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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

# Synthesis and antimicrobial activity of some heterocyclic compounds bearing benzimidazole and pyrazoline motifs

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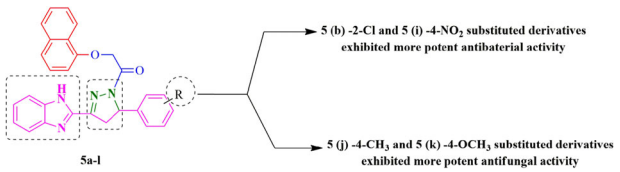
**Abstract** A series of 1-(3-(1*H*-benzoimidazol-2-yl)-5-aryl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalene-1-yloxy)ethanones (**5a–l**) are synthesized and evaluated their antimicrobial activity against gram positive (*S. aureus and S. pyogenes*), gram negative bacteria (*E. coli and P. aeruginosa*), and strains of fungi (*C. albicans, A. niger*, and *A. clavatus*). Compounds were characterized by spectroscopic techniques such as $^{1}$H NMR, $^{13}$C NMR, IR, and mass spectroscopy. The newly synthesized compounds **5b**, **5i** and **5j**, **5k** showed significant antimicrobial activity against tested microorganisms.

## Graphical abstract




**Keywords** Pyrazoline · Benzimidazole · Antimicrobial activity · Antibacterial activity · Antifungal activity

**Electronic supplementary material** The online version of this article (doi:10.1007/s00044-017-2040-5) contains supplementary material, which is available to authorized users.

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## Introduction

Bacteria and fungi have developed resistance strains against currently available antimicrobial agents and therefore it is essential for medicinal chemists to design and synthesize novel antimicrobial agents having less toxicity and more potent effects in much lesser time. In continuation to this, chemists have successfully synthesized effective agents based on heterocyclic compounds. The shining examples are furamizole, nasapadil, tazobactam, and cefatrizine. Benzimidazoles have various types of pharmacological effects, including antimicrobial (Sekar et al. 2016), anthelmatics (Mckellar and Scott 1990), and antiprolifretive (Garuti et al. 2000). Numerous examples show that benzimidazole and its derivatives play an important role in development of antimicrobial agents. Benzimidazole derivatives have been synthesized by the condensation of o-phenylenediamine with acids, their nitriles, imidates and orthoesters (Alaqeel 2017).

Our research group has previously synthesized benzimidazole derivatives and we have received some exiting antimicrobial results (Desai et al. 2014a, b). Therefore, we have focused on benzimidazole-based pyrazoline derivatives which possess diverse chemical structures. These hybrid structures may be useful for the development of antimicrobial agents. The development of efficient preparation of benzimidazole-based pyrazoline played a key role in modern organic synthesis. The pyrazoline scaffold displays important biological activities such as antioxidant (Padmaja et al. 2011), analgesic (Gawad et al. 2012), anti-inflammatory (Kumar et al. 2015), anti-infective (Desai et al. 2014a, b), anti-HIV (Fernandez et al. 2014), antiviral (Ouyang et al. 2008), antidepressant (Kaplancikli et al. 2010), antitumor (Lesyk et al. 2012), and antitubercular (Pathak et al. 2012, Khunt et al. 2012). Mebendazole

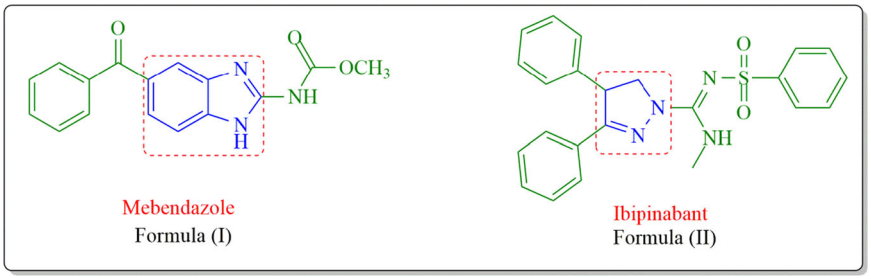
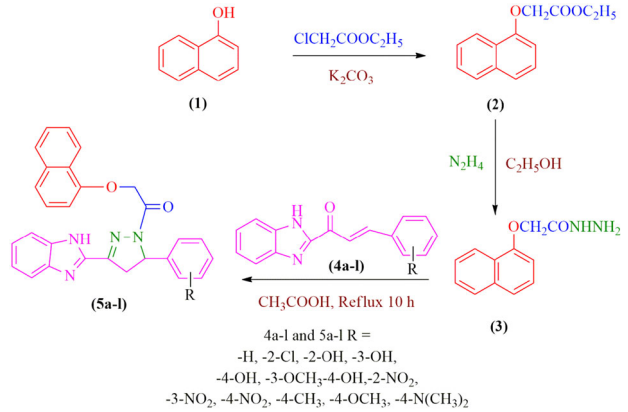



**Fig. 1** Benzimidazole and pyrazoline containing marketed drugs

[Formula (I)] (Ingle and Magar 2011) and ibipinabant [Formula (II)] (Desai et al. 2013) both are well known drugs available in the market (Fig. 1). In the present paper, we have clubbed benzimidazole and pyrazoline moieties in one molecular structure for the synthesis of more potential antimicrobial agents. We have synthesized a series of 1-(3-(1*H*-benzoimidazol-2-yl)-5-aryl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalene-1-yloxy)ethanones (**5a–l**). The structures of targeted compounds were characterized on the basis of $^{13}C$ nuclear magnetic resonance (NMR), $^{1}H$ NMR, infrared (IR), and mass spectroscopy. These derivatives exhibited antimicrobial activity on various strains of bacteria and fungi.




**Scheme 1** Synthetic pathway of compounds (**5a–l**)

## Experimental

### Materials and methods

For determination of melting point open capillary method was used. Thin layer chromatography (TLC) on silica gel plates was used for reaction monitoring. Percentage of C, H, and N was checked by a Perkin-Elmer 2400 CHN analyzer. IR spectra of all compounds were recorded on a Shimadzu IR Prestige-21 (CE) Fourier transform infrared spectrophotometer in KBr; the frequencies were reported in $cm^{-1}$. $^{1}H$ NMR spectra were carried out on Varian Gemini 400 MHz and $^{13}C$ NMR spectra on Varian Mercury 400, 100 MHz in this dimethyl sulfoxide (DMSO)-$d_6$ as a used solvent, and tetramethylsilane used as a internal standard. $^{1}H$ data were given in multiplicity (s, singlet; d, doublet; t, triplet; m, multiple) and chemical shifts were interpreting in $\delta$ ppm. Mass spectroscopic data were scanned on a Shimadzu LCMS 2010 spectrometer. Büchi Rota vapor was used for the distillation.

### Chemistry

The synthesized compounds (**5a–l**) were prepared in four steps. Compound (**2**) was synthesized from a mixture of α-napthol, ethylchloro acetate, and refluxed in water bath. Dry acetone used as a solvent and anhydrous $K_2CO_3$ used as a catalyst. In second step, compound (**2**) and hydrazine hydrate was refluxed in ethanol to yield intermediate *N*-amino-2-napthyloxyacetamide (**3**). In the final step, intermediate (**3**) and 1-(1*H*-benzoimidazol-2-yl)-3-arylprop-2en-1-ones (**4a–l**) were refluxed in acetic acid and cyclised to furnished final compounds (**5a–l**)(Scheme 1).

*Synthesis of ethyl 2-naphthyloxyacetate (**2**), N-amino-2-napthyloxyacetamide (**3**) and 1-(1*H*-benzoimidazol-2-yl)-3-arylprop-2-en-1-ones (**4a–l**)*

Compound ethyl-2-naphthyloxyacetate (**2**) and *N*-amino-2-napthyloxyacetamide (**3**) were prepared according to the method of (Rokade and Dongare 2010; Kumar et al. 2012). Similarly 1-(1*H*-benzoimidazol-2-yl)-3-arylprop-2-en-1-ones were also prepared (Behera et al. 2016).

*Synthesis of 1-(3-(1H-benzoimidazol-2-yl)-5-aryl-4-5dihydro-1H-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanones (**5**)*

A mixture of 1-(1*H*-benzoimidazol-2-yl)-3-phenylprop-2-en-1-one (**4**) (0.001 mol) and compound (**3**) (0.002 mol) were taken in 20 ml glacial acetic acid and refluxed at 130 °C for a period of 10 h. The mixture was concentrated under vacuum and diluted with ice cold water. On completion of the reaction, purity of compounds were checked by TLC using hexane-ethyl acetate (8:2 v/v) as mobile

phase and developed in an iodine chamber. All compounds (**5a–l**) of this series were prepared using the same method.

1-(3-(1*H*-benzoimidazol-2-yl)-5-phenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5a**) Off white (MeOH) (yield 64%) mp 219–222 °C; IR (KBr, $cm^{-1}$): 3442 (N–H stretching, secondary amine), 3060 (C–H stretching, aromatic ring), 2928 (C–H stretching, $–CH_2$ group), 1680 (C=O stretching, aromatic ketone), 1500 (–C=N stretching aromatic ring), 1457 (C=C stretching, aromatic ring), 1230, 1120 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.73$ (s, 1H, –N<u>H</u>), 6.54–8.51 (m, 16H, Ar–<u>H</u>), 5.23 (d, $J_{AC} = 3.09$ Hz, $J_{BC} = 11.08$ Hz, 1H, >CH–$H_C$), 4.92 (d, $J_{AB} = 17.41$ Hz, $J_{BC} = 11.02$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 4.74 (s, 2H, –O–C<u>H</u>$_2$–), 3.64 (d, $J_{AB} = 17.48$ Hz, $J_{AC} = 3.07$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 169.7$ (>C=O), 156.4 (1C, $C_1$ naphthalene ring), 155.1 (1C, $C_3$ pyrazoline ring), 151.7 (1C, $C_2$ benzimidazole ring), 141.1 (1C, $C_1$ aromatic ring), 134.4 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.8 (1C, $C_9$ naphthalene ring), 134.7 (1C, $C_{10}$ naphthalene ring), 128.3 (1C, $C_3$ and $C_5$ aromatic ring), 127.1 (1C, $C_5$ naphthalene ring), 126.0 (1C, $C_6$ naphthalene ring), 126.4 (1C, $C_3$ naphthalene ring), 126.6 (1C, $C_4$ aromatic ring), 126.7 (2C, $C_2$ and $C_6$ aromatic ring), 125.0 (1C, $C_7$ naphthalene ring), 123.8 (1C, $C_8$ naphthalene ring), 123.1 (2C, $C_6$ and $C_5$ benzimidazole ring), 120.7 (1C, $C_4$ naphthalene ring), 115.6 (2C, $C_7$ and $C_4$ benzimidazole ring), 107.0 (1C, $C_2$ naphthalene ring), 67.7 (1C, –O–$CH_2$–), 66.3 (1C, $C_5$ pyrazoline ring), 39.0 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 446.02 ($M^+$); anal. calcd. for ($C_{28}H_{22}N_4O_2$): C, 75.32; H, 4.97; N, 12.55%; found: C, 75.40; H, 5.10; N, 12.62%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(2-chlorophenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5b**) Brown solid (MeOH) (yield 70%) mp 195–197 °C; IR (KBr, $cm^{-1}$): 3440 (N–H stretching, secondary amine), 3063 (C–H stretching, aromatic ring), 2923 (C–H stretching, $–CH_2$ group), 1683 (C=O stretching, aromatic ketone), 1504 (–C=N stretching aromatic ring), 1456 (C=C stretching, aromatic ring), 1231, 1122 (C–O–C stretching), 895 (C–Cl stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.85$ (s, 1H, –N<u>H</u>), 6.42–8.42 (m, 15H, Ar–<u>H</u>), 5.21 (d, $J_{AC} = 3.10$ Hz, $J_{BC} = 11.05$ Hz, 1H, >CH–$H_C$), 4.74 (s, 2H, –O–C<u>H</u>$_2$–), 3.70 (d, $J_{AB} = 17.42$ Hz, $J_{BC} = 11.09$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.22 (d, $J_{AB} = 17.43$ Hz, $J_{AC} = 3.05$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 169.3$ (>C=O), 156.1 (1C, $C_1$ naphthalene ring), 155.7 (1C, $C_3$ pyrazoline ring), 151.4 (1C, $C_2$ benzimidazole ring), 138.4 (1C, $C_1$ aromatic ring), 134.1 (1C, $C_9$ naphthalene ring), 134.2 (1C, $C_{10}$ naphthalene ring), 134.9 (2C, $C_8$ and $C_9$ benzimidazole ring), 132.4 (1C, $C_6$ aromatic ring), 128.6 (1C, $C_3$ aromatic ring), 128.3 (1C, $C_4$ aromatic ring), 128.0 (1C, $C_5$ aromatic ring), 127.3 (1C, $C_5$ naphthalene ring), 126.2 (2C, $C_3$ aromatic ring and $C_6$ naphthalene ring), 126.9 (1C, $C_3$ naphthalene ring), 125.5 (1C, $C_7$ naphthalene ring), 123.8 (1C, $C_8$ naphthalene ring), 123.2 (2C, $C_5$ and $C_6$ benzimidazole ring), 120.7 (1C, $C_5$ naphthalene rig), 115.9 (2C, $C_7$ and $C_4$ benzimidazole ring), 107.8 (1C, $C_2$ naphthalene ring), 67.9 (1C, –$OCH_2$–), 61.6 (1C, $C_4$ pyrazoline ring), 39.0 (1C, $C_5$ pyrazoline ring); MS (*m/z*): 480.1 ($M^+$); anal. calcd. for ($C_{28}H_{21}ClN_4O_2$): C, 69.92; H, 4.40; N, 11.65%; found: C, 69.98; H, 4.48; N, 11.75%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(2-hydroxyphenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5c**) Yellowish white (MeOH) (yield 66%) mp 144–147 °C; IR (KBr, $cm^{-1}$): 3444 (N–H stretching, secondary amine), 3390 (O–H stretching), 3065 (C–H stretching, aromatic ring), 2925 (C–H stretching, $–CH_2$ group), 1681 (C=O stretching, aromatic ketone), 1508 (–C=N stretching aromatic ring), 1452 (C=C stretching, aromatic ring), 1232, 1124 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.81$ (s, 1H, –N<u>H</u>), 6.45–8.40 (m, 15H, Ar–<u>H</u>), 5.32 (s, 1H, –O<u>H</u>), 5.25 (d, $J_{AC} = 3.11$ Hz, $J_{BC} = 11.04$ Hz, 1H, >CH–$H_C$), 4.75 (s, 2H, –O–C<u>H</u>$_2$–), 3.74 (d, $J_{AB} = 17.40$ Hz, $J_{BC} = 11.11$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.25 (d, $J_{AB} = 17.40$ Hz, $J_{AC} = 3.04$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 169.3$ (1C, >C=O), 156.7 (1C, $C_1$ naphthalene ring), 155.1 (1C, $C_3$ pyrazoline ring), 154.3 (1C, $C_2$ aromatic ring), 151.8 (1C, $C_2$ benzimidazole ring), 134.4 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.0 (1C, $C_9$ naphthalene ring), 134.7 (1C, $C_{10}$ naphthalene ring), 130.1 (1C, $C_1$ aromatic ring), 128.4 (1C, $C_4$ aromatic ring), 127.9 (1C, $C_4$ naphthalene ring), 126.8 (1C, $C_6$ naphthalene ring), 126.7 (1C, $C_2$ aromatic ring), 126.0 (1C, $C_3$ naphthalene ring), 125.4 (1C, $C_7$ naphthalene ring), 123.4 (2C, $C_5$ and $C_6$ benzimidazole ring), 121.4 (1C, $C_3$ aromatic ring), 120.4 (1C, $C_4$ naphthalene ring), 115.4 (2C, $C_4$ and $C_7$ benzimidazole), 107.1 (1C, $C_2$ naphthalene ring), 67.3 (1C, –$OCH_2$–), 66.8 (1C, $C_5$ pyrazoline ring), 39.4 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 462.7 ($M^+$); anal. calcd. for ($C_{28}H_{22}N_4O_3$): C, 72.71; H, 4.79; N, 12.11%; found: C, 72.80; H, 4.81; N, 12.15%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(3-hydroxyphenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5d**) Yellow (MeOH) (yield 69%) mp 224–227 °C; IR (KBr, $cm^{-1}$): 3448 (N–H stretching, secondary amine), 3395 (O–H stretching), 3069 (C–H stretching, aromatic ring), 2929 (C–H stretching, $–CH_2$ group), 1686 (C=O stretching, aromatic ketone),

1510 (–C=N stretching aromatic ring), 1455 (C=C stretching, aromatic ring), 1235, 1126 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.77$ (s, 1H, –N<u>H</u>), 6.48–8.49 (m, 15H, Ar–<u>H</u>), 5.38 (s, 1H, –O<u>H</u>), 5.20 (d, $J_{AC} = 3.13$ Hz, $J_{BC} = 11.04$ Hz, 1H, >CH–$H_C$), 3.78 (d, $J_{AB} = 17.41$ Hz, $J_{BC} = 11.12$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 4.80 (s, 2H, –O–C<u>$H_2$</u>–), 3.29 (d, $J_{AB} = 17.43$ Hz, $J_{AC} = 3.01$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 169.3$ (1C, >C=O), 156.0 (1C, $C_1$ naphthalene ring), 155.3 (1C, $C_3$ pyrazoline ring), 151.6 (1C, $C_2$ benzimidazole ring), 142.8 (1C, $C_1$ aromatic ring), 134.9 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.6 (1C, $C_9$ naphthalene ring), 134.5 (1C, $C_{10}$ naphthalene ring), 127.0 (1C, $C_5$ naphthalene ring), 126.9 (1C, $C_6$ naphthalene ring), 126.8 (1C, $C_3$ naphthalene ring), 125.0 (1C, $C_7$ naphthalene ring), 123.8 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.2 (1C, $C_8$ naphthalene ring), 120.7 (1C, $C_4$ naphthalene ring), 119.1 (1C, $C_2$ aromatic ring), 115.0 (2C, $C_4$ and $C_7$ benzimidazole ring), 113.0 (1C, $C_4$ aromatic ring), 112.4 (1C, $C_6$ aromatic ring), 107.4 (1C, $C_2$ naphthalene ring), 67.0 (1C, –$OCH_2$–), 66.4 (1C, $C_5$ pyrazoline ring), 39.0 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 462.7 ($M^+$); anal. calcd. for ($C_{28}H_{22}N_4O_3$): C, 72.71; H, 4.79; N, 12.11%; found: C, 72.81; H, 4.84; N, 12.19%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-hydroxy-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5e**) Buff (MeOH) (yield 61%) mp 168–171 °C; IR (KBr, $cm^{-1}$): 3449 (N–H stretching, secondary amine), 3397 (O–H stretching), 3070 (C–H stretching, aromatic ring), 2926 (C–H stretching, –$CH_2$ group), 1685 (C=O stretching, aromatic ketone), 1509 (–C=N stretching aromatic ring), 1457 (C=C stretching, aromatic ring), 1238, 1127 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.74$ (s, 1H, –N<u>H</u>), 6.44–8.42 (m, 15H, Ar–<u>H</u>), 5.35 (s, 1H, –O<u>H</u>), 5.23 (d, $J_{AC} = 3.14$ Hz, $J_{BC} = 11.02$ Hz, 1H, >CH–$H_C$), 4.85 (s, 2H, –O–C<u>$H_2$</u>–), 3.74 (d, $J_{AB} = 17.42$ Hz, $J_{BC} = 11.11$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.25 (d, $J_{AB} = 17.45$ Hz, $J_{AC} = 3.00$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 169.2$ (1C, >C=O), 156. 5 (1C, $C_4$ aromatic ring), 156.2 (1C, $C_1$ naphthalene ring), 155.4 (1C, $C_3$ pyrazoline ring), 151.9 (1C, $C_2$ benzimidazole ring), 134.8 (1C, $C_1$ aromatic ring), 134.2 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.9 (1C, $C_9$ naphthalene ring), 134.7 (1C, $C_{10}$ naphthalene ring), 127.0 (2C, $C_2$ and $C_6$ aromatic ring), 127.5 (1C, $C_5$ naphthalene ring), 126.3 (1C, $C_6$ naphthalene ring), 126.0 (1C, $C_3$ naphthalene ring), 125.4 (1C, $C_7$ naphthalene ring), 123.4 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.0 (1C, $C_8$ naphthalene ring), 120.1 (1C, $C_4$ naphthalene ring), 115.9 (2C, $C_7$ and $C_4$ benzimidazole ring), 115.0 (2C, $C_3$ and $C_5$ aromatic ring), 107.1 (1C, $C_2$ naphthalene ring), 67.7 (1C, –$OCH_2$–), 66.0 (1C, $C_5$ pyrazoline ring), 39.7 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 462.9 ($M^+$); anal. calcd. for ($C_{28}H_{22}N_4O_3$): C, 72.71; H, 4.79; N, 12.11%; Found: C, 72.80; H, 4.88; N-12.19%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-hydroxy-3-methoxyphenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5f**) Brown (MeOH) (yield 65%) mp 182–185 °C; IR (KBr, $cm^{-1}$): 3452 (N–H stretching, secondary amine), 3400 (O–H stretching), 3075 (C–H stretching, aromatic ring), 2930 (C–H stretching, –$CH_2$ group), 2820 (C–H stretching, –$OCH_3$ group), 1689 (C=O stretching, aromatic ketone), 1506 (–C=N stretching aromatic ring), 1459 (C=C stretching, aromatic ring), 1231, 1129 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.70$ (s, 1H, –N<u>H</u>), 6.49–8.46 (m, 14H, Ar–<u>H</u>), 5.35 (s, 1H, –O<u>H</u>), 5.26 (d, $J_{AC} = 3.19$ Hz, $J_{BC} = 11.09$ Hz, 1H, >CH–$H_C$), 4.86 (s, 2H, –O–C<u>$H_2$</u>–), 3.85 (s, 3H, –OC<u>$H_3$</u>), 3.78 (d, $J_{AB} = 17.46$ Hz, $J_{BC} = 11.17$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.26 (d, $J_{AB} = 17.49$ Hz, $J_{AC} = 3.01$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta = 169.0$ (1C, >C=O), 156.7 (1C, $C_1$ naphthalene ring), 155.7 (1C, $C_3$ pyrazoline ring), 151.7 (1C, $C_2$ benzimidazole ring), 147.0 (1C, $C_3$ aromatic ring), 146.0 (1C, $C_4$ aromatic ring), 134.4 (1C, $C_1$ aromatic ring), 139.0 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.2 (1C, $C_9$ naphthalene ring), 134.7 (1C, $C_{10}$ naphthalene ring), 127.0 (1C, $C_5$ naphthalene ring), (2C, $C_2$ and $C_6$ aromatic ring), 126.7 (1C, $C_6$ naphthalene ring), 126.4 (1C, $C_3$ naphthalene ring), 127.0 (1C, $C_7$ naphthalene ring), 123.8 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.4 (1C, $C_8$ naphthalene ring), 120.9 (1C, $C_4$ naphthalene ring), 115.8 (2C, $C_7$ and $C_4$ benzimidazole ring), 119.0 (1C, $C_6$ aromatic ring), 115.7 (1C, $C_3$ aromatic ring), 110.7 (1C, $C_2$ aromatic ring), 107.7 (1C, $C_2$ naphthalene ring), 67.0 (1C, –$OCH_2$–), 66.0 (1C, $C_5$ pyrazoline ring), 56.7 (1C, –$OCH_3$) 39.0 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 492.5 ($M^+$); anal. calcd. for ($C_{29}H_{24}N_4O_4$): C, 70.72; H, 4.91; N, 11.38%; found: C, 70.82; H, 4.95; N, 11.45%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(2-nitrophenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5g**) Dark yellow (MeOH) (yield 60%) mp 141–143 °C; IR (KBr, $cm^{-1}$): 3454 (N–H stretching, secondary amine), 3076 (C–H stretching, aromatic ring), 2932 (C–H stretching, –$CH_2$ group), 1691 (C=O stretching, aromatic ketone), 1535 (N=O stretching, aromatic ring), 1503 (–C=N stretching aromatic ring), 1463 (C=C stretching, aromatic ring), 1230, 1130 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.89$ (s, 1H, –N<u>H</u>), 6.48–8.49 (m, 15H, Ar–<u>H</u>), 5.52 (d, $J_{AC} = 3.21$ Hz, $J_{BC} = 11.06$ Hz, 1H, >CH–$H_C$), 4.78 (s, 2H, –O–C<u>$H_2$</u>–), 3.75 (d, $J_{AB} = 17.49$ Hz, $J_{BC} = 11.19$ Hz, 1H,

$C_5$-H pyrazoline $H_B$), 3.26 (d, $J_{AB} = 17.52$ Hz, $J_{AC} = 3.05$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}C$ (100 MHz, DMSO-$d_6$): $\delta = 169.0$ (1C, >C=O), 156.7 (1C, $C_1$ naphthalene ring), 155.7 (1C, $C_3$ pyrazoline ring), 151.7 (1C, $C_2$ benzimidazole ring), 147.0 (1C, $C_6$ aromatic ring), 137.0 (1C, $C_1$ aromatic ring), 134.9 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.3 (1C, $C_9$ naphthalene ring), 134.1 (1C, $C_{10}$ naphthalene ring), 134.0 (1C, $C_3$ aromatic ring), 127.4 (1C, $C_2$ aromatic ring), 127.3 (2C, $C_5$ naphthalene ring and $C_2$ aromatic ring), 127.0 (1C, $C_4$ aromatic ring), 126.7 (1C, $C_6$ naphthalene ring), 126.4 (1C, $C_3$ naphthalene ring), 125.0 (1C, $C_7$ naphthalene ring), 124.0 (1C, $C_5$ aromatic ring), 123.7 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.1 (1C, $C_8$ naphthalene ring), 120.0 (1C, $C_4$ naphthalene ring), 115.0 (2C, $C_7$ and $C_4$ benzimidazole ring), 107.9 (1C, $C_2$ naphthalene ring), 67.4 (1C, –$OCH_2$–), 61.0 (1C, $C_5$ pyrazoline ring), 38.0 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 491.2 ($M^+$); anal. calcd. for ($C_{28}H_{21}N_5O_4$): C, 68.42; H, 4.31; N, 14.25%; found: C, 68.51; H, 4.41; N, 14.33%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(3-nitrophenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5h**) Yellowish orange (MeOH) (yield 68%) mp 154–156 °C; IR (KBr, $cm^{-1}$): 3458 (N–H stretching, secondary amine), 3078 (C–H stretching, aromatic ring), 2933 (C–H stretching, –$CH_2$ group), 1690 (C=O stretching, aromatic ketone), 1530 (N=O stretching, aromatic ring), 1507 (–C=N stretching aromatic ring), 1468 (C=C stretching, aromatic ring), 1234, 1136 (C–O–C stretching); $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta = 12.80$ (s, 1H, –N<u>H</u>), 6.45–8.45 (m, 15H, Ar–<u>H</u>), 5.50 (d, $J_{AC} = 3.18$ Hz, $J_{BC} = 11.02$ Hz, 1H, >CH–$H_C$), 4.78 (s, 2H, –O–C<u>$H_2$</u>–), 3.72 (d, $J_{AB} = 17.56$ Hz, $J_{BC} = 11.15$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.20 (d, $J_{AB} = 17.54$ Hz, $J_{AC} = 3.00$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}C$ (100 MHz, DMSO-$d_6$): $\delta = 169.3$ (1C, >C=O), (1C, $C_4$ aromatic ring), 156.0 (1C, $C_1$ naphthalene ring), 155.3 (1C, $C_3$ pyrazoline ring), 151.1 (1C, $C_2$ benzimidazole ring), 147.1 (1C, $C_3$ aromatic ring), 144.0 (1C, $C_1$ aromatic ring), 134.7 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.6 (1C, $C_9$ naphthalene ring), 134.5 (1C, $C_{10}$ naphthalene ring), 133.4 (1C, $C_6$ aromatic ring), 129.4 (1C, $C_5$ aromatic ring), 127.1 (1C, $C_5$ naphthalene ring), 126.6 (1C, $C_6$ naphthalene ring), 126.0 (1C, $C_3$ naphthalene ring), 125.1 (1C, $C_7$ naphthalene ring), 123.7 (1C, $C_8$ naphthalene ring), 123.2 (2C, $C_5$ and $C_6$ benzimidazole ring), 121.2 (1C, $C_5$ aromatic ring), 120.7 (1C, $C_4$ naphthalene ring), 107.0 (1C, $C_2$ naphthalene ring), 115.8 (2C, $C_7$ and $C_4$ benzimidazole ring), 67.6 (1C, –$OCH_2$–), 65.7 (1C, $C_5$ pyrazoline ring), 39.1 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 491.5 ($M^+$); anal. calcd. for ($C_{28}H_{21}N_5O_4$): C, 68.42; H, 4.31; N, 14.25%; found: C, 68.50; H, 4.38; N, 14.31%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-nitrophenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2(napthalen-1-yloxy)ethanone **(5i)** Light orange (MeOH) (yield 62%) mp 150–152 °C; IR (KBr, $cm^{-1}$): 3457 (N–H stretching, secondary amine), 3077 (C–H stretching, aromatic ring), 2928 (C–H stretching, –$CH_2$ group), 1693 (C=O stretching, aromatic ketone), 1525 (N=O stretching, aromatic ring), 1511 (–C=N stretching aromatic ring), 1466 (C=C stretching, aromatic ring), 1240, 1139 (C–O–C stretching); $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta = 12.83$ (s, 1H, –N<u>H</u>), 6.49–8.44 (m, 15H, Ar–<u>H</u>), 5.58 (d, $J_{AC} = 3.23$ Hz, $J_{BC} = 11.07$ Hz, 1H, >CH–$H_C$), 4.72 (s, 2H, –O–C<u>$H_2$</u>–), 3.75 (d, $J_{AB} = 17.58$ Hz, $J_{BC} = 11.13$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.25 (d, $J_{AB} = 17.52$ Hz, $J_{AC} = 2.99$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}C$ (100 MHz, DMSO-$d_6$): $\delta = 169.1$ (1C, >C=O), 156.0 (1C, $C_1$ naphthalene ring), 155.0 (1C, $C_3$ pyrazoline ring), 151.0 (1C, $C_2$ benzimidazole ring), 147.4 (1C, $C_1$ aromatic ring), 145.0 (1C, $C_4$ aromatic ring), 134.7 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.3 (1C, $C_9$ naphthalene ring), 134.2 (1C, $C_{10}$ naphthalene ring), (2C, $C_2$ and $C_6$ aromatic ring), 127.0 (1C, $C_5$ naphthalene ring), 126.4 (1C, $C_6$ naphthalene ring), 126.2 (1C, $C_2$ naphthalene ring), 125.0 (1C, $C_7$ naphthalene ring), 123.7 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.4 (1C, $C_8$ naphthalene ring), 123.5 (2C, $C_2$ and $C_6$ aromatic ring), 123.2 (2C, $C_3$ and $C_5$ aromatic ring), 120.0 (1C, $C_4$ naphthalene ring), 115.2 (2C, $C_7$ and $C_4$ benzimidazole ring), 107.0, (1C, $C_2$ naphthalene ring), 67.7 (1C, –$OCH_2$–), 66.4 (1C, $C_5$ pyrazoline ring), 39.2 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 491.9 ($M^+$); anal. calcd. for ($C_{28}H_{21}N_5O_4$): C, 68.42; H, 4.31; N, 14.25%; found: C, 68.49; H, 4.40; N, 14.34%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-methylphenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5j**) Pale yellow (MeOH) (yield 60%) mp 190–192 °C; IR (KBr, $cm^{-1}$): 3453 (N–H stretching, secondary amine), 3079 (C–H stretching, aromatic ring), 2930 (C–H stretching, –$CH_2$ group), 2889 (C–H stretching, –$CH_3$ group), 1694 (C=O stretching, aromatic ketone), 1512 (–C=N stretching aromatic ring), 1471 (C=C stretching, aromatic ring), 1239, 1141 (C–O–C stretching); $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta = 12.89$ (s, 1H, –N<u>H</u>), 6.48–8.48 (m, 15H, Ar–<u>H</u>), 5.60 (d, $J_{AC} = 3.20$ Hz, $J_{BC} = 11.01$ Hz, 1H, >CH–$H_C$), 4.75 (s, 2H, –O–C<u>$H_2$</u>–), 3.78 (d, $J_{AB} = 17.54$ Hz, $J_{BC} = 11.14$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.20 (d, $J_{AB} = 17.57$ Hz, $J_{AC} = 3.06$ Hz, 1H, $C_4$-H pyrazoline $H_A$), 2.40 (s, 3H, –C<u>$H_3$</u>); $^{13}C$ (100 MHz, DMSO-$d_6$): $\delta = 169.7$ (1C, >C=O), 156.0 (1C, $C_1$ naphthalene ring), 155.8 (1C, $C_3$ pyrazoline ring), 151.0 (1C, $C_2$ benzimidazole ring), 138.4 (1C, $C_1$ aromatic ring), (1C, $C_4$ aromatic ring), 134.8 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.8 (1C, $C_9$ naphthalene ring), 134.2 (1C, $C_{10}$ naphthalene ring), 128.4 (2C, $C_3$ and $C_5$ aromatic ring),

127.4 (1C, $C_5$ naphthalene ring), 126.7 (1C, $C_6$ naphthalene ring), 126.5 (1C, $C_3$ naphthalene ring), 125.4 (1C, $C_7$ naphthalene ring), 125.2 (2C, $C_3$ and $C_5$ aromatic ring), 123.4 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.1(1C, $C_8$ naphthalene ring), 120.4 (1C, $C_4$ naphthalene ring), 115.1 (2C, $C_7$ and $C_4$ benzimidazole ring), 107.2 (1C, $C_2$ naphthalene ring), 67.1 (1C, –$OCH_2$–), 66.7 (1C, $C_5$ pyrazoline ring), 39.9 (1C, $C_4$ pyrazoline ring), 21.4 (1C, –$CH_3$); MS (*m/z*): 460.7 ($M^+$); anal. calcd. for ($C_{29}H_{24}N_4O_2$): C, 75.63; H, 5.25; N, 12.17%; found: C, 75.74; H, 5.36; N, 12.26%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-methoxyphenyl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5k**) Brown (MeOH) (yield 65%) mp 242–244 °C; IR (KBr, $cm^{-1}$): 3454 (N–H stretching, secondary amine), 3080 (C–H stretching, aromatic ring), 2927 (C–H stretching, –$CH_2$ group), 2888 (C–H stretching, –$OCH_3$ group), 1695 (C=O stretching, aromatic ketone), 1514 (–C=N stretching aromatic ring), 1468 (C=C stretching, aromatic ring), 1245, 1138 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.85$ (s, 1H, –N<u>H</u>), 6.43–8.38 (m, 15H, Ar–<u>H</u>), 5.62 (d, $J_{AC} = 3.26$ Hz, $J_{BC} = 11.05$ Hz, 1H, >CH–$H_C$), 4.83 (s, 2H, –O–C<u>$H_2$</u>–), 3.89 (s, 3H, –OC<u>$H_3$</u>), 3.58 (d, $J_{AB} = 17.62$ Hz, $J_{BC} = 11.18$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.12 (d, $J_{AB} = 17.50$ Hz, $J_{AC} = 3.10$ Hz, 1H, $C_4$-H pyrazoline $H_A$); $^{13}$C (100 MHz, DMSO-$d_6$,): $\delta = 169.6$ (1C, >C=O), 158.4 (1C, $C_4$ aromatic ring), 156.4 (1C, $C_1$ naphthalene ring), 155.1 (1C, $C_3$ pyrazoline ring), 151.8 (1C, $C_2$ benzimidazole ring), 147.1 (1C, $C_3$ aromatic ring), (1C, $C_1$ aromatic ring), 134.0 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.8 (1C, $C_9$ naphthalene ring), 134.5 (1C, $C_{10}$ naphthalene ring), 127.0 (1C, $C_5$ aromatic ring), 127.1 (1C, $C_5$ naphthalene ring), 126.1 (1C, $C_6$ naphthalene ring), 126.0 (1C, $C_6$ aromatic ring), 126.0 (1C, $C_3$ naphthalene ring), 125.7 (1C, $C_7$ naphthalene ring), 123.7 (1C, C8 naphthalene ring), 123.4 (2C, $C_5$ and $C_6$ benzimidazole ring), 120.4 (1C, $C_4$ naphthalene ring), 115.1 (2C, $C_7$ and $C_4$ benzimidazole ring), 114.4 (1C, $C_3$ aromatic ring), 107.3 (1C, $C_2$ naphthalene ring), 67.4 (1C, –$OCH_2$–), 66.4 (1C, $C_5$ pyrazoline ring), 55.1 (1C, –$OCH_3$), 39.3 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 476.5 ($M^+$); anal. calcd. for ($C_{29}H_{24}N_4O_3$): C, 73.09; H, 5.08; N, 11.76%; found: C, 73.14, H, 5.11; N, 11.85%.

Physical constant and characterization 1-(3-(1*H*-benzoimidazol-2-yl)-5-(4-(dimethylamino)phenyl)-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanone (**5l**) Brownish yellow (MeOH) (yield 63%) mp 170–172 °C; IR (KBr, $cm^{-1}$): 3458 (N–H stretching, secondary amine), 3086 (C–H stretching, aromatic ring), 2925 (C–H stretching, –$CH_2$ group), 2886 (C–H stretching, –$CH_3$ group), 1690 (C=O stretching, aromatic ketone), 1515 (–C=N stretching aromatic ring), 1473 (–C=C stretching, aromatic ring), 1247, 1133 (C–O–C stretching); $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 12.85$ (s, 1H, –N<u>H</u>), 6.50–8.47 (m, 15H, Ar–<u>H</u>), 5.63 (d, $J_{AC} = 3.24$ Hz, $J_{BC} = 11.03$ Hz, 1H, >CH–$H_C$), 4.79 (s, 2H, –O–C<u>$H_2$</u>–), 3.81 (d, $J_{AB} = 17.61$ Hz, $J_{BC} = 11.20$ Hz, 1H, $C_5$-H pyrazoline $H_B$), 3.26 (d, $J_{AB} = 17.53$ Hz, $J_{AC} = 3.07$ Hz, 1H, $C_4$-H pyrazoline $H_A$), 3.08 (s, 6H, –N (C<u>$H_3$</u>)$_2$); $^{13}$C (100 MHz, DMSO-$d_6$): $\delta = 169.3$ (1C, >C=O), 156.2 (1C, $C_1$ naphthalene ring), 155.2 (1C, $C_3$ pyrazoline ring), 151.1 (1C, $C_2$ benzimidazole ring), 149.2 (1C, $C_4$ aromatic ring), 134.5 (2C, $C_8$ and $C_9$ benzimidazole ring), 134.8 (1C, C9 naphthalene ring), 134.9 (1C, $C_{10}$ naphthalene ring), 131.5 (1C, $C_1$ aromatic ring), 129.3 (2C, $C_2$ and $C_6$ aromatic ring), 129.6 (2C, $C_2$ and $C_6$ aromatic ring), 127.5 (1C, $C_7$ naphthalene ring), 127.7 (1C, $C_5$ naphthalene ring), 126.4 (1C, $C_6$ naphthalene ring), 126.1 (1C, $C_3$ naphthalene ring), 125.5 (1C, $C_7$ aromatic ring), 123.3 (2C, $C_5$ and $C_6$ benzimidazole ring), 123.0 (1C, $C_8$ naphthalene ring), 120.1 (1C, $C_4$ naphthalene ring), 115.5 (2C, $C_7$ and $C_4$ benzimidazole ring), 112.5 (2C, $C_3$ and $C_5$ aromatic ring), 107.5 (1C, $C_2$ naphthalene ring), 67.1 (1C, –$OCH_2$–), 66.7 (1C, $C_5$ pyrazoline ring), 41.7 (2C, –$CH_3$) 39.4 (1C, $C_4$ pyrazoline ring); MS (*m/z*): 489.2 ($M^+$); anal. calcd. for ($C_{30}H_{27}N_5O_2$): C, 73.60; H, 5.56; N, 14.31%; found: C, 73.71; H, 5.61; N, 14.38%.

## Biological evaluation

### *Antimicrobial screening assay*

1-(3-(1*H*-benzoimidazol-2-yl)-5-aryl-4-5dihydro-1*H*-pyrazol-1-yl)-2-(napthalen-1-yloxy)ethanones (**5a–l**) were screened for their antibacterial activity against *Escherichia coli* (MTCC-442), *Pseudomonas aeruginosa* (MTCC-441), *Staphylococcus aureus* (MTCC-96), and *Streptococcus pyogenes* (MTCC-443). MICs of the titled compounds were compared with ampicillin (for bacteria) and griseofulvin (for fungi) was standards and the results are displayed in Table 1. Antifungal activity was screened against three fungi *Candida albicans* (MTCC-227), *Aspergillus niger* (MTCC-282) and *Aspergillus clavatus* (MTCC-1323). Titled compounds were screened in six sets against bacteria and fungi. The MIC of titled compounds was determined as per the National Committee for Clinical Laboratory Standards protocol using Mueller-Hinton Broth (Becton-Dickinson, USA) dilution method (Rattan 2000).

### *Antibacterial activity*

The data of compounds **5a–l** are displayed in Table 1. The data of antibacterial activity clearly showed that compound **5i** (-4-$NO_2$) exhibited very good activity (MIC = 25 µg/ml) against *E. coil, S. aureus,* and *S. pyogenes* and showed

**Table 1** Antibacterial and antifungal activity of compounds (**5a–l**)

| Sr. no. | –R | Minimum bactericidal concentrations ($MIC_B$) in µg/ml | | | | Minimum fungicidal concentrations ($MIC_F$) in µg/ml | | |
|---|---|---|---|---|---|---|---|---|
| | | *E. c.* | *P. a.* | *S. a.* | *S. p.* | *C. a.* | *A. n.* | *A. c.* |
| **5a** | –H | 250 | 250 | 200 | 250 | 100 | 100 | 100 |
| **5b** | -2-Cl | 50 | 50 | 100 | 12.5 | 500 | 500 | 500 |
| **5c** | -2-OH | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| **5d** | -3-OH | 500 | 500 | 500 | 100 | 500 | 100 | >1000 |
| **5e** | -4-OH | 500 | 250 | 100 | 100 | 100 | 500 | 100 |
| **5f** | -3-$OCH_3$-4-OH | 250 | 250 | 250 | 500 | 100 | 500 | 500 |
| **5g** | -2-$NO_2$ | 500 | 250 | 500 | 500 | 500 | 100 | >1000 |
| **5h** | -3-$NO_2$ | 500 | 500 | 250 | 500 | 500 | 1000 | >1000 |
| **5i** | -4-$NO_2$ | 25 | 12.5 | 50 | 25 | 250 | 100 | 250 |
| **5j** | -4-$CH_3$ | 100 | 500 | 500 | 500 | 500 | 50 | >100 |
| **5k** | -4-$OCH_3$ | 50 | 50 | 100 | 50 | 100 | 50 | 25 |
| **5l** | -4-N$(CH_3)_2$ | 250 | 250 | 500 | 500 | 100 | 500 | 500 |
| Ampicillin | | 100 | 100 | 250 | 100 | – | – | – |
| Griseofulvin | | – | – | – | – | 500 | 100 | 100 |

*E.c.* Escherichia coli (MTCC-442), *P.a.* Pseudomonas aeruginosa (MTCC-441), *S.a.* Staphylococcus aureus (MTCC-96), *S.p.* Streptococcus pyogenes (MTCC-443), *C.a.* Candida albicans (MTCC-227), *A.n.* Asperginus niger (MTCC-282), *A.c.* Asperginus clavatus (MTCC-1323)

excellent activity (MIC = 12.5 µg/ml) against *P. aeruginosa*. Compound **5k** (-4-$OCH_3$), showed good activity (MIC = 50 µg/ml) against *E. Coil*, *P. aeruginosa,* and *S. pyogenes*. The remaining compounds of the series possessed moderate antibacterial activity against responsible bacterial strains.

*Antifungal activity*

Antifungal activity was performed using *C. albicans, A. niger,* and *A. clavatus* at various concentrations and MIC values are displayed in Table 1. Synthesized compounds were diluted to 1000 µg/ml concentration, as a stock solution. According to the screening results it was indicated that, Compounds **5j** and **5k** exhibited good antifungal activity against *A. niger* at MIC = 50 µg/ml and compound **5k** possessed very good activity against *A. clavatus* at MIC = 25 µg/ml. Other derivatives showed moderate activity against responsible fungal strains.

## Results and discussion

Characterization of newly synthesized compounds was carried out by standard spectroscopic methods. Interpretation of data was reported in the experimental section. Infrared spectrum of compound **5h** showed stretching vibration at 3458 $cm^{-1}$ indicating the presence of N–H stretching of secondary amines. The absorption band at 3078 $cm^{-1}$ indicated the presence of Ar–H stretching vibration. Stretching at 2933 $cm^{-1}$ had proved the presence of $-CH_2$ group in compound **5h**. The absorption band at 1690 $cm^{-1}$ showed the presence of a >C=O stretching vibration. Absorption bands at 1507, 1468, and 1530 $cm^{-1}$ showed the presence of >C=N, >C=C<, and –N=O– stretching of the aromatic ring. Stretching at 1136 and 1234 $cm^{-1}$ showed the presence of C–O–C bending vibrations.

The $^1$H NMR spectra of final compound **5h** showed that protons attached to C-22, gave singlet at $\delta = 4.78$ (–O–$C\underline{H}_2$–). In pyrazoline ring one proton showed chemical shift at $\delta = 5.50$ (>CH–$H_C$) as a doublet, one proton of pyrazoline $H_B$ and pyrazoline $H_A$ gave doublet of doublet at $\delta = 3.72$ and 3.20. Secondary amine displayed chemical shift at $\delta = 12.80$ as a singlet while the protons of phenyl ring furnished multiple signals at $\delta = 6.45$–$8.45$ (m, 15H, Ar–H) (Fig. 2).

Looking to the $^{13}$C NMR spectra, the chemical shifts of the final compound **5h** have carbons that varied from $\delta =$ 169.3–39.1 ppm. Carbon of ketone (>C=O) group has chemical shift at $\delta = 169.3$. The carbon of $-OCH_2$ group at C-22 attached to the ketone group has a chemical shift value at $\delta = 67.6$. The carbons of pyrazoline ring, C-9, C-10, and C-11 showed chemical shifts at $\delta = 155.3$, 39.1, and 65.7, respectively. The benzimidazole carbons C-12 showed peak at 151.1 ppm, C-15, C-20 appeared at 134.0 ppm. Similarly C-16, C-19 exhibited chemical shifts at 115.8, C-17 while C-18 showed at 123.7 ppm. The carbons of naphthalene ring, C-24, C-26, C-27, and C-29 appeared at 156.0, 123.7,

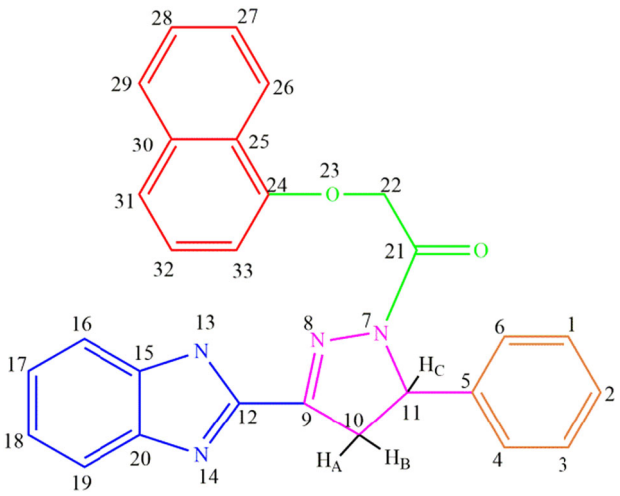



**Fig. 2** Carbon enumerations of compound **5h**

125.1, 126.0, and 127.1. Carbons of C-25 and C-30 exhibited peaks at 134.7, 134.4 while C-31, C-32, and C-33 appeared at 120.6, 126.6, and 107.0. The nitro group in the phenyl ring gave a chemical shift at $\delta = 147.1$.

### Structure–activity relationship (SAR) studies

SAR studies revealed that the presence of the benzimidazole ring is essential for a broad spectrum antimicrobial activity. Substitution pattern on the benzimidazole clubbed pyrazoline derivatives was carefully selected for considering electronic environments of the structures. Antimicrobial data of targeted compounds in Table 1 has clearly shown that diverse electronic varieties are responsible for broad spectrum activity. Compound **5i** containing nitro group at *para* position and in compound **5b** group at *ortho* position showed the highest inhibition against bacterial strains. On the other hand the results exhibited that compounds **5j** and **5k** substituted with methyl and methoxy group at *para* position was found to be the most promising antifungal agents. SAR studies indicates that compounds containing electron withdrawing groups at the *para* position increased antibacterial activity while the presence of the electron releasing group at the *para* position enhanced antifungal activity.

## Conclusion

The titled compounds were screened for their in vitro antibacterial and antifungal activities. It is clearly concluded from Table 1 that structural and electronic variety of the targeted compounds affected their biological activities. On the basis of results of biological activity we have concluded that *para* nitro and *para* chloro are the most distinctive derivatives in the present study because of their prominent in vitro antibacterial potency. For antifungal activity it is proved that *para* position of methoxy and methyl group showed most incremental antifungal activity. SAR studies revealed that *para* position of substituent is essential for potential antimicrobial activity.

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#### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no competing interests.

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