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Synthesis, Identification and Study of the Anti-microbial activity of Novel Chalcone and Epoxy chalcone compounds

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Abstract

In this study, new chalcone and epoxy chalcone synthesized by condensation of 4-acetylbiphenyl with the appropriate aldehydes. The epoxy chalcone prepared via the reaction chalcone with alkaline hydrogen peroxide in methanol. We characterized their mass spectra and ^{1}H, ^{13}C-NMR, and 2D-HSQC spectra to confirm their structure and absolute configuration. The target compounds were then screened for their potential antibacterial and antifungal activities. Most of the tested chalcone compounds had better activity against the fungal strains *Fusarium* and *Aspergillus niger*.

Keywords: Chalcone; Epoxy Chalcone; Green Chemistry; anti-microbial activity.

Introduction

Chalcones have many biological properties due to the enone pharmacophore in their structure and their low molecular weight. They are easy to prepare cost-effectively and could be developed as drug candidates for different diseases. Chalcones showed a broad spectrum of biological properties including anti-inflammatory, anticancer, antibacterial, antifungal, and antiviral [1-6]. They are also intermediates and precursors for different cyclic compounds such as isoxazole, pyrimidines, pyrazolines, etc. [7]. Other applications of chalcones are in an organic solar cell [8], liquid crystals [9], anti-corrosion effects [10], and in polymers [11]. The Weitz-Scheffer reaction uses hydrogen peroxide under alkaline conditions and is the most powerful way to oxidize a chalcone into an epoxy chalcone; it is an example of green chemistry [12-13]. Epoxy chalcone has excellent biological and pharmaceutical activates [14-16] and is intermediates and precursors for a wide range of chiral compounds and natural products [17-19]. As well as, life-threatening infections caused by pathogenic bacteria and fungi that are becoming increasingly general and widely extensive epidemics in the world make many research groups from all over the world is presently novel antibacterial and antifungal agents to overcome the emergence of various infectious diseases and the increasing number of multi drug resistant microbial organisms [20-21]. Here, in this work we prepared new chalcones and epoxy chalcones and characterized them spectroscopically as well as examine products with novel central compounds as potential antibacterial and antifungal agents.

Experimental

Chemicals and Instruments

All the chemicals ordered from Sigma-Aldrich (Saint Louis, USA). A mass spectrophotometer (Shimadzu, QP5050A, Japan) used for the electron impact (EI-Mass) at Tehran University, Iran. Nuclear magnetic resonance measurements carried out in Turkey and Iran. The ^{1}H and ^{13}C-NMR spectrometry carried out at the Tehran University, Iran using a Bruker (500 MHz) spectrometer. Other ^{1}H and ^{13}C NMR spectra and HSQC obtained on a Bruker BioSpin GmbH-400 MHz spectrometer at a laboratory in Turkey using DMSO-d6 as a solvent for all compounds except E2 compounds that used a $CDCl_3$ solvent and tetramethylsilane (TMS) as an internal reference. The TLC plates made of 20-cm silica gel mesh with a thickness of 2 mm (Merck). The names of the compounds given according to the IUPAC system.

Chemistry

Synthesis of Chalcones compounds CH1-CH10

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All the compounds in the study prepared according to the method mentioned in the literature [22]. The synthesis started with the condensation of 4-acetylbiphenyl with the appropriate aldehydes to produce the chalcone compounds.

General Procedure

A mixture of 4-acetylbiphenyl (0.0025 mol) and the appropriate aldehydes (0.0025 mol) dissolved in ethanol (50 mL). A catalytic amount of 10 mL of 10% NaOH added drop-wise to the solution with vigorous stirring. The reaction mixture stirred at room temperature. The progress of the reaction monitored by TLC, and the spot visualized by iodine vapour. On completion of the reaction, the mixture poured into crushed ice and acidified with dilute acetic acid (3% aqueous acetic acid). The resulting crude product filtered, washed successively with distilled water, and dried before being recrystallized from the appropriate solvent to obtain the corresponding chalcones. The (E)-chalcone compounds had different colours depending on the substituent.

Spectral analysis of the chalcones

(E)-1-([1, 1'-biphenyl]-4-yl)-3-(6-methoxynaphthalen-2-yl) prop-2-en-1-one (CH1): This material was prepared from 6-methoxy-2-naphthaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol twice. The product was separated as pale yellow powder, yield 75 %. mp 225 -227 ^{0}C. ^{1}H-NMR (500 MHz, DMSO-d_6): δ 8.25-8.30 (m, 3H, H-7, H-7`, H-21), 8.05-8.11 (dd, 2H, *J* = 15 Hz, β-11-CH=C, H-20), 7.89-7.93 (m, 5H, H-6, H-6`, H-2, H-2`,H-13), 7.79 (d, 2H, *J* = 5 Hz H-3, H-3`),7.52 (t, 2H, *J* =15 Hz, α-10, H-15), 7.44 (t, 1H, *J* = 7.5 Hz, H-1), 7.40 (s, 1H, H-18), 77.22 (dd, 1H, *J* = 5, 10, H-16), 3.92 (s, 3H, H-23). ^{13}C NMR (DMSO-d_6, 500 MHz) δ 187.96 (C-9), 158.07 (C-17), 143.86 (C-11), 138.46 (C-8), 136.06 (C-5), 135.13 (C-4), 130.20 (C-12), 129.71 (C-19), 129.71 (C-14), 128.79 (C-7,C-7`),128.62 (C-2,C-2`), 127.91 (C-13), 127.79 (C-21), 126.89 (C-1), 126.56 (C-6, C-6`),126.49 (C-3, C-3`),124.61 (C-20), 120.60 (C-18), 120.60 (C-16), 118.77 (C-10), 105.82 (C-15), 54.86 (C-22). MS (*m/z*): M^{+1} 364. EI-MS (m/z), ^{1}H and ^{13}C-NMR for compound CH1 figures, 1, 16 and 31.

(*E*)-1-([1, 1'-biphenyl]-4-yl)-3-(4-methoxynaphthalen-1-yl) prop-2-en-1-one) (CH2): This material was prepared from 6-methoxy-2-naphthaldehyde. Wishing by ethanol then recrystallized from ethanol twice. The product was separated as yellow crystals, yield 72%. mp 162-164 ^{0}C. ^{1}H NMR δ 8.55 (d, 1H, *J* =16 Hz, β-11- CH=C), 8.26-8.34 (m, 5H, H-7, H-7`, H-13, H-17, H-20), 7.97 (d, 1H, *J* =16 Hz, α-10-CH=C), 7.88 (d, 2H, *J* = 8, H-6, H-6`), 7.78 (d, 2H, *J* = 8, H-3, H-3`), 7.68 (t, 1H, *J* = 8, H-19), 7.58 (t, 1H, *J* = 8, H-18), 7.51 (t, 2H, *J* = 8, H-2, H-2`), 7.45 (t, 1H, *J* = 8, H-1), 7.12 (d, 1H, *J* = 8, H-14), 4.7 (s, 3H, H-23). ^{13}C NMR (DMSO-d_6, 400 MHz) δ 188.91 (C-9), 157.73 (C-15), 144.87 (C-5), 140.36 (C-11), 139.47 (C-4), 137.19 (C-8), 132.80 (C-12), 129.72 (C-7, C-7`),129.58 (C-2, C-2`),128.85 (C-21), 128.32 (C-1), 127.71 (C-16), 127.50 (C-6, C-6`),127.46 (C-3, C-3`),126.19 (C-10), 125.35 (C-13), 123.93 (C-20), 123.31 (C-17), 122.73 (C-19), 122.26 (C-18), 105.21 (C-14), 56.50 (C-22). MS (*m/z*): M^{+1} 364. HSQC cross peaks: 8.30/123.31 (20), 7.70/128.32 (19), 7.60/126.20 (18), 8.27/122.73 (17), 7.13/105.21 (14), 8.32/127.72 (13), 8.57/140.34 (11-β-δH/δC), 8/122.21 (10-α-δH/δC), 129.72/8.28 (77`),127.44/7.90(66`),7.78/127.52 (33`), 7.52/129.57 (22`), 7.44/128.85 (1), 4.03/57 (δH/δC) OCH_3 (22). EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMS- d_6) for compound CH2, figures 2, 17 and 32. HSQC figures 46 and 47.

***(E)-1-([1, 1'-biphenyl]-4-yl)-3-(3-phenoxyphenyl) prop-2-en-1-one) (CH3)*:** This material was prepared from 3-phenoxybenzaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol: dioxin (1:1) twice. The product was separated as yellowish white powder, yield 75%. mp 145-147 ^{0}C. ^{1}H NMR δ 8.26 (d, 2H, *J* = 10, H-7, H-7`), 8.02 (d, 1H, *J* = 15 Hz, β-11-CH=C), 7.87 ( d, 2H, *J* = 5, H-6,H-6`), 7.78 (d, 2H, *J* = 5, H-3, H-3`), 7.69-7.71 (m, 2H, H-2, H-2`), 7.72 (d, 1H, *J* =15 Hz, α-10-CH=C), 7.40-7.54 (m, 6H, H-13, H-16, H-20, H-21,H-22, H-23), 7.15 (t,1H, *J* = 5, H-19), 7.04-7.08 (m, 3H, H-1, H-17, H-18). ^{13}C NMR (DMSO-d_6, 400 MHz) δ 188.21 (C-9), 156.52 (C-5), 156.40(C-4), 144.28 (C-8), 142.83 (C-11), 138.57 (C-12), 135.92 (C-15), 136.55 (C-14), 129.07 (C-7, C-7`), 129.79(C-19), 128.78 (C-2, C-2`), 128.10 (C-1), 129, 79 (C-17), 126, 72 (C-6,C-6`), 126.66 (C-3, C-3`), 124.26 (C-2, C-3), 123.13 (C-10), 122.62 (C-21), 120.50 (C-22), 118.86 (C-18), 117.99 (C-20), 117.99 (C-16), 117.99 (C-13). MS (*m/z*): M^{+1} 376. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMS-d_6) for compound CH3 figures, 3, 18 and 33.

(E)-1-([1, 1'-biphenyl]-4-yl)-3-(anthracen-9-yl) prop-2-en-1-one) (CH4): This material was prepared from anthracene-9-carbaldehydean. Washing with ethanol was performed followed by recrystallization from ethanol twice. The product was separated as yellow crystals, yield 65%. mp 211-213 ^{0}C. ^{1}H NMR spectrum, δ, ppm: 7.42 (t,1H, *J* = 7.5 Hz, H-1), 7.50 (t, 2H, *J* = 7.5 Hz, H-16, H-22), 7.57-7.62 (m, 4H, H-2, H-2`, H-15, H-23), 7.77-7.81 (m, 3H, α-10-CH=C, H-17, H-21), 7.88 (d, 2H, *J* =5 Hz, H-3, H-3`), 8.16 (d, 2H, *J* = 10 Hz, H-6, H-6`), 8.24-8.31 (m, 4H, H-7, H-7`, H-

14, H-24), 8.66 (d, 1H, *J* = 15 Hz, 1H, β-11-CH=C), 8.71 (s, 1H, H-19). ^{13}C NMR (DMSO-d_6, 500 MHz) δ 144.72 (C-5), 140.31 (C-11), 138.86 (C-4), 136.10 (C-8), 131.29 (C-25), 131.29 (C-13), 130.88 (C-20), 130.88 (C-18), 129.77 (C-14), 129.77 (C-12), 129.51 (C-24), 129.14 (C-7, C-7`),129.05 (C-2, C-2`),128.90 (C-23), 128.90 (C-15), 128.48 (C-19), 128.31 (C-1), 127.11 (C-6, C-6`),127.04 (C-3, C-3`),126.85 (C-16), 126.85 (C-22), 125.65 (C-17), 125.65 (C-21), 125.09 (C-10). MS (*m/z*): M^{+1} 384. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMS-d_6) for compound CH4, figures, 4, 19 and 34.

(2E, 4E)-1-([1, 1'-biphenyl]-4-yl)-5-phenylpenta-2,4-dien-1-one) (CH5): This material was prepared from cinnamaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol: methanol (9:1). The product was separated as yellow powder, yield 65%. mp 162-164 ^{0}C. ^{1}H NMR δ 8.11 (d, 2H, *J* = 5 Hz, H-7, H-7`), 7.87 (d, 2H, *J* = 10 Hz, H-6, H-6`), 7.77 (d, 2H, *J*= 10 Hz, H-3, H-3`), 7.61 (d, 2H, *J* = 5 Hz, H-15, H-19), 7.51-7.58 (m, 3H, β-11-CH=C, H-2, H-2`), 7.42-7.46 (m, 4H, α-10-CH=C, H-16, H-17, H-18), 7.35 (t,1H, *J* = 7.5 Hz, H-1), 7.29 (t, 1H, *J* = 15 Hz 1H, β-13-CH=C), 7.23 (d, 1H, *J* = 15 Hz, 1H, α-12-CH=C). ^{13}C NMR (DMSO-d_6, 500 MHz) δ188.60 (C-9), 144.39 (C-5,C-11), 141.77 (C-13), 138.90 (C-5), 136.47 (C-4), 136.03 (C-8), 129.27 (C-14), 129.12 (C-7, C-7`,C-15), 128.97 (C-2, C-2`,C-19), 128.41 (C-1), 127.29 (C-16, C-17,C-18), 127.01 (C-6, C-6`, C-3, C-3`),125.49 (C-10, C-12). MS (*m/z*): M^{+1} 310. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO-d_6) for compound CH5, figures, 5, 20 and 35.

(E)-1-([1,1'-biphenyl]-4-yl)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)prop-2-en-1-one (CH6): This material was prepared from 2,3-dihydrobenzo[b][1,4]dioxine-6-carbaldehyde. Washing with ethanol was performed followed by recrystallization from xylene. The product was separated as yellow powder, yield, 64 %. mp 108-110 ^{0}C.. ^{1}H NMR δ 8.24 (d, 2H, *J* = 10 Hz, H-7, H-7`), 7.84-7.88 (m, 3H, β-11-CH=C, H-6, H-6`), 7.78 (d, 2H, *J* = 5 Hz, H-3, H-3` ), 7.67 (d, 1H, *J* =15 Hz, α-10-CH=C), 7.52 (t, 2H, *J*=10 Hz, H-2, H-2`), 7.53 (s, 1H, H-13), 7.43(t, 1H, *J* = 7.5 Hz, H-1), 4.29-4.32 (q, 4H, *J* = 5 Hz, H-15, H-15`, H-16, H-16`). ^{13}C NMR (DMSO-d_6, 500 MHz) δ 188.86 (C-9), 146.36 (C-17), 144.82 (C-8), 144.36 (C-11), 144.10 (C-12), 139.44 (C-5), 137.06 (C-4), 129.70 (C-2, C-2`),129.56 (C-7, C-7`),128.83 (C-1), 128.69 (C-14), 127.49 (C-6, C-6`),127.39 (C-3, C-3`),123.60 (C-10), 120.57 (C-18), 117.92 (C-13), 117.73 (C-19), 64.89 (C-15), 64.43 (C-16). MS (*m/z*): M^{+1} 342. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO-d_6) for compound CH6, figures, 6, 21 and 36.

(E)-1-([1,1'-biphenyl]-4-yl)-3-(pyridin-2-yl)prop-2-en-1-one) (CH7): This material was prepared from 2-pyridencarboxaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol twice. The product was separated as yellow powder, yield 55%. mp 133-135^{0}C. ^{1}H NMR δ 8.72 (d, 1H, *J* = 4 Hz, H-16), 8.19-8.23 (m, 3H, H-13, H-7, H-7`), 7.89-7.96 (m, 5H, H-1, H-3, H-3`, H-6, H-6`),7.78 (t, 2H, H-2, H-2`),7.74 (d, 1H, *J* =16 Hz, 1H, β-11-CH=C), 7.55-7.51 (m, 2H, H-14, α-10-CH=C), 7.45 (t, 1H, *J* = 8 Hz, H-15). ^{13}C NMR (DMSO-d_6, 400 MHz) δ 189.46 (C-9), 153.29 (C-12), 150.55 (C-13), 145.23 (C-5), 143.49 (C-11), 139.35 (C-4), 137.70 (C-15), 136.64 (C-8), 129.76 (C-7, C-7`),129.60 (C-2, C-2`),128.95 (C-1), 127.60 (C-6, C-6`),127.51 (C-3, C-3`),125.71 (C-10), 125.46 (C-16), 125.33 (C-14). MS (*m/z*): M^{+1} 285. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO-d_6) for compound CH7 figures, 7, 22 and 37.

(E)-1-([1, 1'-biphenyl]-4-yl)-3-(pyridin-3-yl) prop-2-en-1-one) (CH8): This material was prepared from 3-pyridencarboxaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol twice. The product was separated as pale yellow crystals, yield 58%. mp 150-152^{0}C. ^{1}H NMR δ 8.64 (d, 1H, *J* = 8 Hz, H-14), 8.63 (s, 1H, H-13), 8.39 (d, 2H, *J* = 8 Hz, H-16), 8.28 (d, 2H, *J* = 8 Hz, H-7, H-7`), 8.18 (d, 1H, *J*= 16 Hz, β-11-CH=C), 7.89 (d, 2H, *J* = 8 Hz, H-6, H-6`),7.79 (dd, 3H, H-3, H-3`, α-10-CH=C), 7.50-7.55 (m, 3H, H-15, H-2, H-2`),7.44 (t, 1H, *J* = 8 Hz, H-1). ^{13}C NMR (DMSO-d_6, 400 MHz) δ 188.90 (C-9), 151.50 (C-14), 150.88 (C-13), 145.21 (C-5), 141.00 (C-11), 139.37 (C-4), 136.62 (C-8), 135.65 (C-16), 131.03 (C-17), 129.89 (C-7,C-7`), 129.58 (C-2, C-2`), 128.93 (C-1), 127.54 (C-3, C-3`), 127.50 (C-6, C-6`), 124.44 (C-10), 124.40 (C-15). MS (*m/z*): M^{+1} 285. EI-MS (m/z), ^{1}H and ^{13}C–NMR (DMSO-d_6) for compound CH8 figures, 8, 23 and 38.

(E)-1-([1,1'-biphenyl]-4-yl)-3-(pyridin-4-yl)prop-2-en-1-one) (CH9): This material was prepared from 4-pyridencarboxaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol twice. The product was separated as yellowish white crystal, yield 56%. mp 160-162^{0}C. ^{1}H NMR δ 8.69 (d, 2H, *J* = 4 Hz, H-14, H-15), 8.28 (d, 2H, *J* =8 Hz, H-7, H-7`), 8.22 (d, 1H, *J* =16 Hz, , β-11-CH=C), 7.88-7.92 (m, 4H, H-3, H-3`, H-6, H-6`),7.80 (d, 2H, *J* = 8 Hz, H-16, H-13), 7.71 (d, 1H, *J*=16 Hz, α-10-CH=C), 7.52 (t, 2H, *J* = 8 Hz, H-2, H-2`), 7.44 (t, 1H, *J* = 8 Hz, H-1). ^{13}C–NMR (DMSO-d_6, 400MHz) δ 189.10 (C-9), 150.85 (C-15, C-14), 145.40 (C-5), 142.31 (C-4), 141.48 (C-11), 139.32 (C-8), 136.40 (C-12), 129.99 (C-2, C-2`), 129.60 (C-7, C-7`), 128.98 (C-1), 127.55 (C-6, C-6`, C-3, C-3`), 126.92 (C-10), 123.03 (C-13, C-16). MS (*m/z*): M^{+1} 285.1. EI-MS (m/z), ^{1}H and ^{13}C-

NMR (DMSO-d_6) for compound CH9 figures 9, 24, and 39.

(E)-1-([1, '-biphenyl]-4-yl)-3-(thiophen-2-yl) prop-2-en-1-one) (CH10): This material was prepared from thiophene-2-carbaldehyde. Washing with ethanol was performed followed by recrystallization from ethanol twice. The product was separated as pale yellow powder, yield 70%. mp 153-155 ^{0}C. ^{1}H NMR δ 8.19-8.21 (d, 1H, *J* = 8 Hz, H-7, H-7`), 7.94-7.97 (d, 1H, *J* =16 Hz, 1H, β-11-CH=C), 7.86-7.88 (d, 2H, *J* = 8 Hz, H-6, H-6`), 7.77-7.82 (m, 3H, H-15, H-3, H-3`), 7.72-7.74 (d, 1H, *J* = 4 Hz, H-13), 7.61-7.65 ( d, 1H, *J* = 16 Hz, α-10-CH=C), 7.51-7.55 (t, 2H, *J* = 8 Hz, H-2, H-2`),7.43-7.47 (t, 1H, *J* =8 Hz, H-14),7.21-7.23 (t,1H, *J* = 4 Hz, H-1). ^{13}C–NMR (DMSO-d_6, 400MHz) δ 188.62 (C-9), 144.95 (C-5), 140.23 (C-12), 139.43 (C-4), 137.17 (C-11), 136.83 (C-8), 133.33 (C-13), 130.99 (C-15), 129.61 (C-2, C-2`), 129.59 (C-7, C-7`), 129.23 (C-14), 128.88 (C-1), 127.49 (C-6, C-6`, C-3, C-3`), 120.91 (C-10). MS (*m/z*): M^{+1} 290.1. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO-d_6) for compound CH10 figures, 10, 25 and 40.

Synthesis of Epoxides E1-E5 (General Procedure)

The epoxy-chalcone compounds prepared according to the literature [23]. In general, it followed the Weitz–Scheffer procedure.

Dissolve (0.00135 mol) of the prepared chalcone compounds (CH1-CH10) in methanol (40 mL) treated with 30% hydrogen peroxide (3 ml) and 5 N solution (1.5 mL) with cooling to keep the temperature below 5°C. The progress of the reaction monitored by TLC. On completion of the reaction, the mixture poured into crushed ice and then separated using a separating funnel. It washed twice with 30 ml of water to remove the base and catalyst. It was then dried over anhydrous magnesium sulfate and filtered after which the solvent evaporated under reduced pressure. The solid residue crystallized from a suitable solvent.

Spectral analysis of the Epoxy chalcones

[1, 1'-biphenyl]-4-yl (3-(anthracen-9-yl) oxiran-2-yl)methanone) (E1): The material was prepared from chalcone CH4, recrystallized twice from Hexane and separated as yellow powder, yield 41%. mp 175-177 ^{0}C. ^{1}H-NMR (500 MHz, DMSO-d_6) δ 8.71 (s, 1H, H-19), 8.35-8.41 (m, 4H, *J* = 8 Hz H-6, H-6, H-7, H-7`), 8.16 (d, 2H, *J* = 8 Hz, H-3, H-3`), 7.96 (d, 2H, *J* = 12 Hz, H-14, H-14`), 7.84 (d, 2H, *J* = 8 Hz, H-17, H-17`), 7.54-7.59 (m, 6H, H-2, H-2`, H-15, H-15`, H-16, H-16` ), 7.46 (t, 1H, *J* = 8 Hz, H-1), 5.09 (d, 1H, *J* =2 , β-11 ), 4.94 (d, 1H , *J* = 2, 1H, α-10). $^{13}$C–NMR (DMSO-$d_6$, 400MHz) $\delta$ 194.25 (C-9), 146.11 (C-8), 139.15 (C-12), 134.72 (C-5), 131.15 (C-13, C-13`), 130.04 (C-7, C-7`), 129.40 (C-6, C-6`), 129.95 (C-18, C-18`), 128.62 (C-19), 129.65 (C-2, C-2`, C-4), 129.16 (C-1), 127.66 (C-17, C-17`), 127.60 (C-3, C-3`), 126.94 (C-15, C-15`), 125.92 (C-16, C-16`), 124.95 (C-14, C-14`). MS (*m/z*): $M^{+1}$ 400. HSQC (DMSO-$d_6$, 400 MHz), crosspeaks: (δH/δC): 8.71/128.61 (19), 8.40/124.95 (14,14`), 8.36/130.04 (77`), 8.17/129.40 (66`), 7.83/127.63 (17,17`), 7.99/127.66 (33`), 7.59/126.96 (15,15`), 7.57/125.93 (16,16`), 7.55/129.65 (22`), 7.49/129.16 (1), 5.09 /57.83 (10), 4.96/58.03 (11). EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO-d_6) for compound E1 figures, 11, 26 and 41. HSQC figures 48 and 49.

[1,1'-biphenyl]-4-yl (3-(pyridin-2-yl) oxiran-2-yl) methanone) (E2): The material was prepared from chalcone CH7, recrystallized twice from hexane: ethanol (8:2) and separated as white yellowish crystals, yield 31%. mp 136-138 ^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.66 (d,1H, *J* = 5 Hz, H-16), 8.13 (d, 2H, *J* = 5 Hz, H-7, H-7`), 7.76 (t, 1H, *J* = 7.5 Hz, H-15), 7.72 (d, 2H, *J* = 10 Hz, H-6, H-6`),7.64 (d, 2H, *J* =10 Hz, H-3, H-3`), 7.48 (t, 2H, *J* = 7.5 Hz, H-2, H-2`),7.41-7.45 (m, 2H, H-14, H-13), 7.33 (d, 1H, *J* = 7.5 Hz, H-1), 4.62 (d, 1H, *J* =1.9 Hz, β-11), 4.26 (d, 1H, *J* =1.9 Hz, 1H, α-10). ^{13}C–NMR (DMSO-d_6, 400MHz) δ 193.01(C-9), 154.82 (C-8), 149.99 (C-16), 145.93 (C-12), 139.18 (C-5), 138.48 (C-4), 137.65 (C-15), 129.61 (C-7, C-7`), 129.44 (C-2, C-2`), 129.08 (C-1), 127.67 (C-6, C-6`), 127.53 (C-3, C-3`), 124.59 (C-13), 122.16 (C-14), 59.18 (C-11), 59.03 (C-10). MS (*m/z*): M^{+1} 301. HSQC (DMSO-d_6, 400 MHz), crosspeaks: (δH/δC): 8.63/150.00 (16), 8.13/129.46 (77`), 7.91/137.68 (15), 7.89/127.67 (66`), 7.78/127.57 (33`), 7.56/122.18 (14), 7.45/129.09 (1), 7.52/129.63 (22`), 7.45/124.61 (13), 5.01/59.04 (11), 4.23/59.19 (10). EI-MS (m/z), ^{1}H and ^{13}C-NMR ($CDCl_3$) for compound E2 figures, 12, 27 and 42. HSQC figures 50 and 51.

[1,1'-biphenyl]-4-yl(3-(pyridin-3-yl)oxiran-2-yl)methanone) (E3): The material was prepared from chalcone CH8, recrystallised twice from hexane: water (8:2) and separated as white powder, yield, 33%; mp 138-140 ^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.71 (s, 1H, H-13). 8.60 (d, 1H, *J* = 5 Hz, H-14), 8.14 (d, 2H, *J* = 10 Hz, H-7, H-7`), 7.85-7.89 (m, 3H, H-6, H-6`, H-16), 7.76 (d, 2H, *J* = 10 Hz, H-3, H-3`),7.44-7.53 (m, 4H, H-1, H-2, H-2`, H-15), 5.02 (d, 1H, *J* =1.9 Hz, β-11), 4.26 (d, 1H, *J* =1.9 Hz, α-10). ^{13}C–NMR (DMSO-d_6, 500MHz) δ 192.86 (C-9), 150.54 (C-8, C-13), 148.80 (C-12, C-14), 145.94 (C-5), 134.49 (C-16), 131.97 (C-4), 129.22 (C-2, C-2`), 129.61 (C-7, C-7`), 129.09 (C-1), 127.64 (C-6, C-6`), 127.54 (C-3, C-3`), 124.08 (C-15), 59.78 (C-10), 57.16 (C-11). MS (*m/z*): M^{+1} 301. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO -d_6) for compound E3 figures, 13, 28 and 43.

[1, 1'-biphenyl]-4-yl (3-(3-phenoxyphenyl) oxiran-2-yl)methanone) (E4): The material was prepared from chalcone CH3, recrystallized twice from hexane, and separated as white crystals, yield 48%. mp 101-103^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 (d, 2H, *J* = 8 Hz, H-7, H-7`), 7.88 (d, 2H, *J* =10 Hz, H-6, H-6`),7.76 (d, 2H, *J* =10 Hz, H-3, H-3`),7.51 (t, 2H, *J* = 6 Hz, H-2, H-2`),7.40-7.47 (m, 4H, H-1, H-13, H-17, H-20), 7.25-7.27 (d, 1H, *J* = 8 Hz, H-23), 7.15-7.19 (m, 2H, H-21, H-22), 7.05-7.07 (m, 3H, H-16, H-18, H-19), 7.0 (d, 1H, *J* = 8 Hz, H-23), 4.87 (d, 1H, *J* =1.9, β-H11), 4.17 (d, 1H, *J* =1.9 Hz, α-H10). ^{13}C–NMR (DMSO-d_6, 400MHz) δ 192.92 (C-9), 156.81 (C-12), 157.48 (C-8), 134.53 (C-15), 145.88 (C-5), 139.18 (C-4), 138.61 (C-14), 130.76 (C-13), 129.76 (C-7, C-7`),129.49 (C-2, C-2`), 129.08 (C-1), 127.64 (C-6, C-6`), 127.54 (C-3, C-3`), 130.61 (C-23), 124.17 (C-21), 119.28 (C-16, C-17, C-19, C-20), 121.94 (C-22), 60.33 (C-11), 58.58 (C-10). MS (*m/z*): M^{+1} 392.3. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO -d_6) for compound E4 figures, 14, 29 and 44.

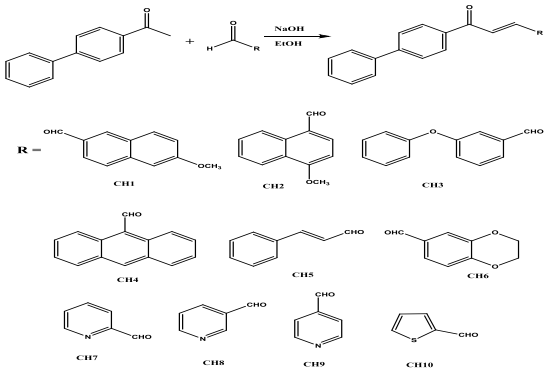
***(E)-1-([1, 1'-biphenyl]-4-yl)-3-(3-phenyloxiran-2-yl) prop-2-en-1-one) (E5)**:* The material was prepared from chalcone CH5, recrystallized twice from hexane, and separated as white powder, yield 37%. mp 125-127^{0}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.79 (m, 1H, α-H13), 4.79 (d, 1H, *J* =2 Hz, β-H12), 6.20 (m,1H, β-H11), 7.00 (d,1H, *J*=16 Hz, α-H10), 7.30 (t, 1H, *J* = 8 Hz, H-17), 7.37 (t, 2H, *J* = 8 Hz, H-16, H-18), 7.50-7.55 (m, 4H, H- 2, H-2`, H-15, H-19 ), 7.76 (d, 2H, *J* = 8 Hz, H-3, H-3`),7.89 (d, 2H, *J* = 8 Hz, H-6, H-6`), 8.13 (d, 2H, *J* = 8 Hz, H-7, H-7`). ^{13}C–NMR (DMSO-d_6, 400MHz) δ 193.53 (C-9), 145.83 (C-5), 136.35 (C-8, C-11), 134.61 (C-14), 134.61 (C-4), 129.61 (C-15, C-19), 129.35 (C-7, C-7`), 129.06 (C-17), 129.25 (C-2, C-2`), 128.29 (C-1), 127.64 (C-6, C-6`), 126.18 (C-10), 127.54 (C-3, C-3`), 59.57 (C-13), 58.57 (C-12). MS (*m/z*): M^{+1} 326.3. EI-MS (m/z), ^{1}H and ^{13}C-NMR (DMSO -d_6) for compound E5, figures, 15, 30 and 45

In vitro antibacterial and antifungal activities study

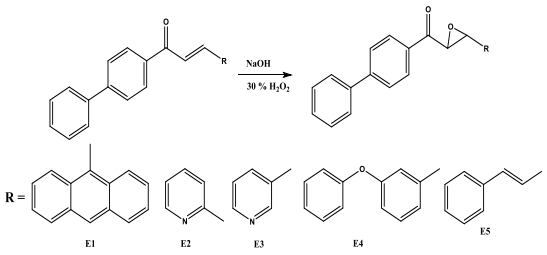
In vitro antibacterial and antifungal activity measured at different concentrations (0.5, 1.0, and 2.0) mg/ml using a disk diffusion method [24] of the chalcone compounds CH1-CH10 against two types of bacteria and two fungus strains studied in Department of Zoology, Faculty of Life Sciences, Government College University, Faisalabad, Pakistan.

Results and Discussion

The synthesis of chalcone and epoxy chalcone compounds performed by the Classian and Weitz–Scheffer reactions, respectively (Scheme 1 and 2). The physical properties and structures of the synthesized compounds showed in Table 1. The structure of the products was identified by mass (EI-Mass) as well as ^{1}H, ^{13}C-NMR, and 2D-HSQC spectra. The structure of the compounds proposed by referring to the literature [25-30]. The MS of all compounds exhibited a peak of the molecular ion [M]+ with high intensity; the molecular ion agrees well with the suggested formula.



Scheme 1. Synthetic pathway to chalcone compounds.



Scheme 2. Synthetic pathway to epoxy chalcone compounds.

Chalcone compounds CH1-CH10

The ^{1}H-NMR spectra for the chalcone compounds showed that there were two possible chalcone structures for the two isomers: trans and cis. Our study and the literature confirmed that the trans isomer is in the majority of chalcone structures. The chalcone compounds characterized by three regions of chemical shifts, i.e., aromatic regions A (4-acetyal biphenyl) and B (R= different aromatic aldehyde) along with vinylic protons α-H and β-H. The protons of Hα and Hβ overlapped with the aromatic protons A and B. In all cases, the two olefinic protons characterized by two doublet signals with a coupling constant of *J* =15 -16 Hz thereby confirming the trans configuration. In contrast, the aromatic ring protons commonly had overlapping signals such as the biphenyl protons, which appeared as multiples in the range of 7.34 - 8.05

ppm for all the compounds. Other peaks attributed to R-B different in their chemical shift and depended on R, which overlapped with the aromatic proton A and the vinylic protons Hα and Hβ. This caused some difficulties in distinguishing between the *J*-coupling of vinylic protons, Hα and Hβ, due to the strong overlap between these protons and the ring protons that resonated in close frequencies. The spectra were similar with minor differences in some cases depending on the different R groups. Most spectra had signaled for the aromatic ring protons and biphenyl protons overlapping with the vinylic protons. The one proton of the olefinic protons distinguished via J-coupling while another proton was difficult to distinguish due to the overlap. In the ^{13}C NMR spectra, all chalcones characterized by four regions. The carbonyl carbon signals appeared at 187-193 ppm due to their conjugation with the double bonds causing low-filled compression with the starting material (ketone). Meanwhile, α-C and β-C appeared in the region of 120-145 ppm. In some cases, his signal overlapped with another signal. Besides, the aromatic carbon signals appeared at 105-158 ppm while the aliphatic signals appeared at 55-65 ppm. In all the compounds, there were more symmetrical atoms in some spectra, which were possible to determine despite the symmetry. In other spectra, they were difficult to determine due to the strong overlap. The full structural determination done by 2D-HSQC for compound CH2 provided other evidence for the formation compound and shows correlation peaks for the most important remote H-C couplings. All spectra indicated that the chalcones were trans.

Epoxy chalcone E1-E5

The reaction between chalcone and the H_2O_2 formation of epoxy chalcone confirmed by the ^{1}H, ^{13}C-NMR, and 2D-HSQC spectra in this reaction. A double bond converted to the epoxy ring thereby causing an up-field shift in all the signals belonging to the protons of the epoxy ring and consequently converting the olefinic protons to aliphatic protons. Also, the structure of the epoxy chalcone could be trans or cis with a *J*-coupling (cis = 3-5 Hz and trans =1-3 Hz). The literature confirms that the trans isomer is in the majority of the epoxy chalcone structures. This ring contraction affects the splitting profile of these protons. In general, all spectra for the epoxy chalcones exhibited a minor *J* value, which is characteristic of the trans-stereochemistry (*J* = 1.9 - 2 Hz) of rigid three-membered ring systems (epoxy chalcone) [31-32].

Compound E5 showed two trans vinylic protons and a trans epoxy ring assigned to the downfield epoxide proton. Compound E5 exhibited two signals for the epoxy ring: The first is a doublet signal at δ 4.79-4.80 ppm (*J*= 2 Hz) attributed to one proton β-H13, and the second signal is multiple in the range of δ 3.79-3.81 ppm attributed for proton α-H12. This proton suffered long-range coupling with three protons β-H13, β-H11, and α-H10. Two signal had seen for the vinylic protons in chalcone. The first signal is a doublet at δ 7.00-7.04 ppm (1H, *J*=16 Hz) attributed to proton α-H10 while the second signal is a multiple at δ 6.20-6.26 ppm attributed to proton β-H11, which suffers long-range coupling with three protons β-H13, β-H11, and α-H12 causing splitting the essential signal to multiples with *J*=16 Hz for one proton confirming the trans configuration of the chalcone. The ^{13}C NMR spectra of epoxy-chalcone had three regions. The first region was at 55.5- 60 ppm at the high field for the aliphatic carbons of the epoxy ring. The second region at 120-160 ppm attributed to the aromatic carbons. The third region is at 190-195 ppm and attributed to carbonyl carbons at the low field due to the lack of conjugation with olefinic carbons and consequently a ring epoxy formation. All spectra showed a strong overlap between the signals due to sturdy symmetry especially in aromatic carbons including biphenyl and aromatic. Besides, the assignments of chemical shifts for the protons and carbon nuclei were further confirmed via 2D-HSQC for the E2 and E4 compounds. In conclusion, all chemical shifts in the ^{1}H, ^{13}CNMRm and 2D-HSQC spectra as shown in the expected regions and confirmed the structure. The data elucidated the trans configuration of the chalcones and epoxy chalcones. See supporting information in the supplementary materials file (Figures 1-51).

Anti-microbial activity

Ten chalcone compounds were then selected and screened for their antibacterial and antifungal activities against a Gram-positive strain *S. aureus* and a Gram-negative strain of *E. coli* as well as *Fusarium* and *Aspergillus niger*. These experiments used gentamicin as control, and the zone of inhibition in millimeters as shown in Table 2. For both the Gram-positive strains of *s. aureus* and Gram-negative strains of *E. coli*, the compounds had no inhibitory activity. However, there was significant antifungal activity against the *Fusarium* strain especially compounds CH5 and CH7. These two had an increase in the N and O atoms in the structure, which might affect activity. Other compounds, particularly the CH3 compound, showed excellent high potency against the *Aspergillus niger* strain. The CH1, CH5, and CH6 compounds similarly had good activity [33-34].

Conclusion.

New chalcones and epoxy chalcones compounds synthesized and characterized by their mass spectra as well as ^{1}H, ^{13}C- NMR, and 2D-HSQC experiments, which confirmed their structures. The data proved that this compound has a trans orientation based on a coupling constant between two protons: ^{3}J αH-βH (15 -16 Hz) for chalcone and epoxy chalcone ^{3}J H-H (1.9 - 2 Hz). The chalcones consider a significant inhibition effect against the fungal strains *Fusarium* and *Aspergillus niger* with no significant inhibition activity against bacteria.

Conflicts of interest

There are no conflicts to declare.

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References

[1] Santosh, L, G., and Vignesh, U. N., Synthesis and pharmacological properties of chalcones: a review., *Res Chem Intermed*., 43, 6043–6077(2017). doi 10.1007/s11164-017-2977-5.

[2] Debarshi, K, M., Sanjay, K, B., and Vivek, A., Anti-cancer Chalcones: Structural and Molecular Target Perspectives. *European Journal of Medicinal Chemistry*. 98, 69-114(2015). doi 10.1016/j.ejmech.2015.05.004.

[3] Zsuzsanna, R,. and Pál, P., Naturally occurring chalcones and their biological activities., *Phytochemistry Reviews*., 15, 87–120(2016). doi 10.1007/s11101-014-9387-8.

[4] Nurkenov, O, A., Ibraev, M, K., Schepetkin, I, A., Khlebnikov, A, I., Seilkhanove, T, M., Arinova, A, E., and Isabaeva, M, B., Synthesis, Structure, and Anti-Infl ammatory Activity of Functionally Substituted Chalcones and Their Derivatives., *Russian Journal of General Chemistry*., 89, 1360–1367(2019). doi 10.1134/S1070363219070028.

[5] Fu, Y, Liu, D., Zeng, H., Ren, X., Song, B., Hu, D., and Gan, X., New chalcone derivatives: synthesis, antiviral activity and mechanism of action. *RSC Adv*., 10, 24483-24490(2020). doi 10.1039/D0RA03684F.

[6] Burmaoglu, S., Algul O., Gobek, A., Aktas A, D., Ulger, M., Gul, E, B., Kaplan, E, Dogen, A., and Aslan G., Design of potent fluoro-substituted chalcones as antimicrobial agents., *Journal of Enzyme Inhibition and Medicinal Chemistry*., 32, 490–495(2017).doi 10.1080/14756366.2016.1265517.

[7] Aijaz, A., Mohmmad, Y, W., Mrudula, P., Abilio, J, F, N, S., Adriano, G, D., Faisal, M, A., and Abdullah, S, Al-B., Synergistic antifungal effect of cyclized chalcone derivatives and fluconazole against Candida albicans., *Med. Chem. Commun.*, 8, 2195-2207(2017). doi 10.1039/c7md00440k.

[8] Kien, Y, T., Mee H T., Hung, Y, W., Nornadia, J., Zhi-Qiang, L., Ming, Y, S., Jyun, Y, T., Jenn-Kai Tsai., Rafizah, R., Wan, M, K., and Meng, G, T., The influence of the push-pull effect and a π-conjugated system in conversion efficiency of bis-chalcone compounds in a dye sensitized solar cell., *Journal of Molecular Structure*., 1143, 42-48(2017). doi.10.1016/j.molstruc.2017.04.059.

[9] Thaker, B, T., and Kanojiya, J, B,. Synthesis, Characterization and Mesophase Behavior of New Liquid Crystalline Compounds Having Chalcone as a Central Linkage., *Mol. Cryst. Liq. Cryst*., 542, 84-98(2011).doi 10.1080/15421406.2011.570123.

[10] Chaouiki, A., Lgaz, H., Salghi, R., Chafiq, M., Oudda., Shubhalaxmi., Bhat, K, S., and Cretescu, I., Ali, I,H., Marzouki, R., and Chung, I-M., Assessing the Impact of Electron-Donating-Substituted Chalcones on Inhibition of Mild Steel Corrosion in HCl Solution: Experimental Results and Molecular-level Insights., *Colloids and Surfaces A: Physicochemical and Engineering Aspects*.,588,1-56(2020). doi.org/10.1016/j.colsurfa.2019.124366.

[11] Alagar, M., Hariharan, A., Srinivasan, K., Kesavan, K., and Murthy, C., A low cure thermo active polymerization of chalcone based benzoxazine and cross linkable olefin blends., *Journal of Polymer Research*., 25:163, 1-11 (2018). doi.org/10.1007/s10965-018-1556-9.

[12] Dana-Georgiana, C., Anna, M, S., and Francesc, M., Highly selective multifunctional nanohybrid catalysts for the one-pot synthesis of α,β-epoxy-chalcones. *Journal of Catalysis*., 334, 120–128(2016). doi.org/10.1016/j.jcat.2015.11.020.

[13] Dalyna, N., Mbelu, K., Victoria, H., and Renuka, M., One-pot synthesis of chalcone epoxides – A green chemistry strategy., *Tetrahedron Letters*., 55,4496-4500(2014).doi.org/10.1016/j.tetlet.

[14] Haiyong, H., Yu, Z., Timothy, C., Rosemarie, F, H., and Seth, D, R., *Arch. Pharm. Chem. Life*

Sci., 8, 429–439(2010).doi 10.1002/ardp.200900261.

[15] Bunu, S, J., Awala, E, V., and Eboh, D, D., Preparation and Antifungal Properties of Chalcone and Halogenated Derivatives., *Saudi J Med Pharm Sci*,6(4),379-389(2020).doi. 10.36348/sjmps.2020.v06i04.009.

[16] Saba, F., and Zainab, N., One Pot and Two Pot Synthetic Strategies and Biological Applications of Epoxy‑Chalcones., *Chemistry Africa*., 2020, 3, 291–302(2020).doi.org/10.1007/s42250-020-00128-5.

[17] Naveen, K, K., and Naseem, A., Regioselective Opening of Chalcone Epoxides with Nitrogen Heterocycles Using Indium(III) Chloride as an Efficient Catalyst., *Synthetic Communications*., 43,2008-2018(2013).doi 10.1080/00397911.2012.667291.

[18] Christelle, L., Epoxy ketones as versatile building blocks in organic synthesis. *Tetrahedron:Asymmetry*., 12, 2359–2383(2001). doi 10.1016/S0957- 4166(01)00412-8.

[19] Simona, B., Daniela, L., and Luigi, V., Ring-Opening of Epoxides in water., *Eur. J. Org. Chem.*, 2011, 2587–2598(2011). doi 10.1002/ejoc.201001693.

[20] Richard, J, F., Yitzhak, T., Antibiotics and Bacterial Resistance in the 21st Century. Perspectives in Medicinal Chemistry. 6, 25–64(2014). doi: 10.4137/ PMc.s14459.

[21] Gaonkar, L., Vignesh, U, N., Synthesis and pharmacological properties of chalcones: a review, *Res Chem Intermed*. 43, 6043–6077(2017). doi: 10.1007/s11164-017-2977-5.

[22] Mohammad, A., Harish, K., and Suroor A, K., Synthesis and pharmacological evaluation of pyrazoline derivatives as new anti-inflammatory and analgesic agents., *Bioorganic & Medicinal Chemistry Letters*.,18, 918–922(2008). doi 10.1016/j.bmcl.2007.12.043.

[23] Ernst, W., and Alfred, S., *Ber*., 54, 2327(1921).

[24] Stompor, M., Zarowska B., Antimicrobial Activity of Xanthohumol and Its Selected Structural Analogues. *Molecules*. 21, 1-10(2016). doi: 10.3390/molecules21050608.

[25] Ibieta, J, G., Bravo, J, A., Coro, Y, Q., Solís, O., and Vila, J, L., *Bolivian Journal of Chemistry*. 34, 89-103(2017).

[26] Doseok, H., Jiye, H., Geunhyeong, J., Dongsoo, K., and Yoongho, L., *Magn. Reson. Chem*., 49, 41–45(2011). doi 10.1002/mrc.2707.

[27] Gabriela I, J., Jose, A, B., and Jose, L, V., Synthesis of Benzylidene Acetophenone Under microwave irradiation; Green Chemistry., *Rev. Bol. Quim*., 2016, 33, 179-182(2016).

[28] Zainuri, D, A., Arshad ,S., Che, Khalib, N., Razak, I, A., Pillai, Renjith, R., Sulaiman, S,F., Hashim, N, S., Ooi, K, L., Armakovic, S., Armakovic, S, J., Panicker, C, Y., and Alsenoy, C, V., Synthesis, XRD crystal structure, spectroscopic characterization (FT-IR,1H and 13C NMR), DFT studies, chemical reactivity and bond dissociation energy studies using molecular dynamics simulations and evaluation of antimicrobial and antioxidant activities of a novel chalcone derivative, (E)-1-(4-bromophenyl)-3-(4-iodophenyl)prop-2en-1-one., *Journal of Molecular Structure*., 1128, 520-533(2017). doi 10.1016/j.molstruc.2016.09.022.

[29] Kumar, P, C, R., Ravindrachary, V., Janardhana, K., Manjunath, H, R., Prakash, K., Vincent, C., and Sridhar, M, A., *Journal of Molecular Structure*.,1005,1-7(2011).doi:10.1016/j.molstruc.2011.07.038.

[30] Neha, S., Mukesh, K., Roshan, L., Amit, K, S., and Meena, S., Acoustical studies of synthesized α,β-unsaturated ketones in ethanol and different percentage composition of DMSO in ethanol., *Journal of Molecular Liquids*., 236, 422–434(2017). doi.org/10.1016/j.molliq.2017.04.023.

[31] Mphahlele, M, J., Maluleka, M, M., and Mampa, R, M., *Crystals.* 9, 1-14(2019). doi 10.3390/cryst9060277.

[32] Marco, A, O, M., Carolina, E-M., María C, L., Gnecco, D., Manuel, S-G., and Raúl, G, E., *J Chem Crystallogr*., 44, 512–519(2014). doi 10.1007/s10870-014-0544-0.

[33] Thanh-D, T., Thi-Thao-Nhu, N., Tuong-Ha, D., Thi-Ngoc-Phuong, H., Cat-Dong, T., and Khac-Minh, T., Synthesis and Antibacterial Activity of Some HeterocyclicChalcone Analogues Alone and in Combination with Antibiotics. *Molecules*. 17,6684-6696(2012). doi.10.3390/molecules17066684.

[34] Kumar, C, S, C., Wan-Sin, L., Chin, W, O., Ching, K, Q., and Hoong-Kun, F., Heteroaryl Chalcones: Design, Synthesis, X-ray Crystal Structures and Biological Evaluation. *Molecules*., 18,12707-12724(2013). doi:10.3390/molecules181012707.