

Synthesis, spectral characterization and *in-vitro* analysis of some novel chalcones derivatives

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Abstract: Chalcones have a variety of biological activity and are a significant component of many natural sources. The acetophenones and various aromatic aldehydes were used in the synthesis of various chalcones by optimised methods of sonication. TLC was used to monitor the reaction, and IR, ¹H-NMR, and ¹³C-NMR spectroscopic methods were used to describe the synthesised products. Finally, the compounds were screened for their ability to inhibit the growth of microbes.

Keywords: Antibacterial, methoxy amino chalcones, Claisen-Schmidt Reaction, flavonoids, antifungal, antidiabetic etc.

INTRODUCTION: Chalcones are widely distributed throughout plants and are thought to be a precursor to flavonoids and isoflavonoids. They are biologically active throughout a broad spectrum, including antibacterial, antifungal, anticancer, and anti-inflammatory properties. The inhibition of lipoxygenase, beta-secretase, acyl-cholinesterase, butyrylcholinesterase, cyclooxygenase, and peroxisome has been documented for some Chalcones. Chalcone has biological activity primarily as a result of the presence of an enone pharmacophore in their structural makeup. The synthesis of various heterocyclic compounds with pharmacological potential is becoming more and more popular [1–4]. Chalcones play a crucial role in the synthesis of numerous such heterocyclic compounds [5–7]. Additionally, they form a significant class of bioactive natural compounds [8–10]. They are made up of open chain flavonoids, which are compounds with two aromatic rings connected by a three carbon - unsaturated carbonyl system. It has been discovered that the antibacterial action of chalcones is caused by the presence of reactive - unsaturated keto function [11–13]. The cytotoxic, anticancer, antiviral, insecticidal, and enzyme inhibitory activities of several chalcones have been examined recently [14, 15]. Numerous chalcones with varied positions for the hydroxyl and alkoxy groups have been found to have antiulcer [16, 17], antibacterial [18–21], antifungal [22], antimalarial [23, 24], antioxidant [25], and antidiabetic [26] properties. We synthesised several chalcone derivatives because of the library of such biological functions of chalcone derivatives.

MATERIALS AND METHODS

By analysing FT-IR, ¹H-, and ¹³C-NMR spectrum data, it was possible to verify the molecular structures of the produced compounds. All of the hydrogen atoms in the olefinic carbon-carbon bond were in the trans conformation, according to assessments of the ¹H-NMR coupling constants. Both the infrared spectra, where the carbonyl peak was seen at a lower wave number than a typical carbonyl peak (about 1650–1660 cm⁻¹), and the ¹³C-NMR spectra showed the presence of a carbonyl group conjugated with the olefinic carbon-carbon bond. Open capillary tubes and a melting point device were used to obtain the uncorrected melting points. The ¹H NMR spectra were recorded in CDCl₃ with TMS as internal standard on a Bruker spectrometer at 400 MHz, while the IR spectra were recorded in KBr pellets on a Nicolet 400 D spectrometer. Their chemical shifts are recorded in (parts per million) units. Using n-hexane and ethyl acetate as the solvent system, TLC was used to determine the purity of the compounds on silica-G plates with a 2 mm thickness. In an iodine chamber, spot visualisation was performed.

SCHEMATIC PROCEDURE FOR SYNTHESIS OF COMPOUNDS:

Chalcones were created through the base-catalyzed Claisen-Schmidt condensation reaction using a mixture of acetophenone derivative (6 mmol) and benzaldehyde derivative (6 mmol) that had been dissolved in ethanol (30 mL). Next, NaOH 40% solution (6 mL) was added dropwise, and the reaction mixture was stirred while the temperature was kept below 10 °C for an hour, followed by four hours at room temperature. The reaction mixture was then put into ice water, the precipitated material was filtered off, and the aqueous ethanol was reconstituted.

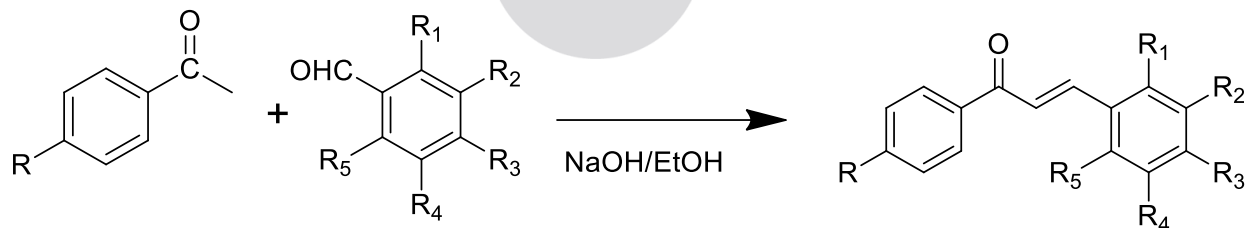
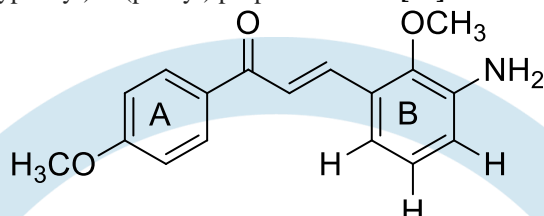
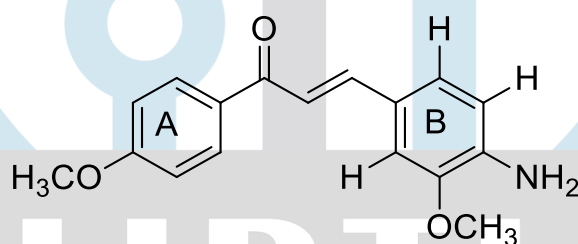


Table – 1: Some important substituents of chalcone

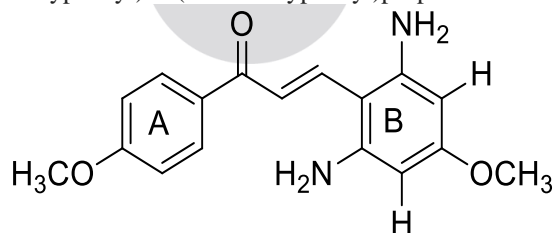
Compounds	R	R ₁	R ₂	R ₃	R ₄	R ₅
1a	OCH ₃	OCH ₃	NH ₂	H	H	H
1b	OCH ₃	H	H	NH ₂	OCH ₃	H
1c	OCH ₃	NH ₂	H	OCH ₃	H	NH ₂
1d	OCH ₃	NH ₂	H	H	H	Br
1e	OCH ₃	H	Br	H	NH ₂	H

Synthesis of (E)-3-(3-amino-2-methoxyphenyl)-1-(p-tolyl) prop-2-en-1-one [1a]**(E)-3-(3-amino-2-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one**

By Using the same method 1-(4-methoxyphenyl) ethanone and 3-amino-2-methoxybenzaldehyde were dissolved in ethanol and add with sodium hydroxide to get (1a) with recrystallization from ethanol gives pale yellow crystals of 1.468g, 84% yield. Mol. Formula: C₁₇H₁₇NO₃ Mol. Wt. 283.32, M.P. 148-151°C. IR (KBr): 3445 and 3348 cm⁻¹ (-NH₂), 1658 cm⁻¹ (C=O), 1544, 1534 cm⁻¹ (>C=C<), 1021 cm⁻¹ (OCH₃), 722 cm⁻¹ (Cl). 1610 (C=Cchain), 1215(C-O-Caryl alkyl ether); ¹H-NMR (CDCl₃) δ 8.10 (*d*, 1H, *J* = 15.8Hz); 7.63 (*d*, 1H, *J* = 15.2 Hz); 7.21 (*d*, 1H, *J* = 8 Hz); 7.13 (*dd*, 1H, *J* = 8.7 Hz); 7.15 (*s*, 1H); 8.19 (*d*, 1H, *J* = 8.7 Hz); 6.77 (*d*, 1H, *J* = 9.1 Hz); 8.24 (*d*, 1H, *J* = 9.2 Hz); 3.90 (*s*, 3H); 3.91 (*s*, 3H); 4.20 (*s*, br, 2H). ¹³C-NMR (CDCl₃) δ 139.55; 125.10; 123.28; 151.14; 126.65; 112.59; 153.33; 114.57; 132.10; 131.74; 114.43; 153.66; 65.20; 65.47; 178.99.

Synthesis of (E)-3-(4-amino-3-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one [1b]**(E)-3-(4-amino-3-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one**

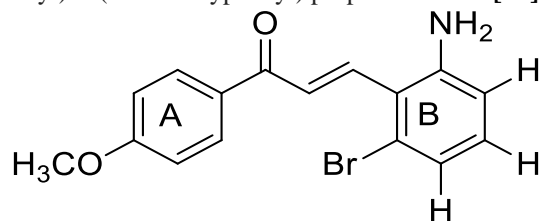
By Using the same method 1-(4-methoxyphenyl) ethanone and 4-amino-3-methoxybenzaldehyde were dissolved in ethanol and add with sodium hydroxide to get (1b) with recrystallization from ethanol gives yellow crystals of 1.68g, 88% yield. Mol. Formula: C₁₇H₁₇NO₃ Mol. Wt. 283.32, M.P. 178-181°C. R_f = 0.50 (*n*-hexane/ethyl acetate: 3/2); IR (KBr): 3340 and 3225 (-NH₂), 1658 cm⁻¹ (C=O), 1596, 1542 cm⁻¹ (>C=C<), 1026 cm⁻¹ (OCH₃), ¹H-NMR (CDCl₃) δ 8.41 (*d*, 1H, *J* = 17.8 Hz); 7.85 (*d*, 1H, *J* = 17.5 Hz); 8.25 (*s*, 2H); 7.66 (*d*, 2H); 7.65 (*s*, 1H); 7.56 (*d*, 1H); 7.63 (*t*, 1H); 7.12 (*t*, 1H); 7.18 (*d*, 1H); 3.82 (*s*, 3H); ¹³C-NMR (CDCl₃) δ 128.43; 128.55; 129.08; 138.42; 191.12; 125.42; 139.93; 127.11; 159.13; 119.90; 130.96; 121.21; 132.50; 56.62.

Synthesis of (E)-3-(2,6-diamino-4-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one [1c]**(E)-3-(2,6-diamino-4-methoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one**

By Using the same method 1-(4-methoxyphenyl) ethanone and 2,6-diamino-4-methoxybenzaldehyde were dissolved in ethanol and add with sodium hydroxide to get (1c) with recrystallization from ethanol gives yellow crystals of 0.56g, 30% yield. Mol. Formula: C₁₇H₁₈N₂O₃ Mol. Wt. 298.34, M.P. 242-245°C, R_f = 0.78 (CHCl₃); IR (KBr): 1650 cm⁻¹ (C=O), 1590, 1548 cm⁻¹ (>C=C<), 1365 cm⁻¹ (OCH₃), ¹H-NMR (CDCl₃) δ 7.57 (*d*, 1H, *J* = 15.9 Hz); 7.93 (*d*, 1H, *J* = 15.8 Hz); 8.12 (*d*, 2H); 7.6 (*d*, 2H); 7.58 (*s*, 1H);

7.31 (s, 1H); 7.05 (d, 1H); 7.31 (t, 1H); 7.22 (d, 1H); 3.74 (s, 3H); $^{13}\text{C-NMR}$ (CDCl_3) δ 138.2; 128.7; 128.1; 133.2; 192.1; 124.0; 145.1; 135.1; 114.3; 160.3; 116.3; 130.4; 121.2; 55.6.

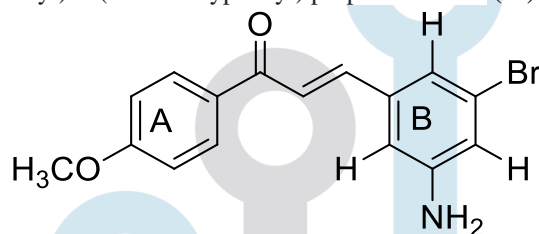
Synthesis of (E)-3-(2-amino-6-bromophenyl)-1-(4-methoxyphenyl) prop-2-en-1-one [1d]



(E)-3-(2-amino-6-bromophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one

By Using the same method 1-(4-methoxyphenyl) ethanone and 2-amino-6-bromobenzaldehyde were dissolved in ethanol and add with sodium hydroxide to get (1d) with recrystallization from ethanol gives yellow crystals of 1.36g and 88% yield. Mol. Formula: $\text{C}_{16}\text{H}_{14}\text{BrNO}_2$ Mol. Wt.332.19, M.P. 165-167 $^\circ\text{C}$, Rf = 0.46(*n*-hexane/ethyl acetate = 3/2); IR (KBr): 1655 cm^{-1} (C=O), 1570, 1520 cm^{-1} (>C=C<), 668 cm^{-1} (Br). $^1\text{H-NMR}$ (CDCl_3) δ 7.80 (d, 1H, J = 13.51 Hz); 7.40 (d, 1H, J = 13.48Hz); 8.02 (d, 2H); 7.52 (d, 2H); 7.51 (s, 1H); 7.58 (d, 2H, J = 6.77 Hz); 7.10 (d, 2H, J = 6.76 Hz); 3.87 (s, 3H); $^{13}\text{C-NMR}$ (CDCl_3) δ 138.8; 129.0; 130.8; 133.1; 191.2; 120.1; 145.2; 128.1; 128.8; 115.1; 162.7; 56.7

Synthesis of (E)-3-(3-amino-5-bromophenyl)-1-(4-methoxyphenyl) prop-2-en-1-one (1e)



(E)-3-(3-amino-5-bromophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one

By Using the same method 1-(4-methoxyphenyl)ethanone and 3-amino-5-bromobenzaldehyde were dissolved in ethanol and add with sodium hydroxide to get (1e) with recrystallization from ethanol to give pale yellow crystals of 1.32 g, Yield 86.7%, $\text{C}_{16}\text{H}_{14}\text{BrNO}_2$ Mol. Wt.332.19, M.P 165-168 $^\circ\text{C}$; Rf = 0.50 (*n*-hexane/ethyl acetate = 9/1); IR (KBr, cm^{-1}): 654.7 (C-Br stretch), 1388.75 (C-N stretch), 2999.31 (C-H stretch, aromatic), 3263.56 (N-H stretch), 1650 (C=O), 1590 (C=C); $^1\text{H-NMR}$ (CDCl_3) δ 8.05 (d, 1H, J = 15.9 Hz); 7.49 (d, 1H, J = 16.2 Hz); 7.64 (d, 2H, J = 8.7 Hz); 7.86 (d, 2H, J = 8.3 Hz); 6.55 (s, 1H); 6.53 (dd, 1H, J_1 = 8.8 and J_2 = 3.2 Hz); 7.56 (d, 1H, J = 8.7 Hz); 3.85 (s, 3H); 3.90 (s, 3H); $^{13}\text{C-NMR}$ (CDCl_3) δ 138.2; 130.6; 132.0; 127.7; 190.6; 120.5; 142.2; 117.4; 131.5; 106.1; 164.4; 99.3; 161.3; 56.4; 56.5.

RESULTS AND DISCUSSION

For the synthesis of Chalcones compounds, a variety of techniques are documented. However, we synthesised chalcones via the Claisen-Schmidt condensation method [27-35]. Chalcones were synthesised using the customary method, which was improved. The sonication technique was used to improve the standard approach. Chalcone can be produced using the traditional method after roughly 24 hours of stirring at room temperature. However, the sonication method made it possible to make chalcone in 15 to 30 minutes. Additionally, less solvent was needed to complete the reaction than with the usual method. Chalcone yield by conventional and optimised methods was discovered to be roughly equal.

ANTIBACTERIAL ACTIVITY

The Cup plate method was used to test all produced compounds for antibacterial activity against a selection of Gram-positive and Gram-negative bacteria. Amoxycillin and streptomycin were utilised as the conventional medications, and dimethyl sulfoxide (DMSO) was used as the solvent. Table 2 shows the antibacterial activity values for all compounds produced using the cup-and-plate method.

For antibacterial research, the following bacterial cultures were employed. Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella aerogenes are some examples of bacteria.

Table 2 lists the findings of studies on antibacterial agents.

At a concentration of 100 g/ml, all produced compounds were tested for antibacterial activity. Amoxycillin and streptomycin were utilised as the conventional medications, and dimethyl sulfoxide (DMSO) was used as the solvent. Antibacterial research revealed that nearly all of the synthetic chemicals were effective against both Gram positive and Gram negative bacteria. Based on the findings of the antibacterial activity, the following observations were made. Except for compound 1c, all other compounds were found to be effective against Bacillus subtilis and shown activity that was lower than Streptomycin, but compound 1a, 1b, and 1e displayed activity that was higher and comparable to Amoxicillin in the case of Gram positive bacteria. All of the synthetic

compounds, with the exception of 1a, 1b, 1d, and 1e, inhibited *Staphylococcus aureus* more potently than Streptomycin and more effectively than Amoxicillin because Amoxicillin did not inhibit this bacterium.

TABLE 2: ANTIMICROBIAL ACTIVITY OF THE SYNTHESIZED COMPOUNDS

S.No.	Gram Positive Bacteria		Gram Negative Bacteria		
	<i>Bacillus Subtilis</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>	<i>Klebsiella aerogenes</i>
1a	13	07	14	12	13
1b	18	10	17	15	16
1c	02	04	05	06	02
1d	10	07	08	09	11
1e	16	09	13	13	14
Amoxicillin	12	-	18	-	-
Streptomycin	21	13	15	24	21

The Mean Zone of Inhibition at a Concentration Level of 100 g/ml of Test Compounds and Standard Drugs is expressed in mm in the following table. *Escherichia coli* was suppressed by all synthetic compounds in the case of Gram negative bacteria, although compound (1b) shown excellent efficacy toward it, even greater than Streptomycin but lower than Amoxicillin. Amoxicillin, a common antibiotic, does not inhibit *Pseudomonas aeruginosa* or *Klebsiella aerogenes*, although all synthetic drugs displayed inhibition zones that were smaller than those of streptomycin. The best activity against both Gram positive and Gram negative bacteria was therefore provided by compound (1b).

CONCLUSION

It was discovered that almost every synthetic chemical was effective against both Gram positive and Gram negative microorganisms. When compared to the reference standard, compound (1b) was shown to exhibit the greatest activity, however other synthetic compounds also displayed activity on par with it. Some conclusions have been drawn about the kind of substituents that can be added to boost the activity based on the results, which can then be further researched.

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