the synthesis of the compound PMPP with monmorillonite K-10 catalyst using microwave irradiation

Time (minutes)	Synthesis results with power strength (Watts)					
	160	320	400	480	560	640
3	0.006 g (yellow solid)	0.004g (yellow solid)		0.045g (yellow solid)		0.077g (orange solid)
5	0.013g (yellow solid)	0.025g (yellow solid)		0.097g (yellow solid)		0.059g (orange solid)
8	0.007g (yellow solid)	0.120g (yellow solid)	0.108g (yellow solid)	0.138g (yellow solid)	0.200g (orange solid)	0.065g (orange solid)
9			0.220g (yellow solid)	0.077g (yellow solid)	0.089g (orange solid)	
10			0.112g (yellow solid)	0.113g (yellow solid)	0.120g (orange solid)	

Characterisation of (E)-1,3-diphenyl-2-propen-1-one (DPP)

The yield was 1.72%; m.p. 51-52°C. UV-Vis spectrum**:** maximum absorbance in ethanol solution at 225.0 and 305.0 nm. Infrared spectrum: peaks (cm^{-1}) in KBr pellet: 1661 (-C=O), 1604 (HC=CH olefinic), 1447 (-C=C- aromatic ring), 735 (aromatic 1,2-disubstituted/ortho), 978 (bend out of the plane for the trans C-H bond), 3059 (C-H aromatic).

^{1}H-NMR Spectrum: Peaks (δ ppm) in $CDCl_3$ solvent: 8.02, doublet, 2H at positions 2' and 6' (C_6H_5-), 7.81, doublet, J=16 Hz, 1H-alpha (-C=C- trans), 7.60-7.63 multiplet, 3H at positions 3', 4', 5' (C_6H_5-), 7.56-7.48, multiplet, 2H at positions 2 and 6 (C_6H_5-), 7.38-7.44 multiplet, 3H at positions 3, 4, 5 (C_6H_5-). (Silverstein *et al.,* 2005a; Pavia *et al.,* 2009a).

Characterisation of (E)-1-phenyl-3-(2-methoxy-phenyl)-2-propen-1-one (PMPP)

UV-Vis spectrum: maximum absorbance (nm) in ethanol solvent at 204, 242, and 342 nm. Infrared spectrum: peaks (cm^{-1}) in KBr pellet: 1017 (C-O-aromatic), 1170 (C-O-aliphatic), 1576 and 1511 (-C=C- aromatic ring), 1599 (HC=CH olefinic), 1657 (-C=O ketone). ^{1}H-NMR Spectrum**:** peaks (δ ppm) in $CDCl_3$ solvent: 3.84, singlet, 3H (CH_3-), 7.98-8.02, multiplet, 2H (C_6H_5-), 7.77, doublet, J=15.6 Hz, 1H (-C=C- trans), 7.61-7.54 multiplet, 3H (C_6H_5-), 7.50-7.47 multiplet, 2H (C_6H_5), 7.42-7.39 multiplet, 1H (C_6H_5-), 6.94-6.92, multiplet, 2H (C_6H_5-). (Silverstein *et al.,* 2005b; Pavia *et al.,* 2009b).

The reaction mechanism for the formation of PMPP is shown in Figure 2. DPP and PMPP compounds form from the starting materials acetophenone and various benzaldehyde derivatives through the Claisen-Schmidt reaction mechanism (Figure 2). The reaction begins with the formation of the enol form of acetophenone

through a tautomeric event (Solomons *et al.,* 2011c). Compared to the keto form in tautomerism, the relatively less stable enol form impacts the reaction yield percentage, which is relatively lower when using an acidic catalyst.

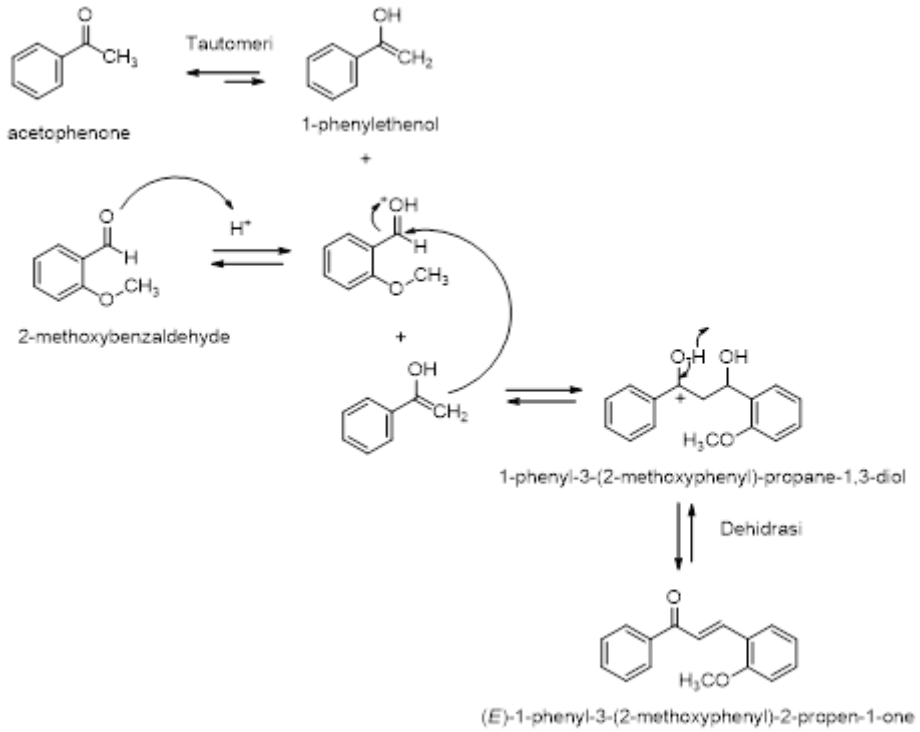

Figure 2: Reaction mechanism for the formation of (*E*)-1-Phenyl-3-(2-methoxyphenyl)-2-propen-1-one (PMPP)

Discussion

In this study, the compound PMPP was synthesised by reacting acetophenone and 2-methoxybenzaldehyde with a montmorillonite K-10 catalyst, employing microwave irradiation at 400 Watts for nine minutes. The synthesis results were validated for reaction completion using TLC, revealing distinct spots compared to the initial compounds. Previous attempts to synthesise PMPP with montmorillonite K-10 catalyst using conventional methods were unsuccessful, prompting the utilisation of microwave irradiation as an alternative approach. Synthesis results of PMPP by way of irradiation method using montmorillonite K-10 (acidic) catalyst yielded a percentage yield of 4.98% and 1.72% for DPP. The UV-Vis spectrophotometry analysis results indicated that DPP has λmax at 308, 228, and 204nm. PMPP has λmax at 342, 242, and 204nm. The wavelengths for acetophenone are 278, 240, and 210nm. These data show that both synthesised compounds exhibit a redshift in λmax towards longer wavelengths (bathochromic shift). This is attributed to the addition of chromophoric groups in DPP and FMPP compounds.

The IR spectrum of PMPP reveals characteristic carbonyl (C=O) peaks at the wavenumber of 1657 cm^{-1}, aromatic C=C at 1576 cm^{-1} and 1511 cm^{-1}, and olefinic C=C functional group at 1599 cm^{-1}. Meanwhile, the IR spectrum of DPP demonstrates the existence of carbonyl (C=O) peaks at the wavenumber of 1661 cm^{-1}, aromatic C=C at 1547 cm^{-1}, and olefinic C=C functional group at 1604 cm^{-1}. The IR spectrum analysis of acetophenone indicates the presence of the carbonyl (dialkyl ketone) group at the wavenumbers of 1688, 1682, and 1599 cm-1, along with the aromatic C=C functional group at 1449 cm^{-1}. The IR spectrum data shows distinct changes in the spectral patterns between the starting compound, acetophenone, and the two synthesised compounds. DPP and PMPP's infrared spectrum patterns are quite similar since the structures of both synthesised compounds are alike, differing only in the methoxy group.

The H-NMR spectrum of the synthesised chalcone compound indicates a doublet absorption peak at a chemical shift of 7.81 ppm (J=16.0 Hz), which corresponds to the H-β proton peak coupled with H-α in the trans (*E*) configuration. Similarly, the ^{1}H-NMR result for the substituted chalcone compound PMPP

demonstrates a doublet peak at a chemical shift of 7.77 ppm (J=15.6 Hz), representing the coupling between H-β and H-α protons. This observation also confirms that these protons are in a trans (*E*).

The acidic catalyst, montmorillonite K-10, creates an environment rich in H^+ ions, promoting acetophenone's tautomeric conversion into the enol form. The acidic catalyst also affects the benzaldehyde compound, where the oxygen atom of the carbonyl group (C=O) binds to H^+ from the catalyst, forming an OH^+ group. A nucleophilic addition reaction occurs at the C=O carbon atom. When an acidic catalyst is used, the enol form of acetophenone acts as a nucleophile, attacking the electropositive C=O carbon atom of benzaldehyde. The nucleophilic assault on the carbonyl carbon atom leads to adding the C=O bond, forming a diol compound (intermediate) and a dehydration reaction. The dehydration reaction occurs from the OH group arising from acetophenone. A water molecule draws a proton of the carbon atom linked to the carbocation, establishing the C=C bond (McMurry, 2008; Solomons *et al.*, 2011b). Pambudi et al. (2019) conducted a study using two types of alkaline catalysts, namely NaOH and NaOH+ZrO_2 montmorillonite (basic montmorillonite), which yielded reaction percentages above 40%. It is recommended to use an alkaline catalyst. Montmorillonite K-10 catalyst is acidic, and in its mechanism, the initial acetophenone material needs to be converted into the enol form through tautomerism. The enol form is less stable compared to the keto form. When an alkaline catalyst is used, the reaction mechanism requires a more stable keto form. This results in a relatively low reaction percentage with the acidic K-10 catalyst.

Conclusion

The compound of (*E)*-1-phenyl-3-(2-methoxyphenyl)-2-propen-1-one (PMPP) can be synthesised through the Claisen Schmidt condensation reaction utilising microwave irradiation at 400 Watts for nine minutes with montmorillonite K-10 catalyst, yielding a percentage yield of 4.98%.

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