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Synthesis and Antimicrobial Activity of Novel Pyrazolone and Pyrazole Analogues Containing Benzimidazole Moiety.

G Manjunath, G Bheemaraju, M Mahesh, and P Venkata Ramana*.

Department of Chemistry, Sri Krishnadevaraya University, Ananthapuramu-515 003,Andhra Pradesh, India.

ABSTRACT

In the present study, a novel series of3-methyl-4-(2-substituted phenylhydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-ones and 1-(3,5-Dimethyl-4-(substituted phenyldiazenyl)- 1*H*-pyrazol-1-yl)-2- (2-((p-tolyloxy)methyl)- 1*H*-benzo[d]imidazol-1-yl) ethanones were synthesized in good yields using 2-(2-((p-tolyloxy)methyl)- 1*H*-benzo[d]imidazol-1-yl)acetohydrazide as a precusor and characterized by IR, NMR, mass spectra and elemental analyses. The newly synthesized pyrazoles and pyrazolones have been screened for their antibacterial activity against gram-positive and gram-negative bacteria using the agar disc diffusion method and antifungal activity against*AspergillusNiger* and *Ustilago maydis.* The compounds showed moderate to very good antibacterial activities.

Keywords: Benzimidazole, pyrazoles, pyrazolones, acetoacetic ester, acetyl acetone, antibacterial activity and antifungal activity.

Corresponding author

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INTRODUCTION

There is a growing interest over the past years for the synthesis of benzimidazole based heterocycles [1] due to the crucial role of benzimidazole [2] unit in the functions of biologically important molecules. They are remarkably effective compounds both with respect to their inhibitory activity and their favorable selectivity ratio. Now a day's many infectious microbial diseases causing problems world-wide because of resistance to a number of antimicrobial agents [3].

Pyrazoles [4-13] has a unique place and contributed significantly to biological, medicine, pharmacology fields. Pyrazole ring containing substituted five membered ring exhibited antibacterial, antifungal, tumor-necrosis inhibitor, antimicrobial, hypoglycemic, hypolipidemic and anti-inflammatory activity. The therapeutic importance of these rings prompted us to develop selective molecules in which a substituent could be arranged in a pharmacophoric pattern to display higher pharmacological activities.

Looking at the importance of benzimidazole and pyrazole nucleus, it was thought that it would be worthwhile to design and synthesize some new benzimidazole derivatives bearing pyrazole moiety and screen them for potential biological activities.

MATERIALS AND METHODS

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The homogeneity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate-hexane, 3:5). The IR spectra were recorded on IR 200 FT-IR spectrometer as KBr pellets. The wave numbers were given in cm^{-1}. The ^{1}HNMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a jeol JNM λ-400 MHz machine. The ^{13}CNMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at 125 MHz.All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The mass spectra were recorded on VG 7070H mass spectrometer. The microanalyses were performed on Perkin-Elmer 240C elemental analyzer.

Synthesis of 2-(p-tolyloxy)acetic acid 2

1 g of p-cresolwas taken in a boiling test tube and was dissolved in 3.5 ml of 33% NaOH and 2.5 ml of 50% solution of mono chloro acetic acid was added. The tube was loosely stoppered and heated on a boiling water bath for about 30 minutes. Cooled and then added dilute hydrochloric acid till the solution was acidic. The precipitate of aryloxy acetic acid[14-15] was filtered, washed with water and recrystallized from water to afford **2**. The melting point of the product obtained was compared with the literature value.

Characterization data of 2

Yield 95%, m.p. 134-136ºC (observed), 136ºC (literature).

Synthesis of 2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazole 3

The mixture of o-Phenylenediamine (0.09 mol) and 2-(p-tolyloxy)acetic acid (0.1 mol) was dissolved in 4N HCl (10 ml) and refluxed at 100°C for 5 hr. The completion of reaction was checked by TLC. The reaction mixture was cooled to room temperature, poured into ice cold water and neutralized with dilute NaOH solution to get 2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazole, **3**.The separated solid was filtered, washed with ice cold water, dried and purified by recrystallization from ethanol.

Characterization data of 3

Yield 95%, m.p. 164-166ºC.
IR (KBr)ν_{max} : 3427 (N-H str.), 2916 (C-H str. in CH_3/CH_2), 1611 (C=N str.), 1178,1056 (sp^2/sp^3 C-O str.) cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.28 (s, 3H, CH_3), 4.65 (s, 1H, NH), 5.35 (s, 2H, CH_2), 6.88-6.90 (d, J = 8 Hz, 2H, Ar-H), 7.07-7.10 (d, J = 8 Hz, 2H,Ar-H), 7.27 (t, J = 3.2 Hz, 2H, benzimidazole-H), 7.62 (dd, J = 3.2 Hz, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 20.5 (CH_3), 64.2 (CH_2), 114.6, 115.3, 123.4, 130.2, 130.2, 130.3,130.4, 131.5, 155.8 (aromatic carbons)ppm.
MS m/*z*: found 238 [M^+]; calcd. 238. Anal.$C_{15}H_{14}N_2O$. Found C 74.86 (75.6), H 5.86 (5.92), N 11.69(11.76).

Synthesis of ethyl 2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetate

A mixture of 2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazole (0.01 mol), ethylchloroacetate (0.01 mol), anhydrous K_2CO_3 (1.38 g, 0.01 mol) and DMF was stirred at room temperature for 8 hr. The reaction mixture was diluted with ice-cold water. The separated solid was filtered, washed with water and recrystallized from ethanol to afford **4**.

Characterization data of 4

Yield 85%, m.p. 118-120ºC.
IR (KBr)ν_{max} : 2981 (sp^3 C-H str. in CH_3/CH_2), 1739 (C=O str. in esters), 1612 (C=N str.), 1588 (C=C str. in aromatics), 1239,1019 (sp^2/sp^3 C-O str.) cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 1.22 (t, J = 8 Hz, 3H, ester CH_3), 2.70 (s, 3H, CH_3), 4.20 (q, J = 8 Hz, 2H, ester CH_2), 5.13 (s, 2H, NCH_2), 5.60 (s, 2H, OCH_2), 6.95 (d, 2H, Ar-H), 7.10 (d, 2H, Ar-H), 7.26 (dd, 2H, benzimidazole-H), 7.41 (dd, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ14.1 (ester CH_3), 24.1 (CH_3) 51.4 (NCH_2), 61.5 (ester CH_2), 66.7 (CH_2O), 114.3, 115.6, 123.2, 130.3, 130.8, 134.2, 139.2, 141.6, 157.8 (aromatic carbons, 166.4(C=O) ppm.
MS m/*z*: found 324 [M^+]; calcd. 324. Anal.$C_{19}H_{20}N_2O_3$. Found C 69.65 (70.35), H 6.19 (6.21), N 8.62(8.64).

Synthesis of2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetohydrazide 5

A solution of ethyl 2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetate,**4**(0.01 mole) and hydrazine hydrate (0.015 mole) in ethanol (25 ml) was refluxed for 5 hr. The reaction mixture was cooled and poured into ice-cold water with stirring. The separated solid was filtered, washed with water and recrystallized from ethanol to afford **5.**

Characterization data of 5

Yield 95%, m.p. 184-186ºC.
IR (KBr)ν_{max} : 3278 (N-H str.), 3061 (C-H str. in aromatics), 1739 (C=O str.), 1667 (C=N str.), 1415 (C-N str.) cm^{-1}.^{1}H NMR (DMSO-d_6) :δ 2.22 (s, 3H, CH_3), 3.97 (s broad, 2H, NH_2), 4.94 (s, 2H, NCH_2), 5.34 (s, 2H, OCH_2), 6.97-6.98 (d, 2H, Ar-H), 7.08-7.10 (d, 2H, Ar-H), 7.20-7.28 (dd, 2H, benzimidazole-H), 7.50-7.52 (dd, 2H, benzimidazole-H), 7.63-7.68 (s ,1H, NH) ppm.^{13}C NMR (DMSO-d_6): δ 24.1 (CH_3), 33.5 (NCH_2), 66.8 (OCH_2), 114.5, 115.1, 123.5, 130.5,130.8, 134.5, 140.2, 141.2, 158.3 (aromatic carbons), 165.9 (C=O) ppm.MS m/*z*: found 310 [M^+]; calcd. 310. Anal.$C_{17}H_{18}N_4O_2$. Found C 64.68 (65.79), H 5.83 (5.85), N 18.19(18.25).

Synthesis of 1-chloro-2-substitutedphenyldiazenes 7a-i

The required primary amine **6** was dissolved in a suitable volume of water containing 2.5-3.5 equivalents of hydrochloride acid by the application of heat if necessary. The solution thus obtained was cooled to 0°C where the amine hydrochloride usually crystallizes. The temperature was maintained at 0°C to 5°C and the aqueous sodium nitrate solution was added portion wise till there was free nitrous acid. The solution was tested for the later with an external indicator paper (moist potassium iodide – starch paper). An excess of acid was maintained to stabilize the diazonium salt solution. However, in those cases where a large excess of acid was harmful, the concentration of the acid was reduced to optimum value.

General procedure for the synthesis of Ethyl-3-oxo-2-(substitutedphenyldiazenyl)butanones 8a-i

A solution of sodium acetate (100g) in 100 ml aqueous alcohol (50%) was added to a solution of Ethylacetoacetate (100 g) in 500 ml of ethanol and the mixture was cooled. To this cold mixture, the corresponding diazonium chloride **7a-i** was added gradually till turbidity was observed. The addition was continued till yellow crystals separated out. These crystals were filtered washed with water and recrystallized from ethanol. The remaining compounds **8b-i**are synthesized on the same lines.

Yield 70-85%, m.p. **8a** 182-184ºC; **8b** 64-66ºC; **8c** 116-118ºC; **8d** 194-196ºC; **8e** 90-92ºC; **8f** 118-120ºC; **8g** 88-90ºC; **8h** 178-180ºC; **8i** 124-126ºC.

General procedure for the synthesis of 3-(substitutedphenyldiazenyl)pentane-2,4-dione 9a-i

A solution of sodium acetate (100g) in 100 ml aqueous alcohol (50%) was added to a solution of acetyl acetone (100 g) in 500 ml of ethanol and the mixture was cooled. To this cold mixture, the corresponding diazonium chloride **7** was added gradually till turbidity was observed. The addition was continued till yellow crystals separated out. These crystals were filtered washed with water and recrystallized from ethanol. The remaining compounds 9**b-i**were synthesized on the same lines.

Yield 70-85%, m.p. **9a** 92-94ºC; **9b** 96-98ºC; **9c** 112-114ºC; **9d** 138-140ºC; **9e** 92-94ºC; **9f** 232-234ºC;**9g** 120-122ºC; **9h** 100-102ºC; **9i** 120-122ºC.

Synthesis of 3-methyl-4-(2-substituted phenylhydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-ones 10a-i

A mixture of methyl 3-oxo-2-(phenyldiazenyl)butanoate**8a-i** (0.01 mole) and 2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetohydrazide **5** (0.01 mole) in ethanol (20 ml) was heated under reflux for 8 hr. on a water bath. After completion of the reaction, ethanol was evaporated; the residue was dissolved in water, neutralized with $NaHCO_3$ and extracted with ether. The ether solution was evaporated under reduced pressure to furnish the pure compound.

Characterization data of 10 a-l

3-methyl-4-(2-phenylhydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10a

Recrystallised from ethanol as yellow crystals.

Yield 85%, m.p. 114-116°C.
IR (KBr)ν_{max} : 3434 (N-H str.), 2923 (C-H str. in CH_3/CH_2), 1739 (C=O str.), 1615 (C=N str.), 1512 (C=C str. in aromatics), 1239,1021 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 1.63 (s, 3H, pyrazoloneCH_3), 2.27 (s, 3H, Ar-CH_3), 5.05 (s, 2H, NCH_2), 5.39 (s, 2H, OCH_2), 6.93-6.94 (d, J = 4 Hz, 3H, Ar-H), 7.07 (d, J = 4 Hz, 2H, Ar-H), 7.09 (d, 2H, Ar-H), 7.28-7.31 (m, 5H, Ar-H, benzimidazole-H and NH), 7.80 (d, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 18.6 (pyrazolone CH_3), 24.5 (Ar-CH_3), 31.8 (NCH_2), 66.5 (OCH_2), 115.1, 115.5, 116.8, 118.9,123.2, 128.9, 129.6, 130.2, 130.7, 134.5, 138.7, 141.8, 143.7, 148.2, 158.0 (aromatic carbons), 162.8 (pyrazolone C=O), 171.5 (C=O) ppm.
MS m/*z*: found 480 [M^+]; calcd. 480. Anal.$C_{27}H_{24}N_6O_3$. Found C 67.12 (67.49), H 4.98 (5.03), N 17.38(17.49).

3-methyl-4-(2-(p-tolyl)hydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10b

Recrystallised from ethanol as yellow crystals.

Yield 75%, m.p. 96-98°C.
IR (KBr)ν_{max} : 3338 (N-H str.), 2862 (C-H str. in CH_3/CH_2), 1680 (C=O str.), 1628 (C=N str.), 1615 (C=C str. in aromatics), 1268 ,1072 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 1.43 (s, 3H, pyrazoloneCH_3), 2.26 (s, 6H, Ar-CH_3), 5.03 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.38-6.42 (m, 2H, Ar-H), 6.92 (m, 2H, Ar-H), 6.94 (m, 2H, Ar-H), 7.08 (m, 2H, Ar-H), 7.18 (m, 1H, NH), 7.24 (dd, 2H, benzimidazole-H), 7.78 (dd, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 19.6 (pyrazolone CH_3), 24.8 (CH_3), 31.2 (NCH_2), 66.8 (OCH_2), 114.8, 115.6, 116.3, 123.4, 128.6, 128.8, 130.1, 130.5, 130.9, 134.9, 139.2, 140.4, 141.8, 148.2, 157.9 (aromatic carbons), 162.8 (pyrazolone C=O), 171.5 (C=O) ppm.
MS m/*z*: found 494 [M^+]; calcd. 494. Anal.$C_{28}H_{26}N_6O_3$. Found C 67.34 (68.00), H 5.24 (5.30), N 16.84(16.99).

3-methyl-4-(2-(o-tolyl)hydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10c

Recrystallised from ethanol as light yellow crystals.

Yield 82%, m.p. 160-162°C.
IR (KBr)ν_{max} : 3321 (N-H str.), 2851 (C-H str. in CH_3/CH_2), 1672 (C=O str.), 1650 (C=N str.), 1620 (C=C str. in aromatics), 1243 ,1082 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 1.63 (s, 3H, pyrazoloneCH_3), 2.26 (s, 3H, Ar-CH_3), 2.28 (s, 3H, Ar-CH_3), 5.04 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.36-6.42 (m, 1H, Ar-H), 6.48(m, 1H, Ar-H), 6.92 (m, 2H, Ar-H), 6.94 (m, 1H, Ar-H), 7.01 (m, 1H, Ar-H), 7.02 (m, 2H, Ar-H), 7.15 (m, 1H, NH), 7.24 (d, 2H, benzimidazole-H), 7.83 (d, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 15.8 (Ar-CH_3), 18.5 (pyrazolone CH_3), 24.7 (Ar-CH_3), 31.2 (NCH_2), 66.8 (OCH_2), 114.6, 115.8, 116.5, 118.9, 123.2, 126.9, 128.6, 128.9, 130.2, 130.5, 130.9, 134.8, 139.2, 141.8, 141.9, 148.5, 157.9 (aromatic carbons), 162.7 (pyrazolone C=O), 171.2 (C=O) ppm.
MS m/*z*: found 494 [M^+]; calcd. 494. Anal.$C_{28}H_{26}N_6O_3$. Found C 67.63 (68.00), H 5.26 (5.30), N 16.82(16.99).

4-(2-(4-chlorophenyl)hydrazono)-3-methyl-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10d

Recrystallised from ethanol as grey crystals.

Yield 88%, m.p. 108-110°C (dec.).
IR (KBr)ν_{max} : 3508-3230 (broad, N-H str.), 2816 (C-H str. in CH_3/CH_2), 1732, 1653 (C=O str.), 1615 (C=N str.), 1157 ,1092 (sp^2/sp^3 C-O str.), 1078 (aromatic C-Cl stretch)cm^{-1}.^{1}H NMR (DMSO-d_6) :δ 1.63 (s, 3H, pyrazoloneCH_3), 2.26 (s, 3H, Ar-CH_3), 5.04 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.42 (d, J = 4 Hz, 2H, Ar-H), 6.92 (m, 2H, Ar-H), 6.97 (m, 2H,Ar-H), 7.01 (m, 1H, NH), 7.18 (m, 2H,Ar-H), 7.26 (dd, 2H, benzimidazole-H), 7.86 (dd, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 18.6 (pyrazolone CH_3), 24.7 (Ar-CH_3), 31.2 (NCH_2), 66.4 (OCH_2), 114.5, 115.6, 117.9, 123.5, 124.6, 128.6, 129.8, 130.3, 130.9, 134.5, 139.2, 141.3, 141.6, 148.9, 157.9, 162.7 (pyrazolone C=O), 171.4 (C=O) ppm.
MS m/*z*: found 514 [M^+]; calcd. 514. Anal.$C_{27}H_{23}ClN_6O_3$. Found C 62.48 (62.97), H 4.46 (4.50), N 16.27(16.32).

4-(2-(2-chlorophenyl)hydrazono)-3-methyl-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10e

Recrystallised from ethanol as red coloured crystals.

Yield 84%, m.p. 176-178°C.
IR (KBr)ν_{max} : 3511-3240 (broad, N-H str.), 2820 (C-H str. in CH_3/CH_2), 1742 (C=O str.), 1650 (C=N str.), 1642 (C=O str. in amide), 1620 (C=N str. in aromatics), 1164 ,1096(sp^2/sp^3 C-O str.), 1081 (aromatic C-Cl str.)cm^{-1}.^{1}H NMR (DMSO-d_6) :δ 1.58 (s, 3H, pyrazoloneCH_3), 2.37 (s, 3H, Ar-CH_3), 5.06 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.37-6.43 (m, 1H, Ar-H), 6.68 (m, 1H, Ar-H), 7.06 (m, 2H, Ar-H), 7.19 -7.26 (m, 2H, Ar-H), 7.39 (d, 2H, Ar-H), 7.48 (m, 1H, NH), 7.58 (d, 2H, benzimidazole-H), 7.82 (d, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 19.6 (pyrazolone CH_3), 24.4 (Ar-CH_3), 31.2 (NCH_2), 66.5 (OCH_2), 114.4, 115.5, 117.8, 120.4, 123.5, 125.7, 127.8, 128.7, 129.9, 130.2, 130.9, 134.5, 138.9, 141.6, 147.9, 148.2, 157.9 (aromatic carbons), 162.7 (pyrazolone C=O), 171.4 (C=O) ppm.
MS m/*z*: found 514 [M^+]; calcd. 514. Anal.$C_{27}H_{23}ClN_6O_3$. Found C 62.41 (62.97), H 4.46 (4.50), N 16.24(16.32).

3-methyl-4-(2-(4-nitrophenyl)hydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10f

Recrystallised from ethanol as yellow crystals.

Yield 88%, m.p. 190-192°C.
IR (KBr)ν_{max} : 3348 (N-H str.), 2912, 2821 (asym/ sym C-H str. in CH_3/CH_2), 1734, 1642 (C=O str.), 1616 (C=N str.), 1321 (sym. N-O str.), 1231 ,1082 (sp^2/sp^3 C-O str.)cm^{-1}.^{1}H NMR (DMSO-d_6) :δ 1.49 (s, 3H, pyrazoloneCH_3), 2.28 (s, 3H, Ar-CH_3), 5.02 (s, 2H, NCH_2), 5.27 (s, 2H, OCH_2), 6.78 (d, 2H, Ar-H), 6.84 (m, 2H, Ar-H), 6.94 (d, 2H, Ar-H), 7.15 (m, 1H, NH), 7.24 (dd, 2H, benzimidazole-H), 7.82 (dd, 2H, benzimidazole-H), 8.14 (m, 2H, Ar-H) ppm.
^{13}C NMR (DMSO-d_6): δ 18.5 (pyrazolone CH_3), 24.6 (Ar-CH_3), 31.2 (NCH_2), 66.8 (OCH_2), 114.4, 115.6, 117.9, 122.2, 123.2, 128.7, 130.2, 130.9, 134.4, 138.5, 139.2, 141.6, 148.4, 149.4, 157.9 (aromatic carbons), 162.7 (pyrazolone C=O), 171.4 (C=O) ppm.
MS m/*z*: found 525 [M^+]; calcd. 525. Anal.$C_{27}H_{23}N_7O_5$. Found C 61.24 (61.71), H 4.32 (4.41), N 18.51(18.66).

3-methyl-4-(2-(2-nitrophenyl)hydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10g

Recrystallised from ethanol as orange crystals.

Yield 74%, m.p. 200-202°C (dec.).
IR (KBr)ν_{max} : 3211 (N-H str.), 2812 (C-H str. in CH_3/CH_2), 1718, 1628 (C=O str.), 1612 (C=N str.), 1482 (asym. N-O str.), 1318 (sym. N-O str.), 1264 ,1102(sp^2/sp^3 C-O str.)cm^{-1}.^{1}H NMR (DMSO-d_6) :δ 1.36 (s, 3H, pyrazoloneCH_3), 2.26 (s, 3H, Ar-CH_3), 5.05 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.91 (d, 2H, Ar-H), 6.71 (m, 1H, Ar-H), 6.89 (m, 1H, Ar-H), 7.06-7.08 (m, 2H, Ar-H), 7.09 (m, 1H, NH), 7.28 (dd, 2H, benzimidazole-H), 7.41 (m, 1H, Ar-H), 7.78 (m, 2H, benzimidazole-H), 8.14 (m, 1H, Ar-H) ppm.
^{13}C NMR (DMSO-d_6): δ 18.6 (pyrazolone CH_3), 24.5 (Ar-CH_3), 31.3 (NCH_2), 66.5 (OCH_2), 114.6, 115.6, 117.4, 119.8, 121.9, 123.2, 130.2, 130.9, 134.5, 135.6, 135.9, 139.2, 141.7, 141.9, 148.5, 157.9 (aromatic carbons), 162.7 (pyrazolone C=O), 171.1(C=O) ppm.
MS m/*z*: found 525 [M^+]; calcd. 525. Anal.$C_{27}H_{23}N_7O_5$. Found C 61.34 (61.71), H 4.36 (4.41), N 18.48(18.66).

4-(2-(4-methoxyphenyl)hydrazono)-3-methyl-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10h

Recrystallised from ethanol as yellow crystals.

Yield 86%, m.p. 154-156°C.
IR (KBr)ν_{max} : 3346 (N-H str.), 2814 (C-H str. in CH_3/CH_2), 1748, 1648 (C=O str.), 1598 (C=N str.), 1248 ,1027 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 1.62 (s, 3H, pyrazoloneCH_3), 2.27 (s, 3H, Ar-CH_3), 3.83 (s, 3H, OCH_3), 5.05 (s, 2H, NCH_2), 5.39 (s, 2H, OCH_2), 6.46-6.48 (m, 2H, Ar-H), 6.80 (m, 2H, Ar-H), 6.97 (d, 2H, Ar-H), 7.07 (d, 2H, Ar-H), 7.10-7.18 (m, 1H, NH), 7.37 (d, 2H, benzimidazole-H), 7.79 (d, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 18.5 (pyrazolone CH_3), 24.2 (Ar-CH_3), 30.9 (NCH_2), 56.2 (OCH_3), 66.5 (OCH_2), 114.6, 115.3, 115.4, 117.4, 123.2, 128.8, 130.2, 131.7, 134.5, 135.6, 139.2, 141.6, 148.2, 150.9, 158.1, 162.7 (pyrazolone C=O), 171.2 (C=O) ppm.
MS m/*z*: found 510 [M^+]; calcd. 510. Anal.$C_{28}H_{26}N_6O_4$. Found C 65.41 (65.87), H 5.09 (5.13), N 16.32(16.46).

4-(2-(2-methoxyphenyl)hydrazono)-3-methyl-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one 10i

Recrystallised from ethanol as golden yellow crystals.

Yield 83%, m.p. 170-172°C.
IR (KBr)ν_{max} : 3349 (N-H str.), 2826 (C-H str. in CH_3/CH_2), 1752, 1656 (C=O str.), 1583 (C=N str.), 1246 ,1080 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 1.53 (s, 3H, pyrazoloneCH_3), 2.27 (s, 3H, Ar-CH_3), 3.82 (s, 3H, OCH_3), 5.05 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.36 (m, 1H, Ar-H), 6.52 (m, 1H, Ar-H), 6.61 (m, 1H, Ar-H), 6.63 (m, 1H, Ar-H), 6.75 (d, 2H, Ar-H), 6.98 (d, 2H, Ar-H), 7.01 (m, 1H, NH), 7.27 (d, 2H, benzimidazole-H), 7.76 (d, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 18.9 (pyrazolone CH_3), 24.6 (Ar-CH_3), 30.9 (NCH_2), 56.2 (OCH_3), 66.3 (OCH_2), 114.3, 115.4, 115.7, 117.6, 119.9, 121.9, 123.2, 128.7, 129.1, 130.2, 130.7, 134.5, 139.2, 141.7, 147.7, 148.2, 157.9, 162.6 (pyrazolone C=O), 170.9 (C=O) ppm.
MS m/*z*: found 510 [M^+]; calcd. 510. Anal.$C_{28}H_{26}N_6O_4$. Found C 65.36 (65.87), H 5.07 (5.13), N 16.31(16.46).

Synthesis of 1-(3,5-Dimethyl-4-(substituted phenyldiazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanones 11a-i

A mixture of 3-(phenyldiazenyl) pentane-2,4-dione (**9a-i**) (0.01 mol) and **2-(2-((p-**tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetohydrazide **5** (0.01 mol) in ethanol (20 ml) was heated under reflux for 8 hr. on a water bath. After completion of the reaction, ethanol was evaporated; the residue was dissolved in water, neutralized with $NaHCO_3$ and extracted with ether. The ether solution was evaporated under reduced pressure to furnish the pure compound.

Characterization data of 11a-i

1-(3,5-dimethyl-4-(phenyldiazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone11a

Recrystallized from ethanol as yellow crystals.

Yield 83%, m.p. 76-78°C.
IR (KBr)ν_{max} : 3163 (C-H str. in CH_3/CH_2), 1739 (C=O str. in ketones), 1625 (C=C str.), 1464 (N=N str.), 1239, 1108 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.27 (s, 3H, Ar-CH_3), 2.50 (s, 3H, pyrazole CH_3), 2.61 (s, 3H, pyrazole CH_3), 5.05 (s, 2H, NCH_2), 5.39 (s, 2H, OCH_2), 6.92 &6.94 (d, J = 8.8 Hz, 2H, Ar-H), 7.06-7.09 (m, 2H, Ar-H), 7.21-7.32 (m,4H, Ar-H & benzimidazole-H), 7.40-7.42 (m, 3H, Ar-H), 7.78-7.81 (d, J=7.8 Hz, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 2.0 (pyrazole CH_3), 8.6 (pyrazole CH_3), 24.4 (Ar-CH_3), 46.0 (NCH_2), 66.0 (OCH_2), 106.4, 114.3, 115.6,123.2, 129.0, 129.2, 129.4, 130.0, 130.2, 130.9, 134.6, 138.7, 139.2, 141.7, 143.6, 157.6 (aromatic carbons), 200.3 (C=O) ppm.
MS m/*z*: found 478 [M^+]; calcd. 478. Anal.$C_{28}H_{26}N_6O_2$. Found C 70.01 (70.28), H 5.43 (5.48), N 17.48(17.50).

1-(3,5-dimethyl-4-(p-tolyldiazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11b

Recrystallised from ethanol as gold crystals.

Yield 80%, m.p. 88-90°C (dec.).
IR (KBr)ν_{max} : 2872 (C-H str. in CH_3/CH_2), 1731 (C=O str. in ketones), 1653(C=N str.),1508 (C=C str.), 1378 (N=N str.), 1238, 1072(sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.37 (s, 3H, Ar-CH_3), 2.41 (s, 3H, Ar-CH_3), 2.56 (s, 3H, pyrazole CH_3), 2.60 (s, 3H, pyrazole CH_3), 5.05 (s, 2H, NCH_2), 5.39 (s, 2H, OCH_2), 6.93 (d, J = 8.8 Hz, 2H, Ar-H), 7.08 (d, J=8 Hz,2H, Ar-H), 7.20-7.22 (m, 2H, Ar-H), 7.27-7.30 (m, 2H, Ar-H), 7.30-7.33 (m, 2H, benzimidazole-H), 7.69-7.80 (m, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 2.0 (pyrazole CH_3), 8.7 (pyrazole CH_3), 24.6 (Ar-CH_3,Ar-CH_3), 45.9 (NCH_2), 66.2 (OCH_2), 106.8, 114.3, 115.6,123.2, 125.9, 128.9, 130.1, 130.3, 130.9, 134.7, 138.6, 138.9, 139.2, 142.1, 143.6, 157.9 (aromatic carbons), 200.3 (C=O) ppm.
MS m/*z*: found 492 [M^+]; calcd. 492. Anal.$C_{29}H_{28}N_6O_2$. Found C 69.92 (70.71), H 5.68 (5.73), N 16.84(17.06).

1-(3,5-dimethyl-4-(o-tolyldiazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11c

Recrystallised from ethanol as light yellow solid.

Yield 74%, m.p. 88-90°C.
IR (KBr)ν_{max} : 2981 (C-H str. in CH_3/CH_2), 1737 (C=O str. in ketones), 1664 (C=N str.), 1514 (C=C str.), 1365 (N=N str.), 1236, 1024(sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.27 (s, 3H, Ar-CH_3), 2.41 (s, 3H, Ar-CH_3), 2.50 (s, 3H, pyrazole CH_3), 2.64 (s, 3H, pyrazole CH_3), 5.05 (s, 2H, NCH_2), 5.39 (s, 2H, OCH_2), 6.93 (d, J = 8.8 Hz, 2H, Ar-H), 7.10 (d, J=8.8 Hz,2H, Ar-H), 7.14 (d, J=8.2 Hz, 2H, Ar-H), 7.27-7.32 (m, 4H, Ar-H,benzimidazole-H), 7.75-7.80 (m, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 1.92 (pyrazole CH_3), 9.2 (pyrazole CH_3), 15.8 (Ar-CH_3), 24.7 (Ar-CH_3), 45.9 (NCH_2), 66.8 (OCH_2), 106.4, 114.6, 115.6, 123.2, 125.9, 128.6, 128.9, 129.2, 129.6, 130.6, 130.7, 134.6, 138.0, 138.7, 139.2, 141.6, 143.6, 158.9 (aromatic carbons), 201.4 (C=O) ppm.
MS m/*z*: found 492 [M^+]; calcd. 492. Anal.$C_{29}H_{28}N_6O_2$. Found C 70.12 (70.71), H 5.66 (5.73), N 16.78(17.06).

1-(4-((4-chlorophenyl)diazenyl)-3,5-dimethyl-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11d

Recrystallised from ethanol as brown solid.

Yield 76%, m.p. 94-96°C.
IR (KBr)ν_{max} : 2920 (C-H str. in CH_3/CH_2), 1739 (C=O str. in ketones), 1667 (C=N str.), 1431 (N=N str.), 1237, 1054(sp^2/sp^3 C-O str.), 1025 (aromatic C-Cl str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.29 (s, 3H, Ar-CH_3), 2.49 (s, 3H, pyrazole CH_3), 2.61 (s, 3H, pyrazole CH_3), 5.05 (s, 2H, NCH_2), 5.37 (s, 2H, OCH_2), 6.90-6.92 (m, 2H, Ar-H), 7.06-7.08 (m, 2H, Ar-H), 7.27-7.29 (m, 2H, Ar-H), 7.33-7.39 (m, 4H, benzimidazole-H,Ar-H), 7.78-7.79 (m, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 2.2 (pyrazole CH_3), 8.9 (pyrazole CH_3), 25.2 (Ar-CH_3), 46.2 (NCH_2), 66.8 (OCH_2), 106.2, 114.4, 115.2, 123.4, 127.2, 128.6, 130.2, 130.4, 130.9, 135.1, 136.2, 138.6, 139.2, 141.6, 143.5, 157.6 (aromatic carbons), 200.2 (C=O) ppm.
MS m/*z*: found 512 [M^+]; calcd. 512. Anal.$C_{28}H_{25}ClN_6O_2$. Found C 65.48 (65.56), H 4.85 (4.91), N 16.21(16.38).

1-(4-((2-chlorophenyl)diazenyl)-3,5-dimethyl-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11e

Recrystallised from ethanol as golden yellow crystals.

Yield 81%, m.p. 96-98°C.
IR (KBr)ν_{max} : 2981 (C-H str. in CH_3/CH_2), 1737 (C=O str. in ketones), 1664 (C=N str.), 1428 (N=N str.), 1246, 1068 (sp^2/sp^3 C-O str.), 1018 (aromatic C-Cl str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.27 (s, 3H, Ar-CH_3), 2.49 (s, 6H, pyrazole CH_3), 5.04 (s, 2H, NCH_2), 5.38 (s, 2H, OCH_2), 6.90-6.92 (m, 2H, Ar-H), 7.06-7.08 (m, 2H, Ar-H), 7.12 (m, 1H, Ar-H), 7.27 (m, 2H, Ar-H), 7.29(d, 2H, benzimidazole-H), 7.31 (m, 1H, Ar-H), 7.68 (d, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 1.8 (pyrazole CH_3), 8.8 (pyrazole CH_3), 24.5 (Ar-CH_3), 45.7 (NCH_2), 65.9 (OCH_2), 106.2, 114.4, 115.6, 123.2, 127.2, 129.3, 130.1, 130.2, 130.4, 130.5, 130.9, 134.3, 136.2, 138.5, 138.9, 141.7, 143.4, 157.6 (aromatic carbons), 200.3 (C=O) ppm.
MS m/*z*: found 512 [M^+]; calcd. 512. Anal.$C_{28}H_{25}ClN_6O_2$. Found C 64.98 (65.56), H 4.87 (4.91), N 16.20(16.38).

1-(3,5-dimethyl-4-((4-nitrophenyl)diazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11f

Recrystallised from ethanol as yellow crystals.

Yield 84%, m.p. 82-84°C.
IR (KBr)ν_{max} : 3018(C-H str. in aromatic compounds), 2936 (C-H str. in CH_3/CH_2), 1734 (C=O str. in ketones), 1618 (C=N str.), 1580(asym. N-O str,),1408 (N=N str.), 1392 (sym. N-O str.),1278, 1085(sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.29 (s, 3H, Ar-CH_3), 2.48 (s, 3H, pyrazole CH_3), 2.60 (s, 3H, pyrazole CH_3), 5.05 (s, 2H, NCH_2), 5.36 (s, 2H, OCH_2), 6.91 (d, J = 8.7 Hz, 2H, Ar-H), 6.95 (d,2H, Ar-H), 7.10 (d, J=8.7 Hz, 2H, benzimidazole-H), 7.28-7.30 (m, 2H, Ar-H), 7.36-7.38 (m, 2H, benzimidazole-H), 7.78-7.80 (m, 2H, Ar-H) ppm.
^{13}C NMR (DMSO-d_6): δ 1.9 (pyrazole CH_3), 8.7 (pyrazole CH_3), 26.8 (Ar-CH_3), 45.8 (NCH_2), 66.8 (OCH_2), 106.4, 114.6, 115.9, 121.2, 123.4, 130.0, 130.1, 130.8, 134.6, 134.9, 138.6, 138.9, 141.8, 143.4, 148.2, 157.9 (aromatic carbons), 198.6 (C=O) ppm.
MS m/*z*: found 523 [M^+]; calcd. 523. Anal.$C_{28}H_{25}N_7O_4$. Found C 63.94 (64.24), H 4.76 (4.81), N 18.45(18.73).

1-(3,5-dimethyl-4-((2-nitrophenyl)diazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11g

Recrystallised from ethanol as orange crystals.

Yield 72%, m.p. 104-106°C.
IR (KBr)ν_{max} : 3024 (aromatic C-H str.), 2948 (C-H str. in CH_3/CH_2), 1721 (C=O str. in ketones), 1622 (C=N str.), 1571 (asym. N-O str.), 1416 (N=N str.), 1390 (sym. N-O str.), 1265, 1072(sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.26 (s, 3H, Ar-CH_3), 2.48 (s, 3H, pyrazole CH_3), 2.60 (s, 3H, pyrazole CH_3), 5.05 (s, 2H, NCH_2), 5.36 (s, 2H, OCH_2), 6.90-6.92 (m, 2H, Ar-H), 7.06-7.08 (m, 2H, C_{13}Ar-H), 7.28-7.30 (m,2H, benzimidazole-H), 7.51-7.53 (m, 2H, Ar-H), 7.72 (m, 1H, Ar-H),7.78 (m, 2H, benzimidazole-H), 8.15 (m, 1H,Ar-H) ppm.
^{13}C NMR (DMSO-d_6): δ 1.9 (pyrazole CH_3), 8.8 (pyrazole CH_3), 25.6 (Ar-CH_3), 46.2 (NCH_2), 66.8 (OCH_2), 107.2, 114.3, 115.4, 121.2, 123.4, 124.5, 130.0, 130.1, 130.2, 130.8, 134.6, 134.9, 135.6, 138.5, 138.7, 141.2, 143.5, 157.9 (aromatic carbons), 198.2(C=O) ppm.
MS m/*z*: found 523 [M^+]; calcd. 523. Anal.$C_{28}H_{25}N_7O_4$. Found C 63.96 (64.24), H 4.79 (4.81), N 18.42(18.73).

1-(4-((4-methoxyphenyl)diazenyl)-3,5-dimethyl-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanone 11h

Recrystallised from ethanol as light yellow crystals.

Yield 75%, m.p. 78-80°C (dec.).
IR (KBr)ν_{max} : 2924 (C-H str. in CH_3/CH_2), 1739 (C=O str. in ketones), 1620 (C=N str.), 1465 (N=N str.), 1241, 1028 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.27 (s, 3H, Ar-CH_3), 2.48 (s, 3H, pyrazole CH_3), 2.60 (s, 3H, pyrazole CH_3), 3.83 (s, 3H, OCH_3), 5.05 (s, 2H, NCH_2), 5.38 (s, 2H, OCH_2), 6.92-6.94 (m, 2H, Ar-H), 6.96-6.99 (m, 2H, Ar-H), 7.07 (d,J=8.4 Hz, 2H, Ar-H), 7.27-7.28 (m, 2H, Ar-H), 7.37 (d, J=8.8 Hz, 2H, benzimidazole-H), 7.79 (d, J=8.8 Hz, 2H, benzimidazole-H) ppm.

^{13}C NMR (DMSO-d_6): δ 2.2 (pyrazole CH_3), 8.7 (pyrazole CH_3), 24.6 (Ar-CH_3), 46.2 (NCH_2), 56.2 (OCH_3), 66.1 (OCH_2), 106.4, 114.4, 114.6, 115.4, 121.2, 123.2, 130.1, 130.2, 130.7, 134.6, 138.2, 138.7, 141.6, 143.3, 157.9, 160.8 (aromatic carbons), 199.4 (C=O) ppm.
MS m/*z*: found 508 [M^+]; calcd. 508. Anal.$C_{29}H_{28}N_6O_3$. Found C 67.92 (68.49), H 5.49 (5.55), N 16.43(16.52).

1-(4-((2-methoxyphenyl)diazenyl)-3,5-dimethyl-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo [d] imidazol -1-yl)ethanone 11i

Recrystallised from ethanol as yellow crystals.

Yield 78%, m.p. 160-162°C.
IR (KBr)ν_{max} : 2946 (C-H str. in CH_3/CH_2), 1734 (C=O str. in ketones), 1632 (C=C str.), 1420 (N=N str.), 1232, 1078 (sp^2/sp^3 C-O str.)cm^{-1}.
^{1}H NMR (DMSO-d_6) :δ 2.27 (s, 3H, Ar-CH_3), 2.48 (s, 3H, pyrazole CH_3), 2.60 (s, 3H, pyrazole CH_3), 3.84 (s, 3H, OCH_3), 5.04 (s, 2H, NCH_2), 5.39 (s, 2H, OCH_2), 6.91-6.94 (m, 2H, Ar-H), 7.06 (m, 1H, Ar-H), 7.08 (m,1H, Ar-H), 7.11 (d, J=8.2 Hz, 2H, Ar-H), 7.27 (m, 1H, Ar-H), 7.28 (m, 1H, Ar-H), 7.38 (d, J=8.6 Hz, 2H, benzimidazole-H), 7.78 (m, 2H, benzimidazole-H) ppm.
^{13}C NMR (DMSO-d_6): δ 1.8 (pyrazole CH_3), 8.6 (pyrazole CH_3), 25.6 (Ar-CH_3), 46.1 (NCH_2), 56.4 (OCH_3), 66.3 (OCH_2), 100.2, 107.0, 114.3, 114.6, 115.2, 121.3, 123.4, 130.1, 130.2, 130.3, 130.9, 134.6, 138.6, 139.2, 141.7, 143.2, 157.6, 159.2 (aromatic carbons), 199.3 (C=O) ppm.
MS m/*z*: found 508 [M^+]; calcd. 508. Anal.$C_{29}H_{28}N_6O_3$. Found C 68.02 (68.49), H 5.50 (5.55), N 16.46(16.52).

Biological activity

The antibacterial and antifungal activity of the synthesized compounds was examined by cup plate method [16] against the following bacterial strains: *Staphylococcus aureus, Bacillus subtilis, Escherichia Coli, Pseudomonas aeruginosa, Salmonella typhi* and fungi *A. Niger, U. maydis,* as compared to the standard drugs Gentamycin and Nystatin for bacterial and fungal growth respectively.

The antimicrobial activities of synthesized compounds were carried by disc diffusion method using nutrient agar medium (NAM) for bacterial and potato dextrose agar (PDA) medium for fungal cultures respectively. NAM was prepared with beef extract (3 g), peptone (5 g), NaCl (5 g) and agar-agar (15 g) in 1000 mL distilled water and pH was adjusted to 7.0. PDA was prepared by adding dextrose (20 g), agaragar (15 g) to potato infusion (1000 mL) and pH was adjusted to 5.5. Potato infusion was made by boiling 200 grams of sliced potatoes in distilled water for 30 minutes and then filtered through Whattman No.1 filter paper and filtrate was made up to 1 litre with distilled water. Both the media were sterilized in an autoclave at 121°C, 15 lbs, pressure for 30 min. After sterilization 20 ml of both media were poured into petri dishes in a laminar air flow and allowed to solidify. After solidification the NAM was inoculated with 100 µl of desired bacteria and PDA was inoculated with 100 µl of desired fungi. Compounds were dissolved in DMSO with a concentration of 100, 500, 1000 ppm and Whattman No.1 filter paper disks were placed in the solution and kept for one minute. After drying the disks were placed on NAM and PDA inoculated with bacteria or fungi and NAM plates were incubated at 37ºC and PDA plates at 30°C. Zones of inhibition were measured after 24 h and 5 days and compared with standard drugs Gentamycin and Nystatin for bacterial and fungal growth respectively. The experiments were repeated thrice and mean values of the radius of zone of inhibition were measured.

Compounds 10f, 10g, 11d, 11e and 11f were found to be more potent than other compounds against *S. aureus* as compared to the control Gentamycin. Compounds 10b, 10c, 10e, 11b, 11g and 11h have potencies that were equal to Gentamycin against *S. aureus.* Compounds 10a, 10i, 11a, 11c and 11i were found weakly potent.

Compounds 10d, 10f, 10g, 11d and 11f were found to be more potent than other compounds against *Bacillus subtilis* as compared to the control Gentamycin. Compounds 10b, 10c, 10e, 10h, 10i, 11b, 11e and 11g have potencies that were equal to Gentamycin against *Bacillus subtilis.* Compounds 10a, 11a, 11c, 11h and 11i were found weakly potent.

Compounds 10c, 10d, 10e,10f, 11d, 11e, 11f and 11g were more potent against *Escherichia Coli* and Compounds 10h, 10i, 11b, 11c, 11h and 11i have potencies that were equal to Gentamycin against *Escherichia Coli.* Compounds 10a and 11awere found weakly potent. .

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Compounds 10c, 10f, 10g, 11d, 11e, 11f and 11g were more potent against *Pseudomonas aeruginosa* where as the compounds 10b, 10d, 10e, 10h, 10i, 11g and 11h were moderately potent. Compounds 10a, 11a, 11h and 11i were weakly potent against *Pseudomonas aeruginosa*.

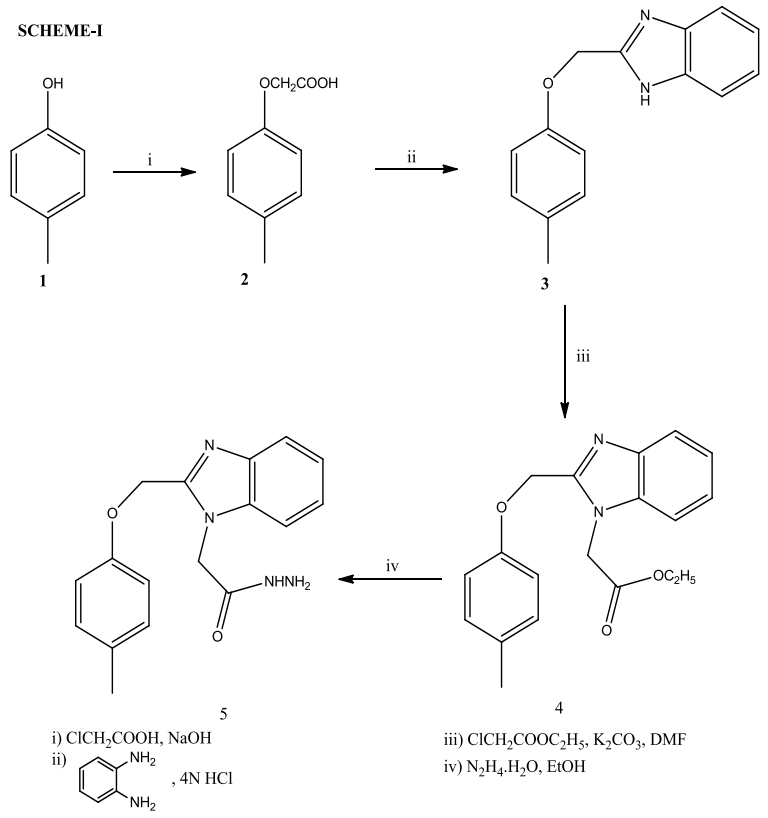
Compounds 10f, 11d, 11e, 11f and 11g were more potent against *Salmonella typhi* whereas the compounds 10b, 10c, 10d, 10e, 10g and 11a were moderately potent. Compounds 10a, 10h, 10i, 11b, 11c, 11h and 11i were weakly potent against *Salmonella typhi.*

Surprisingly majority of the compounds did not exhibited significant antifungal activity against *A. Niger*and *U. maydis.* Compounds 10a, 10d, 10f, 11a, 11b, 11d and 11f exhibited feeble activity. Compound 12d only showed some noticeable activity against *A. Niger* and*U. maydis.*

Compound 5 exhibited moderate to feeble antibacterial inhibition and it does not exhibit any significant antifungal activity. The investigation of antibacterial screening data revealed that all the tested compounds showed moderate to good bacterial inhibition. But majority of the compounds did not exhibit any significant antifungal inhibition.

RESULTS AND DISCUSSION

The synthesized compounds **10a-i**and **11a-i** were prepared as depicted in **SCHEME –I, II & III.** Initially 2-(p-tolyloxy)acetic acid **2** was prepared from p-cresol **1** as its aryloxyacetic acid derivative. 2-((p-tolyloxy)methyl)-1H-benzo[d]imidazole, **3** was prepared by treating 2-(p-tolyloxy)acetic acid **2** with o-Phenylenediamine in 4N HCl. Ethyl 2-(2-((p-tolyloxy)methyl)-1H-benzo[d]imidazol-1-yl)acetate, **4** was prepared by agitating a mixture of 2-((p-tolyloxy)methyl)-1H-benzo[d]imidazole, **3**with ethyl chloro acetate in the presence of K_2CO_3 in DMF. Compound **4** was converted into corresponding acetohydrazide by heating with hydrazine hydrate to give 2-(2-((p-tolyloxy)methyl)-1H-benzo[d]imidazol-1-yl)acetohydrazide **5**.The reaction of aryl diazonium chloride **(7a-i)** with ethyl acetoacetate and acetylacetone yield the corresponding ethyl-2-(aryl hydrazono)-3-oxo butyrate **(8a-i)** and 3-(aryldiazenyl)pentane-2,4-dione **(9 a-i)**.



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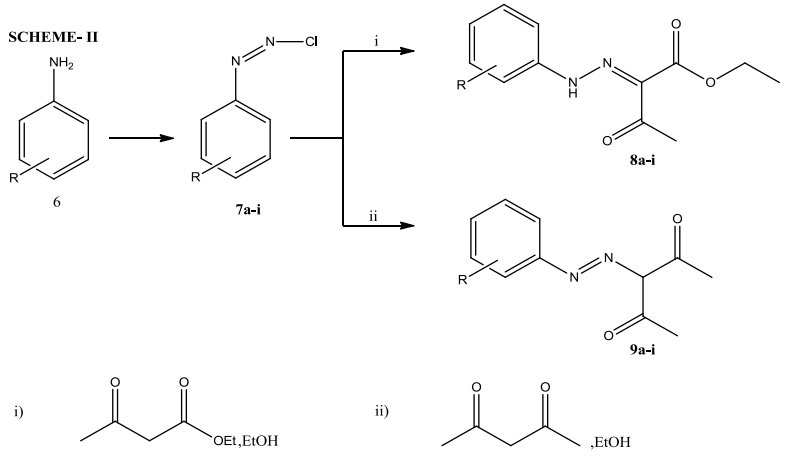
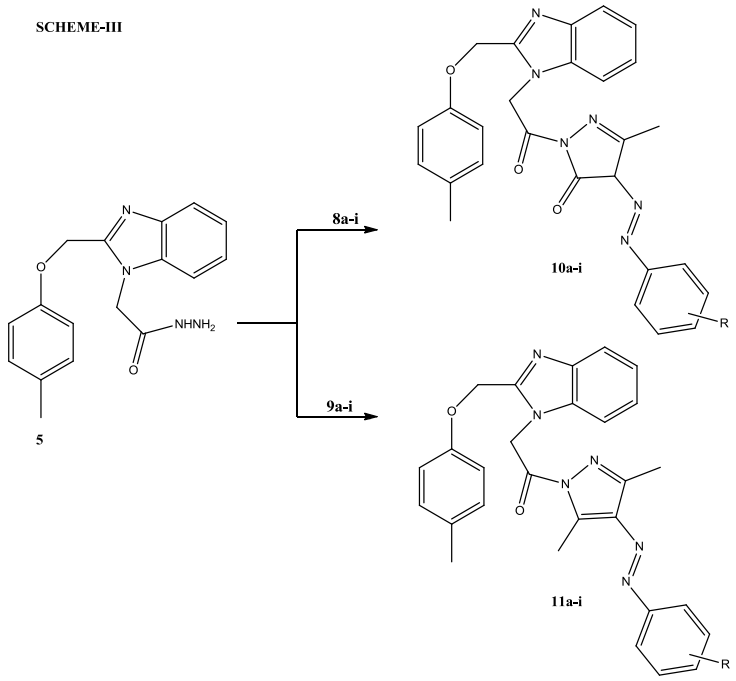
SCHEME- II



R= a) -H, b) 4-CH_3, c) 2-CH_3, d) 4-Cl,
e) 2-Cl, f) 4-NO_2 g) 2-NO_2, h) 4-OCH_3, i) 2-OCH_3

SCHEME-III



R= a) -H, b) 4-CH_3, c) 2-CH_3, d) 4-Cl,
e) 2-Cl, f) 4-NO_2 g) 2-NO_2, h) 4-OCH_3, i) 2-OCH_3

Reaction of compound **5** with **8a-i** in ethanol resulted in the formation of 3-methyl-4-(2-arylhydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1H-benzo[d]imidazol-1-yl)acetyl)-1H-pyrazol-5(4H)-one **(10a-i)** in good yields. The spectral data of **10a-i** confirmed that these compounds exist in hydrazono form. The spectral data of **10a** revealed a strong band at 1739 cm^{-1} due to C=O group. Low frequency carbonyl band may be assigned to C=O group in pyrazolone due to participating in intra- molecular hydrogen-bonding with NH group. The ^1H NMR spectrum of **10a** showed a singlet at δ 7.28 due to the presence of hydrogen-bonded NH group. The mass spectra of **10a** showed molecular ion peak M^+ at m/z 480 corresponding to molecular formula$C_{27}H_{24}N_6O_3$.

Reaction of compound **5** with **9**a-g in the presence of ethanol resulted in the formation of 1-(3,5-dimethyl-4-(aryldiazenyl)-1H-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1H-benzo[d]imidazol-1-yl)ethanone (**11a-i**) in good yields. IR spectra of **11a** revealed a band at 1464 cm^{-1} due to N=N group. The ^1H NMR spectra of

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11ashowed two singlets at δ 2.50, 2.61 indicating the presence of a pair of CH_3 groups in the Pyrazole ring. A singlet was observed at δ 5.39due to OCH_2 protons. The mass spectra of **11a** showed molecular ion peak M^+ at m/z 385 corresponding to molecular formula $C_{28}H_{26}N_6O_2$.

Elemental analyses and spectral data of **10a-i**and **11a-i** are consistent with the assigned structures (see Experimental section).The results pertaining to the evaluation of antimicrobial activities are summarized in **Table-I.**

Table 1: *In- vitro* antibacterial and antifungal activity results of compounds 5, 10a-i and 11a-i

Compound	Zone of inhibition, (mm)																				
	Gram-positive organisms[a]						Gram-negative organisms[a]									Fungi[b]					
	Stapylococcus aureus			*Bacillus subtilis*			*E.coli*			*Pseudomonas aeruginosa*			*Salmonella typhi*			*A.niger*			*U.maydis*		
ppm	1000	500	100	1000	500	100	1000	500	100	1000	500	100	1000	500	100	1000	500	100	1000	500	100
5	3.6	2.1	0.5	3.8	2.2	0.6	3.6	2.1	0.6	3.5	1.9	0.7	3.9	2.1	0.7	NA	NA	NA	NA	NA	NA
10a	3.9	2.0	0.4	4.9	2.1s	0.5	3.6	2.0	0.5	3.2	1.9	0.5	3.0	1.9	0.6	NA	NA	NA	0.9	0.4	NA
10b	6.2	3.0	0.5	5.6	2.6	0.6	6.2	3.0	0.6	5.9	2.8	0.6	6.3	3.1	0.7	NA	NA	NA	NA	NA	NA
10c	6.4	3.2	0.6	5.3	2.5	0.5	5.8	2.7	0.5	6.4	2.0	0.7	6.1	3.0	0/6	NA	NA	NA	NA	NA	NA
10d	4.8	2.5	0.5	8.4	4.3	0.8	8.6	4.2	0.9	5.4	2.3	0.6	4.2	2.8	0.5	2.8	1.2	NA	2.5	1.2	0.6
10e	5.8	2.7	0.6	6.5	3.4	0.6	7.4	3.8	0.7	5.8	2.6	0.6	4.9	2.8	0.5	NA	NA	NA	NA	NA	NA
10f	6.9	3.6	0.6	8.6	4.2	0.8	8.9	4.5	0.8	8.4	4.3	0.7	6.8	3.2	0.6	1.6	0.5	NA	NA	NA	NA
10g	7.2	3.5	0.7	7.8	3.7	0.7	6.4	3.2	0.7	6.8	3.3	0.8	6.5	3.2	0.6	NA	NA	NA	NA	NA	NA
10h	4.9	2.5	0.5	5.1	2.6	0.6	4.8	2.3	0.5	5.2	2.6	0.6	4.9	2.5	0.5	NA	NA	NA	NA	NA	NA
10i	4.6	2.3	0.4	4.9	2.5	0.5	4.5	2.1	0.4	5.6	2.7	0.7	4.6	2.3	0.4	NA	NA	NA	NA	NA	NA
11a	4.6	2.3	0.4	4.8	2.3	0.5	3.2	1.8	0.4	4.6	2.4	0.6	5.2	2.6	0.5	NA	NA	NA	1.6	0.9	0.3
11b	5.4	2.7	0.7	5.0	2.4	0.6	4.6	2.1	0.5	4.8	2.5	0.5	4.8	2.3	0.6	NA	NA	NA	0.5	0.2	NA
11c	4.5	2.3	0.6	4.2	2.0	0.3	4.9	2.5	0.6	4.6	2.3	0.5	4.6	2.2	0.5	NA	NA	NA	NA	NA	NA
11d	6.8	3.1	0.5	8.2	4.0	0.7	9.2	4.4	0.9	8.8	4.2	0.8	8.4	4.1	0.6	2.1	1.0	0.3	NA	NA	NA
11e	6.5	3.0	0.6	6.5	3.4	0.6	7.2	3.7	0.7	7.0	3.6	0.6	6.8	3.2	0.5	NA	NA	NA	NA	NA	NA
11f	7.2	3.6	0.6	7.8	3.8	0.7	8.6	4.4	0.8	8.2	4.1	0.7	8.0	3.9	0.6	NA	NA	NA	2.0	0.9	0.3
11g	5.4	2.7	0.5	5.9	2.8	0.6	6.9	3.7	0.7	6.7	3.6	0.6	6.8	3.8	0.6	NA	NA	NA	NA	NA	NA
11h	4.9	2.4	0.6	4.4	2.1	0.5	4.8	2.2	0.5	4.6	2.1	0.5	4.2	2.0	0.4	NA	NA	NA	NA	NA	NA
11i	4.0	2.0	0.5	4.2	2.0	0.4	4.4	2.1	0.5	4.3	2.0	0.4	4.3	2.1	0.5	NA	NA	NA	NA	NA	NA

[a] Reference drug: Gentamycin
[b] Reference drug : Nystatin
NA No activity

The investigation of antibacterial screening data revealed that all the tested compounds showed moderate to good bacterial inhibition. But majority of the compounds did not exhibit any significant antifungal inhibition.

CONCLUSIONS

In the present study a series of 3-methyl-4-(2-substitutedphenylhydrazono)-1-(2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)acetyl)-1*H*-pyrazol-5(4*H*)-ones and 1-(3,5-dimethyl-4-(substitutedphenyldiazenyl)-1*H*-pyrazol-1-yl)-2-(2-((p-tolyloxy)methyl)-1*H*-benzo[d]imidazol-1-yl)ethanones have been successfully synthesized and the structures established by spectral analysis. The spectral data are consistent with the structure of the newly synthesized compounds. The antimicrobial activity of the synthesized compounds was studied using cup-plate agar diffusion method. The results revealed that majority of the tested compounds exhibited moderate to good activity against the control Gentamycin in antibacterial activity and majority of the compounds does not exhibit any significant antifungal inhibition.

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