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Synthesis, Characterization and Antimicrobial Activities of Chalcones and Their Post Transformation to Pyrazole Derivatives

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An efficient procedure for the synthesis of trisubstituted pyrazoles was developed. Claisen-Schmidt condensation of 2,4,5-trimethoxybenzaldehyde and substituted acetophenone in the presence of aqueous alkaline bases produced chalcones. The cyclocondensation reaction of chalcones and phenyl hydrazine hydrochloride catalyzed by an acid produced trisubstituted pyrazolines in good yields. The synthesized new compounds were characterized by spectral studies and elemental analysis and some of the intermediate chalcones by single crystal X-ray diffraction studies. The compounds were screened *in vitro* for their antimicrobial susceptibilities against different bacteria and fungi species.

Keywords: Antibacterial, Antifungal, Cyclocondensation, Inhibition, Pyrazoline, Spectral.

INTRODUCTION

Chalcones and their derivatives demonstrate a wide range of biological activities and constitutes the central core for the construction of a wide range of bioactive compounds [1,2]. Five membered nitrogen heterocycles, particularly pyrazoles and their derivatives are regarded as important molecules in organic synthesis. They serve as building blocks for the construction of biologically potent molecules. Numerous methods have been developed for synthesis of substituted pyrazoles *viz.* by (i) the reaction of 1,3-diketones with hydrazines, (ii) the reaction of α,β-unsaturated aldehyde and ketones with hydrazines. However, the classical method employed for the synthesis of pyrazolines and pyrazoles involves 1,3-dipolar cycloaddition reactions of nitrile imines to alkenes and alkynes [3,4]. An efficient regioselective synthetic route to multi-substituted pyrazoles by cyclocondensation of β-thioalkyl-α,β-unsaturated ketones with hydrazines was developed by Jin *et al.* [5]. A convenient and efficient synthesis of a series of 1,3-diaryl-4-halo-1*H*-pyrazoles in moderate to excellent yields by 1,3-dipolar cycloaddition of 3-aryl sydnones and 2-aryl-1,1-dihalo-1-alkenes was reported [6].

Pyrazole derivatives have been used as important pharmacores and synthons in the field of organic chemistry and drug designing. For instance, a series of 1-acetyl-3,5-diphenyl-4,5-dihydro-(1*H*)-pyrazoles synthesized were investigated for their ability to inhibit selectively monoamine oxidases, swine kidney diamine oxidase (SKDAO) and bovine serum amine oxidase (BSAO) [7]. Pyrazoles have known to exhibit antifungal, antibacterial, antioxidant [8,9], antitubercular [10] and anticancer [11] activities.

The enormous pharmacological applications associated with pyrazoles prompted us to work in this area. In continuation of our work on pyrazoles and in search of new potential antifungal and antibacterial agents, we herein report the synthesis of a series of new pyrazoles *via* Claisen Schmidt condensation of aromatic aldehydes and aromatic ketones and their *in vitro* antimicrobial susceptibilities against different bacteria and fungi organisms.

EXPERIMENTAL

Melting points were determined by an open capillary tube method and are uncorrected. Purity of the compounds was checked on thin layer chromatography (TLC) plates pre-coated with silica gel using the solvent system ethyl acetate:dichloromethane (1:4 v/v). The spots were visualized under UV light. ^{1}H NMR and ^{13}C NMR spectra were recorded on Agilent-NMR 400 MHz and 100 MHz spectrometer respectively. The solvent $CDCl_3$ with TMS as an internal standard was used to record the spectra. The chemical shifts are expressed in δ ppm. Mass spectra were obtained on Mass Lynx SCN781 spectrometer TOF mode. Elemental analyses was obtained on a Thermo Finnigan Flash EA 1112 CHN analyzer. Purification of com-

pounds was done by column chromatography on silica gel (70-230 mesh Merck).

The synthetic method involves the synthesis of a series of chalcones (**3a-g**) by the reaction of 2,4,5-trimethoxybenzaldehyde (**1**) with substituted acetophenone (**2a-g**) in the presence of base in alcohol medium. The cyclocondensation reaction of chalcones (**3a-g**) with phenyl hydrazine hydrochloride (**4**) and a few drops of concentrated hydrochloric acid in methyl alcohol to obtain pyrazole derivatives (**5a-g**) in good yields. The schematic diagram for the synthesis of chalcones and pyrazolines is outlined in Fig. 1.

Synthesis of chalcones (3a-g): A mixture of 2,4,5-trimethoxybenzaldehyde (**1**, 5 mmol), substituted acetophenone (**2a-g**, 5 mmol) and sodium hydroxide (5 mmol) in 95 % ethyl alcohol (25 mL) was stirred at room temperature for 3 h. The progress of the reaction was monitored by TLC. After the completion of the reaction, the mixture was poured in to ice cold water and kept in the refrigerator for overnight. The solid formed was filtered and washed with cold hydrochloric acid (5 %). Crude products obtained were crystallized from methyl alcohol to obtain pure chalcones (**3a-g**).

(E)-1-Phenyl-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (3a): By reaction of 2,4,5-trimethoxybenzaldehyde (**1**, 10 mmol) and acetophenone (**2a**, 10 mmol) in 82 % yield, m.p. 141-142 °C; ^{1}H NMR: δ 3.845 (s, 9H, OCH_3), 6.718–6.752 (m, 2H, Ar–H), 7.322 (d, 1H, C=CH), 7.458–7.766 (m, 5H, Ar–H), 8.112 (d, 1H, CH=C); Anal. calcd. (%) for $C_{18}H_{18}O_4$ (*m/z*: 298): C, 72.47; H, 6.08; Found (%): C, 72.37; H, 5.98.

(E)-1-(4-Fluorophenyl)-3-(2,4,5-trimethoxyphenyl)-prop-2-en-1-one (3b): By reaction of 2,4,5-trimethoxybenzaldehyde (**1**, 10 mmol) and 4-fluoroacetophenone (**2b**, 10 mmol) in 88 % yield, m.p. 126-127 °C; ^{1}H NMR: δ 3.848 (s, 9H, OCH_3), 6.720–6.749 (m, 2H, Ar–H), 7.310 (d, 1H, C=CH), 7.440–7.780 (m, 4H, Ar–H), 8.120 (d, 1H, CH=C); Anal. calcd. (%) for $C_{18}H_{17}O_4F$ (*m/z*: 316): C, 68.35; H, 5.42; Found (%): C, 68.22; H, 5.28.

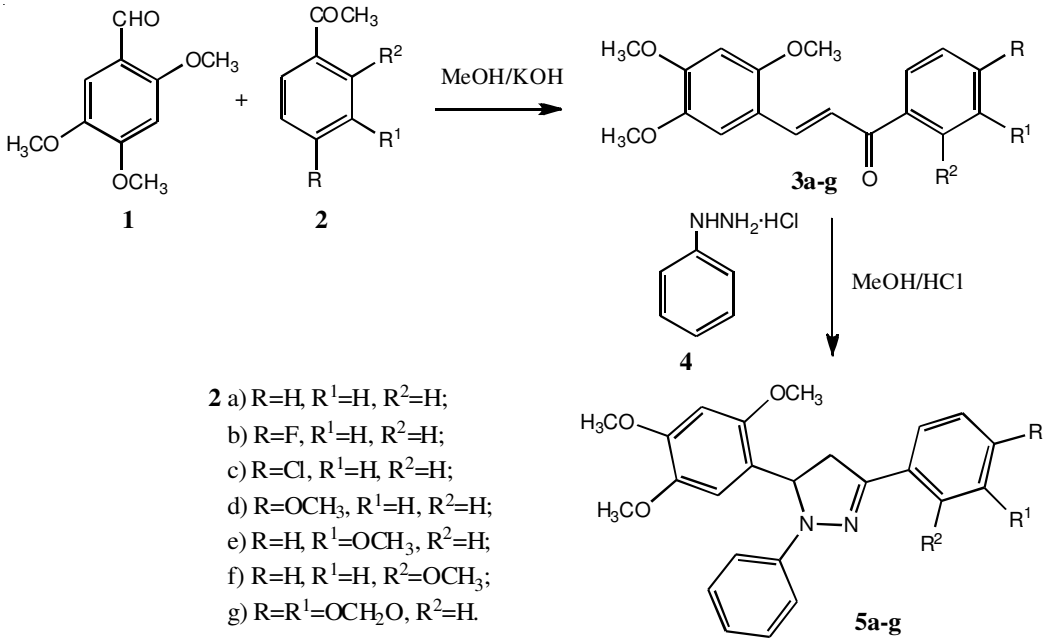
(E)-1-(4-Chlorophenyl)-3-(2,4,5-trimethoxyphenyl)-prop-2-en-1-one (3c): By reaction of 2,4,5-trimethoxybenzaldehyde (**1**, 10 mmol) and 4-chloroacetophenone (**2c**, 10 mmol) in 94 % yield, m.p. 158–159 °C; ^{1}H NMR: δ 3.848 (s, 9H, OCH_3), 6.718–6.751 (m, 2H, Ar–H), 7.316 (d, 1H, C=CH), 7.452–7.778 (m, 4H, Ar–H), 8.116 (d, 1H, CH=C); Anal. calcd. (%) for $C_{18}H_{17}O_4Cl$ (*m/z*: 332): C, 64.97; H, 5.15; Found (%): C, 64.86; H, 5.08.

(E)-1-(4-Methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)-prop-2-en-1-one [12] (3d): By reaction of 2,4,5-trimethoxybenzaldehyde (**1**, 10 mmol) and 4-methoxyacetophenone (**2d**, 10 mmol) in 91 % yield, m.p. 104-105 °C; ^{1}H NMR: δ 3.850 (s, 12H, OCH_3), 6.726–6.744 (m, 2H, Ar–H), 7.324 (d, 1H, C=CH), 7.458–7.781 (m, 4H, Ar–H), 8.184-8.222 (d, 1H, CH=C); Anal. calcd. (%) for $C_{19}H_{20}O_5$ (*m/z*: 328): C, 69.50; H, 6.14; Found (%): C, 69.39; H, 6.05.

(E)-1-(3-Methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)-prop-2-en-1-one (3e): By reaction of 2,4,5-trimethoxybenzaldehyde, **1** (10 mmol) and 3-methoxyacetophenone (**2e**, 10 mmol) in 82 % yield, m.p. 158–159 °C; ^{1}H NMR: δ 3.852 (s, 12H, OCH_3), 6.732–6.752 (m, 2H, Ar–H), 7.330 (d, 1H, C=CH), 7.460–7.787 (m, 4H, Ar–H), 8.202 (d, 1H, CH=C); Anal. calcd. (%) for $C_{19}H_{20}O_5$ (*m/z*: 328): C, 69.50; H, 6.14; Found (%): C, 69.41; H, 6.08.

(E)-1-(2-Methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)-prop-2-en-1-one (3f): By reaction of 2,4,5-trimethoxybenzaldehyde (**1**, 10 mmol) and 2-methoxyacetophenone (**2f**, 10 mmol) in 85 % yield, m.p. 140–141 °C; ^{1}H NMR: δ 3.850 (s, 12H, OCH_3), 6.730–6.754 (m, 2H, Ar–H), 7.311 (d, 1H, C=CH), 7.455–7.788 (m, 4H, Ar–H), 8.172 (d, 1H, CH=C); Anal. calcd. (%) for $C_{19}H_{20}O_5$ (*m/z*: 328): C, 69.50; H, 6.14; Found (%): C, 69.37; H, 6.04.

(E)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (3g) [13]: By reaction of 2,4,5-trimethoxybenzaldehyde (**1**, 10 mmol) and 1-(benzo[d][1,3]-dioxol-5-yl)ethanone (**2g**, 10 mmol) in 89 % yield, m.p. 126-



2 a) R=H, R^1=H, R^2=H;
b) R=F, R^1=H, R^2=H;
c) R=Cl, R^1=H, R^2=H;
d) R=OCH_3, R^1=H, R^2=H;
e) R=H, R^1=OCH_3, R^2=H;
f) R=H, R^1=H, R^2=OCH_3;
g) R=R^1=OCH_2O, R^2=H.

Fig. 1. Schematic diagram for the synthesis of pyrazolines (**5a-g**)

128 °C; ^{1}H NMR: δ 3.848 (s, 9H, OCH_3), 6.031 (s, 2H, OCH_2O), 6.740–6.768 (m, 2H, Ar–H), 7.308 (d, 1H, C=CH), 7.448–7.750 (m, 3H, Ar–H), 8.190 (d, 1H, CH=C); Anal. calcd. (%) for $C_{19}H_{18}O_6$ (*m/z*: 342): C, 66.66; H, 5.30; Found (%): C, 66.52; H, 5.22.

General procedure for the synthesis of pyrazolines (5a-g): To a stirred solution of chalcones (**3a-g**, 0.01 mol) and phenyl hydrazine hydrochloride (**4**, 0.01 mol) in methyl alcohol (15 mL), concentrated hydrochloric acid (7-8 drops) were added. The mixture was refluxed for 3-4 h and the progress of the reaction was monitored by TLC. After completion, the reaction mixture was poured in to ice cold water; solid separated was filtered, washed with ice cold water and dried. The products were purified column chromatography using silica gel (60-120 mesh) and ethyl acetate:dichloromethane (1:4 v/v) as eluent.

1,3-Diphenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5a): By reaction of (E)-1-phenyl-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3a**, 10 mmol) and phenylhydrazine hydrochloride (**4**, 10 mmol) in 81 % yield, m.p. 112–114 °C; ^{1}H NMR: δ 2.990.3.147 (dd, 1H, *J* = 6.7 Hz, 13.6 Hz, C_3-H_a), 3.852 (s, 9H, OCH_3), 3.660-3.738 (dd, 1H, *J* = 6.8 Hz, 14.8 Hz, C_3-H_b), 5.432-5.502 (dd, 1H, *J* = 7.6 Hz, 15.2 Hz, C_2-H), 7.218–7.965 (m, 12H, Ar–H); ^{13}C NMR: δ 40.44 (1C, C-2), 53.48 (1C, C-3), 55.75 (3C), 99.98 (1C), 112.95 (1C), 115.92 (2C), 120.80 (1C), 122.50 (1C), 128.37 (2C), 128.90 (2C), 129.44 (2C), 131.20 (1C), 135.56 (1C), 140.26 (1C), 142.88 (1C), 147.71 (1C), 148.94 (1C), 154.12 (1C, C-4); MS *m/z*: 388 (M^+, 24), 387(100); Anal. calcd. (%) for $C_{24}H_{24}N_2O_3$ (%): C, 74.21; H, 6.23; N, 7.21; Found (%): C, 74.10; H, 6.12; N, 7.08.

3-(4-Fluorophenyl)-1-phenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5b): By reaction of (E)-1-(4-fluorophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3b**, 10 mmol) and phenyl hydrazine hydrochloride (**4**, 10 mmol) in 92 % yield, m.p. 124–125 °C; ^{1}H NMR: δ 2.998-3.142 (dd, 1H, *J* = 7.7 Hz, 13.0 Hz, C_3-H_a), 3.863 (s, 9H, OCH_3), 3.648-3.710 (dd, 1H, *J* = 6.8 Hz, 13.4 Hz, C_3-H_b), 5.454-5.501 (dd, 1H, *J* = 8.3 Hz, *15.8* Hz, C_2-H), 6.986–7.624 (m, 11H, Ar–H); ^{13}C NMR: δ 40.37 (1C, C-2), 53.16 (1C, C-3), 55.65 (3C), 100.08 (1C), 112.44 (1C), 115.82 (2C), 116.42 (2C), 119.16 (1C), 122.34 (1C), 128.95 (2C), 129.66 (2C), 133.22 (1C), 140.78 (1C), 142.10 (1C), 148.55 (1C), 149.14 (1C), 153.99 (1C, C-4), 164.95 (1C); MS *m/z*: 406 (M^+); Anal. calcd. (%) for $C_{24}H_{23}N_2O_3F$ (%): C, 70.92; H, 5.70; N, 6.89; Found (%): C, 70.80; H, 5.56; N, 6.75.

3-(4-Chlorophenyl)-1-phenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5c): By reaction of (E)-1-(4-chlorophenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3c**, 10 mmol) and phenyl hydrazine hydrochloride (**4**, 10 mmol) in 90 % yield, m.p. 99–101 °C; ^{1}H NMR: δ 3.008.3.166 (dd, 1H, *J* = 7.9 Hz, 13.8 Hz, C_3-H_a), 3.850 (s, 9H, OCH_3), 3.672-3.744 (dd, 1H, *J* = 8.0 Hz, 14.9 Hz, C_3-H_b), 5.442-5.496 (dd, 1H, *J* = 9.0 Hz, 16.1 Hz, C_2-H), 7.006–7.624 (m, 11H, Ar–H); ^{13}C NMR: δ 40.30 (1C, C-2), 53.33 (1C, C-3), 55.68 (3C), 99.95 (1C), 112.98 (1C), 115.76 (2C), 119.92 (1C), 122.50 (1C), 128.30 (2C), 128.84 (2C), 129.72 (2C), 134.15 (1C), 136.80 (1C), 142.17 (1C), 143.52 (1C), 148.34 (1C), 149.22 (1C), 153.04 (1C, C-4); MS *m/z*: 424 (M^+, ^{37}Cl), 422 (M^+, ^{35}Cl); Anal. calcd. (%) for $C_{24}H_{23}ClN_2O_3$ (%): C, 68.16; H, 5.48; N, 6.62; Found (%): C, 68.10; H, 5.36; N, 6.54.

3-(4-Methoxyphenyl)-1-phenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5d): By reaction of (E)-1-(4-methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3d**, 10 mmol) and phenyl hydrazine hydrochloride (**4**, 10 mmol) in 96 % yield, m.p. 133–134 °C; ^{1}H NMR: δ 2.992-3.133 (dd, 1H, *J* = 7.2 Hz, 14.5 Hz, C_3-H_a), 3.841 (s, 3H, OCH_3), 3.864 (s, 9H, OCH_3), 3.688-3.732 (dd, 1H, *J* = 8.2 Hz, 15.6 Hz, C_3-H_b), 5.430-5.483 (dd, 1H, *J* = 6.8 Hz, 13.3 Hz, C_2-H), 7.012–7.725 (m, 11H, Ar–H); ^{13}C NMR: δ 39.56 (1C, C-2), 53.08 (1C, C-3), 55.62 (3C), 55.74 (1C), 99.86 (1C), 112.60 (1C), 114.56 (2C), 115.88 (2C), 120.10 (1C), 122.48 (1C), 128.30 (2C), 128.74 (1C), 129.14 (2C), 140.35 (1C), 142.22 (1C), 147.70 (1C), 148.20 (1C), 152.66 (1C, C-4), 161.82 (1C); MS *m/z*: 418 (M^+); Anal. calcd. (%) for $C_{25}H_{26}N_2O_4$ (%): C, 71.75; H, 6.26; N, 6.69; Found (%): C, 71.64; H, 6.13; N, 6.54.

3-(3-Methoxyphenyl)-1-phenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5e): By reaction of (E)-1-(3-methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3e**, 10 mmol) and phenyl hydrazine hydrochloride (**4**, 10 mmol) in 83 % yield, m.p. 1127–129 °C; ^{1}H NMR: δ 2.998.3.201 (dd, 1H, *J* = 7.0 Hz, 14.6 Hz, C_3-H_a), 3.848 (s, 3H, OCH_3), 3.871 (s, 9H, OCH_3), 3.656-3.718 (dd, 1H, *J* = 8.0 Hz, 15.0 Hz, C_3-H_b), 5.416-5.485 (dd, 1H, *J* = 9.1 Hz, 15.2 Hz, C_2-H), 6.992–7.754 (m, 11H, Ar–H); ^{13}C NMR: δ 39.80 (1C, C-2), 53.26 (1C, C-3), 55.62 (3C), 55.70 (1C), 100.06 (1C), 112.44 (1C), 114.60 (2C), 115.80 (2C), 120.24 (1C), 122.53 (1C), 128.28 (2C), 128.70 (1C), 129.34 (2C), 140.60 (1C), 142.76 (1C), 147.92 (1C), 148.40 (1C), 152.84 (1C, C-4), 161.77 (1C); MS *m/z*: 418 (M^+); Anal. calcd. (%) for $C_{25}H_{26}N_2O_4$ (%): C, 71.75; H, 6.26; N, 6.69; Found (%): C, 71.62; H, 6.18; N, 6.60.

3-(2-Methoxyphenyl)-1-phenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5f): By reaction of (E)-1-(2-methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3f**, 10 mmol) and phenyl hydrazine hydrochloride (**4**, 10 mmol) in 83 % yield, m.p. 144–146 °C; ^{1}H NMR: δ 3.028-3.210 (dd, 1H, *J* = 7.5 Hz, 14.2 Hz, C_3-H_a), 3.850 (s, 3H, OCH_3), 3.882 (s, 9H, OCH_3), 3.640-3.696 (dd, 1H, *J* = 8.6 Hz, 15.3 Hz, C_3-H_b), 5.430-5.462 (dd, 1H, *J* = 9.0 Hz, 15.0 Hz, C_2-H), 6.997–7.760 (m, 11H, Ar–H); MS *m/z*: 418 (M^+); Anal. calcd. (%) for $C_{25}H_{26}N_2O_4$ (%): C, 71.75; H, 6.26; N, 6.69; Found (%): C, 71.70; H, 6.15; N, 6.57.

3-(Benzo[d][1,3]dioxol-5-yl)-1-phenyl-5-(2,4,5-trimethoxyphenyl)-4,5-dihydro-1*H*-pyrazole (5g): By reaction of (E)-1-(benzo[d][1,3]dioxol-5-yl)-3-(2,4,5-trimethoxyphenyl)prop-2-en-1-one (**3g**, 10 mmol) and phenyl hydrazine hydrochloride (**4**, 10 mmol) in 78 % yield, m.p. 1106–108 °C; ^{1}H NMR: δ 3.016.3.202 (dd, 1H, *J* = 7.0 Hz, 14.7 Hz, C_3-H_a), 3.862 (s, 9H, OCH_3), 3.655-3.698 (dd, 1H, *J* = 8.1 Hz, 14.5 Hz, C_3-H_b), 5.445-5.478 (dd, 1H, *J* = 9.0 Hz, 15.0 Hz, C_2-H), 6.050 (s, 2H, OCH_2O), 6.984–7.746 (m, 10H, Ar–H); ^{13}C NMR: δ 40.12 (1C, C-2), 53.40 (1C, C-3), 55.85 (3C), 99.50 (1C), 102.26 (1C), 110.55 (1C), 112.96 (1C), 113.70 (1C), 115.82 (2C), 119.90 (1C), 121.22 (1C), 122.73 (1C), 126.12

(1C), 129.65 (2C), 141.00 (1C), 142.88 (1C), 147.22 (1C), 148.84 (1C), 149.66 (1C), 152.20 (1C), 153.24 (1C, C-4); MS *m/z*: 434 (M^+); Anal. calcd. (%) for $C_{25}H_{24}N_2O_5$ (%): C, 69.43; H, 5.59; N, 6.48; Found (%): C, 69.32; H, 5.45; N, 6.37.

RESULTS AND DISCUSSION

^{1}H NMR, elemental analysis and X-ray diffraction crystallographic studies provide the structural proof of the compounds **3a-g**. The structural assignments were made by NMR analysis by considering compound, **3d** as the representative compound among the series. In ^{1}H NMR spectra, the alkenyl proton each for C=CH and CH=C appeared as doublets at δ 6.726–6.744 and 8.184-8.222 ppm respectively. The signals appeared as singlet for twelve protons at δ 3.850 were assigned to OCH_3 protons, while as multiplet for two and four protons each at δ 6.726–6.744 and δ 7.458–7.781 ppm were due to aromatic protons. The analytical data obtained for the compound **3d** were in good agreement with theoretically calculated data. Further, the structure was confirmed by single crystal X-ray diffraction studies and was depicted in ORTEP diagram (Fig. 2) [12]. All the compounds of the series **3a-g** showed similar spectral and analytical data, among them the structure of **3g** was confirmed by single crystal X-ray diffraction studies and was depicted in ORTEP diagram (Fig. 2) [13].

The structural elucidation of the compounds, **3a-g** were provided by ^{1}H NMR, ^{13}C NMR, Mass spectral studies and elemental analysis. The structural assignments were made by NMR analysis by considering compound, **5a** as the representative compound among the series. In ^{1}H NMR spectra, two methylene protons designated as C_3-H_a and C_3-H_b of the newly formed pyrazoline ring is diastereotopic. The C_3-H_a, C_3-H_b and C_2-H protons appeared as a doublet of doublets. The doublet of doublet for C_3-H_a appeared in the region δ 2.990.3.147 (J = 6.7, 13.6 Hz) ppm; doublet of doublet for C_3-H_b appeared in the region δ 3.660-3.738 (J = 6.8, 14.8 Hz) ppm and that of C_2-H in the region δ 5.432-5.502 (J = 7.6, 15.2Hz) ppm. Among C_3-H_a, C_3-H_b and C_2-H protons, C_2-H is the most deshielded due to its close proximity to benzene ring and electronegative nitrogen. C_2-H couples not only with C_3-H_a but also with C_3-H_b and appears as doublet of doublet instead of a triplet. A collection of signal observed singlet for nine protons at δ 3.852 ppm and as multiplet for twelve protons in the region δ 7.218–7.965 ppm were assigned to OCH_3 and aromatic protons respectively.

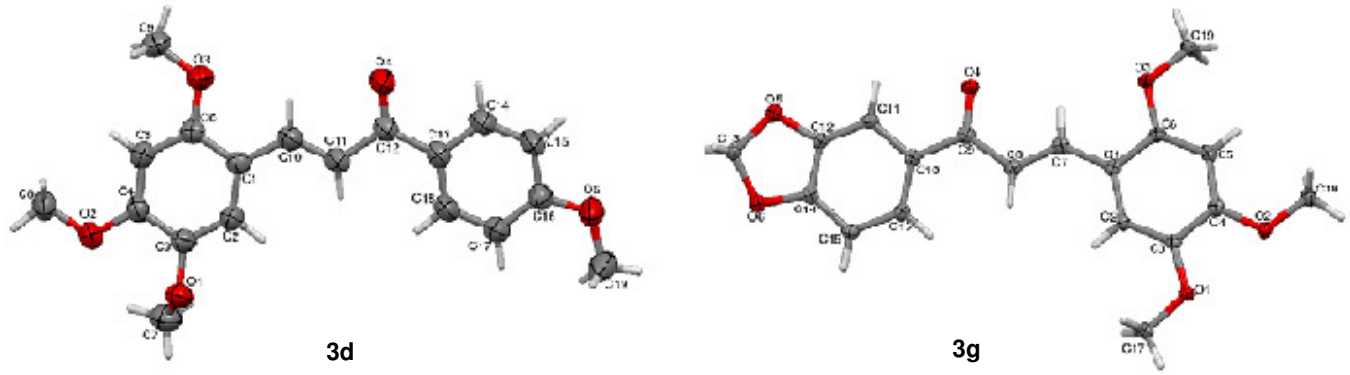
In ^{13}C NMR spectrum, compound **3d** showed a signal at δ 39.56, 53.08 and 152.66 ppm due to C-2, C-3 amd C-4 carbons of the pyrazole ring. A signal appeared for three carbons at δ 55.75 ppm was assigned to three OCH_3 carbons. An array of signals appeared at δ 99.98, 112.95, 115.92, 120.80, 122.50, 128.37, 128.90, 129.44, 131.20, 135.56, 140.26, 142.88, 147.71, 148.94 and 154.12 ppm were ambiguously assigned to aromatic carbons. Compound **3d** showed M^+ ion peak corresponding to its molecular mass and a base peak corresponds to *m/z* (M-1). Further elemental analysis showed that the analytical data obtained for the compound were in good agreement with theoretically calculated values. Similar and consistent pattern signals were observed in the ^{1}H NMR, ^{13}C NMR and Mass spectra of the synthesized series of compounds **3b-g**, which strongly supports the structure proof for the synthesized compounds.

Antimicrobial activity: Antimicrobial studies of synthesized compounds **3a-g** and **5a-g** were assessed by minimum inhibitory concentration (MIC) by serial dilution method [14,15]. The compounds were screened for their antimicrobial activities against Gram-negative bacteria *Escherichia coli,* Gram-positive bacteria *Staphylococcus aureus,* fungi species *Aspergillus nigar* and *Aspergillus flavus.* The experiments were carried out in triplicate; the results were taken as a mean of three determinations. The antibiotics ciprofloxacin and nystatin were used as standard drugs for antibacterial and antifungal studies respectively. The results of MIC's were tabulated in Table-1.

The synthesized chalcones (**3a-g**) and pyrazoles (**5a-g**) exerted a wide range of *in vitro* antimicrobial activities against the tested organisms. Results of the study reveal that the target pyrazole derivatives (**5a-g**) exerted increased antimicrobial susceptibilities in comparison to their intermediate chalcones (**3a-g**) against all the tested organisms. Among the synthesized series, compounds **3c** and **5c** having chloro substitution showed a greater activity against all the tested species. Compounds **3d**, **3e**, **3f**, **5d**, **5e** and **5f** with methoxy substitutions in the aromatic ring found moderately active; while compounds **3g**, **5b** and **5g** showed good activities and compounds **3a** and **3b** exhibited promising inhibitory activities against the tested organisms.

Conclusion

The simple easy accessible procedure for the synthesis of pyrazoles *via* Claisen-Schimidt condensation of aromatic aldehydes and ketones and their *in vitro* antimicrobial activity



3d **3g**

Fig. 2. ORTEP diagram of **3d** and **3g** with 50 % probability ellipsoids

TABLE-1
ANTIMICROBIAL ACTIVITIES OF THE COMPOUNDS **3a-g** AND **5a-g** AGAINST BACTERIAL AND FUNGAL STAINS

Compound	Minimum inhibitory concentration (MIC's) (µg/mL)*			
	S. aureus	*E. coli*	*A. niger*	*A. flavus*
3a	75.0	75.0	25.0	50
3b	50.0	75.0	25.0	50
3c	25.0	25.0	12.5	25
3d	100.0	125.0	50.0	75
3e	100.0	125.0	50.0	75
3f	100.0	125.0	50.0	75
3g	50.0	25.0	25.0	50
5a	50.0	25.0	25.0	25
5b	25.0	25.0	12.5	25
5c	12.5	12.5	12.5	25
5d	50.0	50.0	25.0	50
5e	50.0	50.0	25.0	50
5f	50.0	50.0	25.0	50
5g	25.0	12.5	25.0	25
Ciprofloxacin	25.0	12.5	–	–
Nystatin	–	–	12.5	25

*The results are expressed as mean of three determinations (n = 3).

results revealed the significance of the study. The synthesized compounds exhibited moderate to good antimicrobial activity against the tested microorganisms, compounds having chloro substituents in the aromatic ring demonstrated potent antimicrobial activity. The SAR study of the synthesized compounds remains the topic of interest.

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