al Kimiya: Jurnal Ilmu Kimia dan Terapan
p-ISSN: 2407-1897, e-ISSN: 2407-1927
Vol. 10, No. 1 (13-19), Juni 2023/Dzulhijah 1444

SYNTHESIS AND CHARACTERIZATION OF 1-(1-NAPHTHYL)-5-PHENYL-2,4-PENTADIEN-1-ONE FROM *TRANS*-CINNAMALDEHYDE AND 1-ACETONAPHTHONE

DORI FITRIA[1*], BAYU ARDIANSAH[2], AND ATIA BALKIS[1]

[1]Chemistry Study Program, Faculty of Science and Technology, UIN Sulthan Thaha Saifuddin, Muaro Jambi, Jambi, 36361, Indonesia

[2]Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Indonesia, Depok, 16424, Indonesia

*Corresponding author email: dori.fitria@uinjambi.ac.id

Article Information

Received: Dec 31, 2022
Revised: May 22, 2023
Accepted: Jun 21, 2023
Published: Jun 30, 2023

DOI: 10.15575/ak.v10i1.22896

Keywords:
Chalcone analogues; aldol condensation reaction; cinnamaldehyde; 1-acetylnaphthalene; 1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one

Abstrak/Abstract

Chalcone analogues (1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one) have been synthesized through an aldol condensation reaction between cinnamaldehyde and 1-acetylnaphthalene. The method used in this study is the stirrer method, with the reaction conducted at room temperature for 24 hours using a NaOH catalyst in H_2O/ethanol (50%, v/v). The purity of the product was analyzed using thin-layer chromatography on silica gel plates with n-hexane: ethyl acetate (9:1) employed as the solvent. The resulting product obtained was 0.88 g with a yield of 61.97%. Structure Analysis and elucidation of the synthesized compounds were performed by measuring the vibrations of the functional groups using FTIR, LCMSMS analysis, and determining the ^1H and ^{13}C atoms by HNMR and CNMR analysis. The FTIR, LCMSMS, ^1H, and ^{13}C NMR analysis identified that the synthesized product as chalcone analogues, specifically 1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one.

INTRODUCTION

Cinnamaldehyde is the main component of cinnamon oil, which contains approximately 50-70% and is extracted from the bark of the cinnamon tree [1,2]. The antibacterial properties of cinnamaldehyde have been thoroughly investigated for use in medications, food, and preservation [2]. However, there are limitations in applying cinnamaldehyde due to several drawbacks, such as its pungent smell and high volatility [2,3]. To overcome these issues and enhance the value of cinnamaldehyde, researchers have employed modified chemical approaches. Structurally, Cinnamaldehyde is a simple phenylpropanoid that contains unsaturated aromatic aldehyde groups, which can be modified to form chalcone analogues, known as bioactive compounds with medicinal significance [4].

Chalcone compound can be synthesized from an aldehyde with an aromatic ketone via an aldol condensation reaction [5]–[13]. Cinnamaldehyde which is an aromatic aldehyde when reacted with an aromatic ketone such as acetophenone can form a chalcone analog compound with the name cinnamylideneacetophenones. An effective catalyst for this reaction is a base, specifically NaOH, which is a homogenous catalyst [14,15]. In addition, the reaction for the formation of chalcone analogues can also be catalyzed by a heterogeneous catalyst, for example, organobase Fe_3O_4/SiO_2-guanidine [16] and Fe_3O_4 [17].

Cinnamylideneacetophenones compounds have biological activities, such as cytotoxic against breast cancer cells [14], antibacterial, antituberculosis [15], and anxiolytic activity [18]. In addition, modification of the structure of cinnamaldehyde compounds with other ketones also has biological activity as an antioxidant [19][20]. Due to the diversity of biological activities of chalcone compounds, many researchers have used chalcone as a structural model of the target compound, to explore the potential of chalcone with various structural variations.

In this study, cinnamaldehyde and 1-acetonaphthone were utilized as the precursors for

the synthesis of chalcone analogues. The use of this material is justified by the fact that 2-acetylnaphthalene and different substituted acetophenones were the aromatic ketones employed in earlier investigations, which claimed to have already synthesized chalcone analogues from cinnamaldehyde [14] [15]. To the best of our knowledge, there have been no reports suggesting that an aromatic ketone variant in the form of 1-acetylnaphthalene has ever been used as an aromatic ketone variant for cinnamaldehyde. So, the proposed structural model is a new structural model. To determine whether the synthesized substance matched the required target molecule, FTIR, MS, and NMR spectroscopic studies were used to characterize the compound [21]-[25] [26].

EKSPERIMENT

Material

The chemicals used were analytical grades, such as *trans*-cinnamaldehyde (Merck), 1-acetonaphthone (Sigma Aldrich), filter paper, pH paper, TLC plates F_{254} (Merck), and sodium hydroxide pellet (Merck). The solvents used were ethyl acetate (Merck), n-hexane (Merck), methanol (Merck), ethanol (Merck), and deionized water.

Instrumentation

FTIR analysis was performed using a Thermo Scientific-Nicolet iS50 FT-IR Spectrometer at the ILRC Laboratory, Universitas Indonesia. The Qtof LCMSMS analysis was carried out at the Indonesian National Police's Criminal Investigation Agency, Center for Forensic Laboratory, Sentul, Bogor. ^{1}H-NMR and ^{13}C-NMR analysis was carried out using the Bruker Avance Neo 500 MHz and 126 MHz Nuclear Magnetic Resonance Spectrometer at the ILRC Laboratory, Universitas Indonesia.

Procedure

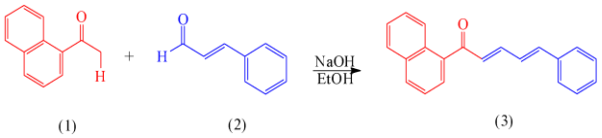
Synthesis of chalcone compound

In a 50 mL Erlenmeyer flask, the mixture containing 1-acetonaphthone (0.85 g, 5 mmol), ethanol (7.5 mL), and sodium hydroxide solution (0.40 g, 10 mmol, in 6 mL water/ethanol 1:1) was stirred at room temperature. *trans*-Cinnamaldehyde (0.66 g, 5 mmol) was then added to the mixture, and it was stirred for 24 h. After that, water (15 mL) was added to the mixture, and then it was extracted with ethyl acetate to wash with brine. The organic phase was dried over sodium sulfate. After the removal of the solvent, the desired product was obtained in good purity.

RESULT AND DISCUSSION

Synthesis of Chalcone Compound

Compound 1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one (3) can be obtained by reacting 1-acetonaphthone (1) with *trans*-cinnamaldehyde (2) using sodium hydroxide as a catalyst, as shown in **Scheme 1**.



Scheme 1. Synthesis of the target compound.

The synthesis of chalcone analogues can be catalyzed by a base, generally, the base used is a homogeneous base catalyst, namely NaOH [14] [15] [27] and KOH [27]. The initial stage of this research was to find out how much yield was produced by the chalcone analog compound. The reaction conditions were carried out using 1-acetylnaphthalene (5 mmol) and cinnamaldehyde (5 mmol), at room temperature, with absolute ethanol solvent, the catalyst used was 10 mmol (2 equivalents) for 24 hours. To find out whether the product has been formed, namely using the TLC test [28], [29]. The eluent ratio is hexane: ethyl (9:1).

Figure 1 is the result of TLC of the starting compound with the product, where A is an acetylnaphthalene compound, B is a cinnamaldehyde compound and P is a product sample produced. The results of the TLC showed that the compound had been formed where the Rf of the synthesized compound was different from the initial compound.

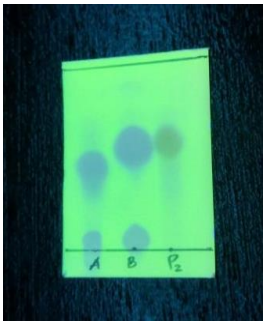
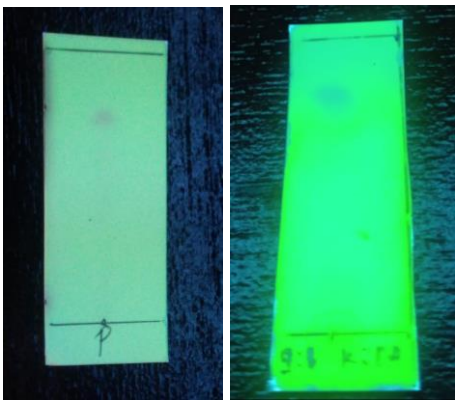


Figure 1. TLC profile of the chalcone synthesis (A = acetylnaphthalene; B = cinnamaldehyde; and P = product), the eluent ratio is hexane: ethyl (9:1).

The 1-(1-naphthyl)-5-phenyl-2,4-pentadien-1-one compound was obtained after the evaporation process using a rotary evaporator because the product formed has a gel texture so it cannot be separated by ordinary filtering. To separate the product from the filtrate before being evaporated with a rotary evaporator, an extraction technique was used using a separating funnel by adding ethyl acetate to the synthesis product which had previously been added with distilled water.



a b

Figure 2. TLC profile of the target compound (The TLC test used hexane: ethyl acetate (a) and chloroform: ethyl acetate (b) eluent each 9:1).

Figure 2 is the result of the product TLC. The TLC test used hexane: ethyl acetate and chloroform: ethyl acetate eluent each 9:1. The TLC test results showed that the compound formed had one spot with an Rf value of 0.7 (hexane: ethyl acetate) and 0.75 (chloroform: ethyl acetate) indicating that the compound was pure.

The ethyl acetate fraction was then evaporated using a rotary evaporator. From the weighing results obtained a product weight of 0.88 g with a yield of 61.97%.

Characterization of The Target Compound

The FTIR spectrum shows a peak at wave number (ύ) 1610 cm^{-1} indicating the presence of a C=O group, the C=O group experiences a resonance effect due to the conjugated double bond in the chalcone analog compound. The presence of C=C is also indicated by a peak in the range of 1573 cm^{-1}. Absorption is specific for chalcone and can also be characterized by the presence of a peak in the 3051 cm-1 regions for C-H sp^2 vibrations, both from aromatic C-H and olefinic C-H. While a peak at wave number (ύ) 3417 cm^{-1} indicates the presence of an OH group, possibly from water vapor during measurement (**Figure 3**).

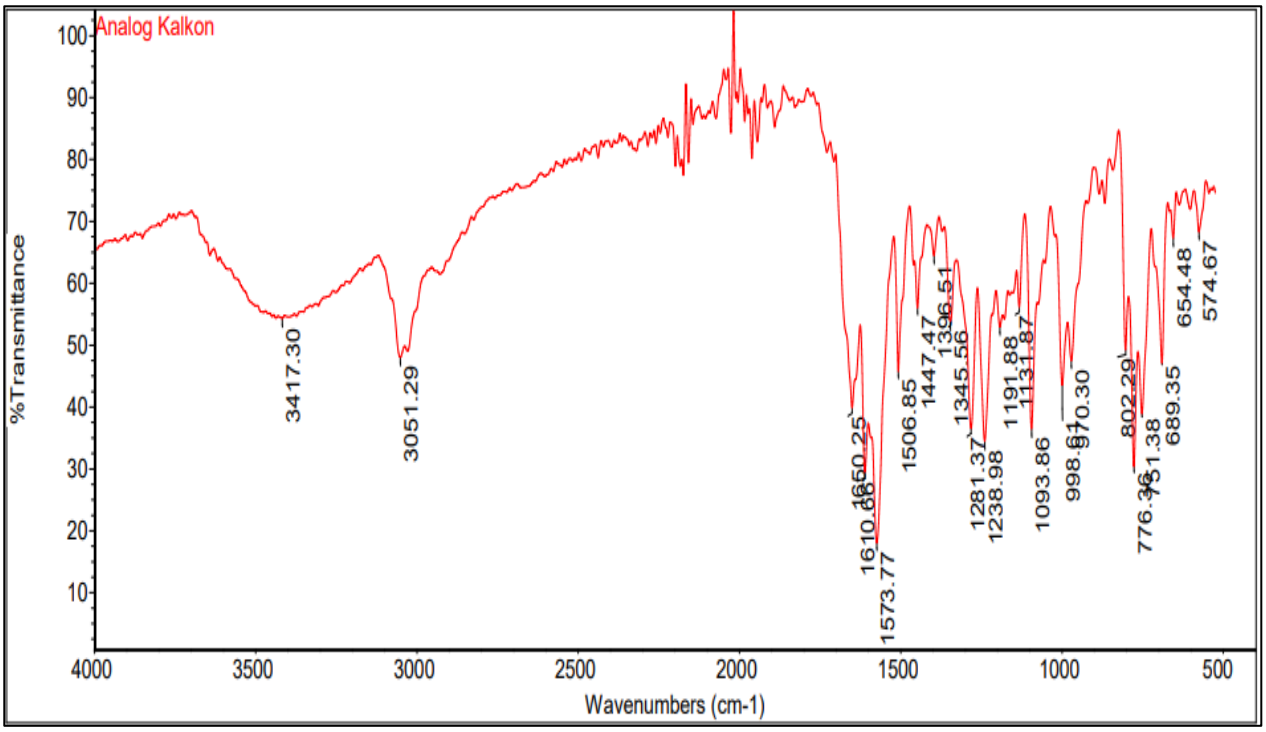


Figure 3. FTIR analysis of the target compound.

The results of the analysis of the mass spectrum of the compound 1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one showed a molecular ion peak at m/z 285.1289 (M+H). The results of the LCMSMS data confirm that the compound synthesized matches the molecular formula $C_{21}H_{16}O$ or matches the target compound (**Figure 4**).

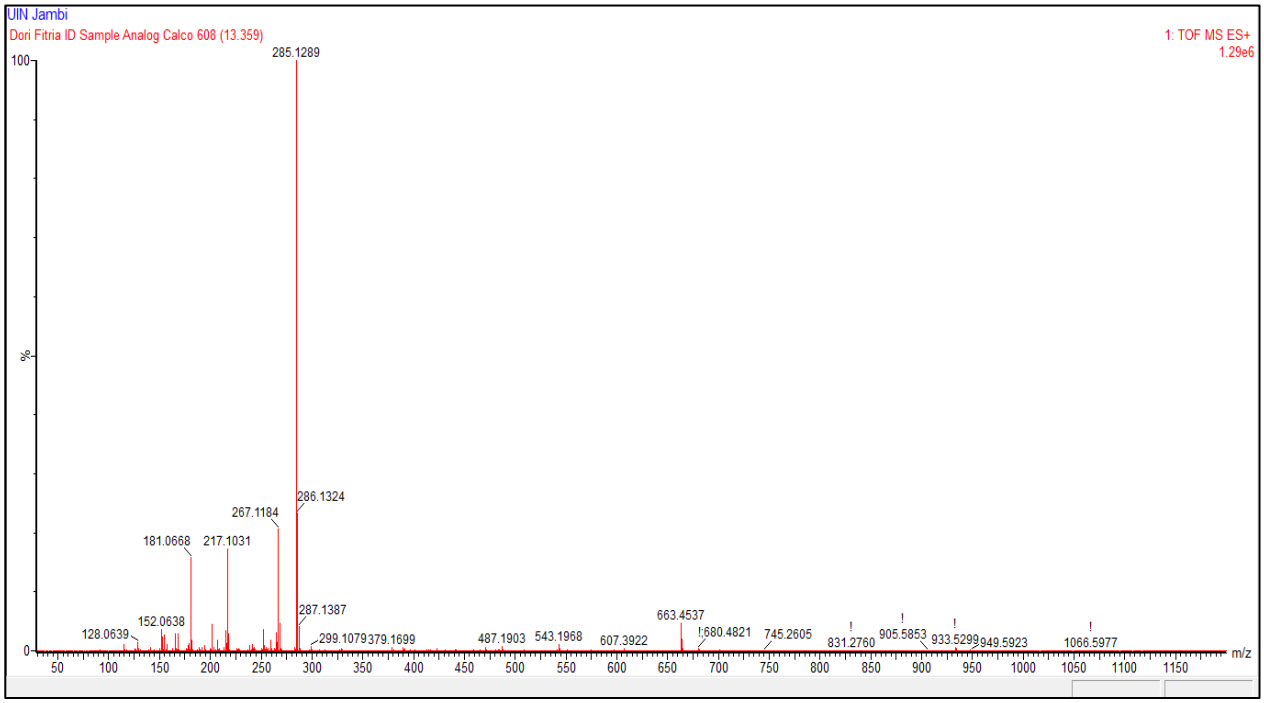


Figure 4. LCMSMS analysis of the target compound.

The H NMR spectrophotometer is used to detect the position of the proton nucleus. In addition, it can also be used to determine the number of protons bonded to carbon, nitrogen, or oxygen atoms. Proton positions are expressed in chemical shifts (δ) expressed in ppm, usually between 0 to 10 ppm. The greater the electron density (σ), the smaller the frequency, and the smaller the chemical shift of the proton (δ) [25]. ^{1}H-NMR analysis using chloroform solvent. The number of H atoms in the chalcone analog compound is 16, according to the data from the analysis.

In addition to measurements using ^{1}H-NMR, measurements were made using ^{13}C-NMR analysis for analysis of carbon shift values to serve as confirmatory data on the molecular structure of products produced using chloroform solvent. The number of C atoms in the chalcone analog compound is 21, but from the data synthesized it is known that there are 18 C atoms. This indicates the presence of equivalent C atoms. From the analysis data, confirmation of the proposed structure is shown in **Table 1**.

The ^{1}H-NMR spectrum of the chalcone analog showed a chemical shift at δ 7.03 (d, 1H); 7.56 ppm (m, 1H); 6.85 ppm (t, 1H); and 6.94 ppm (d, 1H), each compound exhibiting protons at positions C-2, C-3, C-4, and C-5. In unsaturated α,β- ketones, the proton adjacent to the carbonyl (Hα) will have a small δ (shielded) and Hβ will have a larger δ (deshielded) [24]. At positions C-2, C-3, C-4, and C-5, the biggest chemical shift is at position C-3 (Hβ). This can be explained because a resonance occurs in unsaturated α,β-ketones so that the carbon in Hβ (proton on C-3) is relatively more positive than the carbon in Hα (proton on C-2). As a result, the electron density of Hβ is smaller than the electron density of Hα. In addition, there is a geometric or spatial effect of the carbonyl on C-1, so that C-3 is more deshielded than C-2, C-4, and C-5. The chemical shift at δ 8.3058 ppm shows the proton at the position of the C-9' atom with a doublet peak, which is the highest peak. This is because, besides the anisotropic effect, there is also an aromatic effect so that the H in the C-9' position is deshielded. In the aromatic naphthalene ring, the aromatic compound is bonded to the C carbonyl group (ketone), because the C carbonyl group bonded to an aromatic compound attracts electrons, so three types of protons are obtained, namely H ortho, H meta, and H para with a chemical shift (δ) Ho > Hp > Hm. This can be explained because resonance occurs in aromatic compounds, the carbonyl group attracts electrons so that the ortho carbon is relatively more positive than the para carbon and the para carbon is more positive than the meta carbon. As a result, the electron density of H ortho is smaller than the electron density of H para, as well as the electron density of H para is smaller than the electron density of H meta [24]. chemical shift at δ 7.98 (d, 1H); 7.39 ppm (m, 1H);

7.90 ppm (d, 1H), 7.73 ppm (d, 1H); 7.54 ppm (m, 1H); 7.57 ppm (m, 1H) indicates protons at positions C-2', C-3', C-4', C-6', C-7', and C-8'. The second aromatic ring is mono-substituted aromatic, where the prevalence of proton signals is three groups of signals originating from ortho, meta, and para signals. The chemical shift at δ 7.49 ppm (d, 2H) shows the protons in the positions of the C-2" and C-6" atoms (two equivalent protons at the ortho position) with doublet peaks. The chemical shift at δ 7.26 ppm (m, 1H) shows the proton at the position of the C-4" atom (para proton signal) with multiplet peaks. The chemical shift at δ 7.33 ppm (m,2H) shows the protons at the positions of the C-3" and C-5" atoms (from two H protons at equivalent positions meta) with multiplet peaks.

Table 1. Interpretation of ^{1}H NMR data of the compound 1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one.

Atom Label	™$_H$ (ppm)	™$_C$ (ppm)
1	-	195.9
2	7.03 (d, 1H)	126.9
3	7.56 (m, 1H)	146.1
4	6.85 (t, 1H)	125.7
5	6.94 (d, 1H)	142.1
1’	-	137.2
2’	7.98 (d, 1H)	131.4
3’	7.39 (m, 1H)	127.4
4’	7.90 (dd, 1H)	130.5
5’	-	129.3
6’	7.73 (d, 1H)	128.4
7’	7.54 (m, 1H)	126.8
8’	7.57 (m, 1H)	133.9
9’	8.31 (d, 1H)	124.5
10’	-	127.4
1’’	-	136.0
2’’	7.49 (d, 1H)	127.4
3’’	7.33 (m, 1H)	128.9
4’’	7.26 (m, 1H)	126.5
5’’	7.33 (m, 1H)	128.9
6’’	7.49 (d, 1H)	127.4

The ^{13}C-NMR spectrum has a much wider chemical shift, namely 0-230 ppm, compared to ^{1}H-NMR which ranges from 0-10 ppm, sometimes up to 13-14 ppm (if there are hydrogen bonds) [24]. It is known that the chalcone analogues formed consist of alkene, aromatic, and carbonyl groups from ketones. Alkene and aromatic compounds generally have a chemical shift (δ) between 100-160 ppm, while carbonyls from ketones have a chemical shift between 190-230 ppm [24]. The ^{13}C-NMR spectrum of the chalcone derivative showed a chemical shift at δ 137.2 ppm and 136.0 ppm respectively to carbon C-1' and C-1". It is known from the peak intensities during the chemical shift δ 137.2 ppm and 136.0 ppm, which have low intensities which indicate that the C in the chemical shift is quaternary C because there is no H directly bound to the C atom. The chemical shift at δ 195.9 ppm is the C carbonyl of a ketone (C=O). The chemical shift at δ 146.1 and 142.1 ppm indicated the presence of carbon at C-3 and C-5. The chemical shift at δ 126.9 and 125.7 ppm indicated the presence of carbon in C-2 and C-4. The chemical shift at δ 124.5-133.9 ppm indicated the presence of carbon in both aromatic rings. The number of C atoms in the chalcone analogous compound is 21, but from the analysis data, it is known that there are 18 C atoms. This indicates the presence of equivalent C atoms. The C atom is equivalent to C-2" with C-6" and C-3'; C-3" with C-5". The characterization results show that the resulting product is following the target compound. (**Figure 5**).

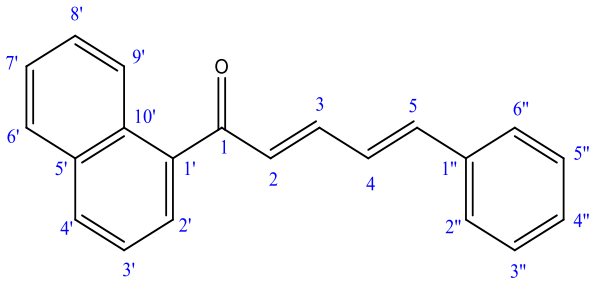


Figure 5. Molecular structure of the target compound.

CONCLUSION

The chalcone analogue compound has been successfully synthesized using the starting materials in the form of cinnamaldehyde as an aromatic aldehyde and 1-acetylnaphthalene as an aromatic ketone with a yield of 61.97%. The results of the characterization of the compound using FTIR, LCMSMS, and NMR showed that the product formed corresponds to the expected target molecule, namely Compound 1-(1-naphthyl)-5-phenyl-2,4-pentadiene-1-one.

ACKNOWLEDGEMENT

This research was supported by the LPPM UIN Sulthan Thaha Saifuddin Jambi through the Ministry of Religion's research grant 2022 with contract No. B-2311/Un.15/PPK/KU.01/06/2022.

REFERENCES

[1] F.A. Al-Bayati and M. J. Mohammed, "Isolation, identification, and purification of cinnamaldehyde from Cinnamomum zeylanicum bark oil. An antibacterial study", *Pharm. Biol.*, **47**(1), 61–66, 2009, doi: 10.1080/13880200802430607.

[2] H. Wang, H. Yuan, S. Li, Z. Li, and M. Jiang, "Synthesis, antimicrobial activity of Schiff base compounds of cinnamaldehyde and amino acids", *Bioorganic Med. Chem. Lett.*, **26**(3), 809–813, 2016, doi: 10.1016/j.bmcl.2015.12.089.

[3] Y.J. Jo, J.Y. Chun, Y.J. Kwon, S.G. Min, G.P. Hong, and M.J. Choi, "Physical and antimicrobial properties of trans-cinnamaldehyde nanoemulsions in water melon juice", *Lwt*, **60**(1), 444–451, 2015, doi: 10.1016/j.lwt.2014.09.041.

[4] A. Adabiardakani, M. Hakimi, and H. Kargar, "Cinnamaldehyde schiff base derivatives: A short review", *World Appl. Program.*, **2**(11), 472–476, 2012.

[5] P.T. da Silva *et al.*, "Structural, vibrational and electrochemical analysis and antibacterial potential of isomeric chalcones derived from natural acetophenone", *Appl. Sci.*, **10**(14), 2020, doi: 10.3390/app10144713.

[6] P.T. da Silva *et al.*, "Synthesis, spectroscopic characterization and antibacterial evaluation by chalcones derived of acetophenone isolated from Croton anisodontus Müll.Arg", *J. Mol. Struct.*, **1226**, 2021, doi: 10.1016/j.molstruc.2020.129403.

[7] M.N. Gomes *et al.*, "Chalcone derivatives: Promising starting points for drug design", *Molecules*, **22**(8), 2017, doi: 10.3390/molecules22081210.

[8] F. Perdana, Y. Eryanti, and A. Zamri, "Synthesis and Toxicity Assessments Some Para-methoxy Chalcones Derivatives," *Procedia Chem.*, **16**, 129–133, 2015, doi: 10.1016/j.proche.2015.12.040.

[9] M.R. Jayapal and N.Y. Sreedhar, "Anhydrous K_2CO_3 as catalyst for the synthesis of chalcones under Microwave Irradiation", *J. Pharm. Sci. Res.*, **2**(10), 644–647, 2010.

[10] M.R. Ahmed, V.G. Sastry, N. Bano, S. Ravichandra, and M. Raghavendra, "Synthesis and cytotoxic, antioxidant activites of new chalcone derivatives", *Rasayan J. Chem.*, **4**(2), 289–294, 2011.

[11] V. Arora, P. Arora, and H. S. Lamba, "Synthesis and evaluation of chalcone derivatives of 2-acetyl naphthalene for antifungal and antibacterial activity", *Der Pharm. Lett.*, **4**(2), 554–557, 2012.

[12] C.B. Patil, S.K. Mahajan, and S.A. Katti, "Chalcone: A versatile molecule", *J. Pharm. Sci. Res.*, **1**(3), 11–22, 2009.

[13] J. Jasril, I. Ikhtiarudin, A. Zamri, H.Y. Teruna, and N. Frimayanti, "New fluorinated chalcone and pyrazoline analogs: Synthesis, docking, and molecular dynamic studies as anticancer agents," *Thai J. Pharm. Sci.*, **41**(3), 93–98, 2017.

[14] D.J. Weldon *et al.*, "One-pot synthesis of cinnamylideneacetophenones and their in vitro cytotoxicity in breast cancer cells", *Bioorganic Med. Chem. Lett.*, **24**(15), 3381–3384, 2014, doi: 10.1016/j.bmcl.2014.05.089.

[15] C.R. Polaquini *et al.*, "Antibacterial & antitubercular activities of cinnamylideneacetophenones", *Molecules*, **22**(10), 1–12, 2017, doi: 10.3390/molecules22101685.

[16] B.A. and D.U.C.R.A.H. Cahyana, and D. Fitria, "Preparation of Fe_3O_4/SiO_2-guanidine organobase catalyst for 1,5-diphenylpenta-2,4-dien-1-one synthesis", *IOP Conf. Ser. Mater. Sci. Eng.*, 188(1), 1–5, 2017, doi: 10.1088/1757-899X/188/1/012026.

[17] D. Fitria, A.H. Cahyana, and A.R. Liandi, "Green Synthesis and Characterization of Cinnamylideneacetophenone Compound Using Fe_3O_4 Magnetic as Catalyst", *EduChemia (Jurnal Kim. dan Pendidikan)*, 6(2), 172, 2021, doi: 10.30870/educhemia.v6i2.10412.

[18] J. da C. Xavier, F.W.Q. Almeida-Neto, P.T. da Silva, E.S. Marinho, M.K.A. Ferreira *et al.*, "Structural characterization, electronic properties, and anxiolytic-like effect in adult zebrafish (Danio rerio) of cinnamaldehyde chalcone", *J. Mol. Struct.*, **1222**, 128954, 2020, doi: 10.1016/j.molstruc.2020.128954.

[19] A.H. Cahyana, A.R. Liandi, Y. Safitri, and R.T. Yunarti, "Synthesis of 1,4-dihydropiridine with aromatic of cinnamaldehyde compound using nife2o4 mnps catalyst and the activity test as antioxidant", *Rasayan J. Chem.*, **13**(3), 1491–1497, 2020, doi: 10.31788/RJC.2020.1335700.

[20] D.P. and B.A.A.H Cahyana, "Citrate-capped

superparamagnetic iron oxide ($Fe3O_4$-CA) nanocatalyst for synthesis of pyrimidine derivative compound as antioxidative agent", *J. Phys. Conf. Ser.*, **188**, 1–4, 2017, doi: 10.1088/1757-899X/188/1/012008.

[21] T.S. De Freitas *et al.*, "Direct antibacterial and antibiotic resistance modulatory activity of chalcones synthesized from the natural product 2-hydroxy-3,4,6-trimethoxyacetophenone", *FEMS Microbiol. Lett.*, 367(15), 1–8, 2020, doi: 10.1093/femsle/fnaa124.

[22] S.A. Khan and A.M. Asiri, "Green synthesis, characterization and biological evaluation of novel chalcones as antibacterial agents", *Arab. J. Chem.*, **10**, S2890–S2895, 2017, doi: 10.1016/j.arabjc.2013.11.018.

[23] T.-D. Tran, T.-T.-N. Nguyen, T.-H. Do, T.-N.-P. Huynh, C.-D. Tran, and K.-M. Thai, "Synthesis and antibacterial activity of some heterocyclic chalcone analogues alone and in combination with antibiotics", *Molecules*, **17**(6), 6684–6696, 2012, doi: 10.3390/molecules17066684.

[24] S. Kosela, "*Cara Mudah dan Sederhana Penentuan Struktur Molekul berdasarkan Spektra Data (NMR, Mass, IR, UV)"*. Jakarta: Lembaga Penerbit Fakultas Ekonomi Universitas Indonesia, 2010.

[25] S. Kosela, "*Penentuan Struktur Molekul dengan Pendekatan Problem dan Solusi Spektra"*. Dian Rakyat - Jakarta, 2013.

[26] L.W. Wijayanti, R.T. Swasono, W. Lee, and Jumina, "Synthesis and evaluation of chalcone derivatives as novel sunscreen agent", *molecules*, **26**, 4–13, 2021, doi: 10.3390/molecules26092698.

[27] N.A.A. Elkanzi, H. Hrichi, R.A. Alolayan, W. Derafa, F.M. Zahou, and R.B. Bakr, "Synthesis of chalcones derivatives and their biological activities: A review", *ACS Omega*, **7**(32), 27769–27786, 2022, doi: 10.1021/acsomega.2c01779.

[28] A. Jain and D.K. Jain, "Synthesis, characterization and biological evaluation of some new heterocyclic derivatives of chalcone as antihyperglycemic agents", *Int. J. Pharm. Sci. Res.*, **10**(12), 5700–5706, 2019, doi: 10.13040/IJPSR.0975-8232.10(12).5700-06.

[29] S. Welday Kahssay, G.S. Hailu, and K.T. Desta, "Design, synthesis, characterization and in vivo antidiabetic activity evaluation of some chalcone derivatives", *Drug Des. Devel. Ther.*, **15**, 3119–3129, 2021, doi: 10.2147/DDDT.S316185.