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Syntheses and biological activity of chalcones-imidazole derivatives

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Abstract A number of novel 13-membered chalcone-imidazole derivatives were prepared and have been synthesized and characterized by IR, ^{1}H NMR, ^{13}C NMR and elemental analysis, the results conformed well to expected structures. Substituted acetophenones and benzaldehydes were condensed using the Claisen–Schmidt base-catalyzed aldol condensation. Methyl on the aromatic ring of chalcones was brominated by NBS, and then the resulting mixture was reacted with imidazole to get the target compound. Several chalcones showed in vitro antibacterial activity against Gram-bacterial. The results showed that these are potential antibacterial compounds.

Keywords Chalcone · Imidazole · Antibacterial activity · Claisen–Schmidt

Introduction

Imidazole and its derivatives are of great significance due to their important roles in biological systems, particularly in enzymes, as proton donors and/or acceptors, coordination system ligands, and the base of charge–transfer processes [1, 2]. Unlike pyrrole (a proton donor) and pyridine (a proton acceptor), 1*H*-imidazole has both proton donor and acceptor properties [3, 4]. Imidazole functionalities have been used for complex reactions with different molecular components such as carboxylic acids to obtain liquid crystalline assemblies [5]. The imidazole nucleus appears in a number of naturally occurring products like the amino acids histidine and purines, which comprise many of the most important bases in nucleic acids. Imidazole derivatives possess a broad spectrum of pharmacological activities such

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as anticonvulsant [6], anti-Parkinson [7] and mono-aminooxidase (MAO) inhibitory [8] activity. Chalcones are known to exhibit various biological activities, such as antioxidant [9], antiinflammatory [10], antimalarial [11], antileishmanial [12], anticancer [13], and antitumor [14]. In addition, chalcones are very important compounds as intermediates in organic syntheses, Their synthesis, characterization, spectroscopic properties, and reactivity have been the subject of many papers [15–21]. On the basis of these observations, and as part of our program in the search for new antibacterial and antifungal bioorganometallics, we have designed and synthesized a number of novel chalcone-imidazole derivatives and evaluated their antimicrobial activity.

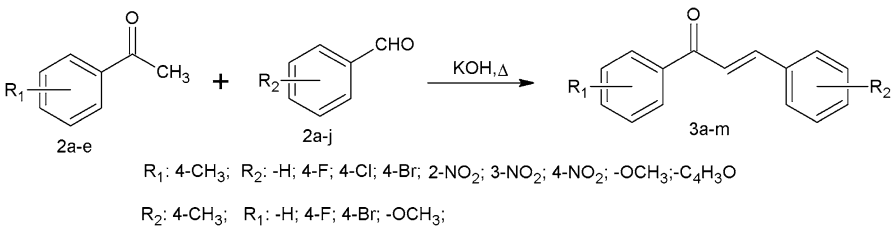
Experimental

Chemistry

All chemicals were commercially availabled, all the solvents were dried before use by the literature methods [22], and moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes. The melting points were determined in an open glass capillary and were uncorrected. C, H, and N analyses were performed with a Fisons EA 1108 (CHNS-O) elemental analyzer. IR spectra were recorded on a Nicolet FT-IR-170SX instrument (KBr discs) in the 4,000–400 cm^{-1} region. NMR spectra were recorded on a Varian Gemini 400 spectrometer, using DMSO-d_6 as the solvent and TMS as the internal standard. Chemical shifts are expressed in ppm.

Prepared chalcone **3a–3m**

The chalcones **(3a–3m)** were synthesized by a base-catalyzed Claisen–Schmidt condensation reaction21 of substituted acetophenones and aldehydes (Scheme 1). The parallel synthesis was carried out in an Advanced ChemTech Instrument model Vantage. In most cases, the starting materials were commercially available. An EtOH solution of substituted acetophenones (1a–e) (1.0 equiv) and aldehydes (2a–j) (1.0 equiv) was added with 50 % KOH (2.5 equiv). The reaction mixture was stirred overnight at room temperature; the pH was adjusted to 3–4 with aq 2 M HCl solution; the precipitate was collected by filtration and purified by recrystallization in EtOH [23].



Scheme 1 Synthetic of route for chalcone **3a–m**

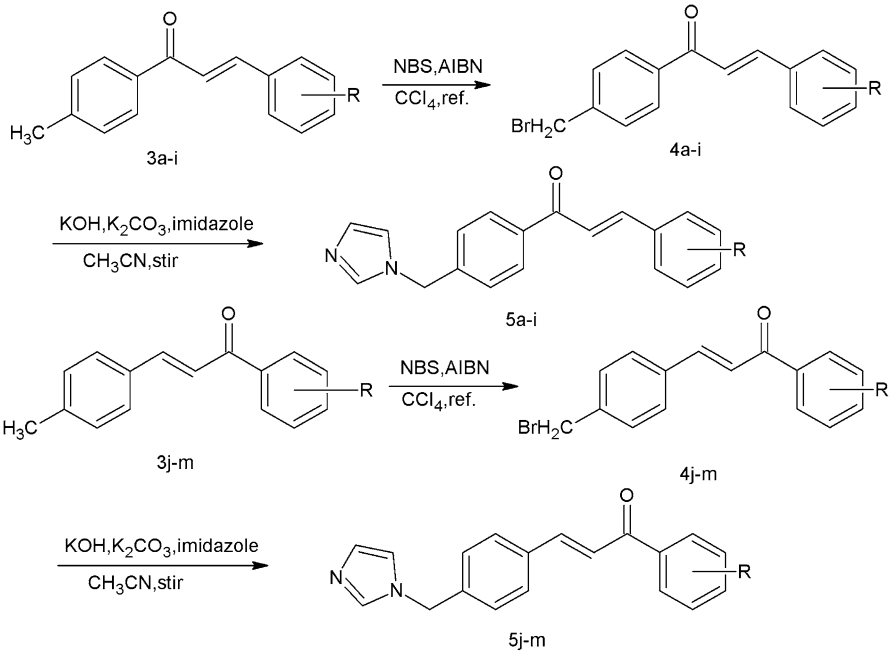
Prepared chalcones-imidazole derivatives **5a–5m**

Five mmol substituted chalcones (**3a–m**), 6 mmol NBS, 25 mL CCl_4 and 0.1 mmol were added into a 50-mL round flask. The mixture refluxed about 11 h with an oil-bath. The mixture was filtered after the reaction ended, and then the liquid mixture was distilled with CCl_4 in vacuum to get the residue.

Five mmol K_2CO_3 and 5 mmol KOH were added with stirring to a solution of the resulting mixture and 6 mmol imidazole in anhydrous CH_3CN (30 mL) at ambient temperature under nitrogen atmosphere. The mixture was stirred for 12 h at ambient temperature [monitored by thin layer chromatography (TLC)]. After removal of the solvent under vacuum, the residue was purified on silica gel by a column using petroleum ether/acetone (6:1) as the eluent to afford the title compound (Scheme 2 and Table 1).

***5a**: (E)-1-(4-((1H-imidazol-1-yl) methyl) phenyl)-3-phenylprop-2-en-1-one*

White-solid; Yield: 16.8 %; mp: 68–70 °C; IR (KBr, cm^{-1}): 1,649 (C=C); 1,581 (C=O); 1,610 (C=N); 3,034, 923 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 7.56 (d, 1H, H_α); 8.06 (d, 1H, H_β); 7.17–7.21 (d, 2H, H2, H6); 7.01–7.05 (d, 2H, H3, H5); 7.54–7.46 (m, 3H, H3′, H4′, H5′); 7.81–7.85 (d, 2H, H2′, H6′); 5, 08 (s, 2H, CH_2); 7.07–7.12 (d, 2H, CH=CH–N); 7.47 (S, 1H, CH=N); ^{13}C-NMR (400 MHz,



Scheme 2 Synthetic of route for chalcone-imidazole derivatives **5a–m**

Table 1 Antimicrobial activity of the newly synthesized compounds (μg/mL)

Comp. No.	Microorganisms and minimal inhibition concentration values					
	Sa	Bc	Ec	Pa	An	Af
5a	29.5	>50	>50	>50	22.5	25.8
5b	13.8	11.6	12.5	10.2	9.5	7.3
5c	19.5	>50	>50	12.5	12.5	12.5
5d	40.5	>50	>50	>50	12.5	25
5e	34	38.5	>50	11.7	16.5	18.5
5f	18.5	16.5	15.6	13.8	12.5	21.7
5g	23.4	45.2	15.6	3.1	10	12.5
5h	>50	>50	45.6	>50	39.7	>50
5i	25	>50	40.5	23.5	35.5	42.5
5j	>50	>50	49.7	19.4	18.5	14.5
5k	17.4	14.8	22.5	12.7	12.5	19.5
5l	34.5	>50	14.9	>50	28.5	>50
5m	>50	>50	>50	>50	36.9	42.8
Ket.	>50	>50	>50	>50	7.8	3.9
Kan.	0.7	0.39	3.9	3.9	>50	>50
Pen.	1.5	0.78	>50	>50	>50	>50

Sa Staphylococcus aureus ATCC 9144, *Bc Bacillus cereus* ATCC 11778, *Ec Escherichia coli* ATCC 25922, *Pa Pseudomonas aeruginosa* ATCC 43288, *An Aspergillus niger* ATCC 9092, *Af Aspergillus fumigatus* ATCC 46645, *Ket*. Ketoconazole, *Kan*. Kanamycin, *Pen*. Penicillin

DMSO-d_6), 191.78 (C=O), 126.81 (Cα), 144.23 (Cβ), 134.48 (C1), 129.81 (C2, 6), 128.92 (C3, 5), 142.17 (C4), 135.27 (C1′), 126.37 (C2′, 6′), 128.13 (C3′, 5′), 127.65 (C4′), 67.78 (CH_2), 136.58 (C1″), 128.47 (C2″), 122.94 (C3″); Anal. Calcd. for $C_{19}H_{16}N_2O$ (228.1584): C, 79.1954; H, 5.5964; N, 9.7217; Found: C, 79.1876; H, 5.5627; N, 9.7181.

***5b**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(2-nitrophenyl)prop-2-en-1-one*

White-Solid; Yield: 15.4 %; mp: 101–103 °C; IR (KBr, cm^{-1}): 1,678 (C=C); 1,581 (C=O); 1,612 (C=N); 3,029, 848 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 5.05 (s, 2H, CH_2); 7.01–7.09 (d, 2H, CH=CH–N); 7.25 (d, 2H, H3, H5); 7.40 (t, 1H, H3′); 7.51–7.63 (m, 4H, H_α, H5′, H6′, CH=N); 7.70 (d, 2H, H2, H6); 8.43 (d, 1H, H_β); 8.14 (t, 1H, H3′); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.56 (C=O), 127.63 (Cα), 148.23 (Cβ), 127.33 (C1), 145.18 (C2), 123.83 (C3), 128.96 (C4), 134.85 (C5), 127.38 (C6), 134.96 (C1′), 129.87 (C2′, 6′), 129.35 (C3′, 5′), 127.93 (C4′), 65.73 (CH_2), 137.84 (C1″), 128.67 (C2″), 123.43 (C3″); Anal. Calcd. for $C_{19}H_{15}N_3O_3$ (333.3455): C, 68.4032; H, 4.5354; N, 12.6058; Found: C, 68.4077; H, 4.5279; N, 12.6013.

***5c**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(3-nitrophenyl)prop-2-en-1-one*

White-Solid; Yield: 23.7 %; mp: 143–145 °C; IR (KBr, cm^{-1}): 1,678 (C=C); 1,567 (C=O); 1,611 (C=N); 3,025, 871, (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 5.13 (s, 2H, CH_2); 7.01–7.09 (d, 2H, CH=CH–N); 7.24 (d, 2H, H3, H5); 7.47–7.69 (m, 5H, H2, H6, H5′, H6′, CH=N); 7.79 (d, 1H, H_α); 8.07 (t, 1H, H3′); 8.15 (d, 1H, H_β); 8.26 (s, 1H, H2′); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.71 (C=O), 127.45 (Cα), 145.37 (Cβ), 136.15 (C1), 120.13 (C2), 147.58 (C3), 123.17 (C4), 129.61 (C5), 132.54 (C6), 134.62 (C1′), 129.73 (C2′, 6′), 129.82 (C3′, 5′), 128.27 (C4′), 65.28 (CH_2), 137.49 (C1″), 128.34 (C2″), 123.51 (C3″); Anal. Calcd. for $C_{19}H_{15}N_3O_3$ (333.3455): C, 68.4032; H, 4.5354; N, 12.6058; Found: C, 68.3984; H, 4.5387; N, 12.6021.

***5d**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one*

Yellow-solid; Yield: 18.3 %; mp: 147–149 °C; IR (KBr, cm^{-1}): 1,701 (C=C); 1,588 (C=O); 1,612 (C=N); 3,032, 865, (ArH); ^{1}HNMR (DMSO-d_6), δ (ppm): 5.03 (s, 2H, CH_2); 7.01–7.08 (d, 2H, CH=CH–N); 7.28 (d, 2H, H3, H4); 7.56 (s, 1H, CH=N); 7.68 (d, 2H, H2, H6); 7.85 (d, 1H, H_α); 8.14 (d, 2H, H2′, H6′); 8.23 (d, 1H, H_β); 8, 56 (d, 2H, H3′, H5′); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.77 (C=O), 127.22 (Cα), 148.12 (Cβ), 141.35 (C1), 127.56 (C2, 6), 123.81 (C3, 5), 147.26 (C4), 134.95 (C1′), 129.74 (C2′, 6′), 129.43 (C3′, 5′), 147.26 (C4′), 66.38 (CH_2), 138.58 (C1″), 128.41 (C2″), 123.47 (C3″); Anal. Calcd. for $C_{19}H_{15}N_3O_3$ (333.3454): C, 68.4032; H, 4.5354; N, 12.6058; Found: C, 68.3943; H, 4.5298; N, 9.7181.

***5e**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(4-methoxyphenyl) prop-2-en-1-one*

Yellow-solid; Yield: 20.7 %; mp: 157–159 °C; IR (KBr, cm^{-1}): 1,689 (C=C); 1,603 (C=O); 1,654 (C=N); 3,017, 831 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 3.81 (S, 3H, OCH_3); 4.96 (S, 2H, CH_2); 7.26–7.20 (m, 6H, H_α, H_β, H2, H3.H5.H6); 7.20 (d, 2H, N–CH=CH); 7.38 (d, 2H, H3, H5); 7.52 (d, 2H, H2, H5); 7.63 (S, 1H, HC=N); 7.81–7.90 (m, 4H, H2′, H3′, H4′, H6′); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.64 (C=O), 126.77 (Cα), 145.48 (Cβ), 127.63 (C1), 127.56 (C2, 6), 114.85 (C3, 5), 159.91 (C4), 134.45 (C1′), 129.82 (C2′, 6′), 129.65 (C3′, 5′), 142.15 (C4′), 65.84 (CH_2), 55.98 (OCH_3), 137.62 (C1″), 128.14 (C2″), 123.47 (C3″); Anal. Calcd. for $C_{20}H_{18}N_2O_2$ (318.3742): C, 75.4521; H, 5.6984; N, 8.7991; Found: C, 75.4493; H, 5.6921; N, 8.8041.

***5f**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(4-fluorophenyl)prop-2-en-1-one*

Brown-solid; Yield: 17.5 %; mp: 163–165 °C; IR (KBr, cm^{-1}): 1,697 (C=C); 1,573 (C=O); 1,639 (C=N); 3,017, 875 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 5.06 (s, 2H, CH_2); 6.94 (d, 2H, H3′, H4′); 7.01–7.07 (d, 2H, CH=CH–N); 7.23 (d, 2H, H3, H5); 7.28 (d, 2H, H2′, H6′); 7.45 (d, 1H, H_α); 7.52 (s, 1H, CH=N); 8.09 (d, 1H, H_β); 7.68 (dd, 2H, H2, H6); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.38 (C=O),

126.92 (Cα), 144.67 (Cβ), 130.81 (C1), 128.37 (C2, 6), 115.47 (C3, 5), 168.74 (C4), 135.48 (C1′), 126.72 (C2′, 6′), 129.25 (C3′, 5′), 127.56 (C4′), 66.89 (CH_2), 137.21 (C1″), 128.47 (C2″), 123.16 (C3″); Anal. Calcd. for $C_{19}H_{15}N_2OF$ (306.3385): C, 74.4957; H, 4.9352; N, 9.1448; F: 6.2016; Found: C, 74.4873; H, 4.9294; N, 9.1508; F: 6.1943.

***5g**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(4-chlorophenyl)prop-2-en-1-one*

Brown-solid; Yield: 25.6 %; mp: 178–180 °C; IR (KBr, cm^{-1}): 1,715 (C=C); 1,609 (C=O); 1,651 (C=N); 3,034, 895, 837 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 5.11 (s, 2H, CH_2); 7.02–7.08 (d, 2H, CH=CH–N); 7.22 (d, 2H, H3′, H4′); 7.26 (d, 2H, H2′, H6′); 7.39 (d, 1H, $H_α$); 7.31 (d, 2H, H3, H5); 7.58 (s, 1H, CH=N); 7.63 (dd, 2H, H2, H6); 8.07 (d, 1H, $H_β$); ^{13}C-NMR (400 MHz, DMSO-d_6), 191.94 (C=O), 126.92 (Cα), 143.85 (Cβ), 129.14 (C1), 127.78 (C2, 6), 112.89 (C3, 5), 138.63 (C4), 135.84 (C1′), 126.91 (C2′, 6′), 128.78 (C3′, 5′), 127.69 (C4′), 66.48 (CH_2), 137.67 (C1″), 128.14 (C2″), 123.68 (C3″); Anal. Calcd. for $C_{19}H_{15}N_2OCl$ (322.7935): C, 70.6981; H, 4.6836; N, 8.6786; Cl: 10.6734; Found: C, 70.6897; H, 4.6874; N, 8.6731; Cl: 10.6682.

***5h**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(4-bromophenyl)prop-2-en-1-one*

Light-brown-Solid; Yield: 28.4 %; mp: 111–113 °C; IR (KBr, cm^{-1}): 1,679 (C=C); 1,583 (C=O); 1,621 (C=N); 3,009, 895 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 4.94 (s, 2H, CH_2); 7.01–7.09 (d, 2H, CH=CH–N); 7.19 (d, 2H, H2′, H6′); 7.28 (d, 2H, H2′, H6′); 7.29 (d, 2H, H3, H5); 7.38 (d, 2H, H3′, H4′); 7.47 (d, 1H, $H_α$); 7.59 (s, 1H, CH=N); 7.71 (dd, 2H, H2, H6); 8.11 (d, 1H, $H_β$); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.56 (C=O), 126.23 (Cα), 145.48 (Cβ), 129.08 (C1), 125.67 (C2, 6), 111.87 (C3, 5), 121.63 (C4), 136.08 (C1′), 127.05 (C2′, 6′), 128.46 (C3′, 5′), 127.37 (C4′), 65.89 (CH_2), 137.48 (C1″), 128.63 (C2″), 123.56 (C3″); Anal. Calcd. for $C_{19}H_{15}N_2OBr$ (367.2445): C, 62.1409; H, 4.1167; N, 7.6282; Br: 21.7577; Found: C, 62.1367; H, 4.1103; N, 7.6199; Br: 21.7524.

***5i**: (E)-1-(4-((1H-imidazol-1-yl)methyl)phenyl)-3-(furan-2-yl)prop-2-en-1-one*

Brown-solid; Yield: 16.9 %; mp: 116–118 °C; IR (KBr, cm^{-1}): 1,711 (C=C); 1,603 (C=O); 1,631 (C=N); 3,004, 895, (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 4.78 (S, 2H, CH_2); 7.20 (d, 2H, NCH=CH); 7.28 (d, 1H, Hα); 7.30–7.63 (m, 3H, H2, H3, H4); 7.65 (S, 1H, CH=N); 7.60–7.95 (m, 4H, H2′, H3′, H4′, H6′); 8.02 (d, 1H, Hβ); ^{13}C-NMR (400 MHz, DMSO-d_6), 187.48 (C=O), 127.41 (Cα), 131.54 (Cβ), 151.62 (C1), 111.42 (C2), 112.76 (C3), 145.94 (C4), 134.85 (C1′), 131.83 (C2′, 6′), 129.49 (C3′, 5′), 127.48 (C4′), 66.75 (CH_2), 138.13 (C1″), 128.48 (C2″), 123.51 (C3″); Anal. Calcd. for $C_{17}H_{14}N_2O_2$ (278.1396): C, 73.4117; H, 5.0732; N, 10.0719; Found: C, 73.4318; H, 5.0692; N, 10.0631.

***5j**: (E)-1-phenylprop-3-(4-((1H-imidazol-1-yl)methyl)phenyl)-2-en-1-one*

White-solid; Yield: 23.5 %; mp: 84–86 °C; IR (KBr, cm^{-1}): 1,689 (C=C); 1,593 (C=O); 1,631 (C=N); 3,034, 913 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 5.07 (S, 2H, CH_2); 7.43–7.62 (m, 6H, Hα, Hβ, H2′, H3′, H4′, H5′); 7.24 (d, 2H, NCH=CH); 7.67 (s, 1H, CH=N), 7.85–7.93 (m, 4H, H2, H3, H5, H6); 8.01 (d, 1H, H6′); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.55 (C=O), 125.43 (Cα), 143.78 (Cβ), 127.17 (C1), 130.40 (C2, 6), 129.08 (C3, 5), 141.22 (C4), 137.92 (C1′), 132.48 (C2′, 6′), 129.31 (C3′, 5′), 134.61 (C4′), 69.34 (CH_2), 136.84 (C1″), 128.17 (C2″), 120.74 (C3″); Anal. Calcd. for $C_{19}H_{16}N_2O$ (288.1584): C, 79.1954; H, 5.5964; N, 9.7217; Found: C, 79. 1903; H, 5.5921; N, 9.7195; N, 12.6058; Found: C, 68.3957; H, 4.5394; N, 12.6013.

***5k**: (E)-1-(4-fluorophenyl)phenylprop-3-(4-((1H-imidazol-1-yl)methyl)phenyl)-2-en-1-one*

White-solid; Yield: 19.4 %; mp: 79–81; IR (KBr, cm^{-1}): 1,705 (C=C); 1,607 (C=O); 1,627 (C=N); 3,034, 895, 837 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 4.98 (s, 1H, CH_2); 7.08–7.16 (m, 4H, H2′, H3′, H5′, H6′); 7.24 (d, 2H, NCH=CH); 7.49 (d, 1H, Hβ); 7.61 (d, 1H, Hα); 7.65 (s, 1H, CH=N); 7.85–7.86 (m, 4H, H2, H3, H5, H6); ^{13}C-NMR (400 MHz, DMSO-d_6), 191.67 (C=O), 126.13 (Cα), 142.97 (Cβ), 126.88 (C1), 131.18 (C2, 6), 128.92 (C3, 5), 140.79 (C4), 139.24 (C1′), 133.88 (C2′, 6′), 129.35 (C3′, 5′), 165.37 (C4′), 68.84 (CH_2), 135.97 (C1″), 128.58 (C2″), 121.22 (C3″); Anal. Calcd. for $C_{19}H_{15}N_2OF$ (306.3385): C, 74.4957; H, 4.9352; N, 9.1448; F: 6.2016; Found: C, 74.4872; H, 4.9247; N, 9.1403; F: 6.1937.

***5l**: (E)-1-(4-bromophenyl)phenylprop-3-(4-((1H-imidazol-1-yl)methyl)phenyl)-2-en-1-one*

Yellow-Solid; Yield: 16.1 %; mp: 144–146 °C; IR (KBr, cm^{-1}): 1,631 (C=C); 1,583 (C=O); 1,610 (C=N); 3,034, 895, 837 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 5.08 (s, 1H, CH_2); 7.15–7.57 (m, 8H, Hα, Hβ, H2, H3, H5, H6, NCH=CH); 7.68 (s, 1H, CH=N); 7.86–7.94 (m, 4H, H2, H3, H5, H6); ^{13}C-NMR (400 MHz, DMSO-d_6), 192.43 (C=O), 127.13 (Cα), 144.35 (Cβ), 126.48 (C1), 131.43 (C2, 6), 129.37 (C3, 5), 141.25 (C4), 138.53 (C1′), 132.48 (C2′, 6′), 128.83 (C3′, 5′), 124.75 (C4′), 69.27 (CH_2), 136.62 (C1″), 128.73 (C2″), 123.35 (C3″); Anal. Calcd. for $C_{19}H_{15}N_2OBr$ (367.2445): C, 62.1409; H, 4.1167; N, 7.6282; Br: 21.7577; C, 62.1335; H, 4.1113; N, 7.6146; Br: 21.7597.

***5m**: (E)-1-(4-methoxyphenyl)phenylprop-3-(4-((1H-imidazol-1-yl)methyl)phenyl)-2-en-1-one*

Yellow-Solid; Yield: 22.5 %; mp: 124–126 °C; IR (KBr, cm^{-1}): 1,721 (C=C); 1,613 (C=O); 1,632 (C=N); 3,034, 837 (ArH); ^{1}H-NMR (400 MHz, DMSO-d_6), δ (ppm): 3, 83 (s, 3H, OCH_3); 4.82 (s, 1H, CH_2); 7.21 (d, 2H, NCH=CH); 7.32–7.61

(m, 6H, Hα, Hβ, H2, H3, H5, H6); 7.82–7.91 (m, 4H, H2, H3, H5, H6); 7.67 (s, 1H, CH=N); ^{13}C-NMR (400 MHz, DMSO-d_6), 193.13 (C=O), 126.78 (Cα), 142.67 (Cβ), 126.88 (C1), 131.35 (C2, 6), 129.43 (C3, 5), 142.19 (C4), 138.31 (C1′), 133.57 (C2′, 6′), 120.14 (C3′, 5′), 168.45 (C4′), 69.27 (CH_2), 136.41 (C1″), 127.92 (C2″), 120.26 (C3″), 53.18 (OCH_3); Anal. Calcd. for $C_{19}H_{16}N_2O$ (318.3742): C, 75.4521; H, 5.6984; N, 8.7991; Found: C, 75.4467; H, 5.6932; N, 8.7914.

Antimicrobial activity

The antibacterial activity of the synthesized compounds was tested against *S. aureus*, *B. cereus*, *E. coli* and *P. aeruginosa* using MH medium (Mueller–Hinton medium: casein hydrolysate 18.5 g, soluble starch 1.5 g, beef extract 1,000 mL), and the antifungal activity of the compounds was tested against *A. niger* and *A. fumigatus* using RPMI-1640 medium [RPMI-1640 (GIBCO BRL) 10 g, $NaHCO_3$ 2.0 g, 0.15 mol/L morpholinepropanesulfonic acid (Sigma) 35 g, triple-distilled water 900 mL, buffered to pH 7.0 with 1 mol/L NaOH (25 °C), metered volume to 1,000 mL, filtered sterilization, conservation in 4 °C]. The MICs of the test compounds were determined by a colorimetric method using the dye MTT [24]. A stock solution of the synthesized compound (50 μg/mL) in DMSO was prepared and graded quantities of the test compounds were incorporated in a specified quantity of sterilized liquid medium (MH medium for antibacterial activity and RPMI-1640 medium for antifungal activity). A specified quantity of the medium containing the compound was poured into microtitration plates. Suspension of the microorganism was prepared to contain about 10^5 cfu/mL and applied to microtitration plates with serially diluted compounds in DMSO to be tested and incubated at 37 °C for 18 h and 36 h for bacteria and fungi, respectively. After the MICs were visually determined on each of the microtitration plates, 50 μL of PBS (phosphate buffered saline 0.01 mol/L, pH 7.5, $Na_2HPO_4{\cdot}12H_2O$ 2.5 g, KH_2PO_4 0.2 g, NaCl 8.0 g, KCl 0.2 g, distilled water 1,000 mL) containing 2 mg of MTT/mL was added to each well. Incubation was continued at room temperature for 5–6 h. The content of each well was removed, and 100 μL of isopropanol containing 5 % 1 mol/L HCl was added to extract the dye. After 12 h of incubation at room temperature, the optical density was measured with a microplate reader at 550 nm. The observed MICs are presented in Table 2.

Results

Chalcone (**3a–m**) synthesis by condensation of acetophenones and aldehydes under the chosen conditions [25–28] (Scheme 1) is attractive since it especially generates (E)-isomer, normally in high yield. As observed from ^{1}H NMR spectra, all chalcones were geometrically pure and with trans-configuration (J Ha–Hb = 15.5–16.0 Hz). Using this method, 13 substituted chalcones (**3a–m**) were obtained in satisfactory yields. Methyl on the aromatic ring of chalcones was brominated by NBS, and then the

Table 2 Prepared calcone-imidazole derivatives

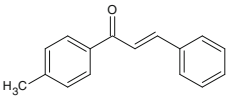
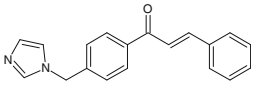
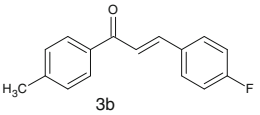
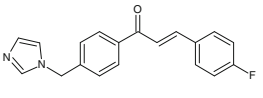
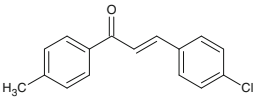
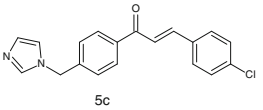
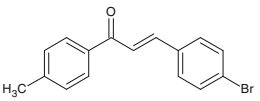
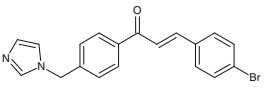
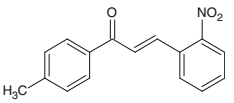
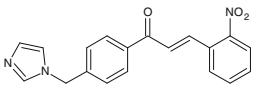
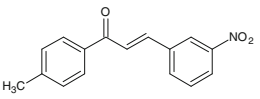
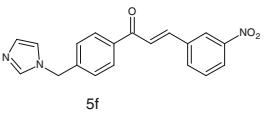
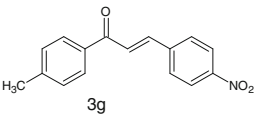
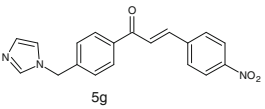
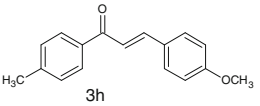
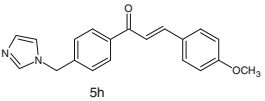
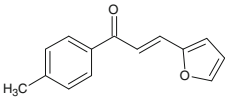
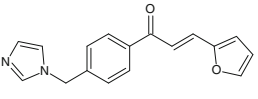
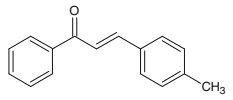
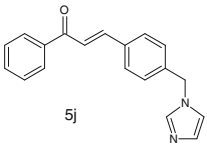
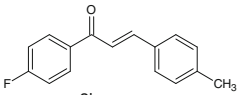
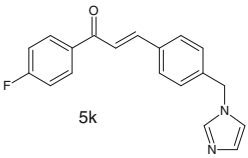
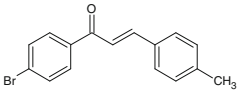
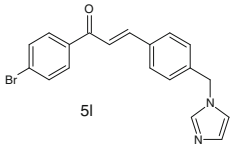
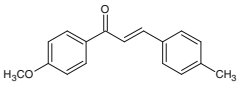
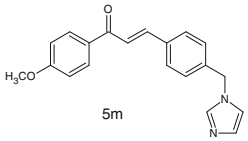
Reagents	Products	Color	Yield[a] (%)	mp (°C)
 3a	 5a	White solid	16.8	68–70
 3b	 5b	White solid	15.4	101–103
 3c	 5c	White solid	23.7	143–145
 3d	 5d	Yellow solid	19.4	147–149
 3e	 5e	Yellow solid	20.7	157–159
 3f	 5f	Brown solid	17.5	163–165
 3g	 5g	Brown solid	25.6	178–180
 3h	 5h	Light-brown solid	28.4	111–113
 3i	 5i	Brown solid	16.9	116–118

Table 2 continued

Reagents	Products	Color	Yield[a] (%)	mp (°C)
 3j	 5j	White solid	23.5	84–86
 3k	 5k	White solid	18.3	79–81
 3l	 5l	Yellow solid	16.1	144–146
 3m	 5m	Yellow solid	22.5	124–126

[a] Isolated yield

resulting mixture was reacted with imidazole to get the target compounds. A novel series of chalcone-imidazole derivatives were obtained in yields of 15.4–28.6 %.

The solid state IR (KBr, cm^{-1}) spectra of these compounds showed C=N group stretching vibrations are seen around 1,610 cm^{-1}. The ^1H NMR (DMSO-d_6, ppm) data of all compounds showed that the vibration of PhC-H 2.35 shifted to 4.90–5.1 confirming Ph–CH_3 substituted by imidazole.

A problem was found in the process of synthesized compounds **4a**–**m** that those could not be purified in the traditional way, hence they are used in the subsequent synthesis without purification. So, we used one-pot synthesis methods to get the title compounds (**5a**–**m**). Steps were shown in chemistry.

The antibacterial activity results presented in Table 2 show the newly synthesized compounds. These new derivatives were screened for their antibacterial activity against *E coli*, *P aeruginosa*, *S typhi*, *B subtilis* and *S aureus*, in which these compounds were tested against one or more bacterial strains. Compounds **5-b** and **5-k** showed higher activity against Gram-negative bacterial and Gram-positive bacterial compared with others; meanwhile compound **5g** showed higher activity against Gram-negative bacterial strains while exhibited lower active against

Gram-positive bacterial strains, which might be due to the presence of a –F or $–NO_2$ group. The potent activities of these chalcone-imidazole derivatives suggest that they are potential candidates for the development of new antibacterial drugs.

The antifungal activity of the compounds was studied with two fungal strains (*Aspergillus niger* ATCC 9092 and *A. fumigatus* ATCC 46645) by the MTT method. The results are summarized in Table 2. Ketoconazole was used as reference for inhibitory activity against fungi. All synthesized compounds exhibited antifungal activity. These results revealed that some of the synthesized compounds exhibited significant antibacterial activity and most of the synthesized compounds showed better antifungal activity.

Conclusions

A novel series of chalcone-imidazole derivatives were characterized by IR, ^{1}HNMR, ^{13}C-NMR and elemental analyses. All the compounds were screened for their antibacterial and antifungal activity. Most of the synthesized compounds showed better antifungal activity. The antibacterial activity of compounds **5b**, **5k** and **5g** against Gram bacterial strains was found to be higher than that for the standard drug.

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