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Cyclization

Copper-Catalyzed Construction of Trinuclear N-Fused Hybrid Scaffolds Using Cyclic Ureas as New Building Blocks

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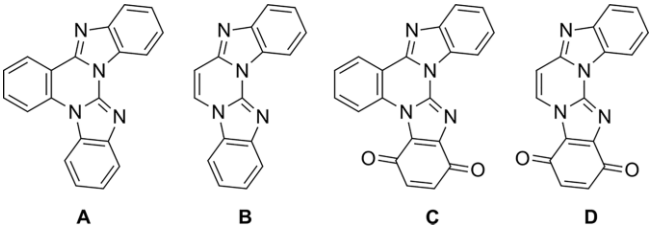
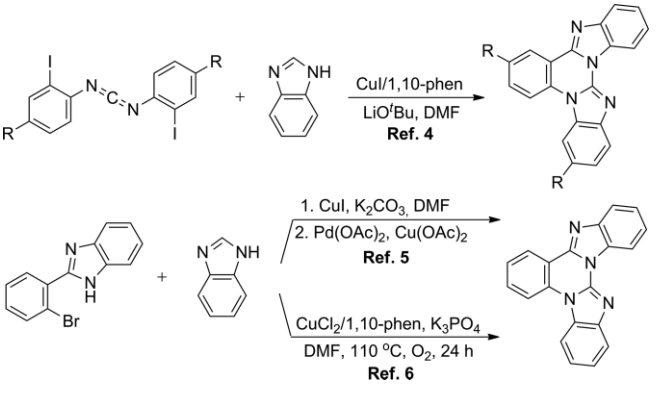
Abstract: 2-(2-Bromoaryl)- and 2-(2-bromovinyl)-benzimidazoles are coupled and cyclized with cyclic ureas as new building blocks in dimethylformamide in the presence of a catalytic amount of a copper catalyst and a base to give the corresponding trinuclear N-fused hybrid scaffolds in good yields. Trinuclear N-fused hybrid scaffolds having methoxy group on benzimidazole moiety are readily oxidized to unprecedented benzimidazolequinone-fused hybrid scaffolds in high yields by treatment of ceric ammonium nitrate in acetonitrile/H_2O.

Introduction

It is known that polynuclear N-fused hybrid scaffolds exhibit diverse biological activities as well as optical properties that are not shown in each N-heterocyclic compounds.[1] Trinuclear N-fused hybrid scaffolds, benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazolines (Scheme 1, **A**) have been synthesized due to such intrinsic activities and properties.[2–6] Lv and coworkers reported that bis(*o*-haloaryl)carbodiimides reacted with benzimidazole in the presence of CuI along with 1,10-phenanthroline to give trinuclear N-fused hybrid scaffolds **A** through a sequential nucleophilic addition/C–N coupling/intramolecular sp^2 C–H arylation process (Scheme 2).[4] Kumar et al. demonstrated that 2-(2-bromophenyl)benzimidazole is coupled and oxidatively cyclized with benzimidazole in the presence of CuI and $Pd(OAc)_2$ along with $Cu(OAc)_2$ as reoxidant to give trinuclear N-fused hybrid scaffold **A** (Scheme 2).[5] An improved copper-catalyzed version for such a similar C–N coupling and oxidative cyclization leading to scaffold **A** was also exemplified by the reaction of 2-(2-bromophenyl)benzimidazole with benzimidazole (Scheme 2).[6] However, last two reports only showed the synthesis of benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo-[1,2-*c*]quinazoline itself.[5,6] Among our efforts directed toward developing new synthetic methods for heterocycles,[7] we reported on several transition metal-catalyzed and transition metal-free protocols for N-fused hybrid scaffolds.[8] This report describes another synthetic method for scaffolds **A** with broad substrate scope by copper-catalyzed coupling and cyclocondensation of 2-(2-bromoaryl)benzimidazoles with 1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one as new building block. The present protocol can be extended to the reaction with 2-(2-bromovinyl)benzimidazoles to produce trinuclear N-fused hybrid scaffolds, benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidines (Scheme 1, **B**). Furthermore, this report also describes the synthesis of unprecedented trinuclear N-fused hybrid scaffolds, **C** and **D** (Scheme 1), from the oxidation of methoxy-substituted **A** and **B** analogues on benzimidazole moiety. To the best of our knowledge, no reports have been found for the synthetic method and biological activity of scaffolds **B**–**D**.



Scheme 1. Trinuclear N-fused hybrid scaffolds.



Scheme 2. Previous synthetic methods for N-fused hybrid scaffolds A.

Results and Discussion

Treatment of equimolar amounts of 2-(2-bromophenyl)-1*H*-benzo[*d*]imidazole (**1a**)[9] and 1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2a**)[10] in dimethylformamide (DMF) in the presence of a catalytic amount of CuI (10 mol-% based on **1a**) and K_2CO_3

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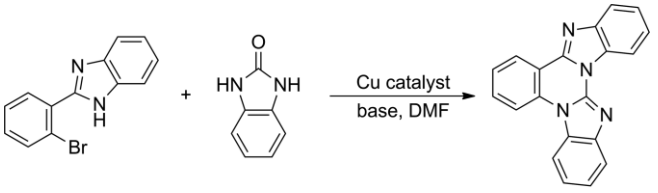
Table 1. Optimization of Conditions for the Reaction of **1a** and **2a**.[a].



1a **2a** **3a**

Entry	Cu cat.	[**2a**]/[**1a**]	Base	Temp [°C]	Time [h]	Conv of **1a** [%]	Yield[b] [%]
1	CuI	1	K_2CO_3	130	12	84	73
2	CuI	1	K_2CO_3	130	24	100	76
3	CuI	1.5	K_2CO_3	130	12	100	83
4	CuI	2	K_2CO_3	130	12	100	82
5	CuI	1.5	K_2CO_3	130	24	100	84
6[c]	CuI	1.5	K_2CO_3	130	12	78	64
7	CuI	1.5	K_2CO_3	100	12	71	62
8	CuI	1.5	K_2CO_3	150	12	100	85
9	CuI	1.5	K_3PO_4	130	12	95	71
10	CuI	1.5	Cs_2CO_3	130	12	100	82
11	CuI	1.5	NaO^{t}Bu	130	12	93	66
12	CuI	1.5	CsF	130	12	62	34
13	CuI	1.5	NaOAc	130	12	68	47
14	CuCl	1.5	K_2CO_3	130	12	79	62
15	CuBr	1.5	K_2CO_3	130	12	83	68
16	Cu powder	1.5	K_2CO_3	130	12	100	34
17	–	1.5	K_2CO_3	130	24	1	0

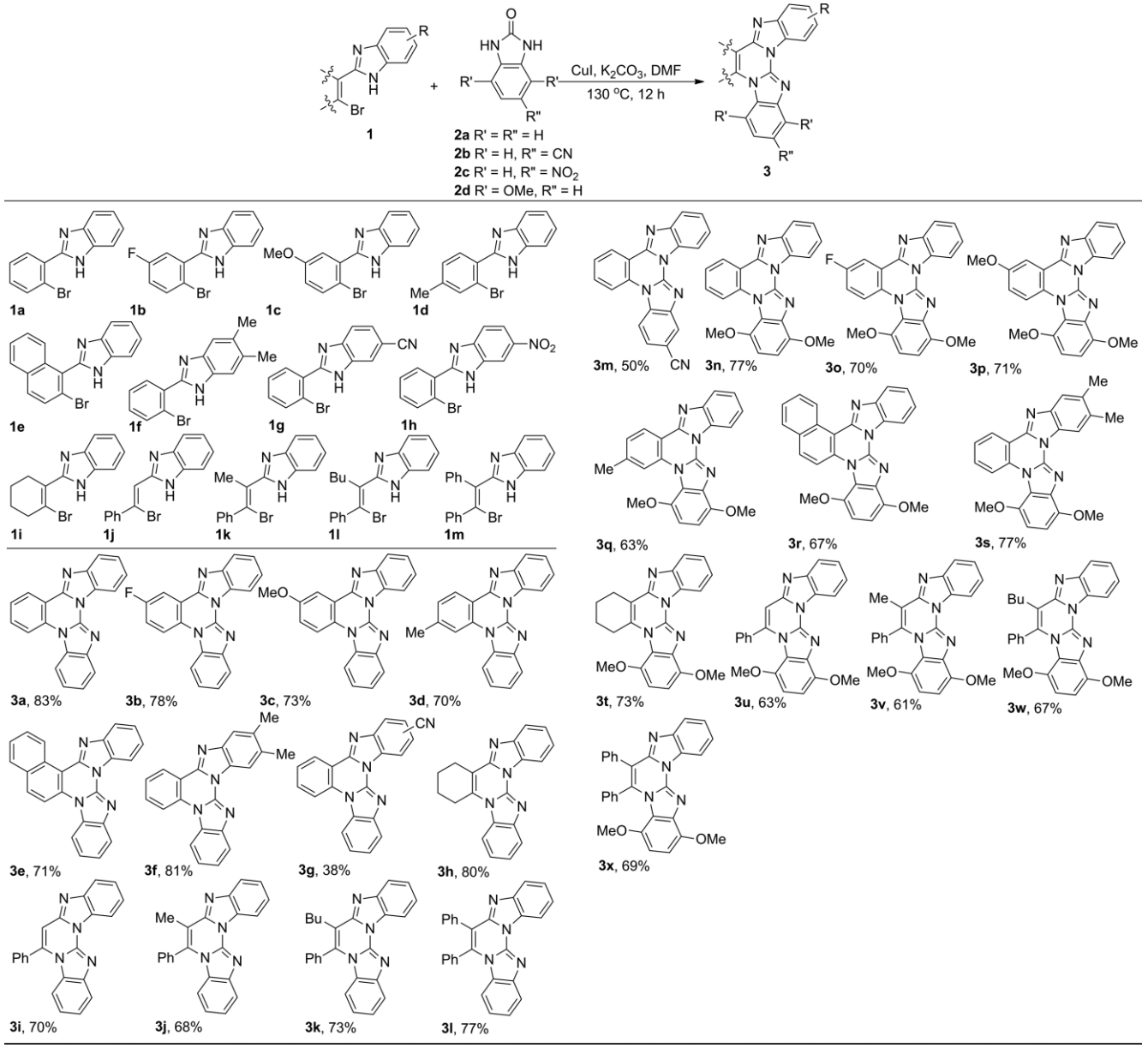
[a] Reaction conditions: **1a** (0.3 mmol), Cu catalyst (0.03 mmol), base (0.6 mmol), DMF (3 mL). [b] Isolated yields. [c] CuI (0.015 mmol).

(2 equiv. to **1a**) at 130 °C for 12 h afforded benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (**3a**)[4–6] in 73 % isolated yield with 84 % conversion of **1a** (Table 1, entry 1). Even though **1a** was completely consumed for 24 h, the yield of **3a** did not show a considerable change (Table 1, entry 2). The molar ratio of **2a** to **1a** affected the yield of **3a** under the employed conditions and the yield increased with the increase of the ratio up to 1.5 (Table 1, entries 1,3,4). Here again, the reaction for 24 h gave no significant change of the yield of **3a** under the molar ratio of [**2a**]/[**1a**] = 1.5 (Table 1, entry 5). The reaction using lower amount of CuI (5 mol-% based on **1a**) resulted in lower yield of **3a** with incomplete conversion of **1a** (Table 1 entry 6). The reaction temperature also affected the yield of **3a** and the conversion of **1a**. A lower reaction temperature resulted in lower yield of **3a** with incomplete conversion of **1a** (Table 1, entry 7), whereas a higher reaction temperature gave a similar yield of **3a** with complete conversion of **1a** (Table 1, entry 8). Performing the reaction using other bases such as K_3PO_4, Cs_2CO_3, NaO^{t}Bu, CsF, and NaOAc under the employed conditions resulted in lower yields of **3a** with incomplete conversion of **1a** except for Cs_2CO_3, which showed a similar activity as K_2CO_3 (Table 1, entries 9–13).

The reaction proceeded with other copper catalysts, such as CuCl, CuBr, and Cu powder, but the yield of **3a** was generally lower than that by the use of CuI (Table 1, entries 14–16). When the reaction was carried out in the absence of a copper catalyst, no product was formed and **1a** was recovered almost intact (Table 1, entry 17). Not shown in Table 1, similar treatment of chloro analogue of **1a**, 2-(2-chlorophenyl)-1*H*-benzo[*d*]imidazole with **2a** under the conditions of entry 3 of Table 1 afforded **3a** in 72 % yield with 87 % conversion of **1a**.

Table 2 shows the results for the coupling and cyclization of 2-(2-bromoaryl)- and 2-(2-bromovinyl)-benzimidazoles **1a**–**m** with 1,3-dihydro-2*H*-benzo[*d*]imidazol-2-ones (**2a**-**d**) under the optimized conditions.[9] The 2-(2-bromoaryl)benzimidazoles **1b**-**d** having electron-donating and -withdrawing substituents on bromoaryl were readily coupled and cyclized with **2a** to give the corresponding trinuclear N-fused hybrid scaffolds **3b**-**d** in similar yields. Benzo-fused 2-(2-bromophenyl)benzimidazole **1e** also reacted with **2a** to give the coupled and cyclized product **3e**. 2-(2-Bromophenyl)benzimidazoles (**1f** and **1g**) having electron-donating methyl and withdrawing cyano substituents also reacted with **2a** to give the coupled and cyclized products (**3f** and **3g**). In the reaction with **1g**, the product was formed as an isomeric mixture in lower yield (38 % yield, 1:1.3). However, no expected product was formed from **1h** having strong electron-withdrawing NO_2 substituent and **2a**. The reaction of cyclic and acyclic 2-(2-bromovinyl)benzimidazoles **1i**–**m** with **2a** also produced the corresponding trinuclear N-fused hybrid scaffolds, benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidines **3h**-**l** in 68–80 % yields. Similar treatment of the above-mentioned 2-(2-bromoaryl)- and 2-(2-bromovinyl)-benzimidazoles **1a**–**f** and **1i**–**m** with 1,3-dihydro-2*H*-benzo[*d*]imidazol-2-ones (**2b** and **2d**)[10,11] under the employed conditions also afforded the corresponding trinuclear N-fused hybrid scaffolds **3m**–**x** irrespective of cyano and methoxy substituents. However, the product yields were slightly lower than that by the reaction with **2a**. Here again, the coupling and cyclization did not proceed with **2c** having strong electron-withdrawing NO_2 substituent. In contrast to several synthetic methods and their applications to OLED for trinuclear N-fused hybrid scaffolds **A**, no reports are known for synthetic method of trinuclear N-fused hy-

Table 2. Scope of Reaction.[a]



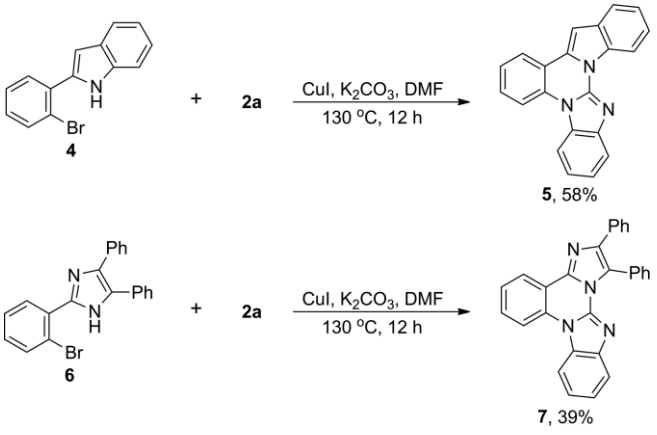
[a] Reaction conditions: **1** (0.3 mmol), **2** (0.45 mmol), CuI (0.03 mmol), K_2CO_3 (0.06 mmol), DMF (3 mL), 130 °C,12 h.

brid scaffolds **B**.[3] 2-(2-Bromophenyl)-1*H*-indole (**4**) and 2-(2-bromophenyl)-4,5-diphenyl-1*H*-imidazole (**6**) were also coupled and cyclized with **2a** under the employed conditions to give the corresponding trinuclear N-fused hybrid scaffolds, **5** and **7** in 58 % and 39 % yields, respectively (Scheme 3).

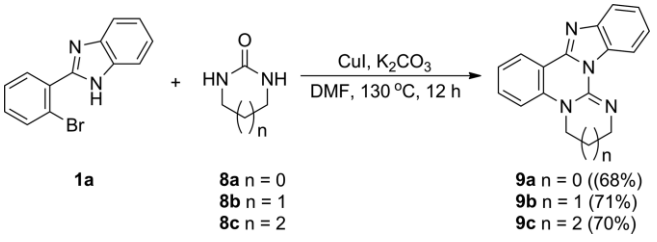
On the basis of the reaction of **1** with **2a**-**d**, the present protocol can be extended to the reaction with cyclic ureas having various ring sizes (Scheme 4). Similar treatment of **1a** with cyclic ureas **8a**–**c** under the employed conditions also afforded the corresponding alicyclic-fused hybrid scaffolds **9a**–**c** in similar yields.[12]

The reaction pathway, although not yet fully understood, seems to proceed by way of an initial formation of C-N coupled intermediate **10** by copper-catalyzed Ullmann-type coupling between **1a** and **2a** (Scheme 5).[13] Intermediate **10** triggers intramolecular cyclocondensation by the nucleophilic attack of NH on adjacent electrophilic carbonyl of **10** and subsequent dehydration to form N-fused trinuclear hybrid scaffold **3a**. We confirmed the formation of **10** in a separate experiment that a similar treatment of **11**, *N*-methyl-substituted analogue of **1a**, with **2a** under the employed conditions furnished C-N coupled product **12** in 68 % yield (Scheme 6).

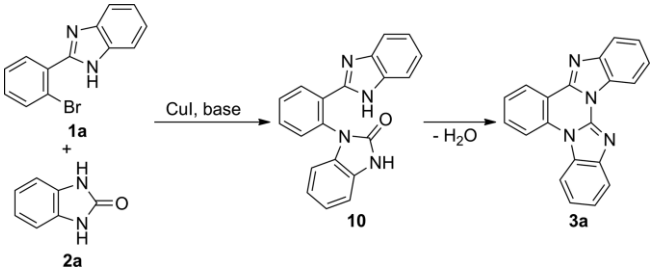
All dimethoxy-substituted trinuclear N-fused hybrid scaffolds **3n**–**x** could be converted into benzimidazolequinone-fused hybrid scaffolds, benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo-[1,2-*c*]-quinazoline-11,14-diones and -pyrimidine-9,12-diones **13a**–**k** with high yields by treatment of ceric ammonium nitrate (CAN) in acetonitrile/H_2O (Table 3).[14] There are no reports on



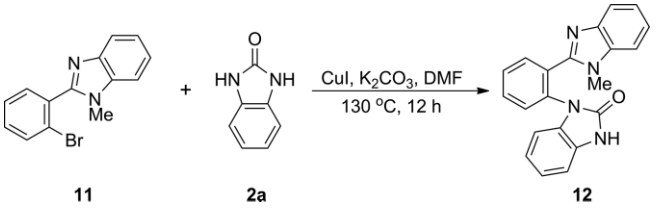
Scheme 3. Synthesis of indole- and imidazole-fused hydrid scaffolds.



Scheme 4. Synthesis of alicyclic-fused hybrid scaffolds.



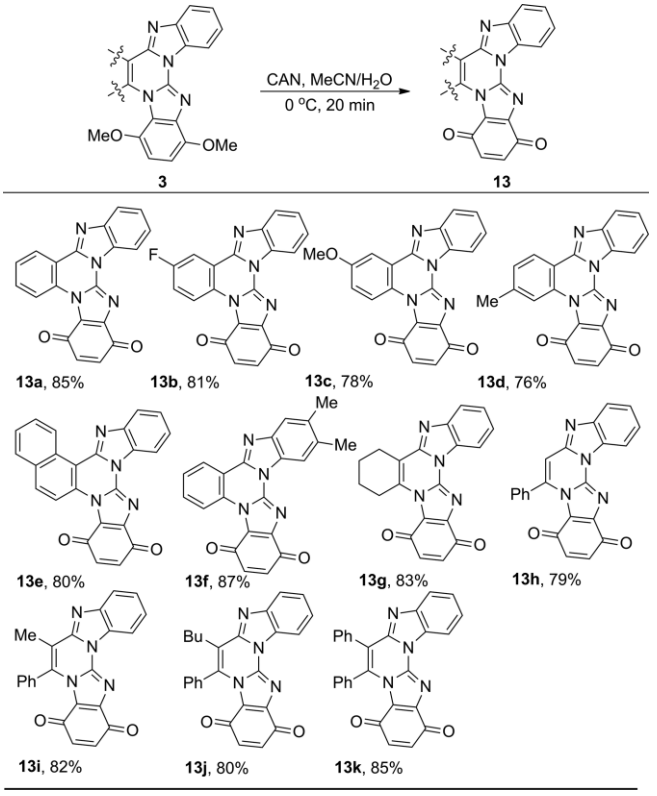
Scheme 5. Reaction pathway.



Scheme 6. Experiment for the mechanism study.

both synthetic methods and biological activities of these N-fused hybrid scaffolds. However, benzimidazole-based 1,4-quinone (1*H*-benzo[*d*]imidazo-4,7-dione)-containing compounds have attracted great attention because of their widely exist in bioreductive quinone-based drugs and biological activities.[15,16]

Table 3. Scope of reaction.[a]



[a] Reaction conditions: **3** (0.2 mmol), CAN (0.8 mmol), acetonitrile/H_2O (4 mL), 0 °C, 20 min.

Conclusions

In summary, construction of trinuclear N-fused hybrid scaffolds were shown by copper-catalyzed coupling and cyclization of 2-(2-bromoaryl)- and 2-(2-bromovinyl)-benzimidazoles, with cyclic ureas as new building blocks. Trinuclear N-fused hybrid scaffolds having methoxy group on benzimidazole moiety could be converted into unprecedented trinuclear N-fused hybrid scaffolds including benzimidazolequinone. We believe that the present reaction will be served as a useful strategy for developing optical materials and bioreductive quinone-based drugs. Further challenges on the construction of polynuclear N-fused hybrid scaffolds using copper-catalyzed coupling/cyclization protocol are expected.

Experimental Section

General Information. ^1H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, in $CDCl_3$ or [D_6]DMSO. Melting points were determined on a microscopic melting point apparatus. High-resolution mass data were recorded using electronic ionization (HRMS-EI, magnetic sector-electric sector double focusing mass analyzer) at Korea Basic Science Institute, Daegu Center, Korea. All reactions were performed in screw-capped vial (5 mL). The isolation of pure products was carried out via thin-layer (a glass plate coated with Kieselgel 60 GF_{254}, Merck) chromatography. 2-(2-Bromoaryl)- and 2-(2-bromovinyl)-benzimidazoles **1a**–**m** were prepared from the corresponding aldehydes and 1,2-phenylenediamines according to

the reported method (see Supporting Information for characterization data and copies of ^{1}H and ^{13}C NMR spectra of **1a**–**m**).[9] Cyclic ureas (**2a**–**c**[10] and **8c**[12]) were synthesized by the corresponding diamines and urea according to literature procedures. 4,7-Dimethoxy-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (**2d**) was prepared from 3,6-dimethoxybenzene-1,2-diamine and urea (see Supporting Information for characterization data and copies of ^{1}H and ^{13}C NMR spectra of **2d**).[11] 3,6-Dimethoxybenzene-1,2-diamine was synthesized by known method from hydroquinone via three step sequence (methylation, nitration, reduction).[14a,17] 2-(2-Bromophenyl)-1*H*-indole (**4**) and 2-(2-bromophenyl)-4,5-diphenyl-1*H*-imidazole (**6**) were synthesized by the reported methods.[18] All other reagents were purchased from commercial sources and used without further purification.

General Procedure for the Synthesis of 3. To a 5 mL screw-capped vial was added **1** (0.3 mmol), **2** (0.45 mmol), CuI (0.006 g, 0.03 mmol), K_2CO_3 (0.083 g, 0.6 mmol) and DMF (3 mL). After stirring at room temperature for 5 min, the reaction mixture was heated at 130 °C for 12 h. The mixture was filtered through a short silica gel column (ethyl acetate) to eliminate inorganic salts and evaporation of the solvent under reduced pressure gave a crude mixture, which was purified by TLC (dichloromethane/methanol = 97:3) to give **3**. Similar experimental procedures were used for the synthesis of **5**, **7**, **9a**–**c**, and **12**. Spectroscopic data for all products are shown below.

Benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3a).[4] R_f = 0.47. White solid (77 mg, 83 %); m.p. 229–232 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.32–7.35 (m, 1H), 7.37–7.40 (m, 1H), 7.45–7.48 (m, 1H), 7.49–7.53 (m, 2H), 7.68–7.72 (m, 1H), 7.82–7.84 (m, 1H), 7.91–7.94 (m, 1H), 8.01 (d, J = 8.0 Hz, 1H) 8.22 (d, J = 8.4 Hz, 1H), 8.66 (dd, J = 7.9 and 1.5 Hz, 1H), 8.69–8.73 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 112.7, 114.5, 114.9, 115.0, 119.6, 120.1, 123.1, 124.3, 124.4, 125.3, 126.6, 130.1, 130.4, 132.0, 134.1, 141.7, 142.5, 143.8, 144.6.

7-Fluorobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3b). R_f = 0.42. White solid (76 mg, 78 %); m.p. 302–303 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.45–7.61 (m, 5H), 7.96 (d, J = 7.5 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.39 (dd, J = 9.1 and 4.1 Hz, 1H), 8.46 (dd, J = 8.3 and 2.8 Hz, 1H), 8.82 (d, J = 7.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 112.6, 112.9 (112.91), 112.9 (112.92), 113.1, 115.3, 116.7 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 117.1 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 119.8 (d, $^2J_{C\text{-}F}$ = 23.8 Hz), 120.1, 120.5, 123.5, 124.7, 125.1, 125.8, 130.5 (d, $^2J_{C\text{-}F}$ = 28.4 Hz), 130.9 (d, $^4J_{C\text{-}F}$ = 2.9 Hz), 141.7, 142.8, 144.0 (d, $^4J_{C\text{-}F}$ = 3.2 Hz). HRMS (EI) calcd. for $C_{20}H_{14}FN_4$ (M^+) 326.0968, found 326.0970.

7-Methoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3c). R_f = 0.51. White solid (74 mg, 73 %); m.p. 267–270 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.93 (s, 3H), 7.28 (dd, J = 9.1 and 3.0 Hz, 1H), 7.34–7.37 (m, 1H), 7.38–7.42 (m, 1H), 7.47–7.52 (m, 2H), 7.86–7.88 (m, 1H), 7.89–7.93 (m, 1H), 8.03 (d, J = 7.9 Hz, 1H), 8.08 (d, J = 3.0, 1H), 8.21 (d, J = 9.2 Hz, 1H), 8.74–8.77 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 56.2, 108.2, 112.6, 115.3, 115.8, 116.7, 119.8, 120.9, 121.0, 123.2, 124.3, 124.7, 125.6, 128.5, 130.3, 130.7, 141.7, 142.7, 143.9, 144.8, 157.1. HRMS (EI) calcd. for $C_{21}H_{14}N_4O$ (M^+) 338.1168, found 338.1171.

8-Methylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3d). R_f = 0.43. White solid (68 mg, 70 %); m.p. 238–240 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.62 (s, 3H), 7.34 (d, J = 8.0 Hz, 1H), 7.41–7.48 (m, 2H), 7.53–7.57 (m, 2H), 7.91–7.93 (m, 1H), 7.94–7.97 (m, 1H), 8.12 (s, 1H), 8.13 (d, J = 7.5 Hz, 1H), 8.60 (d, J = 8.0 Hz, 1H), 8.78–8.81 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 22.4, 112.0, 112.8, 114.9, 119.5, 120.1, 123.0, 124.2, 124.3, 125.3, 126.5, 126.6, 130.2, 130.4, 134.3, 141.9, 142.6, 143.2, 143.9, 144.9. HRMS (EI) calcd. for $C_{21}H_{14}N_4$ (M^+) 322.1218, found 322.1220.

Benzo[*f*]benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3e). R_f = 0.48. White solid (76 mg, 71 %); m.p. 299–301 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.40–744 (m, 1H), 7.47–7.50 (m, 1H), 7.55–761 (m, 3H), 7.78–7.82 (m, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 7.4 Hz, 1H), 8.04–8.11 (m, 1H), 8.11 (d, J = 9.1 Hz, 1H), 8.19 (d, J = 8.2 Hz, 1H), 8.45 (d, J = 9.1 Hz, 1H) 8.87–8.91 (m, 1H), 10.57 (d, J = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 108.2, 113.3, 113.7, 115.1, 119.9, 120.1, 122.7, 124.4, 124.5, 125.3, 126.5, 127.8, 128.3, 129.3 (129.27), 129.3 (129.34), 130.2 (130.18), 130.2 (130.22), 130.4, 133.3, 133.9, 141.9, 143.9, 144.1, 144.7. HRMS (EI) calcd. for $C_{24}H_{14}N_4$ (M^+) 358.1218, found 358.1220.

2,3-Dimethylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3f).[4] R_f = 0.47. White solid (82 mg, 81 %); m.p. 240–242 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.28 (s, 3H), 2.32 (s, 3H), 7.16–7.19 (m, 1H), 7.20–7.24 (m, 1H), 7.27–7.30 (m, 1H), 7.44 (s, 1H), 7.49–7.53 (m, 1H), 7.64–7.66 (m, 1H), 7.81 (d, J = 8.0 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.18 (s, 1H), 8.43 (dd, J = 7.9 and 1.5 Hz. 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 20.5, 20.6, 112.5, 114.6, 114.7, 119.5, 119.8, 122.7, 123.9, 125.0, 126.2, 128.6, 130.0, 131.3, 133.7, 133.8, 134.9, 141.6, 142.2, 142.4, 143.6.

Benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline-2-carbonitrile and benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline-3-carbonitrile (3g). R_f = 0.34. White solid (38 mg, 38 %). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51–7.58 (m, 4H), 7.63–7.67 (m, 2H), 7.81–7.84 (m, 2H), 7.91–7.95 (m, 2H), 7.98–8.02 (m, 2H), 8.05 (d, J = 8.4 Hz, 1H), 8.22–8.24 (m, 2H), 8.30 (d, J = 0.8 Hz, 1H), 8.46 (d, J = 8.4 Hz, 1H), 8.47 (d, J = 8.4 Hz, 1H), 8.79–8.82 (m, 2H), 8.96 (d, J = 8.4 Hz, 1H), 9.23 (d, J = 1.0 Hz, 1H).

6,7,8,9-Tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline (3h). R_f = 0.41. White solid (75 mg, 80 %); m.p. 262–265 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.96–2.01 (m, 2H), 2.09–2.14 (m, 2H), 3.04–3.07 (m, 2H), 3.31–3.33 (m, 2H), 7.20–7.24 (m, 1H), 7.37–7.40 (m, 1H), 7.48–7.53 (m, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.91–7.94 (m, 1H), 8.71–8.74 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.0, 22.21, 23.2, 27.3, 109.4, 113.4, 114.9, 119.5, 119.8, 122.1, 123.6, 124.2, 125.4, 129.8, 129.9, 137.8, 142.1, 142.5, 144.2, 146.5. HRMS (EI) calcd. for $C_{20}H_{16}N_4$ (M^+) 312.1375, found 312.1372.

7-Phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine (3i). R_f = 0.43. White solid (70 mg, 70 %); m.p. 251–253 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.04 (d, J = 8.4 Hz, 1H), 6.91 (s, 1H), 7.00–7.04 (m, 1H), 7.41–7.44 (m, 1H), 7.61–7.71 (m, 5H), 7.80–7.83 (m, 2H), 7.96–7.98 (m, 1H), 8.10–8.13 (m, 1H), 8.96–8.98 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 106.3, 109.2, 114.8, 119.1, 119.4, 121.6, 123.7, 124.0, 125.2, 127.8, 128.0, 129.4, 129.7, 130.3, 131.6, 137.3, 141.9, 142.1, 143.9, 146.9. HRMS (EI) calcd. for $C_{22}H_{14}N_4$ (M^+) 334.1218, found 334.1217.

6-Methyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine (3j). R_f = 0.43. White solid (71 mg, 68 %); m.p. 236–238 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.39 (s, 3H), 5.92 (d, J = 8.4 Hz, 1H), 6.89–6.92 (m, 1H), 7.29–7.32 (m, 1H), 7.54–7.59 (m, 4H), 7.67–7.74 (m, 3H), 7.84–7.86 (m, 1H), 7.98–8.02 (m, 1H), 8.83–8.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 12.8, 109.4, 112.8, 115.0, 119.3, 119.6, 121.8, 123.9, 124.2, 125.4, 129.6, 129.7 (129.70), 129.7 (129.71), 129.9, 130.5, 131.8, 137.5, 142.1, 142.3, 144.1, 147.1. HRMS (EI) calcd. for $C_{23}H_{16}FN_4$ (M^+) 348.1375, found 348.1378.

6-Butyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine (3k). R_f = 0.45. White solid (86 mg, 73 %); m.p.

209–211 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.81 (t, J = 7.4 Hz, 3H), 1.29–1.37 (m, 2H) 1.70–1.76 (m, 2H), 2.78 (t, J = 8.0 Hz, 2H), 5.84 (d, J = 8.4 Hz, 1H), 6.90–6.93 (m, 1H), 7.30–7.33 (m, 1H), 7.54–7.59 (m, 4H), 7.66–7.74 (m, 3H), 7.86 (d, J = 7.8 Hz, 1H), 8.00–8.03 (m, 1H), 8.85–8.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.8, 22.7, 26.9, 31.8, 112.9, 114.3, 115.0, 119.4, 119.7, 121.8, 123.9, 124.2, 125.4, 129.2 (129.18), 129.2 (129.23), 1295, 129.8, 130.5, 131.7, 137.4, 142.4, 144.3, 146.6. HRMS (EI) calcd. for $C_{26}H_{22}N_4$ (M^+) 390.1844, found 390.1846.

6,7-Diphenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]-pyrimidine (3l). R_f = 0.47. White solid (95 mg, 77 %); m.p. 278–280 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.85 (d, J = 8.4 Hz, 1H), 6.91–6.94 (m, 1H), 7.11–7.15 (m, 1H), 7.24–7.28 (m, 4H), 7.31–7.37 (m, 4H), 7.51–7.53 (m, 2H), 7.56–7.60 (m, 2H), 7.87 (d, J = 7.7 Hz, 1H), 8.01–8.04 (m, 1H), 8.86–8.90 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 102.2, 106.3, 109.3, 112.7, 114.8, 119.2, 119.4, 121.7, 123.8, 124.0, 125.3, 127.8, 128.7, 129.4, 129.5, 129.8, 129.9, 130.2, 130.4, 131.6, 137.4, 142.1, 144.0, 146.9. HRMS (EI) calcd. for $C_{28}H_{18}N_4$ (M^+) 410.1531, found 410.1534.

Benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline-13-carbonitrile (3m). R_f = 0.31. White solid (50 mg, 50 %); m.p. 314–316 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.57–7.61 (m, 2H), 7.64–7.67 (m, 1H), 7.73 (dd, J = 8.6 and 1.6 Hz, 1H), 7.84–7.88 (m, 1H), 7.98–8.01 (m, 1H), 8.23 (d, J = 1.3 Hz, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.34 (d, J = 8.4 Hz, 1H) 8.73–8.77 (m, 1H), 8.80 (dd, J = 7.9 and 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 107.9, 113.6, 115.0, 115.1, 115.2, 119.1, 120.0, 124.4, 125.0, 125.9, 126.5, 126.6, 127.1, 130.3, 132.4, 133.0, 133.5, 142.7, 143.5, 143.9, 144.3. HRMS (EI) calcd. for $C_{21}H_{11}N_5$ (M^+) 333.1014, found 333.1013.

11,14-Dimethoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo-[1,2-*c*]quinazoline (3n). R_f = 0.51. White solid (85 mg, 77 %); m.p. 221–223 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.99 (s, 3H), 4.01 (s, 3H), 6.71 (d, J = 8.9 Hz, 1H), 6.81 (d, J = 8.9 Hz, 1H), 7.44–7.47 (m, 1H), 7.58–7.59 (m, 1H), 7.67–7.71 (m, 1H), 7.89–7.93 (m, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.55 (dd, J = 7.9 and 1.5 Hz, 1H), 8.58–8.62 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 55.3, 56.4, 111.3, 113.1, 113.6, 118.2, 118.7, 121.7, 122.9, 123.0, 123.9, 125.2, 128.7, 129.0, 130.6, 132.7, 140.3, 141.1, 142.4, 142.9, 143.2, 144.8. HRMS (EI) calcd. for $C_{22}H_{16}N_4O_2$ (M^+) 368.1273, found 368.1272.

7-Fluoro-11,14-dimethoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]-imidazo[1,2-*c*]quinazoline (3o). R_f = 0.55. White solid (81 mg, 70 %); m.p. 289–292 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.90 (s, 3H), 4.01 (s, 3H), 6.51 (d, J = 8.6 Hz, 1H), 6.82 (d, J = 8.6 Hz, 1H), 7.39–7.41 (m, 2H), 7.60 (dd, J = 8.7 and 5.2 Hz, 1H), 7.87–7.89 (m, 1H), 8.00 (d, J = 7.9 Hz, 1H), 8.58 (dd, J = 9.5 and 2.3 Hz, 1H), 8.72–8.74 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 54.8, 55.6, 110.2 (d, J = 23.7 Hz), 113.2, 114.8, 118.1 (d, J = 23.6 Hz), 120.4, 121.6, 123.9 (d, J = 9.7 Hz), 126.4, 127.4, 128.1 (d, J = 8.3 Hz), 129.1, 131.6, 132.9, 136.1, 137.4, 138.7, 141.1, 145.0, 147.1 (d, J = 4.3 Hz), 161.3 (d, J = 246.6 Hz). HRMS (EI) calcd. for $C_{22}H_{15}N_4O_2$ (M^+) 38d6.1179, found 386.1178.

7,11,14-Trimethoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imid-azo[1,2-*c*]quinazoline (3p). R_f = 0.53. White solid (85 mg, 71 %); m.p. 262–264 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.91 (s, 3H), 3.97 (s, 3H), 3.99 (s, 3H), 6.67 (d, J = 8.8 Hz, 1H), 6.78 (d, J = 8.8 Hz, 1H), 7.25 (dd, J = 9.1 and 2.9 Hz, 1H), 7.53–7.55 (m, 1H), 7.87–7.9 (m, 1H), 8.01 (d, J = 7.9 Hz, 1H), 8.06 (d, J = 2.9 Hz, 1H), 8.19 (d, J = 9.1 Hz, 1H), 8.72–8.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 56.3, 57.0, 57.1, 112.2, 115.5, 117.5, 121.9, 123.2, 125.2, 126.6, 127.9, 128.9, 129.1, 129.9, 130.7, 132.8, 137.4, 137.7, 140.6, 142.8, 146.4, 149.4, 160.3. HRMS (EI) calcd. for $C_{23}H_{18}N_4O_3$ (M^+) 398.1379, found 398.1376.

9,12-Dimethoxy-7-(*p*-tolyl)benzo[4,5]imidazo[1,2-*a*]benzo[4,5]-imidazo[1,2-*c*]pyrimidine (3q). R_f = 0.51. White solid (72 mg, 63 %); m.p. 269–273 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.44 (s, 3H), 3.96 (s, 3H), 3.98 (s, 3H), 6.67 (d, J = 8.5 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H), 7.14–7.18 (m, 1H), 7.31–7.34 (m, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.63 (s, 1H), 7.72 (d, J = 7.7 Hz, 1H), 7.76 (d, J = 8.4 Hz, 1H), 8.65–8.68 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.3, 56.4, 57.2, 112.8, 115.4, 116.0, 119.9, 120.4, 121.2, 123.3, 124.5, 124.8, 125.8, 128.7, 130.4, 130.8, 141.8, 142.8, 144.1, 145.0, 156.1, 157.3. HRMS (EI) calcd. for $C_{23}H_{18}N_4O_2$ (M^+) 382.1430, found 382.1433.

12,15-Dimethoxybenzo[f]benzo[4,5]imidazo[1,2-*a*]benzo[4,5]-imidazo[1,2-*c*]quinazoline (3r). R_f = 0.51. White solid (104 mg, 83 %); m.p. 287–290 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.55 (s, 3H), 4.09 (s, 3H), 6.76 (d, J = 8.6 Hz, 1H), 7.07 (d, J = 8.6 Hz, 1H), 7.52–7.57 (m, 2H), 7.75–7.78 (m, 1H), 7.91 (d, J = 7.4 Hz, 1H), 8.00–8.01 (m, 1H), 8.07 (d, J = 9.1 Hz, 1H), 8.16 (d, J = 8.2 Hz, 1H), 8.42 (d, J = 9.1 Hz, 1H), 8.84–8.87 (m, 1H), 10.53 (d, J = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 55.3, 56.1, 112.2, 112.6, 114.0, 117.2, 118.7, 119.0, 121.6, 123.3, 123.4, 124.2, 125.4, 126.6, 127.1, 128.2, 129.1, 129.3, 132.2, 132.7, 140.8, 141.9, 142.9, 143.6, 146.9, 148.5. HRMS (EI) calcd. for $C_{26}H_{18}N_4O_2$ (M^+) 418.1430, found 418.1427.

11,14-Dimethoxy-2,3-dimethylbenzo[4,5]imidazo[1,2-*a*]benzo-[4,5]imidazo[1,2-*c*]quinazoline (3s). R_f = 0.51. White solid (92 mg, 77 %); m.p. 232–234 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.44 (s, 3H), 2.48 (s, 3H), 3.88 (s, 3H), 4.10 (s, 3H), 6.60 (d, J = 8.6 Hz, 1H), 6.91 (d, J = 8.6 Hz, 1H), 7.43–7.46 (m, 1H), 7.60 (s, 1H), 7.65–7.69 (m, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.34 (s, 1H), 8.59 (dd, J = 7.9 and 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 20.5, 20.6, 55.9, 56.6, 114.6, 114.7, 116.8, 119.5, 119.8, 122.7, 124.0, 125.0, 126.2, 128.6, 130.0, 131.3, 132.6, 133.8, 134.3, 141.6, 142.2, 143.6, 144.7, 148.2. HRMS (EI) calcd. for $C_{24}H_{20}N_4O_2$ (M^+) 396.1586, found 396.1583.

11,14-Dimethoxy-6,7,8,9-tetrahydrobenzo[4,5]imidazo[1,2-*a*]-benzo[4,5]imidazo[1,2-*c*]quinazoline (3t). R_f = 0.53. White solid (82 mg, 73 %); m.p. 251–253 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.99–2.03 (m, 2H), 2.11–2.16 (m, 2H), 3.06–3.09 (m, 2H), 3.33–3.35 (m, 2H), 3.77 (s, 3H), 3.99 (s, 3H), 6.82 (d, J = 8.5 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 7.39–7.42 (m, 1H), 7.87–7.89 (m, 1H), 7.92–7.97 (m, 1H), 8.72–8.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.2, 22.4, 23.3, 27.4, 55.4, 56.0, 113.6, 115.1, 117.6, 119.6, 119.9, 122.3, 123.8, 124.4, 125.5, 130.0, 132.2, 138.0, 142.6, 144.4, 146.7, 148.2. HRMS (EI) calcd. for $C_{22}H_{20}N_4O_2$ (M^+) 372.1586, found 372.1583.

9,12-Dimethoxy-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]-imidazo[1,2-*c*]pyrimidine (3u). R_f = 0.51. White solid (75 mg, 63 %); m.p. 284–286 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.66 (s, 3H), 3.97 (s, 3H), 6.64 (d, J = 8.9 Hz, 1H), 6.77 (d, J = 8.5 Hz, 1H), 6.88–6.92 (m, 1H), 7.29–7.32 (m, 1H), 7.47–7.50 (m, 2H), 7.62 (s, 1H), 7.67–7.74 (m, 3H), 7.84–7.86 (m, 1H), 8.83–8.87 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 56.6, 58.4, 113.6, 115.8, 117.3, 120.1, 120.4, 122.6, 124.7, 124.9, 126.2, 130.4, 130.48, 130.50, 131.3, 132.5, 138.3, 143.1, 144.9, 147.9, 153.5, 155.2. HRMS (EI) calcd. for $C_{24}H_{18}N_4O_2$ (M^+) 394.1430, found 394.1427.

9,12-Dimethoxy-6-methyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]-benzo[4,5]imidazo[1,2-*c*]pyrimidine (3v). R_f = 0.53. White solid (75 mg, 61 %); m.p. 226–228 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.38 (s, 3H), 3.91 (s, 3H), 4.10 (s, 3H), 6.35 (d, J = 8.5 Hz, 1H), 6.72 (d, J = 8.5 Hz, 1H), 7.53–7.58 (m, 4H), 7.66–7.73 (m, 3H), 7.97–8.01 (m, 1H), 8.82–8.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.5, 56.5, 57.4, 112.8, 115.0, 119.3, 119.6, 121.8, 123.9, 124.2, 125.4, 129.2, 129.6, 129.7, 129.9, 130.5, 131.8, 134.2, 137.5, 142.3, 144.1, 147.1, 148.3. HRMS (EI) calcd. for $C_{25}H_{20}N_4O_2$ (M^+) 408.1586, found 428.1587.

6-Butyl-9,12-dimethoxy-7-phenylbenzo[4,5]imidazo[1,2-*a*]-benzo[4,5]imidazo[1,2-*c*]pyrimidine (3w). R_f = 0.55. White solid

(91 mg, 67 %); m.p. 198–200 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.94 (t, J = 7.3 Hz, 3H), 1.42–1.49 (m, 2H), 1.70–1076 (m, 2H), 3.14 (t, J = 7.9 Hz, 2H), 3.59 (s, 3H), 3.96 (s, 3H), 6.54 (d, J = 8.5 Hz, 1H), 6.92 (d, J = 8.5 Hz, 1H), 7.41–7.43 (m, 2H), 7.54–7.62 (m, 4H), 7.74 (d, J = 7.8 Hz, 1H), 7.88–7.91 (m, 1H), 8.73–8.77 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.0, 23.1, 26.8, 31.8, 55.6, 56.6, 113.4, 114.2, 118.5, 118.8, 121.0, 123.0, 123.3, 124.5, 128.3, 128.4, 128.7, 129.0, 129.7, 130.8, 132.4, 136.6, 141.5, 143.4, 145.8, 149.6. HRMS (EI) calcd. for $C_{28}H_{26}N_4O_2$ (M^+) 450.2056, found 450.2053.

9,12-Dimethoxy-6,7-diphenylbenzo[4,5]imidazo[1,2-*a*]benzo-[4,5]imidazo[1,2-*c*]pyrimidine (3x). R_f = 0.51. White solid (97 mg, 69 %); m.p. 303–306 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.95 (s, 3H), 3.99 (s, 3H), 6.67 (d, J = 8.9 Hz, 1H), 6.82 (d, J = 8.9 Hz, 1H), 6.88–6.91 (m, 1H), 7.28–7.31 (m, 1H), 7.34–7.41 (m, 6H), 7.53–7.58 (m, 4H), 7.84–7.85 (m, 1H), 8.82–8.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 55.9, 56.9, 113.8, 115.8, 117.7, 119.1, 121.3, 122.4, 123.0, 125.5, 127.8, 128.7, 129.5, 129.9, 130.2, 132.4, 136.0, 136.5, 137.4, 137.9, 143.5, 145.7, 147.2, 149.2, 153.3, 155.3. HRMS (EI) calcd. for $C_{30}H_{22}N_4O_2$ (M^+) 470.1743, found 470.1744.

Benzo[4,5]imidazo[1,2-*a*]indolo[1,2-*c*]quinazoline (5).[4] R_f = 0.43. White solid (53 mg, 58 %); m.p. 235–237 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.13 (s, 1H), 7.30–7.35 (m, 2H), 7.37–7.41 (m, 2H), 7.47–7.51 (m, 2H), 7.74 (d, J = 7.9 Hz, 1H), 7.86 (dd, J = 7.9 and 0.6 Hz, 1H), 8.00–8.02 (m, 1H), 8.17 (d, J = 8.3 Hz, 1H), 9.02 (dd, J = 8.3 and 0.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 98.6, 112.4, 115.1, 115.8, 117.2, 119.5, 120.4, 122.4, 123.4, 123.7, 123.8, 124.7, 125.0, 129.1, 129.5, 130.4, 131.2, 131.7, 133.4, 143.0, 143.4.

1,2-Diphenylbenzo[4,5]imidazo[1,2-*a*]imidazo[1,2-*c*]quinazoline (7). R_f = 0.61. White solid (48 mg, 39 %); m.p. 289–291 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.24–7.32 (m, 3H), 7.36–7.44 (m, 2H), 7.50–7.67 (m, 9H), 7.74–7.78 (m, 1H), 8.20 (d, J = 7.8 Hz, 1H), 8.42 (d, J = 8.4 Hz, 1H), 8.778 (dd, J = 7.9 and 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 112.8, 114.8, 115.2, 120.8, 123.2, 124.0, 125.3, 125.5, 127.5, 128.0, 128.1, 128.3, 128.9, 130.5, 132.1, 132.8, 133.5, 142.1. HRMS (EI) calcd. for $C_{28}H_{18}N_4$ (M^+) 410.1531, found 410.1529.

2,3-Dihydrobenzo[4,5]imidazo[1,2-*c*]imidazo[1,2-*a*]quinazoline (9a). R_f = 0.41. White solid (53 mg, 68 %); m.p. 183–186 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.76–3.81 (m, 2H), 4.55–4.58 (m, 2H), 7.42–7.48 (m, 2H), 7.51–7.54 (m, 1H), 7.67–7.74 (m, 2H), 7.91 (d, J = 7.9 Hz, 1H), 8.44 (d, J = 7.9 Hz, 1H), 8.58 (dd, J = 7.9 and 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 39.2, 42.1, 113.4, 114.7, 115.3, 119.5, 124.2, 124.4, 125.8, 125.9, 132.9, 137.1, 147.6, 156.5, 160.1, 162.1. HRMS (EI) calcd. for $C_{16}H_{12}N_4$ (M^+) 260.1062, found 260.1060.

3,4-Dihydro-2H-benzo[4,5]imidazo[1,2-*c*]pyrimido[1,2-*a*]quinazoline (9b). R_f = 0.41. White solid (58 mg, 71 %); m.p. 189–191 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.58–3.62 (m, 2H), 3.70–3.73 (m, 2H), 4.36–4.39 (m, 2H), 7.42–7.48 (m, 2H), 7.51–7.54 (m, 1H), 7.67–7.75 (m, 2H), 7.91 (d, J = 8.0 Hz, 1H), 8.45 (d, J = 7.9 Hz, 1H), 8.59 (dd, J = 7.9 and 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 36.6, 37.6, 40.6, 114.5, 115.8, 120.1, 124.4, 124.9, 125.8, 126.5, 131.5, 133.3, 137.6, 147.0, 159.8, 161.8, 162.5. HRMS (EI) calcd. for $C_{17}H_{14}N_4$ (M^+) 274.1218, found 274.1215.

2,3,4,5-Tetrahydrobenzo[4,5]imidazo[1,2-*c*][1,3]diazepino-[1,2-*a*]quinazoline (9c). R_f = 0.41. White solid (61 mg, 70 %); m.p. 215–217 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.02–3.07 (m, 2H), 3.15–3.20 (m, 2H), 4.10–4.13 (m, 2H), 4.37–4.39 (m, 2H), 7.44–7.50 (m, 2H), 7.52–7.56 (m, 1H), 7.69–7.76 (m, 2H), 7.93 (d, J = 7.9 Hz, 1H), 8.46 (d, J = 7.9 Hz, 1H), 8.60 (dd, J = 7.9 and 1.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 36.7, 37.6, 39.2, 42.1, 113.4, 114.8, 115.3, 119.5, 124.3, 124.4, 125.8, 125.9, 131.1, 137.1, 143.8, 156.6, 160.1, 162.1. HRMS (EI) calcd. for $C_{18}H_{16}N_4$ (M^+) 288.1375, found 288.1374.

1-(2-(1-Methyl-1*H*-benzo[*d*]imidazol-2-yl)phenyl)-1,3-dihydro-2*H*-benzo[*d*]imidazol-2-one (12). R_f = 0.34. Pale yellow solid (69 mg, 68 %); m.p. 322–324 °C. ^{1}H NMR (500 MHz, [D_6]DMSO) δ = 3.88 (s, 3H), 7.31–7.34 (m, 1H), 7.36–7.39 (m, 2H), 7.41–7.46 (m,1H), 7.48–7.52 (m, 1H), 7.54–7.58 (m, 1H), 7.68–7.69 (m, 1H), 7.76–7.80 (m, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.98 (dd, J = 7.9 and 1.5 Hz, 1H), 8.01–8.05 (m, 1H), 8.08 (d, J = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, [D_6]DMSO) δ = 31.4, 110.7, 112.5, 113.0, 117.6, 118.1, 118.9, 121.1, 122.4, 123.3, 124.6, 125.4, 128.1, 128.4, 130.0, 132.1, 139.7, 140.5, 141.8, 142.6, 152.3. HRMS (EI) calcd. for $C_{21}H_{16}N_4O$ (M^+) 340.1324, found 340.1321.

General Procedure for the Oxidation of 3 to 13. A solution of ceric ammonium nitrate (CAN) (0.439 g, 0.8 mmol) in acetonitrile/H_2O (1.8 mL/0.2 mL) was added dropwise to a stirred ice-bath cooled solution of **3** (0.2 mmol) in acetonitrile/H_2O (1.4 mL/0.6 mL). After stirring for 20 min in an ice bath, the reaction mixture was poured into cold water and then extracted with ethyl acetate (20 mL, 3 times). Evaporation of the combined solvent under reduced pressure and recrystallization from dichloromethane and hexane mixture gave **13**.

Benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline-11,14-dione (13a). Brown solid (58 mg, 85 %); m.p. 253–255 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.62 (d, J = 10.3 Hz, 1H), 6.80 (d, J = 10.3 Hz, 1H), 7.16–7.19 (m, 1H), 7.29–7.32 (m, 1H), 7.52–7.56 (m, 1H), 7.75–7.78 (m, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H), 8.40 (dd, J = 7.9 and 1.4 Hz, 1H), 8.53–8.57 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 115.4, 116.6, 120.0, 120.4, 123.5, 124.0, 124.6, 124.8, 125.7, 126.3, 127.0, 130.7, 131.6, 132.4, 134.5, 142.1, 144.2, 144.9, 176.3, 180.5. IR (KBr): $\tilde{\nu}$ = 666, 753, 790, 834, 1022, 1066, 1106, 1222, 1259, 1346, 1396, 1501, 1528, 1597, 1644 (C=O), 1678 (C=O), 1733, 2851, 2918, 2959 cm^{-1}. HRMS (EI) calcd. for $C_{20}H_{10}N_4O_2$ (M^+) 338.0804, found 338.0802.

7-Fluorobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline-11,14-dione (13b). Brown solid (58 mg, 81 %); m.p. 311–314 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.64 (d, J = 10.3 Hz, 1H), 6.82 (d, J = 10.3 Hz, 1H), 7.45–7.52 (m, 2H), 7.96 (d, J = 7.5 Hz, 1H), 8.12 (d, J = 7.9 Hz, 1H), 8.37–8.40 (m, 1H), 8.45–8.47 (m, 1H), 8.82 (d, J = 7.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 115.4, 115.9 (d, J = 21.4 Hz), 118.1, 119.2 (d, J = 24.9 Hz), 122.2 (d, J = 9.3 Hz), 123.4, 126.4, 127.8 (d, J = 2.6 Hz), 128.7, 130.9 (d, J = 9.0 Hz), 133.1, 133.5, 133.7, 135.1, 139.4, 144.6, 145.6, 148.1 (d, J = 246.6 Hz), 174.5, 182.4. IR (KBr): $\tilde{\nu}$ = 625, 826, 943, 1023, 1241, 1371, 1438, 1559, 1649 (C=O), 1666 (C=O), 1734, 2857, 2933 cm^{-1}. HRMS (EI) calcd. for $C_{20}H_9FN_4O_2$ (M^+) 356.0710, found 356.0709.

7-Methoxybenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]-quinazoline-11,14-dione (13c). Brown solid (57 mg, 78 %); m.p. 290–294 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.04 (s, 3H), 6.58 (d, J = 10.3 Hz, 1H), 6.72 (d, J = 10.3 Hz, 1H), 7.25 (dd, J = 9.1 and 3.0 Hz, 1H), 7.35–7.39 (m, 1H), 7.66–7.70 (m, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.85 (d, J = 3.0 Hz, 1H), 8.18 (d, J = 9.2 Hz, 1H), 8.71 –8.75 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 57.2, 116.3, 116.9, 117.8, 120.8, 121.3, 122.1, 124.2, 125.3, 125.7, 126.6, 129.6, 131.7, 133.3, 136.4, 142.7, 145.0, 145.9, 158.2, 176.7, 181.1. IR (KBr): $\tilde{\nu}$ = 626, 754, 799, 978, 1021, 1090, 1216, 1257, 1358, 1458, 1506, 1605, 1644 (C=O), 1672 (C=O), 1732, 2850, 2921, 2960 cm^{-1}. HRMS (EI) calcd. for $C_{21}H_{12}N_4O_3$ (M^+) 368.0909, found 368.0911.

7-(*p*-Tolyl)benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine-9,12-dione (13d). Brown solid (54 mg, 76 %); m.p. 300–304 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.46 (s, 3H), 6.57 (d, J = 10.3 Hz, 1H), 6.76 (d, J = 10.3 Hz, 1H), 7.20–7.23 (m, 1H), 7.36–7.40 (m, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.65 (s, 1H), 7.68 (d, J = 7.7 Hz, 1H),

7.86 (d, *J* = 8.2 Hz, 1H), 8.70–8.74 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.6, 115.0, 117.6, 119.1, 120.3, 121.1, 122.1, 122.6, 123.4, 125.5, 126.6, 127.0, 127.9, 130.9, 132.6, 133.0, 144.0, 145.0, 147.2, 177.2, 182.8. IR (KBr): $\tilde{\nu}$ = 664, 753, 799, 1024, 1047, 1086, 1214, 1259, 1321, 1390, 1462, 1516, 1574, 1646 (C=O), 1672 (C=O), 1732, 2849, 2919, 2957 cm^{-1}. HRMS (EI) calcd. for $C_{21}H_{12}N_4O_2$ (M^+) 352.0960, found 352.0963.

Benzo[*f*]benzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]quinazoline-12,15-dione (13e). Brown solid (62 mg, 80 %); m.p. 310–312 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.39 (d, *J* = 10.3 Hz, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 7.20–7.24 (m, 1H), 7.27–7.30 (m, 1H), 7.59–7.62 (m, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 7.4 Hz, 1H), 7.82–7.86 (m, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 8.26 (d, *J* = 9.1 Hz, 1H), 8.67–8.71 (m, 1H), 10.37 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 115.3, 117.1, 122.1, 124.8, 126.4, 126.5, 127.3, 128.5, 129.0, 129.8, 130.3, 131.4, 131.8, 132.2, 132.5, 135.3, 135.9, 137.1, 138.5, 143.9, 145.0, 146.1, 174.9, 180.8. IR (KBr): $\tilde{\nu}$ = 669, 753, 792, 837, 943, 1019, 1065, 1108, 1220, 1259, 1343, 1397, 1503, 1529, 1596, 1645 (C=O), 1676 (C=O), 1734, 2851, 2923, 2955 cm^{-1}. HRMS (EI) calcd. for $C_{24}H_{12}N_4O_2$ (M^+) 388.0960, found 388.0962.

2,3-Dimethylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]-quinazoline-11,14-dione (13f). Brown solid (64 mg, 87 %); m.p. 269–272 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.33 (s, 3H), 2.37 (s, 3H), 6.73 (d, *J* = 10.3 Hz, 1H), 6.82 (d, *J* = 10.3 Hz, 1H), 7.32–7.35 (m, 1H), 7.49 (s, 1H), 7.54–7.58 (m, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 8.23 (s, 1H), 8.48 (dd, *J* = 7.9 and 1.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 20.1, 20.5, 115.2, 116.6, 118.4, 120.1, 120.4, 123.3, 124.6, 125.6, 126.8, 129.2, 130.6, 131.9, 134.4, 134.9, 139.0, 142.8, 143.1, 144.2, 173.6, 181.6. IR (KBr): $\tilde{\nu}$ = 650, 773, 807, 831, 874, 954, 1017, 1078, 1218, 1292, 1382, 1512, 1529, 1615, 1648 (C=O), 1678 (C=O), 1734, 2847, 2919, 2955 cm^{-1}. HRMS (EI) calcd. for $C_{22}H_{14}N_4O_2$ (M^+) 366.1117, found 366.1119.

6,7,8,9-Tetrahydrobenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo-[1,2-*c*]quinazoline-11,14-dione (13g). Brown solid (57 mg, 83 %); m.p. 286–290 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.92–1.97 (m, 2H), 2.05–2.10 (m, 2H), 3.01–3.03 (m, 2H), 3.27–3.30 (m, 2H), 6.59 (d, *J* = 10.3 Hz, 1H), 6.84 (d, *J* = 10.3 Hz, 1H), 7.17–7.20 (m, 1H), 7.33–7.37 (m, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 8.67–8.71 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.2, 22.4, 23.4, 27.5, 115.1, 116.4, 119.7, 120.0, 122.3, 123.8, 124.4, 125.6, 130.1, 133.1, 138.0, 142.3, 144.4, 146.7, 178.1, 180.2. IR (KBr): $\tilde{\nu}$ = 628, 660, 756, 818, 915, 967, 1054, 1110, 1212, 1257, 1393, 1490, 1514, 1622 (C=O), 2863, 2938 cm^{-1}. HRMS (EI) calcd. for $C_{20}H_{14}N_4O_2$ (M^+) 342.1117, found 342.1116.

7-Phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]pyrimidine-9,12-dione (13h). Brown solid (58 mg, 79 %); m.p. 317–319 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.62 (d, *J* = 10.3 Hz, 1H), 6.80 (d, *J* = 10.3 Hz, 1H), 6.87–6.90 (m, 1H), 7.27–7.30 (m, 1H), 7.50–7.53 (m, 2H), 7.62 (s, 1H), 7.65–7.72 (m, 3H), 7.83–7.85 (m, 1H), 8.82–8.85 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 113.8, 115.1, 116.4, 118.1, 118.4, 120.6, 122.9, 1242, 127.1, 128.4 (128.39), 128.4 (128.44), 128.5, 128.7, 130.5, 136.3, 142.9, 145.8, 156.7, 172.3, 181.6. IR (KBr): $\tilde{\nu}$ = 634, 695, 758, 777, 846, 1038, 1219, 1352, 1486, 1512, 1602, 1669 (C=O), 1734, 2929, 3041 cm^{-1}. HRMS (EI) calcd. for $C_{22}H_{12}N_4O_2$ (M^+) 364.0960, found 364.0961.

6-Methyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo-[1,2-*c*]pyrimidine-9,12-dione (13i). Brown solid (62 mg, 82 %); m.p. 261–264 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.52 (s, 3H), 6.36 (d, *J* = 10.3 Hz, 1H), 6.83 (d, *J* = 10.3 Hz, 1H), 7.29–7.32 (m, 1H), 7.41–7.47 (m, 3H), 7.54–7.59 (m, 4H), 8.57–8.61 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.1, 115.3, 115.8, 117.8, 119.9, 122.1, 124.4, 125.7, 129.3, 129.9, 130.0 (129.96), 130.0 (129.98), 130.8, 132.0, 134.2, 137.8, 142.5, 144.4, 147.3, 171.1, 181.6. IR (KBr): $\tilde{\nu}$ = 630, 650, 766, 799, 842, 1065, 1082, 1164, 1227, 1272, 1389, 1447, 1495, 1512, 1581, 1631, 1639 (C=O), 1680 (C=O), 2959, 2976 cm^{-1}. HRMS (EI) calcd. for $C_{23}H_{14}N_4O_2$ (M^+) 378.1117, found 378.1114.

6-Butyl-7-phenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo-[1,2-*c*]pyrimidine-9,12-dione (13j). Brown solid (67 mg, 80 %); m.p. 233–235 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.94 (t, *J* = 7.3 Hz, 3H), 1.29–1.37 (m, 2H), 1.70–1.76 (m, 2H). 3.14 (t, *J* = 7.9 Hz, 2H), 6.37 (d, *J* = 10.3 Hz, 1H), 6.76 (d, *J* = 10.3 Hz, 1H), 7.30–7.34 (m, 1H), 7.54–7.60 (m, 4H), 7.66–7.74 (m, 3H), 8.58–8.61 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.2, 21.6, 27.5. 29.9, 115.2, 116.3, 117.2, 119.6, 122.0, 124.0, 124.3, 125.6, 129.7, 130.0 (130.01), 130.0 (130.03), 130.7, 131.8, 132.6, 137.6, 142.6, 144.5, 146.8, 172.4, 180.2. IR (KBr): $\tilde{\nu}$ = 707, 1111, 1205, 1439, 1501, 1661 (C=O), 1720, 2863, 2953 cm^{-1}. HRMS (EI) calcd. for $C_{26}H_{20}N_4O_2$ (M^+) 420.1586, found 420.1586.

6,7-Diphenylbenzo[4,5]imidazo[1,2-*a*]benzo[4,5]imidazo[1,2-*c*]-pyrimidine-9,12-dione (13k). Brown solid (75 mg, 85 %); m.p. 331–334 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.63 (d, *J* = 10.3 Hz, 1H), 6.82 (d, *J* = 10.3 Hz, 1H), 6.89–6.92 (m, 1H), 7.18–7.22 (m, 1H), 7.34–7.41 (m, 6H), 7.43–7.48 (m, 4H), 7.74–7.76 (m, 1H), 8.73–8.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 115.3, 117.7, 118.7, 119.1, 121.3, 122.5, 122.9, 124.7, 127.8, 128.7, 129.5, 129.9, 130.2, 131.8, 133.5, 136.0, 136.5, 137.4, 137.9, 143.5, 145.7, 149.2, 174.8, 181.4. IR (KBr): $\tilde{\nu}$ = 637, 695, 760, 784, 845, 1019, 1103, 1138, 1220, 1255, 1361, 1488, 1516, 1597, 1662 (C=O), 1683 (C=O), 1735, 2865, 2930, 3042 cm^{-1}. HRMS (EI) calcd. for $C_{28}H_{16}N_4O_2$ (M^+) 440.1273, found 440.1274.

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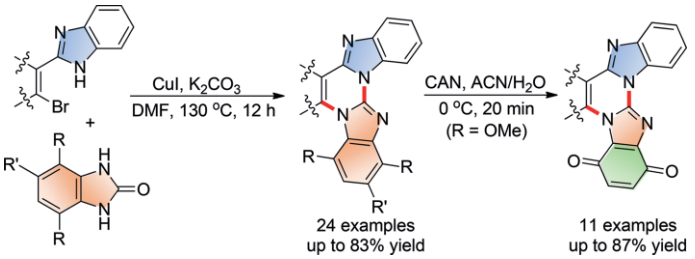

A new synthetic method of trinuclear N-fused hybrid scaffolds has been developed by copper-catalyzed C–N coupling and cycloconedensation of 2-(2-bromoaryl)- and 2-(2-bromovinyl)-benzimidazoles with cyclic ureas as new building blocks. Further studies on the synthesis of polynuclear N-fused hybrid scaffolds using this protocol are expected.

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