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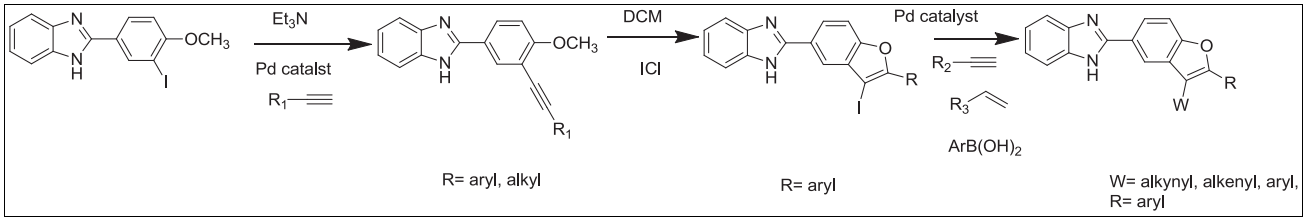

In this article, we report a facile route for the synthesis of novel benzofuranyl benzimidazole derivatives. The methodology involves the Sonagashira reaction of 2-(3-iodo-4-methoxyphenyl)-1*H*-benzimidazole (**3**) with variety of terminal alkynes to have novel benzimidazole alkynyl derivatives followed by iodo-cyclisation to give novel iodo benzofuranyl benzimidazole derivatives. The resulting iodo benzofuranyl benzimidazoles were functionalized further via palladium mediated carbon–carbon bond formation for molecular diversity generating novel heterocyclic compounds.

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INTRODUCTION

In the recent past, synthesis of polyheterocycles [1] has evolved as a major area of research because of diverse and potential biological activity of the series. Especially in the polyheterocycle arena, benzimidazole-based polyheterocycles have evolved as a fascinating target for medicinal chemistry, as these heterocycles show a wide range of interesting biological properties, for example, benzimidazoquinazolines [2], benzimidazo isoquinoline [3], and benzimidazo[2,1-a]isoindolones [4] were reported as antitumor agents. Benzimidazo[2,1-b]quinazolines are potent immune suppressors [5]; benzimidazo[2,1-b]benzo[f]isoquinoline ring system [6] is present in pharmacologically active compounds. Isoindolo[2,1-a]benzimidazolones [7] are also known to be sedatives and tranquilizers.

Among the various benzimidazole heterocycles, benzofuranyl benzimidazole heterocycles have attracted great deal of attention because of hybrid structure of benzofuran and benzimidazole. Individually, benzofuran and benzimidazole heterocycles are known for their broad spectrum of biological activities [8]. So, the combination of these two heterocycles is envisaged to have synergistic effect and be a more biologically potent.

Herein, we report a facile route for the synthesis of novel benzofuranyl benzimidazole derivatives. This methodology gives extensive scope in terms of synthesizing a variety of novel polyheterocyclic compounds. To the best of our knowledge, this methodology has not been evaluated for the synthesis of these novel benzofuranyl benzimidazole derivatives.

RESULTS AND DISCUSSION

The key iodo benzimidazole (**3**) required for our study was prepared according to the similar process reported in the literature [9]. Condensation of *o*-phenylene diamine (**1**) with sodium metabisulfite adduct of the appropriate benzaldehyde in DMF solvent yielded the corresponding iodo benzimidazole (**3**) (Scheme 1).

For the Sonagashira reaction [10] of (**3**) with terminal alkyne, many different conditions were explored (Table 1).

Among the various conditions pursued, we were able to see medium to significant amount of dimerization of terminal alkyne upon using CuI catalyst, whereas in the CuI free reaction condition, the dimerization product is reduced considerably. $PdCl_2(PPh_3)_2$ in triethyl amine as a base and solvent was found to be the optimum condition regarding better yield and negligible side product for the Sonagashira coupling. We chose to use this condition for synthesis of different derivatives. All the benzimidazole alkynyl derivatives (**4a–4i**) were obtained in good to excellent yield, and they all are very well characterized (Scheme 2; Table 2).

After completing the synthesis of benzimidazole alkynyl derivative (**4a–4i**), iodo-cyclisation [11] was carried out. In general, iodo-cyclisation is an efficient reaction and

Scheme 1. Reagent and conditions: (a) sodium metabisulfite, ethanol, RT, DMF, 100°C.

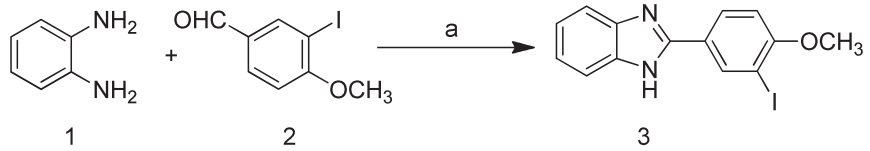


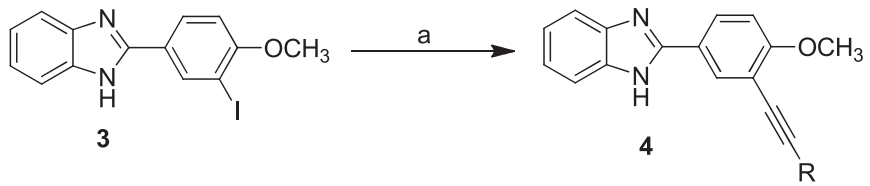
Table 1

Screening of optimized condition for Sonagashira reaction.[a]

Entry	Catalyst	Base (equiv)	Solvent	Solvent yield[b] (%)
1	Pd/C:PPh_3:CuI (1:4:2)	2-Amino ethanol (3.0)	Water	60
2	Pd/C:PPh_3:CuI (1:4:2)	Triethyl amine (3.0)	Water	65
3	Pd/C:PPh_3:CuI (1:4:2)	Triethyl amine (3.0)	Dimethoxy ethane	70
4	Pd/C:PPh_3:CuI (1:4:2)	Triethyl amine (3.0)	Ethanol	70
5	$PdCl_2(PPh_3)2$ (0.1 equiv)	Triethyl amine (15)	—	80
6	Pd/C:PPh_3 (1:4)	Triethyl amine (15)	—	—
7	$PdCl_2(PPh_3)_2$:CuI (0.1 equiv:0.06 equiv)	Triethyl amine (3.0)	THF	75

[a]All reactions were carried out by using **3** (1.0 equiv), phenyl acetylene (1.5 equiv), catalyst, and base at 80°C.
[b]Yields refer to isolated pure products characterized by IR, NMR, and HRMS.

Scheme 2. Reagent and conditions: (a) terminal alkyne, $PdCI_2(PPh_3)_2$, TEA, 80°C.



proceeds under mild reaction conditions and exhibits broad scope in terms of molecular diversity. The intramolecular iodo-cyclisation of alkyne (**4a)** was examined using (1) iodine in dichloromethane at 30°C, (2) iodine/K_2CO_3 in acetonitrile at 30°C, (3) ICl in dichloromethane. There was no product formation in condition (1) and condition (2). In fact, starting material is found to be intact. However, condition (3) gave complete conversion of starting material to required product (Scheme 3).

We chose to use this condition for our different derivative synthesis (**5a** and **5b**), and they are well characterized by NMR and mass (Table 3).

After the synthesis of novel iodo benzofuranyl benzimidazole derivatives (**5a–5b**), we planned to explore the reactivity of iodo group towards the palladium catalyzed carbon–carbon bond formation to yield diversified benzofuranyl benzimidazole derivatives. On this front, Heck, Sonagashira, and Suzuki coupling reactions were carried out (Scheme 4).

The details are given in Table 4.

CONCLUSION

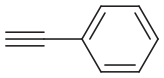
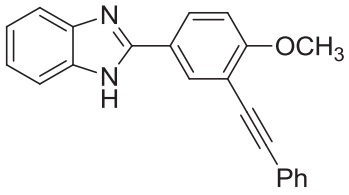
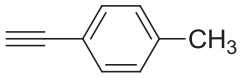
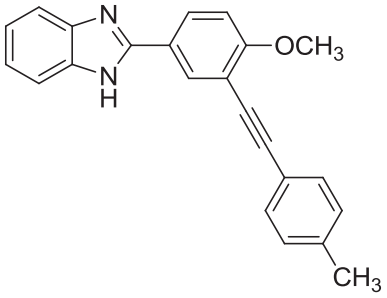
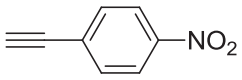
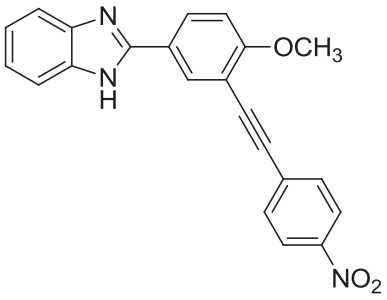
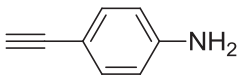
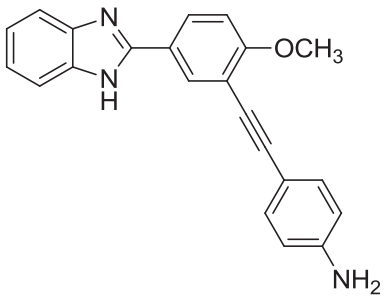
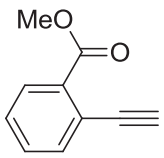
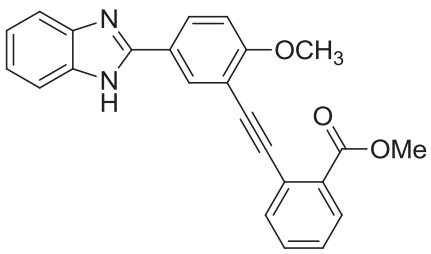
In conclusion, we have developed a simple and efficient route for the synthesis of novel benzofuranyl-benzimidazole derivatives. As a part of these studies, a number of novel benzimidazole alkynyl derivatives have been synthesized, and biological evaluation of these molecules are under progress, which will be reported in due course of time.

EXPERIMENTAL

All solvents and reagents were purchased from the suppliers and used without further purification. Thin layer chromatography was performed on Merck precoated Silica gel $60F_{254}$ plates, visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (60–120 mesh) using *n*-heptane, ethyl acetate. ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 /$CDCl_3$/MeOH-d_4 using 500/400 MHz, on a Bruker/Varian FT NMR. The chemical shifts were reported in δ ppm relative to TMS. Spin multiplicities are given as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), m (multiplet), and b (broad). Coupling constants (*J*) are given in hertz. Infrared spectra were recorded on an FTIR spectrometer. HRMS was determined using waters Q-Tof premier micro mass apparatus. Melting points were determined using a scientific open capillary melting point apparatus and are uncorrected. Chromatographic purity by HPLC (Waters-Empower software) using area normalization method and the condition is as follows. Column: XBridge C18, 5 µm (4.6*150 mm), mobile phase A: 10 mM ammonium acetate in water, Mobile Phase B: acetonitrile, gradient (T/%B) = 0/10, 3/10, 35/90, 40/90, 42/10, 48/10, 52/10. Flow 1.0 mL/min; UV 235 nm.

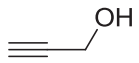
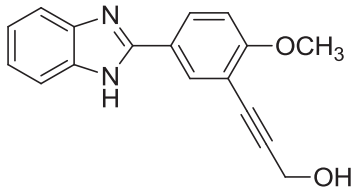
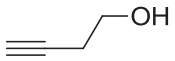
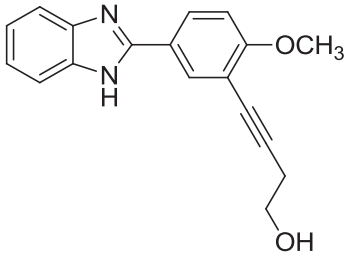
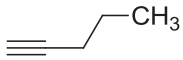
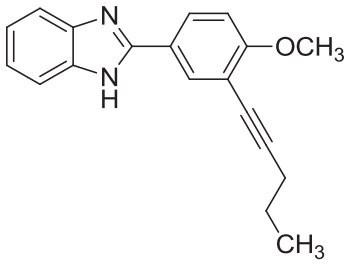
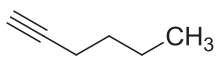
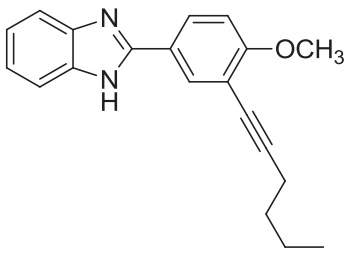
Table 2

Synthesis of 2-(3-alkynyl-4-methoxy phenyl)-1*H*-benzimidazole.[a]

Entry	Alkyne	Product (**4**)	Time (h)	Yield[b] (%)
a			2	80
b			2	82
c			1.5	83
d			2	80
e			3	85

(*Continued*)

Table 2
(Continued)

Entry	Alkyne	Product (**4**)	Time (h)	Yield[b] (%)
f			3	81
g			3	83
h			4	80
i			4	78

[a]All reactions were carried out by using **3** (1.0 equiv), terminal alkyne (1.5 equiv), catalyst, (10 mol%) and triethyl amine (15 equiv) at 80°C.
[b]Yields refer to isolated pure products characterized by IR, NMR, and HRMS.

2-(3-Iodo-4-methoxyphenyl)-1*H*-benzimidazole (3). To a solution of 3-iodo-4-methoxy benzaldehyde (**2**) (20 g, 0.0763 mol) in ethanol (200 mL) was added a solution of sodium metabisulfite (8.14 g, 0.0428 mol) in 10 mL of water at room temperature. The reaction mass was stirred at room temperature for 30 min and then kept in the refrigerator for 4 h. The precipitated solid was filtered and dried at 50°C (26.5 g; yield = 95%). This salt (26 g, 0.075 mol) was added to a solution of *o*-phenylene diamine (**1**) (7.67 g, 0.075 mol) in 50 mL of DMF at room temperature; the reaction mass was heated to 100°C for 4 h. After completion of starting material, the reaction mass was cooled to room temperature and poured in to water, precipitated solid was filtered and dried at 50°C to offered title compound (22.4 g; yield = 90.0%).

Compound **3**: Off-white solid; mp 215–217°C; IR (KBr, *v*): 3500, 1601, 1435, 1261, 1047, 743 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.64 (d, $J = 2.0$ Hz, 1H, Ar-H), 8.20 (dd, $J = 2.0$ Hz, $J = 8.8$ Hz, 1H, Ar-H), 7.60 (dd, $J = 3.2$ Hz, $J = 6.0$ Hz, 2H, Ar-H), 7.22 (dd, $J = 3.2$ Hz, $J = 6.0$ Hz, 2H, Ar-H), 6.95 (d, $J = 8.8$ Hz, 1H, Ar-H), 3.97 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 159.5, 150.3, 137.3, 128.6, 128.5, 124.9, 122.6, 114.9, 112.2, 86.9, 57.1; HRMS (*m*/*z*): calculated for $C_{14}H_{12}IN_2O$ $(M + H)^+$ 351.0671, found 351.0670; HPLC Purity: 99.5%; HPLC retention time: 19.87 min.

General procedure for the preparation of alkynyl benzimidazole (4a–4i). To a mixture of iodo benzimidazole (**3**) (0.5 g, 1.43 mmol) in TEA (2.2 g, 22 mmol) was added $PdCl_2$ $(PPh_3)_2$ (0.1004 g, 0.143 mmol) followed by alkyne (1.5 equiv) at room temperature under nitrogen atmosphere; this reaction

Scheme 3. Reagent and conditions: (a) iodine monochloride, DCM, RT.

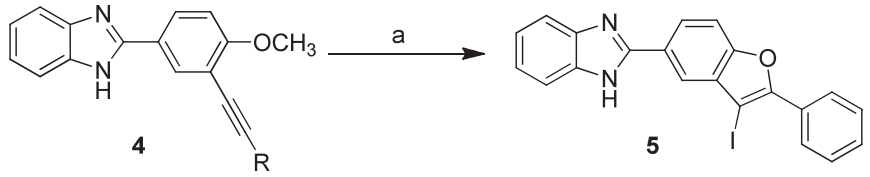
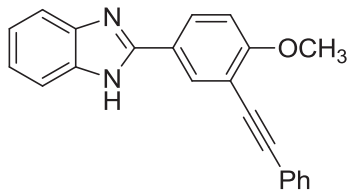
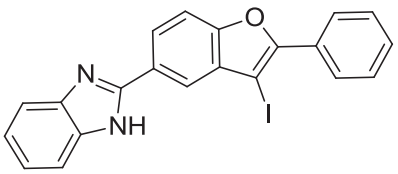
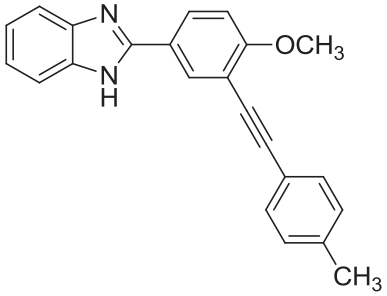
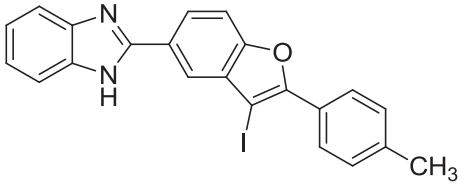


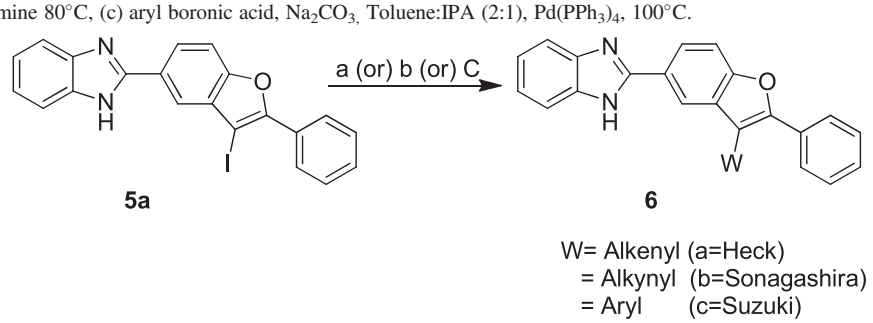
Table 3

Synthesis of 2-(3-iodo-2-subsituted-1-benzofuran-5-yl)-1*H*-benzimidazole.[a]

Entry	Starting material	Product (**5**)	Time (h)	Yield[b] (%)
a			0.5	85
b			1	80

[a]All reactions were carried out by using **4** (1.0 equiv), iodine monochloride (1.5 equiv), dichloro methane solvent (10 volume) at RT.
[b]Yields refer to isolated pure products characterized by IR, NMR, and HRMS.

Scheme 4. Reagent and conditions: (a) alkene, tetra-butyl ammonium chloride, sodium carbonate, palladium acetate. DMF, 85°C, (b) terminal alkyne, $PdCl_2(PPh_3)_2$, triethyl amine 80°C, (c) aryl boronic acid, Na_2CO_3, Toluene:IPA (2:1), $Pd(PPh_3)_4$, 100°C.

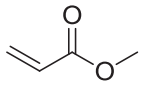
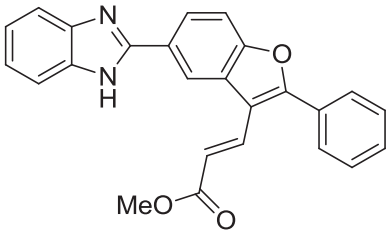
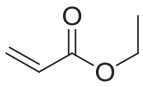
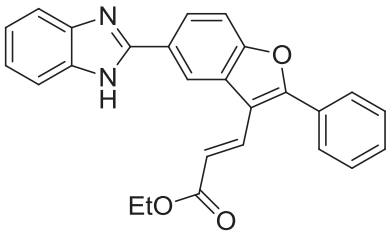
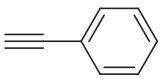
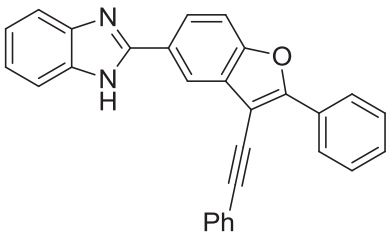
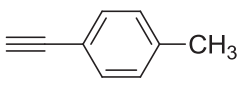
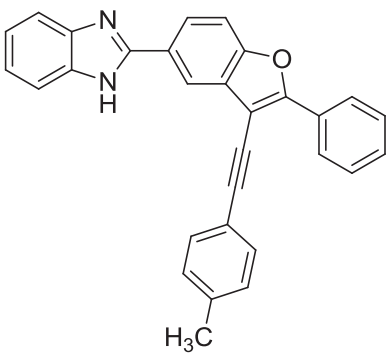
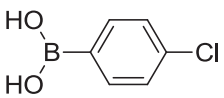
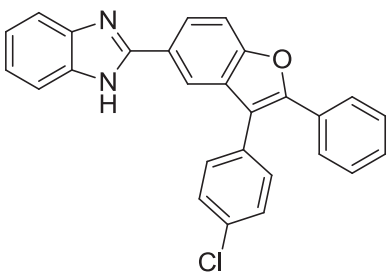


mixture was stirred at 80°C for the time mentioned in Table 2. After completion of reaction, as monitored by TLC, cooled the reaction mass to room temperature and poured into water (50 mL) and extracted with ethyl acetate (3 × 25 mL). The organic layers were collected, combined, and washed with water, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using *n*-heptane-EtOAc mixture to give the desired product.

***2-[4-Methoxy-3-(phenyl ethynyl)phenyl]-1H*-benzimidazole (4a).** Off-white solid; mp 312–314°C; IR (KBr, *v*): 3444, 1607, 1284, 1022, 742 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.96 (s, 1H, NH), 8.29 (d, J = 2.0 Hz, 1H, Ar-H), 8.20 (dd, J = 2.0 Hz, J = 8.5 Hz, 1H, Ar-H), 7.45–7.58 (m, 7H, Ar-H), 7.2–7.31 (m, 3H, Ar-H), 3.95 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 161.2, 150.9, 144.1, 135.4, 131.8, 131.4, 129.3, 129.2, 123.1, 122.9, 122.2, 119.0, 112.5, 112.2,

Table 4

Heck, Sonagashira, and Suzuki coupling reaction of **5a**.

Entry	Starting material	Product (**6**)	Time (h)	Yield[a] (%)
a			6	82
b			7	80
c			4	83
d			4	83
e			8	83

[a]Yields refer to isolated pure products characterized by IR, NMR, and HRMS.

111.7, 93.9, 85.9, 56.6. HRMS (*m/z*): calculated for $C_{22}H_{17}N_2O$ $(M+H)^+$ 325.1592, found 325.1601; HPLC Purity: 99.2%; HPLC retention time: 23.66 min.

2-{4-Methoxy-3-[(4-methylphenyl) ethynyl]phenyl}-1H-benzimidazole (4b). Off-white solid; mp 231–234°C; IR (KBr, *v*): 3434, 1606, 1431, 1276, 1022, 820, 747 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.88 (s, 1H, NH), 8.27 (d, $J=2.0$ Hz, 1H, Ar-H), 8.19 (dd, $J=2.0$ Hz, $J=8.5$ Hz, 1H, Ar-H), 7.63 (d,,$J=7.5$ Hz , 1H, Ar-H), 7.51 (d, $J=7.0$ Hz, 1H, Ar-H), 7.46 (d,,$J=8.0$ Hz, 2H, Ar-H), 7.26–7.30 (m, 3H, Ar-H), 7.18–7.21 (m,2H, Ar-H), 3.94 (s, 3H, OCH_3), 2.35 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 161.1, 150.9, 144.1, 139.1, 135.4, 131.7, 131.4, 129.9, 128.9, 123.1, 122.9, 122.2, 119.9, 119.0, 112.4, 111.7, 94.1, 85.3, 56.6, 21.5; HRMS (*m/z*): calculated for $C_{23}H_{19}N_2O$ $(M+H)^+$ 339.1821, found 339.1804; HPLC Purity: 99.3%; HPLC retention time: 25.14 min.

2-{4-Methoxy-3-[(4-nitrophenyl)ethynyl]phenyl}-1H-benzimidazole (4c). Pale yellow solid; mp 244–246°C; IR (KBr, *v*): 3359, 2203, 1510, 1343, 855, 748 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.91 (s, 1H, NH), 8.24–8.35 (m, 4H, Ar-H), 7.83 (d, $J=8.5$ Hz, 2H, Ar-H), 7.64 (d, $J=7.5$ Hz, 1H, Ar-H), 7.51 (d, $J=7.5$ Hz, 1H, Ar-H), 7.18–7.35 (m, 3H, Ar-H), 3.97 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 161.4, 150.7, 147.3, 132.9, 131.8, 130.0, 129.7, 124.5, 123.2, 122.9, 122.2, 119.1, 112.6, 111.2, 92.2, 91.0, 56.7; HRMS (*m/z*): calculated for $C_{22}H_{16}N_3O_3$ $(M+H)^+$ 370.1556, found 370.1537; HPLC Purity: 99.5%; HPLC retention time: 23.68 min.

4-{[5-(1H-Benzimidazol-2-yl)-2-methoxyphenyl]ethynyl} aniline (4d). Pale-brown solid; mp 186–188°C; IR (KBr, *v*): 3374, 2204, 1622, 1517, 1279, 744 cm^{-1}; ^1H NMR (CH_3OH-d_4, 500 MHz): δ 8.16 (d, $J=2.0$ Hz, 1H, Ar-H), 8.05 (dd, $J=2.0$ Hz, $J=9.0$ Hz, 1H, Ar-H), 7.59–7.65 (m, 2H, Ar-H), 7.25–7.29 (m, 4H, Ar-H), 7.19 (d, $J=9.0$ Hz, 1H, Ar-H), 6.70 (d, $J=8.5$ Hz, 2H, Ar-H), 4.66 (s, 2H, NH_2), 3.99 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 160.8, 151.1, 149.9, 144.1, 135.4, 132.9, 130.9, 128.1, 122.9, 122.8, 122.1, 119.0, 114.2, 113.4, 112.2, 111.6, 108.8, 95.9, 83.0, 56.4; HRMS (*m/z*): calculated for $C_{22}H_{18}N_3O$ $(M+H)^+$ 340.1774, found 340.1765 HPLC Purity: 99.2%; HPLC retention time: 19.3 min.

Methyl 2{[5-(1H-benzimidazol-2-yl)-2-methoxyphenyl] ethynyl} benzoate (4e). Off-white solid; mp 138–141°C; IR (KBr, *v*): 3445, 1714, 1433, 1276, 747 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.92 (s, 1H, NH), 8.29 (d, 1H, Ar-H, $J=2.0$ Hz), 8.21 (dd, 1H, Ar-H, $J=2.0$ Hz, $J=8.5$ Hz), 7.93 (d, 1H, Ar-H, $J=8.0$ Hz), 7.72 (d, 1H, Ar-H, $J=7.5$ Hz), 7.64–7.68 (m, 2H, Ar-H), 7.51–7.56 (m, 2H, Ar-H), 7.2–7.32 (m, 3H, Ar-H,), 3.96 (s, 3H, $COOCH_3$), 3.91 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 166.7, 161.3, 150.9, 134.3, 132.7, 132.2, 131.6, 130.5, 129.4, 129.2, 123.1, 122.8, 122.2, 119.0, 112.5, 112.4, 111.7, 92.5, 90.5, 56.6, 52.8; HRMS (*m/z*): calculated for $C_{24}H_{19}N_2O_3$ $(M+H)^+$ 383.1563, found 383.1751; HPLC Purity: 99.1%; HPLC retention time: 22.8 min.

3-[5-(1H-Benzimidazol-2-yl)-2-methoxyphenyl]prop-2-yn-1-ol (4f). Off-white solid; mp 186–188°C; IR (KBr, *v*): 3434, 1449, 1270, 1017, 733 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.86 (s, 1H, NH), 8.15–8.18 (m, 2H, Ar-H), 7.49-7.63 (m, 2H, Ar-H), 7.16–7.25 (m, 3H, Ar-H), 5.44 (t, $J=6.0$ Hz, 1H, OH), 4.36 (d, 2H, CH_2, $J=6.0$ Hz), 3.93 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 161.2, 150.9, 144.1, 135.4, 129.2, 122.9, 122.8, 122.1, 119.0, 112.4, 111.6, 94.5, 80.1, 56.4, 50.1; HRMS (*m/z*) calculated for $C_{17}H_{15}N_2O_2$ $(M+H)^+$ 279.1363, found 279.1396; HPLC Purity: 99.0%; HPLC retention time: 14.43 min.

4-[5-(1H-Benzimidazol-2-yl)-2-methoxyphenyl]buty-3-yn-1-ol (4g). Off-white solid; mp 219–221°C; IR (KBr, *v*): 3444, 1608, 1284, 1046, 743 cm^{-1}; ^1H NMR (CH_3OH-d_4, 500 MHz): δ 7.6–8.10 (m, 4H, Ar-H), 7.25 (dd, 2H, Ar-H, $J=3.0$ Hz, $J=6.0$ Hz), 7.17 (d, 1H, Ar-H, $J=9.0$ Hz), 3.95 (s, 3H, OCH_3), 3.78 (t, 2H, OCH_2, $J=7.0$ Hz), 2.70 (t, 2H, CH_2, $J=7.0$ Hz); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 161.2, 151.0, 131.6, 128.2, 122.9, 122.4, 113.1, 112.2, 93.35, 77.4, 60.3, 56.3, 24.0; HRMS (*m/z*): calculated for $C_{18}H_{17}N_2O_2$ $(M+H)^+$ 293.1542, found 293.1573; HPLC Purity: 99.2%; HPLC retention time: 14.65 min.

2-[4-Methoxy-3-(pent-1-yn-1-yl)phenyl]-1H-benzimidazole (4h). Off-white solid; mp 174–176°C; IR (KBr, *v*): 3435, 1607, 1269, 1024, 745 cm^{-1}; ^1H NMR (CH_3OH-d_4, 500 MHz): δ 7.59−8.09 (m, 4H, Ar-H), 7.25 (dd, $J=3.0$ Hz, $J=6.0$ Hz, 2H, Ar-H), 7.16 (d, $J=8.5$ Hz, 1H, Ar-H), 3.95 (s, 3H, OCH_3), 2.46 (t, $J=7.0$ Hz, 2H, $–CH_2$), 1.67 (m, 2H, $–CH_2$,), 1.11 (t, $J=7.0$ Hz, 3H, $–CH_3$); ^{13}C NMR (DMSO-d_6 125 MHz): δ 161.2, 131.4, 128.1, 122.9, 122.1, 113.2, 112.2, 95.4, 77.1, 56.3, 22.2, 21.3, 13.8. HRMS (*m/z*): calculated for $C_{19}H_{19}N_2O$ $(M+H)^+$ 291.1749, found 291.1734; HPLC Purity: 99.4%; HPLC retention time: 22.1 min.

2-(3-Hex-1-yn-1-yl)-4-methoxyphenyl]-1H-benzimidazole (4i). Off-white solid; mp 199–201°C; IR (KBr, *v*): 3445,2958, 1445, 1271, 1023, 746 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.84 (s, 1H, NH), 7.49–8.13 (m, 4H, Ar-H), 7.18–7.21 (m, 3H, Ar-H), 3.94 (s, 3H, OCH_3), 2.46–2.51 (m, 2H, CH_2), 1.43–1.57 (m, 4H, CH_2–CH_2), 0.93 (t, $J=7$ Hz , 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 161.2, 151.1, 144.1, 135.4, 131.4, 128.1, 122.9, 122.8, 122.1, 118.9, 113.2, 112.2, 111.6, 95.5, 76.9, 56.3, 30.8, 21.9, 19.0, 13.9; HRMS (*m/z*) calculated for $C_{20}H_{21}N_2O$ $(M+H)^+$ 305.1905, found 305.1922; HPLC Purity: 99.4%; HPLC retention time: 23.9 min.

General procedure for the preparation of compound 5a/5b. To a solution of **4a/4b** (1.54 mmol) in DCM (5 mL) was added iodine mono chloride (2.3 mmol) at room temperature. The reaction mass was stirred under nitrogen atmosphere, and the progress of the reaction was monitored by TLC. After completion of starting material, reaction mass was poured in to water (50 mL) and product extracted with ethyl acetate (3*100 mL). The organic layers were collected, combined, dried over anhydrous sodium sulfate and concentrated to have the desired product.

2-(3-Iodo-2-phenyl-1-benzofuran-5-yl)-1H-benzimidazole (5a). Off-white solid; mp 207–209°C; IR (KBr, *v*): 3391, 1632, 1457, 1054, 746 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 12.97 (s, 1H, NH), 8.38 (d, $J=1.5$ Hz, 1H, Ar-H), 8.27 (dd, $J=1.5$ Hz, $J=8.5$ Hz, 1H, Ar-H), 8.10–8.17 (m, 2H, Ar-H), 7.95–8.01(m,1H, Ar-H,), 7.76–7.79 (m, 2H, Ar-H), 7.54–7.63 (m, 3H, Ar-H), 7.42–7.47 (m, 2H, Ar-H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 155.7. 154.8. 150.2, 135.0, 133.7, 130.5, 129.5, 129.3, 127.7, 125.9, 125.1, 122.1, 121.8, 114.8, 113.1, 63.9; HRMS (*m/z*): calculated for $C_{21}H_{14}IN_2O$ $(M+H)^+$ 437.0239, found 437.0226; HPLC Purity: 99.7%; HPLC retention time: 26.9 min.

2-[3-Iodo-2-(4-methylphenyl)-1-benzofuran-5-yl]-1H-benzimidazole (5b). Off-white solid; mp 219–221°C; IR (KBr, *v*): 3435, 1627, 1440, 1274, 1061, 745 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz): δ 13.12 (s, 1H, NH), 8.25–8.28 (m, 2H, Ar-H), 8.05

(d, $J = 8.0$ Hz, 2H, Ar-H), 7.22–7.82 (m, 7H, Ar-H,), 2.40 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 154.7, 154.3, 151.6, 140.2, 133.4, 129.9, 127.6, 126.8, 126.6, 125.1, 120.1, 112.4, 63.1, 21.5; HRMS (*m/z*): calculated for $C_{22}H_{16}IN_2O$ $(M+H)^+$ 451.0606, found 451.0601; HPLC Purity: 99.5%; HPLC retention time: 28.7 min.

General procedure for Heck coupling (6a–6b). To a solution of **5a** (0.5 g, 1.15 mmol) in dimethyl formamide (10 mL) was added appropriate alkene (4.6 mmol), sodium carbonate (0.37 g, 3.45 mmol), tetra-butyl ammonium chloride (0.32 g, 1.15 mmol) followed by Palladium acetate (0.12 mmol) at room temperature under nitrogen atmosphere. The reaction mass was heated at 85°C for 6–7 h; after completion of starting material as indicated by TLC, the reaction mass was cooled to room temperature, and water (50 mL) was added into the reaction mass and extracted with ethyl acetate (3 × 50 mL). The organic layers were collected and washed with water and brine. The ethyl acetate extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using *n*-heptane-EtOAc to give the desired product.

Methyl-3-[5-(1H-benzimidazol-2-yl)-2-phenyl-1-benzofuran-3yl]prop-2-enoate (6a). Off-white solid; mp 173–176°C; IR (KBr, *v*): 3445, 1716, 1654, 1432, 1172, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 10.55 (s, 1H, NH), 8.50 (s, 1H, Ar-H), 8.16 (d, $J = 8.5$ Hz, 1H, Ar-H), 7.74–8.05 (m, 5H, Ar-H), 7.61 (d, $J = 9.0$ Hz, 1H, Ar-H), 7.51–7.56 (m, 3H, Ar-H), 7.30–7.32 (m, 2H, Ar-H), 6.75 (d, $J = 16.0$ Hz, 1H, CH═CH), 3.84 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 167.4, 162.9, 158.9, 155.1, 151.7, 135.5, 135.1, 131.0, 129.8, 129.0, 128.9, 126.9, 126.8, 125.3, 123.1, 122.3, 119.6, 119.2, 112.9, 112.7, 111.8, 52.2; HRMS (*m/z*): calculated for $C_{25}H_{19}N_2O_3$ $(M+H)^+$ 395.2658, found 395.2636. HPLC Purity: 99.3%; HPLC retention time: 25.85 min.

Ethyl-3-[5-(1H-benzimidazol-2-yl)-2-phenyl-1-benzofuran-3yl]prop-2-enoate (6b). Off-white solid; mp 89–91°C; IR (KBr, *v*): 3444, 1632, 1441, 1179, 745 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 13.14 (s, 1H, NH), 8.72 (s, 1H, CH), 8.34 (d, $J = 8.0$ Hz, 1H, Ar-H), 7.61–7.88 (m, 9H, Ar-H), 7.24 (d, $J = 8.0$ Hz, 2H, Ar-H), 6.93 (d, $J = 16$ Hz, 1H, CH═CH), 4.25 (d, $J = 6.5$ Hz, 2H, CH_2), 1.30 (t, $J = 6.5$ Hz, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 166.9, 158.9, 155.1, 151.7, 144.2, 135.5, 135.0, 130.9, 129.8, 129.0, 128.9, 126.9, 126.7, 125.3, 123.1, 122.2, 119.8, 119.3, 112.9, 112.7, 111.8, 60.8, 14.7; HRMS (*m/z*): calculated for $C_{26}H_{21}N_2O_3$ $(M+H)^+$ 409.1956, found 409.1958; HPLC Purity: 99.7%; HPLC retention time: 27.37 min.

General procedure for Sonagashira coupling (6c–6d). To a mixture of **5a** (0.5 g, 1.15 mmol) in TEA (3 mL) was added $PdCl_2$ $(PPh_3)_2$ (0.08 g 0.115 mmol) followed by alkyne (1.725 mmol) at room temperature under nitrogen atmosphere; this reaction mixture was stirred at 80°C for 4 h. After completion of starting material as confirmed by TLC, the reaction mass was cooled to room temperature and diluted with water (50 mL).The product was extracted with ethyl acetate (3 × 50 mL). The organic layers were collected, combined, and subjected to water followed by brine washings. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using *n*-heptane-EtOAc to give the desired product.

2-[2-Phenyl-3-(phenylethynyl)-1-benzofuran-5-yl]-1H-benzimidazole (6c). Off-white solid; mp 140–142°C; IR (KBr): 3435, 1627, 1439, 744, 688 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 13.12 (s, 1H, NH), 8.27–8.56 (m, 4H, Ar-H), 8.15 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.45–7.95 (m, 10H, Ar-H), 7.22–7.23 (m, 2H, Ar-H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 157.2, 154.8, 154.2, 151.6, 131.9, 130.6, 130.3, 130.0, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 127.7, 126.8. 126.7, 126.1, 125.4, 125.3, 122.7, 122.4, 120.2, 118.4, 112.7, 112.5, 99.1, 97.8, 80.5 HRMS (*m/z*): calculated for $C_{29}H_{19}N_2O$ $(M+H)^+$ 411.1920, found 411.1917; HPLC Purity: 99.5%; HPLC retention time: 25.14 min.

2-{3[(4-Methylphenyl)ethynyl]-2-phenyl-1-benzofuran-5-yl}-1H-benzimidazole (6d). Off-white solid; mp 258–261°C; IR (KBr): 3437, 1438, 1272, 813, 745, 686 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 13.1 (s, 1H, NH), 8.29–8.55 (m, 4H, Ar-H), 7.87 (d, $J = 8.5$ Hz, 1H, Ar-H), 7.51–7.69 (m, 7H, Ar-H), 7.23–7.34 (m, 4H, Ar-H), 2.38 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 157.0, 154.2, 151.6, 139.7, 131.9, 130.6, 130.0, 129.7, 129.4, 129.3, 126.8, 126.1, 125.4, 119.4, 118.4, 112.7, 99.3, 98.1, 79.9, 21.6; HRMS (*m/z*): calculated for $C_{30}H_{21}N_2O$ $(M+H)^+$ 425.2076, found 425.2085; HPLC Purity: 99.3%; HPLC retention time: 32.8 min.

General procedure for Suzuki coupling (6e). To a solution of **5a** (0.5 g, 1.15 mmol) in Toluene:IPA (2:1) solvent mixture (10 mL) was added 2.0 M of sodium carbonate (3 eq), followed by boronic acid (0.27 g, 1.73 mmol) and $Pd(PPh_3)_4$ (0.133, 0.115 mmol) at room temperature. The reaction mixture was heated to 100°C and stirred at this temperature for 8 h; after completion of starting material confirmed by TLC, cool the reaction mass to room temperature and add water (50 mL) product extracted with ethyl acetate (3 × 50 mL). The organic layers were collected, combined, and subjected to water followed by brine washings; the organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography using *n*-heptane-EtOAc to give the desired product.

2-[3-(4-Chlorophenyl)-2-phenyl-1-benzofuran-5-yl]-1H-benzimidazolete (6e). Off-white solid; mp 308–311°C; IR (KBr): 3445, 1434, 1267, 1088, 743 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.97 (s, 1H, NH), 7.86–8.27 (m, 3H, Ar-H), 7.52–7.67 (m, 8H, Ar-H), 7.20–7.46 (m, 5H, Ar-H); ^{13}CNMR (DMSO-d_6, 125 MHz): δ 154.6, 151.8, 133.4, 131.9, 130.9, 130.3, 129.9, 129.8, 129.7, 129.4, 127.2, 126.3, 124.6, 118.2, 116.7, 112.4; HRMS (*m/z*): Calcd for $C_{27}H_{18}ClN_2O$ $(M+H)^+$ 421.1440, found 421.1409.

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