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Synthesis, Characterization and Biological Evaluation Of Some Novel 2-[(5-Aryl)-4,5-Dihydro-1*H*-Pyrazole-3-Yl]-1H-Benzimidazoles As Potential Antimicrobial Agents

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ABSTRACT: *Various novel 2-[(5-aryl)-4,5-dihydro-1H-pyrazole-3-yl]-1H-benzimidazoles **(6a-h)** have been synthesized from 1-(1H-benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones **(5a-h)** by suing different o-phenylenediamines **(1a-d)** and lactic acid **2** as starting materials and by involving 2-(α-hydroxy)ethyl benzimidazoles **(3a-d)** and 2-acetyl benzimidazoles **(4a-d)** as intermediates. The chemical structures of these compounds have been established by IR, ^{1}H-NMR and Mass spectral data. The newly synthesized compounds were screened for their ability towards antimicrobial activity.*

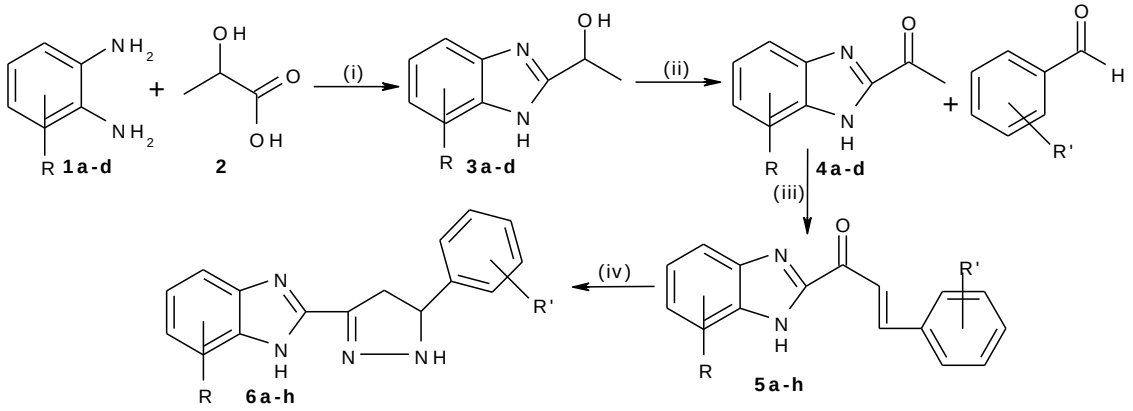
KEY WORDS: *Pyrazoles, benzimidazolines, antimicrobial activity*

I. INTRODUCTION:

The resistance to antimicrobial drugs is widespread, the development of new antimicrobial agents and understanding their mechanism of action are becoming vital nowadays.[1] The incorporation of the benzimidazole nucleus is an important synthetic strategy in studies of antimicrobial drug discovery.[2] Benzimidazoles have been an important pharmacophores and privileged structures in medicinal chemistry,[3] encompassing a diverse range of biological activities including anticancer,[4] cytotoxic,[5] antihypertensive,[6] antiviral,[7] vasodilator,[8] anti-arrhythmic, antiulcer, anthelmintical, inotropic, antihistamine, antifungal, anti-inflammatory.[9] However many strategies are available for benzimidazole synthesis.[10-14] The exploitation of a simple molecule with different functionalities for the synthesis of heterocyclics is a worthwhile contribution in the heterocyclic chemistry. The pyrazoles are prominent nitrogen-containing heterocyclics and, therefore, various procedures have been worked out for their synthesis.[15] Numerous pyrazoles and their derivatives have been found to possess useful bioactivity such as antihyperglycemic, analgesic, anti-inflammatory, antipyretic, antibacterial, hypoglycemic, sedative-hypnotic activity,[16-22] antimicrobial,[23] central nervous system[24] and immunosuppressive.[25]

II. RESULTS AND DISCUSSION:

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. Thus we have designed and synthesized a series of novel 2-[(5-aryl)-4,5-dihydro-1*H*-pyrazole-3-yl]-1*H*-benzimidazoles **(6a-h)** in good to excellent yields by using commercially available *o*-phenylenediamines **(1a-d)** and lactic acid **2** (Scheme 1). The synthetic route leading to the title compounds is summarized in scheme 1. The initial intermediate, 2-(α-hydroxy)ethyl benzimidazoles **(3a-d)** was prepared through cyclization between *o*-phenylenediamines **(1a-d)** and lactic acid **2** in HCl solution under reflux for 25-26 h. The compound **3a-d** was turned into the intermediate, 2-acetyl benzimidazoles **(4a-d)** on oxidation with $K_2Cr_2O_7$ in presence of H_2SO_4 at ambient temperature on uniform stirring for 4-5. The final intermediate, 1-(1*H*-benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones **(5a-h)** has been prepared from the reaction between compound **4a-d** and different aromatic aldehydes in alkaline medium (60% KOH) by using ethanol solvent on constant stirring at room temperature for 3-4 h. The title compounds, 2-[(5-aryl)-4,5-dihydro-1*H*-pyrazole-3-yl]-1*H*-benzimidazoles **(6a-h)** have been prepared from the subsequent ring closure reaction of compound **5a-h** with hydrazine hydrate in acetic acid at reflux temperature for 5-6 h. The chemical structures of all the newly synthesized compounds were confirmed by their IR, ^{1}H-NMR and mass spectral data. Further the compounds **6a-h** were used to evaluate their antimicrobial activity.



Scheme 1: (i) HCl, reflux, 25-26 h, (ii) $K_2Cr_20_7$, H_2SO_4, 4-5 h, (iii) EtOH, 60% KOH, 3-4 h, (iv) AcOH, reflux, 5-6h.

1/3/4a-d R = a) H, b) 4-CH_3, c) 4-Cl; d) 4-NO_2. **5/6a-h** R= a) H, b) H, c) H, d) 4-CH_3, e) 4-CH_3, f) 4-Cl, g) 4-Cl, h) 4-NO_2.

5/6a-h R'= a) H, b) 4-OCH_3, c) 3,4-OCH_3, d) H, e) 4-C_2H_5, f) 4-C_2H_5, g) 4-NO_2, h) 4-C_2H_5.

Table 1: Antimicrobial activity of 2-[(5-aryl)-4,5-dihydro-1*H*-pyrazole-3-yl]-1*H*-benzimidazoles **(6a-h)**

Compound	**Antibacterial activity**				**Antifungal activity**	
	B. subtilus	*S. aureus*	*E. coli*	*K. pneumoniae*	*F. oxysporum*	*A. niger*
6a	05	05	05	05	02	02
6b	13	13	09	10	05	05
6c	15	15	13	12	04	03
6d	13	15	13	13	05	04
6e	10	09	10	08	03	03
6f	13	13	08	07	04	03
6g	13	15	09	11	05	05
6h	09	09	10	05	03	03
Streptomycin	16	16	16	16	-	-
Fluconazole	-	-	-	-	06	06

ANTIBACTERIAL ACTIVITY

The *in vitro* antibacterial activity of the newly synthesized compounds was evaluated against two representative gram-positive bacteria viz., *B. subtilus* and *S. aureus*, two gram-negative bacteria viz., *E. coli* and *K .pneumoniae* through 'Cup-plate method'[26] using Streptomycin as standard drug by using DMSO as solvent and these results were confirmed by an experiment run at a concentration of 40 μg/ml (Table 1). It has been observed that the compounds exhibited interesting biological activity however, with a degree of variation. Among all the synthesized compounds, Compound **6c** against *B. subtilus* and *S. aureus*, compounds **6c, 6d** and **6g** against *S. aureus* were determined to be of excellent activity. Compounds **6b, 6d, 6f** and **6g** against *B. subtilus*, compounds **6b** and **6f** towards *S. aureus*, the tested compounds **6c** and **6d** against *E. coli* and the compound **6d** against *K. pneumoniae* were exhibited intermediate activity. While the remaining compounds showed moderate to low activity against all the organisms employed under the conditions of this experiment.

ANTIFUNGAL ACTIVITY

The newly prepared compounds were also screened for growth inhibition against two fungal organisms namely *F. oxysporum* and *A. niger* by using Fluconazole as standard drug with same method and solvent. The activity of the tested compounds is listed in Table 1. At 40 μg/ml concentration, Compounds **6b, 6d** and **6g** showed the greatest biological activity against *F. oxysporum* since the growth was almost completely inhibited during the entire incubation period and compounds **6b and 6g** are most active against *A. niger.* Compounds **6c** and **6f** showed pronounced growth inhibition against *F. oxysporum* and compound **6d** against *A. niger*. The remaining compounds were moderate to less active.

EXPERIMENTAL

All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by

column chromatography on silica gel of 60-120 mesh. IR spectra were obtained on a Perkin Elmer BX serried FTIR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a Varian 300 MHz spectrometer for ^{1}H NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

Synthesis of 2-(α-hydroxy)ethyl benzimidazoles (3a-d)

o-Phenylenediamine **(1a-d)** (0.01 mol) was treated with lactic acid **(2)** (0.01 mol) in presence of 4N hydrochloric acid (5 mL) and refluxed on water both for 24 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled and neutralized with NH_3 solution to get solid which is separated through filter and recrystallized from absolute ethanol to afford **3a-d** in pure form.

Synthesis of 2-acetyl benzimidazoles (4a-d)

To a solution of 2-(α-hydroxy)ethyl benzimidazole **(3a-d)** (0.01 mol) in dil.H_2SO_4 (5%, 40 mL) was drop wise added the solution of $K_2Cr_2O_7$ (0.15 mol) and aqueous H_2SO_4 (25%, 80 mL) with constant stirring at room temperature over a period of 20 min. Further the reaction mixture was stirred at room temperature for 2 h. After completion of the reaction, (monitored by TLC), the reaction mixture neutralized with NH_3 solution (1:1) and formed solid was filtered, washed with water and dried, recrystallized from ethyl acetate to achieve **4a-d** in pure form.

Synthesis of 1-(1H-benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones (5a-h)

2-Acetyl benzimidazole **(4a-d)** (0.01 mol) and aromatic benzaldehyde (0.01 mol) were mixed in ethanol (20 mL) and added 60% aq. KOH (5 mL) and the mixture was constantly stirred at room temperature for 4 h. After completion of reaction (monitored by TLC) the reaction mixture was poured into ice cold water and neutralized with dil HCl solution to get solid which is recrystallized from ethanol to get **5a-d** in pure form.

Synthesis of 2-[(5-aryl)-4,5-dihydro-1*H*-pyrazole-3-yl]-1*H*-benzimidazoles (6a-h)

1-(1*H*-Benzimidazol-2-yl)-3-(substituted phenyl)prop-2-en-1-ones **(5a-h)** (0.01 mol) and hydrazine hydrate (0.04 mol) was dissolved in glacial acetic acid (10 ml) and refluxed the reaction mixture on water both for 5-6 h. After completion of reaction (monitored by TLC) the reaction mixture was poured into ice cold water and neutralized with ammonia solution. The formed solid was filtered, dried and recrystallized from ethyl acetate to obtain compounds **6a-h** in pure form.

1-(1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3a) Yellow solid, yield 90%, mp 180-182 ^{o}C. IR (KBr) cm^{-1}: 2971, 1623, 1458, 1215, 1103. ^{1}H NMR ($CDCl_3$) δ: 10.30 (1H, bs), 7.52 (2H, m, *J*=7.8 Hz), 7.12 (2H, m, *J*=7.6), 4.8 (1H, s), 3.05 (1H, q, *J*=7.4 Hz), 1.62 (3H, d, *J*=7.2 Hz). MS *m/z*: 163 (M^++1).

1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3b) Dark yellow solid, yield 90%, mp 160-162 ^{o}C. IR (KBr) cm^{-1}: 3038, 2701, 1629, 1449, 1316, 1101. ^{1}H NMR ($CDCl_3$) δ: 9.61 (1H, bs), 7.32 (3H, m, *J*=8.0 Hz), 4.85 (1H, s), 3.05 (1H, q, *J*=7.8 Hz), 1.62 (3H, d, *J*=7.4 Hz). MS *m/z*: 177 (M^++1).

1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3c) Brown solid, yield 65%, mp 171-173 ^{o}C. IR (KBr) cm^{-1}: 2981, 1623, 1444, 1210, 1082. ^{1}H NMR ($CDCl_3$) δ: 12.50 (1H, s), 7.55 (2H, d, *J*=7.2 Hz), 7.20 (1H, d, *J*=7.4 Hz), 4.91 (1H, m, *J*=6.8 Hz), 1.52 (3H, d, *J*=7.0 Hz). MS *m/z*: 197 (M^++1).

1-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3d) Brown solid, yield 75%, mp 148-150 ^{o}C. IR (KBr) cm^{-1}: 3342, 3215, 3024, 2865, 2240, 1420, 1248. ^{1}H NMR ($CDCl_3$) δ: 8.63 (1H, s), 7.91 (1H, d, *J*=7.0 Hz), 7.76 (1H, d, *J*=7.2 Hz), 6.64 (1H, s), 6.59 (1H, d, *J*=7.4 Hz), 5.16 (1H, m, *J*=7.6 Hz), 1.77 (1H, d, *J*=7.8 Hz). MS *m/z*: 208 (M^++1).

1-(1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4a) Yellow solid, yield 78%, mp 189-191 ^{o}C. IR (KBr) cm^{-1}: 3289, 3059, 3015, 1674, 1580, 1445, 1235, 1147. ^{1}H NMR ($CDCl_3$) δ: 13.02 (1H, s), 7.85 (1H, d, *J*=7.8 Hz), 7.52 (1H, d, *J*=7.6 Hz), 7.32 (2H, t, *J*=7.4 Hz), 2.74 (3H, s). MS *m/z*: 161 (M^++1).

1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4b) Yellow solid, yield 80%, mp 170-172 ^{o}C. IR (KBr) cm^{-1}: 3365, 2919, 2852, 1693. ^{1}H NMR ($CDCl_3$) δ: 11.23 (1H, s), 7.65 (1H, d, *J*=8.0 Hz), 7.48 (1H, d, *J*=7.8 Hz), 7.24 (1H, s), 3.42 (3H, s), 2.45 (3H, s). MS *m/z*: 174 (M^++1).

1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4c) Yellow solid, yield 65%, mp 185-187 ^{o}C. IR (KBr) cm^{-1}: 3294, 3066, 3021, 1677, 1574, 1335, 1219, 1060. ^{1}H NMR ($CDCl_3$) δ: 10.70 H, s), 7.82 (1H, t, *J*=7.6 Hz), 7.51 (1H, m, *J*=7.4 Hz), 7.30 (1H, m, *J*=7.2 Hz), 2.81 (3H, s). MS *m/z*: 195 (M^++1).

1-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4d) Pale yellow solid, yield 70%, mp 155-157 ^{o}C. IR (KBr) cm^{-1}: 3360, 3040, 2865, 2160, 1720, 1356, 1240. ^{1}H NMR ($CDCl_3$) δ: 8.91 (1H, s), 8.77 (1H, s), 8.13 (1H, d, *J*=7.2 Hz), 8.09 (1H, d, *J*=7.4 Hz), 2.79 (3H, s). MS *m/z*: 206 (M^++1).

(*E*)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-phenyl-2-propen-1-one (5a) Pale yellow solid, yield 69%, mp 162-164 ^{o}C. IR (KBr) cm^{-1}: 3276, 2856, 1589, 1487, 1238. ^{1}H NMR ($CDCl_3$) δ: 8.77 (1H, s), 8.11 (2H, d, *J*=8.8 Hz),

7.76 (2H, dd, *J*=8.4 Hz), 7.43 (2H, d, *J*=8.2 Hz), 7.23 (2H, dd, *J*=7.8 Hz), 6.90 (1H, d, *J*=8.0 Hz). MS *m/z*: 249 (M^++1).

(*E*)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-(4-methoxy-phenyl)-2-propen-1-one (5b) Dark yellow solid, yield 78%, mp 175-177 ^oC. IR (KBr) cm^{-1}: 3282, 2848, 1601, 1508, 1245. ^1H NMR ($CDCl_3$) δ: 12.28 (1H, s), 7.51-7.02 (8H, m, *J*=8.6 Hz), 6.12-5.64 (1H, dd, *J*=8.2 Hz), 3.82 (3H, s), 3.44-3.38 (1H, dd, *J*=8.2 Hz). MS *m/z*: 279 (M^++1).

(*E*)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-(3,4-dimethoxyphenyl)-2-propen-1-one (5c) Yellow solid, yield 72%, mp 210-212 ^oC. IR (KBr) cm^{-1}: 3232, 1655, 1612, 1545, 1253, 1177, 833. ^1H NMR ($CDCl_3$) δ: 8.77 (1H, s), 8.11 (2H, d, *J*=7.8 Hz), 7.76 (2H, dd, *J*=8.0 Hz), 7.59 (1H, d, *J*=8.2 Hz), 7.13 (1H, s), 6.90 (1H, d, *J*=8.4 Hz), 6.82 (1H, d, *J*=8.4 Hz), 6.79 (1H, d, *J*=7.8 Hz), 3.80 (6H, s). MS *m/z*: 309 (M^++1).

(*E*)-1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-3-phenyl-2-propen-1-one (5d) Yellow solid, yield 72%, mp 178-180 ^oC. IR (KBr) cm^{-1}: 3245, 2925, 1662, 1624, 1564, 1243, 1210, 846. ^1H NMR ($CDCl_3$) δ: 8.76 (1H, s), 7.71 (1H, d, *J*=7.8 Hz), 7.66 (1H, d, *J*=7.8 Hz), 7.56 (1H, d, *J*=8.0 Hz), 7.43 (2H, d, *J*=8.2 Hz), 7.39 (1H, dd, *J*=7.8 Hz), 7.36 (1H, d, *J*=7.6 Hz), 7.23 (1H, dd, *J*=8.0 Hz), 6.94 (1H, d, *J*=7.8 Hz), 2.43 (3H, s). MS *m/z*: 263 (M^++1).

(*E*)-3-(4-ethylphenyl)-1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-2-propen-1-one (5e) Yellow solid, yield 65%, mp 168-170 ^oC. IR (KBr) cm^{-1}: 3230, 2932, 1654, 1612, 1572, 1234, 1222, 864. ^1H NMR ($CDCl_3$) δ: 8.77 (1H, s), 7.73 (1H, d, *J*=8.0 Hz), 7.68 (1H, d, *J*=7.8 Hz), 7.61 (1H, d, *J*=7.4 Hz), 7.39 (1H, d, *J*=8.4 Hz), 7.26 (2H, d, *J*=8.4 Hz), 7.20 (2H, d, *J*=7.6 Hz), 6.94 (1H, d, *J*=7.4 Hz), 2.47 (2H, q, *J*=8.0 Hz), 2.43 (3H, s), 1.37 (3H, t, *J*=7.2 Hz). MS *m/z*: 291 (M^++1).

(*E*)-1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-3-(4-ethylphenyl)-2-propen-1-one (5f) Brown solid, yield 55%, mp 173-175 ^oC. IR (KBr) cm^{-1}: 3255, 2956, 1674, 1635, 1594, 1256, 1243, 884. ^1H NMR ($CDCl_3$) δ: 8.75 (1H, s), 7.88 (1H, d, *J*=7.8 Hz), 7.79 (1H, d, *J*=7.4 Hz), 7.60 (1H, d, *J*=8.0 Hz), 7.58 (1H, d, *J*=7.4 Hz), 7.26 (2H, d, *J*=8.0 Hz), 7.21 (2H, d, *J*=7.4 Hz), 6.94 (1H, d, *J*=7.6 Hz), 2.47 (3H, q, *J*=7.2 Hz), 1.37 (3H, t, *J*=7.8 Hz). MS: *m/z* 311.7 (M^++1).

(*E*)-1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-3-(4-nitrophenyl)-2-propen-1-one (5g) Red solid, yield 45%, mp 212-214 ^oC. IR (KBr) cm^{-1}: 3243, 2946, 1663, 1644, 1584, 1236, 1254, 906. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 8.77 (1H, s), 8.07 (2H, d, *J*=7.8 Hz), 7.89 (1H, d, *J*=8.0 Hz), 7.78 (1H, d, *J*=7.6 Hz), 7.73 (2H, d, *J*=8.0 Hz), 7.62 (2H, s), 7.58 (1H, d, *J*=8.2 Hz), 6.94 (1H, d, *J*=8.0 Hz). MS *m/z*: 328 (M^++1).

(*E*)-3-(4-ethylphenyl)-1-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-2-propen-1-one (5h) Brown solid, yield 53%, mp 168-170 ^oC. IR (KBr) cm^{-1}: 3234, 2941, 1668, 1654, 1576, 1246, 1263, 879. ^1H NMR ($CDCl_3$) δ: 9.09 (1H, s), 8.75 (1H, s), 8.30 (1H, d, *J*=8.2 Hz), 8.29 (1H, d, *J*=8.0 Hz), 7.61 (1H, d, *J*=7.6 Hz), 7.26 (2H, d, *J*=7.4 Hz), 7.20 (2H, d, *J*=7.6 Hz), 6.90 (1H, d, *J*=8.0 Hz), 2.47 (2H, q, *J*=8.2 Hz), 1.37 (3H, t, *J*=7.8 Hz). MS *m/z*: 322 (M^++1).

2-[5-(phenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-1*H*-benzimidazol (6a) Brown solid, yield 72%, mp 158-160 ^oC. IR (KBr) cm^{-1}: 3374, 3034, 2224, 1558, 1432, 846. ^1H NMR ($CDCl_3$) δ: 7.92 (1H, s), 7.90 (1H, d, *J*=8.4 Hz), 7.61 (2H, d, *J*=7.8 Hz), 7.50 (2H, dd, *J*=8.2 Hz), 7.41 (2H, d, *J*=7.6 Hz), 7.24 (1H, dd, *J*=8.0 Hz), 7.17 (2H, dd, *J*=7.6 Hz), 4.90 (1H, m, *J*=8.0 Hz), 3.43 (2H, d, *J*=7.4 Hz). MS: *m/z* 263.3 (M^++1).

2-[5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-1*H*-benzimidazol (6b) Orange solid, yield 74%, mp 169-171 ^oC. IR (KBr) cm^{-1}: 3408, 3016, 2942, 2136, 1574, 1426, 1244, 846. ^1H NMR ($CDCl_3$) δ: 7.92 (1H, s), 7.90 (1H, d, *J*=7.8 Hz), 7.50 (2H, dd, *J*=8.0 Hz), 7.41 (2H, d, *J*=8.4 Hz), 7.18 (2H, d, *J*=7.4 Hz), 6.86 (2H, d, *J*=8.2 Hz), 4.90 (1H, m, *J*=7.6 Hz), 3.43 (2H, d, *J*=7.2 Hz), 3.33 (3H, s). MS *m/z*: 293 (M^++1).

2-[5-(3,4-dimethoxyphenyl)-4,5-dihydro-1*H*-pyra-zol-3-yl]-1*H*-benzimidazol (6c) Yellow solid, yield 69%, mp 154-156 ^oC. IR (KBr) cm^{-1}: 3374, 3015, 2932, 2124, 1586, 1374, 1124, 932. ^1H NMR ($CDCl_3$) δ: 7.92 (1H, s), 7.90 (1H, d, *J*=7.6 Hz), 7.50 (2H, dd, *J*=8.0 Hz), 7.41 (2H, d, *J*=7.2 Hz), 7.05 (1H, s), 6.95 (1H, d, *J*=8.4 Hz), 6.67 (1H, d, *J*=8.2 Hz), 4.90 (1H, m, *J*=7.4 Hz), 3.70 (6H, s), 3.43 (2H, d, *J*=8.0 Hz). MS *m/z*: 323 (M^++1).

2-(5-phenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-5-methyl1*H*-benzimidazol (6d) Pale yellow, yield 70%, mp 146-148 ^oC. IR (KBr) cm^{-1}: 3344, 3024, 2932, 2124, 1565, 1487, 876. ^1H NMR ($CDCl_3$) δ: 7.92 (1H, s), 7.90 (1H, d, *J*=8.8 Hz), 7.61 (2H, d, *J*=7.8 Hz), 7.24 (1H, dd, *J*=8.4 Hz), 7.20 (1H, d, *J*=7.6 Hz), 7.17 (2H, dd, *J*=7.4 Hz), 7.12 (1H, d, *J*=7.2 Hz), 7.09 (1H, s), 4.90 (1H, m, *J*=8.0 Hz), 3.43 (2H, d, *J*=8.2 Hz), 2.43 (3H, s). MS *m/z*: 277 (M^++1).

2-[5-(4-ethylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-5-methyl-1*H*-benzimidazol (6e) Red solid, yield 68%, mp 172-174 ^oC. IR (KBr) cm^{-1}: 3412, 3018, 2948, 2172, 1588, 1424, 968. ^1H NMR ($CDCl_3$) δ: 7.92 (1H, s), 7.90 (1H, d, *J*=8.8 Hz), 7.36 (2H, d, *J*=8.4 Hz), 7.20 (1H, d, *J*=8.0 Hz), 7.12 (1H, d, *J*=7.8 Hz), 7.09 (1H, s), 7.01 (2H, d, *J*=7.4 Hz), 4.90 (1H, m, *J*=7.8 Hz), 3.43 (2H, d, *J*=7.4 Hz), 2.43 (3H, s), 2.39 (2H, q, *J*=7.8 Hz), 1.06 (3H, t, *J*=8.0 Hz). MS *m/z*: 304 (M^++1).

2-[5-(4-ethylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-5-chloro-1*H*-benzimidazol (6f) Pale yellow solid, yield 71%, mp 144-146 ^oC. IR (KBr) cm^{-1}: 3422, 3014, 2878, 2116, 1532, 1432, 1042, 784. ^1H NMR ($CDCl_3$) δ: 7.92

(1H, s), 7.90 (1H, d, *J*=7.8 Hz), 7.38 (1H, s), 7.36 (1H, d, *J*=7.6 Hz), 7.34 (2H, d, *J*=8.0 Hz), 7.28 (1H, d, *J*=8.2 Hz), 7.01 (2H, d, *J*=8.4 Hz), 4.90 (1H, m, *J*=8.2 Hz), 3.43 (2H, d, *J*=7.6 Hz), 2.39 (2H, q, *J*=7.8 Hz), 1.06 (3H, t, *J*=7.4 Hz). MS *m/z*: 325 (M^++1).

2-[5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-5-chloro-1*H*-benzimidazol (6g) Orange solid, yield 66%, mp 174-176 ^oC. IR (KBr) cm^{-1}: 3420, 3026, 2118, 1582, 1432, 892. ^1H NMR ($CDCl_3$) δ: 7.92 (1H, s), 7.90 (1H, d, *J*=7.8 Hz), 7.88 (2H, d, *J*=7.4 Hz), 7.64 (2H, d, *J*=7.6 Hz), 7.38 (1H, s), 7.36 (1H, d, *J*=8.2 Hz), 7.28 (1H, d, *J*=8.4 Hz), 4.90 (1H, m, *J*=8.0 Hz), 3.43 (2H, d, *J*=8.2 Hz). MS *m/z*: 342 (M^++1).

2-[5-(4-ethylphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl]-5-nitro-1*H*-benzimidazol (6h) Yellow solid, yield 66%, mp 160-162 ^oC. IR (KBr) cm^{-1}: 3416, 3034, 2948, 2124, 1586, 1430, 1224, 886. ^1H NMR ($CDCl_3$) δ: 8.31 (1H, d, *J*=7.8 Hz), 8.26 (1H, s), 7.92 (1H, s), 7.90 (1H, d, *J*=8.0 Hz), 7.79 (1H, d, *J*=7.6 Hz), 7.36 (2H, d, *J*=8.0 Hz), 7.01 (2H, d, *J*=7.4 Hz), 4.90 (1H, m, *J*=8.2 Hz), 3.43 (2H, d, *J*=7.2 Hz), 2.39 (2H, q, *J*=8.0 Hz), 1.06 (3H, t, *J*=7.4 Hz). MS *m/z*: 336 (M^++1).

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