Synthesis of diynes from 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene and imidazole/benzimidazole *via* a CuI/$Pd(OAc)_2$ catalysed cascade reaction

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A novel reaction between 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene and imidazole/benzimidazole catalysed by CuI and $Pd(OAc)_2$ gave the corresponding highly sterically hindered diynes *via* a cascade elimination/Ullmann-type C–N coupling process.

Keywords: diynes, 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene, imidazole, elimination, Ullmann-type coupling

The imidazole/benzimidazole framework represents a privileged structural motif of importance in biologically active natural products and pharmaceutical compounds. In particular, 1,2-disubstituted benzimidazole derivatives have shown a wide range of biological activities.[1–4] Diynes are also biologically active and are versatile synthons for many natural products and pharmaceutical molecules.[5–7] Diynes have been recognised as a particularly useful fragment which undergoes the Bergman cyclisation[8] and produces a DNA-damaging *p*-benzyne diradical.[9,10] Several studies to construct this potential synthon have been reported. Consequently, it is interesting to prepare imidazole/benzimidazole-containing diynes.

Ullmann-type coupling reactions have been successfully applied to assemble various heterocyclic compounds *via* one-pot strategies, due to their efficiency and low cost.[11–15] Various indole,[16–19] naphthothiophene[20] and benzofuran[21–23] derivatives have been synthesised from *gem*-dibromovinyl benzene and its derivatives.

Since 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene is a good precursor of an alkynyl bromide, we thought that it would couple with imidazole/benzimidazole to form the corresponding aryl diynes. We now report a CuI and $Pd(OAc)_2$ catalysed cascade reaction to construct imidazole/benzimidazole-containing diynes.

Firstly, 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene (**1a**) and benzimidazole (**2a**) were chosen as starting materials and the reaction was carried out in toluene at 90 °C in the presence of CuI (10% mmol), $Pd(OAc)_2$ (10% mmol), 1,10-phenanthroline (20% mmol) and K_2CO_3 (2.0 equiv.). Fortunately, 17% yield of the desired product 1-((2-(phenylethynyl)phenyl)ethynyl)-1*H*-benzo[*d*]imidazole (**3a**) was isolated (entry 1, Table 1). We then optimised the reaction. When the temperature was raised to 100 °C, the yield increased to 25% (entry 2, Table 1). However, the reaction mixture was complicated at a temperature of 140 °C (entry 3, Table 1). Different ligands were also screened. Comparing the yields with TMEDA, L-proline and DMEDA, 1, 10-phenanthroline showed the best activity (entries 4, 5 and 6, Table 1). Subsequently, different copper catalysts were investigated, and CuI was proven to be the best (entries 7, 8 and 9, Table 1). A series of palladium co-catalysts including $PdCl_2$, $Pd(dppf)Cl_2$, $Pd(PPh_3)Cl_2$ and $Pd_2(dba)_3$ were examined, and $Pd(OAc)_2$ turned out to be the most effective (entries 10, 11, 12 and 13, Table 1). A screen of bases revealed that Cs_2CO_3 was the preferred base (entries 16, 17, 18 and 19, Table 1). The effect of solvents was significant. The reaction did not occur in DMF, DMSO, DCE and CH_3CN (entries 20, 21, 22 and 23, Table 1). By optimising various reaction parameters, the combination of CuI (10% mmol), $Pd(OAc)_2$ (10% mmol), 1, 10-phenanthroline (20% mmol), Cs_2CO_3 (2.0 equiv.) in toluene at 100 °C was found to be the best reaction conditions for this transformation.

With the optimised reaction conditions in hand, the scope of the cascade reaction was explored. First, substrates with different R^2 substituents in the 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene component were screened. The results are shown in Table 2. Electron-donating groups (*p*-Me, *p*-OMe and *m*-Me) facilitate the reaction (compounds **3a**, **3b**, **3c** and **3f**; Table 2) whilst electron-withdrawing groups (*p*-F, *p*-Cl, 4-F and 5-CF_3) decreased the yields to a certain extent (compounds **3d**, **3e**, **3k** and **3l**; Table 2). Alkyl groups could also be used and the corresponding products were obtained in moderate yields (compounds **3h**, **3i**, **3j**; Table 2). When R^2 was a *tert*-butyl only 32% of the corresponding product was isolated (compound **3i**, Table 2), since the high steric hindrance affected the reaction. Similarly, a relatively lower yield (46%) was obtained when R^2 was a naphthyl group (compound **3g**, Table 2). At the same time, different R^1 substituents were also investigated. It was shown that electron-withdrawing groups such as F and CF_3 would hinder the process (compounds **3k** and **3l**, Table 2).

The effect of substituted imidazoles and benzimidazoles were also examined. Due to the different nucleophilic properties, imidazole and benzimidazole differed from each other in the yields of the corresponding products. Generally benzimidazoles gave higher yields (compare **3a** in Table 2 to **3q** in Table 4). Compared to the electron-withdrawing group, the electron-donating group facilitated the cascade reaction. 57% yield of the corresponding product could be isolated when 5, 6-dimethyl benzimidazole was chosen as the nucleophile, compared to 55% yield of 5-nitrobenzimidazole (compounds **3o** and **3p**, Table 3).

Similar effects were also observed in the case of the reactions with imidazoles. 4-Methylimidazole was more reactive, compared to imidazole (compounds **3q** and **3r**, Table 4). At the same time, as a weaker nucleophilic reagent compared to benzimidazole, parallel experiments between imidazole and different 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzenes were conducted. Similar to the reactions of benzimidazole, the electron-withdrawing 1-(2,2-dibromovinyl)-2-(phenylethynyl) benzenes down-regulated the reaction, in contrast to the electron-donating group in the 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene (compounds **3s**, **3t**, **3u** and **3v**, Table 4). Generally, stronger nucleophiles benefit the CuI-catalysed Ullmann reaction and accelerate the whole cascade reaction.

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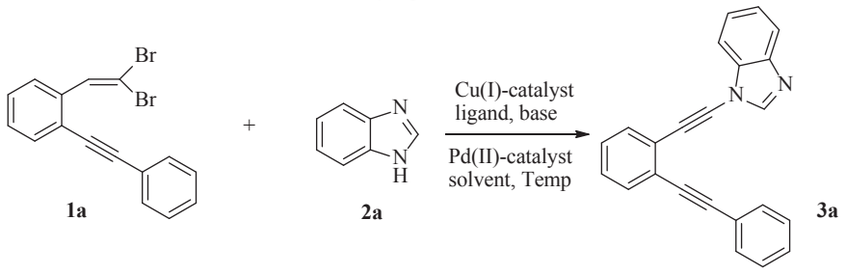
Table 1 The optimisation of the Cu/Pd co-mediated cascade coupling reaction[a]



Entry	Cu(I)-cat	Ligand	Pd(II)-cat	Base	Solvent	Temp/°C	Yield/%[b]
1	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	K_2CO_3	Toluene	90	17
2	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	K_2CO_3	Toluene	100	25
3	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	K_2CO_3	Toluene	140	ND
4	CuI	TMEDA	$Pd(OAc)_2$	K_2CO_3	Toluene	100	Trace
5	CuI	L-Proline	$Pd(OAc)_2$	K_2CO_3	Toluene	100	Trace
6	CuI	DMEDA	$Pd(OAc)_2$	K_2CO_3	Toluene	100	Trace
7	CuBr	1,10-Phenanthroline	$Pd(OAc)_2$	K_2CO_3	Toluene	100	Trace
8	CuCl	1,10-Phenanthroline	$Pd(OAc)_2$	K_2CO_3	Toluene	100	Trace
9	Cu_2O	1,10-Phenanthroline	$Pd(OAc)_2$	K_2CO_3	Toluene	100	13
10	CuI	1,10-Phenanthroline	$PdCl_2$	K_2CO_3	Toluene	100	Trace
11	CuI	1,10-Phenanthroline	$Pd(dppf)Cl_2$	K_2CO_3	Toluene	100	Trace
12	CuI	1,10-Phenanthroline	$Pd(PPh_3)Cl_2$	K_2CO_3	Toluene	100	Trace
13	CuI	1,10-Phenanthroline	$Pd_2(dba)_3$	K_2CO_3	Toluene	100	Trace
14	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Cs_2CO_3	Toluene	100	62
15	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	K_3PO_4	Toluene	100	46
16	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Et_3N	Toluene	100	Trace
17	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Li_2CO_3	Toluene	100	ND
18	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	*t*-BuOK	Toluene	100	45
19	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Na_2CO_3	Toluene	100	ND
20	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Cs_2CO_3	DMF	100	ND
21	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Cs_2CO_3	DMSO	100	ND
22	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Cs_2CO_3	DCE	100	ND
23	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Cs_2CO_3	CH_3CN	100	ND
24	CuI	1,10-Phenanthroline	–	Cs_2CO_3	Toluene	100	ND
25	–	–	$Pd(OAc)_2$	Cs_2CO_3	Toluene	100	ND
26[c]	CuI	1,10-Phenanthroline	$Pd(OAc)_2$	Cs_2CO_3	Toluene	100	Trace

[a]Unless otherwise stated, the amount of substrates were 0.5 mmol, and all the reactions were under an atmosphere of N_2.
[b]Isolated yield based on 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene (**1a**).
[c]CuI (10% mmol), 1,10-phenanthroline (20% mmol) and Cs_2CO_3 (1.0 equiv.) were added in the first step, and after being heated for 12 h at 100 °C, $Pd(OAc)_2$ (10% mmol) and Cs_2CO_3 (1.0 equiv) were added in the second step. Heating was continued for another 12 h at 100 °C.

Conclusion

In conclusion, a cascade reaction coupled with an elimination using CuI and $Pd(OAc)_2$ co-catalysed Ullmann-type C–N coupling has been discovered. A variety of substituted imidazole and benzimidazole diynes with a high steric hindrance and their derivatives have been synthesised. These products are potentially biologically active.

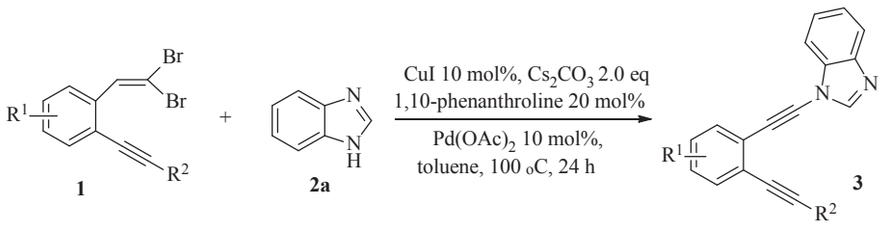
Experimental

All the reactions were conducted under an atmosphere of nitrogen. All the copper sources, palladium sources, bases, solvents, aldehydes and acetylenes were commercially available. DMF, DCE, DMSO and CH_3CN were distilled with the presence of CaH_2 under reduced pressure; toluene was distilled from sodium. Analytical TLC was performed on pre-coated silica gel plates (GF 254), visualised with a UV254 lamp. Column chromatography was performed on silica gel 60 (200–300 mesh) with petrol and ethyl acetate as eluents. All products were identified by ^{1}H NMR, ^{13}C NMR, MS and IR. Unknown compounds were also characterised by high resolution mass spectrometry (Waters Micromass GCT). NMR spectra were recorded for ^{1}H NMR at 400 MHz and for ^{13}C NMR at 100 MHz (Bruker Avance 400 MHz). Chemical shifts (δ, ppm) were recorded with TMS as internal standard. Coupling constants are reported in Hertz (Hz). Mass spectra were obtained using EI ionisation (Agilent 5975). Melting points were uncorrected.

Coupling reaction: 1-(2,2-dibromovinyl)-2-(phenylethynyl) benzenes (0.5 mmol), imidazole/benzimidazole (0.5 mmol), CuI (10% mmol), 1, 10-phenanthroline (20% mmol), $Pd(OAc)_2$ (10% mmol) and Cs_2CO_3 (2.0 equiv) were added to an oven-dried Schlenk tube charged with a magnetic stir bar. The Schlenk tube was capped with a Teflon screwcap, and then evacuated and backfilled with N_2 (with N_2 balloon) for 3 times. Then toluene (3 mL) was added as the solvent. The tube was placed in a 100 °C oil bath for 24 h. The reaction was monitored by TLC. After the reaction finished, the mixture was filtered and washed with EtOAc (15 mL × 3), and then concentrated by rotatory evaporation. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (5 : 1–3 : 1 v/v) as eluent to give the corresponding product.

1-((2-(Phenylethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3a**): Red solid; yield: 62%; m.p. 81–83 °C; IR (neat) ν 3060, 2262, 1612, 1497, 1458, 1399, 1240, 1098, 1071, 885, 691 cm^{-1}; ^{1}H NMR (400 MHz,

Table 2 The effect of different substituents on behalf of 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene[a]



Entry	R^1	R^2	Product	Yield/%[b]
1	H	C_6H_5	**3a**	62
2	H	*p*-$CH_3C_6H_4$	**3b**	73
3	H	*p*-$CH_3OC_6H_4$	**3c**	69
4	H	*p*-FC_6H_4	**3d**	54
5	H	*p*-ClC_6H_4	**3e**	58
6	H	*m*-$CH_3C_6H_4$	**3f**	71
7	H	Naphthyl	**3g**	46
8	H	*n*-Hexyl	**3h**	72
9	H	*t*-Bu	**3i**	32
10	H	Cyclopropyl	**3j**	63
11	5-CF_3	C_6H_5	**3k**	51
12	4-F	C_6H_5	**3l**	55
13	4-F	*p*-FC_6H_4	**3m**	58
14	4-F	*n*-Hexyl	**3n**	59

[a]Reaction condition: 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene (0.5 mmol), benzimidazole (0.5 mmol), CuI (10% mmol), 1,10-phenanthroline (20% mmol), $Pd(OAc)_2$ (10% mmol) and Cs_2CO_3 (2.0 equiv.) in toluene under an atmosphere of N_2 at 100 °C for 24 h.
[b]Isolated yield based on 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene.

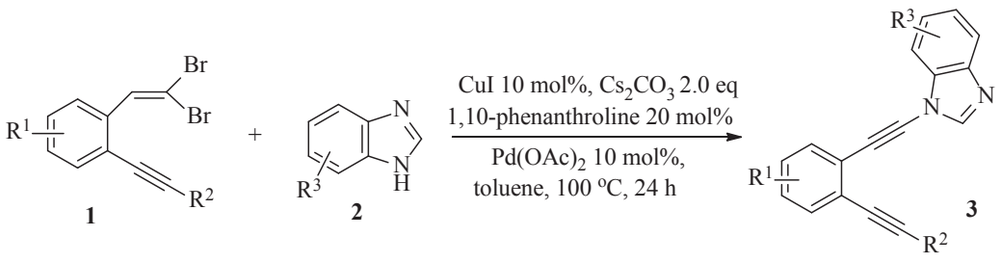
$CDCl_3$) δ 8.15 (s, 1H), 7.82 (d, *J*=8.0 Hz, 1H), 7.67 (d, *J*=8.0 Hz, 1H), 7.63–7.57 (m, 2H), 7.54–7.52 (m, 2H), 7.36–7.32 (m, 6H), 7.20 (t, *J*=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.31, 141.90, 134.36, 132.10, 131.75, 131.22, 128.66, 128.41, 128.31, 128.15, 125.42, 124.74, 124.02, 123.96, 122.81, 120.70, 111.24, 93.68, 87.91, 80.25, 72.85; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{14}N_2$: 318.1157; found: 318.1153.

1-((2-(p-Tolylethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3b**): Red solid; yield 73%; m.p. 86–88 °C; IR (neat) *v* 3060, 2921, 2252, 1612, 1501, 1480, 1290, 1175, 885, 817 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 7.68 (d, *J*=8.0 Hz, 1H), 7.61–7.57 (m, 2H), 7.42 (d, *J*=8.0 Hz, 2H), 7.37–7.33 (m, 3H), 7.23 (t, *J*=8.0 Hz, 1H), 7.14 (d, *J*=8.0 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.33, 141.82, 138.87, 134.31, 132.02, 131.62, 131.17, 129.15, 128.30, 127.95, 125.59, 124.74, 124.01, 123.78, 120.64, 119.67, 111.25, 93.92, 87.25, 80.11, 72.88, 21.48; HRMS (EI): $[M]^+$ calcd for $C_{24}H_{16}N_2$: 332.1313; found: 332.1312.

1-((2-((4-Methoxyphenyl)ethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3c**): Yellow solid; yield 69%; m.p. 111–112 °C; IR (neat) *v* 3061, 2962, 2262, 1607, 1505, 1399, 1288, 1248, 1030, 832, 746 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 1H), 7.61–7.57 (m, 2H), 7.46 (d, *J*=8.0 Hz, 2H), 7.37–7.33 (m, 3H), 7.25 (t, *J*=8.0 Hz, 1H), 6.86 (d, *J*=8.0 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.90, 143.36, 141.89, 134.37, 133.26, 131.96, 131.22, 128.35, 127.84, 125.81, 124.77, 124.04, 123.70, 120.69, 114.86, 114.06, 111.27, 93.84, 86.69, 80.09, 72.95, 55.31; HRMS (EI): $[M]^+$ calcd for $C_{24}H_{16}N_2O$: 348.1263, found: 348.1262.

1-((2-((4-Fluorophenyl)ethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3d**): Red solid; yield 54%; m.p. 74–76 °C; IR (neat) *v*

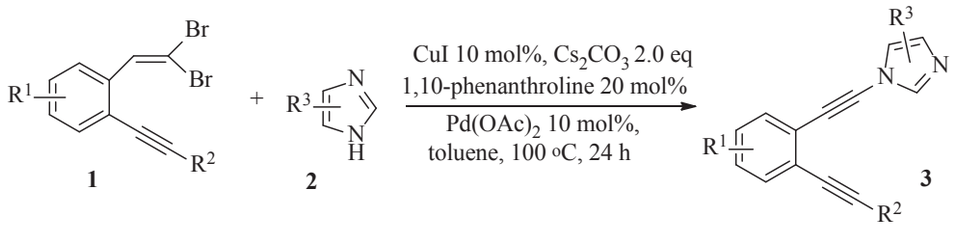
Table 3 The scope of substituted benzimidazoles used in the Cu/Pd-co-catalysed cascade reaction[a]



Entry	R^1	R^2	R^3	Product	Yield/%[b]
1	H	C_6H_5	5, 6-dimethyl	**3o**	57
2	H	C_6H_5	5-NO_2	**3p**	55
3	5-CF_3	C_6H_5	5, 6-dimethyl	**3w**	54

[a]Reaction condition: 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene (0.5 mmol), nucleophile (0.5 mmol), CuI (10% mmol), 1, 10-phenanthroline (20% mmol), $Pd(OAc)_2$ (10% mmol) and Cs_2CO_3 (2.0 equiv.) in toluene under an atmosphere of N_2 at 100 °C for 24 h.
[b]Isolated yield based on 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene.

Table 4 The scope of substituted imidazoles used in the Cu/Pd-co-catalysed cascade reaction[a]



Entry	R^1	R^2	R^3	Product	Yield/%[b]
1	H	C_6H_5	H	**3q**	47
2	H	C_6H_5	4-Me	**3r**	51
3	H	*p*-$CH_3C_6H_4$	H	**3s**	48
4	H	*p*-FC_6H_4	H	**3t**	44
5	4-F	C_6H_5	H	**3u**	39
6	H	*n*-Hexyl	H	**3v**	53

[a]Reaction condition: 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene (0.5 mmol), nucleophile (0.5 mmol), CuI (10% mmol), 1, 10-phenanthroline (20% mmol), $Pd(OAc)_2$ (10% mmol) and Cs_2CO_3 (2.0 equiv.) in toluene under an atmosphere of N_2 at 100 °C for 24 h.
[b]Isolated yield based on 1-(2,2-dibromovinyl)-2-(phenylethynyl)benzene.

3064, 2254, 1598, 1504, 1459, 1228, 1175, 1096, 837, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.84 (d, *J*=8.0 Hz, 1H), 7.65 (d, *J*=8.0 Hz, 1H), 7.63–7.59 (m, 2H), 7.52–7.48 (m, 2H), 7.40–7.34 (m, 3H), 7.23 (t, *J*=8.0 Hz, 1H), 7.05–7.01 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.95, 161.46, 143.32, 141.91, 135.88, 134.36, 133.74, 133.66, 132.10, 131.34, 128.43, 128.29, 125.29, 124.77, 124.13, 123.90, 120.81, 118.94, 118.90, 115.89, 115.67, 111.15, 92.56, 87.62, 80.24, 72.79; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{13}FN_2$: 336.1063; found: 336.1063.

1-((2-((4-Chlorophenyl)ethynyl)phenyl)ethynyl)-1H-benzo[d] imidazole (**3e**): Yellow solid; yield 58%; m.p. 94–96 °C; IR (neat) *v* 3063, 2253, 1612, 1495, 1458, 1290, 1092, 1013, 828, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.84 (d, *J*=8.0 Hz, 1H), 7.64 (d, *J*=8.0 Hz, 1H), 7.62–7.58 (m, 2H), 7.44 (d, *J*=8.0 Hz, 2H), 7.38–7.34 (m, 3H), 7.30 (d, *J*=8.0 Hz, 2H), 7.24 (t, *J*=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.27, 141.84, 134.71, 134.29, 132.92, 132.10, 131.33, 128.75, 128.38, 125.07, 124.76, 124.14, 123.89, 121.25, 120.76, 111.07, 92.42, 88.83, 80.24, 72.71; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{13}ClN_2$: 352.0767; found: 352.0764.

1-((2-(m-Tolylethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3f**): Red solid; yield 71%; m.p. 53–54 °C; IR (neat) *v* 3060, 2922, 2255, 1609, 1497, 1458, 1172, 783, 748, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 1H), 7.62–7.58 (m, 2H), 7.36–7.33 (m, 5H), 7.22 (t, *J*=8.0 Hz, 2H), 7.16 (d, *J*=8.0 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.34, 141.90, 138.11, 134.36, 132.37, 132.04, 131.21, 129.56, 128.81, 128.34, 128.30, 128.07, 125.56, 124.74, 124.03, 123.93, 122.57, 120.70, 111.30, 93.95, 87.58, 80.21, 72.86, 21.12; HRMS (EI): $[M]^+$ calcd for $C_{24}H_{16}N_2$: 332.1313; found: 332.1312.

1-((2-(Naphthalen-1-ylethynyl)phenyl)ethynyl)-1H-benzo[d] imidazole (**3g**): Red oil; yield 46%; IR (neat) *v* 3058, 2924, 2255, 1612, 1501, 1458, 1173, 1011, 800, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J*=8.0 Hz, 1H), 8.15 (s, 1H), 7.87–7.81 (m, 3H), 7.78–7.73 (m, 2H), 7.68–7.63 (m. 2H), 7.46–7.39 (m, 4H), 7.31 (t, *J*=8.0 Hz, 1H), 7.18–7.09 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.48, 141.82, 134.45, 133.18, 132.23, 131.87, 130.77, 129.23, 128.65, 128.31, 128.28, 126.83, 126.55, 125.97, 125.21, 124.76, 124.07, 123.88, 120.67, 120.47, 111.27, 92.69, 92.02, 80.25, 72.95; HRMS (EI): $[M]^+$ calcd for $C_{27}H_{16}N_2$: 368.1313; found: 368.1306.

1-((2-(Oct-1-yn-1-yl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3h**): Red oil; yield 72%; IR (neat) *v* 3062, 2925, 2256, 1613, 1501, 1459, 1173, 1019, 758, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 7.74 (d, *J*=8.0 Hz, 1H), 7.55–7.52 (m. 1H), 7.50–7.48 (m, 1H), 7.44–7.37 (m, 2H), 7.31–7.29 (m, 2H), 2.48 (t, *J*=6.0 Hz, 2H), 1.62–1.56 (m, 2H), 1.43–1.38 (m, 2H), 1.21–1.19 (m, 4H), 0.83–0.80 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.39, 141.96, 134.54, 132.15, 131.44, 128.41, 127.39, 126.58, 124.67, 124.01, 123.65, 120.77, 111.05, 95.27, 79.49, 79.20, 72.90, 31.23, 28.70, 28.59, 22.42 19.70, 13.97; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{22}N_2$: 326.1783; found: 326.1786.

1-((2-(3,3-Dimethylbut-1-yn-1-yl)phenyl)ethynyl)-1H-benzo[d] imidazole (**3i**): Yellow solid; yield 32%; m.p. 75–77 °C; IR (neat) *v* 3062, 2968, 2927, 2255, 1613, 1500, 1458, 1294, 1173, 885 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 7.75 (d, *J*=8.0 Hz, 1H), 7.56–7.53 (m. 1H), 7.49–7.47 (m, 1H), 7.45–7.37 (m, 2H), 7.33–7.29 (m, 2H), 1.32 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.49, 141.99, 134.52, 132.20, 131.73, 128.47, 127.37, 126.64, 124.69, 124.04, 123.57, 120.80, 111.15, 103.39, 79.38, 77.73, 72.81, 30.88, 28.21; HRMS (EI): $[M]^+$ calcd for $C_{21}H_{18}N_2$: 298.1470; found: 298.1473.

1-((2-(Cyclopropylethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3j**): Red oil; yield 63%; IR (neat) *v* 3063, 2256, 1612, 1500, 1459, 1291, 1174, 884, 845, 809 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 7.81 (d, *J*=8.0 Hz, 1H), 7.53–7.50 (m. 1H), 7.47–7.37 (m, 3H), 7.31–7.27 (m, 2H), 1.57–1.51 (m, 1H), 0.94–0.88 (m, 2H), 0.86–0.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.39, 141.94, 134.52, 132.13, 131.17, 128.29, 127.36, 126.22, 124.68, 124.03, 123.84, 120.76, 111.17, 98.24, 79.58, 74.39, 72.96, 8.90, 0.41; HRMS (EI): $[M]^+$ calcd for $C_{20}H_{14}N_2$: 282.1157; found: 282.1153.

1-((2-(Phenylethynyl)-5-(trifluoromethyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3k**): Red solid; yield 51%; m.p. 148–149 °C; IR (neat) *v* 3083, 2923, 2259, 1611, 1497, 1437, 1326, 1172, 1121, 835, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.85–7.83 (m, 2H), 7.73 (d, *J*=8.0 Hz, 1H), 7.66 (d, *J*=8.0 Hz, 1H), 7.60 (d, *J*=8.0 Hz, 1H), 7.56–7.54 (m, 2H), 7.41–7.34 (m, 4H), 7.23 (t, *J*=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.21, 141.87, 134.21, 132.51, 131.91, 130.35, 130.02, 129.27, 128.76, 128.00 (q, *J*=3.7 Hz, C_{Ar-CF3}), 124.99, 124.77, 124.33, 122.15, 120.87, 111.20, 96.10, 86.80, 81.55, 72.00; HRMS (EI): $[M]^+$ calcd for $C_{24}H_{13}F_3N_2$: 386.1031; found: 386.1035.

1-((4-Fluoro-2-(phenylethynyl)phenyl)ethynyl)-1H-benzo[d] imidazole (**3l**): Red solid; yield 55%; m.p. 83–85 °C; IR (neat) *v* 3061, 2923, 2256, 1599, 1570, 1492, 1453, 1166, 820, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 7.65 (d, *J*=8.0 Hz, 1H), 7.59–7.55 (m, 1H), 7.52–7.51 (m, 2H), 7.38–7.31 (m, 5H), 7.23 (t, *J*=8.0 Hz, 1H), 7.09 (td, J_1=8.0 Hz, J_2=6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.28, 160.79, 143.30, 141.88, 134.32, 133.25, 133.17, 131.84, 129.04, 128.49, 127.66, 127.55, 124.82, 124.12, 122.30, 120.77, 120.21 (d, *J*=2.0 Hz, C_{Ar-F}), 119.07, 118.83, 116.14, 115.92, 111.18, 94.76, 86.83 (d, *J*=3.0 Hz), 79.88, 71.89; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{13}FN_2$: 336.1063; found: 336.1061.

1-((4-Fluoro-2-((4-fluorophenyl)ethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3m**): Red solid; yield 58%; m.p. 103–104 °C; IR (neat) *v* 3066, 2216, 1597, 1569, 1507, 1454, 1398, 1230, 1165, 836,

743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.84 (d, J=8.0 Hz, 1H), 7.63 (d, J=8.0 Hz, 1H), 7.58–7.55 (m, 1H), 7.50–7.46 (m, 2H), 7.36 (t, J=8.0 Hz, 1H), 7.30 (dd, J_1=8.0 Hz, J_2=2.4 Hz, 1H), 7.25 (t, J=8.0 Hz, 1H), 7.09 (td, J_1=8.0 Hz, J_2=2.4 Hz, 1H), 7.02 (t, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.14, 163.29, 161.64, 160.80, 143.26, 141.91, 134.32, 133.84, 133.76, 133.36, 133.26, 127.53, 127.43, 124.80, 124.17, 120.85, 120.14, 119.04, 118.80, 118.43, 118.39, 116.22, 115.97, 115.75, 111.05, 93.64, 86.55, 79.88, 71.82; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{12}F_2N_2$: 354.0969; found: 354.0966.

1-((4-Fluoro-2-(oct-1-yn-1-yl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3n**): Red oil; yield 59%; IR (neat) *v* 2929, 2857, 2257, 1603, 1568, 1491, 1454, 1291, 873, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.85 (dd, J_1=8.0 Hz, J_2=0.8 Hz, 1H), 7.71 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.52–7.49 (m, 1H), 7.44–7.36 (m, 2H), 7.18 (dd, J_1=8.0 Hz, J_2=2.8 Hz, 1H), 7.01 (td, J_1=8.0 Hz, J_2=2.8 Hz, 1H), 2.47 (t, J=8.0 Hz, 3H), 1.62–1.54 (m, 2H), 1.41–1.37 (m, 2H), 1.21–1.16 (m, 4H), 0.83–0.79 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.38, 160.89, 143.35, 141.94, 134.51, 133.40, 133.31, 128.86, 128.76, 124.70, 124.04, 120.81, 119.92, 119.90, 119.13, 118.91, 115.34, 110.96, 96.65, 79.13, 78.37, 78.35, 71.92, 31.18, 28.55, 28.52, 22.38, 19.64, 13.94; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{21}FN_2$: 344.1689; found: 344.1689.

5,6-Dimethyl-1-((2-(phenylethynyl)phenyl)ethynyl)-1H-benzo[*d*]imidazole (**3o**): Red oil; yield 57%; IR (neat) *v* 2923, 2250, 1596, 1497, 1464, 1162, 1159, 1047, 840, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.63–7.57 (m, 3H), 7.54–7.52 (m, 2H), 7.39–7.32 (m, 6H), 2.36 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.70, 140.40, 134.34, 133.06, 132.77, 132.11, 131.75, 131.22, 128.60, 128.45, 128.19, 128.15, 125.33, 124.18, 122.87, 120.71, 111.31, 93.65, 87.92, 80.77, 72.42, 20.20, 20.08; HRMS (EI): $[M]^+$ calcd for $C_{25}H_{18}N_2$: 346.1470; found: 346.1475.

6-Nitro-1-((2-(phenylethynyl)phenyl)ethynyl)-1H-benzo[d]imidazole (**3p**): Yield solid; yield 55%; IR (neat) *v* 2925, 2361, 1593, 1522, 1492, 1343, 1176, 1058, 759, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.23 (s, 1H), 8.15 (d, J=9.6 Hz, 1H), 7.74 (d, J=6.8 Hz, 1H), 7.51–7.44 (m, 2H), 7.31–7.27 (m, 3H), 7.21 (d, J=8.8 Hz, 1H), 7.14 (d, J=6.8 Hz, 2H), 7.07 (d, J=6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.86, 146.43, 144.66, 144.32, 143.44, 140.07, 135.83, 134.18, 130.62, 129.92, 129.53, 128.98, 128.87, 128.15, 127.78, 124.07, 120.10, 119.76, 117.41, 112.29; HRMS (EI): $[M]^+$ calcd for $C_{23}H_{13}N_3O_2$: 363.1008; found: 363.1005.

1-((2-(Phenylethynyl)phenyl)ethynyl)-1H-imidazole (**3q**): Red oil; yield 47%; IR (neat) *v* 2923, 2263, 1598, 1494, 1470, 1310, 1099, 1012, 812, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.58 (d, J=8.0 Hz, 1H), 7.54–7.51 (m, 3H), 7.37–7.32 (m, 5H), 7.22 (s, 1H), 7.11 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.03, 131.93, 131.53, 129.36, 128.74, 128.63, 128.54, 128.14, 125.86, 123.64, 122.83, 121.74, 93.82, 87.63, 81.72, 69.65; HRMS (EI): $[M]^+$ calcd for $C_{19}H_{12}N_2$: 268.1000; found: 268.1000.

4-Methyl-1-((2-(phenylethynyl)phenyl)ethynyl)-1H-imidazole (**3r**): Red oil; yield 51%; IR (neat) *v* 2963, 2923, 2259, 1598, 1495, 1409, 1292, 1071, 757, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.59–7.56 (m, 1H), 7.54–7.50 (m, 3H), 7.37–7.32 (m, 5H), 6.90 (s, 1H), 2.95 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.41, 138.64, 131.90, 131.56, 131.46, 128.68, 128.51, 128.40, 128.11, 125.78, 123.99, 122.95, 117.73, 93.76, 87.76, 76.29, 69.05, 13.46; HRMS (EI): $[M]^+$ calcd for $C_{20}H_{11}N_2$: 282.1157; found: 282.1154.

1-((2-(p-Tolylethynyl)phenyl)ethynyl)-1H-imidazole (**3s**): Red oil; yield 48%; IR (neat) *v* 2921, 2257, 1593, 1502, 1472, 1310, 1099, 1012, 815, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.57 (d, J=8.0 Hz, 1H), 7.52 (d, J=8.0 Hz, 1H), 7.41 (d, J=8.0 Hz, 2H), 7.37–7.30 (m, 2H), 7.22 (s, 1H), 7.17 (d, J=8.0 Hz, 2H), 7.11 (s, 1H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.00, 138.97, 131.80, 131.45, 131.41, 129.29, 128.58, 127.93, 126.06, 123.55, 121.72, 119.73, 94.09, 87.02, 81.65, 69.69; HRMS (EI): $[M]^+$ calcd for $C_{20}H_{11}N_2$: 282.1157; found: 282.1156.

1-((2-((4-Fluorophenyl)ethynyl)phenyl)ethynyl)-1H-imidazole (**3t**): Red oil; yield 44%; IR (neat) *v* 2923, 2259, 1597, 1472, 1228, 1065, 1012, 836, 758, 648 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.58–7.45 (m, 4H), 7.39–7.33 (m, 2H), 7.22 (s, 1H), 7.13 (s, 1H), 7.22 (s, 1H), 7.06 (t, J=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 164.00, 161.50, 133.50, 133.41, 131.91, 131.64, 129.48, 128.66, 128.20, 125.76, 119.00, 116.01, 115.79, 92.71, 87.36, 81.76, 69.58; HRMS (EI): $[M]^+$ calcd for $C_{19}H_{11}N_2$: 286.0906; found: 286.0905.

1-((4-Fluoro-2-(phenylethynyl)phenyl)ethynyl)-1H-imidazole (**3u**): Red oil; yield 39%; IR (neat) *v* 2924, 2261, 1600, 1571, 1394, 1066, 1012, 819, 757, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.52–7.50 (m, 3H), 7.38–7.37 (m, 3H), 7.30–7.27 (m, 1H), 7.22 (s, 1H), 7.11 (s, 1H), 7.07 (t, J=8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.46, 160.97, 139.96, 133.53, 133.44, 131.62, 129.39, 129.09, 128.59, 128.13, 128.03, 122.36, 121.70, 119.92, 119.89, 118.91, 118.67, 116.06, 115.84, 94.92, 86.59 (d, J=13.2 Hz), 81.37, 68.75; HRMS (EI): $[M]^+$ calcd for $C_{19}H_{11}FN_2$: 286.0906; found: 286.0902.

1-((2-(Oct-1-yn-1-yl)phenyl)ethynyl)-1H-imidazole (**3v**): Red oil; yield 53%; IR (neat) *v* 3117, 2929, 2858, 2262, 1594, 1473, 1310, 1170, 1065, 758, 649 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.49–7.44 (m, 2H), 7.32–7.25 (m, 2H), 7.21 (s, 1H), 7.11 (s, 1H), 2.47 (t, J=6.8 Hz, 3H), 1.65–1.57 (m, 2H), 1.49–1.44 (m, 2H), 1.28–1.27 (m, 4H), 0.87 (t, J=6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.01, 132.02, 131.63, 129.21, 128.58, 127.36, 126.73, 123.33, 121.74, 95.32, 80.97, 78.92, 69.70, 31.27, 28.68, 28.55, 22.47, 19.59, 14.03; HRMS (EI): $[M]^+$ calcd for $C_{19}H_{20}N_2$: 276.1626; found: 276.1622.

5,6-Dimethyl-1-((2-(phenylethynyl)-5-(trifluoromethyl)phenyl) ethynyl)-1H-benzo[d]imidazole (**3w**): White solid; yield 54%; m.p. 133–135 °C; IR (neat) *v* 2923, 2262, 1609, 1498, 1379, 1259, 1125, 1070, 756, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.84 (s, 1H), 7.72 (t, J=8.0 Hz, 1H), 7.59–7.54 (m, 4H), 7.41–7.33 (m, 4H), 2.36 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.57, 140.38, 134.59, 133.33, 132.56, 132.46, 131.88, 130.29, 129.96, 129.18, 128.58, 127.89, 124.96, 124.60, 122.18, 122.09, 120.85, 111.23, 96.00, 86.82, 82.08, 71.57, 20.24, 20.12; HRMS (EI): $[M]^+$ calcd for $C_{26}H_{17}F_3N_2$: 414.1344; found: 414.1345.

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