Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

Synthesis and Biological Activity of Novel Imidazole Based Chalcone Derivatives.

Ms. Manisha Hooda[1], Dr. Pallavi Bhardwaj[2*], Dr. Jyoti Tanwar[3*]

[1] Research Scholar, Department of Chemistry, Baba Mastnath University, Asthal Bohar, Rohtak,

[2*]Associate Professor Deputy Dean, Department of Chemistry, Baba Mastnath University Rohtak,

[3*]Assistant Professor, Department of Chemistry, Hindu Girls College, Sonepat, Maharishi Dayanand University, Rohtak

(Received: 16 November 2024 Revised: 20 December 2024 Accepted: 04 January 2025)

KEYWORDS

Antimicrobial activity, Chalcones, Claisen-Schmidt, Imidazole, Nuclear magnetic resonance

ABSTRACT:

Aim: To synthesize novel imidazole-based chalcone derivatives and assess their biological activities for potential drug development.

Method: The novel imidazole-based chalcone derivatives were synthesized by reacting benzylamine, dihydroxyacetone, and potassium thiocyanate, forming (1-benzyl-2-mercapto-1H-imidazol-5-yl) methanol. The introduction of methyl or ethyl iodide, coupled with oxidation using magnesium dioxide, yielded the target compounds by alkylation and oxidation method. Claisen-Schmidt condensation with various acetophenones under methanolic sodium hydroxide facilitated further derivatization. Structural elucidation involved Spectroscopic analysis and mass spectrometry, followed by antimicrobial activity testing.

Results: Compounds (9a-9j') demonstrated varied antibacterial efficacy. Compound 9b exhibited notable activity against B. cereus and E. coli (MIC 125 µg/mL and 62.5 µg/mL). Compound 9e showed significant antibacterial activity across strains (MIC 50-125 µg/mL), and 9c consistently inhibited S. aureus, B. cereus, and P. aeruginosa (MIC 250 µg/mL). Compounds 9g and 9j' displayed diverse antibacterial effects, indicating potential selectivity.

Conclusions: In conclusion, the synthesized imidazole-based chalcone derivatives exhibit promising antimicrobial potential, supported by methodological alignment and consistent observations in antibacterial and antifungal activities. The innovative inclusion of oxidation steps enhances structural diversity, emphasizing their efficacy against bacterial and fungal infections.

1. Introduction

The prevalence of azoles in both natural and synthetic compounds, coupled with their pivotal role as synthetic intermediates, has attracted significant attention across industrial and academic domains [1-5]. Azole-based heterocyclic derivatives, renowned for their diverse biological activities and therapeutic potential, have emerged as focal points in medicinal chemistry research [6-10].

The azole scaffold is a crucial element found in many medications that have been authorized for clinical use and in compounds that are being investigated, highlighting its significance in contemporary drug development endeavours [11-13]. Azole ring-containing compounds, such as imidazole, triazoles, and oxazole, have shown significant efficacy against a range of ailments, including microbial infections, cancer, inflammation, and neurological problems [14,15]. Azole derivatives, including triazoles and imidazole, are extensively used as antifungal medicines because they may effectively hinder fungal cytochrome P450 enzymes that play a vital role in the production of ergosterol, a critical element of fungal cell membranes [16-19].

Imidazole-based chalcone derivatives represent a class of compounds with promising potential in medicinal chemistry due to their diverse biological activities [20-22]. Chalcones, characterized by their α, β-unsaturated

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

ketone structure, have long been recognized for their pharmacological properties. Imidazole, on the other hand, serves as a privileged scaffold in drug discovery owing to its structural versatility and pharmacological relevance [23-27]. The fusion of imidazole with chalcone moieties presents an intriguing avenue for the synthesis of novel compounds with enhanced biological profiles.

Several studies have underscored the pharmacological significance of imidazole-based compounds. For instance, research by Sharma et al., (2021) demonstrated the anticancer potential of imidazole derivatives against various cancer cell lines, highlighting their role as cytotoxic agents [28]. Additionally, investigations by Patel et al., (2021) revealed the antimicrobial activity of imidazole-based compounds against pathogenic microorganisms, suggesting their utility as antimicrobial agents [29].

Moreover, the biological activities of chalcone derivatives have been extensively explored in the literature. Studies by Li et al., (2020) elucidated the antioxidant properties of chalcones, emphasizing their potential in combating oxidative stress-related diseases [30]. Furthermore, research conducted by Rashid et al., (2019) highlighted the anti-inflammatory effects of chalcone derivatives, indicating their therapeutic relevance in inflammatory conditions [31].

In this perspective, the synthesis and biological evaluation of novel imidazole-based chalcone derivatives represent an important and fascinating area of study. Through the integration of the structural characteristics and pharmacological attributes of imidazole and chalcone, these compounds have the potential for the creation of highly effective therapeutic agents that may target a wide range of disorders, such as cancer, microbial infections, oxidative stress, and inflammation [32-36].

This research paper aims to explore the synthesis strategies employed for the preparation of imidazole-based chalcone derivatives and investigate their biological activities through comprehensive in vitro and in vivo evaluations. Through this endeavour, insights into the pharmacological potential of these compounds can be gained, paving the way for their future development as clinically relevant therapeutics.

2. Methods

2.1 Materials

Benzyl amine, dihydroxyacetone, potassium thiocyanate, acetic acid, 1-butanol, methyl iodide or ethyl iodide, sodium hydroxide, magnesium dioxide (MnO2), chloroform, acetophenones, methanolic sodium hydroxide, oxone, tetrahydrofuran (THF) and water were the reagent used in the synthesis of compounds. The chemicals and reagents were procured from Sigma Aldrich.

2.2 Synthesis of Imidazole-Based Chalcone Derivatives

The synthesis of imidazole-based chalcone derivatives, namely compounds 7a and 7b, was carried out using a multi-step approach described in Scheme 1. To, a solution of acetic acid and 1-butanol benzylamine (1), dihydroxyacetone (2), and potassium thiocyanate (3) were mixed. The reaction mixture after reaction, containing (1-Benzyl-2-mercapto-1H-imidazol-5-yl) methanol was agitated for 72 hours. Later, a solution of N-(4-methylphenyl)-2-aminothiocarbonylpropanoic acid (compound (4)) in methanol was treated with methyl iodide ethyl iodide and then coupled with an aqueous solution of sodium hydroxide. This led to the synthesis of 2-(4-methylphenyl)-4-thioxo-4,5-dihydro-1H-imidazole-5-carboxylic acid and 2-(4-methylphenyl)-4-thioxo-1H-imidazole-5-carbaldehyde (compounds 5, 6). Subsequently, compounds 5 and 6 were oxidized using magnesium dioxide (MnO_2) under reflux conditions with chloroform as a solvent, resulting in the formation of 2-(4-methylphenyl)-1H-imidazole-4-thiol (compound 7). Subsequently, Claisen-Schmidt condensation processes were conducted using compound 7a or 7b with different acetophenones (8a-8j) in presence of methanolic sodium hydroxide solution resulting in the formation of compounds 9a-9j'. In addition, compound 9j was oxidised using Oxone in a mixture of THF and water, forming the oxidized methyl sulfonyl molecule 9k. The chemical integrity and content of all synthesized compounds were verified using nuclear magnetic resonance (^{1}H NMR, ^{13}C NMR) and mass spectrometry studies, confirming their structural properties. The use of this complete synthetic strategy facilitated the production of imidazole based chalcone derivatives having well-defined structures and potential biological activity.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

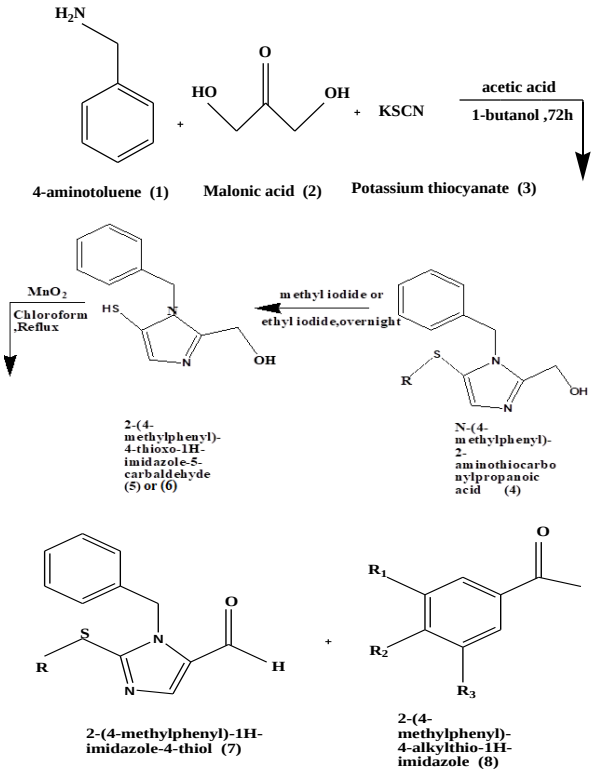


Figure 1: Scheme 1- Reagents and conditions.

Table 1. - Compounds 7a-9j

Compounds	R_1	R_2	R_3	R_4
7a	H	H	H	Me
7b	H	H	H	Et
8a	H	Br	H	-
8b	H	F	H	-
8c	H	Cl	H	-
8d	H	NO_2	H	-
8e	H	OPh	H	-
8f	H	CH_3	H	-
8g	Ph	Ph	H	-
8h	H	Ph	H	-
8i	H	OCH_3	H	-
8j	OCH_3	OCH_3	OCH_3	-
9a	H	Br	H	SMe
9b	H	F	H	SMe
9c	H	Cl	H	SMe
9d	H	NO_2	H	SMe
9e	H	OPh	H	SMe
9f	H	CH_3	H	SMe
9g	Ph	Ph	H	SMe
9i	H	OCH_3	H	SMe
9j	OCH_3	OCH_3	OCH_3	SMe
9K	OCH_3	OCH_3	OCH_3	SO_2Me
9a'	H	Br	H	SEt
9b'	H	F	H	SEt
9c'	H	Cl	H	SEt
9e'	H	OPh	H	SEt
9g'	Ph	Ph	H	SEt
9h'	H	Ph	H	SEt
9i'	H	OCH_3	H	SEt
9j'	OCH_3	OCH_3	OCH_3	Set

2.3 Characterization

The synthesized novel imidazole-based chalcone derivatives were spectroscopically characterized using advanced analytical instruments. Mass spectrometry was conducted using a Bruker MicroTOF-Q mass spectrometer, sourced from Bruker India Scientific Pvt. Ltd., to determine the molecular weights and structural properties of the compounds. Nuclear magnetic resonance (NMR) spectroscopy, including both carbon (^{13}C) and proton (^{1}H) NMR, was performed using a Bruker AVANCE III 500 MHz NMR spectrometer, also supplied by Bruker India Scientific Pvt. Ltd. These instruments provided high-resolution spectra, enabling precise determination of the molecular structures of the synthesized chalcone derivatives.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

2.4 Antimicrobial activity

The synthesized compounds were evaluated for antibacterial and antifungal properties against various bacteria and fungi. Bacterial assessment involved S. aureus, B. cereus, E. coli, and P. aeruginosa cultured in Mueller-Hinton (MH) medium, while A. niger and A. fumigatus were cultivated in RPMI-1640 medium for antifungal evaluation. Minimum inhibitory concentrations (MICs) were determined using the MTT colourimetric technique. Compounds, at 50 µg/mL concentration in DMSO, were added to a sterilized liquid medium in microtitration plates along with microbial suspensions (105 cfu/mL). Incubation at 37 °C (bacteria) and 36 °C (fungi) followed. MICs were visually determined, and MTT solution (2 mg/mL in PBS) was added, incubated, and then separated using isopropanol containing 5% 1 M hydrochloric acid. Optical density at 550 nm was measured using a microplate reader. The MIC values reflected the compounds' ability to inhibit microbial growth, indicating their potential as antimicrobial agents and providing insights into therapeutic applications.

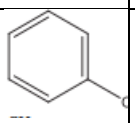
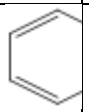
2.5 Statistical Analysis

The statistical tests were run using the SPSS (Version 26) programme. While numbers and percentages were utilised to depict categorical data, the mean and standard deviation were used to characterise all continuous variables. Descriptive statistics were used to determine the frequencies and proportions.

3. Results

The different Chalcone Derivatives were synthesized using Claisen-Schmidt condensation reaction. This involves potent bases like NaOH or KOH in polar solvents such as MeOH or DMF. Thin-layer chromatography confirms the purity of compound, and spectrum analysis confirm the structured analysis. Table 2 below displays the physical data of different imidazole triazole -chalcones derivatives.

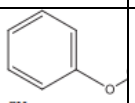
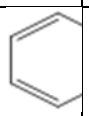
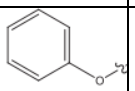
Table 2: Physical data of synthesized imidazothiazole-chalcones derivatives (9a-9j')

Compounds	R_1	R_2	R_3	R_4	M.P. (°C)	Yield (%)
9a	H	Br	H	SCH_3	237-239	62.27
9b	H	F	H	SCH_3	287-290	66.11
9c	H	Cl	H	SCH_3	271-274	52.85
9d	H	N_2O	H	SCH_3	251-253	50.02
9e	H		H	SCH_3	280-281	61.98
9f	H	CH_3	H	SCH_3	267-269	63.79
9g			H	SCH_3	246-249	58.28
9i	H	OCH_3	H	SCH_3	249-250	67.49
9j	OCH_3	OCH_3	OCH_3	SCH_3	282-284	68.14
9k	OCH_3	OCH_3	OCH_3	SO_2CH_3	279-280	64.58
9a'	H	Br	H	S-Ethyl	222-228	61.78
9b'	H	F	H	S-Ethyl	262-	76.87

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

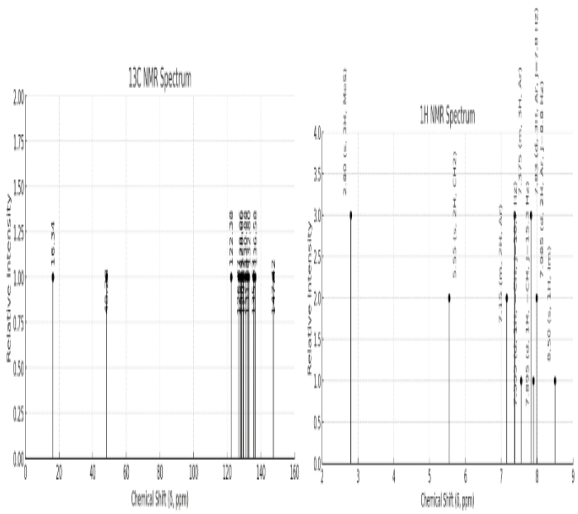
					265	
9c’	H	Cl	H	S-Ethyl	272-274	50.89
9e’	H		H	S-Ethyl	252-258	78.67
9g’			H	S-Ethyl	276-280	45.56
9h’	H		H	S-Ethyl	212-218	78.45
9i’	H	OCH_3	H	S-Ethyl	247-250	32.98
9j’	OCH_3	OCH_3	OCH_3	S-Ethyl	222-228	58.89

3.1 Synthesis (a)3-(1-benzyl-2-(methylthio or ethylthio)-1Himidazol-4-yl)-1-phenylpropan-1-one (9a-9j’)

A solution containing sodium hydroxide (2 moles/litre), consisting of 2 ml, was combined with either 1-benzyl-2-mercapto-1H-imidazole-5-carbaldehyde derivative 7a or 7b, with a quantity of 1.0 ml, in a solution of methanol with a volume of 5.0 ml. Subsequently, the appropriate acetophenone, specifically 8a-8j, with a quantity of 1 mmol, was added to the mixture. The resulting mixture was stirred at room temperature for a duration of 24 to 48 hours, with the progress of the reaction monitored using thin-layer chromatography (TLC). Following completion, 2 N hydrochloric acid was added until a solid was produced. After filtering and rinsing with cold ethanol, the raw material was refined by recrystallization in methanol.

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazole-4-yl)-1-(4-bromophenyl) prop-2-en-1-one (9a)**

Yield :62% melting point = 202–204 °C. The ^{1}H NMR 200 MHz DMSO-d6 (δ) in ppm: 2.80 (singlet, 3H, methylthio group), 5.55 (singlet, 2H, methylene group), 7.14–7.17 (multiplet, 2H, aromatic protons), 7.32–7.43 (multiplet, 3H, aromatic protons), 7.53–7.58 (doublet, 1H, vinyl proton, J = 18.7 Hz), 7.76–7.90 (doublet, 3H, 4-bromophenyl protons H4 and H6, J = 7.8 Hz), 7.87–7.92 (doublet, 1H, vinyl proton, J = 15.3 Hz), 7.97–8.00 (doublet, 2H, 4-bromophenyl protons H3 and H5, J = 8.8 Hz), 8.50 (singlet, 1H, imidazole proton). ^{13}C NMR spectra at 75 MHz in DMSO-d6 (δ) at 16.34, 48.23, 122.381, 126.87, 128.06, 128.55, 128.60, 129.52, 130.88, 131.88, 132.8, 135.63, 136.58, and 147.42. The LC-MS: m/z 414.2 (M + H) +.



Compound (9a)

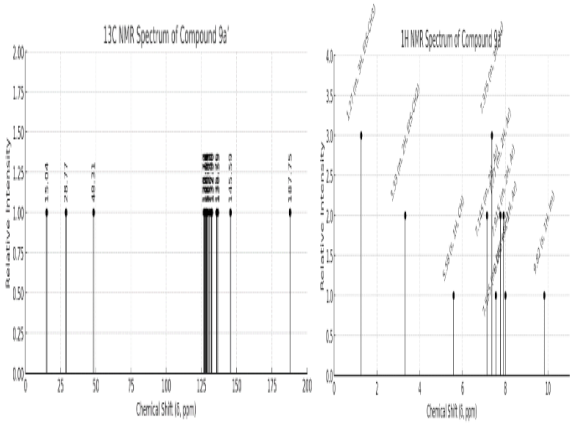
- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(4-bromophenyl) prop-2-en-1-one (9a’)**

Yield :74% melting point =154–156 ◦C. The ^{1}H NMR δ (ppm) 1.24–1.29, 3.29–3.36, 5.58, 7.13–7.16, 7.32–7.43, 7.53–7.58, 7.75–7.79, 7.89–7.94, 7.99–8.02, and 9.82. The ^{13}C NMR analysis δ (ppm) 15.04, 28.77, 48.31, 126.77, 127.19, 128.06, 128.51, 128.64, 129.49, 130.89, 132.00, 132.36, 135.76, 136.55, 145.59, and 187.75. The LC-MS :427.3 (M + H) +.

Journal of Chemical Health Risks

www.jchr.org

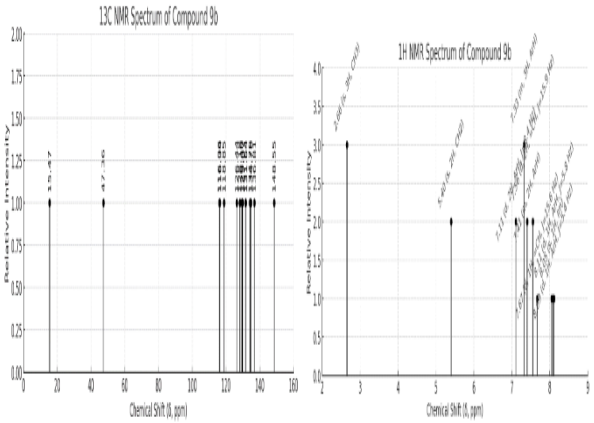
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727



Compound (9a')

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(4- fluorophenyl) prop-2-en-1-one (9b)**

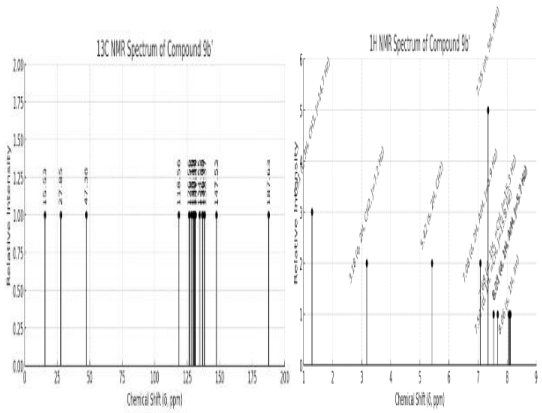
Yield: 42%, melting point =182 -184 °C. The ^{1}H NMR (300 MHz, DMSO-d6) at δ (ppm): 2.65-2.66 (singlet, 3H, CH3, J = 4.6 Hz), 5.40 (singlet, 2H, CH2), 7.09-7.12 (doublet, 2H, ArH, J = 8.4 Hz), 7.28-7.37 (multiplet, 3H, ArH), 7.39-7.42 (multiplet, 2H, ArH), 7.53-7.58 (doublet, 2H, HC = CH, J = 15.9Hz), 7.64-7.70 (doublet, 1H, HC = CH, J = 15.6 Hz), 8.05 (singlet, 1H, imidazole), 8.08-8.10 (doublet, 1H, ArH, J = 5.4 Hz), 8.10-8.12 (doublet, 1H, ArH, J = 5.8 Hz). ^{13}C NMR spectrum (80 MHz, DMSO-d6) displays signals at the following chemical shifts (δ in ppm): 15.47, 47.36, 116.06 (CF), 116.34 (CF), 118.85, 126.44, 128.18, 129.40, 129.87, 131.54, 131.64, 134.26, 134.78, 136.81, 148.55. Analysed by LC-MS (ESI), peaks observed at 353.4 (M + H) + and 375.5 (M + Na) +.



Compound (9b)

- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(4-fluorophenyl) prop-2-en-1-one (9b')**

Yield: 41%., Melting point =134-136°C. ^{1}H NMR spectrum (300 MHz-DMSO d6) at δ (ppm) 1.27-1.31 (triplet, 3H, CH_3, J = 14.7 Hz), 3.12-3.23 (quartet, 2H, CH_2, J = 7.2), 5.42 (singlet, 2H, CH_2), 7.07-7.09 (doublet, 2H, ArH, J = 6.9 Hz), 7.28-7.41 (multiplet, 5H, ArH), 7.51-7.56 (doublet, 1H, HC = CH, J = 15.8 Hz), 7.65-7.70 (doublet, 1H, HC = CH, J = 15.3 Hz), 8.06 (singlet, 1H, imidazole), 8.07-8.09 (doublet, 1H, ArH, J = 5.7 Hz), and 8.10-8.12 (doublet, 1H, ArH, J = 5.7 Hz). The compound's elemental analysis data was as follows: 15.53, 27.85, 47.38, 118.56, 126.56, 128.16, 129.39, 130.17, 130.58, 131.39, 134.55, 136.73, 136.90, 138.37, 147.53, and 187.63. LC-MS (ESI) analysis at 367.4 (M + H) +.

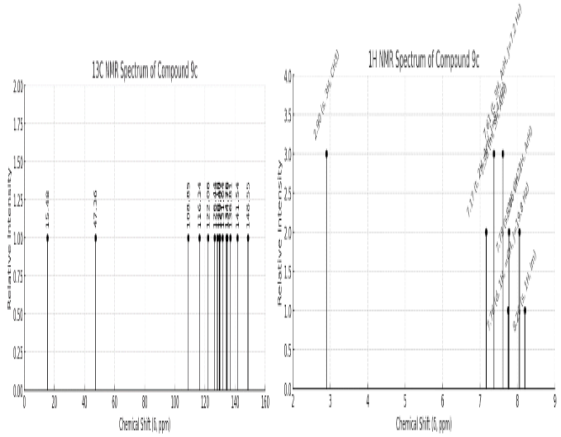


Compound (9b')

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(4- chlorophenyl) prop-2-en-1-one (9c)**

Yield: 59%, Melting point =183-185 °C. The ^{1}H NMR spectrum (250 MHz, DMSO-d6) displays peaks at δ (ppm): 2.90 (singlet, 3H, CH_3), 7.75-7.80 (singlet, 2H, CH_2), 7.14-7.19 (triplet, 2H, ArH), 7.29-7.46 (multiplet, 3H, ArH), 7.56-7.66 (triplet, 3H, ArH), 7.72-7.79 (doublet, 1H, HC = CH, J = 19.8 Hz), 8.03-8.08 (multiplet, 2H, ArH), and 8.20 (singlet, 1H, imidazole). The ^{13}C NMR spectrum (72 MHz, DMSO-d6) shows peaks at the following chemical shifts (δ in ppm): 15.48, 47.36, 122.06 (CF), 116.34 (CF), 108.85, 126.44, 128.18, 129.40, 129.87, 141.54, 131.64, 134.26, 134.78, 136.81, 148.55. The compound's LCMS (ESI) spectrum shows a peak at 374.4 (M + H) +.

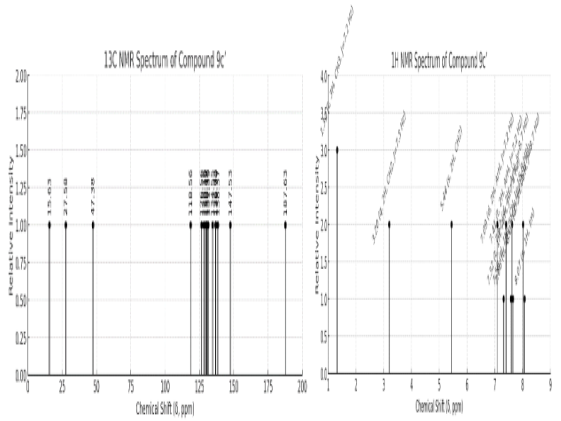
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727



Compound **(9c)**

- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(4-chlorophenyl) prop-2-en-1-one (9c')**

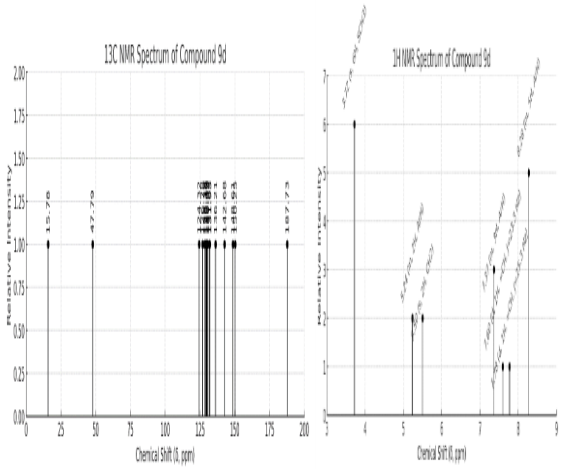
Yield :63%. Melting point =148-150 ◦C. ^{1}H NMR spectrum (300 MHz-DMSO d6) shows peaks at δ (ppm) 1.27-1.37 (t, 3H, CH_3, J = 7.2 Hz), 3.17-3.22 (q, 2H, CH_2, J = 7.3 Hz), 5.44 (s, 2H, CH_2), 7.06-7.12 (d, 2H, ArH, J = 7.2 Hz), 7.29-7.34 (t, 1H, ArH, J = 7.4 Hz), 7.38-7.43 (t, 2H, ArH, J = 7.2 Hz), 7.56-7.59 (d, 1H, HC = CH, J = 15.8 Hz), 7.60-7.64 (d, 2H, ArH, J = 8.7 Hz), 7.63-7.68 (d, 1H, HC = CH, J = 15.6 Hz), 8.00-8.03 (d, 2H, ArH, J = 8.7 Hz), and 8.07 (s, 1H, imidazole). The ^{13}C NMR spectrum (75 MHz-DMSO d6) shows peaks at δ (ppm) 15.63, 27.58, 47.38, 118.56, 126.56, 128.16, 129.30, 130.17, 130.58, 131.39, 134.55, 136.73, 136.90, 138.37, 147.53, and 187.63, m/z 383.4 (M + H) + in the LC-MS (ESI) analysis.



Compound (9c')

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(4- nitrophenyl) prop-2-en-1-one (9d)**

Yield : 12%; Melting point = 166–169 ◦C; ^{1}H NMR (300 MHz-DMSO d6): The chemical shifts (δ) in parts per million (ppm) are as follows: 3.72 (singlet, 6H, SCH_3), 5.50 (singlet, 2H, CH_2), 5.17–5.30 (multiplet, 2H, ArH), 7.30–7.43 (multiplet, 3H, ArH), 7.57–7.62 (doublet, 1H, CH = CH, J = 23.3 Hz), 7.77–7.78 (doublet, 1H, CH = CH, J = 15.3 Hz), 8.21–8.34 (multiplet, 5H, ArH). ^{13}C NMR (75 MHz DMSO d6): The chemical shifts (δ) in parts per million (ppm) are as follows: 15.78, 47.79, 129.14, 124.32, 126.78, 128.38, 129.47, 130.09, 130.35, 131.63, 131.95, 136.21, 142.68, 148.61, 150.25, 187.73. LC-MS (ESI): (M + H) + ratio of 380.4.

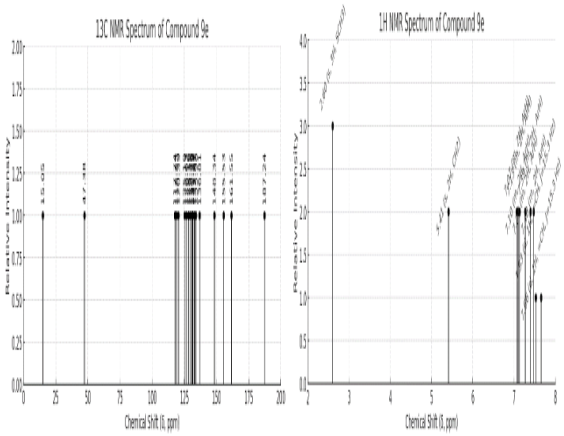


Compound (9d)

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(4- phenoxy phenyl) prop-2-en-1-one (9e)**

Yield: 46%; Melting point = 144–146 oC ; ^{1}H NMR spectrum (200 MHz-DMSO d6) as shown in Figure 2: δ (ppm) 2.60 (singlet, 3H, SCH_3), 5.41 (singlet, 2H, CH_2), 7.05–7.08 (multiplet, 2H, ArH), 7.08–7.11 (multiplet, 2H, ArH), 7.11–7.15 (multiplet, 2H, ArH), 7.23–7.31 (multiplet, 2H, ArH), 7.37–7.42 (multiplet, 2H, ArH), 7.44–7.51 (multiplet, 2H ArH), 7.51–7.54 (doublet, 1H, CH = CH, J = 15.3 Hz), 7.63–7.68 (doublet, 1H, CH = CH, J = 15.3 Hz);^{13}C NMR spectrum (75 MHz-DMSO d6): δ (ppm) 15.05, 47.38, 117.74, 118.83, 120.39, 125.19, 126.63, 128.16, 129.38, 130.79, 131.25, 131.58, 132.91, 133.98, 136.81, 148.34, 155.53, 161.55, 187.24; LC-MS (ESI): 427.3 (M + Na)+.

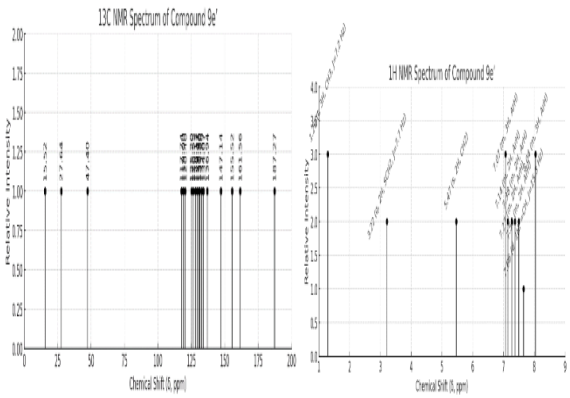
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727



Compound (9e)

- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(4- phenoxy phenyl) prop-2-en-1-one (9e')**

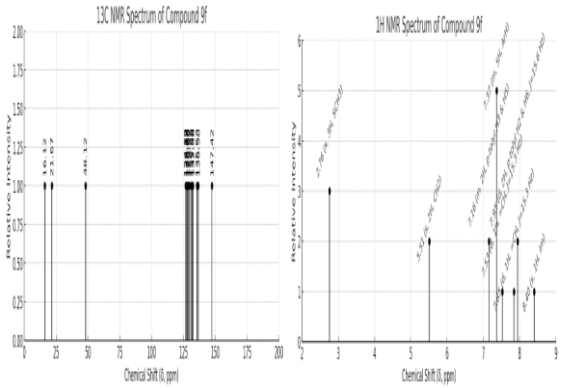
Yield:41%. The melting point =129 -132°C. ^{1}H NMR spectrum (300 MHz, DMSO-d6) displays increases at δ 1.27-1.31 (triplet, 3H, CH_3, J = 7.2 Hz), 3.16-3.27 (quartet, 2H, SCH_2, J = 7.7 Hz), 5.47 (singlet, 2H, CH_2), 7.05-7.09 (multiplet, 3H, ArH), 7.13-7.15 (multiplet, 2H, ArH), 7.23-7.31 (multiplet, 2H, ArH), 7.35-7.40 (multiplet, 2H, ArH), 7.45-7.55 (multiplet, 2H, ArH), 7.63-7.68 (doublet, 1H, CH = CH, J = 15.3 Hz), and 8.03-8.05 (multiplet, 3H, ArH). ^{13}C NMR spectra (75 MHz, DMSO-d6) display peaks at δ 15.52, 27.64, 47.40, 117.74, 119.00, 120.40, 125.20, 126.55, 128.13, 129.37, 129.41, 130.80, 131.26, 132.89, 134.07, 136.94, 147.14, 155.52, 161.56, and 187.27. The compound's molecular weight was found to be 441.6 (M + 1) + and 463.3 (M + Na) + using LC-MS (ESI).



Compound (9e')

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(p-tolyl) prop2-en-1-one (9f)**

Yield: 81%; Melting point =116–124 ◦C; ^{1}H NMR spectrum (300 MHz, DMSO-d6) displays increases at δ 2.39-2.76 (triplet, 3H, SCH3, J = 7.2 Hz), 3.16-3.27 (quartet, 2H, SCH_2, J = 7.7 Hz), 5.51 (singlet, 2H, CH_2), 7.14-7.17 (multiplet, 3H, ArH), 7.13-7.15 (multiplet, 2H, ArH), 7.30-7.43 (multiplet, 2H, ArH), 7.35-7.40 (multiplet, 2H, ArH), 7.45-7.55 (multiplet, 2H, ArH), 7.50-7.55 (doublet, 1H, CH = CH, J = 15.3 Hz), and 7.93-7.96 (multiplet, 2H, ArH). ^{13}C NMR spectra (15.6 MHz, DMSO-d6) display peaks at δ16.12, 21.67, 48.12, 126.79, 126.87, 127.13, 128.06, 128.55, 128.60, 129.52, 130.88, 131.88, 132.38, 135.63, 136.58, and 147.42 ppm. The compound's molecular weight was found to be 349.4 m/z (M +H) + using LC-MS (ESI).

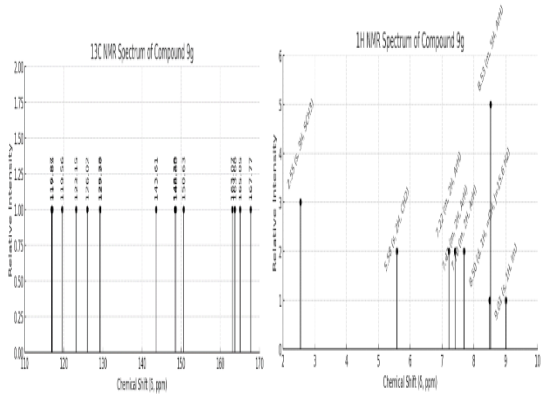


Compound (9f)

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(naphthalen2-yl) prop-2-en-1-one (9g)**

Yield: 60%, Melting point range = 216-218 oC. ^{1}H NMR spectrum was 500 MHz in DMSO d6. Chemical shifts: 2.55 (singlet, 3H, SCH_3), 5.58 (singlet, 2H, CH_2), 7.19–7.24 (multiplet, 2H, ArH), 7.34–7.48 (multiplet, 2H, ArH), 8.50 (doublet, 1H, CH = CH, J = 15.6 Hz), 7.66–7.73 (multiplet, 2H, ArH), 8.53 (multiplet, 5H, ArH), and 9.01 (singlet, 1H, imidazole). The ^{13}C NMR spectrum (126 MHz-DMSO d6) shows chemical shifts (δ) in parts per million (ppm) at the following values: 116.87, 117.05, 119.56, 123.15, 126.02, 129.23, 129.30, 143.61, 148.39, 148.60, 150.63, 163.07, 163.68, 165.05, 167.77 as observed in Figure. The compound's molecular weight was found to be 385.5 m/z (M +H) + using LC-MS (ESI).

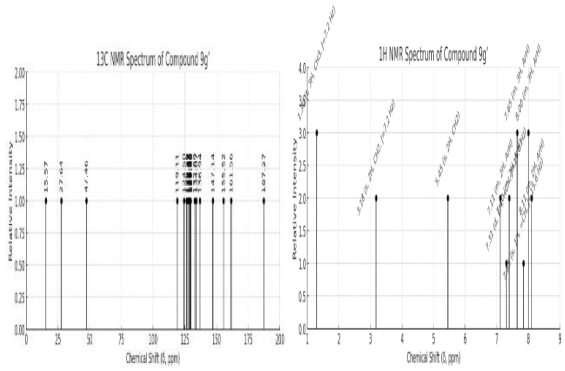
Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727



Compound (9g)

- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(naphthalen-2- yl) prop-2-en-1-one (9g')**

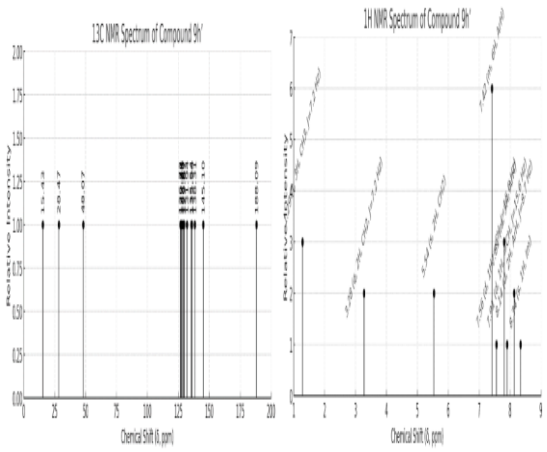
Yield :57%, Melting point (MP) = 103 -105 oC , ^{1}H NMR (DMSO d6 at 300 MHz): The following are the chemical shifts (δ) expressed in parts per million (ppm): 1.28–1.32 (triplet, 3H, methyl group, J = 7.2 Hz), 3.14–3.22 (singlet, 2H, methylene group, J = 7.2 Hz), 5.45 (singlet, 2H, methylene group), 7.10–7.12 (multiplet, 2H, aromatic protons), 7.28–7.33 (doublet, 1H, CH = CH, J = 15.6 Hz), 7.37–7.42 (multiplet, 2H, aromatic protons), 7.60–7.70 (multiplet, 3H, aromatic protons), 7.82–7.87 (singlet, 1H, CH = CH, J = 15.6 Hz), 7.94–8.06 (multiplet, 3H, aromatic protons), 8.099–8.12 (multiplet, 2H, aromatic protons). ^{13}C NMR (75 MHz-DMSO d6): The following were the chemical shifts (δ) expressed in parts per million (ppm): The following numbers were 15.57, 27.64, 47.46, 119.115, 124.50, 126.56, 127.42, 128.17, 128.88, 129.05, 129.40, 129.65 as shown in Figure.



Compound (9g')

- **(E)-1-([1,1′-biphenyl]-4-yl)-3-(1-benzyl-2-(ethylthio)-1Himidazol-4-yl) prop-2-en-1-one (9h')**

Yield :55%; Melting point = 196–201 ◦C; ^{1}H NMR (200 MHz-DMSO d6): δ (ppm)1.26–1.31 (triplet, 3 hydrogen atoms, methyl group, J = 7.2 Hz), 3.24–3.31 (quartet, 2 hydrogen atoms, methylene group, J = 7.2 Hz), 5.54 (singlet, 2 hydrogen atoms, methylene group), 7.32–7.51 (multiplet, 6 hydrogen atoms, aromatic ring), 7.52–7.60 (doublet, 1 hydrogen atom, CH = CH group, J = 15.6 Hz), 7.732–7.88 (multiplet, 3 hydrogen atoms, aromatic ring), 7.88–7.93 (doublet, 1 hydrogen atom, CH = CH group, J = 15.6 Hz), 8.12–8.152 (doublet, 2 hydrogen atoms, J = 8.7 Hz), 8.262–8.42 (singlet, 1 hydrogen atom, imidazole); ^{13}C NMR(75 MHz-DMSO d6): δ (ppm), 15.43, 28.47, 48.07, 126.72, 127.33, 127.45, 127.512, 128.42, 128.49, 129.37, 129.47, 129.572, 129.619, 131.944, 135.944, 135.54, 138.311, 145.103, 188.09; LC-MS (ESI): 425.3 (M + H)+[37].



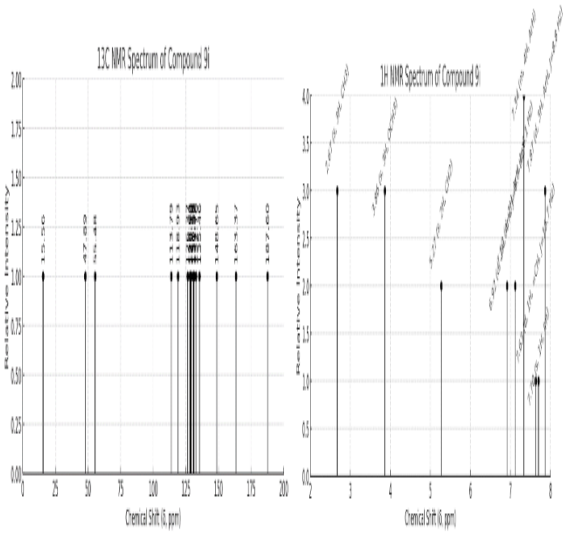
Compound (9h')

- **(E)-3-(1-benzyl-2-(methylthio)-1H-imidazol-4-yl)-1-(4- methoxyphenyl) prop-2-en-1-one (9i)**

Yield :78%; Melting point = 150–157 ◦C; ^{1}H NMR spectrum (300 MHz-DMSO d6) shows peaks at the following chemical shifts: 2.67 ppm (singlet, 3H, CH3), 3.86 ppm (singlet, 3H, OCH_3), 5.27 ppm (singlet, 2H, CH_2), 6.90–6.93 ppm (doublet, 2H, ArH, J = 8.7 Hz), 7.11–7.13 ppm (doublet, 2H, ArH, J = 6.10 Hz), 7.27–7.40 ppm (multiplet, 4H, ArH), 7.58–7.68 ppm (doublet, 1H, HC = CH, J = 15.7 Hz), 7.70 ppm (singlet, 1H, imidazole), 7.85–7.88 ppm (doublet, 3H, ArH, J = 8.8 Hz). ^{13}C NMR spectrum (75 MHz, $CDCl_3$) shows peaks

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

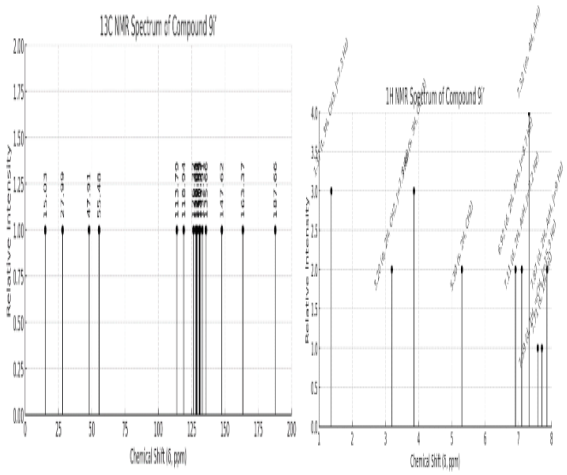
at the following chemical shifts: 15.56, 47.89, 55.48, 113.79, 118.93, 126.37, 128.08, 128.54, 129.10, 130.59, 130.92, 131.39, 132.70, 135.46, 148.65, 163.37, 187.60 ppm. The LC-MS (ESI) analysis shows: 365.4 (M + H) + and 389.4 (M + Na) +.



Compound (9i)

- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(4- methoxyphenyl) prop-2-en-1-one (9i')**

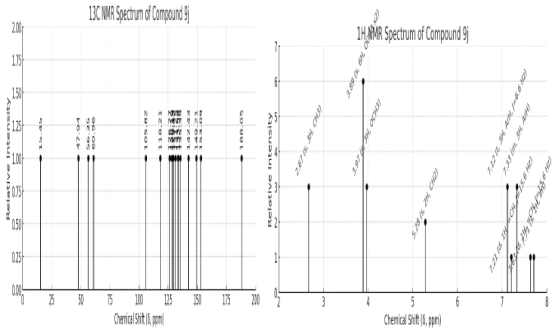
Yield: 78%. Melting point = 143-145 oCelsius. ^{1}H NMR spectrum (measured at 300 MHz using DMSO-d6 as the solvent) shows peaks at chemical shifts (δ) of 1.35-1.39 (triplet, 3 hydrogen atoms, methyl group, coupling constant J = 7.3 Hz), 3.16-3.23 (quartet, 2 hydrogen atoms, methylene group, J = 7.3 Hz), 3.86 (singlet, 3 hydrogen atoms, methoxy group), 5.30 (singlet, 2 hydrogen atoms, methylene group), 6.90-6.93 (doublet, 2 hydrogen atoms, aromatic protons, J = 8.7 Hz), 7.09-7.12 (doublet, 2 hydrogen atoms, aromatic protons, J = 7.2 Hz), 7.26-7.38 (multiplet, 4 hydrogen atoms, aromatic protons), 7.56-7.61 (doublet, 1 hydrogen atom, vinyl proton, J = 15.3 Hz), 7.71 (singlet, 1 hydrogen atom, imidazole), and 7.85-7.88 (doublet, 2 hydrogen atoms, aromatic protons, J = 9 Hz). The ^{13}C NMR spectrum (measured at 75 MHz using $CDCl_3$ as the solvent) shows peaks at chemical shifts (δ) of 15.03, 27.99, 47.91, 55.48, 113.79, 118.94, 126.32, 128.02, 128.68, 129.07, 130.59, 130.93, 131.22, 132.91, 135.66, 147.62, 163.37, and 187.66. A molecular ion peak of 379.4 (M + H) + in the LC-MS (ESI) analysis.



Compound (9i')

- **(E)-3-(1-benzyl-2-(methyl thio)-1H-imidazol-4-yl)-1-(3,4,5- trimethoxy phenyl) prop-2-en-1-one (9j)**

Yield ;86% ,Melting point =171–177 °C. ^{1}H NMR spectrum (400 MHz, DMSO-d6), peaks are seen at the specified chemical shifts: 2.67 ppm (singlet, 3H, CH3), 3.89 ppm (singlet, 6H, OCH3), 3.97 ppm (singlet, 3H, OCH_3), 5.28 ppm (singlet, 2H, CH_2), 7.11–7.13 ppm (triplet, 3H, ArH, J = 6.6 Hz), 7.18–7.23 ppm (doublet, 1H, HC = CH, J = 15.6 Hz), 7.28–7.38 ppm (multiplet, 3H, ArH), 7.60–7.66 ppm (doublet, 1H, HC = CH, J = 15.6 Hz), and 7.71 ppm (singlet, 1H, imidazole). The ^{13}C NMR spectrum (80 MHz, CDCl3) shows peaks at chemical shifts of 15.45, 47.94, 56.35, 60.96, 105.82, 118.21, 126.27, 128.10, 129.13, 129.43, 131.25, 133.36, 133.57, 135.39, 142.43, 149.21, 153.09, and 188.05 ppm. LC-MS (ESI) analysis m/z 425.4 (M + H) + and 447.4 (M + Na) +.

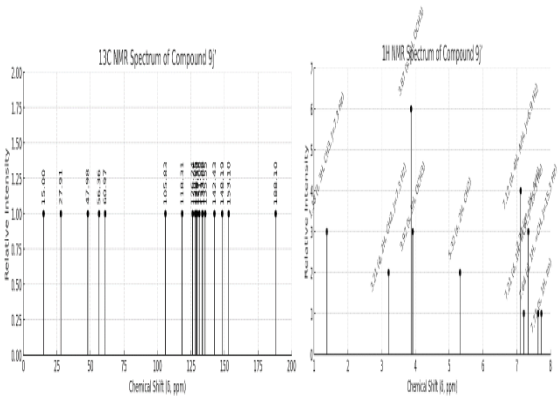


Compound (9j)

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

- **(E)-3-(1-benzyl-2-(ethylthio)-1H-imidazol-4-yl)-1-(3,4,5- trimethoxy phenyl) prop-2-en-1-one (9j')**

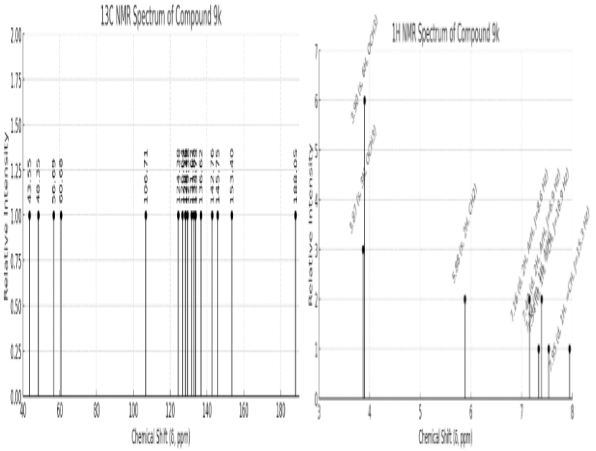
Yield :61%, Melting point range =72-94 ◦C. The ^{1}H NMR spectrum (300 MHz-DMSO d6) shows peaks at δ (ppm) 1.35-1.40 (t, 3H, CH_3, J = 7.3 Hz), 3.17-3.24 (q, 2H, CH_2, J = 7.3 Hz), 3.87 (s, 6H, OCH_3), 3.92 (s, 3H, OCH_3), 5.32 (s, 2H, CH_2), 7.10-7.13 (d, 4H, ArH, J = 6.9 Hz), 7.18-7.24 (d, 1H, HC = CH, J = 15.3 Hz), 7.29-7.39 (m, 3H, ArH), 7.61-7.66 (d, 1H, HC = CH, J = 15.3 Hz), and 7.73 (s, 1H, imidazole). ^{13}C NMR spectrum (75 MHz, CDCl3) shows peaks at δ (ppm) 15.00, 27.91, 47.98, 56.36, 60.97, 105.83, 118.31, 126.24, 128.05, 129.10, 129.52, 131.08, 133.36, 133.62, 135.55, 142.43, 148.19, 153.10, and 188.10. Molecular ion peak at 439.5 (M + H) + in the LC-MS (ESI) analysis.



Compound (9j')

- **(E)-methyl 1-benzyl-5-(3-oxo-3-(3,4,5-tri methoxyphenyl) prop-1-en-1-yl)-1H-imidazole-2-sulfinate (9k)**

Yield 87%; Melting point = 169–177 ◦C; ^{1}H NMR spectrum (300 MHz-DMSO d6) shows peaks at the following chemical shifts: 3.87 ppm (singlet, 3H, OCH3), 3.90 ppm (singlet, 6H, OCH_3), 5.88 ppm (singlet, 2H, CH_2), 7.11–7.20 ppm (doublet, 2H, ArH, J = 8.6 Hz), 7.30–7.37 ppm (multiplet, 1H, ArH), 7.38–7.41 ppm (doublet, 2H, ArH, J = 6.9 Hz), 7.38–7.43 ppm (multiplet, 2H, ArH), 7.51–7.56 ppm (doublet, 1H, HC = CH, J = 18.9 Hz), and 7.92–7.97 ppm (doublet, 1H, HC = CH, J = 15.3 Hz). ^{13}C NMR spectrum (75 MHz-DMSO d6) shows peaks at the following chemical shifts: 43.55 ppm, 48.35 ppm, 56.69 ppm, 60.68 ppm, 106.71 ppm, 124.38 ppm, 126.64 ppm, 128.16 ppm, 128.35 ppm, 129.38 ppm, 131.62 ppm, 132.83 ppm, 133.75 ppm, 136.62 ppm, 142.76 ppm, 145.75 ppm, and 153.40 ppm. The LC-MS (ESI) analysis shows m/z 457.5 (M + H) + and m/z 479.4 (M + Na) +.



Compound (9k)

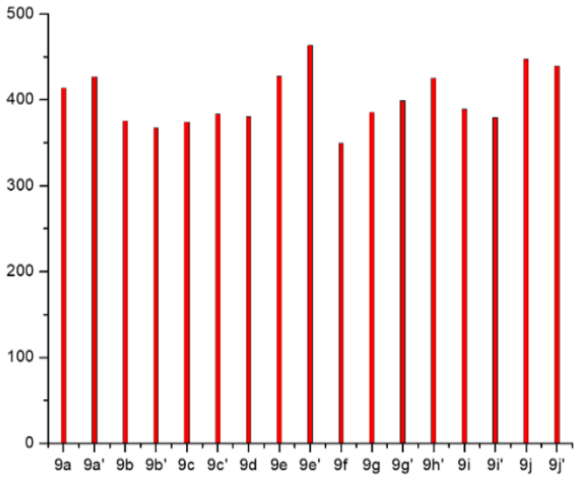


Figure 2: Mass Spectrometry of Synthesized compounds

3.2 Biological Evaluation

The compounds (9a–9j') tested against a range of microorganisms for their antifungal and antibacterial

qualities. The MTT colorimetric assay yielded the MICs, which at a rate of 66.11% provided insightful information about the compounds' potential as antibacterial agents.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

- **Antibacterial Assessment**

The antibacterial evaluation involved prominent bacterial strains, including S. aureus, B. cereus, E. coli, and P. aeruginosa. The components were examined at a 50 µg/mL concentration in DMSO, and their inhibitory effects were assessed in Mueller-Hinton (MH) medium. Visual analysis was used to establish the minimum concentration (MIC) at which microbial growth was suppressed [38,39]. The results were summarized in Table 3 below:

Table 3: Antibacterial activity of synthesized compounds (9a-9j')

Compounds	*S. aureus*	*B. cereus*	*E. coli*	*P. aeruginosa*
9a	**250**	**200**	**200**	**250**
9b	**250**	**125**	**62.5**	**250**
9c	**250**	**250**	**200**	**250**
9d	**250**	**100**	**100**	**125**
9e	**125**	**50**	**50**	**125**
9f	**125**	**50**	**62**	**100**
9g	**100**	**70**	**56**	**200**
9i	**200**	**50**	**250**	**200**
9j	**100**	**200**	**100**	**100**
9k	**250**	**150**	**62.5**	**250**
9a'	**200**	**160**	**100**	**50**
9b'	**50**	**100**	**50**	**50**
9c'	**10**	**60**	**10**	**160**
9e'	**50**	**100**	**25**	**140**
9g'	**135**	**200**	**100**	**250**
9h'	**150**	**250**	**200**	**210**
9i'	**200**	**170**	**100**	**230**
9j'	**140**	**180**	**250**	**200**

The synthetic compounds, 9a–9j, demonstrated antibacterial activity against a range of bacterial strains, including S. aureus, B. cereus, E. coli, and P. aeruginosa. The Minimum Inhibitory Concentrations (MIC), expressed in micrograms per millilitre (µg/mL), were established for each compound against each species of bacteria.

Among the compounds, 9b exhibited noteworthy antibacterial efficacy, particularly standing out against B. cereus and E. coli, with MIC values of 125 µg/mL and 62.5 µg/mL, respectively as shown in Figure 5. Similarly, compound 9e demonstrated significant activity against all bacterial strains tested, with MIC values ranging from 50 µg/mL to 125 µg/mL.

Compound 9c consistently displayed inhibitory effects against S. aureus, B. cereus, and P. aeruginosa, with MIC values of 250 µg/mL across all strains as shown in the figure below. Compounds 9g and 9j' showcased varied activity against different bacterial strains, hinting at potential selectivity. Notably, 9g exhibited a lower MIC against E. coli (56 µg/mL) compared to other strains, while 9j' demonstrated higher potency against P. aeruginosa with an MIC of 250 µg/mL. Compound 9c' demonstrated low MIC values across all bacterial strains, indicating broad-spectrum antibacterial activity. Conversely, 9h' exhibited high MIC values, suggesting lower efficacy against the tested bacterial strains as represented in Figure 6. Overall, the synthesised compounds exhibited varied antibacterial properties, with some demonstrating potential effectiveness against certain bacterial strains. The findings provide useful insights into the possible uses of these compounds as antibacterial agents, indicating the necessity for additional research and advancement.

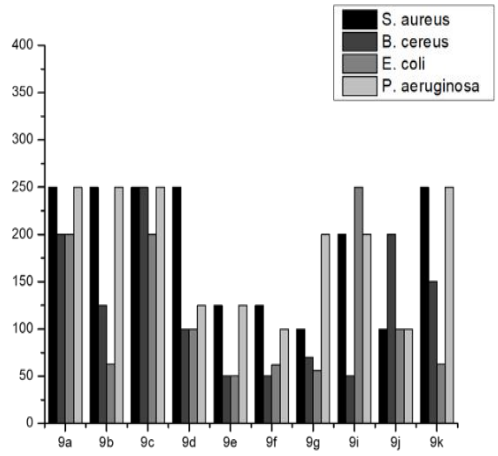


Figure 3: Antibacterial Assessment for compounds (9a-9k)

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

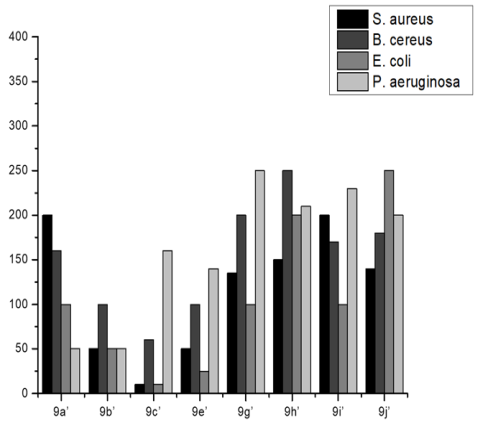


Figure 4: Antibacterial Assessment for compounds (9a'-9j')

- **Antifungal Assessment**

For antifungal evaluation, A. niger and A. fumigatus were cultured in the RPMI-1640 medium. Similarly, compounds were added at a concentration of 50 µg/mL, and MIC values were determined. The results were presented in Table 4.

Table 4: Antifungal activity of synthesized compounds (9a-9j')

Compounds	*A. niger*	*A. fumigatus*
9a	500	400
9b	100	600
9c	500	200
9d	800	300
9e	200	600
9f	200	800
9g	500	800
9i	600	300
9j	250	700
9k	250	900
9a'	400	1000
9b'	300	500
9c'	300	600
9e'	900	400
9g'	300	200
9h'	400	800
9i'	500	600
9j'	700	300

The antifungal activity of the synthesized compounds (9a-9j') against two fungal strains, A. niger and A. fumigatus with the Minimum Inhibitory Concentrations (MIC) in micrograms per millilitre (µg/mL) were determined for each compound against each fungal species. Compound 9b displayed notable antifungal efficacy, particularly against A. niger with a MIC value of 100 µg/mL, and A. fumigatus with an MIC of 600 µg/mL. Compound 9e also demonstrated noteworthy efficacy against both fungal strains, showing MIC values of 200 µg/mL against A. niger and 600 µg/mL against A. fumigatus Compound 9d demonstrated higher MIC values, indicating lower antifungal efficacy against A. niger (800 µg/mL) and A. fumigatus (300 µg/mL). On the other hand, compounds 9f, 9k, 9a', 9c', 9e', 9g', 9h', 9i', and 9j' exhibited varying degrees of antifungal activity against both fungal strains. Compounds 9c and 9g demonstrated consistent inhibitory effects against A. niger (500 µg/mL) and A. fumigatus (200 µg/mL) and (800 µg/mL), respectively. Compound 9j' showed selective activity with a lower MIC against A. niger (700 µg/mL) compared to A. fumigatus (300 µg/mL). Conversely, compounds 9a', 9b', and 9i' displayed distinct antifungal efficacy against A. fumigatus with MIC values of 1000 µg/mL, 500 µg/mL, and 600 µg/mL, respectively.

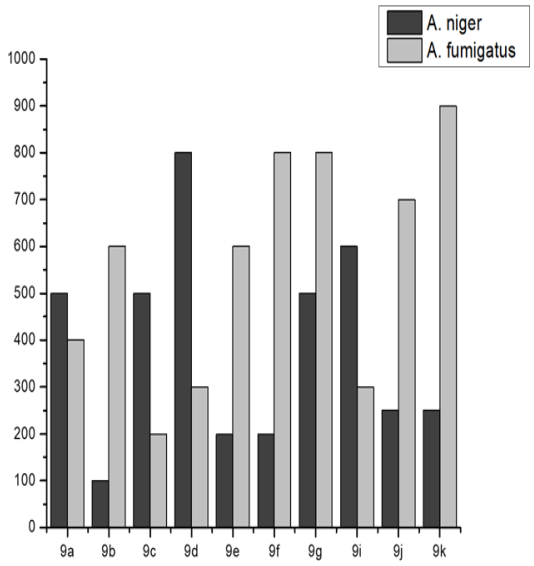


Figure 5: Antifungal Assessment for compounds (9a-9k)

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

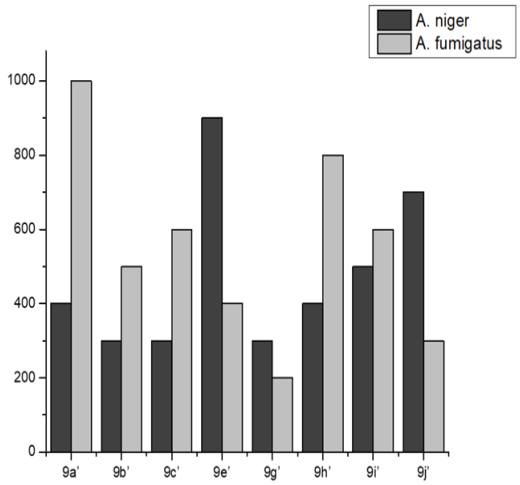


Figure 6: Antifungal Assessment for compounds (9a'-9j')

4. Discussion

4.1 Synthesis of Imidazole-based chalcone derivatives

The synthesis of imidazole-based chalcone derivatives involved a multi-step approach, resulting in well-defined compounds. Characterization using Nuclear Magnetic Resonance (NMR) spectroscopy and mass spectrometry validated their chemical structures, aligning with similar methodologies employed in previous studies [40-45].

Comparing these findings with existing research, the methodology employed shared similarities with other studies exploring chalcone derivatives. Tran et al., (2012), Modzelewska et al., (2006), Baviskar et al., (2009), and Vogel et al., (2010) used a multi-step synthesis method that included Claisen-Schmidt condensation. They then analysed the chalcone derivatives using NMR and mass spectrometry for investigation. This convergence in synthetic strategies reinforces the reliability and reproducibility of the presented work [46-49]. Furthermore, Jaisiewicz et al., (2023); and Dorababu et al., (2020) utilized new bioactive compounds, a methodology based on combining two molecules with biological properties into a new hybrid molecule used to design and synthesize a series of ten indole derivatives bearing imidazole, benzothiazole-2-thione, or benzoxazole-2-thione moieties at the C-3 position [50,51]. The oxidation step using Oxone to obtain the oxidized methyl sulfonyl molecule 9k adds a distinctive element to the synthesis, contributing to the structural diversity of the final compounds. This methodology aligns with Liu et al., (2013) work on incorporating oxidation steps to enhance the chemical diversity of chalcone derivatives, indicating a shared focus on structural intricacies [52].

The verification of the synthesized compounds' structural properties through nuclear magnetic resonance (^{1}H NMR, ^{13}C NMR) and mass spectrometry studies was a crucial aspect, ensuring the reliability of the results. Similar verification protocols are echoed in studies by Oskuei et al., (2021) [53] and Sangeetha et al., (2021), underlining the importance of robust characterization techniques for novel compounds [54].

Overall, the synthesis process showcased a detailed and well-supported methodology, incorporating innovative elements like oxidation stages and thorough structural verification, paving the way for potential applications in medicinal chemistry.

4.2 Antimicrobial Study

The antimicrobial evaluation of the synthesized compounds against bacterial and fungal strains provided valuable insights into their potential applications. The selective antibacterial efficacy of compound 9b against B. cereus and E. coli, as well as the broad-spectrum antibacterial activity of compound 9c, aligns with similar observations in studies by Osmaniye et al., (2018) and Tratrat et al., (2019) [55,56]. These consistent findings contribute to establishing a robust foundation for the antibacterial potential of imidazole-based chalcone derivatives.

Moreover, the antifungal assessment reveals promising results, with compounds 9b and 9e demonstrating notable efficacy against A. niger and A. fumigatus. This aligns with the work of Tank et al., (2022); Abonia et al., (2012); Pankaj et al., (2020), who also reported significant antifungal activity in chalcone derivatives against A. niger [57-59] Additionally, the selectivity observed in compound 9j' mirrors findings in Sattu et al., (2018), suggesting a nuanced impact on different fungal strains [60].

The reliability of antimicrobial outcomes, in comparison to comparable studies, underscores the potential of these compounds in combating bacterial and fungal diseases,

laying the groundwork for the development of innovative antibacterial medications.

5. Conclusion

In conclusion, the synthesis and characterization of imidazole-based chalcone derivatives, coupled with their comprehensive antimicrobial evaluation, offer a promising avenue for the development of potential therapeutic agents. The methodological alignment with comparable studies and the consistent observations in antibacterial and antifungal activities contribute to the robustness and reliability of the presented research. The structural diversity achieved through oxidation steps adds an innovative dimension to the synthesis. These findings underscore the potential of imidazole-based chalcone derivatives as effective agents against bacterial and fungal infections. Future research endeavours can leverage these insights to further optimize and advance the development of novel antimicrobial drugs.

References

1. Hughes RA, Thompson SP, Alcaraz L, Moody CJ. Total synthesis of the thiopeptide antibiotic amythiamicin D. Journal of the American Chemical Society. 2005 Nov 9;127(44):15644-51.
2. Glover C, Merritt EA, Bagley MC. Synthesis of saramycetic acid. Tetrahedron Letters. 2007 Sep 24;48(39):7027-30.
3. Musiol R, Kowalczyk W. Azole antimycotics-a highway to new drugs or a dead end?. Current medicinal chemistry. 2012 Mar 1;19(9):1378-88.
4. Amin A, Qadir T, Sharma PK, Jeelani I, Abe H. A Review on The Medicinal And Industrial Applications of N-Containing Heterocycles. The Open Medicinal Chemistry Journal. 2022 Nov 16;16(1).
5. Sinha SK, Ghosh P, Jain S, Maiti S, Al-Thabati SA, Alshehri AA, Mokhtar M, Maiti D. Transition-metal catalyzed C–H activation as a means of synthesizing complex natural products. Chemical Society Reviews. 2023;52(21):7461-503.
6. Zhang HZ, Gan LL, Wang H, Zhou CH. New progress in azole compounds as antimicrobial agents. Mini reviews in medicinal chemistry. 2017 Jan 1;17(2):122-66.
7. Zhang L, Peng XM, Damu GL, Geng RX, Zhou CH. Comprehensive review in current developments of imidazole-based medicinal chemistry. Medicinal research reviews. 2014 Mar;34(2):340-437.
8. Gujjarappa R, Sravani S, Kabi AK, Garg A, Vodnala N, Tyagi U, Kaldhi D, Singh V, Gupta S, Malakar CC. An overview on biological activities of oxazole, isoxazoles and 1, 2, 4-oxadiazoles derivatives. Nanostructured Biomaterials: Basic Structures and Applications. 2022 Mar 8:379-400.
9. Salerno L, Floresta G, Ciaffaglione V, Gentile D, Margani F, Turnaturi R, Rescifina A, Pittalà V. Progress in the development of selective heme oxygenase-1 inhibitors and their potential therapeutic application. European Journal of Medicinal Chemistry. 2019 Apr 1; 167:439-53.
10. Chugh A, Kumar A, Verma A, Kumar S, Kumar P. A review of antimalarial activity of two or three nitrogen atoms containing heterocyclic compounds. Medicinal Chemistry Research. 2020 Oct; 29:1723-50.
11. Tratrat C. 1, 2, 4-Triazole: A privileged scaffold for the development of potent antifungal agents-a brief review. Current Topics in Medicinal Chemistry. 2020 Sep 1;20(24):2235-58.
12. Kharb R, Shahar Yar M, C Sharma P. New insights into chemistry and anti-infective potential of triazole scaffold. Current medicinal chemistry. 2011 Jul 1;18(21):3265-97.
13. Arshad MF, Alam A, Alshammari AA, Alhazza MB, Alzimam IM, Alam MA, Mustafa G, Ansari MS, Alotaibi AM, Alotaibi AA, Kumar S. Thiazole: A versatile standalone moiety contributing to the development of various drugs and biologically active agents. Molecules. 2022 Jun 21;27(13):3994.
14. Peng XM, Cai GX, Zhou CH. Recent developments in azole compounds as antibacterial and antifungal agents. Current topics in medicinal chemistry. 2013 Aug 1;13(16):1963-2010.
15. Dwivedi AR, Kumar R, Kumar V. Recent synthetic strategies for monocyclic azole nucleus and its role in drug discovery and development. Current Organic Synthesis. 2018 May 1;15(3):321-40.
16. Malik P, Chaudhry N, S Kitawat B, Kumar R, K Mukherjee T. Relationship of azole resistance with the structural alteration of the target sites: Novel synthetic compounds for better antifungal activities. The Natural Products Journal. 2014 Jun 1;4(2):131-9.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

17. Bossche HV, Marichal P, Gorrens J, Coene MC, Willemsens G, Bellens D, Roels I, Moereels H, Janssen PA. Biochemical approaches to selective antifungal activity. Focus on azole antifungals. Mycoses. 1989 Nov; 32:35-52.
18. Scalese G, Mosquillo MF, Pérez-Díaz L, Gambino D. Biosynthesis of ergosterol as a relevant molecular target of metal-based antiparasitic and antifungal compounds. Coordination Chemistry Reviews. 2024 Mar 15; 503:215608.
19. Hlavica P. Evaluation of structural features in fungal cytochromes P450 predicted to rule catalytic diversification. Biochimica et Biophysica Acta (BBA)-Proteins and Proteomics. 2013 Jan 1;1834(1):205-20.
20. Hu F, Zhang L, Nandakumar KS, Cheng K. Imidazole scaffold-based compounds in the development of therapeutic drugs. Current Topics in Medicinal Chemistry. 2021 Nov 1;21(28):2514-28.
21. Teli G, Chawla PA. Hybridization of imidazole with various heterocycles in targeting cancer: a decade's work. ChemistrySelect. 2021 May 20;6(19):4803-36.
22. Rulhania S, Kumar S, Nehra B, Gupta GD, Monga V. An insight into the medicinal perspective of synthetic analogs of imidazole. Journal of molecular structure. 2021 May 15; 1232:129982.
23. Constantinescu T, Lungu CN. Anticancer activity of natural and synthetic chalcones. International journal of molecular sciences. 2021 Oct 20;22(21):11306.
24. Marotta L, Rossi S, Ibba R, Brogi S, Calderone V, Butini S, Campiani G, Gemma S. The green chemistry of chalcones: Valuable sources of privileged core structures for drug discovery. Frontiers in Chemistry. 2022 Sep 12; 10:988376.
25. Ouyang Y, Li J, Chen X, Fu X, Sun S, Wu Q. Chalcone derivatives: Role in anticancer therapy. Biomolecules. 2021 Jun 16;11(6):894.
26. Mastachi-Loza S, Ramírez-Candelero TI, Benítez-Puebla LJ, Fuentes-Benítes A, González-Romero C, Vázquez MA. Chalcones, a Privileged Scaffold: Highly Versatile Molecules in [4+ 2] Cycloadditions. Chemistry–An Asian Journal. 2022 Oct 17;17(20):e202200706.
27. Kachhi M, Parsewar Y, Sachdev H, Mane S, Garud S, Jain H, Deshmukh SM, Fegade N. CHALCONES IN MEDICINAL CHEMISTRY: AN IN-DEPTH ANALYSIS OF STRUCTURE-ACTIVITY RELATIONSHIPS AND PHARMACOLOGICAL SIGNIFICANCE.
28. Sharma P, LaRosa C, Antwi J, Govindarajan R, Werbovetz KA. Imidazoles as potential anticancer agents: An update on recent studies. Molecules. 2021 Jul 11;26(14):4213.
29. Pandya KM, Patel JJ, Patel AH, Patel NB, Desai P. Substituted Imidazole-Pyrazole Clubbed Scaffolds: Microwave Assisted Synthesis and Examined Their In-vitro Antimicrobial and Antituberculosis Effects. Letters in Organic Chemistry. 2021 Jul 1;18(7):574-82.
30. Li D, She X, Calderone R. The antifungal pipeline: the need is established. Are there new compounds?. FEMS yeast research. 2020 Jun;20(4): foaa023.
31. ur Rashid H, Xu Y, Ahmad N, Muhammad Y, Wang L. Promising anti-inflammatory effects of chalcones via inhibition of cyclooxygenase, prostaglandin E2, inducible NO synthase and nuclear factor κb activities. Bioorganic Chemistry. 2019 Jun 1; 87:335-65.
32. Constantinescu T, Lungu CN. Anticancer activity of natural and synthetic chalcones. International journal of molecular sciences. 2021 Oct 20;22(21):11306.
33. Thapa P, Upadhyay SP, Suo WZ, Singh V, Gurung P, Lee ES, Sharma R, Sharma M. Chalcone and its analogs: Therapeutic and diagnostic applications in Alzheimer's disease. Bioorganic chemistry. 2021 Mar 1; 108:104681.
34. Awolade P, Cele N, Kerru N, Gummidi L, Oluwakemi E, Singh P. Therapeutic significance of β-glucuronidase activity and its inhibitors: A review. European journal of medicinal chemistry. 2020 Feb 1; 187:111921.
35. Rulhania S, Kumar S, Nehra B, Gupta GD, Monga V. An insight into the medicinal perspective of synthetic analogs of imidazole. Journal of molecular structure. 2021 May 15; 1232:129982.
36. Nasrollahzadeh MS, Eskandarpour V, Maleki MF, Eisvand F, Mashreghi M, Hadizadeh F, Tayarani-Najaran Z, Ghodsi R. Design, synthesis and biological evaluation of novel imidazole-based benzamide and hydroxamic acid derivatives as potent histone deacetylase inhibitors and anticancer agents. Journal of Molecular Structure. 2024 Feb 5; 1297:136951.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(1), 36-53 | ISSN:2251-6727

37. Rozmer Z, Berki T, Maász G, Perjési P. Different effects of two cyclic chalcone analogues on redox status of Jurkat T cells. Toxicology in Vitro. 2014 Dec 1;28(8):1359-65.
38. National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. Approved standard M7-A6. 6th. NCCLS; Wayne, PA, USA: 2003.
39. National Committee for Clinical Laboratory Standards. Performance Standards for Antimicrobial Susceptibility Testing. Informational supplement M100-S13. 12th. NCCLS; Wayne, PA, USA: 2003.
40. Liu T, Yao X, Zhang R, Wu T, Liu Z, Li D, Dong Q. Design, synthesis and biological evaluation of novel indole-piperazine derivatives as antibacterial agents. Bioorganic & Medicinal Chemistry Letters. 2023 Jun 1; 89:129320.
41. Tratrat C, Haroun M, Xenikakis I, Liaras K, Tsolaki E, Eleftheriou P, Petrou A, Aldhubiab B, Attimarad M, Venugopala KN, Harsha S. Design, synthesis, evaluation of antimicrobial activity and docking studies of new thiazole-based chalcones. Current Topics in Medicinal Chemistry. 2019 Feb 1;19(5):356-75.
42. Kalanithi M, Rajarajan M, Tharmaraj P, Sheela CD. Spectral, biological screening of metal chelates of chalcone based Schiff bases of N-(3-aminopropyl) imidazole. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2012 Feb 15; 87:155-62.
43. Rulhania S, Kumar S, Nehra B, Gupta GD, Monga V. An insight into the medicinal perspective of synthetic analogs of imidazole. Journal of molecular structure. 2021 May 15; 1232:129982.
44. Peng XM, Cai GX, Zhou CH. Recent developments in azole compounds as antibacterial and antifungal agents. Current topics in medicinal chemistry. 2013 Aug 1;13(16):1963-2010.
45. Shalmali N, Ali MR, Bawa S. Imidazole: an essential edifice for the identification of new lead compounds and drug development. Mini reviews in medicinal chemistry. 2018 Feb 1;18(2):142-63.
46. Tran TD, Nguyen TT, Do TH, Huynh TN, Tran CD, Thai KM. Synthesis and antibacterial activity of some heterocyclic chalcone analogues alone and in combination with antibiotics. Molecules. 2012 Jun 1;17(6):6684-96.
47. Modzelewska, A.; Pettit, C.; Achanta, G.; Davidson, N.E.; Huang, P.; Khan, S.R. Anticancer activities of novel chalcone and bis-chalcone derivatives. Bioorg. Med. Chem. 2006, 14, 3491–3495.
48. Baviskar, B.A.; Baviskar, B.; Shiradkar, M.R.; Deokate, U.A.; Khadabadi, S.S. Antimicrobial activity of some novel. Benzimidazolyl chalcones. E-J. Chem. 2009, 6, 196–200.
49. Vogel, S.; Heilmann, J. Synthesis, cytotoxicity, and antioxidative activity of minor prenylated chalcones from Humulus lupulus. J. Nat. Prod. 2008, 71, 1237–1241.
50. Jasiewicz B, Babijczuk K, Warżajtis B, Rychlewska U, Starzyk J, Cofta G, Mrówczyńska L. Indole Derivatives Bearing Imidazole, Benzothiazole-2-Thione or Benzoxazole-2-Thione Moieties—Synthesis, Structure and Evaluation of Their Cytoprotective, Antioxidant, Antibacterial and Fungicidal Activities. Molecules. 2023 Jan 10;28(2):708.
51. Dorababu, A. Indole—A Promising Pharmacophore in Recent Antiviral Drug Discovery. RSC Med. Chem. 2020, 11, 1335–1353.
52. Liu HR, Liu XJ, Fan HQ, Tang JJ, Gao XH, Liu WK. Design, synthesis and pharmacological evaluation of chalcone derivatives as acetylcholinesterase inhibitors. Bioorganic & medicinal chemistry. 2014 Nov 1;22(21):6124-33.
53. Oskuei SR, Mirzaei S, Jafari-Nik MR, Hadizadeh F, Eisvand F, Mosaffa F, Ghodsi R. Design, synthesis and biological evaluation of novel imidazole-chalcone derivatives as potential anticancer agents and tubulin polymerisation inhibitors. Bioorganic Chemistry. 2021 Jul 1; 112:104904.
54. Sangeetha V. Design, Synthesis, Characterization and Biological Evaluation of Novel Benzimidazole Chalcone Derivatives as Antitubercular Agents Targeting Glutamine Synthetase 1 (Doctoral dissertation, College of Pharmacy, Madras Medical College, Chennai).
55. Osmaniye D, Kaya Cavusoglu B, Saglik BN, Levent S, Acar Cevik U, Atli O, Ozkay Y, Kaplancikli ZA. Synthesis and anticandidal activity of new imidazole-chalcones. Molecules. 2018 Apr 4;23(4):831.

56. Tratrat C, Haroun M, Xenikakis I, Liaras K, Tsolaki E, Eleftheriou P, Petrou A, Aldhubiab B, Attimarad M, Venugopala KN, Harsha S. Design, synthesis, evaluation of antimicrobial activity and docking studies of new thiazole-based chalcones. Current Topics in Medicinal Chemistry. 2019 Feb 1;19(5):356-75.
57. Tank MJ, Kucha NA, Mitchla SM, Patel FT, Malik GM. Synthesis and biological activities of Chalcone and Pyrimidine derivatives of imidazothiazole moiety. Chemistry & Biology Interface. 2022 Mar 1;12(2).
58. Abonia R, Insuasty D, Castillo J, Insuasty B, Quiroga J, Nogueras M, Cobo J. Synthesis of novel quinoline-2-one based chalcones of potential anti-tumor activity. European journal of medicinal chemistry. 2012 Nov 1; 57:29-40.
59. Pankaj C. Butani, Bhagvanji M. Bheshdadia,1 Kartik D. Ladva, Synthesis, characterization & biological evaluation of some novel, 6-(2,3-dihydrobenzo[b][1,4] dioxin-5-yl)- imidazo[2,1-b]thiazole derivatives, Chemistry & Biology interface, Journal of ISCB, 2020, 10, 1, 1-13
60. Sattu H, Swathi P. SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF IMIDAZOLO-CHALCONE DERIVATIVES.