

Facile synthesis of alkoxyphthalimide derivatized benzimidazole assembled pyrazoles, pyrimidines and isoxazoles, *via* common intermediate chalcone

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In the present investigation, synthesis of 2-(3-aryl-2-phenyl-3,4-dihydropyrazol-5-yl)-1-N-alkoxyphthalimidobenzimidazole **9a-h**, 4-(1-N-alkoxyphthalimidobenzimidazol-2-yl)-6-arylpyrimidin-2-amine **10a-h** and 2-(5-aryl-4,5-dihydroisoxazol-3-yl)-1-N-alkoxyphthalimidobenzimidazole **11a-h** are described. Mild dichromate oxidation of 1-benzimidazol-2-yl-ethanol **1** gives 1-benzimidazol-2-yl-ethanone **2** which on Claisen condensation with various aromatic aldehydes yields the corresponding 3-aryl-1-(benzimidazol-2-yl)-prop-2-en-1-one **3a-d** derivatives. Compound **3a-d** act as key intermediates for all the three series of final compounds. In one pathway **3a-d** is converted to its alkoxyphthalimide derivatives **5a-h** by condensation with ω -bromoalkoxyphthalimides **4a-b**, which cyclize with PhNHNH₂/pyridine, guanidine nitrate/10% NaOH and hydroxylamine hydrochloride/CH₃COOH to give **9a-h**, **10a-h** and **11a-h** respectively. In an alternative route, reaction of **3a-d** with all the three reagents affords 2-(3-aryl-2-phenyl-3,4-dihydropyrazol-5-yl)benzimidazole **6a-d**, 4-(benzimidazol-2-yl)-6-arylpyrimidin-2-amine **7a-d** and 2-(5-aryl-4,5-dihydroisoxazol-3-yl)benzimidazole **8a-d** which on condensation with ω -bromoalkoxyphthalimides **4a-b** give the final compounds **9a-h**, **10a-h** and **11a-h**. Structure elucidations of all the compounds have been accomplished by elemental analysis, IR, ¹H NMR and mass spectral data.

Keywords: Benzimidazole, ω -bromoalkoxyphthalimide, pyrazole, pyrimidine, isoxazole

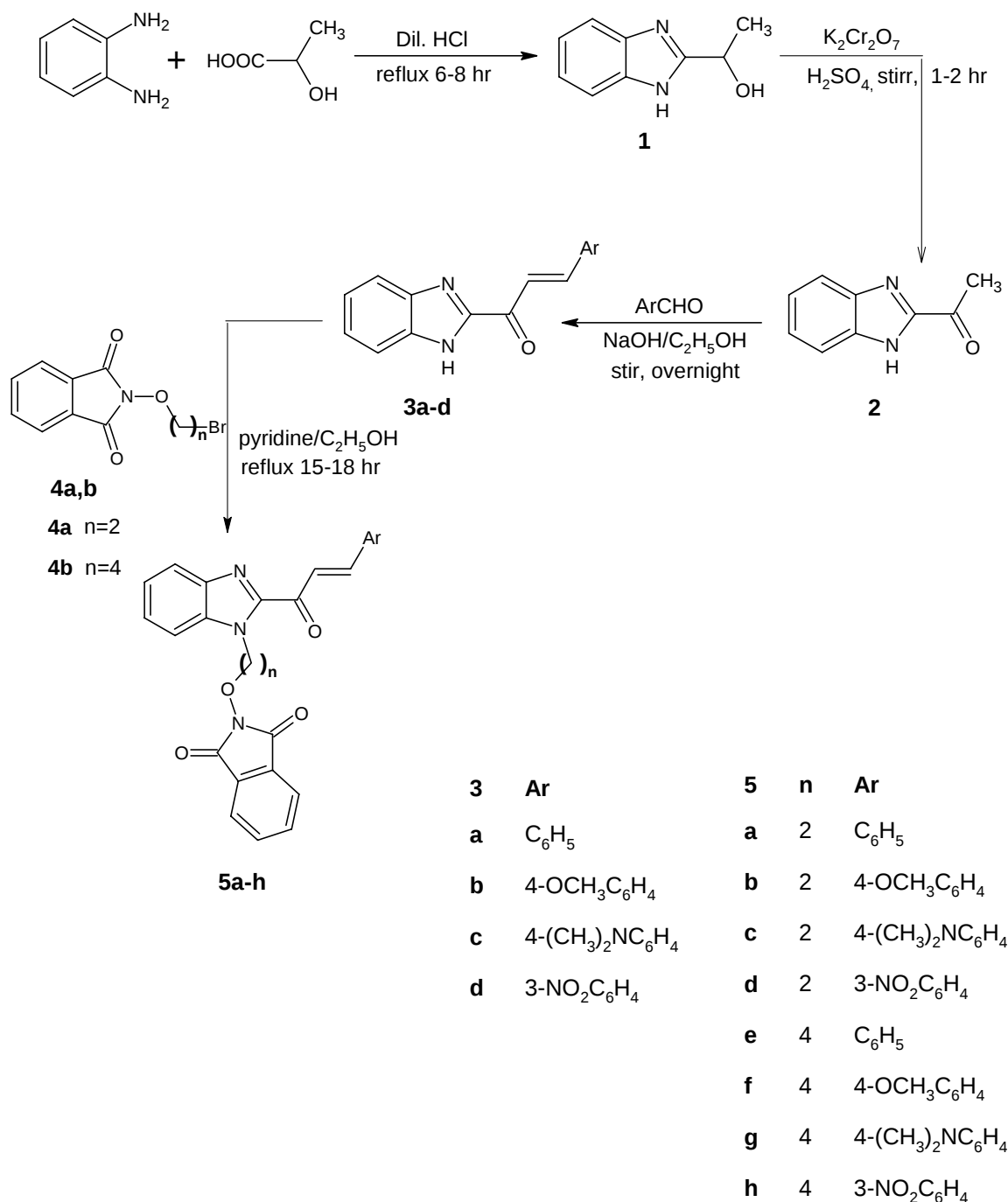
Derivatives of imidazole, pyrazole, pyrimidine and isoxazole have played a crucial role in the history of heterocyclic chemistry and been used extensively as important pharmacophores and synthons in the field of organic chemistry and drug designing. Owing to their versatile chemotherapeutic importance, a significant amount of research effort has been focussed on these nuclei.

Benzimidazole derivatives have evoked considerable attention in recent years as these are endowed with a wide range of pharmaceutical activities like antifungal¹, antihypertensive², antioxidant³, cardiogenic⁴, antithrombotic⁵, HIV-IPR inhibitor⁶, IL-1 inhibitor⁷, anticonvulsant⁸, anti-hepatitis B and C virus activity⁹, etc. The pyrazole nucleus is a ubiquitous feature of pharmacological interest and has been proven to be a fertile source of medicinal agents such as cytotoxic¹⁰, antibacterial¹¹, antiamoebic¹², 5- α reductase inhibitor¹³, cyclooxygenase-II (COX-IISS)¹⁴, antiproliferative¹⁵ and anticancer¹⁶. Pyrimidine derivatives serve both as biomimetic and reactive pharmacophores due to their diverse medicinal properties such as antitumor¹⁷, anticancer (lungs, breast and CNS cancer)¹⁸,

immunodilator¹⁹, antifolate²⁰, antiviral²¹, etc. Pyrimidine derivatives have activities like tyrosine kinase inhibitors²², COX-2 inhibitor²³, calcium channel blockers plus antihypertensive²⁴ and also activity against Y181C HIV-1 mutant strain²⁵. Isoxazoles are widely investigated for therapeutic uses like antiepileptic²⁶, PPAR- δ agonists²⁷, acetylcholine-esterase inhibitor²⁸, anti-inflammatory²⁹, acrosin inhibitor and antifungal activity³⁰, etc.

Diverse biological activities like anticonvulsant³¹, anticancer³², diuretic³³, fungicidal³⁴ and trypanocidal³⁵ have been observed for alkoxyphthalimide and related functionalities. The ability to inhibit growth of malarial parasite *Plasmodium falciparum*³⁶ have also been observed for several aminoxy derivatives. Heterocyclic rings attached to alkoxyphthalimide group have been synthesized³⁷ and tested for antimicrobial and antimalarial³⁸ activity.

Led by the above facts coupled with the desire for synthesizing various alkoxyphthalimide derivatives herein is reported the synthesis of some new heterocycles incorporating above moieties together in order to prepare the molecules having enhanced biological properties.

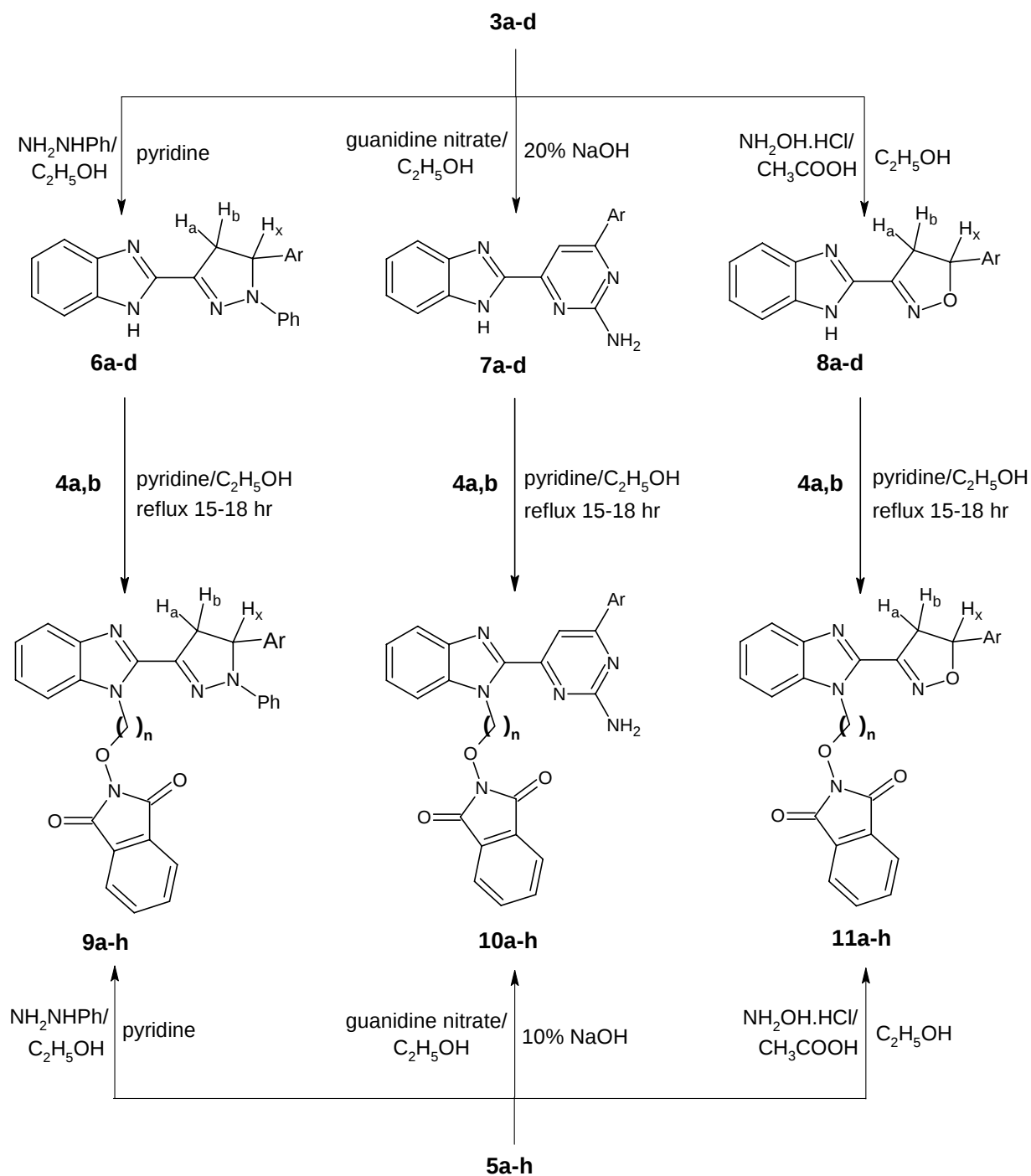


Scheme I

Result and Discussion

The Synthetic route for obtaining the final products is presented in **Scheme I** and **II**. The required intermediate 1-benzimidazol-2-yl-ethanone **2** was prepared by oxidation of 1-benzimidazol-2-yl-ethanol **1** using acid dichromate. Formation of **2** was confirmed by the IR absorption spectra at 1713 cm^{-1} due to carbonyl group and disappearance of O-H

stretching band at 3400 cm^{-1} in compound **1**. This is further supported by disappearance of ^1H NMR signal at δ 8.7 for O-H group. Compound **1** was prepared by refluxing *o*-phenylenediamine with lactic acid in dil. HCl. Compound **2** was converted to chalcones **3a-d** by treating it with corresponding aromatic aldehydes in NaOH/ethanol. IR and ^1H NMR spectral data established the structure of these compounds. IR



Scheme II

absorption band at $1654\text{--}1667\text{ cm}^{-1}$ indicated the presence of α,β -unsaturated carbonyl functionalities. Compounds **3a-d** were then condensed with ω -bromoalkoxyphthalimides **4a,b** in presence of catalytic amount of pyridine to furnish 2-(3-arylprop-2-enoyl)-1-N-alkoxyphthalimidobenzimidazole **5a-h**. Structure of **5a** was confirmed by disappearance of IR

peak for N-H functionality, appearance of C-O and N-O stretching band at 1075 and 1355 cm^{-1} respectively and two triplets at δ 2.7 and 3.0 for N-CH₂ and O-CH₂ of ethoxyphthalimide moiety in the ¹H NMR spectrum. 2-(3-Arylprop-2-enoyl)-1-N-alkoxyphthalimidobenzimidazole **5a-h** when treated with PhNHNH₂/pyridine, guanidine nitrate/10%NaOH and

hydroxylamine hydrochloride/CH₃COOH separately, afforded **9a-h**, **10a-h** and **11a-h** respectively. Formation of these compounds have been confirmed by disappearance of C=O stretching band at 1667 cm⁻¹ for α,β -unsaturated carbonyl group in all the three cases. Structure of **9a-h** was further confirmed by the presence of double doublet respectively of three hydrogens H_a, H_b and H_x present in pyrazole ring, which appeared at δ 3.25-3.44, 3.91-4.25 and 6.12-6.20 respectively. Formation of pyrimidine ring in compounds **10a-h** was inferred by IR spectra which exhibited an intense band in the region 3430-3361, corresponding to NH₂ group and the ¹H NMR spectra exhibited a singlet at δ 6.64-6.3 for NH₂ proton. Structure of **11a-h** was also established on the basis of different values of ¹H NMR signal for H_a, H_b and H_x, the values being δ 3.29-3.64, 3.96-4.32 and 6.63-6.89 for three double doublets and also N-O broadening peak in IR spectra. In an alternative pathway **9a-h**, **10a-h** and **11a-h** (Scheme II) were synthesized by reversal of the last two steps. In this reaction sequence, **3a-d** were first cyclized with the above mentioned reagents to give **6a-d**, **7a-d** and **8a-d**. These were further condensed with ω -bromoalkoxyphthalimides **4a-d** to yield the final compounds. Physical and analytical data of synthesized compounds are summarized in Table I and II.

Experimental Section

Melting points of all synthesized compounds were determined in open capillaries and are uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer 1300 FT IR spectrometer and ¹H NMR spectra were recorded on a Bruker WM-400 (400 MHz FT NMR) spectrometer using TMS as internal standard. Mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer. All compounds gave satisfactory micro analytical results. Homogeneity of the synthesized compounds was checked by TLC using silica gel-G plates, *n*-hexane-ethyl acetate as developing solvent and the spots were visualized using iodine vapour. ω -Bromoalkoxyphthalimides **4a,b** were prepared³⁹ by reported methods.

Synthesis of 1-benzimidazol-2-yl-ethanol, 1

A mixture of *o*-phenylenediamine (1.08 g, 0.01 mole) and lactic acid (0.7 mL, 0.01 mole) in 4 *N* HCl (40 mL) was refluxed for 6-8 hr on a water bath. The reaction mixture was allowed to cool and neutralized with aqueous NaOH solution. The separated solid was

filtered, washed with water, dried and purified by recrystallization from absolute ethanol.

IR (KBr): 3300 (N-H str.), 2978 (C-H str., CH₃), 3050 (C-H str., Ar-H), 1620 (C=N str.), 3400 cm⁻¹ (O-H str.); ¹H NMR (CDCl₃): δ 8.1 (s, 1H, OH), 8.6 (s, 1H, NH), 7.8-7.25 (m, 4H, Ar-H), 1.92 (d, 3H, CH₃).

Synthesis of 1-benzimidazol-2-yl-ethanone, 2

A mixture of **1** (8.1 g, 0.05 mole) in 5% sulphuric acid (100 mL) was treated dropwise with K₂Cr₂O₇ (19.8 g) solution in water (75 mL) and conc. H₂SO₄ (45 mL) and stirred for 1-2 hr. The separated solid was filtered, washed thoroughly with water, dried and purified by recrystallization from ethanol.

IR (KBr): 3408 (N-H str.), 2094, 2942 (C-H str., CH₃), 1713 (C=O str.), 1618 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃): δ 9.1 (s, 1H, NH), 7.7-7.18 (m, 4H, Ar-H), 2.1 (s, 3H, CH₃).

Synthesis of 1-(benzimidazol-2-yl)-3-phenylprop-2-en-1-one, 3a

To a stirred solution of **2** (1.6 g, 0.01 mole) and NaOH (3 g dissolved in minimum amount of water) in 90% ethanol (20 mL) was added portionwise benzaldehyde (1 mL, 0.01 mole). The stirring was continued for another 1 hr and then kept overnight. The contents of the flask were poured into water and neutralised with acetic acid. The separated solid was filtered, washed with water, dried and purified by recrystallization from ethanol.

IR (KBr): 3264-3444 (N-H str.), 3080 (C-H str., Ar-H), 1667 (C=O str.), 1597 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃): δ 9.32 (s, 1H, NH), 7.8-7.1 (m, 9H, Ar-H), 5.6 (d, 1H, =CH-Ar).

Similarly, other compounds **3b-d** were also synthesized. Their spectral characterization data are presented here:

1-(Benzimidazol-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one, 3b

IR (KBr): 3400 (N-H str.), 1654 (C=O str.), 1575 (C=N str.), 1088 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 9.08 (s, 1H, NH), 7.88-7.32 (m, 8H, Ar-H), 5.57 (d, 1H, =CH-Ar), 3.3 (s, 3H, OCH₃).

1-(Benzimidazol-2-yl)-3-[4-(dimethylamino)phenyl]prop-2-en-1-one, 3c

IR (KBr): 3430 (N-H str.), 2913 (C-H str., CH₃), 1663 (C=O str.), 1601 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃): δ 9.21 (s, 1H, NH), 7.79-7.27 (m, 8H, Ar-H), 5.61 (d, 1H, =CH-Ar), 3.19 (s, 6H, N(CH₃)₂).

Table I — Physical and analytical characterization data of compounds **3a-d**, **5a-h**, **6a-d**, **7a-d** and **8a-d**

Compd	Mol. formula	Mol. Wt.	Ar	n	Yield (%)	m.p. °C	Found (calcd) %	
							C	N
3a	C ₁₆ H ₁₂ N ₂ O	248.27	C ₆ H ₅	-	77	187	77.28 (77.40)	11.11 (11.28)
3b	C ₁₇ H ₁₄ N ₂ O ₂	278.30	4-OCH ₃ C ₆ H ₄	-	74	244	73.25 (73.37)	10.01 (10.07)
3c	C ₁₈ H ₁₇ N ₃ O	291.34	4-(CH ₃) ₂ NC ₆ H ₄	-	63	205	74.12 (74.20)	14.26 (14.42)
3d	C ₁₆ H ₁₁ N ₃ O ₃	293.27	3-NO ₂ C ₆ H ₄	-	69	200	65.46 (65.53)	14.14 (14.33)
5a	C ₂₆ H ₁₉ N ₃ O ₄	437.44	C ₆ H ₅	2	67	148	71.22 (71.39)	9.55 (9.61)
5b	C ₂₇ H ₂₁ N ₃ O ₅	467.47	4-OCH ₃ C ₆ H ₄	2	68	186	69.11 (69.37)	8.91 (8.99)
5c	C ₂₈ H ₂₄ N ₄ O ₄	480.51	4-(CH ₃) ₂ NC ₆ H ₄	2	70	158	69.76 (69.99)	11.51 (11.66)
5d	C ₂₆ H ₁₈ N ₄ O ₆	482.44	3-NO ₂ C ₆ H ₄	2	65	135	64.59 (64.73)	11.54 (11.61)
5e	C ₂₈ H ₂₃ N ₃ O ₄	465.49	C ₆ H ₅	4	71	142	72.09 (72.24)	9.01 (9.03)
5f	C ₂₉ H ₂₅ N ₃ O ₅	495.52	4-OCH ₃ C ₆ H ₄	4	63	161	70.16 (70.29)	8.32 (8.48)
5g	C ₃₀ H ₂₈ N ₄ O ₄	508.56	4-(CH ₃) ₂ NC ₆ H ₄	4	61	142	70.40 (70.85)	10.94 (11.02)
5h	C ₂₈ H ₂₂ N ₄ O ₆	510.49	3-NO ₂ C ₆ H ₄	4	66	130	65.72 (65.88)	10.89 (10.97)
6a	C ₂₂ H ₁₈ N ₄	338.40	C ₆ H ₅	-	77	202	78.01 (78.08)	16.41 (16.56)
6b	C ₂₃ H ₂₀ N ₄ O	368.43	4-OCH ₃ C ₆ H ₄	-	74	260	74.76 (74.98)	15.16 (15.21)
6c	C ₂₄ H ₂₃ N ₅	381.47	4-(CH ₃) ₂ NC ₆ H ₄	-	73	236	75.44 (75.56)	18.25 (18.36)
6d	C ₂₂ H ₁₇ N ₅ O ₂	383.40	3-NO ₂ C ₆ H ₄	-	68	242	68.86 (68.92)	18.19 (18.27)
7a	C ₁₇ H ₁₃ N ₅	287.31	C ₆ H ₅	-	72	238	71.02 (71.06)	24.22 (24.37)
7b	C ₁₈ H ₁₅ N ₅ O	317.34	4-OCH ₃ C ₆ H ₄	-	69	269	68.02 (68.13)	22.03 (22.07)
7c	C ₁₉ H ₁₈ N ₆	330.38	4-(CH ₃) ₂ NC ₆ H ₄	-	75	255	68.91 (69.07)	25.27 (25.44)
7d	C ₁₇ H ₁₂ N ₆ O ₂	332.31	3-NO ₂ C ₆ H ₄	-	65	251	61.29 (61.44)	25.17 (25.29)
8a	C ₁₆ H ₁₃ N ₃ O	263.29	C ₆ H ₅	-	71	205	72.87 (72.99)	15.88 (15.96)
8b	C ₁₇ H ₁₅ N ₃ O ₂	293.31	4-OCH ₃ C ₆ H ₄	-	66	222	69.44 (69.61)	14.24 (14.33)
8c	C ₁₈ H ₁₈ N ₄ O	306.36	4-(CH ₃) ₂ NC ₆ H ₄	-	61	220	70.42 (70.57)	18.20 (18.29)
8d	C ₁₆ H ₁₂ N ₄ O ₃	308.29	3-NO ₂ C ₆ H ₄	-	68	211	62.16 (62.33)	18.11 (18.17)

Table II — Physical and analytical characterization data of compounds **9a-h**, **10a-h** and **11a-h**

Compd	Mol. formula	Mol. Wt.	Ar	n	Yield (%)	m.p. °C	Found (calcd) %	
							C	N
9a	C ₃₂ H ₂₅ N ₅ O ₃	527.57	C ₆ H ₅	2	55	172	72.71 (72.85)	13.21 (13.27)
9b	C ₃₃ H ₂₇ N ₅ O ₄	557.59	4-OCH ₃ C ₆ H ₄	2	59	228	70.89 (71.08)	12.48 (12.56)
9c	C ₃₄ H ₃₀ N ₆ O ₃	570.64	4-(CH ₃) ₂ NC ₆ H ₄	2	65	190	71.41 (71.56)	14.59 (14.73)
9d	C ₃₂ H ₂₄ N ₆ O ₅	572.57	3-NO ₂ C ₆ H ₄	2	54	125	67.04 (67.13)	14.50 (14.68)
9e	C ₃₄ H ₂₉ N ₅ O ₃	555.62	C ₆ H ₅	4	51	168	73.29 (73.50)	12.42 (12.60)
9f	C ₃₅ H ₃₁ N ₅ O ₄	585.65	4-OCH ₃ C ₆ H ₄	4	58	221	71.63 (71.78)	11.82 (11.96)
9g	C ₃₆ H ₃₄ N ₆ O ₃	598.69	4-(CH ₃) ₂ NC ₆ H ₄	4	57	183	71.05 (72.22)	13.97 (14.04)
9h	C ₃₄ H ₂₈ N ₆ O ₅	600.62	3-NO ₂ C ₆ H ₄	4	61	119	67.79 (67.99)	13.81 (13.99)
10a	C ₂₇ H ₂₀ N ₆ O ₃	476.48	C ₆ H ₅	2	59	207	68.00 (68.06)	17.58 (17.64)
10b	C ₂₈ H ₂₂ N ₆ O ₄	506.51	4-OCH ₃ C ₆ H ₄	2	63	240	66.28 (66.40)	16.50 (16.59)
10c	C ₂₉ H ₂₅ N ₇ O ₃	519.55	4-(CH ₃) ₂ NC ₆ H ₄	2	61	231	66.91 (67.04)	18.71 (18.87)
10d	C ₂₇ H ₁₉ N ₇ O ₅	521.48	3-NO ₂ C ₆ H ₄	2	59	227	62.04 (62.19)	18.72 (18.80)
10e	C ₂₉ H ₂₄ N ₆ O ₃	504.53	C ₆ H ₅	4	56	197	68.87 (69.04)	16.59 (16.66)
10f	C ₃₀ H ₂₆ N ₆ O ₄	534.56	4-OCH ₃ C ₆ H ₄	4	61	234	67.18 (67.40)	15.59 (15.72)
10g	C ₃₁ H ₂₉ N ₇ O ₃	547.60	4-(CH ₃) ₂ NC ₆ H ₄	4	63	215	67.76 (67.99)	17.81 (17.90)
10h	C ₂₉ H ₂₃ N ₇ O ₅	549.53	3-NO ₂ C ₆ H ₄	4	65	209	63.19 (63.38)	17.77 (17.84)
11a	C ₂₆ H ₂₀ N ₄ O ₄	452.46	C ₆ H ₅	2	58	182	68.84 (69.02)	12.22 (12.38)
11b	C ₂₇ H ₂₂ N ₄ O ₅	482.48	4-OCH ₃ C ₆ H ₄	2	54	232	67.05 (67.21)	11.49 (11.61)
11c	C ₂₈ H ₂₅ N ₅ O ₄	495.52	4-(CH ₃) ₂ NC ₆ H ₄	2	62	210	67.61 (67.87)	14.05 (14.13)
11d	C ₂₆ H ₁₉ N ₅ O ₆	497.45	3-NO ₂ C ₆ H ₄	2	64	194	62.61 (62.77)	14.00 (14.08)
11e	C ₂₈ H ₂₄ N ₄ O ₄	480.51	C ₆ H ₅	4	58	174	69.74 (69.99)	11.51 (11.66)
11f	C ₂₉ H ₂₆ N ₄ O ₅	510.54	4-OCH ₃ C ₆ H ₄	4	66	226	68.04 (68.22)	10.72 (10.97)
11g	C ₃₀ H ₂₉ N ₅ O ₄	523.58	4-(CH ₃) ₂ NC ₆ H ₄	4	55	206	68.60 (68.82)	13.14 (13.38)
11h	C ₂₈ H ₂₃ N ₅ O ₆	525.51	3-NO ₂ C ₆ H ₄	4	59	187	63.79 (63.99)	13.20 (13.33)

1-(Benzimidazol-2-yl)-3-(3-nitrophenyl)prop-2-en-1-one, 3d

IR (KBr): 3417 (N-H str.), 1665 (C=O str.), 1607 (C=N str.), 1529, 1349 cm^{-1} (N=O str., NO_2); ^1H NMR (CDCl_3): δ 9.30 (s, 1H, NH), 7.91-7.40. (m, 8H, Ar-H), 5.56 (d, 1H, =CH-Ar).

Synthesis of 2-(3-phenylprop-2-enoyl)-1-N-ethoxyphthalimidobenzimidazole, 5a

To a three necked flask, provided with a reflux condenser, a dropping funnel and a mechanical stirrer, a solution of compound **3a** (2.48 g, 0.01 mole) and ω -bromoethoxyphthalimide **4a** (2.70 g, 0.01 mole) in absolute alcohol were charged. To this stirred solution catalytic amount of pyridine was added dropwise and the mixture was refluxed for 15-18 hr. After cooling, the mixture was concentrated to one third of the original volume by removing the solvent under reduced pressure. The separated solid was filtered, dried and purified by recrystallization from ethanol.

IR (KBr): 3072 (C-H str., Ar), 2980 (C-H str., CH_2), 1685-1644 (C=O str.), 1355 (N-O str.), 1075 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.9-7.68 (m, 13H, Ar-H), 5.43 (d, 1H, =CH-Ar), 2.7 (t, 2H, NCH_2), 3.0 (t, 2H, OCH_2).

Compounds **5b-h** were also prepared by similar method with minor change in reaction conditions. Spectral data of these compounds are presented here:

2-[3-(4-Methoxyphenyl)prop-2-enoyl]-1-N-ethoxyphthalimidobenzimidazole, 5b

IR (KBr): 3066 (C-H str., Ar), 2977 (C-H str., CH_2), 1710-1650 (C=O str.), 1343 (N-O str.), 1047 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.81-7.32 (m, 12H, Ar-H), 5.38 (d, 1H, =CH-Ar), 3.32 (s, 3H, CH_3), 2.61 (t, 2H, NCH_2), 3.12 (t, 2H, OCH_2).

2-[3-[4-(Dimethylamino)phenyl]prop-2-enoyl]-1-N-ethoxyphthalimidobenzimidazole, 5c

IR (KBr): 2948 (C-H str., CH_2), 1732-1670 (C=O str.), 1332 (N-O str.), 1042 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.98-7.41 (m, 12H, Ar-H), 5.65 (d, 1H, =CH-Ar), 2.73 (t, 2H, NCH_2), 3.22 (t, 2H, OCH_2), 2.9 (s, 6H, $\text{N}(\text{CH}_3)_2$).

2-[3-(3-Nitrophenyl)prop-2-enoyl]-1-N-ethoxyphthalimidobenzimidazole, 5d

IR (KBr): 2962 (C-H str., CH_2), 1698-1664 (C=O str.), 1341 (N-O str.), 1025 (C-O str.), 1503, 1326 cm^{-1} (N=O str.); ^1H NMR (CDCl_3): δ 7.84-7.2 (m, 12H,

Ar-H), 5.51 (d, 1H, =CH-Ar), 2.69 (t, 2H, NCH_2), 3.16 (t, 2H, OCH_2).

2-(3-Phenylprop-2-enoyl)-1-N-butoxyphthalimidobenzimidazole, 5e

IR (KBr): 3081 (C-H str., Ar), 2982 (C-H str., CH_2), 1723-1644 (C=O str.), 1335 (N-O str.), 1083 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.9-7.3 (m, 13H, Ar-H), 5.69 (d, 1H, =CH-Ar), 2.71 (t, 2H, NCH_2), 3.08 (t, 2H, OCH_2), 2.11 (m, 2H, $\text{CH}_2\text{-CH}_2$).

2-[3-(4-Methoxyphenyl)prop-2-enoyl]-1-N-butoxyphthalimidobenzimidazole, 5f

IR (KBr): 3084 (C-H str., Ar), 2948 (C-H str., CH_2), 1720-1687 (C=O str.), 1376 (N-O str.), 1072 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.87-7.35 (m, 12H, Ar-H), 5.43 (d, 1H, =CH-Ar), 3.41 (s, 3H, CH_3), 2.91 (t, 2H, NCH_2), 3.32 (t, 2H, OCH_2), 2.14 (m, 2H, $\text{CH}_2\text{-CH}_2$).

2-[3-(4-Dimethylaminophenyl)prop-2-enoyl]-1-N-butoxyphthalimidobenzimidazole, 5g

IR (KBr): 2988 (C-H str., CH_2), 1689-1644 (C=O str.), 1385 (N-O str.), 1057 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.8-7.21 (m, 12H, Ar-H), 5.4 (d, 1H, =CH-Ar), 2.96 (s, 6H, $\text{N}(\text{CH}_3)_2$), 2.69 (t, 2H, NCH_2), 3.22 (t, 2H, OCH_2), 2.18 (m, 2H, $\text{CH}_2\text{-CH}_2$).

2-[3-(3-Nitrophenyl)prop-2-enoyl]-1N-butoxyphthalimidobenzimidazole, 5h

IR (KBr): 3065 (C-H str., Ar), 2969 (C-H str., CH_2), 1693-1654 (C=O str.), 1342 (N-O str.), 1029 cm^{-1} (C-O str.); ^1H NMR (CDCl_3): δ 7.88-7.45 (m, 12H, Ar-H), 5.58 (d, 1H, =CH-Ar), 2.69 (t, 2H, NCH_2), 3.22 (t, 2H, OCH_2), 2.04 (m, 2H, $\text{CH}_2\text{-CH}_2$), 2.97 (s, 6H, $\text{N}(\text{CH}_3)_2$).

Synthesis of 2-(2,3-diphenyl-3,4-dihydropyrazol-5-yl)benzimidazole, 6a

To a mixture of **3a** (2.48 g, 0.01 mole) and phenyl hydrazine (1.08 g, 0.01 mole) in absolute alcohol, catalytic amount of pyridine was added and the reaction mixture was refluxed for 5-8 hr. After cooling, the reaction mixture was poured slowly into crushed ice with stirring. The solid product obtained was filtered, washed, dried and purified by recrystallization from ethanol.

IR (KBr): 3428 (N-H str.), 3070 (C-H str., Ar-H), 1576 (C=N str.), 1121 cm^{-1} (N-N str.); ^1H NMR

(CDCl₃): δ 9.43 (s, 1H, NH), 7.8-7.13 (m, 14H, Ar-H), 3.36 (dd, 1H, H_a), 3.99 (dd, 1H, H_b), 6.22 (dd, 1H, H_x).

Compounds **6b-d** were prepared by similar method with minor change in reaction conditions. Their spectral data are presented here:

2-[3-(4-Methoxyphenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]benzimidazole, 6b

IR (KBr): 3472 (N-H str.), 3041 (C-H str., Ar-H), 1535 (C=N str.), 1129 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 9.63 (s, 1H, NH), 7.85-7.31 (m, 13H, Ar-H), 3.42 (dd, 1H, H_a), 4.13 (dd, 1H, H_b), 6.43 (dd, 1H, H_x), 3.42 (t, 2H, OCH₂).

2-[3-(4-Dimethylaminophenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]benzimidazole, 6c

IR (KBr): 3442 (N-H str.), 3063 (C-H str., Ar-H), 1522 (C=N str.), 1135 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 9.47 (s, 1H, NH), 7.9-7.23 (m, 13H, Ar-H), 3.53 (dd, 1H, H_a), 4.21 (dd, 1H, H_b), 6.38 (dd, 1H, H_x), 2.9 (s, 6H, N(CH₃)₂).

2-[3-(3-Nitrophenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]benzimidazole, 6d

IR (KBr): 3439 (N-H str.), 3081 (C-H str., Ar-H), 1562 (C=N str.), 1115 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 9.71 (s, 1H, NH), 7.91-7.3 (m, 13H, Ar-H), 3.47 (dd, 1H, H_a), 4.11 (dd, 1H, H_b), 6.48 (dd, 1H, H_x).

Synthesis of 4-(benzimidazol-2-yl)-6-phenylpyrimidin-2-amine, 7a

Compound **3a** (2.48 g, 0.01 mole) and guanidine nitrate (1.22 g, 0.01 mole) were dissolved in absolute alcohol and refluxed for 1 hr. 10% NaOH solution was added to the reaction mixture and refluxing continued for 8 hr. The reaction mixture was cooled and poured on crushed ice to get a light brown coloured product, **7a**, which was purified by recrystallization from ethanol.

IR (KBr): 3436-3359 (N-H str.), 3075 (C-H str., Ar-H), 1597 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃): δ 9.62 (s, 1H, NH), 7.8-7.12 (m, 10H, Ar-H), 6.38 (s, 2H, NH₂).

Compounds **7b-d** were prepared by similar method with minor change in reaction conditions. Their spectral data are presented here:

4-(Benzimidazol-2-yl)-6-(4-methoxyphenyl)pyrimidin-2-amine, 7b

IR (KBr): 3453-3372 (N-H str.), 3063 (C-H str., Ar-H), 1567 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃):

δ 9.84 (s, 1H, NH), 7.91-7.32 (m, 9H, Ar-H), 6.49 (s, 2H, NH₂), 3.47 (s, 3H, OCH₃).

4-(Benzimidazol-2-yl)-6-(4-dimethylaminophenyl)pyrimidin-2-amine, 7c

IR (KBr): 3476-3328 (N-H str.), 3055 (C-H str., Ar-H), 1527 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃): δ 9.53 (s, 1H, NH), 7.9-7.28 (m, 9H, Ar-H), 6.36 (s, 2H, NH₂), 2.84 (s, 6H, N(CH₃)₂).

4-(Benzimidazol-2-yl)-6-(3-nitrophenyl)pyrimidin-2-amine, 7d

IR (KBr): 3436-3398 (N-H str.), 3063 (C-H str., Ar-H), 1580 cm⁻¹ (C=N str.); ¹H NMR (CDCl₃): δ 9.51 (s, 1H, NH), 7.9-7.41 (m, 9H, Ar-H), 6.29 (s, 2H, NH₂).

Synthesis of 2-(5-phenyl-4,5-dihydroisoxazol-3-yl)-benzimidazole, 8a

Anhydrous sodium acetate (1.64 g, 0.02 mole) was dissolve in hot acetic acid. Compound **3a** (2.48 g, 0.01 mole) was taken in absolute alcohol (10 mL) and to it hydroxylamine hydrochloride (0.69 g, 0.01 mole) in absolute alcohol (10 mL) was added. The solution of sodium acetate in acetic acid was transferred to this reaction mixture and refluxed for 10 hr. It was poured into ice cold water, the product obtained was filtered and purified by recrystallization from ethanol.

IR (KBr): 3430 (N-H str.), 3063 (C-H str., Ar-H), 1582 (C=N str.), 1360 cm⁻¹ (N-O str.); ¹H NMR (CDCl₃): δ 9.68 (s, 1H, NH), 7.9-7.29 (m, 9H, Ar-H), 3.36 (dd, 1H, H_a), 4.12 (dd, 1H, H_b), 6.58 (dd, 1H, H_x).

Compounds **8b-d** were similarly prepared with minor change in reaction conditions, *e.g.*, reflux time, amount of solvent, *etc.* Their spectral data are presented here:

2-[5-(4-Methoxyphenyl)-4,5-dihydroisoxazol-3-yl]-benzimidazole, 8b

IR (KBr): 3413 (N-H str.), 3072 (C-H str., Ar-H), 1349 cm⁻¹ (N-O str.); ¹H NMR (CDCl₃): δ 9.37 (s, 1H, NH), 7.8-7.16 (m, 8H, Ar-H), 3.34 (dd, 1H, H_a), 4.16 (dd, 1H, H_b), 6.59 (dd, 1H, H_x), 3.48 (s, 3H, OCH₃).

2-[5-(4-Dimethylaminophenyl)-4,5-dihydroisoxazol-3-yl]benzimidazole, 8c

IR (KBr): 3448 (N-H str.), 3046 (C-H str., Ar-H), 1352 (N-O str.), 1084 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 9.68 (s, 1H, NH), 7.92-7.4 (m, 8H, Ar-H),

3.46 (dd, 1H, H_a), 3.98 (dd, 1H, H_b), 6.62 (dd, 1H, H_x), 2.84 (s, 6H, N(CH₃)₂).

2-[5-(3-Nitrophenyl)-4,5-dihydroisoxazol-3-yl]-1benzimidazole, 8d

IR (KBr): 3426 (N-H str.), 3067 (C-H str., Ar-H), 1346 (N-O str.), 1057 (C-O str.), 1562 cm⁻¹ (N=O str.); ¹H NMR (CDCl₃): δ 9.98 (s, 1H, NH), 7.94-7.25 (m, 8H, Ar-H), 3.61 (dd, 1H, H_a), 4.2 (dd, 1H, H_b), 6.67 (dd, 1H, H_x).

Synthesis of 2-(2,3-diphenyl-3,4-dihydropyrazol-5-yl)-1-N-ethoxyphthalimidobenzimidazole, 9a

Method I: Compound **5a** (4.37 g, 0.01 mole) and phenyl hydrazine (1.08 g, 0.01 mole) were dissolved in absolute alcohol. To this solution catalytic amount of pyridine was added and reaction mixture was refluxed for 5-8 hr. After cooling, the reaction mixture was poured slowly into crushed ice. The solid product so obtained was filtered, washed, dried and purified by recrystallization from glacial acetic acid.

Method II: Condensation of 6a with 4a. To a mixture of compound **6a** (3.38 g, 0.01 mole) and ω-bromoethoxyphthalimide **4a** (2.70 g, 0.01 mole) in absolute alcohol, catalytic amount of pyridine was added dropwise and the reaction mixture was refluxed for 15-18 hr. Excess of solvent was removed *in vacuo* and the concentrated mass poured on crushed ice in order to get crude product that was filtered, washed, dried and purified by recrystallization from ethanol.

IR (KBr): 3072 (C-H str., Ar-H), 2919 (C-H str., CH₂), 1717 (C=O str., CO-N-CO), 1382 (N-O str.), 1049 (C-O str.), 1115 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 7.79-7.36 (m, 18H, Ar-H), 2.94 (t, 2H, NCH₂), 3.29 (t, 2H, OCH₂), 3.38 (dd, 1H, H_a), 3.91 (dd, 1H, H_b), 6.12 (dd, 1H, H_x); MS: *m/z* 527 [M]⁺.

Compounds **9b-h** were also prepared by similar method with the minor modifications in mole ratio of reagents, changing in reflux time, *etc.* Characteristic spectral data of these compounds are presented here:

2-[3-(4-Methoxyphenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]-1-N-ethoxyphthalimidobenzimidazole, 9b

IR (KBr): 3077 (C-H str., Ar-H), 2953 (C-H str., CH₂), 1722, 1674 (C=O str., CO-N-CO), 1365 (N-O str.), 1057 (C-O str.), 1118 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 7.81-7.32 (m, 17H, Ar-H), 3.31 (s, 3H, OCH₃), 2.72 (t, 2H, NCH₂), 3.32 (t, 2H, OCH₂), 3.25 (dd, 1H, H_a), 4.1 (dd, 1H, H_b), 6.15 (dd, 1H, H_x); MS: *m/z* 557 [M]⁺.

2-[3-(4-Dimethylaminophenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]-1-N-ethoxy-phthalimidobenzimidazole, 9c

IR (KBr): 3085 (C-H str., Ar-H), 2922 (C-H str., CH₂), 1756, 1703 (C=O str., CO-N-CO), 1381 (N-O str.), 1043 (C-O str.), 1128 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 7.8-7.21 (m, 17H, Ar-H), 3.1 (s, 6H, N(CH₃)₂), 2.92 (t, 2H, NCH₂), 3.2 (t, 2H, OCH₂), 3.29 (dd, 1H, H_a), 3.91 (dd, 1H, H_b), 6.20 (dd, 1H, H_x); MS: *m/z* 570 [M]⁺.

2-[3-(3-Nitrophenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]-1-N-ethoxyphthalimido-benzimidazole, 9d

IR (KBr): 3062 (C-H str., Ar-H), 2926 (C-H str., CH₂), 1719, 1661 (C=O str., CO-N-CO), 1379 (N-O str.), 1055 (C-O str.), 1125 (N-N str.), 1495 cm⁻¹ (N=O str., NO₂); ¹H NMR (CDCl₃): δ 7.7-7.56 (m, 18H, Ar-H), 2.9 (t, 2H, NCH₂), 3.22 (t, 2H, OCH₂), 3.28 (dd, 1H, H_a), 3.90 (dd, 1H, H_b), 6.18 (dd, 1H, H_x); MS: *m/z* 572 [M]⁺.

2-(2,3-Diphenyl-3,4-dihydropyrazol-5-yl)-1-N-butoxyphthalimidobenzimidazole, 9e

IR (KBr): 3079 (C-H str., Ar-H), 2925 (C-H str., CH₂), 1720, 1678 (C=O str., CO-N-CO), 1355 (N-O str.), 1050 (C-O str.), 1121 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 7.81-7.46 (m, 18H, Ar-H), 2.9 (t, 2H, NCH₂), 3.25 (t, 2H, OCH₂), 3.25 (dd, 1H, H_a), 4.32 (dd, 1H, H_b), 6.20 (dd, 1H, H_x), 2.21 (m, 2H, CH₂-CH₂); MS: *m/z* 555 [M]⁺.

2-[3-(4-Methoxyphenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]-1-N-butoxyphthalimidobenzimidazole, 9f

IR (KBr): 3049 (C-H str., Ar-H), 2923 (C-H str., CH₂), 1731, 1689 (C=O str., CO-N-CO), 1375 (N-O str.), 1032 (C-O str.), 1124 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 7.9-7.46 (m, 17H, Ar-H), 3.35 (s, 3H, OCH₃), 2.9 (t, 2H, NCH₂), 3.06 (t, 2H, OCH₂), 3.44 (dd, 1H, H_a), 4.24 (dd, 1H, H_b), 6.16 (dd, 1H, H_x), 2.1 (q, 2H, CH₂-CH₂); MS: *m/z* 585 [M]⁺.

2-[3-(4-Dimethylaminophenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]-1-N-butoxy-phthalimidobenzimidazole, 9g

IR (KBr): 3081 (C-H str., Ar-H), 2938 (C-H str., CH₂), 1732, 1687 (C=O str., CO-N-CO), 1376 (N-O str.), 1039 (C-O str.), 1116 cm⁻¹ (N-N str.); ¹H NMR (CDCl₃): δ 7.89-7.23 (m, 17H, Ar-H), 3.15 (s, 6H,

$N(CH_3)_2$), 2.87 (t, 2H, NCH_2), 3.21 (t, 2H, OCH_2), 3.44 (dd, 1H, H_a), 3.25 (dd, 1H, H_b), 6.17 (dd, 1H, H_x), 2.12 (m, 2H, CH_2-CH_2); MS: m/z 598 $[M]^+$.

2-[3-(3-Nitrophenyl)-2-phenyl-3,4-dihydropyrazol-5-yl]-1-N-butoxyphthalimido-benzimidazole, 9h

IR (KBr): 3088 (C-H str., Ar-H), 2940 (C-H str., CH_2), 1721, 1658 (C=O str., CO-N-CO), 1377 (N-O str.), 1049 (C-O str.), 1119 (N-N str.), 1523 cm^{-1} (N=O str., NO_2); 1H NMR ($CDCl_3$): δ 7.91-7.32 (m, 18H, Ar-H), 2.8 (t, 2H, NCH_2), 3.2 (t, 2H, OCH_2), 3.39 (dd, 1H, H_a), 4.13 (dd, 1H, H_b), 6.12 (dd, 1H, H_x), 2.22 (m, 2H, CH_2-CH_2); MS: m/z 601 $[M]^+$.

Synthesis of 4-(1-N-ethoxyphthalimidobenzimidazol-2-yl)-6-phenylpyrimidin-2-amine, 10a

Method I: A mixture of compound **5a** (4.37 g, 0.01 mole) and guanidine nitrate (1.22 g, 0.01 mole) were dissolved in absolute alcohol and refluxed for 1 hr. 10% NaOH solution was added dropwise to the reaction mixture and refluxing continued for 8 hr. The reaction mixture was cooled and poured slowly into crushed ice. The solid obtained was filtered, washed, dried and purified by recrystallization from ethanol.

Method II: Condensation of 7a with 4a. A mixture of compound **7a** (2.87 g, 0.01 mole) and ω -bromoethoxyphthalimide **4a** (2.70 g, 0.01 mole) were dissolved in absolute alcohol, pyridine was added to this reaction mixture as a base. The reaction mixture was refluxed for 15-18 hr. After cooling, the mixture was concentrated to one third by removing the solvent under reduced pressure. The separated solid was filtered, dried and purified by recrystallization from ethanol.

IR (KBr): 3426, 3361 (N-H str., NH_2), 3066 (C-H str., Ar-H), 2954 (C-H str., CH_2), 1745-1674 (C=O str., CO-N-CO), 1375 (N-O str.), 1105 cm^{-1} (C-O str.); 1H NMR ($CDCl_3$): δ 7.80-7.68 (m, 14H, Ar-H), 6.38 (s, 2H, NH_2), 2.93 (t, 2H, NCH_2), 3.65 (t, 2H, OCH_2); MS: m/z 746 $[M]^+$.

Compounds **10b-h** were synthesized by similar method with minor modifications, *e.g.*, reflux time, recrystallization solvent, *etc.* Their characteristic spectral data are presented here:

4-(1-N-ethoxyphthalimidobenzimidazol-2-yl)-6-(4-methoxyphenyl)pyrimidin-2-amine, 10b

IR (KBr): 3430, 3350 (N-H str., NH_2), 3043 (C-H str., Ar-H), 2970 (C-H str., CH_2), 1775-1688 (C=O str., CO-N-CO), 1350 (N-O str.), 1078 cm^{-1} (C-O

str.); 1H NMR ($CDCl_3$): δ 7.95-7.28 (m, 13H, Ar-H), 6.48 (s, 2H, NH_2), 3.39 (s, 3H, OCH_3), 2.9 (t, 2H, NCH_2), 3.49 (t, 2H, OCH_2); MS: m/z 506 $[M]^+$.

4-(1-N-ethoxyphthalimidobenzimidazol-2-yl)-6-(4-dimethylaminophenyl)pyrimidin-2-amine, 10c

IR (KBr): 3442, 3355 (N-H str., NH_2), 3051 (C-H str., Ar-H), 2928 (C-H str., CH_2), 1776-1679 (C=O str., CO-N-CO), 1363 (N-O str.), 1087 cm^{-1} (C-O str.); 1H NMR ($CDCl_3$): δ 7.79-7.21 (m, 13H, Ar-H), 6.5 (s, 2H, NH_2), 3.18 (s, 6H, $N(CH_3)_2$), 2.82 (t, 2H, NCH_2), 3.43 (t, 2H, OCH_2); MS: m/z 519 $[M]^+$.

4-(1-N-ethoxyphthalimidobenzimidazol-2-yl)-6-(3-nitrophenyl)pyrimidin-2-amine, 10d

IR (KBr): 3432, 3349 (N-H str., NH_2), 3035 (C-H str., Ar-H), 2924 (C-H str., CH_2), 1789-1686 (C=O str., CO-N-CO), 1378 (N-O str.), 1090 (C-O str.), 1541 cm^{-1} (N=O str., NO_2); 1H NMR ($CDCl_3$): δ 7.97-7.3 (m, 13H, Ar-H), 6.30 (s, 2H, NH_2), 2.89 (t, 2H, NCH_2), 3.62 (t, 2H, OCH_2); MS: m/z 521 $[M]^+$.

4-(1-N-butoxyphthalimidobenzimidazol-2-yl)-6-phenylpyrimidin-2-amine, 10e

IR (KBr): 3463, 3321 (N-H str., NH_2), 3059 (C-H str., Ar-H), 2961 (C-H str., CH_2), 1721-1644 (C=O str., CO-N-CO), 1358 (N-O str.), 1107 cm^{-1} (C-O str.); 1H NMR ($CDCl_3$): δ 7.80-7.19 (m, 14H, Ar-H), 6.64 (s, 2H, NH_2), 2.85 (t, 2H, NCH_2), 3.78 (t, 2H, OCH_2), 2.19 (m, 2H, CH_2-CH_2); MS: m/z 504 $[M]^+$.

4-(1-N-butoxyphthalimidobenzimidazol-2-yl)-6-(4-methoxyphenyl)pyrimidin-2-amine, 10f

IR (KBr): 3432, 3375 (N-H str., NH_2), 3048 (C-H str., Ar-H), 2939 (C-H str., CH_2), 1762-1629 (C=O str., CO-N-CO), 1371 (N-O str.), 1097 cm^{-1} (C-O str.); 1H NMR ($CDCl_3$): δ 7.88-7.24 (m, 14H, Ar-H), 6.41 (s, 2H, NH_2), 3.44 (s, 3H, OCH_3), 2.81 (t, 2H, NCH_2), 3.59 (t, 2H, OCH_2), 2.13 (m, 2H, CH_2-CH_2); MS: m/z 534 $[M]^+$.

4-(1-N-butoxyphthalimidobenzimidazol-2-yl)-6-(4-dimethylaminophenyl)pyrimidin-2-amine, 10g

IR (KBr): 3462, 3344 (N-H str., NH_2), 3071 (C-H str., Ar-H), 2914 (C-H str., CH_2), 1725-1649 (C=O str., CO-N-CO), 1359 (N-O str.), 1086 cm^{-1} (C-O str.); 1H NMR ($CDCl_3$): δ 7.8-7.18 (m, 14H, Ar-H), 6.61 (s, 2H, NH_2), 3.27 (s, 6H, $N(CH_3)_2$), 2.95 (t, 2H, NCH_2), 3.63 (t, 2H, OCH_2), 1.95 (m, 2H, CH_2-CH_2); MS: m/z 547 $[M]^+$.

4-(1-N-butoxyphthalimidobenzimidazol-2-yl)-6-(3-nitrophenyl)pyrimidin-2-amine, 10h

IR (KBr): 3472, 3354 (N-H str., NH₂), 3057 (C-H str., Ar-H), 2924 (C-H str., CH₂), 1766-1639 (C=O str., CO-N-CO), 1348 (N-O str.), 1092 (C-O str.), 1533 cm⁻¹ (N=O str., NO₂); ¹H NMR (CDCl₃): δ 7.86-7.25 (m, 14H, Ar-H), 6.58 (s, 2H, NH₂), 3.44 (s, 6H, N(CH₃)₂), 2.87 (t, 2H, NCH₂), 3.6 (t, 2H, OCH₂), 2.12 (m, 2H, CH₂-CH₂); MS: *m/z* 549 [M]⁺.

Synthesis of 2-(5-phenyl-4,5-dihydroisoxazol-3-yl)-1-N-ethoxyphthalimidobenzimidazole, 11a

Method I: Solution of anhydrous sodium acetate (1.64 g, 0.02 mole) in hot acetic acid was added in a mixture of **5a** (4.37 g, 0.01 mole) and hydroxylamine hydrochloride (0.69 g, 0.01 mole) in absolute alcohol. The reaction mixture was refluxed for 10 hr and kept overnight. Excess of solvent was distilled off under reduced pressure and then poured into ice cold water. The solid obtained was filtered and purified by recrystallization from ethanol.

Method II: Condensation of 8a with 4a. To a mixture of compound **8a** (2.63 g, 0.01 mole) and ω-bromoethoxyphthalimide **4a** (2.70 g, 0.01 mole) in absolute alcohol, pyridine was added as a base. The reaction mixture was then refluxed for 15-18 hr. Subsequently, ethanol was distilled off and the crystals were filtered, dried and purified by recrystallization from ethanol.

IR (KBr): 3082 (C-H str., Ar-H), 2922 (C-H str., CH₂), 1789, 1721 (C=O str., CO-N-CO), 1372 (N-O str.), 1085 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 7.96-7.33 (m, 13H, Ar-H), 2.97 (t, 2H, NCH₂), 3.69 (t, 2H, OCH₂), 3.38 (dd, 1H, H_a), 3.99 (dd, 1H, H_b), 6.72 (dd, 1H, H_x); MS: *m/z* 452 [M]⁺.

Compounds **11b-h** were prepared by similar method with minor change in reaction conditions, *e.g.*, reflux time, *etc.* Their characteristic spectral data are presented here:

2-[5-(4-Methoxyphenyl)-4,5-dihydroisoxazol-3-yl]-1-N-ethoxyphthalimidobenzimidazole, 11b

IR (KBr): 3078 (C-H str., Ar-H), 2945 (C-H str., CH₂), 1780, 1691 (C=O str., CO-N-CO), 1360 (N-O str.), 1080 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 7.8-7.16 (m, 12H, Ar-H), 3.07 (t, 2H, NCH₂), 3.75 (t, 2H, OCH₂), 3.29 (dd, 1H, H_a), 4.18 (dd, 1H, H_b), 6.69 (dd, 1H, H_x), 3.58 (s, 3H, OCH₃); MS: *m/z* 482 [M]⁺.

2-[5-(4-Dimethylaminophenyl)-4,5-dihydroisoxazol-3-yl]-1-N-ethoxyphthalimido-benzimidazole, 11c

IR (KBr): 3038 (C-H str., Ar-H), 2960 (C-H str., CH₂), 1756, 1671 (C=O str., CO-N-CO), 1354 (N-O str.), 1081 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 7.81-7.1 (m, 12H, Ar-H), 3.14 (t, 2H, NCH₂), 3.86 (t, 2H, OCH₂), 3.43 (dd, 1H, H_a), 3.96 (dd, 1H, H_b), 6.71 (dd, 1H, H_x), 2.94 (s, 6H, N(CH₃)₂); MS: *m/z* 495 [M]⁺.

2-[5-(3-Nitrophenyl)-4,5-dihydroisoxazol-3-yl]-1-N-ethoxyphthalimidobenzimidazole, 11d

IR (KBr): 3067 (C-H str., Ar-H), 2945 (C-H str., CH₂), 1795, 1704 (C=O str., CO-N-CO), 1329 (N-O str.), 1057 (C-O str.), 1562 cm⁻¹ (N=O str.); ¹H NMR (CDCl₃): δ 7.94-7.25 (m, 12H, Ar-H), 2.98 (t, 2H, NCH₂), 3.94 (t, 2H, OCH₂), 3.64 (dd, 1H, H_a), 4.25 (dd, 1H, H_b), 6.68 (dd, 1H, H_x); MS: *m/z* 497 [M]⁺.

2-(5-Phenyl-4,5-dihydroisoxazol-3-yl)-1-N-butoxyphthalimidobenzimidazole, 11e

IR (KBr): 3027 (C-H str., Ar-H), 2953 (C-H str., CH₂), 1786, 1732 (C=O str., CO-N-CO), 1362 (N-O str.), 1063 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 7.7-7.13 (m, 13H, Ar-H), 2.86 (t, 2H, NCH₂), 3.89 (t, 2H, OCH₂), 3.41 (dd, 1H, H_a), 4.32 (dd, 1H, H_b), 6.63 (dd, 1H, H_x); MS: *m/z* 480 [M]⁺.

2-[5-(4-Methoxyphenyl)-4,5-dihydroisoxazol-3-yl]-1-N-butoxyphthalimidobenzimidazole, 11f

IR (KBr): 3065 (C-H str., Ar-H), 2925 (C-H str., CH₂), 1781, 1652 (C=O str., CO-N-CO), 1378 (N-O str.), 1078 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 7.79-7.16 (m, 12H, Ar-H), 3.12 (t, 2H, NCH₂), 4.19 (t, 2H, OCH₂), 3.30 (dd, 1H, H_a), 4.22 (dd, 1H, H_b), 6.69 (dd, 1H, H_x), 3.45 (s, 3H, OCH₃); MS: *m/z* 510 [M]⁺.

2-[5-(4-Dimethylaminophenyl)-4,5-dihydroisoxazol-3-yl]-1-N-butoxyphthalimido-benzimidazole, 11g

IR (KBr): 3084 (C-H str., Ar-H), 2955 (C-H str., CH₂), 1769, 1689 (C=O str., CO-N-CO), 1373 (N-O str.), 1059 cm⁻¹ (C-O str.); ¹H NMR (CDCl₃): δ 7.8-7.21 (m, 12H, Ar-H), 3.12 (t, 2H, NCH₂), 3.95 (t, 2H, OCH₂), 3.61 (dd, 1H, H_a), 4.30 (dd, 1H, H_b), 6.89 (dd, 1H, H_x), 2.86 (s, 6H, N(CH₃)₂); MS: *m/z* 523 [M]⁺.

2-[5-(3-Nitrophenyl)-4,5-dihydroisoxazol-3-yl]-1-N-butoxyphthalimidobenzimidazole, 11h

IR (KBr): 3082 (C-H str., Ar-H), 2945 (C-H str., CH₂), 1791, 1712 (C=O str., CO-N-CO), 1345 (N-O

str.), 1071 (C-O str.), 1574 cm^{-1} (N=O str); ^1H NMR (CDCl_3): δ 7.9-7.25 (m, 12H, Ar-H), 2.98 (t, 2H, NCH_2), 3.85 (t, 2H, OCH_2), 3.47 (dd, 1H, H_a), 4.11 (dd, 1H, H_b), 6.72 (dd, 1H, H_x); MS: m/z 525 $[\text{M}]^+$.

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