Rhodium-Catalyzed Cascade Annulative Coupling of 3,5-Diarylisoxazoles with Alkynes

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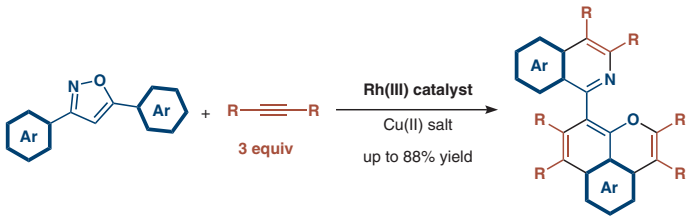

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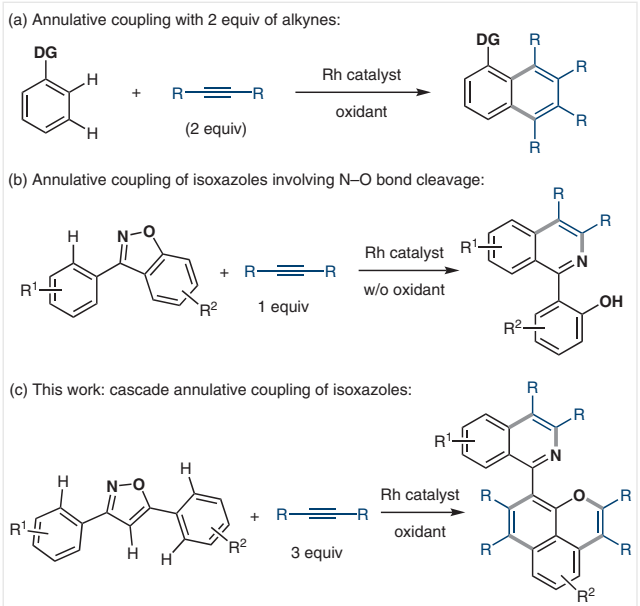
Abstract A rhodium-catalyzed cascade annulative coupling of 3,5-diarylisoxazoles with three equivalents of an alkyne proceeds smoothly in the presence of a Cu(II) oxidant, where the sequential construction of isoquinoline and naphtho[1,8-*bc*]pyran frameworks connected by a biaryl linkage is achieved by a single operation. Most of the obtained polycyclic compounds exhibit visible fluorescence in both the solution and the solid state. The hexaphenylated isoquinoline-naphthopyran conjugate (R = Ph) as a representative product shows a green emission which can be turned off by making an isoquinolinium salt with an acid. The emission is also reversibly turned on by treatment with a base.

Key words C–H activation, annulative coupling, isoquinoline, rhodium catalyst, polyaromatic compounds

Polycyclic aromatic and heteroaromatic compounds have attracted much research interest owing to their substantial and increasing importance as functional organic materials involving light-emitting devices, solar cells, and semiconductors.[1] Accordingly, the development of new synthetic methods for such fused-aromatic systems is in high demand.

Transition-metal-catalyzed direct annulative coupling reactions of directing group substituted aromatic substrates with alkynes have been extensively studied in the last few decades because of their high efficiency and operational simplicity.[2,3] In particular, the reactions of this type are powerful synthetic tools for constructing various benzo-fused heteroaromatic molecules through the annulation accompanied by the incorporation of a heteroatom-containing directing group. Under certain circumstances, alkynes may also be multiply annulated onto the aromatic substrates to lead to higher π-extended carbocyclic systems. For example, the dehydrogenative coupling reactions with two equivalents of alkynes under various catalytic conditions including rhodium catalysis have been utilized as straightforward methods for the synthesis of benzo-fused arenes [Scheme 1 (a)].[2,4,5] These annulative cyclization reactions are potentially useful in exploring novel functional molecules since highly elaborate aromatics can be obtained from readily available starting materials.[6]



Scheme 1 Rh-catalyzed annulative coupling reactions

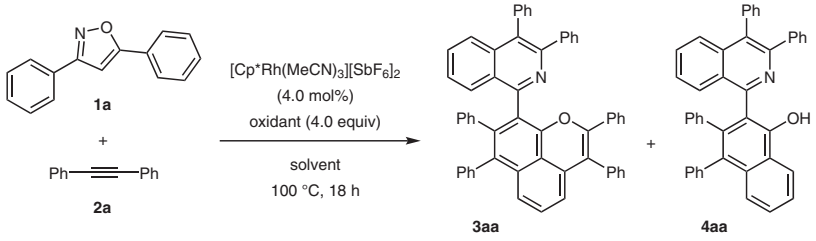
Recently, we have developed the synthesis of 1-substituted isoquinolines[7] through coupling using aryl-substituted isoxazoles as the starting substrates as a new repertoire of the rhodium-catalyzed direct transformation chemistry, where the N–O bond of the ring system acts as the internal oxidant [Scheme 1 (b)].[8] In the course of our continuous in-

vestigation into the annulative coupling with alkynes, we have found that 3,5-diarylisoxazoles can undergo cascade oxidative annulation to give rise to the corresponding isoquinoline-conjugated naphtho[1,8-*bc*]pyran frameworks with the incorporation of three equivalents of alkyne [Scheme 1 (c)]. The naphtho[1,8-*bc*]pyran skeleton is involved in various natural and synthetic compounds,[9] and their synthesis through the catalytic oxidative annulation on 1-naphthols and related substrates has been achieved by our group[3c] and the groups of Ackermann,[10] Wang,[3h,11] and Li.[12] In this publication, the scope of this novel catalytic transformation using the isoxazoles and alkynes as the building blocks and the optical properties of the obtained biaryl-type coupling products are described.

As an initial attempt, we examined the reaction of 3,5-diphenylisoxazole (**1a**) with excess diphenylacetylene (**2a**, 3.6 equiv) in the presence of $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (Cp^* = pentamethylcyclopentadienyl) (4.0 mol%) as catalyst and $Cu(OAc)_2$ (4.0 equiv) as oxidant at 100 °C for 18 hours (Table 1, entry 1), and the corresponding 1:3 coupling product **3aa** was obtained in 66% NMR yield. Acetate salts of Ag(I) and Mn(III) were not suitable as the oxidants for the present reaction (entries 2 and 3). A number of solvents were then tested (entries 4–7) and the highest yield was achieved using 1,4-dioxane (86%, entry 6). Interestingly, reducing the amount of **2a** to 3.1 equivalents resulted in a product yield of 94% (83% after purification) within 9 hours (entry 8). No reaction took place in the absence of any Rh catalyst (entry 9). Throughout the optimization study, a 1:2 coupling product **4aa** was sometimes detected in small quantities (<5% yield). This implies that the annulative coupling on the naphthol moiety of **4aa** is the last step of the catalytic sequence that leads to **3aa** (see discussion below).

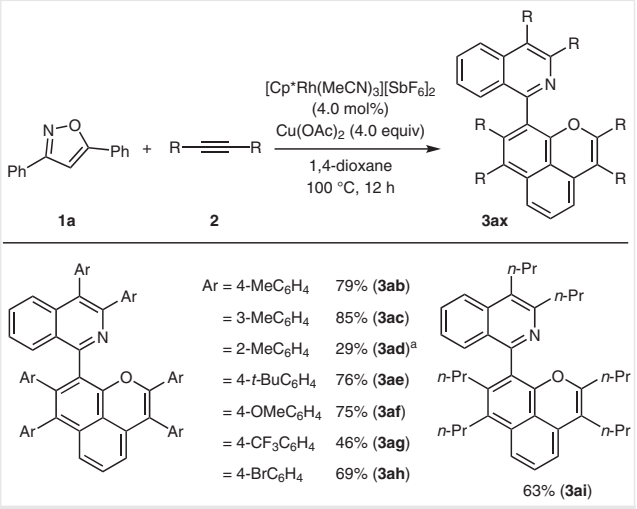
With the reaction conditions of entry 8 in Table 1, we examined the substrate scope of alkynes (Scheme 2). Good to excellent yields were achieved with variously substituted diphenylacetylenes **2** with the exception of **2d** and **2g**. The lower product yields with **2d** and **2g** are probably because of their weaker coordinating properties due to the steric bulkiness and the electron-deficient nature, respectively. Of note is that the C–Br linkage in **2h** remained intact during the reaction. An aliphatic alkyne, oct-4-yne (**2i**) was also applicable to furnish the corresponding product in 63% yield. No productive results were obtained with silyl- or carbonyl-substituted alkynes (not shown).

Table 1 Optimization Studies for the Coupling of **1a** and **2a**[a]



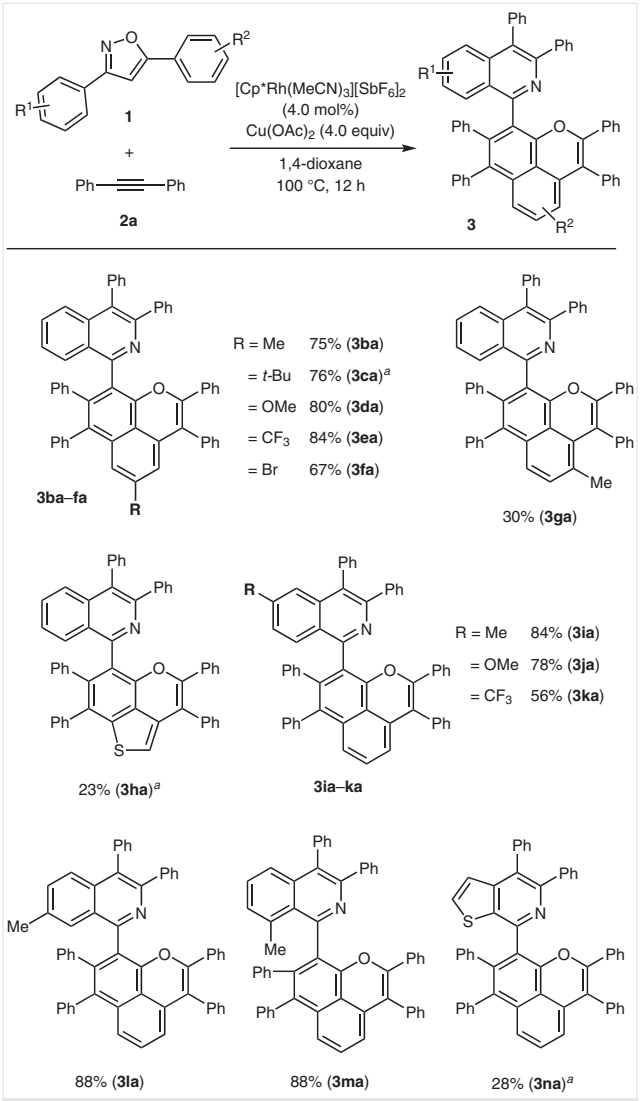
Entry	**2a** (equiv)	Oxidant	Solvent	Yield[b] (%)	
				3aa	**4aa**
1	3.6	$Cu(OAc)_2$	$PhCF_3$	66	n.d.
2	3.6	AgOAc	$PhCF_3$	n.d.	n.d.
3	3.6	$Mn(OAc)_3{\cdot}2H_2O$	$PhCF_3$	8	4
4	3.6	$Cu(OAc)_2$	DCE	62	3
5	3.6	$Cu(OAc)_2$	*o*-xylene	34	5
6	3.6	$Cu(OAc)_2$	1,4-dioxane	86	n.d.
7	3.6	$Cu(OAc)_2$	DMF	n.d.	n.d.
8[c]	3.1	$Cu(OAc)_2$	1,4-dioxane	94 (83)[d]	n.d.
9[e]	3.1	$Cu(OAc)_2$	1,4-dioxane	n.d.	n.d.

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.62 or 0.72 mmol), oxidant (0.8 mmol), $[Cp^*Rh(MeCN)_3][SbF_6]_2$ (4.0 mol%), solvent (4.0 mL).
[b] Determined by NMR analysis; n.d. = not detected.
[c] Reaction time: 9 h.
[d] Isolated yield.
[e] Without the Rh catalyst.

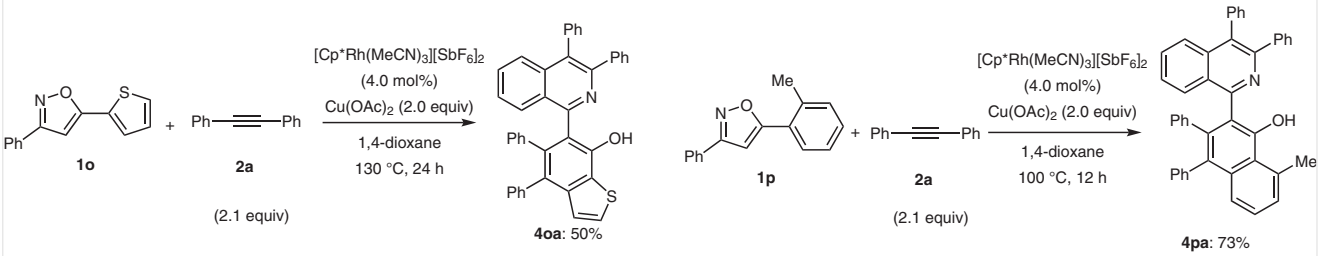


Scheme 2 Substrate scope for alkynes. [a] Reaction at 120 °C.

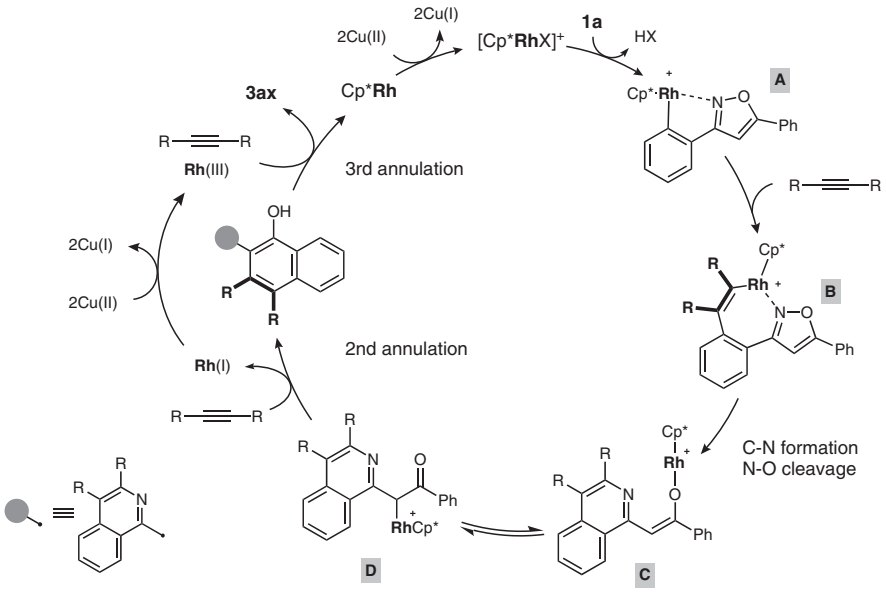
We then carried out the reactions of various 3,5-diarylisoxazoles **1b–n** with diphenylacetylene (**2a**) (Scheme 3). A variety of substituents can be installed onto the naphtho[1,8-*bc*]pyran subunit by using isoxazoles **1b–g** with different substituents on the 5-aryl group. It is noteworthy that the reaction of **1g** resulted in the selective formation of **3ga** in which the methyl group is placed at the C4 position of the ring system. This peculiar regioselectivity seems to be achieved as the second annulation takes place at the sterically more accessible site (see discussion below). Additionally, the catalytic system can be utilized for the construction of a thienochromene framework to give **3ha** as a single isomer albeit with a low yield. The structures of **3ga** and **3ha** were unambiguously determined by X-ray crystallography.[13] Apparently, functionality on the 3-aryl group of the isoxazoles falls into the isoquinoline subunit. Thus, the 1:3 coupling products **3ia–ma** were obtained in high yields with use of isoxazoles **1i–m** having a substituent on the 3-aryl group. No significant drop of the product yield was observed even in the presence of an *ortho*-methyl substituent (**3ma**). A thienopyridine moiety was also constructed albeit with low yield (**3na**). When isoxazoles **1o** and **1p** were employed, the corresponding 1:2 coupling products **4oa** and **4pa** were formed selectively. This is apparently due to the fact that no Csp^2–H bond for the third annulation is available in the products (Scheme 4).



Scheme 3 Substrate scope for isoxazoles. [a] Reaction at 130 °C for 24 h.



Scheme 4 Annulative coupling with two equivalents of alkynes

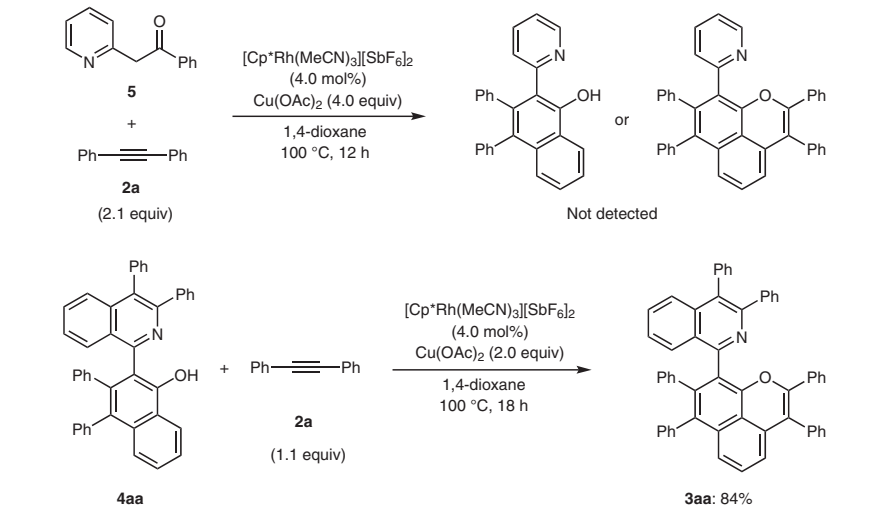


Scheme 5 Proposed reaction mechanism

A proposed catalytic cycle for the reaction of **1a** with **2** is illustrated in Scheme 5. The reaction is initiated by coordination-assisted C–H bond activation to form a five-membered rhodacycle complex **A**. Then, alkyne insertion and subsequent formal S_N-type reaction[8g,14] onto the nearby N–O bond gives a Rh alkoxide species **C**, which is in equilibrium with a carbon-enolate complex **D**. From this stage, oxidative annulation undergoes with incorporating the second alkyne molecule to construct the naphthol moiety.

According to the following control experiment, it is assumed that the catalytic Rh species may be liberated only after the second annulative coupling. We adopted α-(2-pyridyl)acetophenone (**5**), which is structurally analogous to the 1:1 coupling product, to the optimal reaction conditions; however, no C–C bond forming reaction was triggered (Scheme 6, upper). Finally, another oxidative coupling proceeded with the third alkyne molecule to furnish the 1:3 coupling products **3**. This step was confirmed separately by the reaction of **4aa** with **2a** affording the product **3aa** in a high yield (Scheme 6, lower). In total, four C–C bonds, one C–N bond, and one C–O bond are formed in a one-shot manner.

It has been reported that a series of naphtho[1,8-*bc*]pyran derivatives exhibit relatively strong fluorescence even in their solid state.[3c,9c] Consequently, we investigated the optical properties of the present coupling products



Scheme 6 Control experiments

(Figure 1). When excited at 342 nm, **3aa** emitted a green fluorescence with a broad spectral width ranging from 450 nm to 600 nm in chloroform solution [Figure 1 (b)]. No obvious bathochromic shift was observed in the solid state measurement and the quantum efficiency was comparable: 0.15 for the $CHCl_3$ solution and 0.11 for the powder [Figure 1 (d) and Table S1].

Interestingly, **3aa** showed a characteristic spectral change in response to the formation of an isoquinolinium salt. We first prepared a hydrochloric salt of **3aa** (**3aa**·HCl) and measured its spectra. The color changed from light yellow to deep orange with expansion of the absorption edge up to 600 nm [Figure 1 (a) and (c)]. On the other hand, the emission intensity was considerably decreased in the solution and eventually quenched in the solid state [Figure 1 (d)]. This difference between the solution and the solid is due to the fact that the salt can partly dissociate into free **3aa** and HCl in chloroform. Indeed, more obvious spectral change was observed when excess HCl (1.0 mol/L in Et_2O) was added [Figure 1 (a) and (b)] to the solution. The reversibility of this event is realized by the sequential addition of HCl and Et_3N. We also synthesized an N-methylated isoquinolinium salt **3aa**·MeOTf as a reference, and as expected, similar spectra to those of **3aa** in the presence of the excess HCl were obtained in the solution since the dissociation of the CH_3–N bond is not possible in this case.

Substituents on the naphthopyran or isoquinoline motif did not largely affect the luminescence property, and the tested molecules (**3ae**, **3af**, **3ag**, **3ca**, **3da**, **3ea**, and **3ja**) recorded similar fluorescence spectra within 20 nm shift of the peak top. In contrast, the compound **3ai** which is derived from an aliphatic alkyne showed blue-green emission with the peak top at around 470 nm (Figure 2).

Additionally, we looked into the potential axial chirality of the coupling products. As a representative example, compound **3ag** can be separated into a pair of enantiomers in a chiral HPLC analysis (see the Supporting Information). Further studies on their chiroptical properties are underway in our group.

In summary, we have developed a rhodium-catalyzed cascade annulative coupling reaction of 3,5-diarylisoxazoles with alkynes. In this catalytic system, three equivalents of alkynes are consolidated and isoquinoline-conjugated naphtho[1,8-*bc*]pyran frameworks are efficiently constructed by a single manipulation. The starting isoxazole derivatives are readily available and can be stored without any special treatments. The coupling products exhibit fluorescence in both the solution and solid state, and additionally, its turn-off/on is reversibly achievable by treatment with an acid and a base.

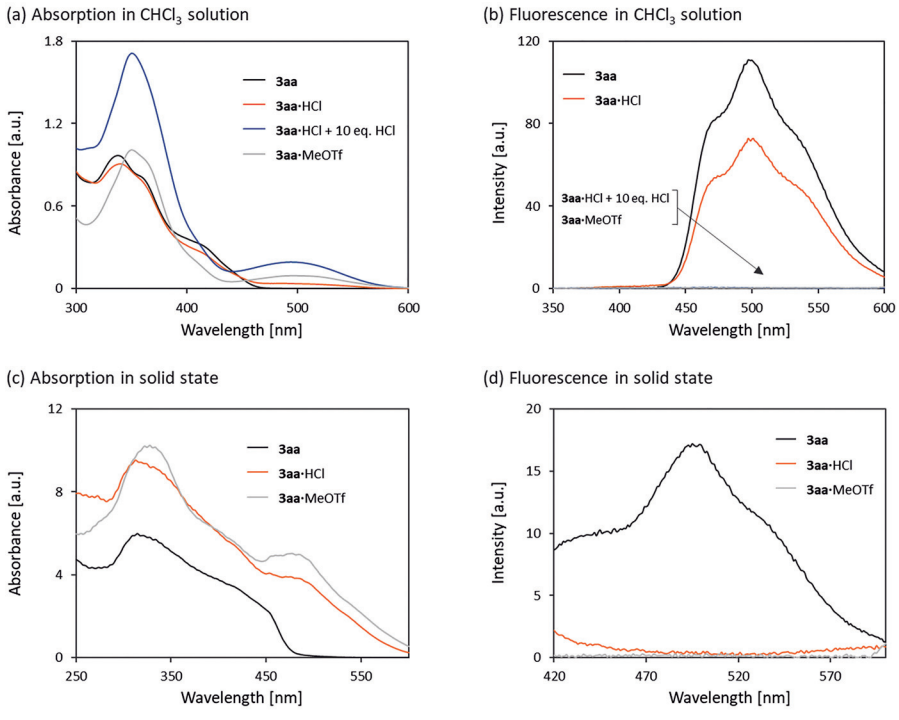


Figure 1 (a) UV-vis absorption and (b) fluorescence spectra of **3aa** (black), **3aa**·HCl (orange), **3aa**·HCl + 10 equiv of HCl (blue), and **3aa**·MeOTf (gray) in $CHCl_3$ solution (5.0×10^{-5} mol/L); the fluorescence spectra of **3aa**·HCl + 10 equiv of HCl and **3aa**·MeOTf overlap close to the baseline. (c) UV-vis absorption and (d) fluorescence spectra of **3aa** (black), **3aa**·HCl (orange), and **3aa**·MeOTf (gray) in solid state.

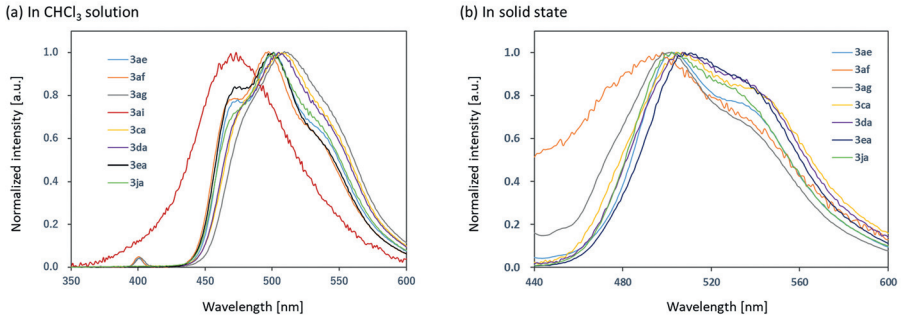


Figure 2 Normalized fluorescence spectra of **3ae** (blue), **3af** (orange), **3ag** (gray), **3ai** (red), **3ca** (yellow), **3da** (purple), **3ea** (navy), and **3ja** (green) at room temperature. (a) Spectra in $CHCl_3$ solution (left, 5.0×10^{-6} mol/L). (b) Spectra in solid state (right).

All manipulations were performed under N_2 using standard Schlenk techniques unless otherwise noted. DMF and 1,4-dioxane were dried and deoxygenated by a Glass Counter Solvent Dispending System (Nikko Hansen & Co., Ltd.). $PhCF_3$, DCE, and *o*-xylene were distilled from CaH_2 and stored with molecular sieves 4Å. CH_2Cl_2 was degassed with N_2 bubbling and dried with molecular sieves 4Å. THF (stabilizer free) was purchased from Wako Pure Chemical Industries as dehydrated solvent and used without purification. Silica gel column chromatography was performed using Wakosil® C-200 (64–210 μm) or Kanto Chemical 60N (40–100μm). 3,5-Diphenylisoxazole (**1a**) was synthesized according to the literature procedure.[15] The other isoxazoles were synthesized by the copper-catalyzed cycloaddition of oxime chlorides with terminal alkynes according to the literature procedure.[16] Alkynes **2b**–**h**,[17] rhodium complexes,[3b,18] and α-(2-pyridyl)-acetophenone (**5**)[19] were synthesized according to the literature. All other reagents were commercially available and used without further purification.

NMR spectra were measured at 400 MHz (^{1}H NMR), at 100 MHz (^{13}C NMR), and at 376 MHz (^{19}F NMR) in 5 mm NMR tubes. ^{1}H NMR chemical shifts were reported relative to the resonance of TMS (δ = 0.00) or the residual solvent signals at δ = 7.26 for $CDCl_3$. ^{13}C NMR chemical shifts were reported relative to the residual solvent signals at δ = 77.2 for $CDCl_3$. Melting points were measured with Mettler Toledo MP90. HRMS were recorded by APCI-TOF. GC analyses were carried out with Shimadzu GC8APF equipped with a silicon OV-17 column (2.6 mm × 1.5 m). GC-MS spectra were recorded on Shimadzu GCMS-QP2010 SE with a CBP-1 column (0.5 mm × 25 m). Preparative gel permeation chromatography (GPC) was conducted with Showa Denko H-2001/H-2002 (eluent: $CHCl_3$) or YMC T2000 (eluent: EtOAc) column. Absorption and fluorescence spectra were recorded on JASCO V-750 and JASCO FP8500 spectrometers. Quantum efficiency was determined using an integration sphere system.

Isoxazole Derivatives 1;[15,16,20] General Procedure

Oxime chloride (1.0 mmol) and terminal alkyne (1.0 mmol) were dissolved in H_2O/*t*-BuOH (1:1, 6.0 mL) under an N_2 atmosphere. To the solution, sodium ascorbate (0.1 mmol, 1.0 mol/L in water), $CuSO_4 \cdot 5H_2O$ (0.02 mmol in 0.10 mL of water), and $NaHCO_3$ (4.33 mmol, 4.33 equiv) were added at r.t. The mixture was stirred overnight and then it was poured into EtOAc; the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Unless otherwise noted, the residue was subjected to column chromatography (silica gel, hexane/EtOAc 9:1), and further purification was conducted by recrystallization (hexane layered over EtOAc solution).

3,5-Diphenylisoxazole (1a)[20d]

White solid; yield: 281 mg (64%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 1 H), 7.43–7.52 (m, 6 H), 7.83–7.89 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.5, 125.9, 126.8, 127.5, 129.0, 129.0, 129.2, 130.1, 130.3, 163.0, 170.4.

3-Phenyl-5-(*p*-tolyl)isoxazole (1b)[20d]

White solid; yield: 98 mg (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 6.78 (s, 1 H), 7.29–7.31 (m, 2 H), 7.45–7.50 (m, 3 H), 7.73–7.75 (m, 2 H), 7.86–7.88 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 96.9, 124.8, 125.8, 126.8, 128.9, 129.3, 129.7, 129.9, 140.5, 162.9, 170.6.

5-(4-*tert*-Butylphenyl)-3-phenylisoxazole (1c)

Purified by column chromatography (hexane/EtOAc 15:1); white solid; yield (2.0-mmol scale): 276 mg (50%); mp 95–97 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 9 H), 6.79 (s, 1 H), 7.46–7.52 (m, 5 H), 7.76–7.79 (m, 2 H), 7.86–7.88 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.2, 34.9, 97.0, 124.8, 125.7, 126.0, 126.8, 128.9, 129.3, 130.0, 153.7, 162.9, 170.6.

HRMS (APCI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{20}NO$: 278.1539; found: 278.1538.

5-(4-Methoxyphenyl)-3-phenylisoxazole (1d)[20e]

White solid; yield: 122 mg (48%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (s, 3 H), 6.71 (s, 1 H), 6.99–7.01 (m, 2 H), 7.45–7.51 (m, 3 H), 7.77–7.80 (m, 2 H), 7.84–7.88 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 96.1, 114.4, 120.4, 126.8, 127.5, 128.9, 129.3, 129.9, 161.2, 163.0, 170.4.

3-Phenyl-5-[4-(trifluoromethyl)phenyl]isoxazole (1e)[20c]

White solid; yield: 130 mg (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94 (s, 1 H), 7.48–7.52 (m, 3 H), 7.76 (d, *J* = 8.2 Hz, 2 H), 7.87–7.89 (m, 2 H), 7.96–7.98 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 98.9, 123.7 (q, *J* = 271.0 Hz), 126.1 (q, *J* = 3.8 Hz), 126.8, 128.8, 128.8, 129.0, 130.3, 130.6, 131.9 (q, *J* = 32.7 Hz), 163.2, 168.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.9.

5-(4-Bromophenyl)-3-phenylisoxazole (1f)[20d]

White solid; yield: 112 mg (37%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 1 H), 7.48–7.49 (m, 3 H), 7.62–7.64 (m, 2 H), 7.70–7.72 (m, 2 H), 7.85–7.87 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.9, 124.6, 126.4, 126.8, 127.3, 128.9, 129.0, 130.1, 132.3, 163.1, 169.3.

3-Phenyl-5-(*m*-tolyl)isoxazole (1g)[20c]

Purified by column chromatography and GPC (EtOAc); white solid; yield: 80 mg (34%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 6.81 (m, 1 H), 7.25–7.27 (m, 1 H), 7.35–7.39 (m, 1 H), 7.45–7.50 (m, 3 H), 7.63–7.66 (m, 2 H), 7.86–7.88 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 97.4, 123.0, 126.4, 126.8, 127.4, 128.9, 129.2, 130.0, 131.0, 138.8, 163.0, 170.6.

3-Phenyl-5-(thiophen-3-yl)isoxazole (1h)

White solid; yield (2.0-mmol scale): 116 mg (25%); mp 120–122 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.69 (s, 1 H), 7.43–7.50 (m, 5 H), 7.83–7.87 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.3, 124.3, 125.4, 126.8, 127.1, 128.9 (2 C), 129.1, 130.0, 162.9, 166.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{10}NOS$: 228.0478; found: 228.0467.

5-Phenyl-3-(*p*-tolyl)isoxazole (1i)[20d]

White solid; yield (3.0-mmol scale): 188 mg (27%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3H), 6.81 (s, 1 H), 7.28–7.30 (m, 2 H), 7.43–7.52 (m, 3 H), 7.75–7.78 (m, 2 H), 7.82–7.85 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 97.4, 125.8, 126.3, 126.7, 127.6, 129.0, 129.6 (2 C), 130.2, 162.9, 170.2.

3-(4-Methoxyphenyl)-5-phenylisoxazole (1j)[20e]

White solid; yield (3.0-mmol scale): 150 mg (20%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87 (s, 3 H), 6.78 (s, 1 H), 6.99–7.01 (m, 2 H), 7.43–7.51 (m, 3 H), 7.79–7.85 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 97.3, 114.3, 121.7, 125.8, 127.6, 128.2, 129.0, 130.2, 161.0, 162.6, 170.2.

5-Phenyl-3-[4-(trifluoromethyl)phenyl]isoxazole (1k)[20f]

White solid; yield: 59 mg (20%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (s, 1 H), 7.48–7.54 (m, 3 H), 7.75 (d, *J* = 8.1 Hz, 2 H), 7.85–7.87 (m, 2 H), 7.99–8.01 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.4, 123.9 (q, *J* = 270.7 Hz), 125.9, 126.0 (q, *J* = 3.7 Hz), 126.0, 127.2, 129.1, 130.5, 131.4 (q, *J* = 32.4 Hz), 132.6, 161.9, 171.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.8.

5-Phenyl-3-(*m*-tolyl)isoxazole (1l)[20b]

Purified by column chromatography and GPC ($CHCl_3$); white solid; yield (3.0-mmol scale): 344 mg (49%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 6.83 (s, 1 H), 7.29–7.30 (m, 1 H), 7.30–7.34 (m, 1 H), 7.45–7.52 (m, 3 H), 7.65–7.67 (m, 1 H), 7.70–7.71 (m, 1 H), 7.84–7.86 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 97.6, 124.0, 125.9, 127.4, 127.5, 128.8, 129.0 (2 C), 130.2, 130.8, 138.7, 163.1, 170.3.

5-Phenyl-3-(*o*-tolyl)isoxazole (1m)[20a]

Purified by column chromatography and GPC (EtOAc); yellow oil; yield (2.5-mmol scale): 258 mg (44%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.53 (s, 3 H), 6.70 (s, 1 H), 7.27–7.38 (m, 3 H), 7.43–7.51 (m, 3 H), 7.55–7.57 (m, 1 H), 7.83–7.86 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 100.2, 125.9, 126.0, 127.5, 128.9, 129.0, 129.5, 129.5, 130.2, 131.1, 136.9, 163.7, 169.6.

5-Phenyl-3-(thiophen-2-yl)isoxazole (1n)[20g]

White solid; yield (3.0-mmol scale): 141 mg (21%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.76 (s, 1 H), 7.13–7.15 (m, 1 H), 7.43–7.53 (m, 5 H), 7.81–7.83 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.5, 125.9, 127.2, 127.4, 127.7, 127.7, 129.0, 130.4, 130.9, 158.2, 170.4.

3-Phenyl-5-(thiophen-2-yl)isoxazole (1o)[20c]

Purified by column chromatography (hexane/EtOAc 10:1); white solid; yield: 97 mg (43%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.69 (s, 1 H), 7.13–7.15 (m, 1 H), 7.45–7.47 (m, 4 H), 7.55–7.56 (m, 1 H), 7.83–7.86 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 97.3, 126.9, 127.1, 128.0, 128.1, 128.7, 128.9, 129.3, 130.1, 163.0, 164.4.

3-Phenyl-5-(*o*-tolyl)isoxazole (1p)[20c]

Purified by column chromatography and GPC ($CHCl_3$); yellow oil; yield: 93 mg (39%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57 (s, 3 H), 6.72 (s, 1 H), 7.30–7.39 (m, 3 H), 7.46–7.51 (m, 3 H), 7.75–7.78 (m, 1 H), 7.87–7.90 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 100.6, 126.3, 126.8, 127.1, 128.6, 128.9, 129.3, 130.0, 130.1, 131.4, 136.3, 162.6, 170.6.

Rh-Catalyzed Annulative Coupling (Scheme 2 and Scheme 3); General Procedure

A glass tube equipped with a magnetic stir bar was charged with isoxazole **1** (0.2 mmol), alkyne **2** (0.62 mmol, 3.1 equiv), $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (0.008 mmol, 4.0 mol%), and $Cu(OAc)_2$ (0.8 mmol, 4.0 equiv). The tube was evacuated and backfilled with N_2 (3 ×) followed by addition of 1,4-dioxane (4.0 mL) via syringe. The resulting mixture was heated at 100 °C for 12 h. After cooling to r.t., the mixture was poured into water and extracted with EtOAc (3 ×). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was subjected to column chromatography (silica gel) to afford the corresponding product. Further purification was performed by GPC if required.

Note: the coupling products **3** exhibit broadened and split peaks in NMR spectra owing to the presence of rotamers, and the following data are reported as appeared in the spectra.

3,4-Diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinoline (3aa)

Purified by column chromatography (hexane/EtOAc 5:1); yellow solid; yield: 125 mg (83%); mp 167–169 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.54 (dd, *J* = 1.0, 7.1 Hz, 1 H), 6.70–6.72 (m, 4 H), 6.80–6.89 (m, 4 H), 6.97–7.03 (m, 2 H), 7.11 (s, 5 H), 7.13–7.33 (m, 12 H), 7.34–7.40 (m, 5 H), 7.48–7.53 (m, 2 H), 7.55–7.58 (m, 1 H), 8.16–8.17 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.4, 117.4, 118.7, 121.9, 123.1, 125.7, 126.4, 126.5, 126.7, 127.1, 127.2, 127.3, 127.4, 127.5, 127.7, 127.8, 127.9, 128.0, 128.0, 128.2, 128.4, 128.5, 129.3, 129.4, 129.7, 130.0, 130.3, 130.9, 131.0, 131.2, 131.4, 131.5, 131.6, 131.8, 132.3, 133.7, 133.9, 135.6, 136.1, 137.5, 139.1, 139.7, 140.7, 141.1, 148.7, 149.7, 149.9, 156.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{57}H_{38}NO$: 752.2948; found: 752.2946.

2-(3,4-Diphenylisoquinolin-1-yl)-3,4-diphenylnaphthalen-1-ol (4aa)

Purified by column chromatography (hexane/EtOAc 10:1) and GPC; yellow solid; crystals suitable for X-ray measurement were obtained by pentane vapor diffusion into the EtOAc solution; mp 258–260 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55–6.70 (m, 3 H), 6.76–6.85 (m, 1 H), 6.90–6.92 (m, 2 H), 7.01–7.02 (m, 1 H), 7.07–7.10 (m, 3 H), 7.15–7.23 (m, 5 H), 7.26–7.47 (m, 8 H), 7.50–7.56 (m, 2 H), 7.78 (d, *J* = 8.1 Hz, 1 H), 8.48–8.50 (m, 1 H), 9.20 (br, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.6, 123.0, 124.8, 125.2, 125.3, 125.5, 126.3, 126.3, 126.4, 126.5, 126.6, 127.1, 127.2, 127.4, 127.5, 127.8, 127.9, 128.5, 130.2, 130.2, 131.1, 131.2, 131.4, 131.7, 132.1, 133.8, 136.5, 137.1, 138.6, 139.4, 139.8, 140.2, 148.8, 150.7, 157.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{43}H_{30}NO$: 576.2322; found: 576.2321.

1-(2,3,7,8-Tetra-*p*-tolylbenzo[*de*]chromen-9-yl)-3,4-di-*p*-tolylisoquinoline (3ab)

Purified by column chromatography (hexane/EtOAc 5:1) and GPC; yellow solid; yield: 132 mg (79%); mp 180–182 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.06 (s, 3 H), 2.15 (s, 3 H), 2.25 (s, 3 H), 2.31 (s, 3 H), 2.39 (s, 6 H), 6.42–6.60 (m, 4 H), 6.61–6.82 (m, 4 H), 6.84–6.96 (m, 2 H), 7.02–7.21 (m, 16 H), 7.43–7.50 (m, 2 H), 7.56 (d, *J* = 7.7 Hz, 1 H), 8.09–8.12 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 21.2, 21.2, 21.3, 21.4, 21.4, 116.0, 116.7, 118.8, 121.7, 122.9, 125.7, 126.2, 127.2, 127.3, 127.6, 127.9, 128.0, 128.1, 128.4, 128.6, 128. 7, 129.0, 129.1, 129.5, 130.0, 130.2, 130.7, 130.8, 131.0, 131.0, 131.2, 131.40, 131.4, 132.7, 132.8, 134.0, 134.8, 134.8, 135.6, 136.3, 136.3, 136.8, 137.2, 137.9, 138.4, 140.6, 148.5, 149.6, 149.8, 157.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{63}H_{50}NO$: 836.3887; found: 836.3884.

1-(2,3,7,8-Tetra-*m*-tolylbenzo[*de*]chromen-9-yl)-3,4-di-*m*-tolylisoquinoline (3ac)

Purified by column chromatography (hexane/EtOAc 10:1); yellow solid; yield: 142 mg (85%); mp 150–152 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66–2.44 (m, 18 H), 6.40–6.76 (m, 8 H), 6.80–7.18 (m, 15 H), 7.20–7.40 (m, 3 H), 7.54–7.59 (m, 3 H), 8.19 (br, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 21.3, 21.4, 21.4, 21.5, 116.2, 117.4, 118.6, 121.7, 123.1, 125.9, 125.9, 126.3, 126.4, 126.9, 127.0, 127.4, 127.6, 127.7, 128.1, 128.2, 128.3, 128.4, 128.6, 128.7, 129.0, 129.1, 129.3, 129.6, 131.1, 131.2, 131.6, 131.7, 132.1, 132.2, 132.3, 132.5, 133.6, 133.9, 135.6, 135.7, 136.1, 136.1, 136.8, 137.2, 137.6, 137.9, 138.8, 138.9, 139.2, 139.6, 140.8, 141.0, 148.4, 149.6, 149.7, 157.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{63}H_{50}NO$: 836.3887; found: 836.3878.

1-(2,3,7,8-Tetra-*o*-tolylbenzo[*de*]chromen-9-yl)-3,4-di-*o*-tolylisoquinoline (3ad)

Purified by column chromatography (hexane/EtOAc 10:1) and GPC; yellow solid; yield: 48 mg (29%); crystals suitable for X-ray measurement are obtained from MeOH solution layered with hexane; mp 187–189 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44–2.42 (m, 18 H), 6.30–6.42 (m, 1 H), 6.57–6.70 (m, 1 H), 6.70–7.16 (m, 15 H), 7.16–7.21 (m, 10 H), 7.35–7.50 (m, 2 H), 7.99–8.12 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 19.2, 19.3, 19.4, 19.4, 19.6, 19.7, 19.7, 19.8, 19.9, 19.9, 20.1, 20.1, 20.2, 20.3, 20.6, 20.6, 20.9, 20.9, 21.3, 115.7, 115.8, 115.9, 117.1, 117.6, 117.8, 118.0, 118.6, 119.1, 119.2, 122.0, 122.1, 122.7, 122.8, 122.9, 123.4, 124.3, 124.5, 124.6, 124.9, 125.2, 125.3, 125.5, 125.8, 125.9, 126.1, 126.2, 126.3, 126.4, 126.8, 126.9, 126.9, 127.0, 127.0, 127.1, 127.4, 127.6, 127.7, 127.8, 127.8, 128.2, 128.3, 128.4, 128.7, 128.8, 129.2, 129.5, 129.5, 129.6, 129.6, 129.7, 129.7, 129.8, 129.9, 130.1, 130.2, 130.4, 130.7, 130.7, 130.9, 131.0, 131.3, 131.5, 131.8, 132.0, 132.1, 132.7, 132.9, 133.0, 133.2, 133.3, 133.5, 133.6, 133.7, 134.2, 134.7, 134.8, 135.6, 135.6, 136.1, 136.2, 136.4, 136.6, 136.7, 136.9, 136.9, 136.9, 137.1, 137.2, 137.3, 137.4, 137.5, 137.6, 137.8, 138.0, 138.1, 138.6, 140.0, 140.4, 140.5, 140.8, 149.7, 150.0, 151.0, 151.2, 151.3, 155.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{63}H_{50}NO$: 836.3887; found: 836.3882.

3,4-Bis(4-*tert*-butylphenyl)-1-[2,3,7,8-tetrakis(4-*tert*-butylphenyl)benzo[*de*]chromen-9-yl]isoquinoline (3ae)

Purified by column chromatography (hexane/EtOAc 20:1) and GPC; yellow solid; yield: 165 mg (76%); mp 205–207 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (s, 9 H), 1.17 (s, 9 H), 1.21 (s, 9 H), 1.27 (s, 9 H), 1.34 (s, 9 H), 1.36 (s, 9 H), 6.50–6.52 (m, 1 H), 6.58 (d, *J* = 8.6 Hz, 2 H), 6.80–6.82 (m, 3 H), 6.95 (d, *J* = 8.5 Hz, 2 H), 7.04–7.07 (m, 3 H), 7.10–7.24 (m, 9 H), 7.28–7.32 (m, 3 H), 7.41 (m, 3 H), 7.46–7.54 (m, 2 H), 7.62–7.64 (m, 1 H), 8.18–8.20 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.1, 31.2, 31.3, 31.4, 31.4, 31.5, 34.1, 34.3, 34.4, 34.6, 34.7, 116.0, 116.8, 118.9, 121.7, 122.9, 123.1, 124.0, 124.1, 124.5, 124.5, 125.8, 126.1, 126.2, 127.4, 127.7, 1278.0, 128.2, 129.0, 129.4, 129.9, 130.4, 130.7, 130.8, 130.9, 131.0, 131.1, 131.1, 131.3, 132.8, 133.8, 134.7, 136.3, 136.3, 137.0, 138.4, 141.0, 148.0, 148.4, 148.9, 149.1, 149.7, 149.8, 149.9, 150.8, 157.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{81}H_{86}NO$: 1088.6704; found: 1088.6674.

3,4-Bis(4-methoxyphenyl)-1-[2,3,7,8-tetrakis(4-methoxyphenyl)benzo[*de*]chromen-9-yl]isoquinoline (3af)

Purified by column chromatography (hexane/EtOAc 2:1) and GPC; yellow solid; yield: 139 mg (75%); mp 187–189 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.57 (d, *J* = 5.8 Hz, 3 H), 3.64 (d, *J* = 5.8 Hz, 3 H), 3.73 (d, *J* = 5.8 Hz, 3 H), 3.78 (d, *J* = 5.8 Hz, 3 H), 3.83–3.84 (m, 6 H), 6.25 (br, 1 H), 6.33–6.37 (m, 2 H), 6.46–6.55 (m, 2 H), 6.55–6.65 (m, 2 H), 6.65–6.72 (m, 2 H), 6.77–6.84 (m, 3 H), 6.84–7.00 (m, 4 H), 7.00–7.20 (m, 9 H), 7.26–7.34 (m, 1 H), 7.42–7.51 (m, 2 H), 7.57–7.60 (m, 1 H), 8.06–8.09 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.0, 55.1, 55.2, 55.3, 112.1, 112.6, 112.9, 113.4, 113.6, 113.8, 114.8, 115.6, 115.8, 118.9, 121.7, 122.6, 125.7, 126.2, 126.4, 127.2, 127.5, 128.1, 128.5, 129.6, 130.0, 130.6, 131.6, 131.7, 132.0, 132.2, 132.3, 132.4, 132.5, 132.6, 132.9, 133.9, 134.2, 136.5, 140.4, 148.5, 149.6, 149.6, 157.0, 157.3, 157.9, 158.4, 158.6, 158.9, 159.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{63}H_{50}NO_7$: 932.3582; found: 932.3563.

1-{2,3,7,8-Tetrakis[4-(trifluoromethyl)phenyl]benzo[*de*]chromen-9-yl}-3,4-bis[4-(trifluoromethyl)phenyl]isoquinoline (3ag)

Purified by column chromatography (hexane/EtOAc 5:1); yellow solid; yield: 107 mg (46%); mp 341–343 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.58–6.60 (m, 1 H), 6.72 (d, *J* = 8.2 Hz, 2 H), 6.78 (d, *J* = 7.8 Hz, 1 H), 6.97–7.04 (m, 4 H), 7.11–7.13 (m, 2 H), 7.18–7.22 (m, 2 H), 7.28–7.42 (m, 6 H), 7.47–7.62 (m, 6 H), 7.67–7.76 (m, 5 H), 8.28–8.30 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 117.6, 118.0, 118.3, 121.9, 122.2, 122.5, 122.7, 123.7, 124.5, 124.6, 124.7, 124.7, 124.9, 125.3, 125.4, 125.8, 125.9, 126.5, 126.8, 127.2, 127.5, 127.9, 128.4, 128.6, 129.0, 129.2, 129.3, 129.6, 129.8, 129.9, 130.2, 130.4, 130.5, 130.6, 130.9, 131.1, 131.4, 131.5, 131.6, 131.7, 132.1, 133.7, 135.6, 136.3, 138.5, 139.6, 140.3, 142.0, 142.9, 143.6, 147.9, 148.7, 149.8, 156.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.54, –62.56, –62.61, –62.65, –62.69, –69.92.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{63}H_{32}F_{18}NO$: 1160.2191; found: 1160.2174.

3,4-Bis(4-bromophenyl)-1-[2,3,7,8-tetrakis(4-bromophenyl)benzo[*de*]chromen-9-yl]isoquinoline (3ah)

Purified by column chromatography (hexane/EtOAc 10:1); yellow solid; yield: 170 mg (69%); mp 203–205 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.42–6.50 (m, 2 H), 6.50–6.56 (m, 2 H), 6.82–6.92 (m, 4 H), 6.96–7.00 (m, 3 H), 7.07–7.08 (m, 3 H), 7.13–7.24 (m, 5 H), 7.27–7.30 (m, 2 H), 7.38–7.41 (m, 1 H), 7.41–7.45 (m, 2 H), 7.51–7.60 (m, 6 H), 8.13 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.9, 116.9, 118.3, 120.4, 121.1, 121.6, 121.7, 121.9, 122.2, 122.8, 123.3, 125.8, 127.2, 127.3, 128.6, 128.8, 129.9, 130.1, 130.4, 130.7, 130.9, 131.2, 131.5, 131.5, 131.7, 132.0, 132.34, 132.7, 132.7, 132.9, 132.9, 133.0, 133.0, 133.3, 133.7, 133.9, 135.7, 135.7, 137.4, 138.2, 139.4, 139.4, 148.0, 148.8, 149.6, 156.7.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{57}H_{32}Br_6NO$: 1225.7529; found: 1225.7500.

3,4-Dipropyl-1-(2,3,7,8-tetrapropylbenzo[*de*]chromen-9-yl)isoquinoline (3ai)

Purified by column chromatography (hexane/EtOAc 40:1); yellow oil; yield: 69 mg (63%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.43 (t, *J* = 7.3 Hz, 3 H), 0.61 (t, *J* = 7.3 Hz, 3 H), 0.76–0.87 (m, 2 H), 0.94 (t, *J* = 7.3 Hz, 3 H), 1.01 (t, *J* = 7.3 Hz, 3 H), 1.08–1.13 (m, 6 H), 1.21–1.27 (m, 1 H), 1.47–1.54 (m, 3 H), 1.65–1.87 (m, 6 H), 1.95 (t, *J* = 7.2 Hz, 2 H), 2.12–2.19 (m, 1 H), 2.28–2.32 (m, 2 H), 2.59–2.66 (m, 1 H), 2.89–2.91 (m, 2 H), 2.92–3.14 (m, 4 H), 6.75 (d, *J* = 7.2 Hz, 1 H), 7.29–7.35 (m, 2 H), 7.49 (d, *J* = 8.7 Hz, 1 H), 7.56–7.65 (m, 2 H), 8.02 (d, *J* = 8.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 14.2, 14.4, 14.7, 14.8, 19.6, 21.2, 23.5, 23.8, 24.3, 24.4, 28.4, 29.8, 30.7, 31.6, 33.2, 37.4, 111.2, 111.6, 118.6, 119.4, 121.5, 123.1, 125.2, 126.7, 127.1, 127.4, 127.6, 128.0, 129.3, 131.5, 133.3, 135.6, 138.4, 148.3, 151.7, 152.4, 156.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{39}H_{50}NO$: 548.3887; found: 548.3867.

1-(5-Methyl-2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)-3,4-diphenylisoquinoline (3ba)

Purified by column chromatography (hexane/EtOAc 3:1); yellow solid; yield: 114 mg (75%); mp 159–161 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 6.39 (s, 1 H), 6.68–6.70 (m, 4 H), 6.79–6.88 (m, 4 H), 6.99–7.02 (m, 3 H), 7.10 (s, 5 H), 7.16–7.21 (m, 4 H), 7.23 (m, 2 H), 7.247.30 (m, 4 H), 7.33–7.42 (m, 5 H), 7.48–7.52 (m, 2 H), 7.55–7.57 (m, 1 H), 8.16–8.18 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.4, 117.3, 117.9, 118.3, 120.2, 122.2, 125.6, 125.7, 126.3, 126.5, 126.7, 127.1, 127.2, 127.4, 127.4, 127.6, 127.7, 127.8, 128.0, 128.4, 128.6, 129.3, 129.3, 129.7, 130.0, 130.3, 130.4, 130.9, 131.1, 131.2, 131.5, 131.6, 131.7, 131.8, 132.2, 133.8, 134.2, 135.7, 136.0, 137.6, 138.2, 139.3, 139.9, 140.8, 141.2, 148.8, 149.7, 149.9, 157.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO$: 766.3104; found: 766.3101.

1-(5-*tert*-Butyl-2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)-3,4-diphenylisoquinoline (3ca)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 122 mg (76%); mp 238–240 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11 (s, 9 H), 6.65–6.71 (m, 5 H), 6.80–6.89 (m, 4 H), 6.99–7.03 (m, 2 H), 7.07–7.12 (m, 5 H), 7.16–7.32 (m, 10 H), 7.32–7.43 (m, 5 H), 7.46–7.53 (m, 2 H), 7.55–7.58 (m, 1 H), 8.15–8.17 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9, 35.1, 115.2, 117.6, 118.0, 118.4, 120.1, 125.6, 125.7, 126.3, 126.4, 126.7, 127.1, 127.2, 127.3, 127.4, 127.6, 127.8, 127.8, 127.9, 128.4, 128.6, 129.2, 129.3, 129.7, 130.1, 130.3, 130.9, 131.1, 131.2, 131.4, 131.6, 131.6, 131.9, 133.9, 135.7, 136.0, 137.6, 139.3, 139.9, 140.7, 141.1, 148.5, 149.6, 149.8, 151.0, 157.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{61}H_{46}NO$: 808.3574; found: 808.3583.

1-(5-Methoxy-2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)-3,4-diphenylisoquinoline (3da)

Purified by column chromatography (hexane/EtOAc 5:1); yellow solid; yield: 126 mg (80%); mp 155–157 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.59 (s, 3 H), 6.23 (d, *J* = 2.2 Hz, 1 H), 6.56 (d, *J* = 2.2 Hz, 1 H), 6.68–6.73 (m, 4 H), 6.80–6.89 (m, 4 H), 6.98–7.05 (m, 3 H), 7.10 (s, 5 H), 7.18–7.23 (m, 6 H), 7.27–7.40 (m, 7 H), 7.46–7.52 (m, 2 H), 7.55–7.56 (m, 1 H), 8.15–8.18 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.9, 101.9, 108.4, 117.0, 117.5, 125.7, 125.7, 126.4, 126.4, 126.7, 127.1, 127.2, 127.4, 127.4, 127.6, 127.7, 127.8, 128.0, 128.0, 128.1, 128.4, 128.6, 129.3, 129.7, 130.0, 130.1, 130.3, 130.8, 131.0, 131.2, 131.3, 131.5, 131.8, 133.6, 134.2, 135.4, 135.6, 136.0, 137.5, 139.4, 139.9, 141.1, 141.3, 149.2, 149.6, 149.8, 157.0, 159.7.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO_2$: 782.3054; found: 782.3045.

3,4-Diphenyl-1-[2,3,7,8-tetraphenyl-5-(trifluoromethyl)benzo[*de*]chromen-9-yl]isoquinoline (3ea)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 138 mg (84%); mp 160–162 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.67–6.71 (m, 5 H), 6.82–6.89 (m, 4 H), 6.98–7.07 (m, 2 H), 7.09–7.13 (m, 5 H), 7.15–7.25 (m, 6 H), 7.27–7.35 (m, 3 H), 7.37–7.44 (m, 5 H), 7.50–7.55 (m, 3 H), 7.57–7.60 (m, 1 H), 8.09–8.12 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.4, 117.0, 120.4, 120.4, 120.9, 122.8, 122.9, 125.5, 125.9, 126.1, 126.7, 126.9, 127.0, 127.1, 127.2, 127.2, 127.4, 127.5, 127.9, 128.2, 128.2, 128.4, 128.5, 128.6, 129.6, 129.6, 129.8, 129.9, 130.0, 130.2, 130.3, 130.7, 130.9, 131.2, 131.2, 131.4, 131.5, 131.6, 132.3, 133.0, 133.2, 134.0, 134.7, 136.1, 137.4, 138.1, 139.1, 141.0, 142.1, 149.5, 149.9, 150.0, 156.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –63.03.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{37}F_3NO$: 820.2822; found: 820.2848.

1-(5-Bromo-2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)-3,4-diphenylisoquinoline (3fa)

Purified by column chromatography (hexane/EtOAc 4:1) and GPC; yellow solid; yield: 110 mg (67%); mp 172–174 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (m, 1 H), 6.68–6.70 (m, 4 H), 6.80–6.89 (m, 4 H), 6.98–7.05 (m, 2 H), 7.10 (s, 5 H), 7.12–7.31 (m, 9 H), 7.32–7.43 (m, 6 H), 7.49–7.53 (m, 2 H), 7.55–7.58 (m, 1 H), 8.10–8.13 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.5, 119.2, 119.3, 120.4, 123.6, 124.9, 125.8, 125.9, 126.6, 126.7, 126.8, 128.0, 128.2, 128.4, 128.6, 129.5, 129.5, 129.6, 129.8, 130.2, 130.5, 130.7, 130.9, 131.1, 131.3, 131.5, 133.3, 134.5, 134.8, 135.0, 136.1, 137.4, 138.4, 139.3, 141.0, 141.9, 149.7, 149.9, 149.9, 156.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{57}H_{37}BrNO$: 832.2037; found: 832.1912.

1-(4-Methyl-2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)-3,4-diphenylisoquinoline (3ga)

Purified by column chromatography (hexane/EtOAc 5:1); yellow solid; yield: 47 mg (30%); crystals suitable for X-ray measurement were obtained from CH_2Cl_2 solution layered with pentane; mp 157–159 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 3 H), 6.65–6.71 (m, 4 H), 6.79–6.86 (m, 4 H), 6.95–7.01 (m, 5 H), 7.05–7.11 (m, 4 H), 7.15–7.41 (m, 14 H), 7.48–7.54 (m, 3 H), 8.15–8.17 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 117.7, 118.7, 123.1, 123.5, 125.6, 125.7, 126.2, 126.3, 126.4, 126.5, 126.6, 127.0, 127.0, 127.2, 127.3, 127.4, 127.6, 127.7, 127.8, 127.9, 128.3, 128.8, 129.2, 129.6, 130.0, 130.3, 130.9, 131.2, 131.5, 131.5, 131.7, 132.0, 132.9, 134.4, 135.9, 137.6, 138.5, 139.3, 139.6, 139.7, 141.1, 149.6, 149.7, 150.2, 157.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO$: 766.3104; found: 766.3120.

3,4-Diphenyl-1-(2,3,6,7-tetraphenylthieno[4,3,2-*de*]chromen-8-yl)isoquinoline (3ha)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 35 mg (23%); crystals suitable for X-ray measurement were obtained from CH_2Cl_2 solution layered with pentane; mp 164–166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.39 (m, 1 H), 6.72 (m, 2 H), 6.86–6.94 (m, 6 H), 6.99–7.11 (m, 7 H), 7.16–7.35 (m, 12 H), 7.39–7.42 (m, 2 H), 7.51–7.55 (m, 2 H), 7.56–7.60 (m, 1 H), 8.17–8.19 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.2, 115.9, 119.7, 125.8, 126.0, 126.5, 126.7, 126.8, 127.0, 127.1, 127.3, 127.3, 127.4, 127.6, 127.8, 128.2, 128.3, 128.4, 128.9, 129.1, 129.6, 129.7, 129.8, 130.1, 130.1, 131.20, 131.5, 133.6, 135.9, 136.0, 137.5, 139.3, 139.5, 140.3, 140.0, 142.1, 148.5, 149.7, 149.9, 155.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{55}H_{36}NOS$: 758.2512; found: 758.2511.

6-Methyl-3,4-diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinoline (3ia)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 129 mg (84%); mp 157–159 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 6.53–6.55 (m, 1 H), 6.70–6.73 (m, 4 H), 6.81–6.88 (m, 4 H), 6.99–7.05 (m, 2 H), 7.07–7.11 (m, 5 H), 7.13–7.32 (m, 12 H), 7.33–7.43 (m, 6 H), 8.04–8.06 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.2, 116.3, 117.4, 118.9, 121.9, 123.1, 124.6, 125.7, 125.8, 126.4, 126.6, 127.0, 127.2, 127.4, 127.4, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.6, 128.8, 129.0, 129.3, 129.4, 130.0, 130.1, 130.3, 130.9, 131.0, 131.1, 131.2, 131.4, 131.6, 131.8, 132.4, 133.7, 133.8, 135.7, 136.3, 137.7, 139.2, 139.7, 140.0, 140.7, 141.3, 148.6, 149.7, 150.1, 156.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO$: 766.3104; found: 766.3104.

6-Methoxy-3,4-diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinoline (3ja)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 122 mg (78%); mp 157–159 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 3 H), 6.52–6.54 (m, 1 H), 6.71–6.85 (m, 6 H), 6.87–6.91 (m, 3 H), 6.97–7.05 (m, 2 H), 7.09–7.16 (m, 8 H), 7.17–7.32 (m, 9 H), 7.34–7.41 (m, 5 H), 8.02–8.04 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 103.9, 116.3, 117.4, 118.8, 121.9, 123.0, 123.2, 125.7, 126.4, 126.5, 126.6, 127.0, 127.2, 127.4, 127.7, 127.8, 127.9, 128.0, 128.0, 128.2, 128.5, 128.6, 128.8, 129.2, 129.4, 129.4, 130.1, 130.2, 130.9, 131.0, 131.2, 131.3, 131.4, 131.6, 131.7, 132.3, 133.7, 133.8, 135.7, 133.7, 133.8, 135.7, 137.8, 138.1, 139.2, 139.7, 140.6, 141.4, 148.6, 149.7, 150.6, 156.1, 160.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO_2$: 782.3054; found: 782.3053.

3,4-Diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)-6-(trifluoromethyl)isoquinoline (3ka)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 83 mg (56%); mp 188–190 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.57–6.58 (m, 1 H), 6.68–6.70 (m, 4 H), 6.83–6.90 (m, 4 H), 7.00–7.02 (m, 2 H), 7.09–7.14 (m, 5 H), 7.16–7.26 (m, 10 H), 7.32–7.44 (m, 6 H), 7.68 (d, *J* = 8.8 Hz, 1 H), 7.89 (s, 1 H), 8.32 (d, *J* = 8.7 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.6, 117.6, 117.9, 121.8, 122.1, 123.2, 123.6, 123.6, 125.2, 125.9, 126.5, 127.1, 127.3, 127.5, 127.7, 127.8, 128.0, 128.0, 128.1, 128.2, 128.4, 128.5, 128.7, 129.0, 129.3, 130.0, 130.2, 130.9, 131.0, 131.1, 131.3, 131.3, 131.3, 131.5, 131.5, 131.8, 132.3, 133.6, 134.1, 135.3, 135.4, 136.3, 138.9, 139.5, 140.5, 148.7, 149.9, 151.4, 157.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.78.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{37}F_3NO$: 820.2822; found: 820.2815.

7-Methyl-3,4-diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinoline (3la)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 135 mg (88%); mp 158–160 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.47 (s, 3 H), 6.55 (d, *J* = 7.1 Hz, 1 H), 6.69–6.76 (m, 4 H), 6.79–6.83 (m, 1 H), 6.84–6.90 (m, 3 H), 6.95–7.04 (m, 3 H), 7.11–7.12 (m, 5 H), 7.14–7.31 (m, 10 H), 7.33–7.41 (m, 6 H), 7.44–7.46 (m, 1 H), 7.88 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 116.3, 117.4, 119.0, 121.9, 123.1, 125.6, 125.7, 126.2, 126.4, 126.5, 126.6, 127.0, 127.3, 127.4, 127.4, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 129.3, 129.4, 130.1, 130.3, 130.9, 131.0, 131.1, 131.2, 131.4, 131.5, 131.6, 131.9, 132.5, 133.8, 133.8, 134.3, 135.7, 136.3, 137.7, 139.2, 139.8, 140.8, 141.3, 148.7, 149.2, 149.8, 156.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO$: 766.3104; found: 766.3102.

8-Methyl-3,4-diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinoline (3ma)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 135 mg (88%); crystals suitable for X-ray measurement were obtained by slow evaporation of hexane solution; mp 157–159 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.59 (s, 3 H), 6.53 (dd, *J* = 1.0, 7.0 Hz, 1 H), 6.67 (s, 1 H), 6.76–6.81 (m, 4 H), 6.86–6.95 (m, 4 H), 7.01–7.06 (m, 2 H), 7.10–7.20 (m, 11 H), 7.22–7.31 (m, 6 H), 7.33–7.38 (m, 5 H), 7.42–7.45 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.8, 116.3, 117.4, 122.0, 123.1, 123.4, 124.7, 125.6, 126.4, 126.7, 127.0, 127.3, 127.4, 127.6, 127.7, 127.7, 127.8, 128.0, 128.1, 128.3, 128.6, 129.0, 129.1, 129.5, 129.7, 129.8, 130.1, 130.9, 131.0, 131.2, 131.4, 131.5, 131.6, 132.4, 133.7, 133.8, 135.5, 135.6, 137.6, 138.1, 139.2, 139.4, 139.8, 141.1, 148.7, 148.8, 148.8, 155.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{58}H_{40}NO$: 766.3104; found: 766.3105.

4,5-Diphenyl-7-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)thieno[2,3-*c*]pyridine (3na)

Purified by column chromatography (hexane/EtOAc 4:1); yellow solid; yield: 43 mg (28%); mp 172–174 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55 (dd, *J* = 1.4, 6.7 Hz, 1 H), 6.76–6.77 (m, 1 H), 6.82–6.84 (m, 1 H), 6.86–6.95 (m, 5 H), 7.00–7.08 (m, 2 H), 7.10–7.20 (m, 11 H), 7.22–7.24 (m, 8 H), 7.33–7.45 (m, 4 H), 7.54 (d, *J* = 5.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.4, 117.5, 118.9, 121.9, 123.1, 123.5, 125.9, 126.4, 126.8, 127.1, 127.3, 127.5, 127.7, 127.9, 127.9, 128.1, 128.2, 128.4, 128.5, 128.7, 129.3, 130.4, 130.6, 131.0, 131.1, 131.4, 131.5, 131.5, 132.5, 133.7, 134.0, 135.6, 136.6, 138.2, 139.1, 139.4, 140.1, 140.6, 145.6, 148.7, 149.8, 150.1, 150.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{55}H_{36}NOS$: 758.2512; found: 758.2511.

6-(3,4-Diphenylisoquinolin-1-yl)-4,5-diphenylbenzo[*b*]thiophen-7-ol (4oa)

Purified by column chromatography (hexane/EtOAc 5:1) and GPC; yellow solid; yield: 54 mg (50%); crystals suitable for X-ray measurement were obtained by slow evaporation of $CHCl_3$ solution; mp 152–154 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.49–6.57 (m, 2 H), 6.66–6.78 (m, 1 H), 6.79–7.10 (m, 8 H), 7.11–7.18 (m, 5 H), 7.29–7.47 (m, 8 H), 7.71 (d, *J* = 8.4 Hz, 1 H), 9.90 (br, 1 H) °C.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 119.5, 124.7, 125.1, 125.5, 126.1, 126.3, 126.5, 126.9, 127.3, 127.3, 127.4, 127.5, 127.78, 128.1, 128.5, 129.3, 130.0, 130.1, 130.3, 130.9, 131.3, 132.3, 136.3, 137.0, 138.3, 139.1, 134.0, 140.0, 141.1, 148.6, 149.3, 157.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{41}H_{28}NOS$: 582.1886; found: 582.1897.

2-(3,4-Diphenylisoquinolin-1-yl)-8-methyl-3,4-diphenylnaphthalen-1-ol (4pa)

Purified by column chromatography (hexane/EtOAc 10:1) and GPC; yellow solid; yield: 86 mg (73%); crystals suitable for X-ray measurement were obtained by hexane vapor diffusion into EtOAc solution; mp 170–172 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.04 (s, 3 H), 6.58–6.65 (m, 2 H), 6.73–6.78 (m, 2 H), 6.84 (d, *J* = 7.7 Hz, 2 H), 7.03–7.10 (m, 2 H), 7.17–7.23 (m, 4 H), 7.24–7.30 (m, 2 H), 7.30–7.42 (m, 8 H), 7.43–7.46 (m, 1 H), 7.48–7.50 (m, 1 H), 7.59–7.61 (m, 1 H), 7.84–7.86 (m, 1 H), 8.76 (br, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.4, 118.8, 124.0, 125.2, 125.3, 125.5, 126.2, 126.3, 126.5, 126., 127.1, 127.3, 127.4, 127.7, 127.9, 128.1, 128.5, 130.2, 130.3, 130.4, 131.2, 131.5, 131.6, 132.3, 135.6, 136.3, 136.7, 137.1, 138.3, 140.0, 140.1, 140.3, 148.8, 153.2, 158.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{44}H_{32}NO$: 590.2478; found: 590.2494.

3,4-Diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinoline Hydrochloride (3aa·HCl)

To a solution of **3aa** (0.1 mmol) in CH_2Cl_2 (1.0 mL) was added HCl solution (1 mol/L in Et_2O, 1.0 mL) at r.t. After stirring for 1 h, volatiles were removed under reduced pressure to give isoquinolinium salt **3aa**·HCl as a red solid; yield: 74 mg (93%); mp 187–189 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.58–6.59 (m, 1 H), 6.67–6.90 (m, 8 H), 7.01–7.08 (m, 3 H), 7.08–7.42 (m, 22 H), 7.61 (br, 3 H), 8.26 (br, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.7, 117.7, 121.8, 123.3, 126.0, 126.5, 126.6, 127.3, 127.5, 127.8, 127.8, 127.9, 128.1, 128.2, 128.5, 128.7, 129.2, 129.4, 129.9, 130.1, 130.6, 130.8, 131.0, 131.1, 131.2, 131.3, 131.8, 132.1, 132.4, 133.7, 134.4, 135.4, 138.9, 139.4, 140.4, 148.8, 150.1.

HRMS (APCI): *m*/*z* [M – Cl]$^+$ calcd for $C_{57}H_{38}NO$: 752.2948; found: 752.2925.

2-Methyl-3,4-diphenyl-1-(2,3,7,8-tetraphenylbenzo[*de*]chromen-9-yl)isoquinolinium Triflate (3aa·MeOTf)

To a solution of **3aa** (0.1 mmol) in CH_2Cl_2 (1.0 mL) was added MeOTf solution (0.10 mmol in 0.5 mL of CH_2Cl_2) at r.t. After stirring for 1 h, volatiles were removed under reduced pressure to give isoquinolinium salt **3aa**·MeOTf as a red solid; yield: 78 mg (85%); mp 181–183 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.98 (s, 3 H), 6.49–6.56 (m, 2 H), 6.71–6.85 (m, 5 H), 6.92–7.10 (m, 6 H), 6.94–7.24 (m, 8 H), 7.28–7.42 (m, 10 H), 7.42–7.54 (m, 2 H), 7.70–7.72 (m, 1 H), 8.10–8.14 (m, 2 H), 8.50–8.52 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.6, 108.3, 118.8, 118.9, 119.3, 121.4, 122.5, 124.1, 127.3, 127.4, 127.7, 127.9, 128.3, 128.37, 128.40, 128.5, 128.8, 129.0, 129.1, 129.2, 129.2, 129.3, 129.3, 129.6, 129.86, 129.91,

130.1, 130.4, 130.5, 130.86, 130.94, 131.1, 131.3, 132.1, 132.3, 132.5, 132.7, 133.4, 134.0, 136.0, 136.8, 137.2, 137.29, 137.4, 137.8, 138.9, 145.3, 150.0, 157.8.

HRMS (APCI): *m*/*z* [M – MeOTf + H]$^+$ calcd for $C_{57}H_{38}NO$: 752.2948; found: 752.2935.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610376.

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