

Review

Recent Advances in Using Transition-Metal-Catalyzed C–H Functionalization to Build Fluorescent Materials

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SUMMARY

Organic fluorescent molecules have broad applications in modern technology, such as in security systems, chemosensors, bioprobes, field-effect transistors, memory devices, organic light-emitting diodes, etc. The transition-metal-catalyzed C–H bond functionalization approach represents a distinct, facile, and atom-efficient tactic for the construction of organic fluorescent molecules, which are often difficult to prepare using typical synthetic methods. In this review, four types of C–H bond functionalization reactions for the preparation of fluorescent materials are discussed: (1) transition-metal-catalyzed C–H/C–X cross-coupling reactions; (2) transition-metal-catalyzed C–H/C–H cross-coupling reactions; (3) transition-metal-catalyzed C–H addition and/or annulation reactions; and (4) transition-metal-catalyzed C–H/C–M or C–H/Het–H bond functionalization. The objective of this review is to characterize the current state of the art in using transition-metal-catalyzed C–H functionalization to build fluorescent molecules as well as their application in electroluminescent materials, mechanofluorochromic materials, labels, sensors for bioimaging, etc.

INTRODUCTION

Fluorescent materials have been significantly impacting and improving the quality of human lives. Organic fluorescent molecules have been attracting much research interest from both scientific and engineering arenas owing to their widespread use in various applications, including organic light-emitting diodes, field-effect transistors, memory devices, security systems, chemosensors, bioprobes, etc.^{1–9} In the last few decades, research studies on organic fluorescent molecules have rapidly grown, and transition-metal-catalyzed C–H functionalization has become one of the most important methods to construct various organic fluorescent molecules.^{10,11}

Molecules with a fluorescent chromophore absorb energy ($h\nu_A$) in the form of electromagnetic radiation and then pass through the internal conversion (IC) from the higher electronic excited state (S_n) to the lowest excited singlet state (S_1). As defined, the radiation transition from the lowest excited singlet state to the electronic ground state (S_0) is called fluorescence (Figure 1).^{1–3} The radiation process is expressed as $S_1 \rightarrow S_0 + h\nu_F$, where h is the Plank constant and ν_F is the frequency of the emitted light. Organic compounds with such light-emitting properties are called organic fluorescent molecules.^{1–3}

Transition-metal-catalyzed C–H functionalization reactions have emerged as a powerful synthetic tactic in the past couple of decades and have generated great interest among scientists in material chemistry research due to their significant

The Bigger Picture

Organic fluorescent materials have demanded significant attention due to their applications in organic light-emitting diodes, memory devices, security systems, chemosensors, bioprobes, etc. In recent years, the use of transition-metal-catalyzed C–H functionalization reactions in building fluorescent materials has demonstrated remarkable progress. Various types of C–H functionalization reactions, including the transition-metal-catalyzed C–H/C–X and C–H/C–H cross-coupling, C–H addition/annulation, and C–H/C–M or C–H/Het–H cross-coupling, to construct various fluorescent frameworks have been developed. Compared with conventional synthetic methods, this approach affords the synthetic chemists several unique privileges: (1) it does not require pre-functionalization of starting materials; (2) it can avoid the use of stoichiometric organometallic reagents; and (3) it can facilitate the design of short and efficient reaction routes and minimize side reactions.

advantages: they can provide more atom and step economic syntheses of complex organic materials than other methods, usually use fewer toxic reagents, and can even enable unprecedented synthetic transformations.^{10–19} This approach represents a unique opportunity to access novel building blocks and manipulate the specific properties of organic fluorescent molecular structures. As a result, a variety of transition-metal-catalyzed C–H functionalization reactions have been developed in recent years to construct novel organic fluorescent molecules.^{10,11}

In this review, we survey the progress achieved in the synthesis of organic fluorescent materials by C–H functionalization reactions. Especially, we will emphasize and discuss using the transition-metal-catalyzed C–H/C–X, C–H/C–H cross-coupling reactions, C–H addition/annulation reactions, and C–H/C–M or C–H/Het–H bond functionalization to build fluorescent molecules (Scheme 1). We will briefly discuss the challenges and proposed mechanisms of these reactions. We will also discuss the organic fluorescent molecules and their use as electroluminescent materials, mechanofluorochromic materials, labels, sensors for bioimaging, etc. We hope to offer the readers a robust understanding of the state of development in the field, prior to focusing on the practical applications of C–H functionalization in the synthesis of organic fluorescent materials.

TRANSITION-METAL-CATALYZED C–H FUNCTIONALIZATION TO BUILD FLUORESCENT MATERIALS

Transition-Metal-Catalyzed C–H/C–X Cross-Coupling Reactions to Build Fluorescent Materials

As one of the powerful methods for carbon-carbon (C–C) bond construction, transition-metal-catalyzed C–H/C–X cross-coupling has been rapidly developing in the past few decades.^{20–24} When compared with conventional cross-coupling reactions, this process does not require pre-functionalized starting materials and can avoid the use of stoichiometric organometallic reagents, allowing it to be more environmentally and economically beneficial.^{20–24} As a result, transition-metal-catalyzed C–H/C–X cross-coupling has been considered as an increasingly viable approach in modern organic chemistry.

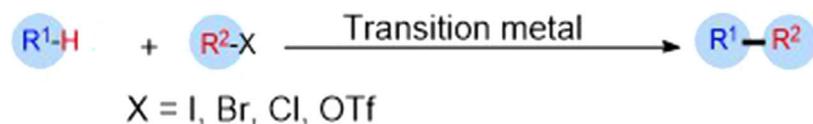
Perylene-3,4,9,10-tetracarboxylic acid bisimides (PBIs) have received widespread attention in academia and industry because of their wide applications, including organic field-effect transistors, light-emitting diodes, solar cells, photovoltaic devices, etc.²⁵ Photophysical properties of PBIs can be conveniently modified by substitution at the *meta* position. In 2009, Wang and co-workers reported the palladium-catalyzed *meta*-selective alkylation of perylene bisimides with cheap and readily available alkyl halides (Scheme 2).²⁶ A variety of alkyl bromides with different lengths of alkyl chains were tolerated under standard conditions with moderate yields. These new compounds exhibited strong fluorescence emissions. The conventional methods for preparing these compounds relies primarily on the Suzuki coupling, which requires additional synthetic steps and the use of poisonous bromine (Scheme 3).²⁶ In comparison, the direct C–H bond functionalization reactions have been considered as economic and environmentally friendly protocols to construct PBIs. In addition, the catalytic cycle was proposed as shown in Scheme 4. Oxidative addition of a Pd(0) complex with an alkyl halide generates alkylpalladium(II) intermediate **5A**. Subsequently, intermediate **5A** undergoes intermolecular ligand exchange to form intermediate **5B**. Then, the C–H bond activation of PBIs and **5B** affords the key transition state **5C**. The alkylpalladium(II) intermediate **5D** is formed through deprotonation of intermediate **5C**. The reductive elimination of intermediate **5D** generates the product and regenerates the palladium (0) catalyst.

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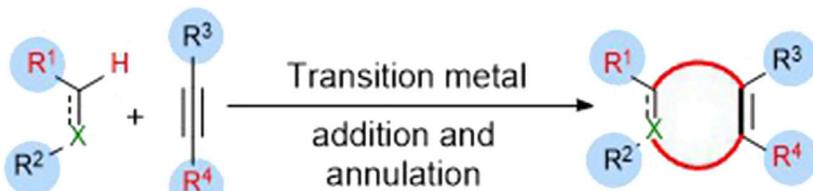
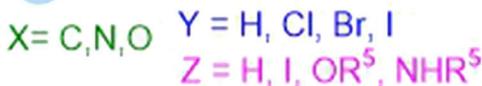
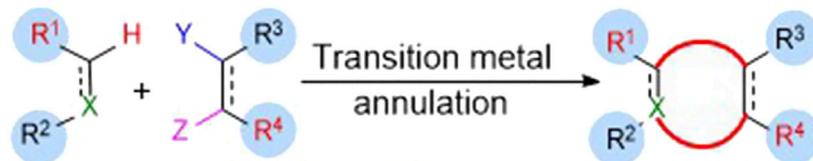
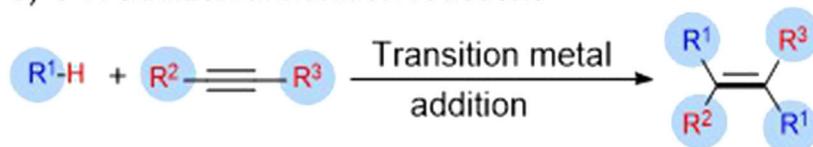
1) C-H/C-X cross-coupling reactions



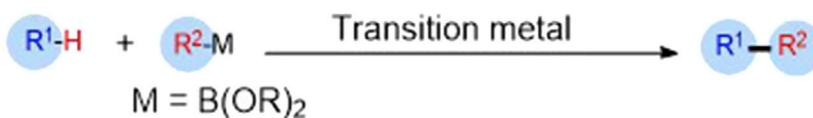
2) C-H/C-H cross-coupling reactions



3) C-H addition/annulation reactions

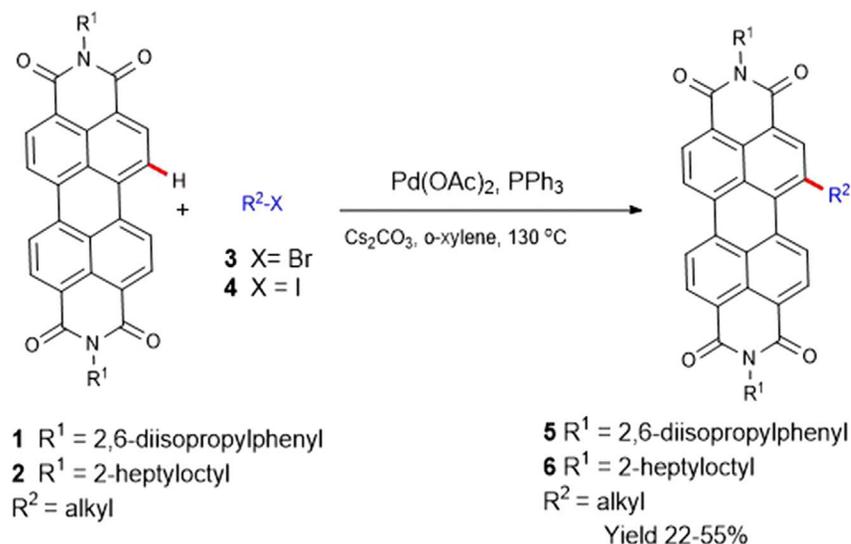


4) C-H/C-M or C-H/Het-H bond functionalizations



Scheme 1. Four Types of C–H Bond Functionalization Reactions to Build Fluorescent Materials

π -Conjugated heteroaryl-aryl motifs have emerged as a fluorescent molecular framework and have attracted considerable interest among materials chemistry research scientists.^{10,11} These structural scaffolds could be synthesized through multi-step condensation reactions, classical transition-metal-catalyzed Ar–X/Ar–M cross-coupling reactions, or the Liebeskind-Srogl coupling reactions (Scheme 5).^{10,11,28} However, molecular diversity was significantly restricted due to the tiresome multi-step synthesis and requirement of pre-functionalization of starting materials. Additionally, some core heteroaryl halides, pseudohalides, and heteroaryl



Scheme 2. Pd-Catalyzed Alkylation of PBIs with Alkyl Halides

organometallic compounds are difficult to obtain and may even be unsuitable to participate in the transition-metal-catalyzed coupling process, which may be a bottleneck for the synthesis and screening of fluorescent heterocyclic materials.¹¹ Thus, transition-metal-catalyzed C–H/C–X cross-coupling reactions would be one of the most ideal strategies to solve these issues. 8-Aryl xanthenes are important biologically active molecules. In 2011, You and co-workers reported the first copper-catalyzed direct C–H/C–X cross-coupling of Xanthine derivatives with non-activated aryl bromides and discovered a new series of organic fluorescent molecules (Scheme 6).²⁷ The authors found that the cross-coupling products, 8-arylsubstituted xanthenes, exhibited significantly strong photonic luminescence. In terms of electronic characteristics, the *N,N*-dimethylanilines section acts as the electron donor (D), and the caffeine unit serves as the electron acceptor (A) to construct donor-acceptor (D-A) π -conjugated fluorescent dyes. Based on this guideline, the authors designed and synthesized a new fluorescent molecule **9b**, which successfully marked Lewis lung cancer cells (LL2) and human embryo kidney 293 cells (HEK 293). Preliminary

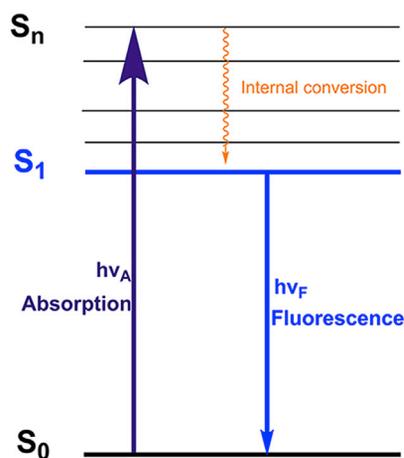


Figure 1. Schemes of Excited-State Relaxation

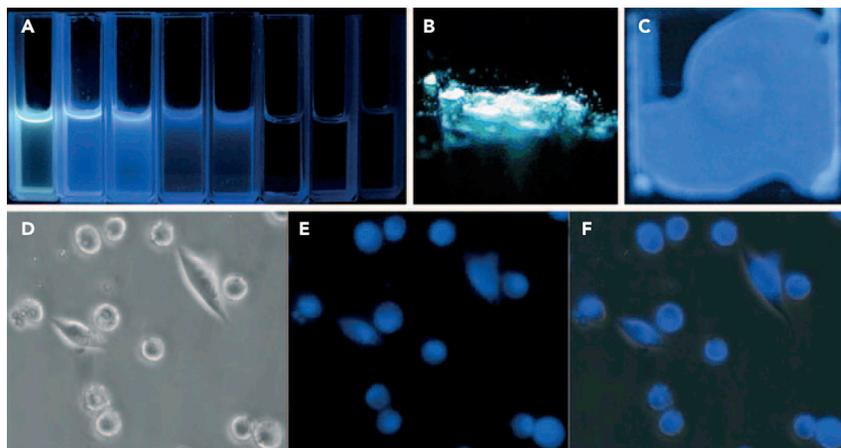
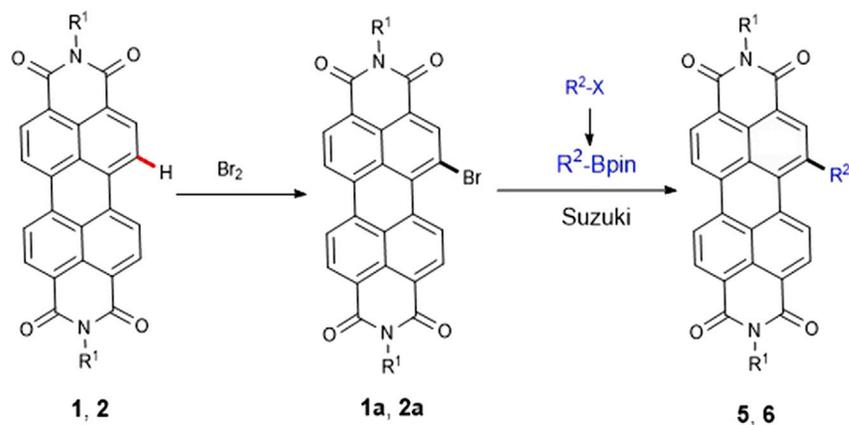


Figure 2. Photophysical Property of 9a–9f

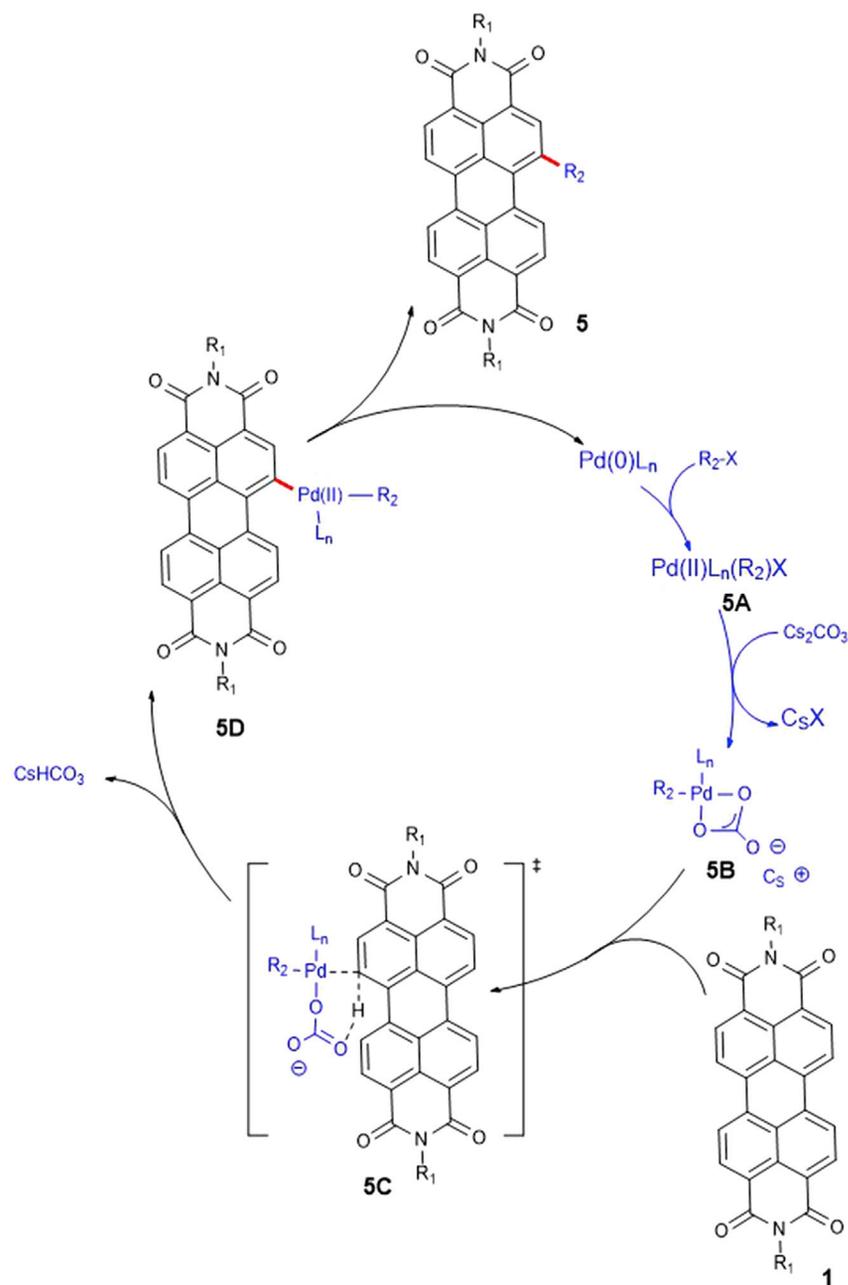
(A) Fluorescence images of **9a–9f**, benzylic theophylline, benzylic theobromine, and caffeine in CHCl_3 .
 (B) Fluorescence image of **9b** (powder).
 (C) Fluorescence image of **9b** (thin film).
 (D) Bright-field transmission image of LL2 cells incubated with **9b**.
 (E) Fluorescence image of LL2 cells incubated with **9b**.
 (F) Overlay of the fluorescence and bright-field transmission images of LL2 cells incubated with **9b**.
 Reprinted with permission from You et al.²⁷ Copyright 2009 Wiley-VCH Verlag GmbH & Co. KGaA.

test results showed that this new fluorescent molecule is a potentially effective reagent for biological imaging (Scheme 6; Figure 2).

In 2012, Lan and co-workers reported full-color-tunable fluorescence libraries through palladium-catalyzed direct C–H bond (hetero)arylation of *N*-heteroarenes with aryl chlorides (Scheme 7).²⁹ This protocol avoids the traditional Suzuki coupling which requires additional synthetic steps to prepare iodo heterocycles and arylboronic acids (Scheme 8).²⁹ A set of *N*-heteroarenes such as caffeine, theophylline, theobromine purines, imidazoles, thiazoles, oxazoles, 1,2,3-triazoles, and *N*-heteroarene *N*-oxides were converted to the corresponding heteroaryl-aryl motifs under the standard conditions. These coupling products displayed a full coverage of solid-state emission wavelengths from red emission to blue emission (405–616 nm). Furthermore, the direct use of coupling products methyl 3-(4-formylphenyl)indolizine-2-carboxylate and methyl

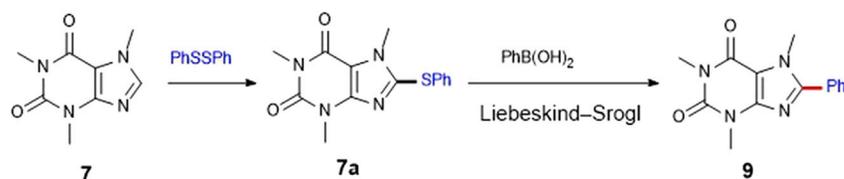


Scheme 3. The Conventional Synthetic Method for 5–6

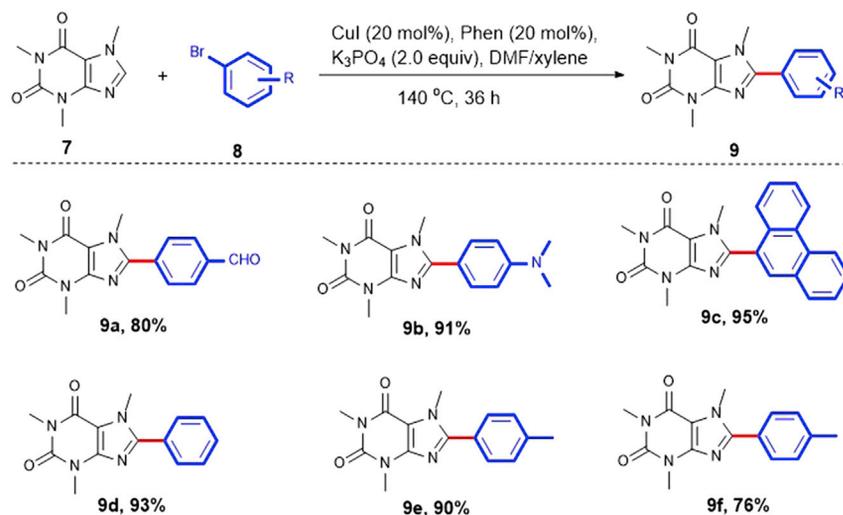


Scheme 4. The Plausible Reaction Mechanism for the Formation of **5**

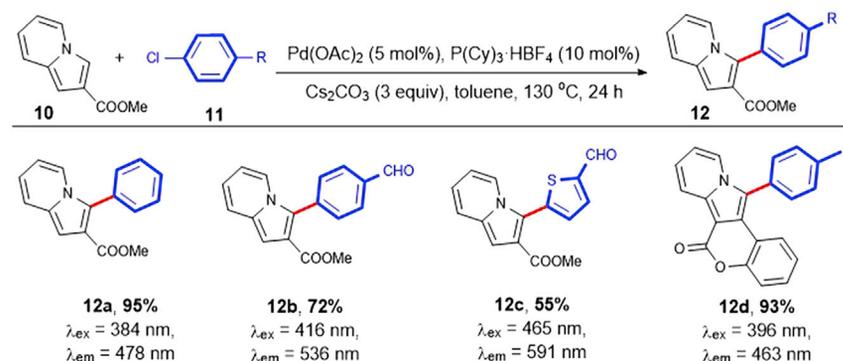
3-(5-formylthiophen-2-yl)indolizine-2-carboxylate as starting materials to react with malononitrile generated useful bioimaging fluorescence probes **14a** and **14b** (Scheme 9; Figure 3), which have successfully marked A375 cells (Figure 3).



Scheme 5. The Conventional Synthetic Method for **9**

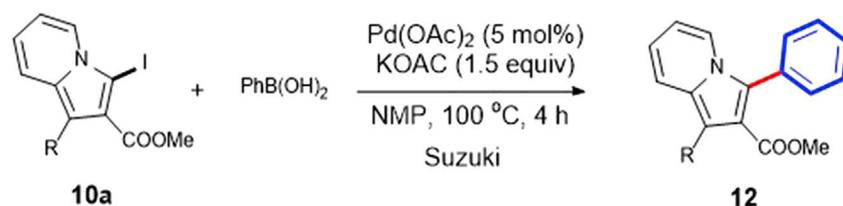


Scheme 6. Copper-Catalyzed Direct C–H/C–Br Cross-Coupling Xanthine with Aryl Bromides

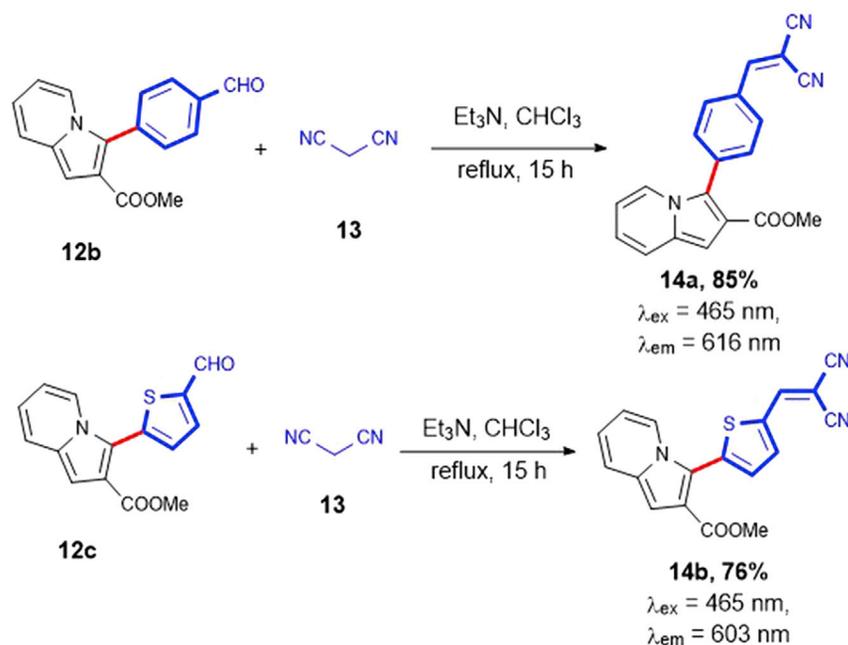


Scheme 7. Palladium-Catalyzed Direct C–H Bond (Hetero)Arylation of N-Heteroarenes with Aryl Chlorides

4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY)-based π -conjugated molecules are important fluorescent materials, which are being applied extensively in material science such as fluorescent imaging agents, sensors, and organic optoelectronic materials.³⁰ The development of efficient and concise methods to obtain BODIPY-based π -conjugated functional molecules is of great research interest in academia and industry. The traditional syntheses of functional BODIPY-based π -conjugated functional materials mainly use the Suzuki or Stille coupling, which needs additional steps or the use of toxic or environmentally harmful chemicals (Scheme 10).³¹ In 2015, Yu and co-workers demonstrated the Pd-catalyzed direct C–H



Scheme 8. The Conventional Synthetic Method for 12



Scheme 9. The Synthesis of Fluorescent Materials **14a** and **14b**

arylation method for the efficient syntheses of BODIPY-based π -conjugated functional molecules (Schemes 11 and 12).³¹ This method provided an efficient strategy for the construction of BODIPY-based π -conjugated molecules in moderate to good yields (47%–72%). The coupling products displayed strong fluorescence emission, which have potential applications in fluorescence bioimaging and organic light-emitting devices (Figure 4).

In 2015, Lan and co-workers disclosed a Cu-catalyzed direct C–H (hetero)arylation of [1,2,4]triazolo[4,3-a]pyridine for screening blue-emitting materials.³² The reaction used PPh_3 as the ligand and CuI as the catalyst (Scheme 13). Products 3-aryl-[1,2,4]triazolo[4,3-a]pyridines displayed bright deep-blue emissions with moderate to high quantum yields in the polystyrene (PS) film (5 wt %), high photostability, and good thermal stability. The conventional methods for synthesizing these compounds generally involve an annulation reaction using 2-pyridylhydrazones or acylated 2-hydrazinopyridines as synthetic precursors.³² These methods

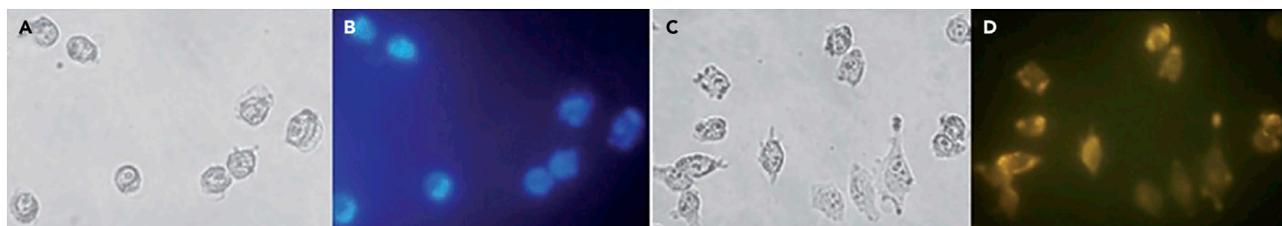


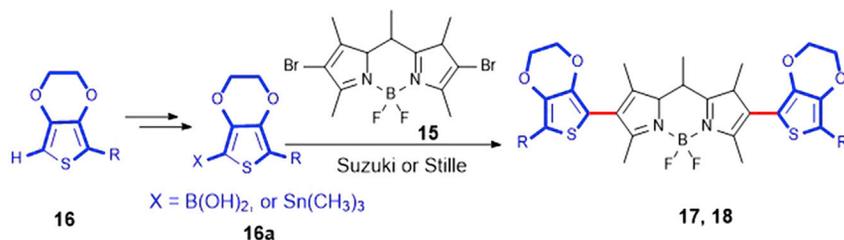
Figure 3. Bioimaging Fluorescence Probes Marked A375 Cells

(A) The bright-field transmission image of A375 cells incubated with **12b**.

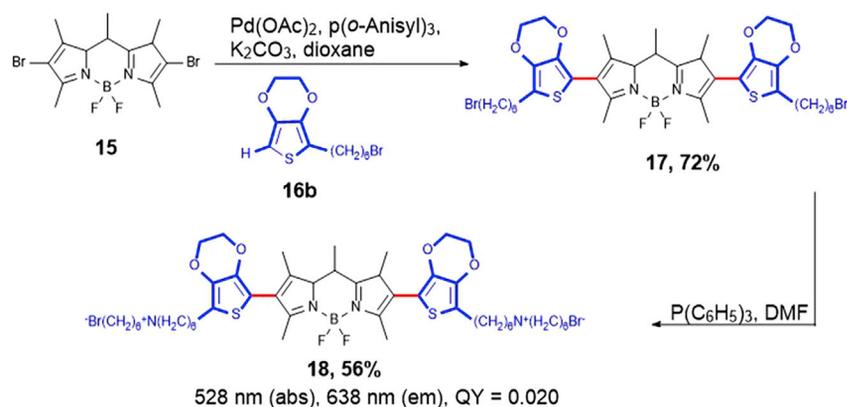
(B) Fluorescence image of A375 cells incubated with **12b**.

(C) The bright-field transmission image of A375 cells incubated with **14b**.

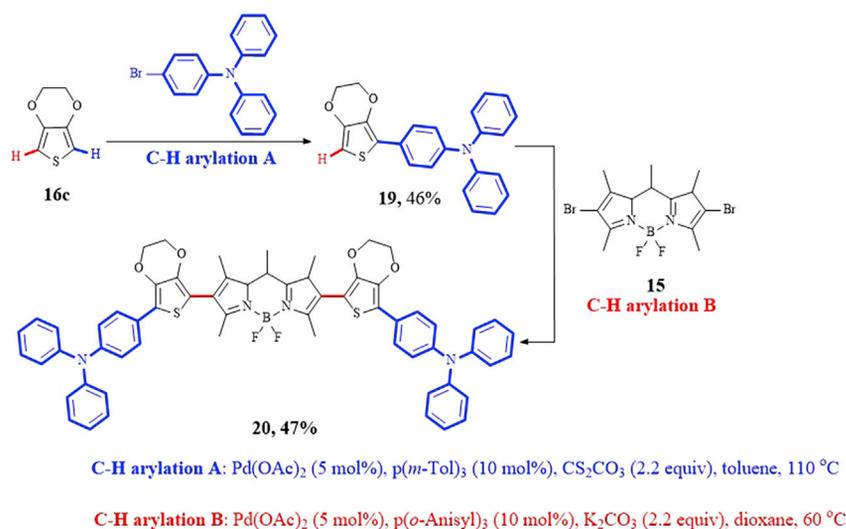
(D) The fluorescence image of A375 cells incubated with **14b**. Adapted from Liu et al.²⁹ with permission, copyright 2012 Wiley-VCH Verlag GmbH & Co. KGaA.



Scheme 10. The Conventional Synthetic Method for **17** and **18**



Scheme 11. Synthesis of the Bio-Imaging probe **18**



Scheme 12. Synthesis of BODIPY-Based π -Conjugated Functional Molecule **20** through Sequential C–H Arylations

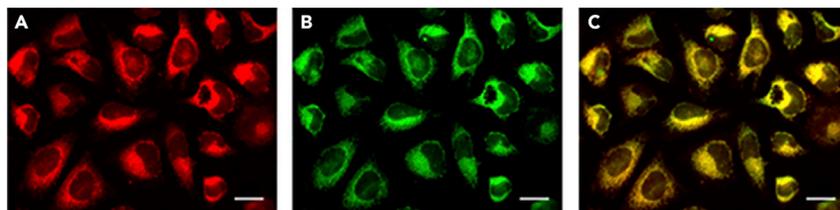


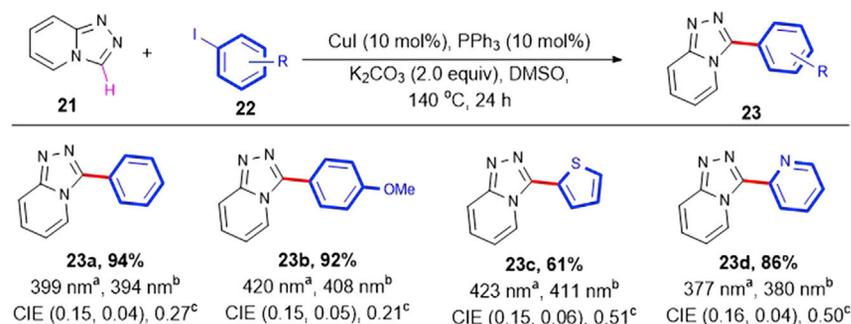
Figure 4. The Fluorescence Bioimaging of Probe 18

(A and B) Fluorescence images of HeLa cells stained with (A) the bioimaging probe 18 and (B) MitoTracker Green FM (MT).

(C) Merged view of the images in (A) and (B). Reprinted with permission from Chong et al.³¹ Copyright 2015 American Chemical Society.

suffer from often highly toxic or carcinogenic hydrazine reagents or harsh reaction conditions. Additionally, tedious multi-step procedures are required for preparation of precursors (Scheme 14).

Piezochromic luminescent molecular materials have gained great interest from both industry and academia. They are considered as “smart” stimuli-responsive materials, which have shown great potential for various applications, including rewritable optical media, security systems, optical displays, chemosensors, etc.^{33,34} Organic piezochromic luminescent materials have the following common characteristics: the molecular packing modes can be changed by external stimulus, leading to mechanochromic luminescent behavior. The mechanochromic properties of organic fluorescent materials mainly depend on molecular packing, which is associated with intermolecular interactions such as dipole-dipole interactions, π - π , and hydrogen bonds. The highly twisted conformation most likely results in weak intermolecular interactions and relatively loose molecular packing, which is susceptible to external stimuli, inducing a mechanofluorochromic response. In 2016, Lan and co-workers reported a programmed C–H/C–X reaction to synthesize 2,7-diaryl-[1,2,4]triazolo [1,5-a]pyrimidines (2,7-diaryl-TAPs), which opens up a new avenue to rapidly access a library of D-A-type luminogens for the discovery of novel mechanochromic materials (Scheme 15; Figure 5).³⁵ In this work, different substituents (2,7-diaryl-TAPs) were synthesized in moderate to excellent yields by using the programmed C3-H arylation, Dimroth rearrangement, and copper-catalyzed C7-H arylation (Scheme 15). Photophysical investigation showed that 2,7-diaryl-TAPs with an electron-withdrawing group on the 2-aryl and an electron-donating group on the 7-aryl possessed a relatively large dipole moment and displayed remarkable blue shift of emission by

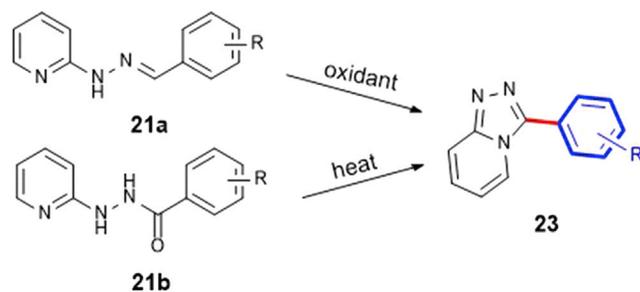


Scheme 13. Cu-Catalyzed Direct C–H (Hetero)arylation of [1,2,4]Triazolo[4,3-a]Pyridine

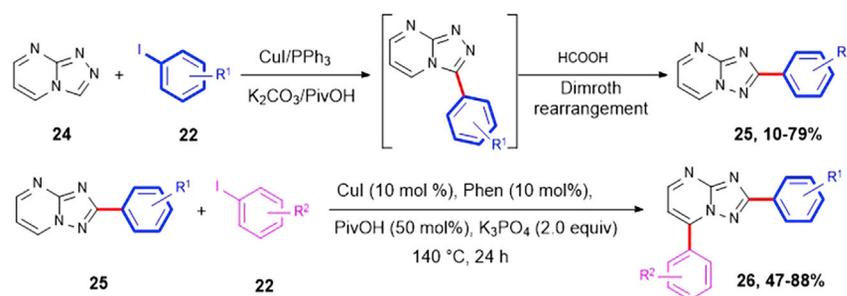
^aEmission maximum in CH_2Cl_2 (10 μM).

^bEmission maximum in the PS film (5 wt %).

^cCIE₁₉₃₁ coordinate and absolute quantum yield in the PS film (5 wt %).



Scheme 14. The Conventional Synthetic Method for 23



Scheme 15. Synthesis of 2,7-Diaryl-TAPs by a Programmed C–H/C–X Reaction

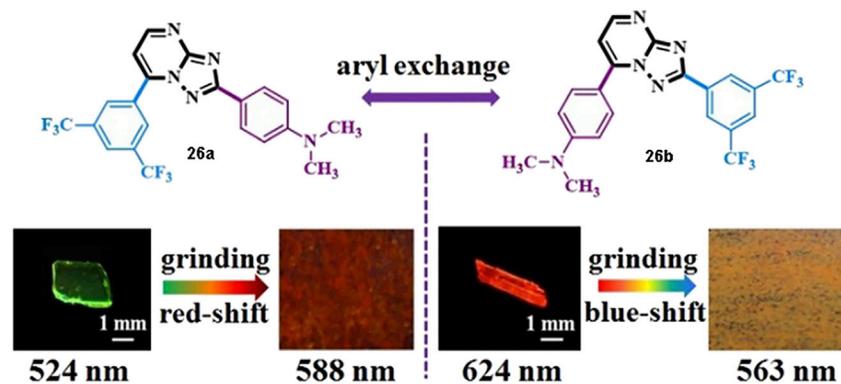
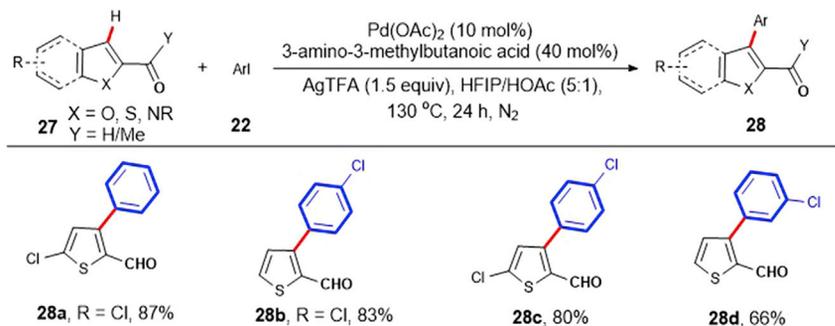


Figure 5. Photographs of Single Crystals and Ground Samples of 26a and 26b under UV Light (365 nm)

Adapted from Wu et al.³⁵ with permission, copyright 2016 American Chemical Society.



Scheme 16. Synthesis of 3-aryl-(2-Aldehyde)Thiophenes 28a–28d

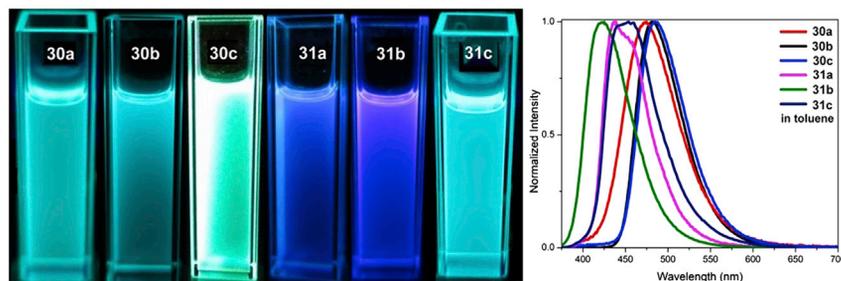


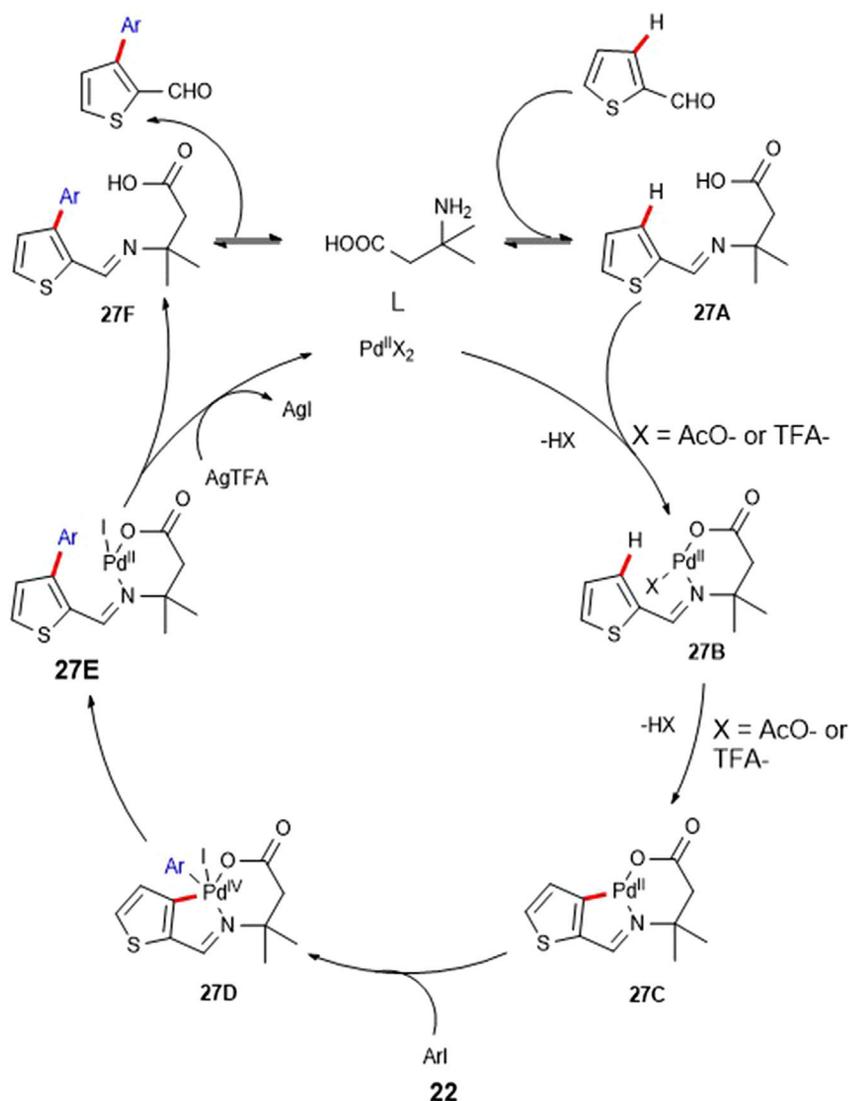
Figure 6. Fluorescence Images and Normalized Emission Spectra of 30a–30c and 31a–31c in Toluene (5.0×10^{-5} M)

Adapted from Li et al.³⁷ with permission, copyright 2018 Wiley-VCH Verlag GmbH & Co. KGaA.

external stimulus. When the two aryls were interchanged, the resulting fluorescent molecules showed a relatively small dipole moment and displayed a red emission by external stimulus.

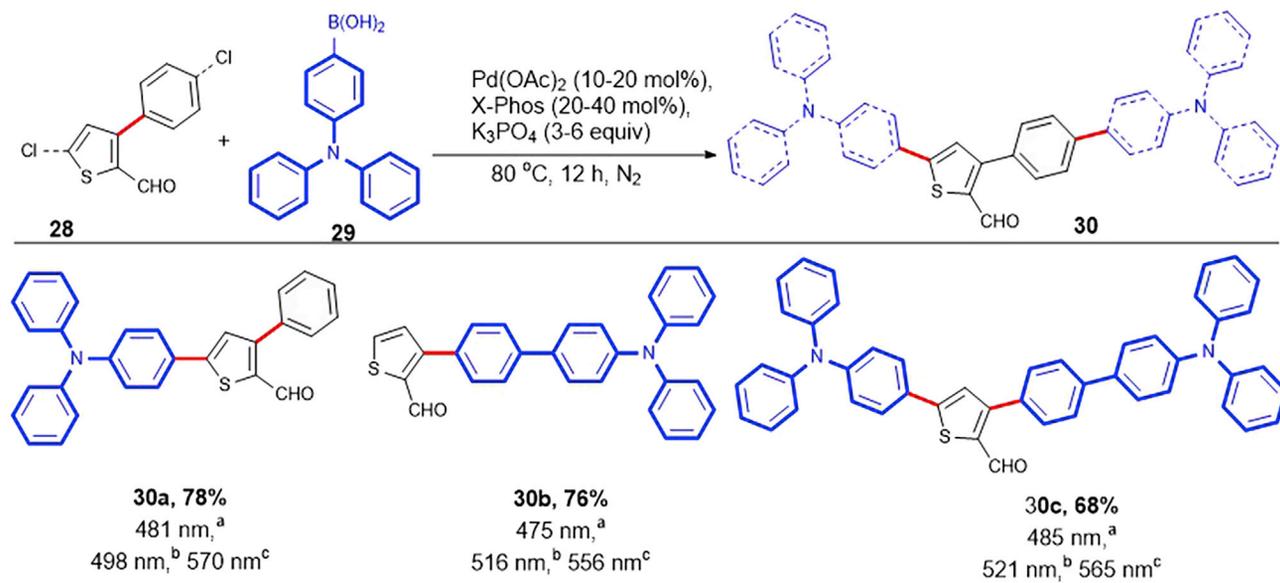
The transient directing group-enabled C–H functionalization process has emerged as a powerful synthetic strategy and has aroused great interest among scientists in chemical research because of its significant advantages: it does not need pre-functionalized starting materials, can avoid the use of stoichiometric organometallic reagents, and does not require extra steps to construct and remove a directing group.³⁶ In 2018, Ge and co-workers reported a novel strategy for the blue- and red-shift mechanochromic luminogens by transient ligand-enabled palladium-catalyzed C–H functionalization of heteroaromatic aldehydes and subsequent Suzuki cross-coupling reactions (Scheme 16; Figure 6).³⁷ A series of structurally diverse carbonyl tethered heterobiaryls were constructed using thiophene-2-carbaldehydes and iodobenzenes (Scheme 16). The plausible mechanism for the palladium-catalyzed transient ligand-directed cross-coupling of thiophene-2-carbaldehyde with iodobenzene was proposed (Scheme 17). The imine intermediate **27A** is generated by condensation of thiophene-2-carbaldehyde and the transient ligand. Coordination of **27A** with palladium species gives cyclic palladium complex **27B**, which then undergoes a C–H activation step to give rise to the [5,6]-bicyclic palladium intermediate **27C**. Oxidative addition of **27C** with iodobenzene generates the palladium(IV) species **27D**. Finally, the reductive elimination of **27D** produces the final product. Furthermore, TPA-containing β -aryl-substituted thiophene-2-carbaldehyde compounds were obtained by palladium-catalyzed Suzuki cross-coupling of (4-(diphenylamino)phenyl)boronic acid with chloro substituted 3-aryl-(2-aldehyde)thiophenes (Scheme 18). In addition, TPA-containing 3-arylthiophene-2-oxazoles were afforded by transforming the aldehyde group into oxazole using the tosylmethylisocyanide (Scheme 19). The TPA-containing 3-arylthiophene-2-carbaldehydes exhibited red-shifted mechanochromic behaviors. Interestingly, TPA-containing 3-arylthiophene-2-oxazoles displayed remarkable blue shift of emission (Figure 7). This protocol offers an opportunity to rapidly build up novel mechanofluorochromic materials with two different chromism trends.

Furthermore, authors studied the mechanochromic mechanism of **30–31** by analyzing differential scanning calorimetry curves, powder X-ray diffraction patterns, and crystal packing structure (Figure 8). Experimental data demonstrate that external force stimulation can induce conformation planarization and thus enhances intermolecular π - π stacking interactions and is responsible for the red-shifted emission. The observed blue-shift fluorescence after grinding the powder of TPA-containing 3-arylthiophene-2-oxazoles can be ascribed to weakened intermolecular π - π interactions.



Scheme 17. The Plausible Mechanism for the Formation of 28

Recently, Ge and co-workers reported the palladium-catalyzed C–H/C–Cl cross-coupling of TPA-bearing oxazoles (32) with (z)-1-chloro-4-styrylbenzene or (z)-1,2-bis(4-chlorophenyl)ethane (33) to build cis-olefin-based organic mechanochromic materials (Scheme 20).³⁸ The photophysical properties of TPA-bearing (z)-2-(4-styrylphenyl)oxazoles (34a–34d) were measured in toluene solution and before and after grinding (Scheme 20; Figure 9). As shown in Figure 9, emission wavelengths of 34a–34d were in the blue region (452 to 490 nm) in toluene. Notably, 34b showed deep-blue emission with CIE₁₉₃₁ of (0.15, 0.08), which is very close to EBU coordinates (0.15, 0.06). Oxazoles 34a–34d exhibited blue-shifted mechanochromic luminescence properties (Figure 9B). Specifically, the original powder of 34a–34d displayed yellow emission with emission maximum of 503–568 nm. Upon grinding, the emission color shifted to blue green ($\lambda_{em} = 483\text{--}502\text{ nm}$) (Figure 9). The fluorescence blue shift, after grinding the powder 34a–34d, could be ascribed to weakened intermolecular $\pi\text{--}\pi$ interactions.



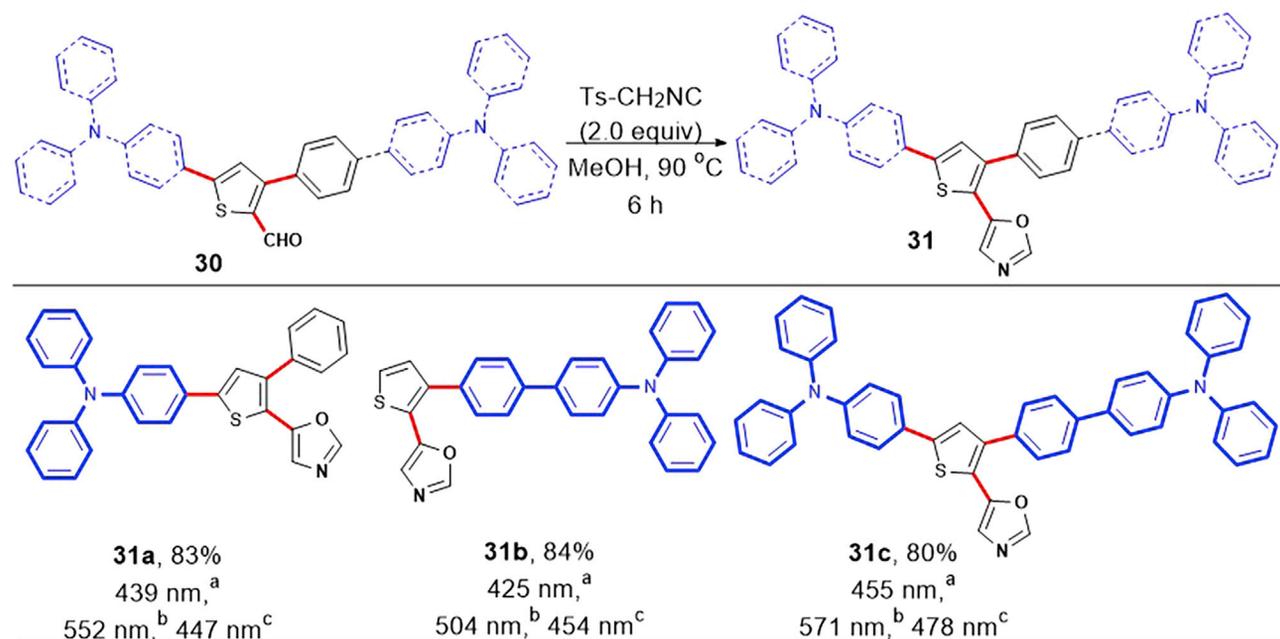
Scheme 18. Synthesis of TPA-Bearing 3-Phenyl-(2-Carbaldehyde)Thiophenes

^aEmission maximum in toluene (5×10^{-5} M).

^bEmission maximum in pristine powder.

^cEmission maximum in ground powder.

Very recently, Ge and co-workers designed and synthesized a series of novel organic mechanochromic materials, TPA-bearing 2-(4-(oxazol-2-yl)phenyl)acetonitrile-3-benzylbenzothio/furanphe. In this work, palladium-catalyzed direct γ -C–H bond



Scheme 19. Synthesis of TPA-Containing 3-Phenyl-(2-Oxazole)Thiophenes

^aEmission maximum in toluene (5×10^{-5} M).

^bEmission maximum in pristine powder.

^cEmission maximum in ground powder.

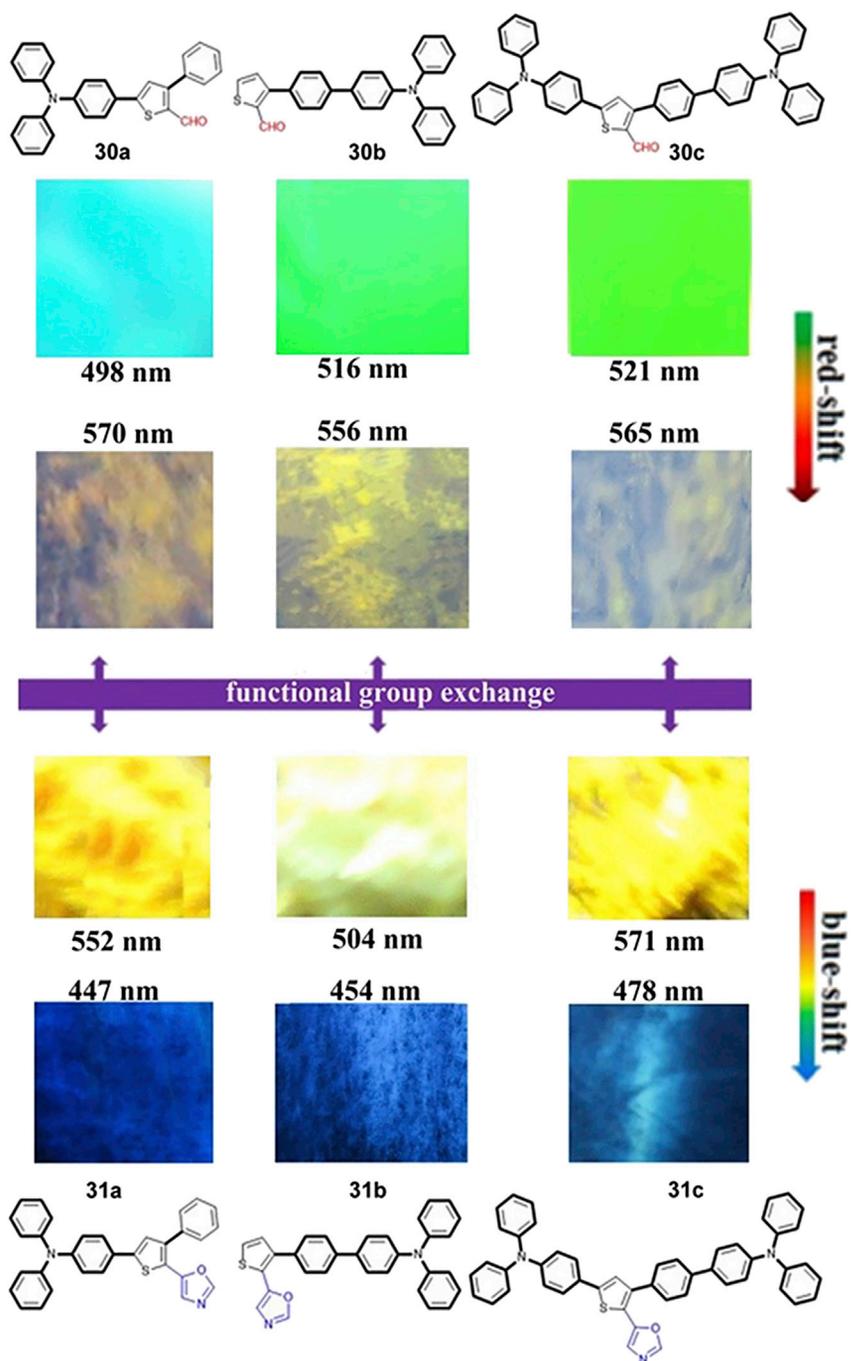


Figure 7. Fluorescent Images of 30 and 31 before and after Grinding

Adapted from Li et al.³⁷ with permission, copyright 2018 Wiley-VCH Verlag GmbH & Co. KGaA.

arylation of 3-methylbenzothiophene-2-carbaldehyde/3-methylbenzofuran-2-carbaldehyde with iodobenzene was performed (Scheme 21).³⁹ Then, the direct use of 3-benzylbenzothiophene-2-carbaldehyde and 3-benzylbenzofuran-2-carbaldehyde as starting materials to react with TPA-bearing 2-(4-(oxazol-2-yl)phenyl)acetonitrile produced novel organic functional molecules 38 (Scheme 22; Figure 10). The luminous properties of 38a and 38b were investigated with respect to emission

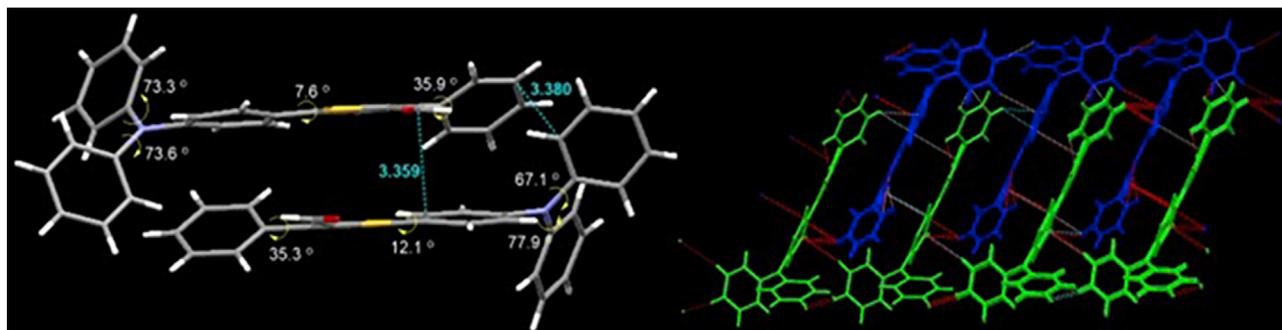
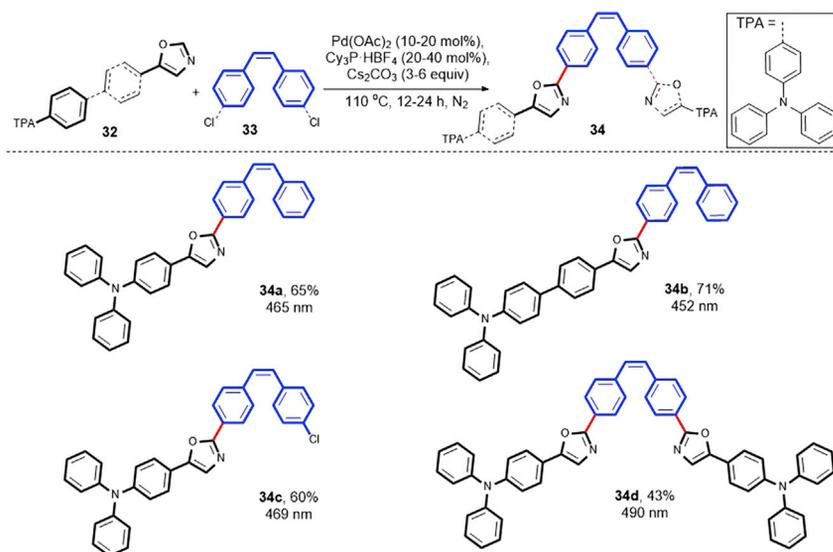


Figure 8. The Crystal Packing Structure of 30a

Adapted from Li et al.³⁷ with permission, copyright 2018 Wiley-VCH Verlag GmbH & Co. KGaA.



Scheme 20. Synthesis of TPA-Containing (z)-2-(4-Styrylphenyl)Oxazoles

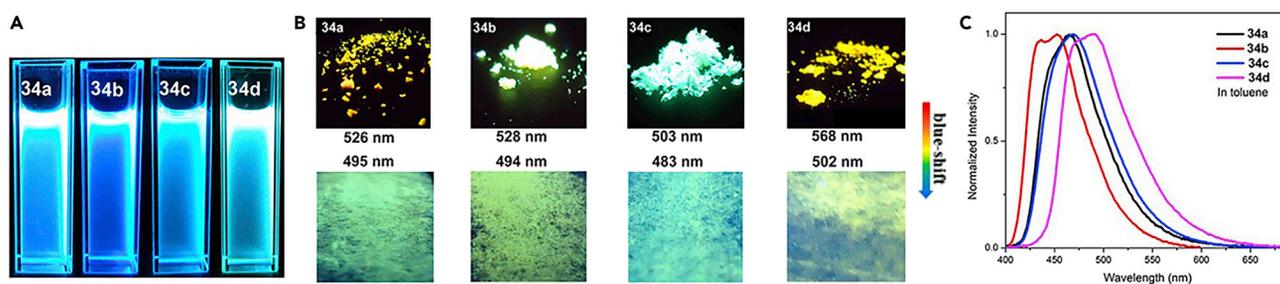
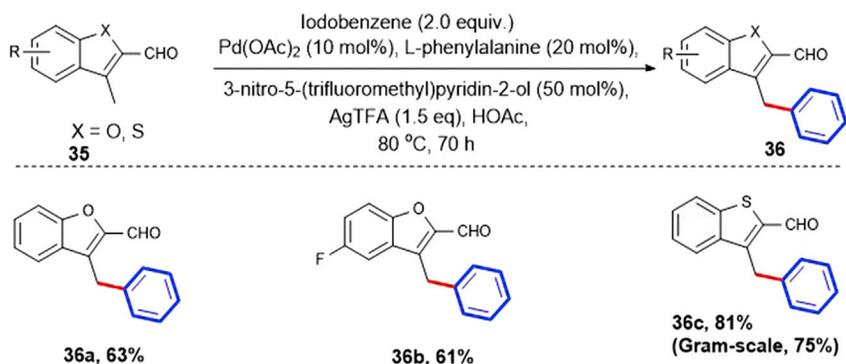


Figure 9. Fluorescence Images and Emission Spectra of 34a–34d

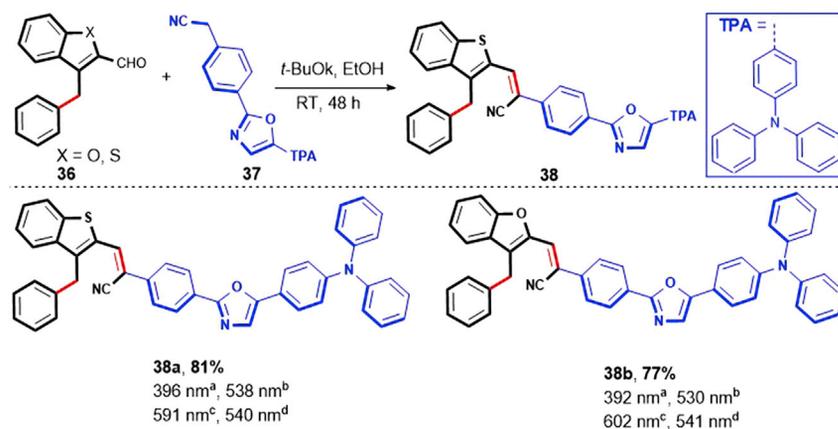
(A) Fluorescence images of 34a–34d in toluene (2.0×10^{-5} M) under UV light (365 nm).

(B) Fluorescent images of 34a–34d before and after grinding.

(C) Normalized emission spectra of 34a–34d in toluene (2.0×10^{-5} M). Adapted from Li and Ge³⁸ with permission, copyright 2019 AAAS.



Scheme 21. Synthesis of 3-Benzylbenzothiofuran-2-Carbaldehyde and 3-Benzylbenzofuran-2-Carbaldehyde by Transient Ligand-Enabled Palladium Catalyzed C–H Functionalization



Scheme 22. Synthesis of TPA-Containing 2-(4-(Oxazol-2-yl)Phenyl)Acetonitrile-3-Benzylbenzothio/Fur-Anphens

^{a,b}Absorption maximum and emission maximum in toluene (1×10^{-5} M).

^cEmission maximum in pristine powder.

^dEmission maximum in ground powder.

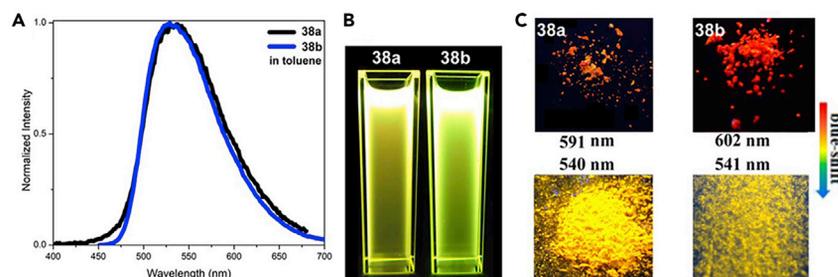
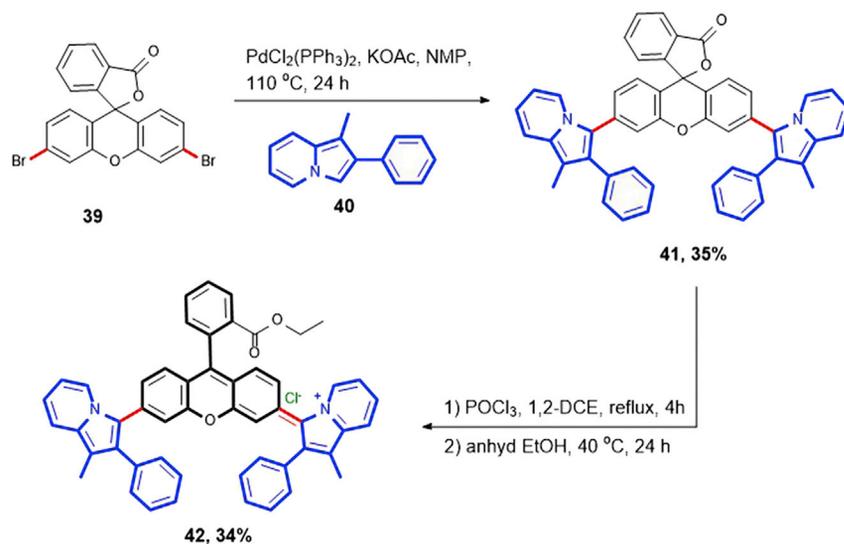


Figure 10. Fluorescence Emission Spectra and Fluorescent Images of 38a and 38b

(A) Normalized emission spectra of 38a and 38b in toluene (1.0×10^{-5} M).

(B) Fluorescence images of 38a and 38b in toluene (1.0×10^{-5} M) under UV light (365 nm).

(C) Fluorescent images of 38a and 38b before and after grinding. Adapted from Li et al.³⁹ with permission, copyright 2020 Wiley-VCH Verlag GmbH & Co. KGaA.



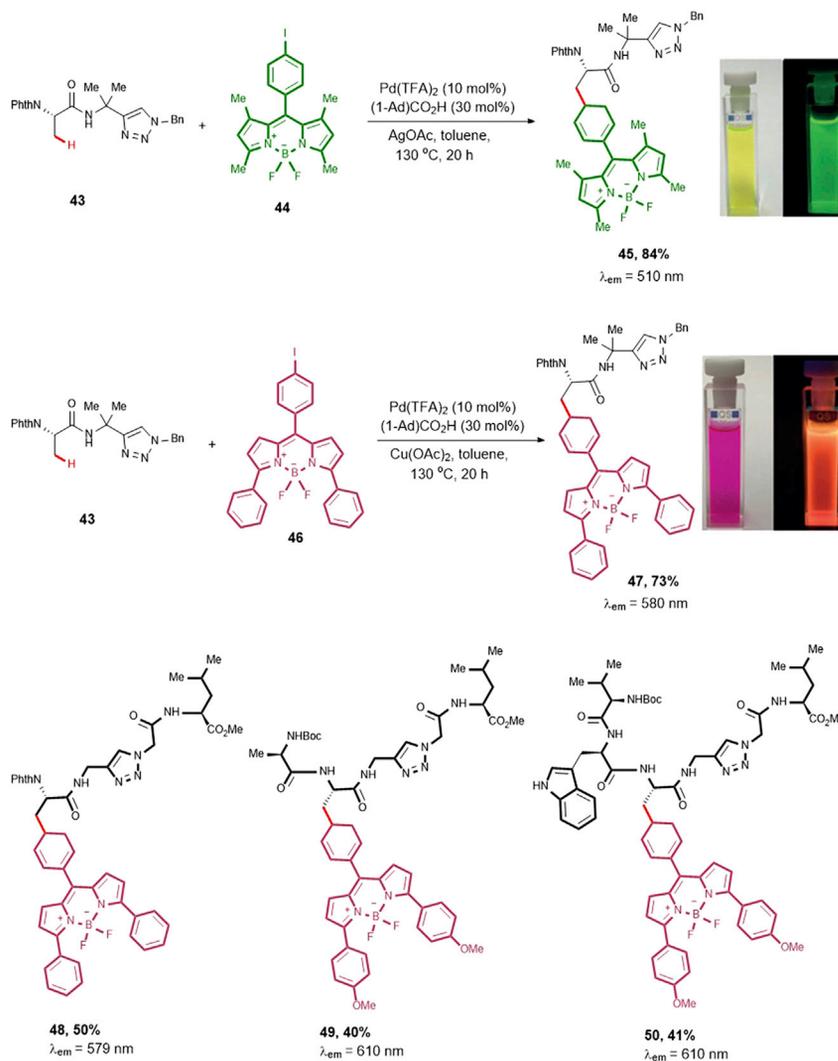
Scheme 23. Synthesis of Fluorescent Molecule 42 from 39

maxima in toluene solution and before and after grinding (Figure 10). Both of two compounds (38a and 38b) clearly displayed blue-shifted mechanochromic luminescence properties (Figure 10). The powder X-ray diffraction measurements of the unground powder of 38a exhibited many sharp and intense reflection peaks. After grinding, no reflection peak was observed, indicating that the crystalline state was converted into the amorphous powder by mechanical stimulus. The fluorescence emission blue shift, after grinding the powder 38a and 38b, could be attributed to the alteration of the molecular packing modes and weakened intermolecular π - π interactions.

In 2019, Scott and co-workers reported the palladium-catalyzed C–H/C–Br cross-coupling of 1-methyl-2-phenylindolizine with 3,6-dibromoxanthene to prepare a near-infrared (NIR) II emissive dye.⁴⁰ However, although the corresponding C–H functionalization product rhodindolizine spirolactone was nonfluorescent, upon opening of the lactone ring by simple operation, a xanthene-based emissive dye was obtained and exhibited an emission peak at 1,092 nm in the NIR II region (Scheme 23).

Transition-metal-catalyzed C–H functionalization reactions open a new avenue for efficient synthesis of common organic fragments and also offer a great opportunity for the late-stage functionalization of structurally complex molecules.¹⁰ In 2018, Ackermann and co-workers disclosed a late-stage BODIPY diversification of structurally complex amino acids and peptides by palladium-catalyzed C(sp³)–H activation (Scheme 24).⁴¹ A series of fluorescent chromophore-bearing structurally complex amino acids and peptides have been designed and synthesized, which offer a novel peptidomimetic BODIPY sensors. This finding provides important insights in the late-stage functionalization of complex molecules and significantly advances the field.

π -Conjugated polymers have emerged as promising fluorescent materials and have aroused great interest among organic and material scientists. In 2018, Tomita and co-workers used the Ru-catalyzed regiospecific direct double arylation reactions to construct π -conjugated polymers, poly(p-phenylene) derivatives bearing 2,5-bis(3-



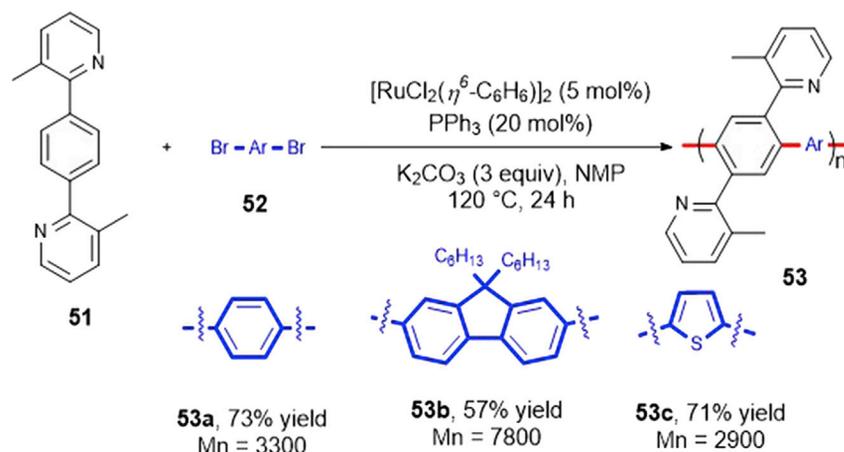
Scheme 24. Palladium-Catalyzed C(sp³)-H Activation in Building Novel Peptidomimetic BODIPY Sensors

Adapted from Wang et al.⁴¹ with permission, copyright 2018 Wiley-VCH Verlag GmbH & Co. KGaA.

methylpyridin-2-yl) substituents, with high number-average molecular weight in good yields (Scheme 25).⁴² These π -conjugated polymers **53a–53c** exhibited relatively strong fluorescent emissions in chloroform (λ_{max} : 385, 397, and 467 nm, respectively).

Transition-Metal-Catalyzed C–H/C–H Cross-Coupling Reactions to Build Fluorescent Materials

The carbon-carbon bond formation is one of the most important processes in modern organic chemistry since it enables key steps in the synthesis of complex organic products from simple reaction precursors. In the classic methods, construction of C–C bonds often requires the pre-functionalization of starting materials. Despite broad application in synthetic chemistry, the process requires additional synthetic steps and thus reduces the overall efficiency. In addition, stoichiometric amounts of toxic metal waste are often generated in this process, which constitutes an environmental problem. For these reasons, C–C bond formation by transition-metal-catalyzed direct C–H/C–H cross-coupling reactions have emerged as one of the most



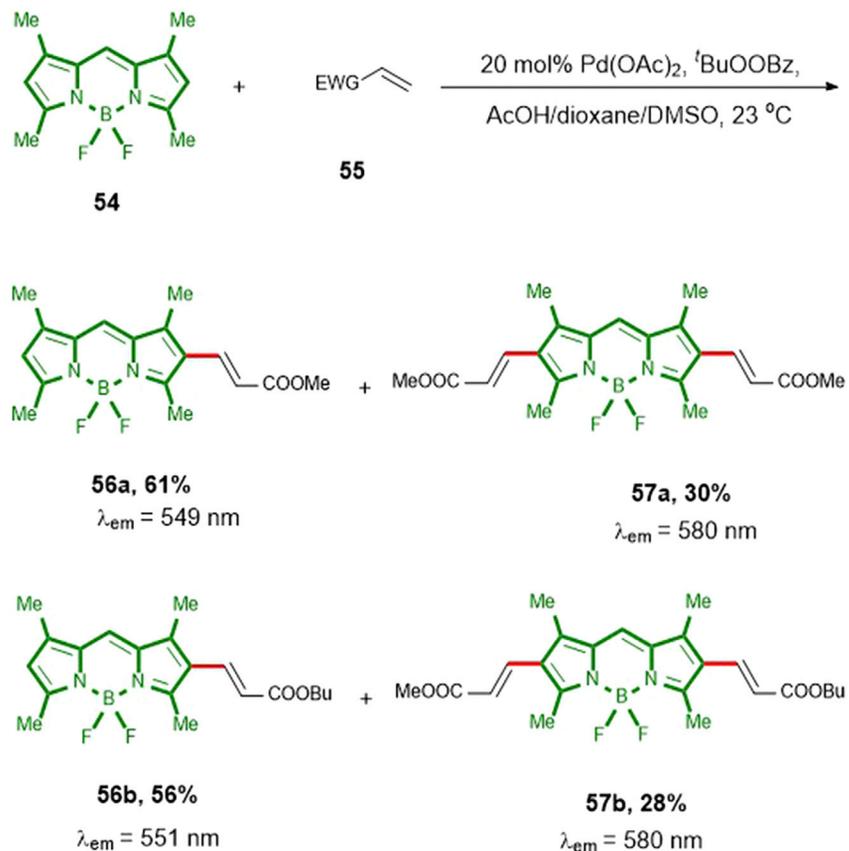
Scheme 25. Polycondensation of **51** and **52**.

straightforward and effective methods to construct bi(hetero) aryls because only a “H₂” is released as a side product.^{10–19}

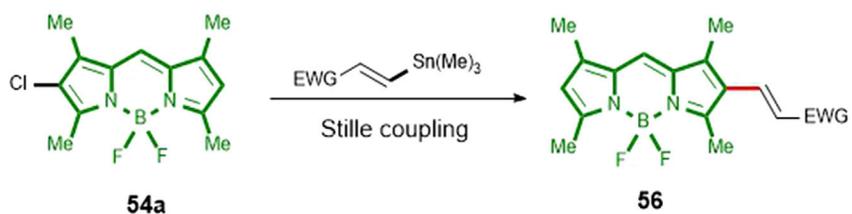
In 2007, Burgess and co-workers described a palladium-mediated Heck-type cross-coupling reaction between 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) dyes and alkenes to forge the conjugation of the tetramethyl-BODIPY system (Scheme 26).⁴³ Typical approaches for the synthesis of these dyes mainly use the Stille coupling, which requires halogenating BODIPY followed by highly toxic organometallic couplings (Scheme 27).⁴³ These products as new fluorescent probes exhibited strong fluorescence emissions that span 525–570 nm and high fluorescence quantum yields (Figure 11).

In 2012, You et al. reported a Pd/Cu-catalyzed dehydrogenative Heck coupling between various biologically relevant *N*-heteroarenes and alkenes (Scheme 28).⁴⁴ The traditional preparation of these compounds relies on the Liebeskind-Srogl coupling reaction, which needs the tiresome multi-step synthesis and pre-functionalization of starting materials (Scheme 29).²⁸ The coupling products, alkenylated *N*-heteroarenes, displayed strong fluorescence emission that covered the spectra from 417 to 566 nm (Figures 12 and 13). Furthermore, these organic materials have been proven to be useful bioimaging fluorescence probes.

Bi(hetero)aryl scaffolds are widely present in organic functional materials, pharmaceuticals, agrochemicals, natural products, ligands, and organic synthetic intermediates.¹¹ The development of efficient and concise methods for the construction of bi(hetero)aryls is of great research interest in academia and industry. In 2016, You and co-workers described an efficient synthesis of donor-acceptor-type biheteroaryl fluorophores via palladium-catalyzed C–H/C–H cross-coupling of electron-deficient 2*H* indazoles with electron-rich heteroarenes (Scheme 30).⁴⁵ The conventional methods for preparing these compounds usually need the tedious multi-step synthesis (Scheme 31).⁴⁶ These donor-acceptor-type biheteroaryl dyes presented full-color-tunable fluorescence emissions with high quantum yields and large Stokes shifts. The near-infrared fluorophore dye **65** with emission wavelength 709 nm was synthesized by the Knoevenagel condensation of **62e** with malononitril (Scheme 32; Figure 14), which has been demonstrated to be the smallest near-infrared probe for *in vivo* mitochondria imaging.



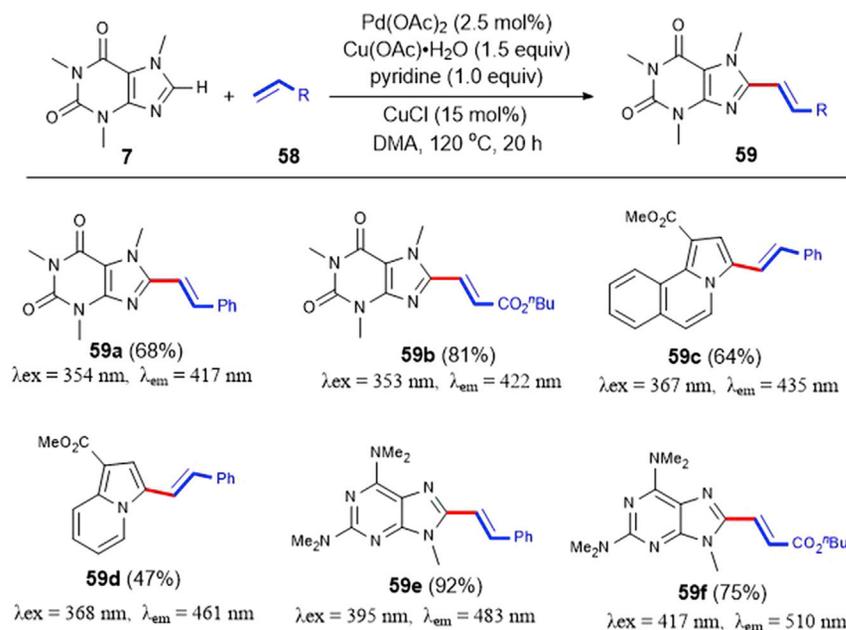
Scheme 26. Palladium-Mediated Heck-Type Cross-Coupling between 54 and Alkenes



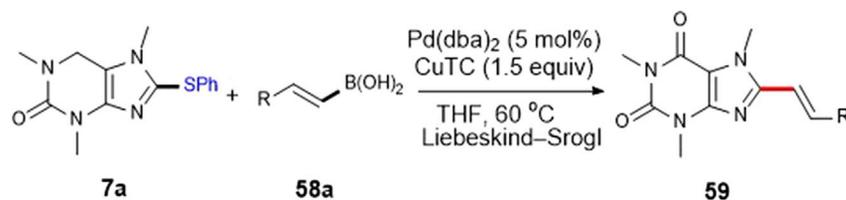
Scheme 27. The Conventional Synthetic Method for 56



Figure 11. Photograph of Dyes 57a, 57b, 56b, and 56a in Ethanol under UV Irradiation
Adapted from Thivierge et al.⁴³ with permission, copyright 2007 American Chemical Society.



Scheme 28. Palladium-Catalyzed Dehydrogenative Heck Coupling between Various Biologically Relevant *N*-Heteroarenes and Alkenes



Scheme 29. The Conventional Synthetic Method for 59

The excited-state intramolecular proton-transfer (ESIPT) molecules enable a dual-emission behavior involving the normal enol-form emission with a relatively short wavelength (blue-light component) and the proton-transfer keto-form emission with a relatively long wavelength (orange-light component) and thus are considered as ideal candidates to design single-molecular white-light-emitting materials.^{5,47} 2-(2-Hydroxyphenyl)azoles are an important class of organic functional molecules with the ESIPT characteristics. Unfortunately, 2-(2-hydroxyphenyl)azoles typically show

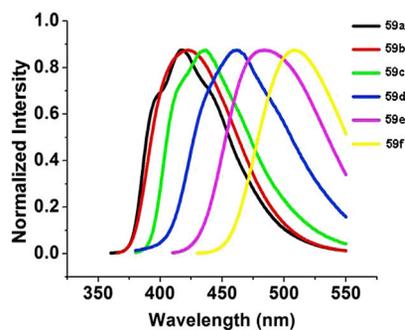


Figure 12. Normalized Emission Spectra of 59a–59f in CH_2Cl_2
 Adapted from Huang et al.⁴⁴ with permission, copyright 2012 Royal Society of Chemistry.

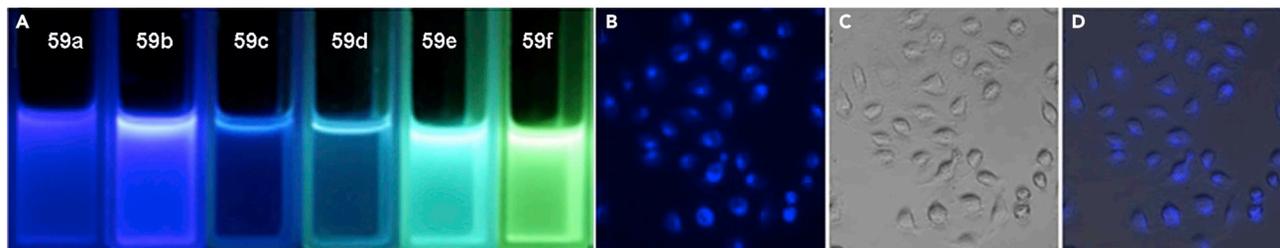


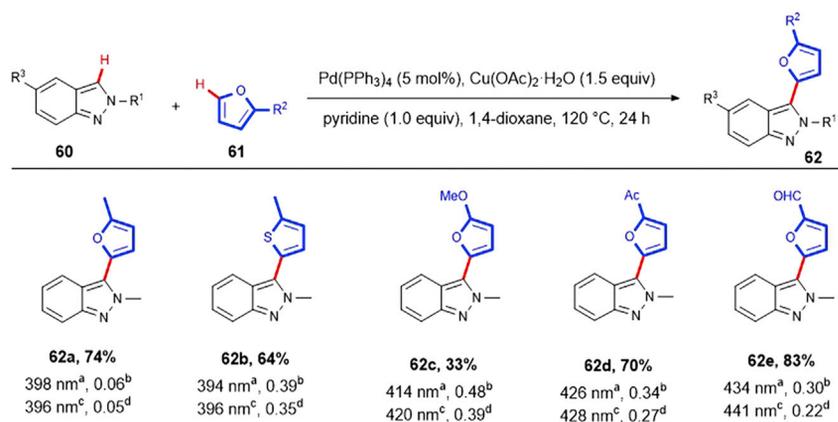
Figure 13. Fluorescence Images of 59a–59f and Bioimaging Fluorescence Probe 59f

(A) Fluorescence images of 59a–59f in CH₂Cl₂.

(B) Fluorescence image of SMMC-7721 cells incubated with 59f (5 mM).

(C) Bright-field transmission image of SMMC-7721 cells incubated with 59f.

(D) Overlay of fluorescence and bright-field transmission images of SMMC-7721 cells incubated with 59f. Adapted from Huang et al.⁴⁴ with permission, copyright 2012 Royal Society of Chemistry.



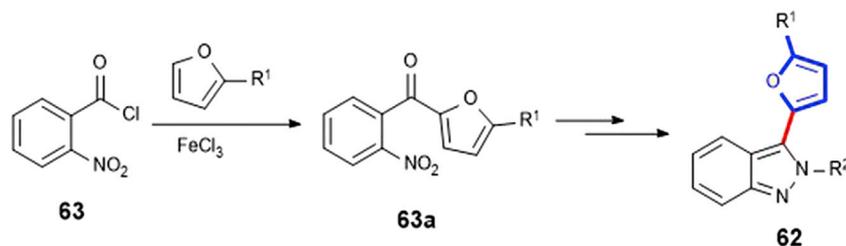
Scheme 30. Direct Oxidative C–H/C–H Cross-Coupling of 2H-Indazoles with Various Heteroarenes and Photophysical Data of the Resulting Catalytic Products

^aEmission maximum in CH₂Cl₂ at 10.0 μM.

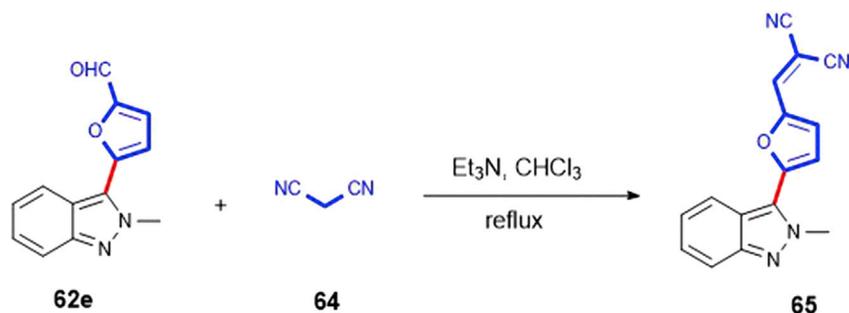
^bAbsolute quantum yield in CH₂Cl₂ at 10.0 μM determined with an integrating sphere system.

^cEmission maximum in CH₃CN at 10.0 μM.

^dAbsolute quantum yield in CH₃CN at 10.0 μM determined with an integrating sphere system.



Scheme 31. The Conventional Synthetic Method for 62



Scheme 32. Synthesis of Near-Infrared Fluorophore Dye **65**

solely the keto-form emission in the solid state or in nonpolar solvent because of a strong intramolecular hydrogen-bonding interaction, which leads to the lack of original short wavelength enol-form emission and thus hardly forms a broadband emission covering the whole visible range (Scheme 33). In addition, the 2-(2-hydroxyphenyl)azoles often exhibit weak or quenching emission feature due to the intramolecular hydrogen-bonding fixation and, thus, are more prone to aggregate. Lan, You et al. developed a rhodium(III)-catalyzed system in 2015 for the direct internal oxidative C–H/C–H cross-coupling between heteroarenes and phenols using a traceless oxidation directing strategy to discover new organic optoelectronic materials.⁴⁸ The traceless oxidation directing strategy has aroused great interest among scientists in chemical research because of its significant advantages: it serves as both a traceless directing group and an internal oxidant, can avoid the use of stoichiometric amounts of an external oxidant, and does not require extra steps to remove

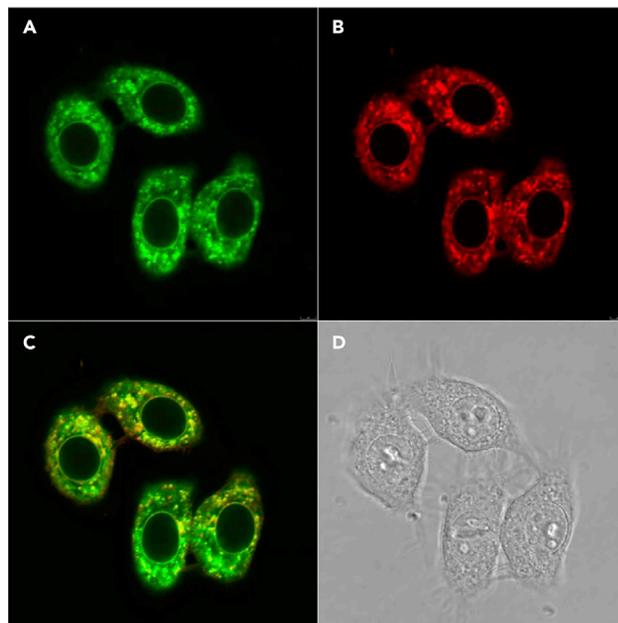
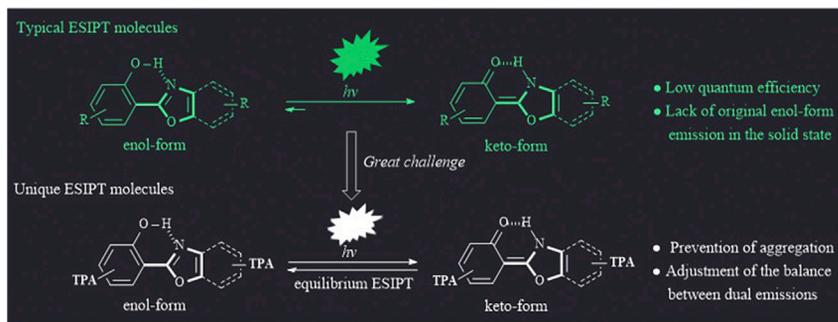


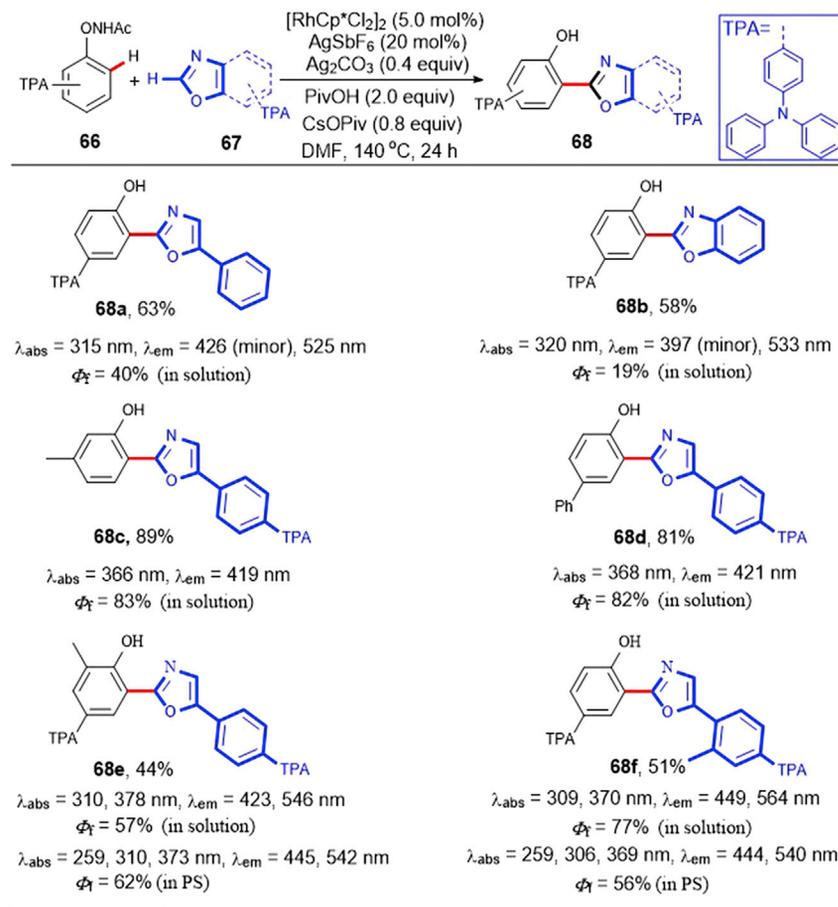
Figure 14. Co-staining of HepG2 Cells with **65** and a Commercially Available Mitochondria-Specific Tracker MTG (A–D) (A) fluorescent image of HepG2 cells stained with MTG ($\lambda_{\text{ex}} = 488 \text{ nm}$, $\lambda_{\text{em}} = 500\text{--}540 \text{ nm}$), (B) fluorescent image of HepG2 cells stained with **65** ($20.0 \mu\text{M}$, $\lambda_{\text{ex}} = 552 \text{ nm}$, $\lambda_{\text{em}} = 650\text{--}750 \text{ nm}$), (C) merged image of (A and B), and (D) bright-field image. Adapted from Cheng et al.⁴⁵ with permission, copyright 2016 American Chemical Society.



Scheme 33. Structures and ESIPT Mechanism of 2-(2-Hydroxyphenyl)azoles

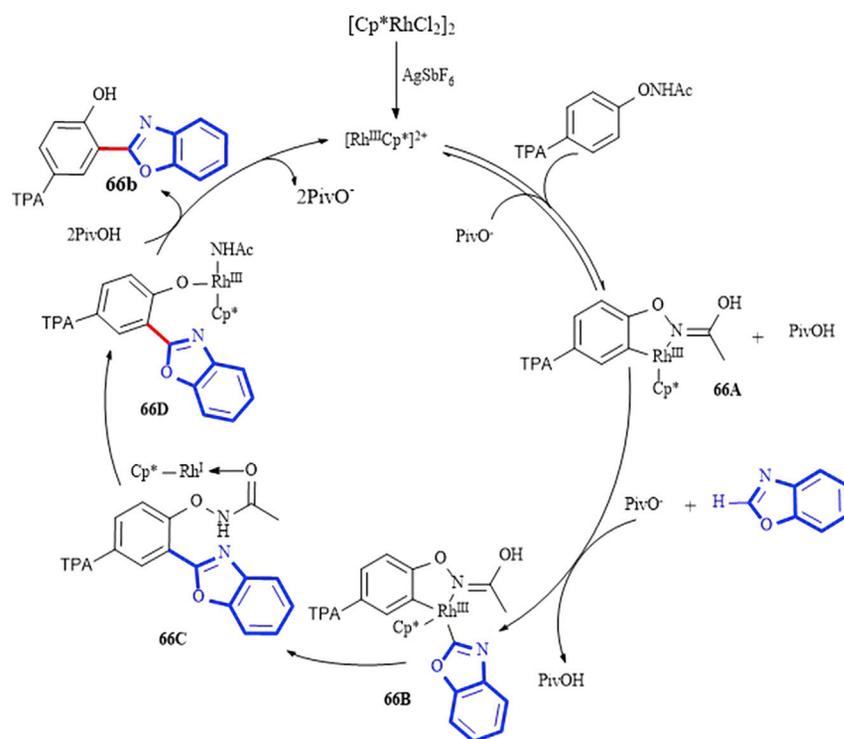
TPA: triphenylamineunits.

a directing group. The heteroarylation products 2-(2-hydroxyphenyl)azoles were obtained in good to excellent yields by using catalytic amounts of $[\text{RhCp}^*\text{Cl}_2]_2$, 10 mol % AgSbF_6 , 0.2 equiv Ag_2CO_3 , 2.0 equiv PivOH , 0.8 equiv CsOPiv in DMF under atmosphere of N_2 . A broad range of *N*-phenoxyacetamides and oxazoles provided the desired products in good to excellent yields under standard conditions (Scheme 34).



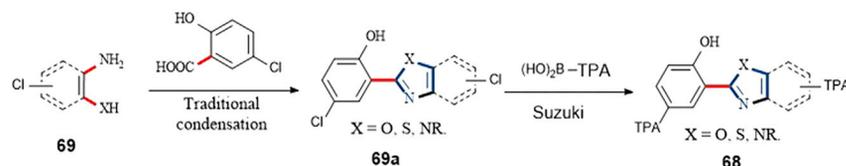
Scheme 34. Synthesis of TPA-Bearing 2-(2-Hydroxyphenyl)Oxazoles

Absolute quantum yields and absorption and emission maxima were measured in toluene (5.0×10^{-5} M), in toluene (1.0×10^{-6} M) and in the PS films (0.2 wt %), respectively.



Scheme 35. The Tentative Mechanism for the Cross-Coupling of *N*-aryloxyacetamide with 1,3-Azole

A tentative mechanism was proposed. First, coordination of the amide nitrogen atom to Rh^{III} followed by *ortho*-C–H activation of **66a** generated the six-membered rhodacycle **66A**. The subsequent formation of the key benzoxazolyl-Rh^{III}-phenyl intermediate **66B** was achieved with benzo[d]oxazole. Then, reductive elimination produced **66C**. Finally, the oxidative addition generated Rh^{III} intermediate **66D**, which upon protonation by PivOH, generated product **68b** (Scheme 35). Furthermore, authors designed and synthesized a series of novel ESIPT molecules with strong dual emission. It has been well-documented that the triphenylamine (TPA) group possesses good electron-donating property, hole-transporting capability, and nonplanar characteristic.^{37–39} The aggregation behaviors of 2-(2-hydroxyphenyl)azoles could be restrained by incorporating the TPA group, which could endow TPA-bearing 2-(2-hydroxyphenyl)azoles with a strong emission. The energy levels of the keto form and enol form of 2-(2-hydroxyphenyl)azoles could be adjusted by TPA, which offers an opportunity to generate dual emission. Therefore, two bis-triphenylamine (TPA)-bearing 2-(2-hydroxyphenyl)azoles **26** and **27** were synthesized by using this transition-metal-catalyzed C–H/C–H cross-coupling reaction. The conventional methods for preparing these scaffolds use condensation reactions to obtain 2-(2-hydroxyphenyl)azoles followed by Suzuki couplings to introduce triphenylamine, which suffers from tedious multiple-step synthesis (Scheme 36).⁴⁸



Scheme 36. The Conventional Synthetic Method for **68**

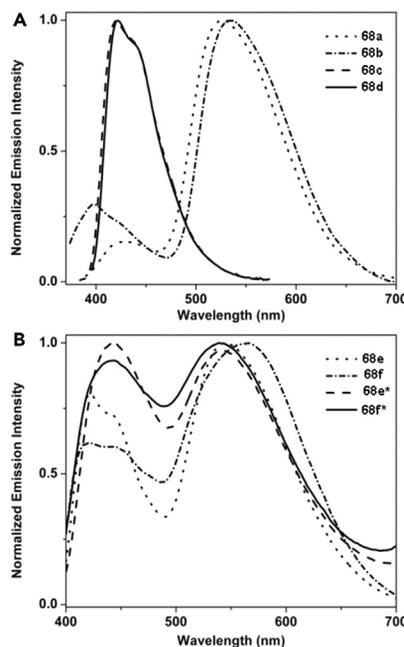


Figure 15. Emission spectra of 68a–68f in Toluene and PS Films

Adapted from Li et al.⁴⁸ with permission, copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.

These molecules displayed the ESIPT equilibrium between the enol form and the keto form in toluene and the PS film, and showed bright white-light emissions with high quantum yields and thermal stabilities (Figures 15 and 16).

In subsequent studies, the You group further synthesized two new white-light emitting molecules **68g** and **68h** using the rhodium(III)-catalyzed oxidative C–H/C–H cross-coupling strategy and prepared white organic light-emitting devices base on them (Scheme 37; Figure 17).⁴⁹ A **68g**-based device showed green-white electroluminescence with CIE₁₉₃₁ (0.25, 0.41) and a high singlet exciton yield (63%), which exceeds the theoretical limit of 25% in conventional fluorescent OLEDs (Figure 17). The device exhibited a high external quantum efficiency (EQE) up to 5.3%, which is the highest EQE in single-molecular organic white-light-emitting materials. Experimental data and theoretical calculations indicated that **68g** possesses a highly hybridized local and charge-transfer (HLCT) excited-state character. In addition, the **68h**-based device exhibited sky-blue emission with CIE₁₉₃₁ (0.18, 0.16) and an EQE of 8.0%, which is the highest EQE in the recorded HLCT materials.

2-(2'-Hydroxyphenyl)azoles are a kind of typical ESIPT molecules.^{5,47} For example, 2-(5-phenyloxazol-2-yl)phenol (HPO) only showed the ESIPT keto-form emission in the excited state. In 2017, You and co-workers synthesized TPA-bearing 2-(2'-hydroxyphenyl)oxazoles by rhodium(III)-catalyzed oxidative C–H/C–H cross-coupling strategy. Moreover, they discovered that it is a unique kind of 2-(2'-Hydroxyphenyl)azole, which only showed the sole enol-form emission in both solution and solid states (Schemes 38 and 39).⁵⁰ Theoretical calculations further provided a supplementary support for these experimental results (Figure 18). The energy levels of the keto-form species of the first excited-state HPO and **68i** were 1.09 and 6.41 kcal mol⁻¹, respectively. For HPO, the enol form is easy to transfer to keto form in the excited state due to its low energy level, whereas the transformation of **68i** from the excited-state enol form to keto form is difficult because of its significantly high energy level. This transformation is a significantly endergonic process, demonstrating

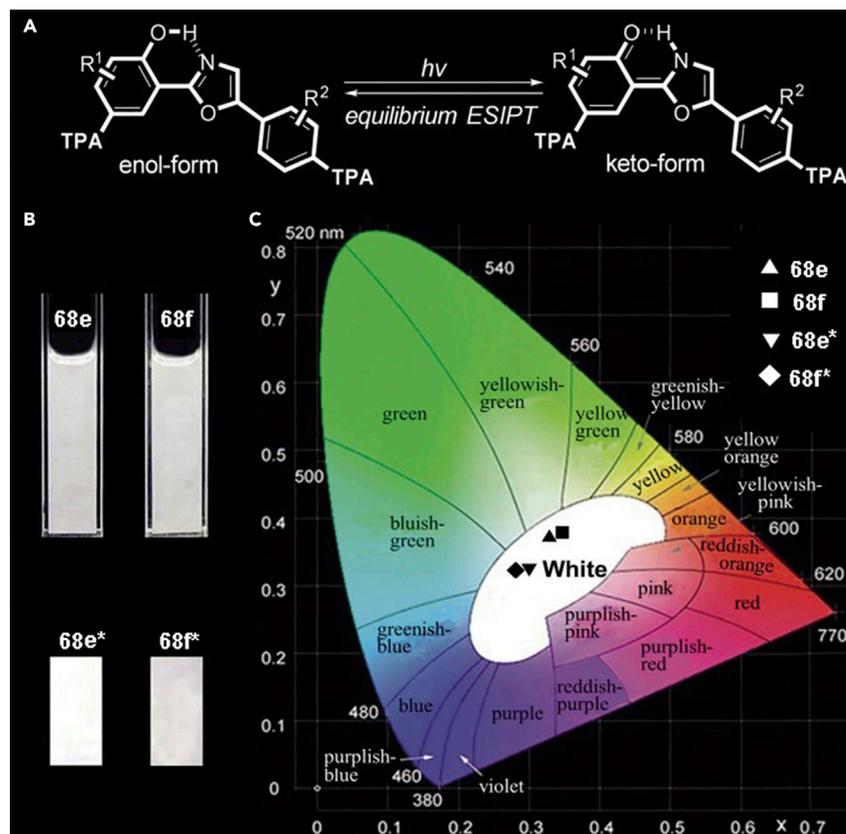
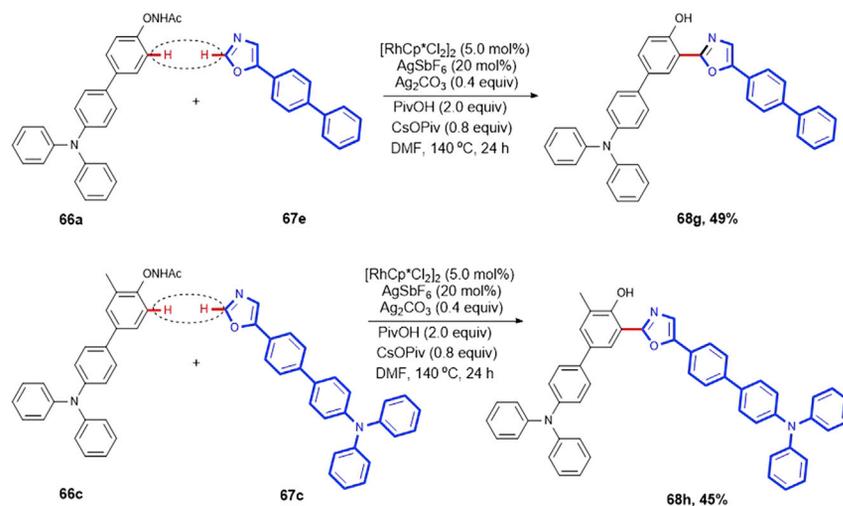


Figure 16. Emission Color Coordinates and Fluorescence Images of 68e and 68f in Toluene and in PS Films

Adapted from Li et al.⁴⁸ with permission, copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.

that the thermodynamic equilibrium favors the enol species of 68i and thus leads to the lack of keto-form emission. The 68i-based device shows highly efficient deep-blue emission with the CIE₁₉₃₁ (0.15, 0.08), which is very close to the CIE₁₉₃₁ (0.14,



Scheme 37. Synthetic Routes of 68g and 68h

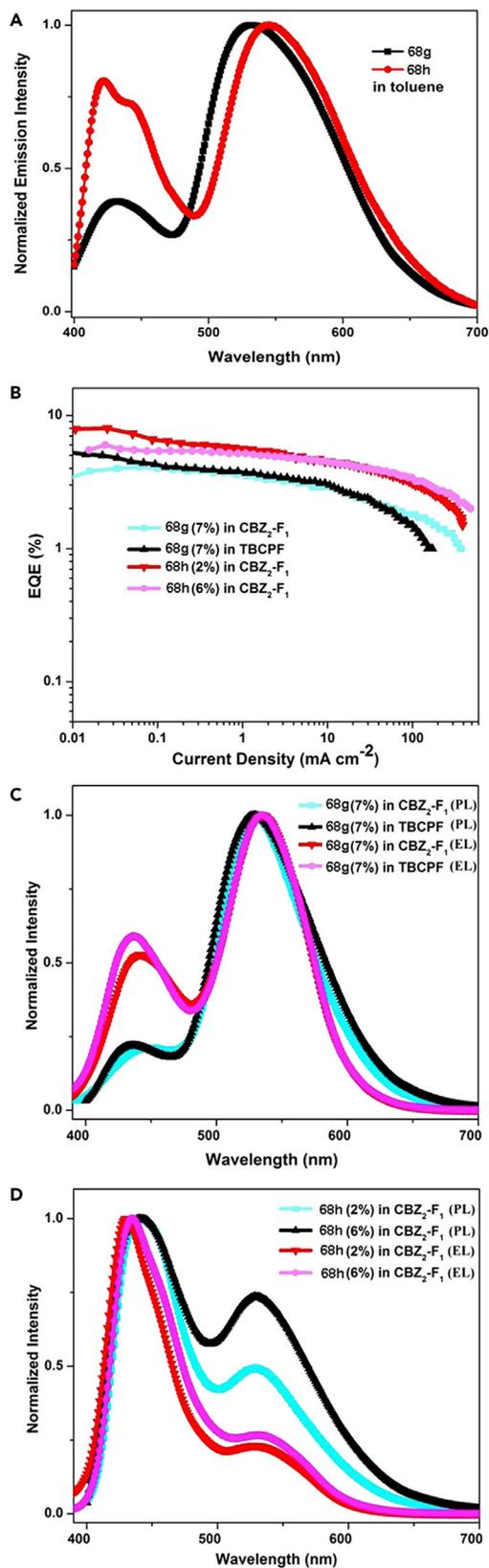


Figure 17. Photophysical and Electroluminescence Properties of 68g–68f

- (A) Normalized emission spectra of **68g** and **68h**.
 (B) EQE–current density curves of devices based on **68g** and **68f**.
 (C) Normalized EL spectra of **68g**-based devices and PL spectra of **68g** in the film.
 (D) Normalized EL spectra of **68f**-based devices and PL spectra of **68f** in the film. Adapted from Li et al.⁴⁹ with permission, copyright 2018 Royal Society of Chemistry.

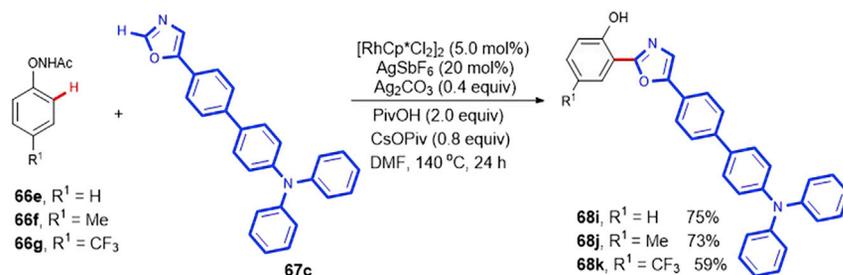
0.08) of the NTSC standard blue (Figure 19). In addition, this device exhibited an EQE up to 7.1%, indicating a breakthrough in exciton utilization efficiency. This is the first example of highly efficient pure blue OLEDs based on the sole enol-form emission of 2-(2'-hydroxyphenyl)azoles.

Recently, Lan and co-workers disclosed the Rh(III)-catalyzed oxidative C–H/C–H cross-coupling of [1,2,4]triazolo[1,5-a]pyrimidines with indoles and pyrroles to afford the ESIPT fluorophores (Scheme 40).⁵¹ In this work, 7-(Pyrrol-2-yl)-[1,2,4]triazolo[1,5-a]pyrimidines and 7-(indol-2-yl)-[1,2,4]triazolo[1,5-a]pyrimidines were synthesized in moderate to excellent yields. A large library of ESIPT fluorophores could be obtained by removing the pyrimidyl directing group using sodium methoxide (Scheme 41). These ESIPT fluorophores exhibited bright emission and high quantum yields in both solution and solid states (Figure 20).

π -Conjugated polymers have been considered as promising fluorescent materials for the fabrication of optoelectronic devices. The transition-metal-catalyzed direct C–H/C–H polymerization of non-preactivated (hetero)arenes would be one of the most straightforward and effective approaches to construct π -conjugated polymers, which would eliminate the extra steps to prepare bifunctional monomers. In 2014, the You group disclosed the Cu-catalyzed oxidative C–H/C–H polymerization of benzodiimidazoles to prepare polybenzodiimidazoles with moderate number-average molecular weight in good yields (Schemes 42 and 43).⁵² These polybenzodiimidazoles exhibit strong blue fluorescence emissions in chloroform and PS film (Figure 21).

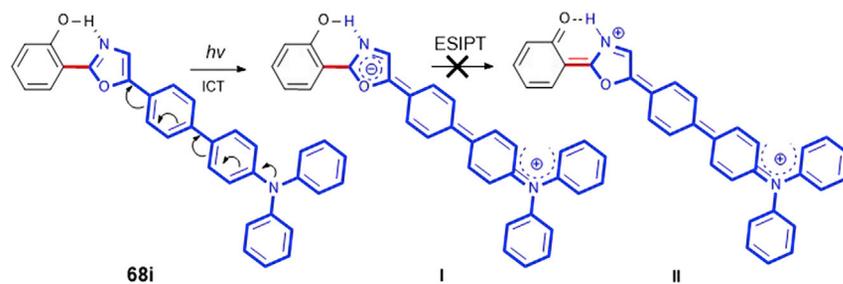
In 2015, Li and co-workers reported Pd-catalyzed oxidative C–H/C–H homopolymerization of thiazole derivatives with thiophene to construct π -conjugated polymers **76a–76c** (Scheme 44).⁵³ Emission maxima of **76a–76c** were observed at 609, 626, and 645 nm in the film state, respectively.

In 2018, the Kanbara group developed Pd-catalyzed cross-dehydrogenative coupling reaction of 2,2',3,3',5,5',6,6'-octafluorobiphenyl with thiophenes to prepare π -conjugated polymers **79**, which show green photoluminescence ($\lambda_{\text{max}} = 503$ nm) in thin film (Scheme 45).⁵⁴ The corresponding electroluminescent (EL)



Scheme 38. Synthetic Routes of 68i–68k

XPhos: 2-(dicyclohexylphosphino)-2',4',6'-triiisopropylbiphenyl.



Scheme 39. The ICT and ESIPT Mechanism of 68i

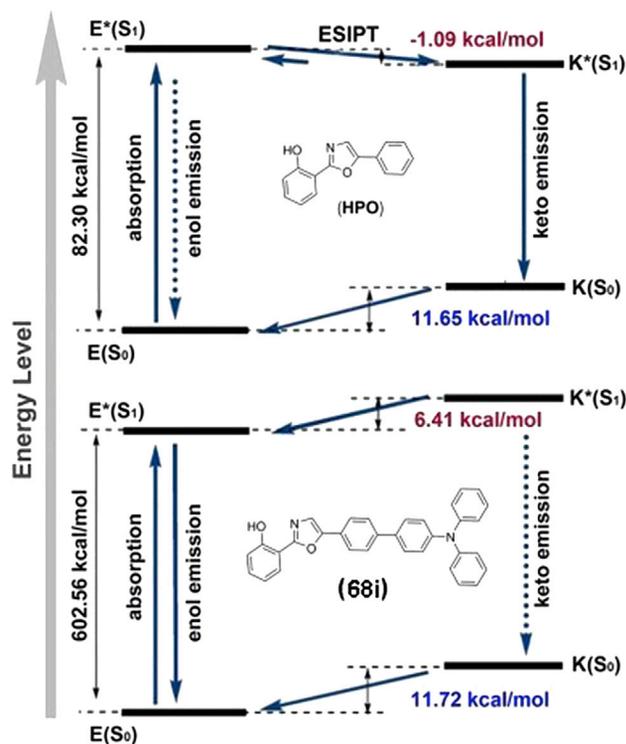


Figure 18. Diagrams of the ESIPT Processes and Calculated Energy Levels of HPO and 68i

Adapted from Li et al.⁵⁰ with permission, copyright 2017 Wiley-VCH Verlag GmbH & Co. KGaA.

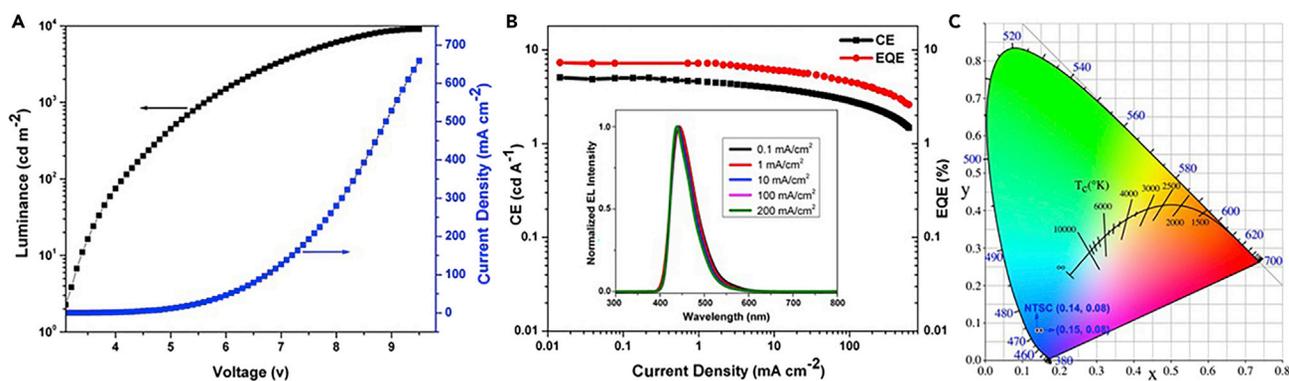
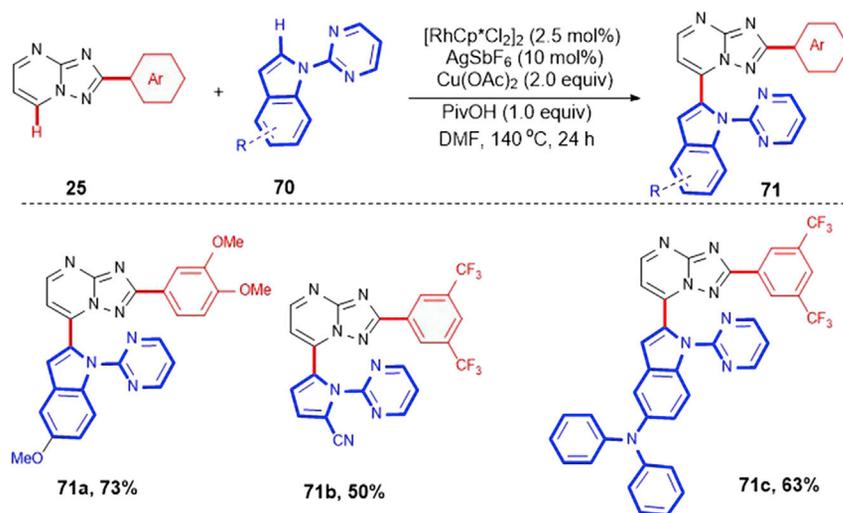


Figure 19. Electroluminescence Property of 68i

(A) Luminance–current density–voltage characteristics of the 68i-based device.

(B) The EL efficiency-current density and EQE-current density curve.

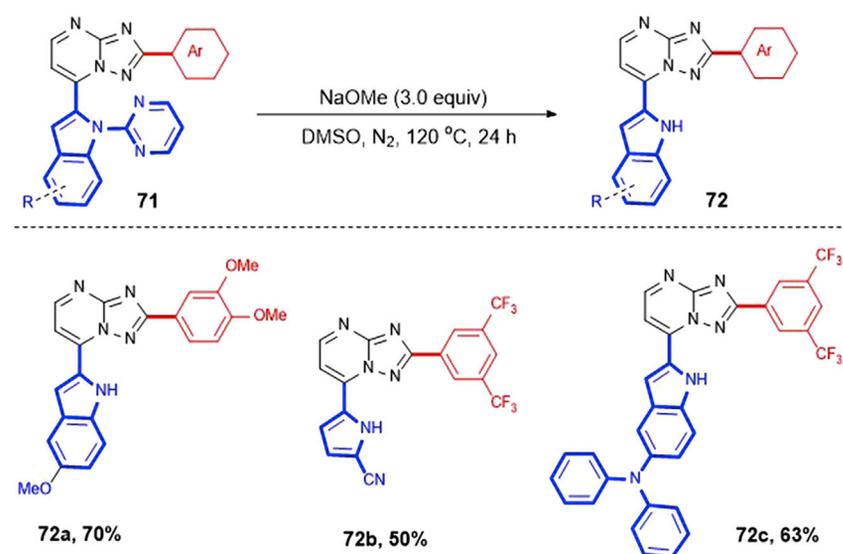
(C) CIE1931 coordinates of the device. Adapted from Li et al.⁵⁰ with permission, copyright 2017 Wiley-VCH Verlag GmbH & Co. KGaA.



Scheme 40. Rh(III)-Catalyzed Oxidative C–H/C–H Cross-Coupling

spectrum also displays green emits (Figure 22). Furthermore, the same group synthesized the bithiazole-based semiconducting polymers **81a** and **81b** by the Cu-catalyzed aerobic oxidative C–H/C–H coupling reaction in 2018 (Scheme 46).⁵⁵ The polymer **81b** exhibits a green emission ($\lambda_{\text{max}} = 530\text{ nm}$) and relatively high emission quantum yield (10.4%). The electroluminescent spectrum of **81b** was like its photoluminescence spectrum (Figure 23).

In 2019, Zhu and co-workers used Rh(III)-catalyzed *N*-nitroso-directed C–H olefination reaction to construct π -conjugated polymer **83** with high yield (Scheme 47).⁵⁶ The fluorescent polymer **83** was chosen as a sensor to detect metal ions Hg^{2+} .



Scheme 41. Removal of the Pyrimidyl Directing Group

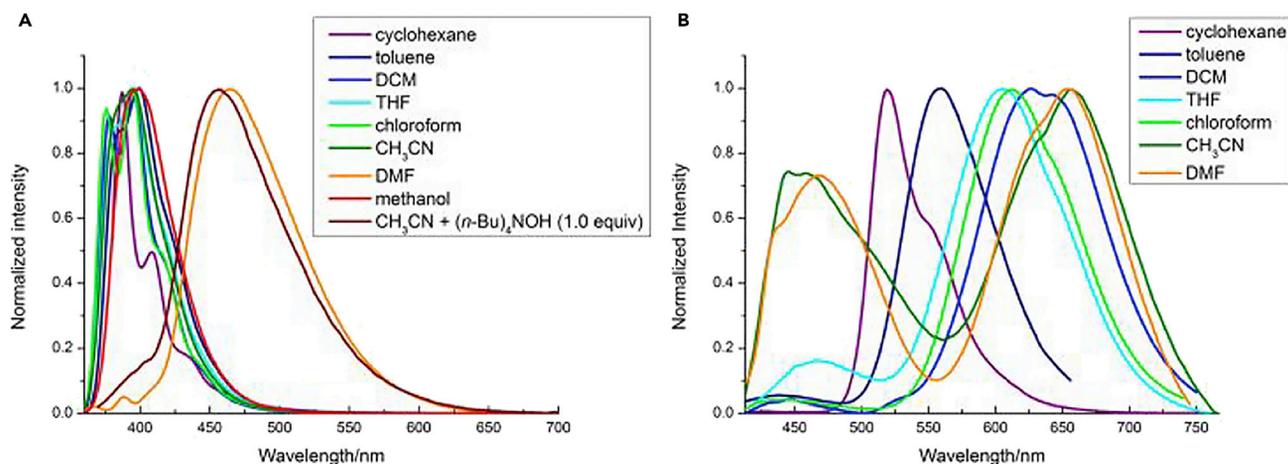
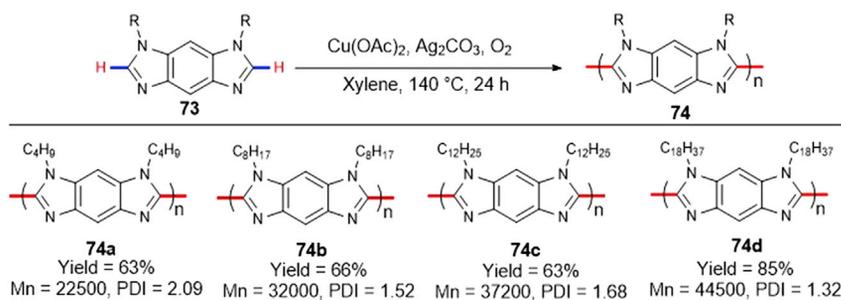
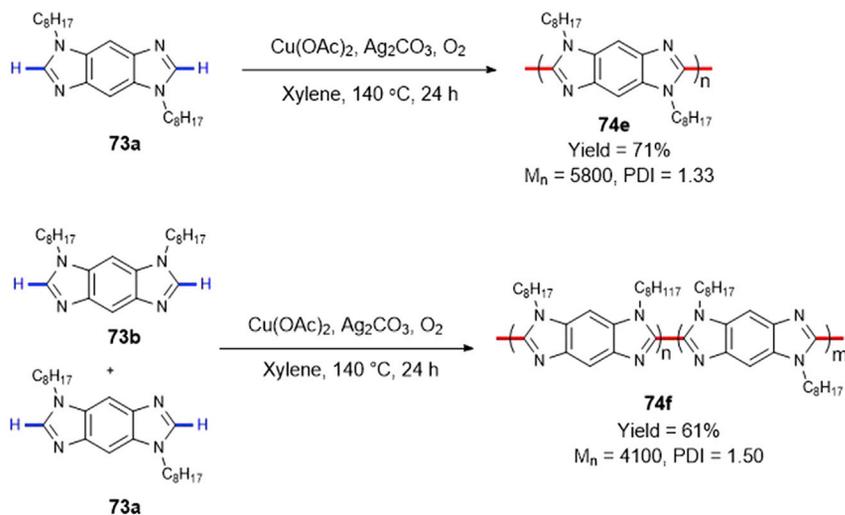


Figure 20. Normalized Emission Spectra of 71b and 71c

Reprinted with permission from You et al.⁵¹ Copyright 2019 American Chemical Society.



Scheme 42. Cu-Catalyzed Oxidative C–H/C–H Polymerization of 73



Scheme 43. Cu-Catalyzed Oxidative C–H/C–H Polymerization of 73a and 73b

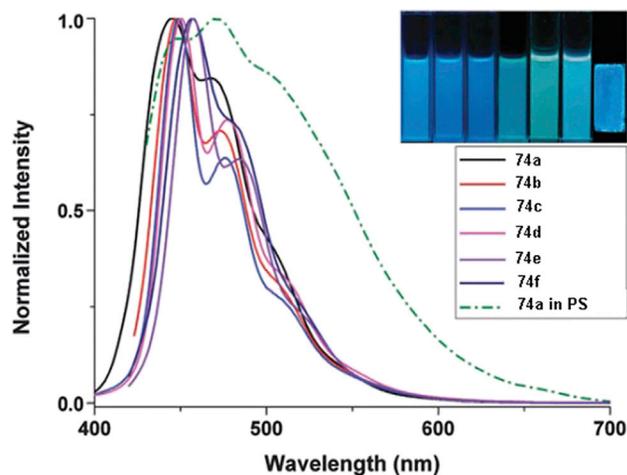
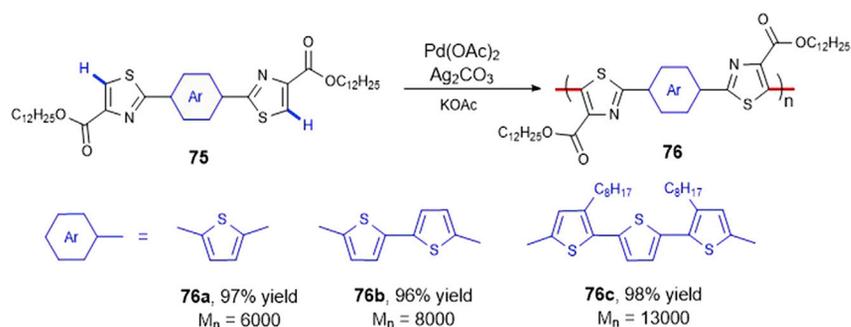
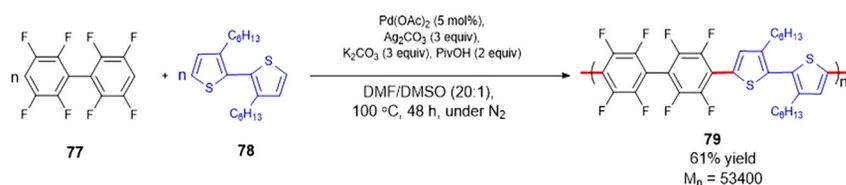


Figure 21. Fluorescence Spectra of Polymers 74a–74f in CHCl₃ and 74a in the PS Film
Adapted from Huang et al.⁵² with permission, copyright 2014 Royal Society of Chemistry.



Scheme 44. Synthesis of Polymers 76a–76c through Pd-Catalyzed Oxidative C–H/C–H Coupling



Scheme 45. Pd-Catalyzed Cross-Dehydrogenative Polycondensation

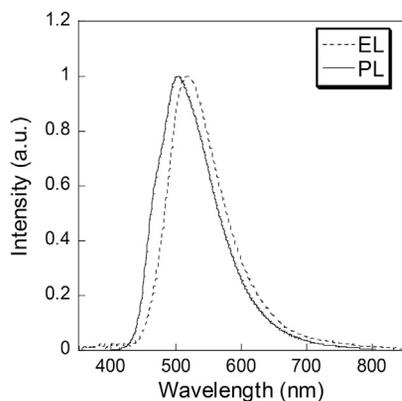
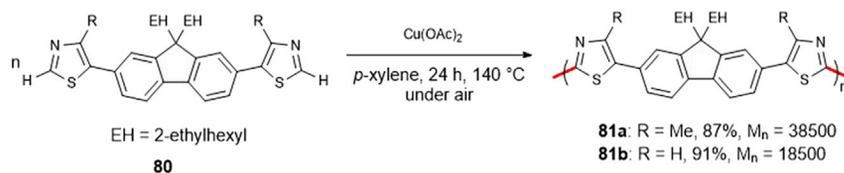


Figure 22. The Photoluminescence Spectrum of a Thin Film of 79 and a Electroluminescent Spectrum of OLED using 79 at 10 V

Reprinted with permission from Aoki et al.⁵⁴
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Scheme 46. Cu-Catalyzed Polycondensation Reactions

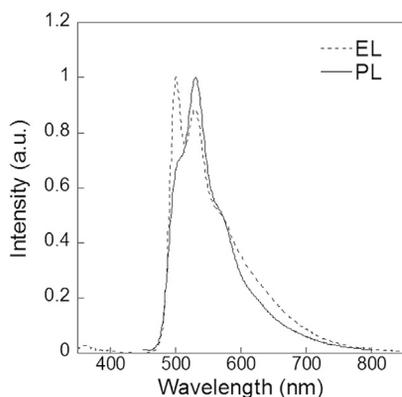
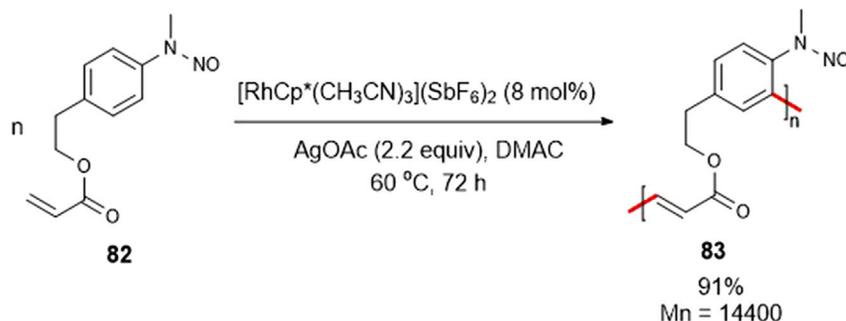


Figure 23. The Photoluminescence Spectrum of a Thin Film of 81b and the Electroluminescent Spectrum of an OLED with 81b at 7 V

Adapted from Faradhiyani et al.⁵⁵ with permission, copyright 2018 Royal Society of Chemistry.

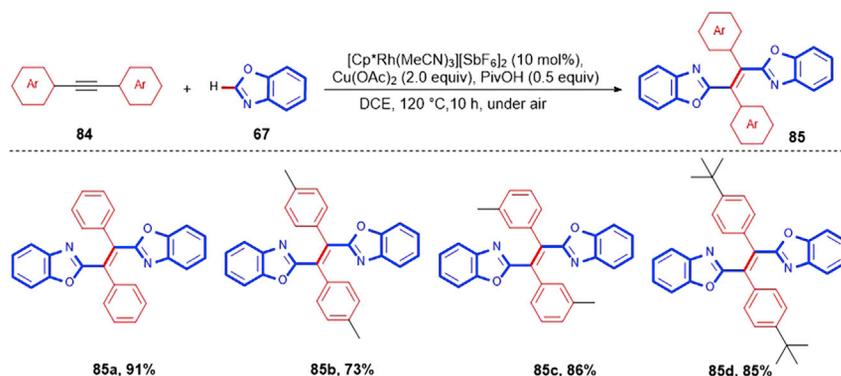


Scheme 47. Synthesis of Poly 83

Transition-Metal-Catalyzed C–H Addition/Annulation Reactions to Build Fluorescent Materials

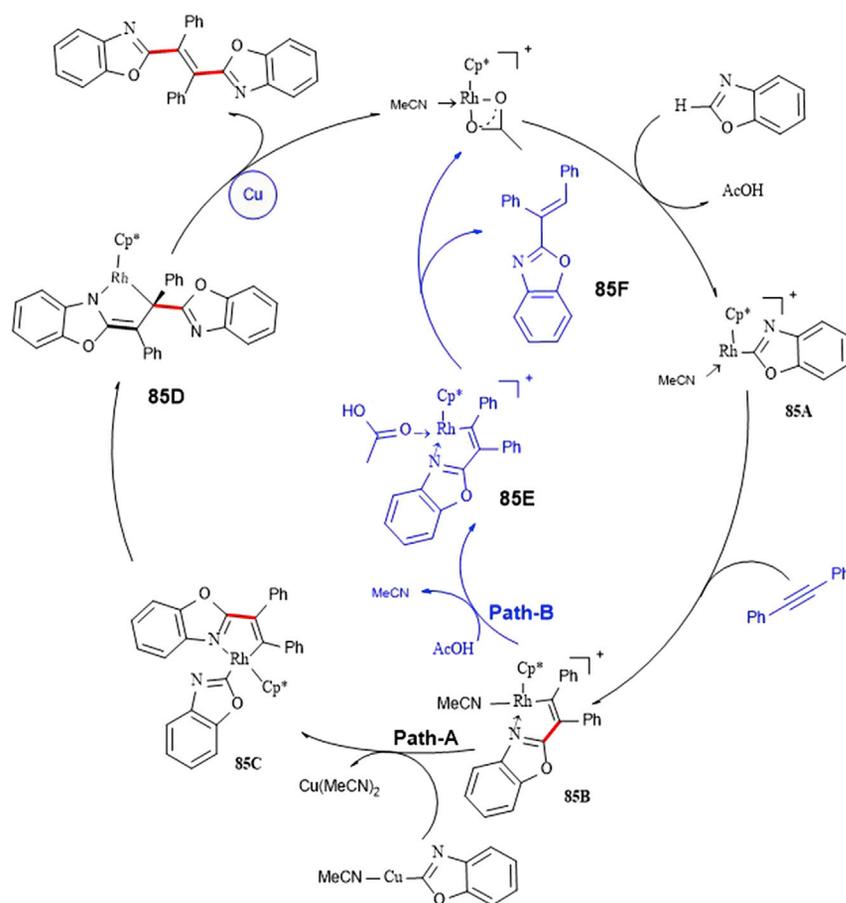
Transition-Metal-Catalyzed C–H Addition Reactions to Build Fluorescent Materials

Tetraarylethylenes as prototypical aggregation-induced emission (AIE) materials have excellent fluorescent properties and have been extensively used in organic light-emitting devices, fluorescent biosensors, and mechanochromic materials.⁴ Tetraarylethylene derivatives can be synthesized through classical olefin formation methods such as the McMurry and the Wittig reactions and classical transition-metal-catalyzed addition of diaryl alkynes with arylating reagents.^{57,58} However, these methods typically suffer from several disadvantages such as rigorous reaction conditions, prefunctionalized substrates, tedious multiple-step synthesis, and low synthetic efficiency, which significantly restricts the rapid construction of structurally diverse tetraarylethylenes. Thus, transition-metal-catalyzed C–H addition and oxidative coupling of alkynes with (hetero)aryl molecules to build tetraarylethylene derivatives would be the most ideal strategy to solve the problems, because this strategy is highly efficient, atom economical, does not require pre-functionalized substrates, and can avoid the use of stoichiometric organometallic reagents.^{10–17}



Scheme 48. Rhodium-Catalyzed C–H Addition/Oxidative Coupling of Alkynes with Azoles

In 2017, Lan and You described a rhodium and copper co-catalyzed C–H addition/oxidative coupling reaction of alkynes with azoles to build a new AIE molecule library.⁵⁹ This reaction showed a broad substrate scope, high yield, and excellent trans-selectivity, thus, providing an opportunity to rapidly assemble a series of tetra(hetero)-arylethylenes (Scheme 48). A tentative mechanism was also proposed



Scheme 49. Proposed Mechanism of Rhodium-Catalyzed Trans-selective C–H Addition/Oxidative Coupling

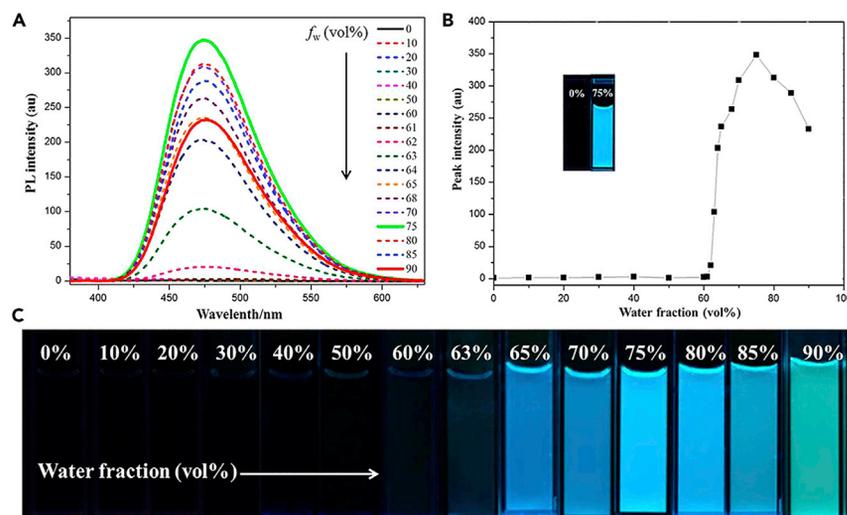


Figure 24. Photophysical Property of 85d

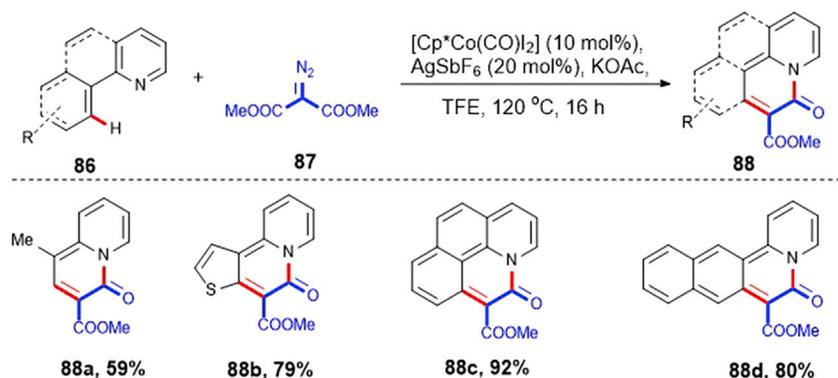
(A) PL spectra of **85d** in THF-water mixtures with different water fractions (f_w).
 (B) Plots of fluorescence intensity versus water fraction in THF/water mixtures. Inset: fluorescent photographs of **85d** in THF/water mixtures ($f_w = 0\%$ and 75%), taken under the illumination of a UV lamp.
 (C) Fluorescence photographs of **85d** (1×10^{-5} M) in THF/water mixtures with different fractions of water. Reprinted with permission from Tan et al.⁵⁹ Copyright 2017 American Chemical Society.

(Scheme 49). First, the cationic rhodium complex reacts with benzoxazole to form an oxazolyrhodium intermediate **85A**. Subsequently, insertion of the alkyne forms the vinylrhodium complex **85B**. In path A, the neutral oxazolyvinylrhodium intermediate **85C** is formed with oxazolyrcopper. Then, nucleophilic addition of the oxazolyl produces the metallahydropyrrole intermediate **85D**. Under the assistance of a Cu(II) species, The desired products could be released from **85D** and the rhodium catalyst can be regenerated. In path B, the intermediate **85E** is formed, which then undergoes a protonation to give the side product **85F** and rhodium catalyst. Notably, these new molecules exhibited strong fluorescence emission with high fluorescence quantum yields in mixtures of high water/THF ratios and solid powder (Figure 24). Furthermore, experimental data demonstrated that these tetra(hetero)arylethylenes were AIE active, which unlocks an opportunity to rapidly screen fluorescence materials for organic light-emitting devices and fluorescent biosensors.

Transition-Metal-Catalyzed C–H Annulation Reactions to Build Fluorescent Materials

Conjugated polycyclic ring systems have attracted great research interest in recent years because of their potential applications in fluorescent bioimaging, organic light-emitting diodes, chemosensors, and nanographene materials.^{60,61} The design and synthesis of novel conjugated polycyclic ring systems with attractive fluorescent properties is highly sought.

In 2015, Glorius and co-workers reported the $[\text{Cp}^*\text{Co}(\text{CO})\text{I}_2]$ -catalyzed coupling of diazo compounds with aromatic and heteroaromatic compounds to build extended π -systems (Scheme 50).⁶⁰ These were a new class of conjugated polycyclic hydrocarbons, which showed broad and intense absorption and emission bands. Additionally, these molecules displayed tunable emission wavelengths both in solution and in the solid state (Figure 25).



Scheme 50. Cobalt(III)-Catalyzed Coupling of Diazo Compounds with Heteroaromatic Compounds via C–H Activation/Annulation

Later on, the Glorius group described the C–H activation and cyclization of 2-arylpyridines with pyridotriazoles by using $[\text{Cp}^*\text{Rh}(\text{CH}_3\text{CN})_3](\text{SbF}_6)_2$ as the catalyst (Scheme 51).⁶¹ Further study showed that a new class of fluorescent scaffolds has been successfully constructed and applied for the detection of metal ions (Figure 26).

In 2017, the Itami group described a one-step annulative π -extension reaction of polycyclic aromatic hydrocarbons and heteroaromatics to obtain various π -extended aromatics by using palladium-catalyzed C–H functionalization method (Scheme 52).⁶² This method avoids the traditional Suzuki coupling reaction, which requires tedious multiple-steps to prepare 2,2'-dibromo-1,1'-biphenyls and arylboronic acids (Scheme 53).⁶³ The molecule 94g exhibited a bright blue-green emission with a broad emission spectrum in dichloromethane and maximum emission wavelength at 464 nm (Figure 27). Its powder displayed a bright yellow fluorescence emission.

In 2018, The same research group developed palladium-catalyzed annulative dimerization of diverse chlorophenylenes to synthesize fused aromatics with a triphenylene core, which are difficult to access otherwise (Scheme 54).⁶⁴ These new fused aromatics represent an emerging class of π -conjugated molecules, which have considerable potential as fluorescence materials for optoelectronic devices. The easy access to fused aromatics with a triphenylene core has highlighted the great

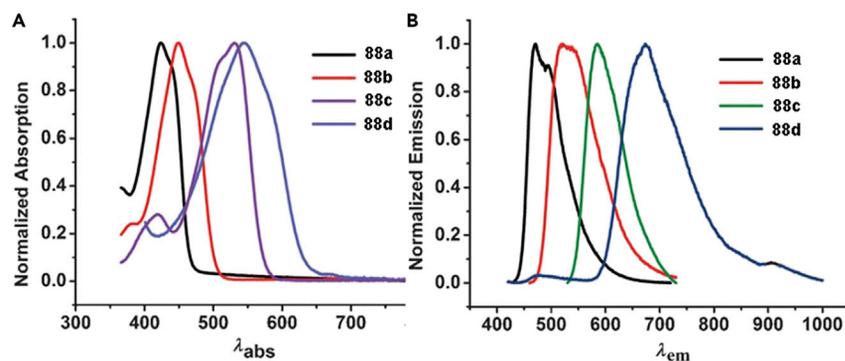
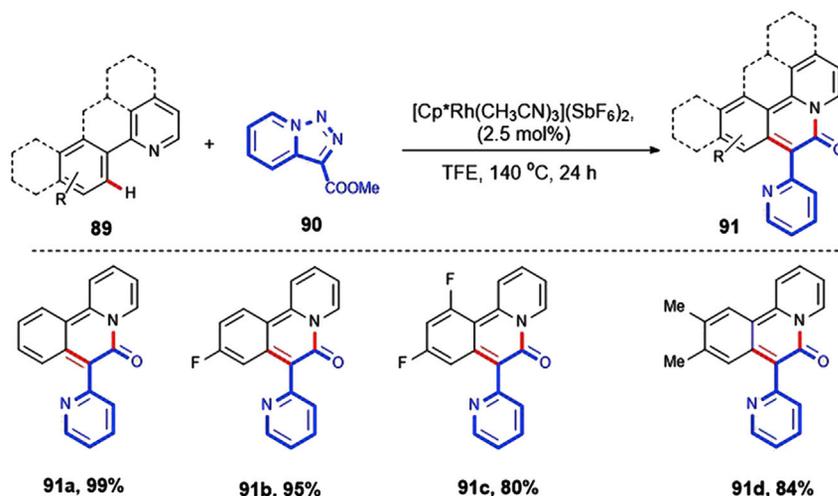


Figure 25. Absorption and Emission Spectra of 88a–88d

Absorption (A) and emission (B) spectra of 88a–88d in CH_2Cl_2 at RT (10^{-5} M). Adapted from Zhao et al.⁶⁰ with permission, copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.



Scheme 51. Rh^{III}-Catalyzed C–H Bond Activation/Annulation

appeal of C–H functionalization reactions in discovering and building novel organic functional molecules.

A rhodium-catalyzed annulation of ethyl benzimidates with α -aroyl sulfur ylides was achieved using NaOAc as the base by the Cheng group in 2012.⁶⁵ A series of functionalized isoquinazolones were obtained in moderate to high moderate yields (Scheme 55). These pyrano[4,3,2-ij]isoquinoline derivatives were a novel type of

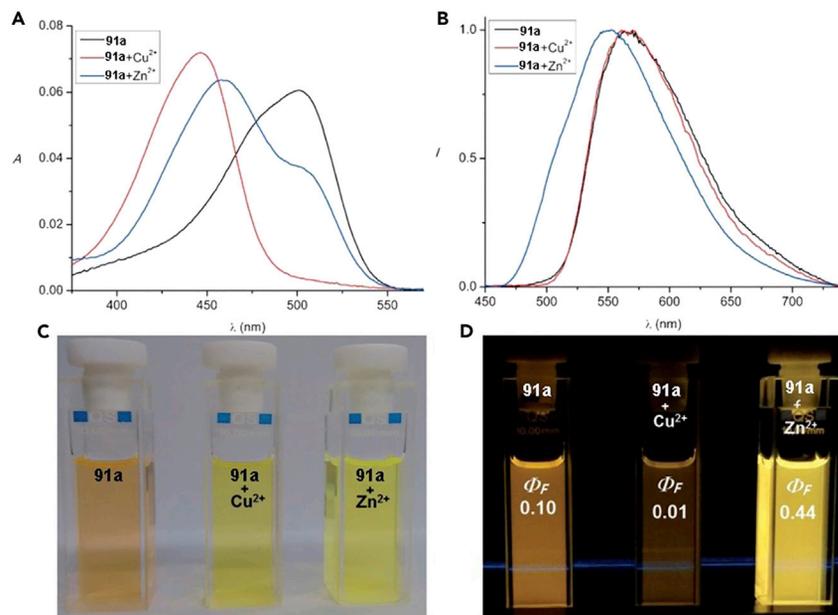
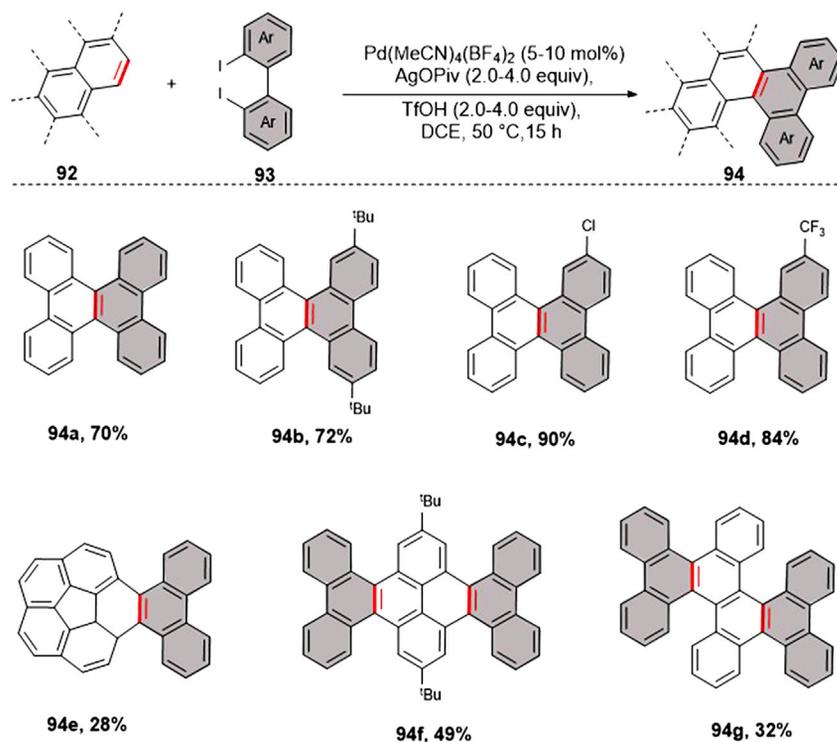


Figure 26. Photophysical Property and Photos of **91a**

(A and B) Absorption (A) and emission (B) spectra of compound **91a** in the presence of Cu(ClO₄)₂ or Zn(ClO₄)₂.

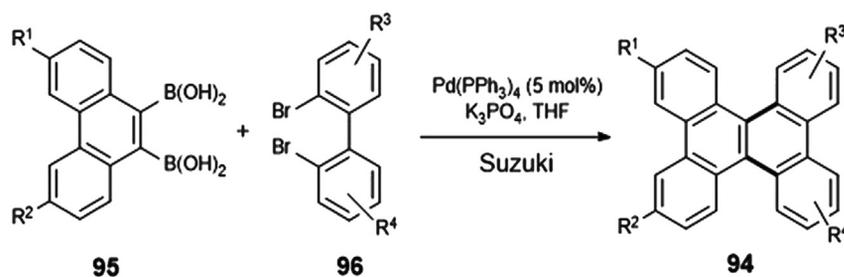
(C and D) Photos of **91a** in a solution of CH₂Cl₂ and with Cu(ClO₄)₂ and Zn(ClO₄)₂ under ambient light (C) and UV light (D). Adapted from Kim et al.⁶¹ with permission, copyright 2015 Wiley-VCH Verlag GmbH & Co. KGaA.



Scheme 52. The Palladium-Catalyzed Annulative π -Extension Reaction

fluorescent materials with emission maxima around 465 nm and Stokes shifts up to 141 nm (Figure 28).

Nitrogen-containing heterocycles are important scaffolds in material science due to their excellent photophysical properties.¹⁰ The development of efficient methods to synthesize these molecules is of great research interest in academia and industry. In 2015, Wu and co-workers reported the palladium-catalyzed cyclization and C–H activation cascade reaction of 2-amino-*N*-arylbenzohydrazides with triethyl orthobenzoates to synthesize indazolo[3,2-*b*]quinazolinone derivatives in moderate to excellent yields (Scheme 56).⁶⁶ A possible mechanism for this reaction was proposed (Scheme 57). The 2-phenyl-3-(phenylamino)quinazolinone (**105A**) is generated by condensation and cyclization of 2-amino-*N*-phenylbenzohydrazide **103** and triethyl orthobenzoate. Next, C–H activation of **105A** gives the cyclic palladium complex **105B**, which then undergoes “rollover” cyclometalation to form the six-membered palladacycle intermediate **105C**. Finally, the reductive elimination of intermediate



Scheme 53. The Conventional Synthetic Method for **94**

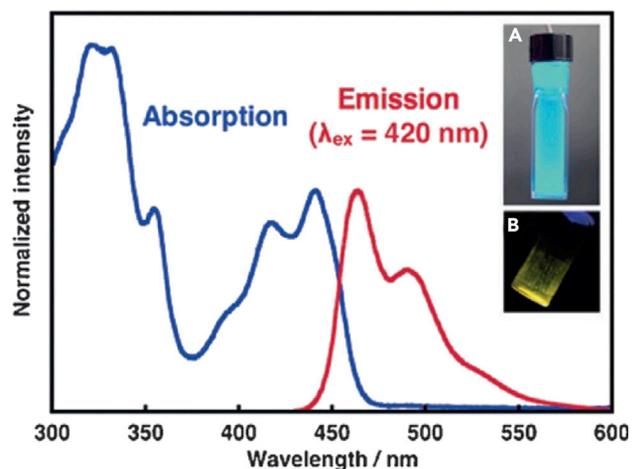


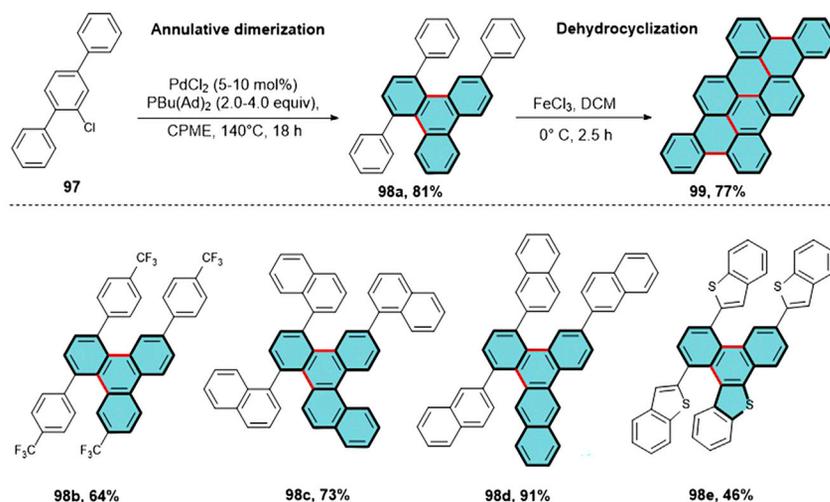
Figure 27. Normalized UV-Vis Absorption and Emission Spectra of 94g in CH₂Cl₂

(A) Blue-green emission of **94g** in CH₂Cl₂ excited by UV light.

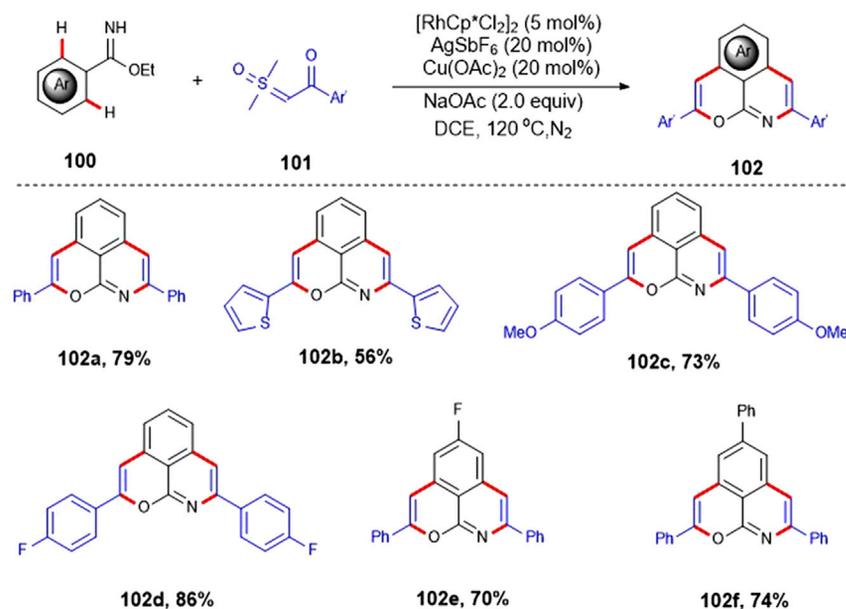
(B) Solid-state yellow emission of **94g** excited by UV light. Adapted from Matsuoka et al.⁶² with permission, copyright 2017 Wiley-VCH Verlag GmbH & Co. KGaA.

105C affords the desired product and Pd(0) species. Indazolo[3,2-*b*]quinazolinones displayed absorption peaks at 241 and 357 nm and blue fluorescence emission in the range of 403–430 nm in CHCl₃. These novel fluorescent dyes exhibited outstanding Stokes shifts between 68 and 81 nm and high fluorescence efficiency, demonstrating that indazolo[3,2-*b*]quinazolinones are a new class of blue fluorophores in the field of organic fluorescent materials.

In 2017, B. Charette and co-workers disclosed a palladium-catalyzed cyclodehydration and intramolecular C–H arylation reaction to construct a series of benzo[*a*]imidazo[2,1,5-*c,d*]indolizines in good yields (Scheme 58).⁶⁷ A plausible concerted metalation-deprotonation mechanism was proposed, involving: (1) the oxidative addition of Pd(0) to intermediate Pd(II) (**107A**) by aryl bromide **106**, (2) the anion exchange to generate the palladium intermediate **107B**, (3) the C–H activation to give



Scheme 54. Palladium-Catalyzed Annulative Dimerization of Aryl Halides



Scheme 55. Rhodium-Catalyzed Annulation between Ethyl Benzimidates and α -Aryloxy Sulfoxides

rise to the six-membered palladium ring **107D**, (4) reductive elimination to produce the desired product **107a** (Scheme 59). These benzo[a]imidazo[2,1,5-c,d]indolizines generally showed blue fluorescence emissions that span 461–489 nm (Figure 29).

Coumarin compounds have been extensively applied in many fields because of their excellent biological properties, including anti-inflammatory, antioxidant, antimicrobial, and anticancer capabilities.⁶⁸ In addition, they have shown excellent photophysical properties such as strong light absorption, high fluorescence quantum yields with large Stokes shifts. Very recently, Gogoi and co-workers reported a Pd(II)-catalyzed oxidative annulation reaction of 4-hydroxycoumarin and arylcarboxylic acid to synthesize a wide range of structurally diversified bis-coumarins in

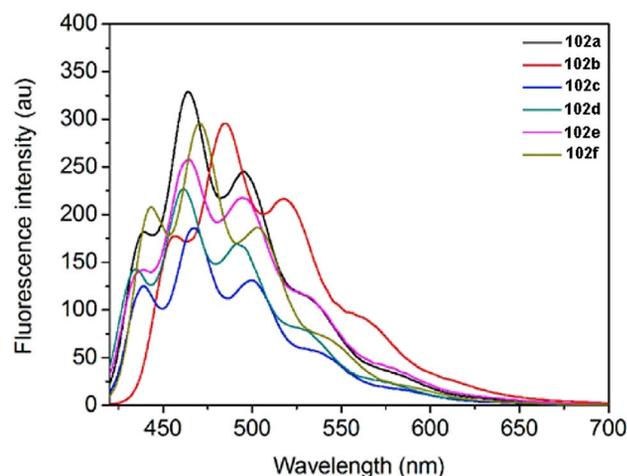
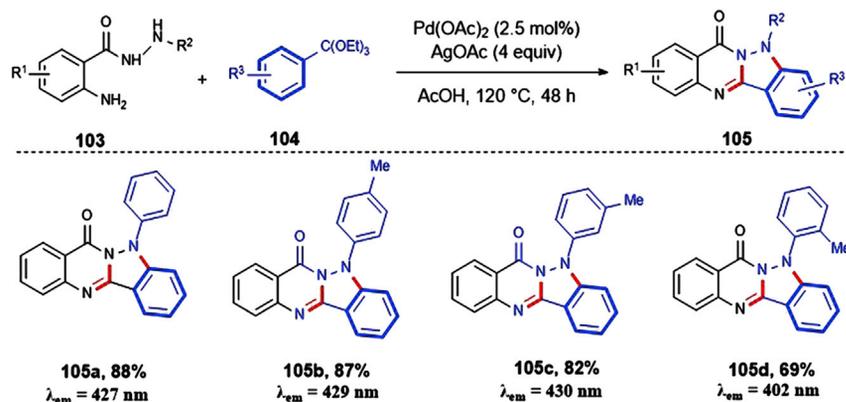


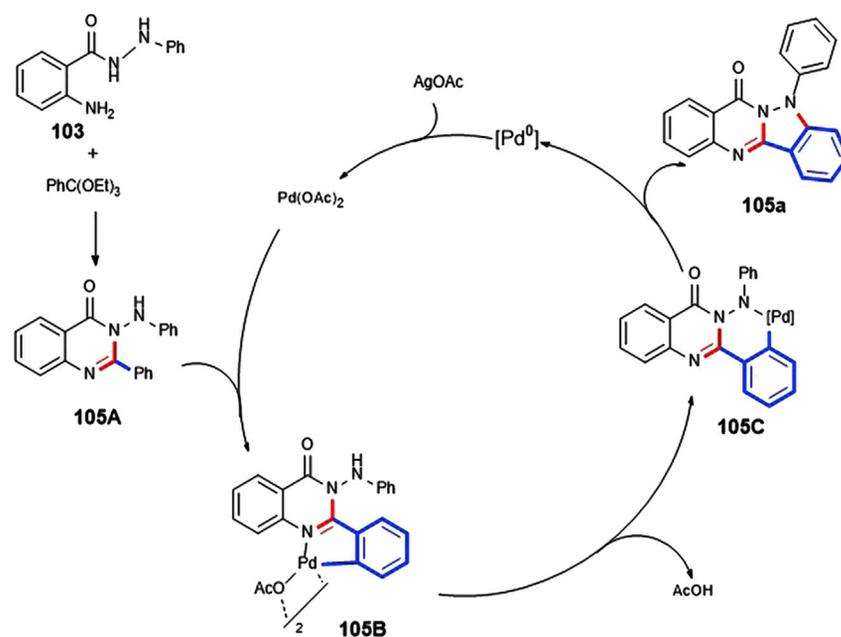
Figure 28. Normalized Emission Spectra of 102a–102f in CH₂Cl₂
Adapted from Wu et al.⁶⁵ with permission, copyright 2018 American Chemical Society.



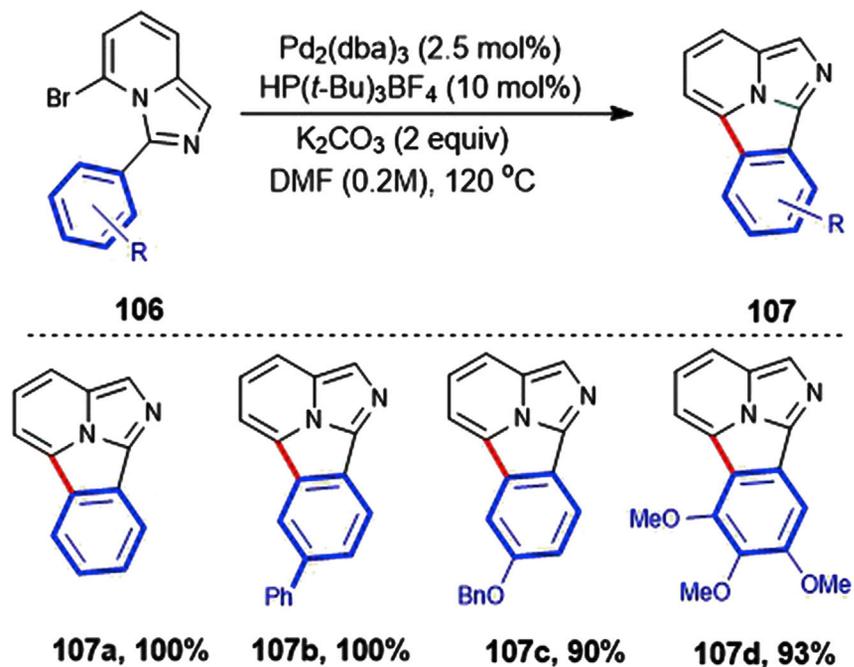
Scheme 56. The Palladium-Catalyzed Cyclization/C–H Activation Cascade Reaction

moderate to high yields (Scheme 60).⁶⁸ This method avoids traditional low-efficiency condensation reactions (Scheme 61). The photophysical properties of these bis-coumarins were investigated, and some of these compounds exhibited strong fluorescence emission with high fluorescence quantum yields (Figure 30). As a result, these molecules have potential applications in fluorescent probes, dye-sensitized solar cells, OLEDs, and other electronic devices.

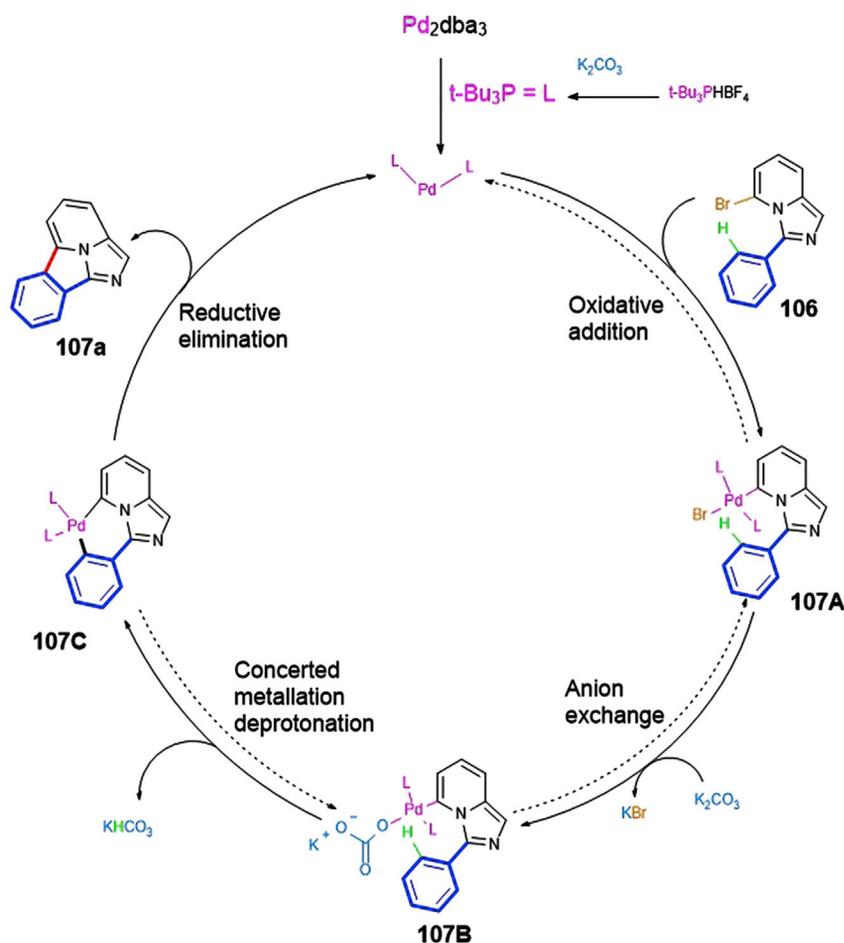
Recently, the one-pot synthesis of phenanthrone-type polyheterocycles was demonstrated by Lan and co-workers (Scheme 62).⁶⁹ In this process, rhodium(III)-catalyzed *ortho*-heteroarylation of indolyl ketones through oxidative C–H/C–H cross-coupling and subsequent copper(II)-promoted intramolecular cyclization produced the fluorescent material molecules. A plausible pathway was proposed in Scheme 63. First, the reactive cationic rhodium species $[\text{Cp}^*\text{Rh}^{\text{III}}]$ is generated from $[\text{Cp}^*\text{RhCl}_2]_2$ in the presence of AgSbF_6 . Then, the rhodium species reacts with 112 through chelation-assisted C–H activation to produce five-membered cyclorhodium intermediate



Scheme 57. The Plausible Mechanism for the Formation of Indazolo[3,2-b]Quinazolinones



Scheme 58. Synthesis of Benzo[a]imidazo[2,1,5-c,d]Indolizines



Scheme 59. The Plausible Mechanism for the Intramolecular C–H Arylation of 106

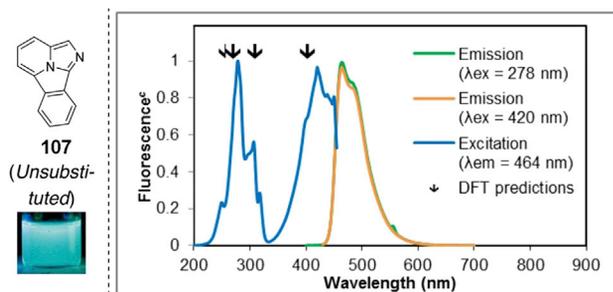
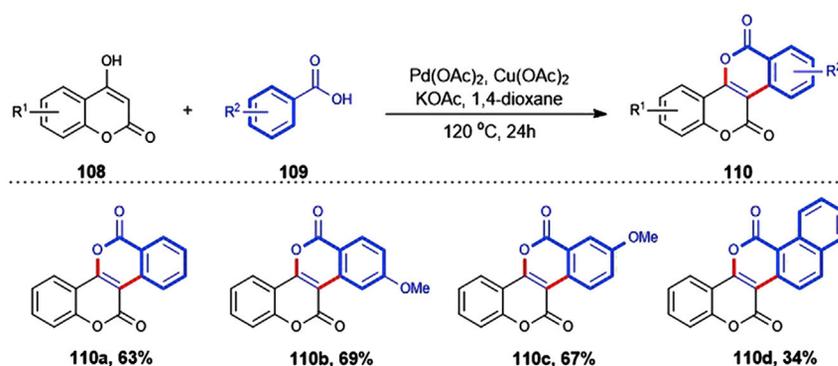
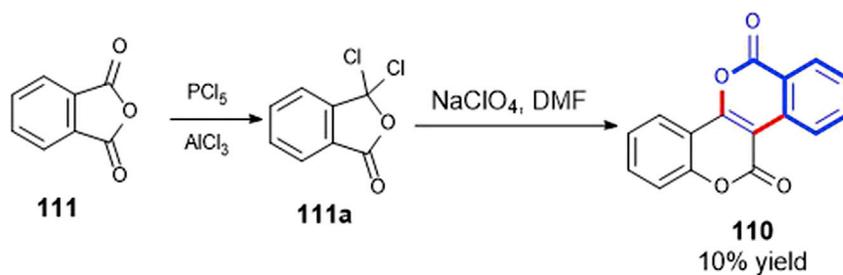


Figure 29. The Emission and Excitation Spectra of 107a

Photo of 107a in a solution of MeOH. Adapted from Lévesque et al.⁶⁷ with permission, copyright 2017 American Chemical Society.



Scheme 60. Synthesis of 110



Scheme 61. The Conventional Synthetic Method for 110

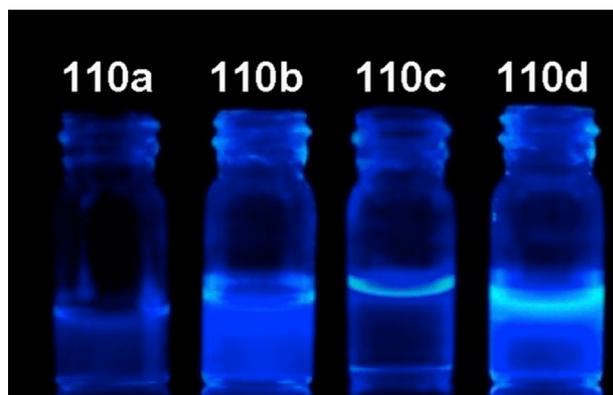
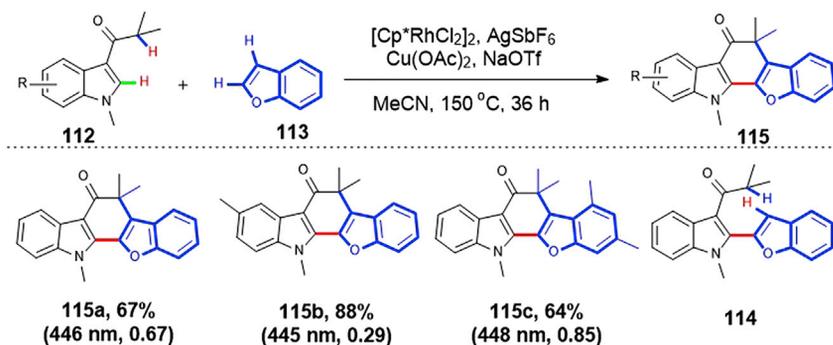


Figure 30. Photos of Compounds 110a–110d under UV Irradiation

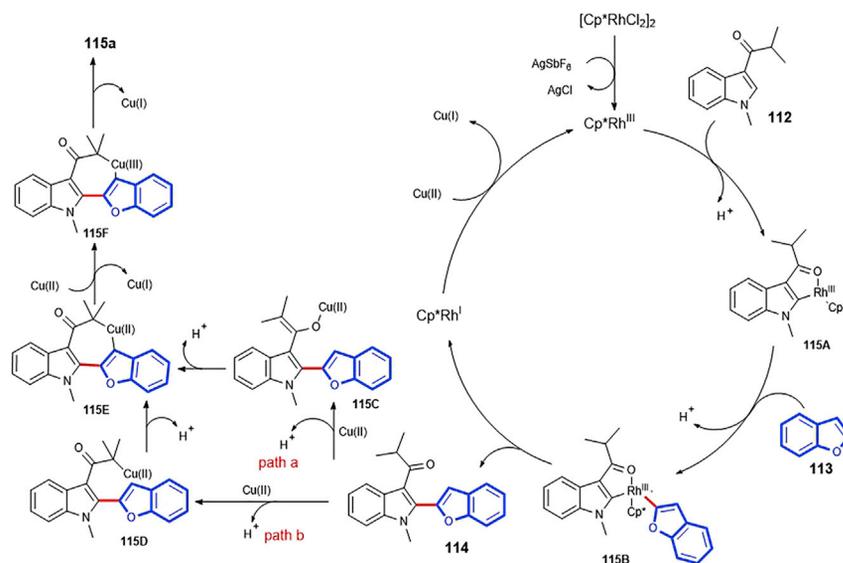
Adapted from Sharma et al.⁶⁸ with permission, copyright 2020 American Chemical Society.



Scheme 62. Synthesis of Phenanthrone-type Polyheterocycles

Emission maxima and fluorescence quantum yields in CH_2Cl_2 (1.0×10^{-5} M) are reported in parentheses.

115A, which then reacts with **113** to give diarylrhodium complex **115B**. Subsequently, the reductive elimination of **115B** generates the intermediate **115** and Rh(I) species. The latter is oxidized to Rh(III) species by the oxidant Cu(OAc)_2 . **115** reacts with Cu(OAc)_2 to produce **115C** (path a) or **115D** (path b), which then undergoes an intramolecular C–H activation to give the seven-membered cyclocopper intermediate **115E**. The cyclocopper intermediate **115E** is oxidized by another Cu(II) species to generate the Cu(III) complex intermediate **115F**. Finally, the reductive elimination of **115F** produces the final product. A novel class of blue-emitting fluorophores with high quantum yields was constructed using this highly efficient one-pot synthetic strategy. Surprisingly, the cyclization product **115a** exhibited a high fluorescence quantum yield of 67% with a narrower FWHM (full widths at half-maximum) (66 nm), while the uncyclized intermediate **114** showed a relatively low quantum yield of 12% (Figure 31). Moreover, the cyclization product **115c** displayed a very high quantum yield of 85% and pure blue emission at approximately 441 nm with CIE₁₉₃₁ coordinates of (0.15, 0.09), which is very close to EBU coordinates of (0.15, 0.06) (Figure 31).



Scheme 63. The Plausible Mechanistic Pathway

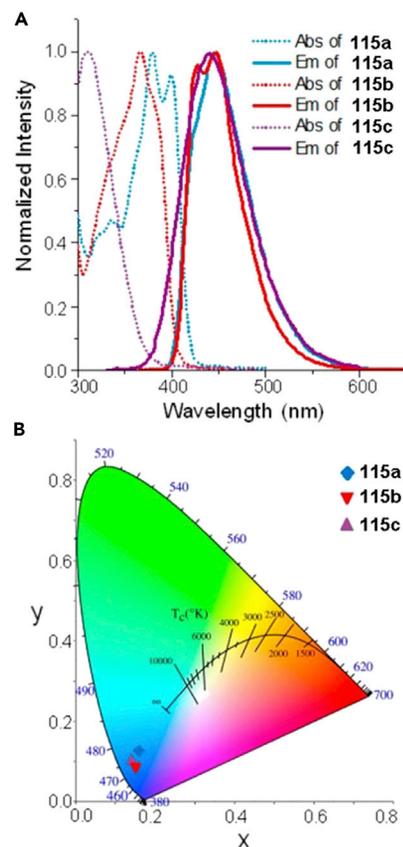


Figure 31. Photophysical Property of 115a-115c

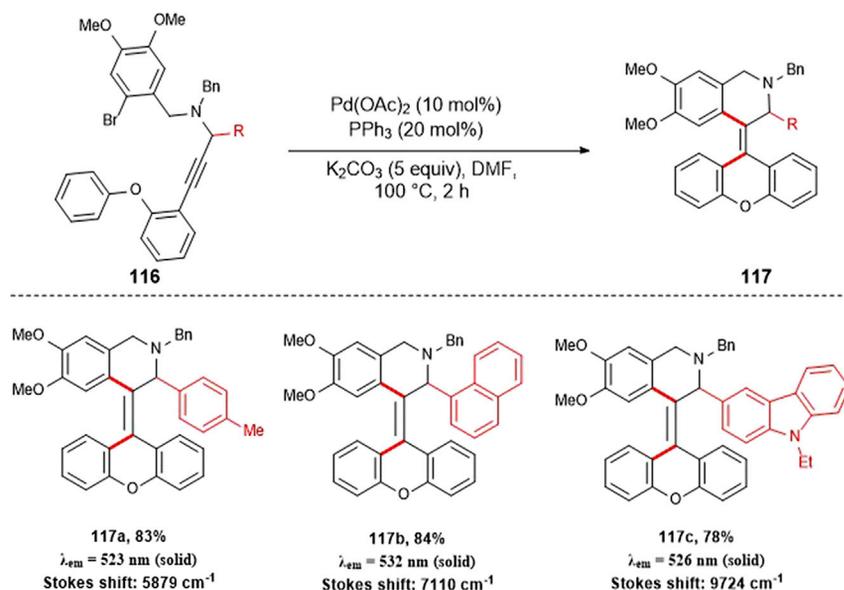
(A) Normalized absorption spectra (dotted lines) and fluorescence emission spectra (solid lines) in DCM (1×10^{-5} M).

(B) Emission color coordinates of 115a–115c in the CIE₁₉₃₁ chromaticity diagram. Adapted from Pu et al.⁶⁹ with permission, copyright 2019 American Chemical Society.

Transition-Metal Catalyzed C–H Addition and Annulation Reactions to Build Fluorescent Materials

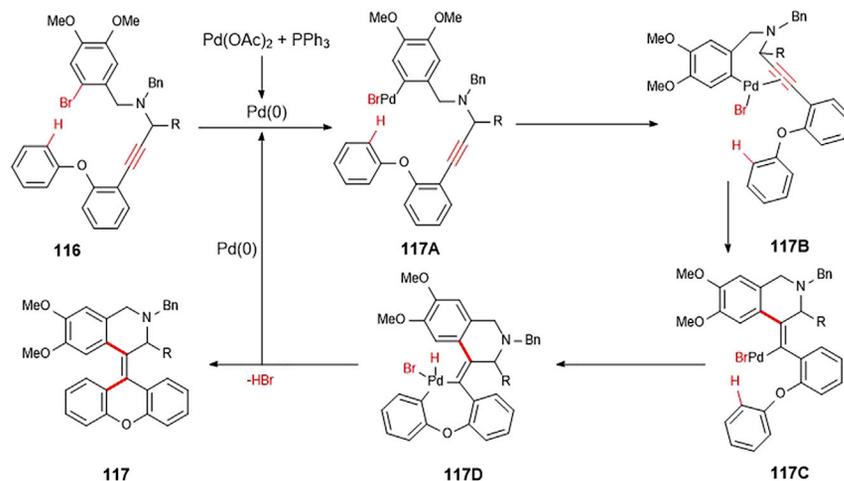
Conjugated tetra-substituted olefins were widely used in photo-responsive organic materials, molecular devices, and biological studies.⁷⁰ The development of efficient and simple methods for the construction of conjugated tetra-substituted olefins has attracted much attention from organic chemists. In 2013, Perumal reported the palladium-catalyzed cyclization/C–H activation of 2-bromobenzyl-*N*-propargylamine derivatives to synthesize a new class of tetra-substituted olefins (Scheme 64).⁷¹ A plausible mechanism was proposed. First, the aryl palladium complex 117A is generated by oxidative addition of aryl bromide 116 with Pd(0) species. Then, π -coordination of the internal alkyne to form palladium intermediate 117B and subsequent insertion provides the carbopalladation complex 117C, which then undergoes a C–H activation step to give the seven-membered palladium ring 117D. Finally, reductive elimination of 117D forms the final product and Pd(0) species (Scheme 65). A series of tetra-substituted olefins could be obtained by this method. These compounds were demonstrated as novel AIE materials, which showed intense solid-state fluorescence emission and large Stoke shifts.

In 2013, the rhodium(III)-catalyzed C–H bond addition of azobenzenes to aldehydes was demonstrated by Ellman and Lavis (Scheme 66).⁷² A new class of readily

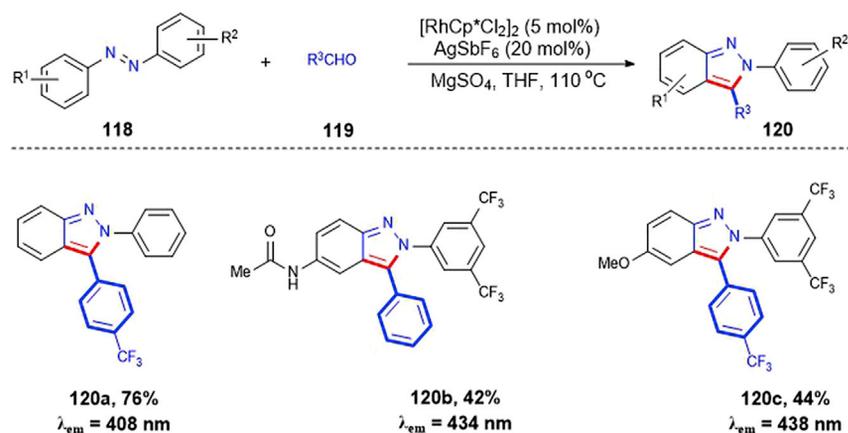


Scheme 64. Palladium-Catalyzed Cyclization/C–H Activation of 2-Bromobenzyl-N-Propargylamine Derivatives

prepared fluorophores was obtained by this protocol. The conventional methods for preparing these materials usually involve multi-step reactions, inaccessible synthetic precursors, or unavoidable pre-functionalization (Scheme 67). These novel dyes showed high extinction coefficients and large Stokes shifts, which has a great potential as biological probes. Furthermore, a plausible mechanism involving a rhodium(III)-catalyzed C–H bond addition process was proposed (Scheme 68). First, the coordination of the azo functional group to Rh^{III} and subsequent *ortho*-C–H bond activation produce a rhodium intermediate, which then reacts with aldehyde 119 to give the alcohol 120B. Subsequently, 120B undergoes an intramolecular nucleophilic substitution to form 120C, which rapidly aromatizes to generate the desired product 120.

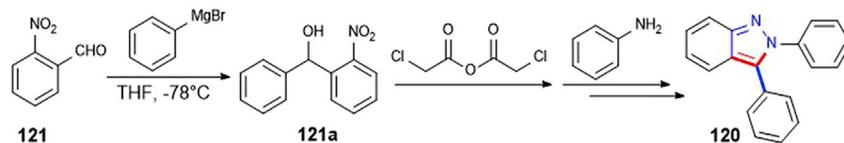


Scheme 65. The Plausible Mechanism for Formation of Tetrasubstituted Olefins

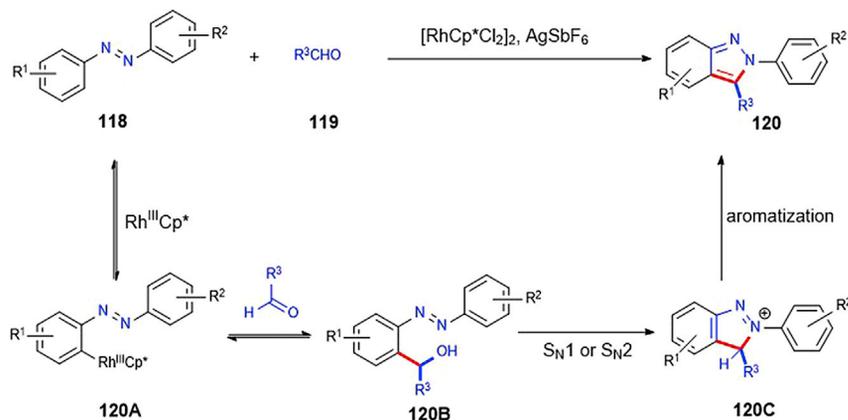


Scheme 66. Rhodium(III)-Catalyzed C–H Bond Addition of Azobenzenes to Aldehydes

Fluorescence measurements taken in 10 mM HEPES pH 7.3.

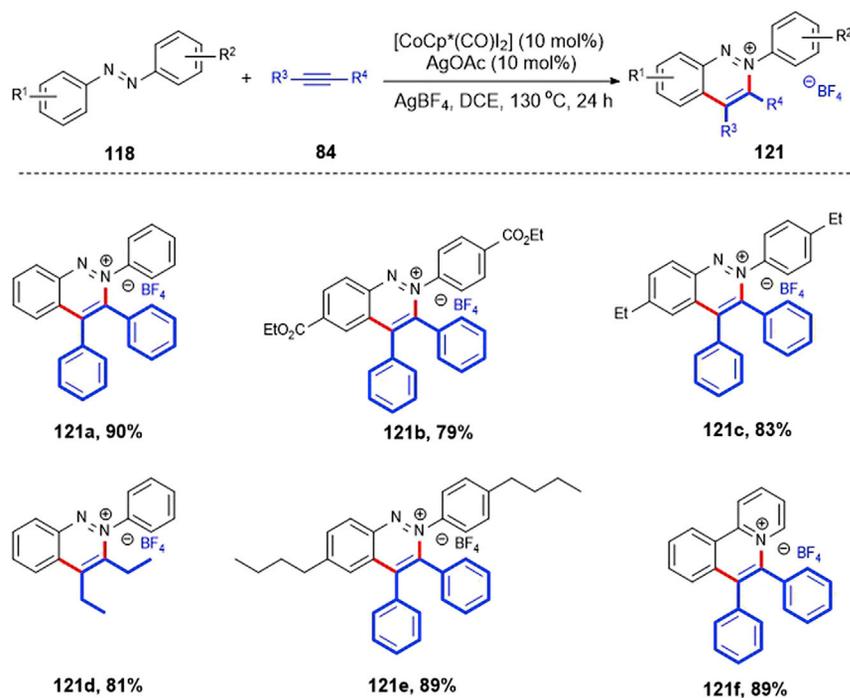


Scheme 67. The Conventional Synthetic Method for 120



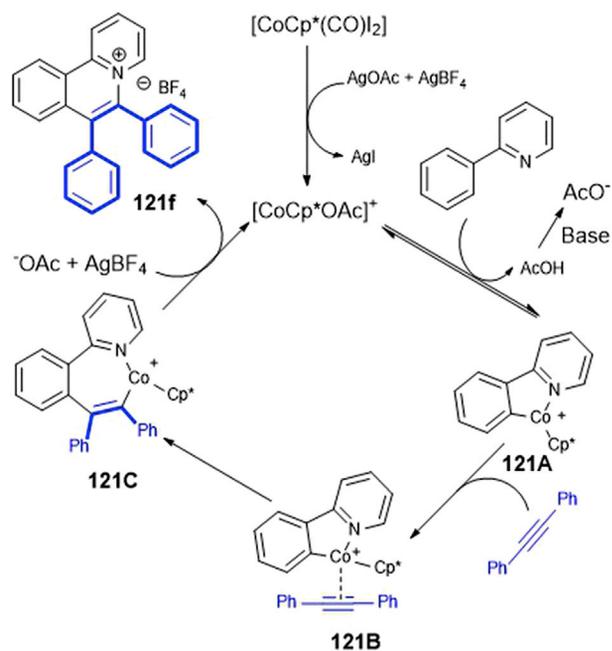
Scheme 68. A Plausible Mechanism for the Formation of 120

Alkynes can be used as very useful building blocks for π -extension. The transition-metal-catalyzed sequential C–H activation and cyclization of alkynes to extend π -systems has emerged as a powerful synthetic strategy and has aroused great interest among scientists in chemical research.^{10,11} N-heterocyclic quaternary ammonium salts are found in the core structures of many organic fluorescent materials.¹⁰ In 2015, Chien-Hong Cheng and co-workers reported cobalt-catalyzed oxidative annulation reactions of nitrogen-containing arenes with alkynes to obtain quaternary ammonium salts, including pyridisoquinolinium, isoquinolinium, quinolinium, and cinnolinium salts, in good to excellent yields (Scheme 69).⁷³ A plausible mechanism involving a C–H activation and annulation process was proposed (Scheme 70). Specifically, the cobalt (III) complex $[\text{Cp}^*\text{Co}(\text{OAc})]^+$ is generated by the exchange of iodide ligands in $[\text{CoCp}^*(\text{CO})_2]$ with AgOAc . Then, nitrogen-directed reversible



Scheme 69. Synthesis of Cinnolinium Salts **121a–121f**

ortho C–H bond cleavage gives rise to the five-membered cobalt intermediate **121A**. Subsequently, π -coordination of the alkyne affords **121B**. Following this, insertion of the alkyne into the Co–C bond forms the seven-membered cobaltacyclic intermediate **121C**. Finally, reductive elimination of **121C** produces the final product. Furthermore, the photophysical properties of the selected quaternary



Scheme 70. A Plausible Reaction Mechanism for the Formation of **121**

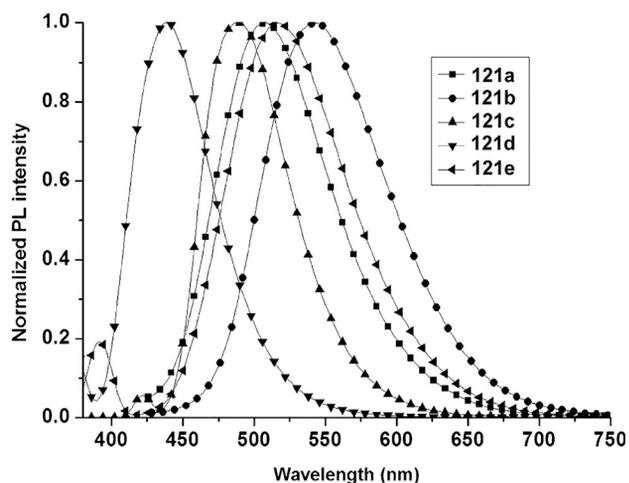
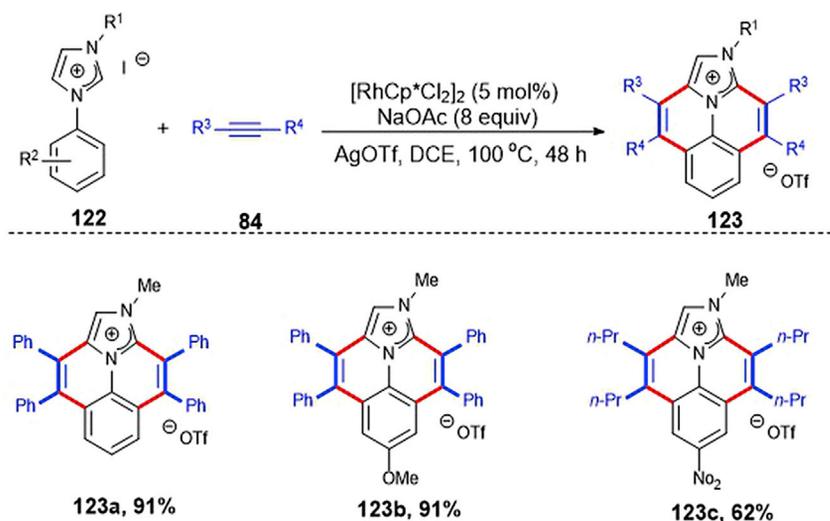


Figure 32. Photoluminescence Spectra of Selected Cinnolinium Salts (121a–121e) in DCM

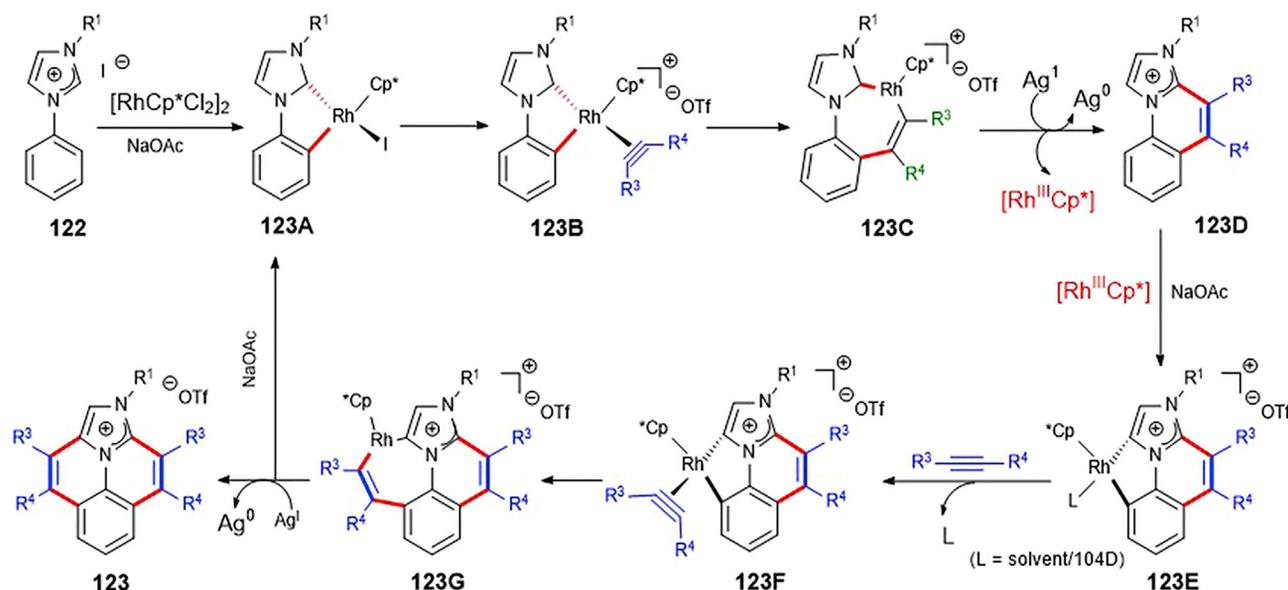
Adapted from Prakash et al.⁷³ with permission, copyright 2016 Wiley-VCH Verlag GmbH & Co. KGaA.

ammonium salts were studied, which showed violet-to-green fluorescence emissions at 430–550 nm (Figure 32). These fluorescent materials have great potential in the preparation of organic light-emitting diodes. This represented the first example of achieving cobalt-catalyzed C–H oxidative annulation of arenes with alkynes under an external oxidant and thus would inspire the development of novel applicable OLED materials.

Alkynes can be used as non-pre-functionalized starting materials to build conjugated polycyclic ring systems through sequential C–H activation and cyclization.^{10,11} The conjugated imidazolium salts are a type of very promising fluorescent materials. In 2015, Choudhury and co-workers described a rhodium(III)-catalyzed cascade double aromatic C–H activation annulation to synthesize a set of benzo[*ij*]imidazo[2,1,5-*de*]-quinolininium scaffold-containing polycyclic heteroaromatic molecules (Scheme 71).⁷⁴ A plausible catalytic route is shown in Scheme 72. First, coordination of the



Scheme 71. Rhodium(III)-Catalyzed C–H Activation-Annulation

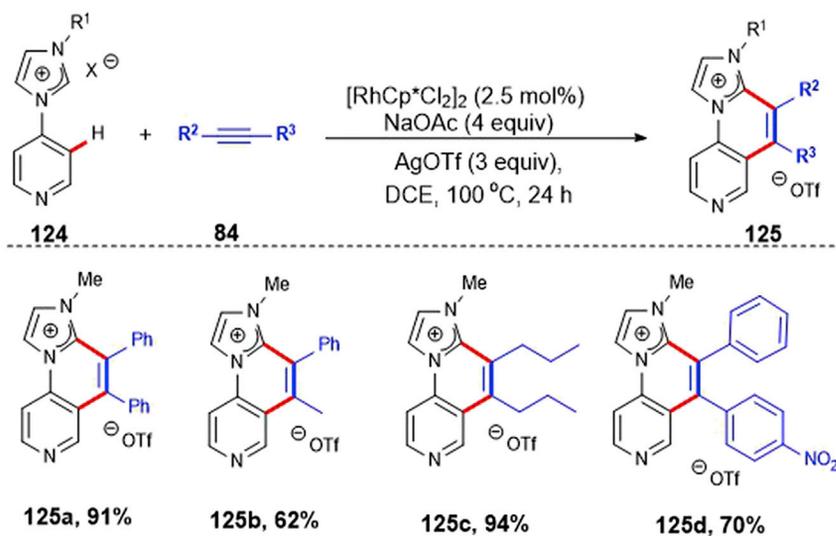


Scheme 72. The Plausible Catalytic Cycle for the Formation of 123

NHC ligand to Rh^{III} and subsequent *ortho*-C–H bond activation produce a five-membered rhodacycle 123A. Then, iodine abstraction from intermediate 123A by AgOTf followed by π-coordination of the alkyne forms the rhodacycle intermediate 123B. Subsequent insertion provides the seven-membered rhodacycle intermediate 123C. Next, reductive elimination affords the mono-annulated product 123D and a Cp*Rh^{III} species. Subsequently, 123D reacts with Cp*Rh^{III} in the presence of NaOAc to give rhodacycle intermediate 123E, which then undergoes π-coordination with an alkyne to generate rhodacycle intermediate 123F. Subsequent insertion forms the intermediate 123G which undergoes reductive elimination to generate the product 123 and the Cp*Rh^{III} species. A series of nicely decorated polycyclic heteroaromatic molecules containing benzo[*ij*]imidazo[2,1,5-*de*]quinolizinium architectures were designed and synthesized. These molecules showed strong fluorescence emission at 455–465 nm range, which have great potential as new luminescent materials.

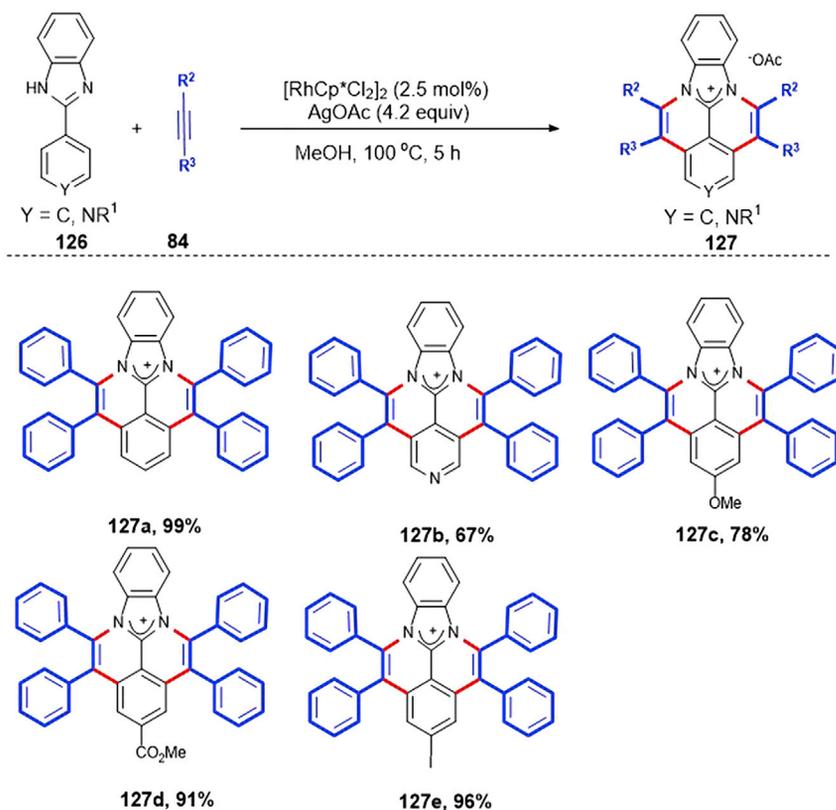
In a following study, a rhodium(III)-catalyzed intermolecular annulation of poorly reactive pyridine backbones with a variety of internal alkynes was achieved using AgOTf as the oxidant and halide abstractor by the same group (Scheme 73).⁷⁵ A variety of nicely decorated imidazo-[1,2-*a*][1,6] naphthyridinium motifs were obtained from this newly developed protocol and showed strong blue to green fluorescence emission. Especially, some of imidazo-[1,2-*a*][1,6] naphthyridinium motif-containing mono- and bis-annulated products showed strong fluorescence emission at a broad range of 360–475 nm wavelength.

In 2017, the Saá group reported the Rh(III)-catalyzed double-oxidative annulation of 2-arylbenzimidazoles with alkynes to obtain a novel class of *N*-doped cationic PAHs (polycyclic aromatic hydrocarbons) in excellent yields (Scheme 74; Figure 33).⁷⁶ These novel PAHs exhibited strong fluorescence emission, which has promising applications in optoelectronic materials. In addition, phenyl- and diphenylmethanedi-amine derivatives could be obtained by reducing the azafluoranthemium salt in the presence of LiAlH₄ or PhLi.



Scheme 73. Rh^{III}-Catalyzed NHC-Directed Annulation of Pyridine Backbones

In recent years, the development of polycyclic heteroaromatic (PHA) materials has attracted considerable attention in view of their great potential for various applications such as fluorescent devices and organic semiconductors, etc.^{10,11} However, realizing a design strategy for synthesis of polycyclic heteroaromatic materials is a



Scheme 74. Synthesis of Fluorophore Dyes 127a–127e via Rh^{III}-Catalyzed Annulation of Pyridine Backbones

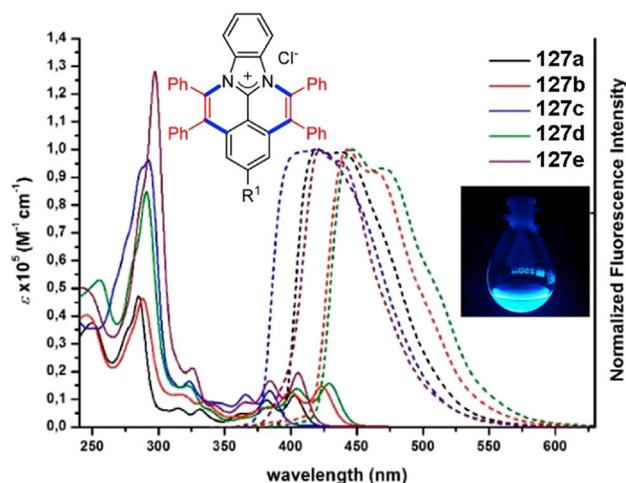
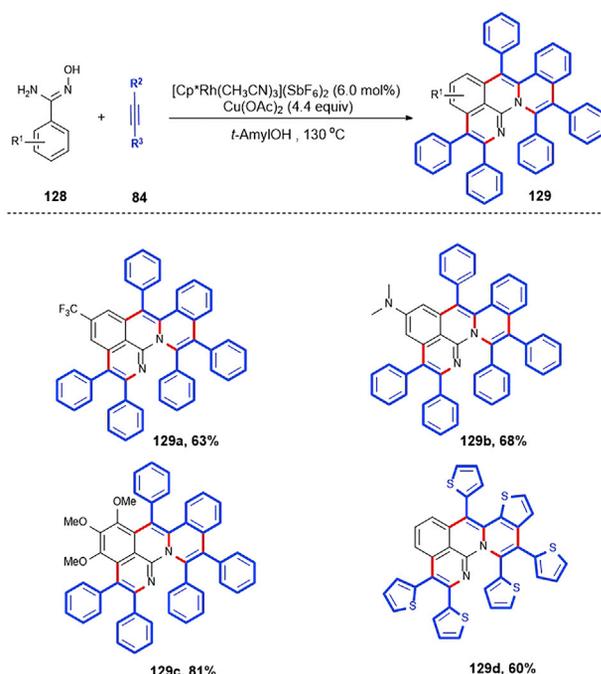


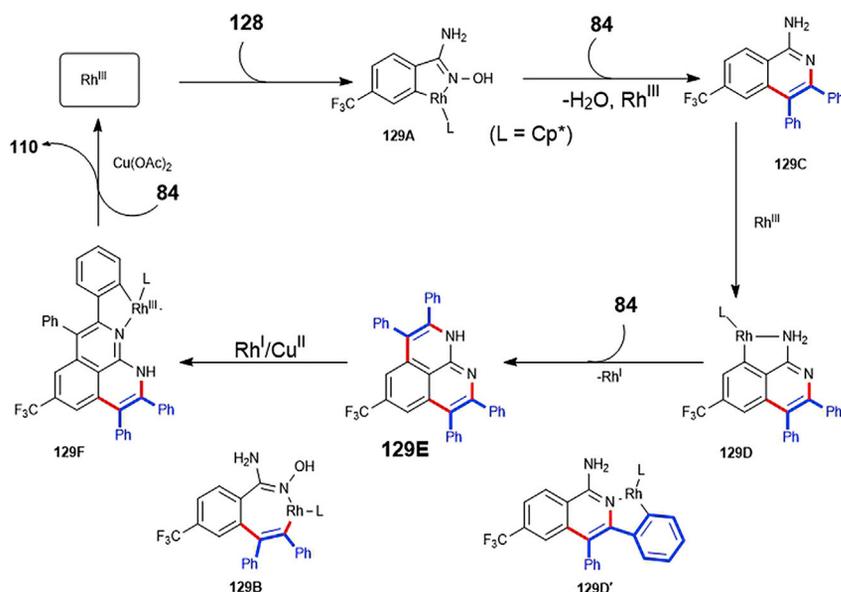
Figure 33. Photoluminescence Spectra of 127a–127e in DCM

Adapted from Villar et al.⁷⁶ with permission, copyright 2017 American Chemical Society.

challenging task. In 2014, Cheng and Chuang developed the rhodium-catalyzed multiple C–H activation and annulation of *N*-hydroxybenzamidines and alkynes to obtain highly substituted naphthyrindine-based polyheteroaromatic compounds in good and excellent yields (Scheme 75).⁷⁷ $[\text{Cp}^*\text{Rh}(\text{CH}_3\text{CN})_3](\text{SbF}_6)_2$ was used as the catalyst and *tert*-amyl alcohol as the solvent in this study. A plausible mechanism involving a C–H activation process was proposed (Scheme 76). First, the coordination of the oxime nitrogen atom to Rh^{III} and subsequent *ortho*-C–H bond activation produce a five-membered intermediate **129A**, which then undergoes π -coordination with an alkyne and subsequent insertion to provide the seven-membered



Scheme 75. Synthesis of Fluorophore Dyes 129a–129d via Rhodium-Catalyzed C–H Bond Activation of *N*-hydroxybenzamidines and Alkynes



Scheme 76. The Proposed Mechanism for the Formation of **129**

cyclorhodium intermediate **129B**. This intermediate then undergoes reductive elimination to form 1-aminoisoquinoline **129C** and a Rh^{III} species. Subsequently, coordination of the amine nitrogen atom of **129C** to the Rh^{III} followed by C–H bond activation, insertion of an alkyne, and then reductive elimination affords **129E** and a Rh^{I} complex. The Rh^{I} is re-oxidized by $\text{Cu}(\text{OAc})_2$ to form the Rh^{III} species. Furthermore, the intermediate **129E** undergoes C–H bond activation, alkyne insertion, and reductive elimination to obtain the final desired product **129**. A series of highly substituted polyheteroaromatic compounds have been designed and synthesized, offering a simple and effective protocol to construct unique π -conjugated systems. The photophysical properties of **129a–d** were investigated, **129a–c** exhibited emission maxima at 500–530 nm with broad bandwidths. **129d** showed very strong green emission and a narrower bandwidth of 75 nm (Figure 34).

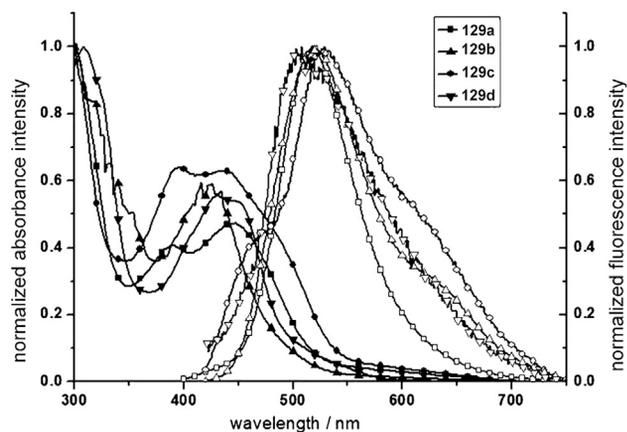
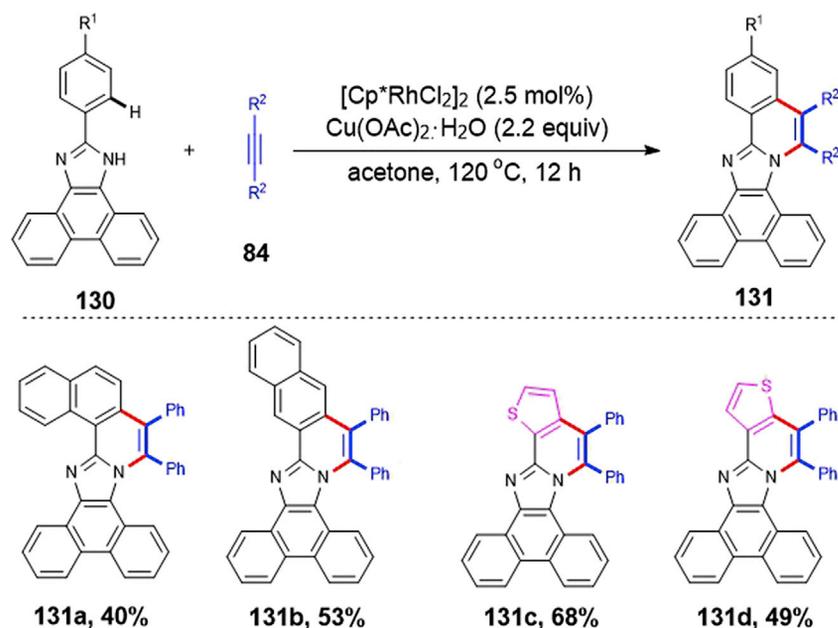


Figure 34. Absorption and Fluorescence Spectra of **129a–129d** in Dichloromethane

Adapted from Jayakumar et al.⁷⁷ with permission, copyright 2014 Wiley-VCH Verlag GmbH & Co. KGaA.



Scheme 77. Rhodium(III)-Catalyzed C–H Activation and Alkyne Annulation

1H-Phenanthro[9,10-d]imidazoles are a rigid π -conjugated heterocyclic skeleton and often show excellent electron injection and transport properties and good thermal stability.⁷⁸ These demonstrated that they are a class of good organic semiconductor materials in organic light-emitting diodes (OLEDs) and solar cells. In 2014, the Hua group disclosed rhodium(III)-catalyzed C–H activation and alkyne annulation to construct π -extension of 2-aryl-phenanthroimidazoles (Scheme 77).⁷⁸ After adding Fe^{3+} into the acetone solution of **131c**, the fluorescence intensity showed 4.6 times enhancement and slight blue shift, demonstrating that the compound **131c** is a fluorescent probe for Fe^{3+} detection (Figure 35).

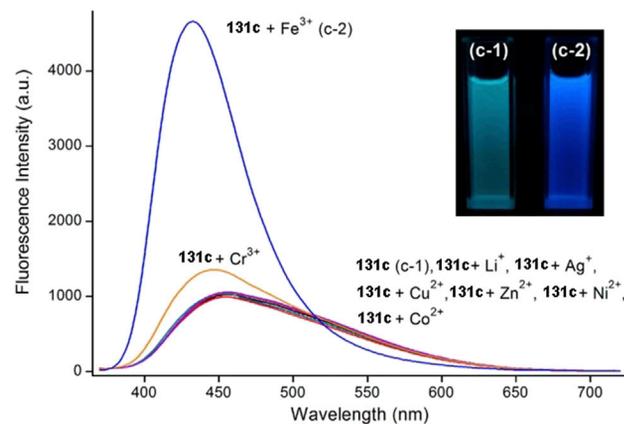
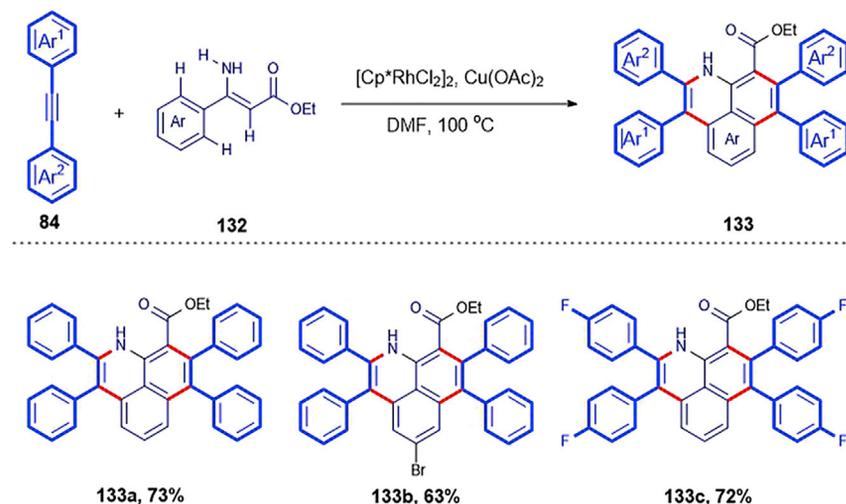


Figure 35. Fluorescence Emission Spectra of 131c in Acetone Solvent (50 μM) with Different Metal Ions (50 μM)

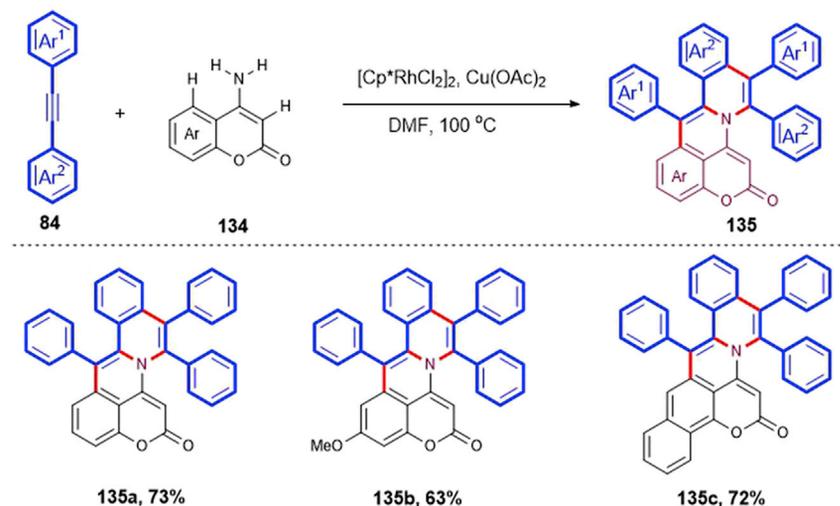
Insert: photo of **131c** acetone solvent without (c-1) or with (c-2) Fe^{3+} under a UV lamp ($\lambda_{\text{ex}} = 365 \text{ nm}$). Adapted from Zheng and Hua⁷⁸ with permission, copyright 2014 American Chemical Society.



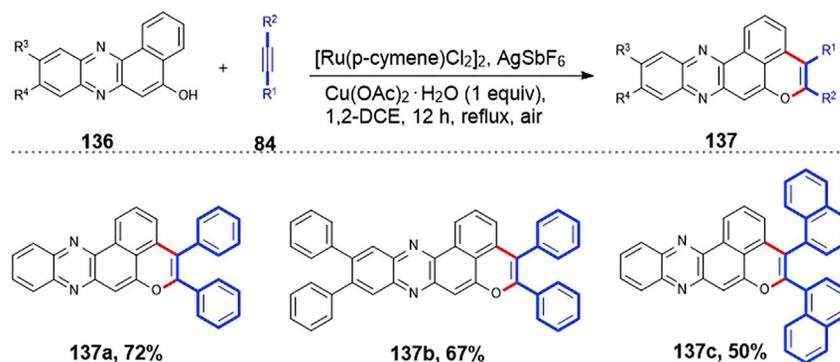
Scheme 78. Rh-Catalyzed Tandem Oxidative Annulation of β -Enamino Esters with Alkynes

Polyheteroaromatic compounds as an optoelectronic conjugated materials often display excellent electro- and photochemical properties, which have potential applications in organic luminescence device.^{10,11} In 2015, the Sun group reported rhodium-catalyzed C–H bond activation of β -enamino esters and 4-aminocoumarins and annulation with alkynes to obtain polyheteroaromatic compounds in moderate to good yields (Schemes 78 and 79).⁷⁹ Compounds **133** and **135** exhibited strong fluorescence emission at 450–470 nm with broad bandwidths.

In 2017, Perumal and co-workers reported the ruthenium(II)-catalyzed regioselective C–H/O–H oxidative annulation reaction to obtain a diverse library of isochromeno [8,1-ab]phenazines (Scheme 80).⁸⁰ These isochromeno[8,1-ab]phenazines displayed strong fluorescence emissions ($\lambda_{max,em}$: 532–632 nm in dichloromethane; 565–640 nm in thin film) and large Stokes shifts (up to $4,853\text{ cm}^{-1}$ in DCM; $5,747\text{ cm}^{-1}$ in thin film) with high fluorescence quantum yields (up to 86% in DCM) (Figure 36).



Scheme 79. Rh-Catalyzed Tandem Oxidative Annulation of 4-Aminocoumarins with Alkynes



Scheme 80. Ru-Catalyzed Regioselective C–H/O–H Oxidative Annulation Reaction to Synthesis of Isochromeno[8,1-ab]Phenazines

This newly developed protocol was successfully applied to build far-red (FR) fluorescent probes for live cancer cell imaging. The plausible mechanism for the formation of isochromeno[8,1-ab]phenazines is shown in Scheme 81. The reactive cationic ruthenium species $[\text{Ru(p-cymene)OAc}]\text{SbF}_6$ is generated by the exchange of ligands in $[\text{RuCl}_2(\text{p-cymene})]_2$ with AgSbF_6 and Cu(OAc)_2 . Then, coordination of the oxygen atom to the ruthenium species forms the intermediate 137A, which then undergoes a C–H activation to give the five-membered ruthenacycle intermediate 137B. Subsequently, π -coordination of the alkyne generates 137C. The insertion of the alkyne into the Ru–C bond forms the seven-membered cycloruthenium intermediate 137D. Finally, reductive elimination of 137D produces the final product. The ruthenium catalyst is regenerated by Cu(OAc)_2 .

In 2018, You and Lan developed palladium-catalyzed direct C–H functionalization or annulation of BODIPYs with alkynes to obtain a series of asymmetric benzo[b]-fused BODIPYs (Scheme 82).⁸¹ The conventional methods for preparing these compounds usually involve the Knoevenagel-type condensation reaction, which needs the tiresome multi-step synthesis (Scheme 83).⁸¹ In this study, $\text{Pd(PhCN)}_2\text{Cl}$ (10 mol %) and AgOPiv (4.0 equiv) were used as the catalyst and base, respectively. A plausible mechanism is shown in Scheme 84. First, BODIPY-2-yl palladium species 139A is

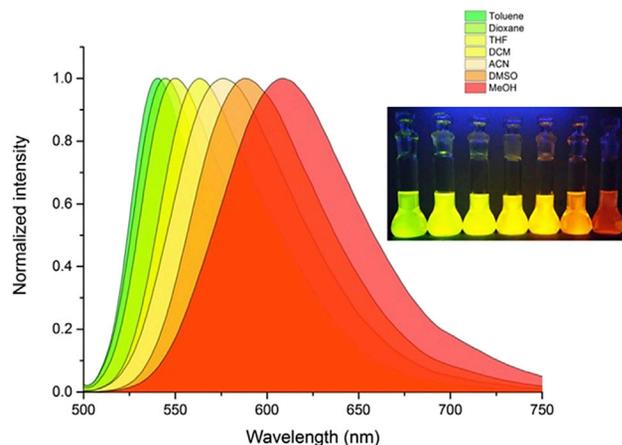
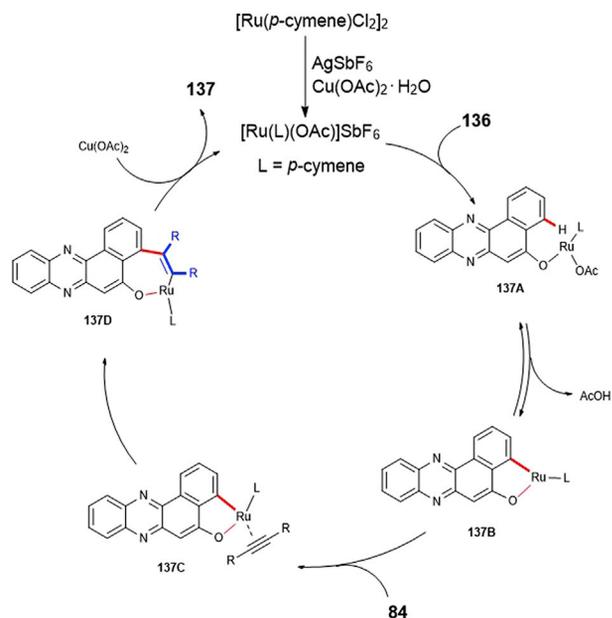
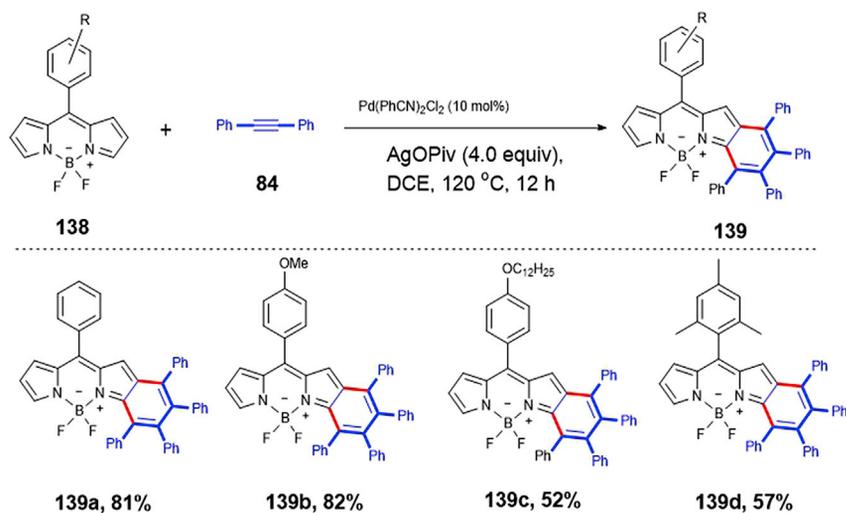


Figure 36. Emission spectra of 137b in Various Solvents

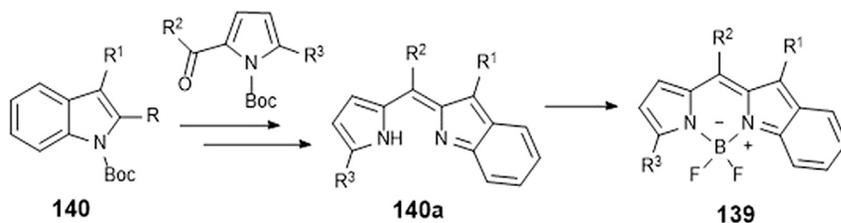
Adapted from Mayakrishnan et al.⁸⁰ with permission, copyright 2017 American Chemical Society.



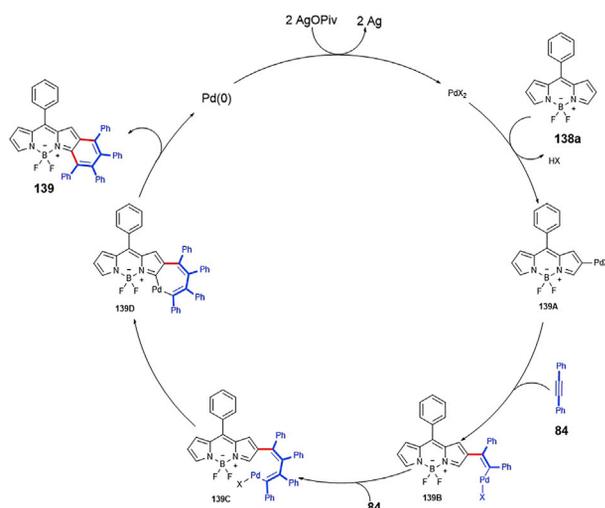
Scheme 81. A Plausible Mechanism for the Formation of 137



Scheme 82. Palladium-Catalyzed Direct C–H Functionalization or Annulation of BODIPYs with Alkynes



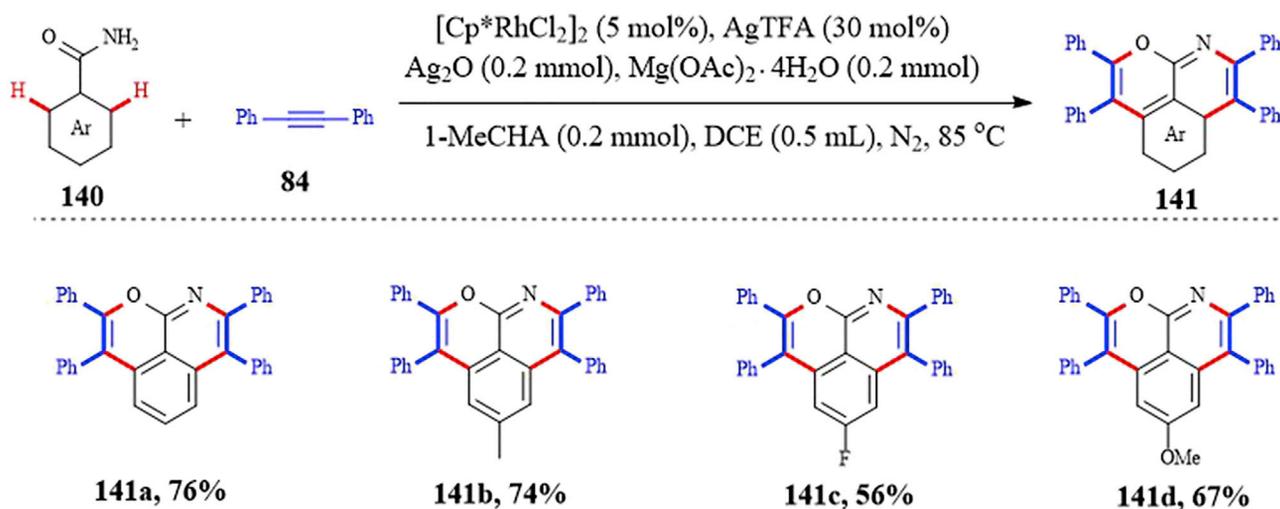
Scheme 83. The Conventional Synthetic Method for 139



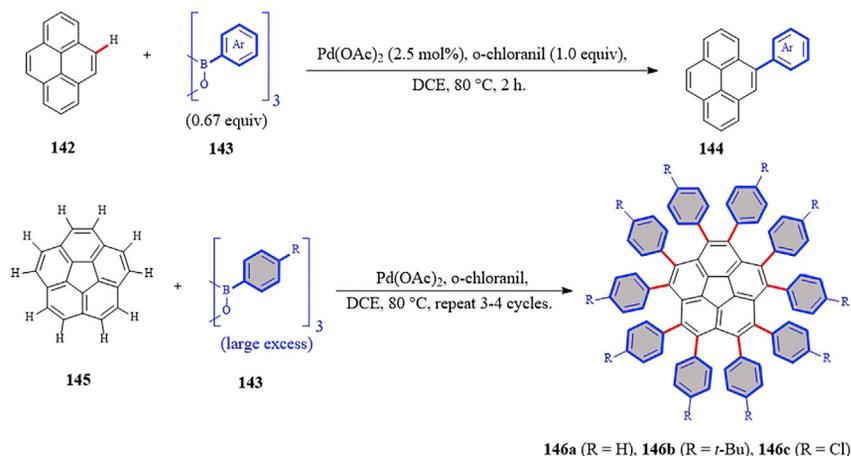
Scheme 84. The Plausible Mechanism for the Formation of 139

generated by direct electrophilic palladation at the 2-position of BODIPY. Next, alkyne insertion produces the vinylpalladium species 139B. Subsequently, another molecule of alkyne inserts into the Pd–C bond to form the butadienyl palladium intermediate 139C. Then, the intermediate 139C undergoes an intramolecular electrophilic palladation at the 3-position of BODIPY to produce the intermediate 139D. Finally, the reductive elimination generates the benzo[b]-fused BODIPY 139 and Pd(0) species. These benzo[b]-fused BODIPYs showed remarkably red-shifted fluorescence emissions and larger Stokes shifts than classical BODIPY dyes. Some benzo[b]-fused BODIPYs have specific lysosome-labeling capacities and turn-on fluorescence emission in cells by cell imaging experiments and cytotoxicity assays.

In 2019, You and co-workers reported a highly efficient double *ortho*-C–H activation/annulation protocol of benzamides with aryl alkynes (Scheme 85).⁸² This study represents a very important example of the double *ortho*-C–H activation of benzamides



Scheme 85. Rh-Catalyzed Double *Ortho*-C–H Activation/Annulation of Benzamides with Aryl Alkynes



Scheme 86. Palladium-Catalyzed Direct C–H Functionalization to Synthesize Decaphenylcorannulenes

and subsequent *N,O*-double annulations with aryl alkynes, which provides a facile route to extended π -conjugated polycyclic heteroaromatics with a double-helical structure. Furthermore, a double-helical extended π -conjugated polycyclic heteroarene could be obtained via Scholl oxidation of corresponding PHA. This new material exhibited blue emission with high fluorescence quantum yield.

Transition-Metal-Catalyzed C–H/C–M or C–H/Het-H Bond Functionalization to Build Fluorescent Materials

Transition-Metal-Catalyzed C–H/C–M Cross-Coupling Reactions to Build Fluorescent Materials

In 2012, Itami and co-workers developed a palladium-catalyzed direct C–H arylation of aromatics for the synthesis of decaphenylcorannulenes **146** (Scheme 86).⁸³ Pd(OAc)₂/o-chloranil was employed as the catalyst. The reaction showed unique regioselectivity, in which all 10 C–H positions on the rim of corannulene could be arylated. Decaphenylcorannulene (**146**) exhibited multiple fluorescence emission peaks at 373, 390, and 470 nm in the CH₂Cl₂ solution.

Transition-Metal-Catalyzed C–H/Het-H Bond Functionalization to Build Fluorescent Materials

Organic polymers are widely used in organic optoelectronic devices, such as optical sensors, OLEDs, organic field-effect transistors, and organic photovoltaics.^{10,11} Recently, Tang and co-workers reported the palladium and benzoic acid-catalyzed polymerization to generate a series of regio- and stereo-regular poly(allylic ether)s through C(sp³)-H activation of internal diynes and diols (Scheme 87).⁸⁴ These thin films of poly(allylic ether)s exhibited high refractive indices and low optical dispersions. The polymer containing tetra-phenylethene moiety exhibited strong fluorescence emission.

Recently, Ding and co-workers reported a rhodium-(III)-catalyzed direct C–H amidation of 2-arylbenzo-[d]thiazoles to prepare organic white-light emission materials (Scheme 88).⁸⁵ 2-Phenylbenzo[d]thiazoles reacted with 3-phenyl-1,4,2-dioxazol-5-ones to produce 2-arylbenzo[d]thiazole derivatives. Typical approaches for the synthesis of these dyes mainly involve a three-step process consisting of nitration, ammoniation, and amidation (Scheme 89).⁸⁵ Furthermore, bright organic white-light emission molecules have been screened via manipulation of the electron-donating

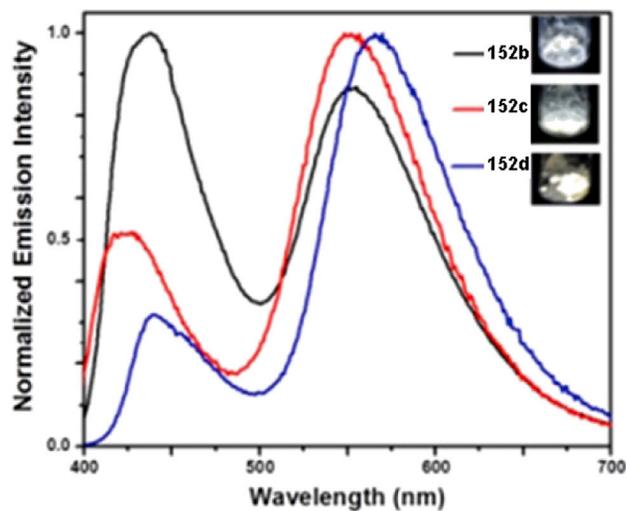


Figure 37. Normalized Emission Spectra of 152b-152d in the Solid State
Adapted from Liu et al.⁸⁵ with permission, copyright 2019 American Chemical Society.

CONCLUSIONS AND FUTURE DIRECTIONS

The development of synthetic organic fluorescent materials via C–H functionalization reactions is detailed in this review. The use of transition-metal-catalyzed C–H functionalization reactions in building fluorescent materials has achieved significant progress in recent years. Various fluorescent frameworks have been constructed based on this process. In fact, transition-metal-catalyzed C–H bond functionalization has been considered as an increasingly attractive approach for the preparation of synthetic organic fluorescent materials compared with conventional cross-coupling

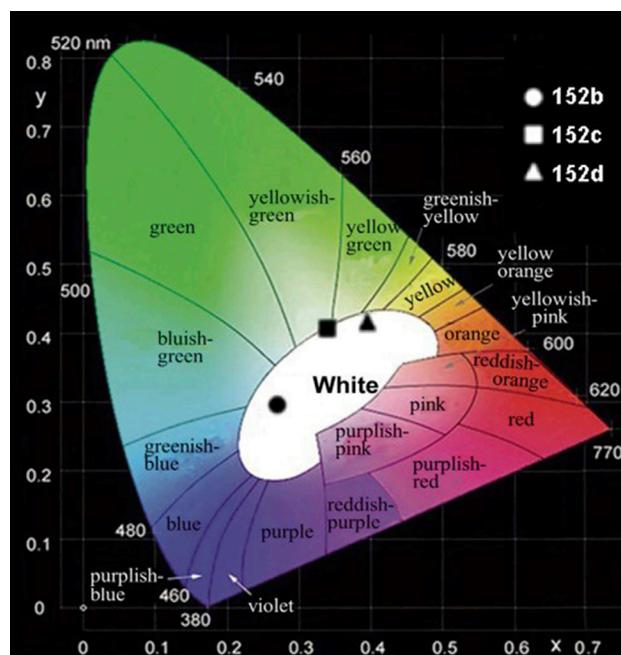
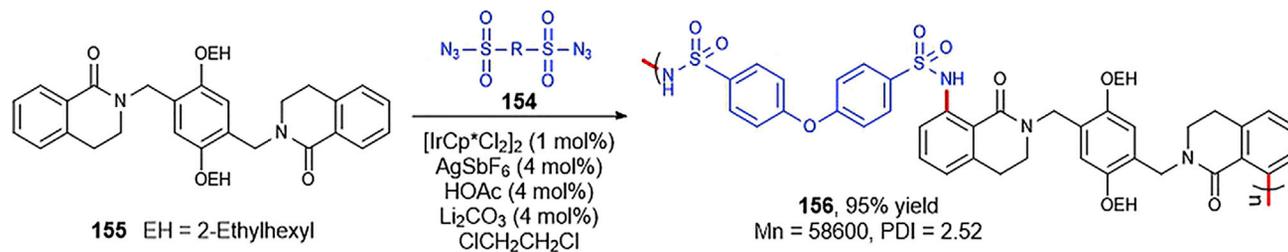


Figure 38. The Emission Color Coordinate of 152b-152d in the CIE_{1,931} Chromaticity Diagram
Adapted from Liu et al.⁸⁵ with permission, copyright 2019 American Chemical Society.



Scheme 90. Synthesis of the Polysulfonamide **156**

reactions, as this process can avoid tedious multi-step synthesis and pre-functionalization of starting materials. Thus, it is both environmentally and economically uniquely privileged.

A broadly applicable transition-metal-catalyzed C–H bond functionalization strategy to build fluorescent materials has yet to be developed, considering that many C–H bond functionalization reactions are not yet truly mainstream, and many issues need to be addressed. Currently, precious transition metals such as rhodium and palladium are still the most widely used catalysts and C–H bond functionalization reactions usually require a catalyst loading of 1–10 mol % to be practical and effective. On one hand, exploration of inexpensive and effective catalysts, including the iron, cobalt, nickel, and copper species, would be a very effective way to cut costs. On the other hand, developing new technologies for recycling valuable transition-metal catalysts would also be cost effective and warrants further investigation. Moreover, harsh reaction conditions are often required, such as high reaction temperatures, strongly acidic conditions, and the use of stoichiometric amounts of oxidizing agents. These factors could significantly restrict the large-scale industrial application of these protocols. Thus, the development of milder reaction conditions for these processes is still highly desired. Exploration of powerful synthetic strategies such as the use of transient directing groups, tuning of sterics and/or electronics of substrates and catalytic system, and using an ancillary ligand to overcome the regioselectivity issue require further attention. Furthermore, the development of fluorescent polymers via C–H functionalization reactions is still in its infancy. Additional efforts should be made for developing various fluorescent polymer materials using this strategy.

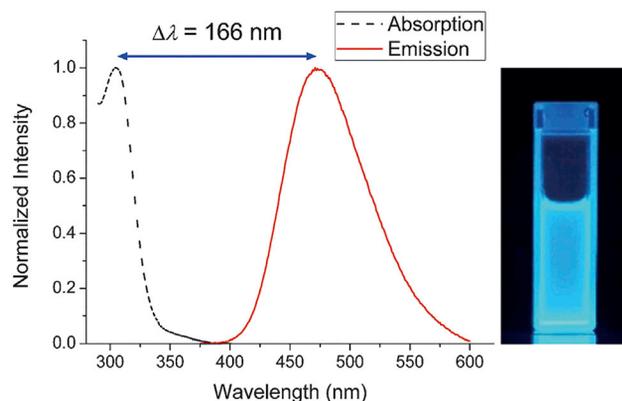


Figure 39. Absorption and Emission Spectra of **156** in THF Solution

Adapted from Jang et al.⁸⁶ with permission, copyright 2017 Wiley-VCH Verlag GmbH & Co. KGaA.

As demonstrated, the transition-metal-catalyzed C–H bond functionalization approach represents an efficient and straightforward route to access various organic fluorescent frameworks that cannot be easily prepared by conventional synthetic methods. Considering the rapid development of this approach in recent years, we strongly believe that transition-metal-catalyzed C–H bond functionalization reactions will soon become a key technology for the efficient synthesis and discovery of organic fluorescent materials in academia and industry.

ACKNOWLEDGMENTS

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AUTHOR CONTRIBUTIONS

H.G. proposed the topic of the review. B.L. investigated the literature and prepared the manuscript. A.A. and H.G. helped to revise the manuscript.

REFERENCES

1. Glasbeek, M., and Zhang, H. (2004). Femtosecond studies of solvation and intramolecular configurational dynamics of fluorophores in liquid solution. *Chem. Rev.* **104**, 1929–1954.
2. Sinkeldam, R.W., Greco, N.J., and Tor, Y. (2010). Fluorescent analogs of biomolecular building blocks: design, properties, and applications. *Chem. Rev.* **110**, 2579–2619.
3. Berezin, M.Y., and Achilefu, S. (2010). Fluorescence lifetime measurements and biological imaging. *Chem. Rev.* **110**, 2641–2684.
4. Hu, R., Leung, N.L.C., and Tang, B.Z. (2014). AIE macromolecules: syntheses, structures and functionalities. *Chem. Soc. Rev.* **43**, 4494–4562.
5. Lv, H.M., Yi Chen, Y.C., Lei, J., Au, C.T., and Yin, S.F. (2015). An ESIP-T-based ratiometric fluorescent probe for the imaging of nitroxy in living cells. *Anal. Methods* **7**, 3883–3887.
6. Wang, F., Cao, X., Mei, L., Zhang, X., Hu, J., and Yan, T. (2018). Twisted penta-carbazole/benzophenone hybrid compound as multifunctional organic host, dopant or non-doped emitter for highly efficient solution-processed delayed fluorescence OLEDs. *Chin. J. Chem.* **36**, 241–246.
7. Yuan, W., Yang, H., Duan, C., Cao, X., Zhang, J., Xu, H., et al. (2020). Molecular configuration fixation with C–H⋯F hydrogen bonding for thermally activated delayed fluorescence acceleration. *Chem* **6**, 1–11.
8. Cao, X., Zhang, D., Zhang, S., Tao, Y., and Huang, W. (2017). CN-containing donor-acceptor-type small-molecule materials for thermally activated delayed fluorescence OLEDs. *J. Mater. Chem. C* **5**, 7699–7714.
9. Yuan, W., Zhang, M., Zhang, X., Cao, X., Sun, N., Wan, S., and Tao, Y. (2018). The electron inductive effect of CF₃ on penta-carbazole containing blue emitters: trade-off between color purity and luminescent efficiency in TADF OLEDs. *Dyes Pigm.* **159**, 151–157.
10. Wencel-Delord, J., and Glorius, F. (2013). C–H bond activation enables the rapid construction and late-stage diversification of functional molecules. *Nat. Chem.* **5**, 369–375.
11. Yang, Y., Lan, J., and You, J. (2017). Oxidative C–H/C–H coupling reactions between two (hetero)arenes. *Chem. Rev.* **117**, 8787–8863.
12. Wang, W., Lorion, M.M., Shah, J., Kapdi, A.R., and Ackermann, L. (2018). Late-stage peptide diversification by position-selective C–H activation. *Angew. Chem. Int. Ed. Engl.* **57**, 14700–14717.
13. Yin, B., Fu, M., Wang, L., Liu, J., and Zhu, Q. (2020). Dual ligand-promoted palladium-catalyzed nondirected C–H alkenylation of aryl ethers. *Chem. Commun. (Camb.)* **56**, 3293–3296.
14. Liu, C., Yuan, J., Gao, M., Tang, S., Li, W., Shi, R., and Lei, A. (2015). Oxidative coupling between two hydrocarbons: an update of recent C–H functionalizations. *Chem. Rev.* **115**, 12138–12204.
15. Murakami, K., Yamada, S., Kaneda, T., and Itami, K. (2017). C–H functionalization of azines. *Chem. Rev.* **117**, 9302–9332.
16. Daugulis, O., Roane, J., and Tran, L.D. (2015). Bidentate, monoanionic auxiliary-directed functionalization of carbon–hydrogen bonds. *Acc. Chem. Res.* **48**, 1053–1064.
17. Yeung, C.S., and Dong, V.M. (2011). Catalytic dehydrogenative cross-coupling: forming carbon–carbon bonds by oxidizing two carbon–hydrogen bonds. *Chem. Rev.* **111**, 1215–1292.
18. Gensch, T., Hopkinson, M.N., Glorius, F., and Wencel-Delord, J. (2016). Mild metal-catalyzed C–H activation: examples and concepts. *Chem. Soc. Rev.* **45**, 2900–2936.
19. Gandeepan, P., Müller, T., Zell, D., Cera, G., Warratz, S., and Ackermann, L. (2019). 3d Transition Metals for C–H Activation. *Chem. Rev.* **119**, 2192–2452.
20. Yu, J.Q. (2015). *Science of Synthesis: Catalytic Transformations via C–H Activation* (Thieme Verlag).
21. Lyons, T.W., and Sanford, M.S. (2010). Palladium-catalyzed ligand-directed C–H functionalization reactions. *Chem. Rev.* **110**, 1147–1169.
22. Yu, J.Q., and Shi, Z.J. (2010). *Topics in Current Chemistry: C–H Activation* (Springer).
23. Nareddy, P., Jordan, F., and Szostak, M. (2017). Recent developments in ruthenium-catalyzed C–H arylation: array of mechanistic manifolds. *ACS Catal.* **7**, 5721–5745.
24. Alberico, D., Scott, M.E., and Lautens, M. (2007). Aryl–aryl bond formation by transition-metal-catalyzed direct arylation. *Chem. Rev.* **107**, 174–238.
25. Schmidt-Mende, L., Fechtenkötter, A., Müllen, K., Moons, E., Friend, R.H., and Mackenzie, J.D. (2001). Self-organized discotic liquid crystals for high-efficiency organic photovoltaics. *Science* **293**, 1119–1122.
26. Yue, W., Li, Y., Jiang, W., Zhen, Y., and Wang, Z. (2009). Direct meta-selective alkylation of perylene bisimides via palladium-catalyzed C–H functionalization. *Org. Lett.* **11**, 5430–5433.
27. Zhao, D., Wang, W., Yang, F., Lan, J., Yang, L., Gao, G., and You, J. (2009). Copper-catalyzed direct C arylation of heterocycles with aryl bromides: discovery of fluorescent core frameworks. *Angew. Chem. Int. Ed. Engl.* **48**, 3296–3300.
28. He, Z., Luo, F., Li, Y., and Zhu, G. (2013). Copper-catalyzed direct thiolation of xanthenes and related heterocycles with disulfides. *Tetrahedron Lett.* **54**, 5907–5910.
29. Liu, B., Wang, Z., Wu, N., Li, M., You, J., and Lan, J. (2012). Discovery of a full-color-tunable fluorescent core framework through direct C–H (hetero)arylation of N–heterocycles. *Chem. Eur. J.* **18**, 1599–1603.
30. Loudet, A., and Burgess, K. (2007). BODIPY dyes and their derivatives: syntheses and spectroscopic properties. *Chem. Rev.* **107**, 4891–4932.
31. Chong, H., Lin, H.A., Shen, M.Y., Liu, C.Y., Zhao, H., and Yu, H.H. (2015). Step-economical

- syntheses of functional BODIPY-EDOT π -conjugated materials through direct C–H arylation. *Org. Lett.* **17**, 3198–3201.
32. Wu, J., You, Q., Lan, J., Guo, Q., Li, X., Xue, Y., and You, J. (2015). Cu Catalyzed direct C–H (hetero)arylation of [1,2,4]triazolo[4,3-a]pyridine to construct deep-blue-emitting luminophores. *Org. Biomol. Chem.* **13**, 5372–5375.
 33. Sagara, Y., and Kato, T. (2009). Mechanically induced luminescence changes in molecular assemblies. *Nat. Chem.* **1**, 605–610.
 34. Davis, D.A., Hamilton, A., Yang, J., Cremer, L.D., Van Gough, D.V., Potisek, S.L., Ong, M.T., Braun, P.V., Martinez, T.J., White, S.R., et al. (2009). Force-induced activation of covalent bonds in mechanoresponsive polymeric materials. *Nature* **459**, 68–72.
 35. Wu, J., Cheng, Y.Y., Lan, J.B., Wu, D., Qian, S.Y., Yan, L.P., He, Z., Li, X.Y., Wang, K., Zou, B., and You, J. (2016). Molecular engineering of mechanochromic materials by programmed C–H arylation: making a counterpoint in the chromism trend. *J. Am. Chem. Soc.* **138**, 12803–12812.
 36. Zhang, F.L., Hong, K., Li, T.J., Park, H., and Yu, J.Q. (2016). Functionalization of C(sp³)–H bonds using a transient directing group. *Science* **351**, 252–256.
 37. Li, B., Seth, K., Niu, B., Pan, L., Yang, H., and Ge, H. (2018). Transient-ligand-enabled ortho-arylation of five-membered heterocycles: facile access to mechanochromic materials. *Angew Chem Int Ed Engl.* **57**, 3401–3405.
 38. Li, B., and Ge, H. (2019). Highly selective electrochemical hydrogenation of alkynes: rapid construction of mechanochromic materials. *Sci. Adv.* **5**, eaaw2774.
 39. Li, B., Lawrence, B., Li, G., and Ge, H. (2020). Ligand-controlled direct γ -C–H arylation of aldehydes. *Angew. Chem. Int. Ed. Engl.* **59**, 3078–3082.
 40. Rathnamalala, C.S.L., Gayton, J.N., Dorris, A.L., Autry, S.A., Meador, W., Hammer, N.I., Delcamp, J.H., and Scott, C.N. (2019). Donor-acceptor-donor NIR II emissive rhodindolizine dye synthesized by C–H bond functionalization. *J. Org. Chem.* **84**, 13186–13193.
 41. Wang, W., Lorion, M.M., Martinazzoli, O., and Ackermann, L. (2018). BODIPY peptide labeling by late-stage C(sp³)–H activation. *Angew. Chem. Int. Ed. Engl.* **57**, 10554–10558.
 42. Yamashita, A., Nishiyama, H., Inagi, S., and Tomita, I. (2018). Synthesis of π -conjugated poly(arylene)s by polycondensation of 1,4-bis(3-methylpyridin-2-yl)benzene and aryl dibromides through regioselective C–H functionalization process. *J. Polym. Sci. Part A: Polym. Chem.* **56**, 2771–2777.
 43. Thivierge, C., Bandichhor, R., and Burgess, K. (2007). Spectral dispersion and water solubilization of BODIPY dyes via palladium-catalyzed C–H functionalization. *Org. Lett.* **9**, 2135–2138.
 44. Huang, Y., Song, F., Wang, Z., Xi, P., Wu, N., Wang, Z., Lan, J., and You, J. (2012). Dehydrogenative heck coupling of biologically relevant N-heteroarenes with alkenes: discovery of fluorescent core frameworks. *Chem. Commun. (Camb.)* **48**, 2864–2866.
 45. Cheng, Y., Li, G., Liu, Y., Shi, Y., Gao, G., Wu, D., Lan, J., and You, J. (2016). Unparalleled ease of access to a library of biheteroaryl fluorophores via oxidative cross-coupling reactions: discovery of photostable NIR probe for mitochondria. *J. Am. Chem. Soc.* **138**, 4730–4738.
 46. Selwood, L., Fernandez, D.A., Bellamy, T., Kling, M., and Madge, J. (2001). A convenient route to the soluble guanylate cyclase activator YC-1 and its N2 regioisomer. *Heterocycles* **55**, 1813–1816.
 47. Kwon, J.E., and Park, S.Y. (2011). Advanced organic optoelectronic materials: harnessing excited-state intramolecular proton transfer (ESIPT) process. *Adv. Mater.* **23**, 3615–3642.
 48. Li, B., Lan, J., Wu, D., and You, J. (2015). Rhodium(III)-catalyzed ortho-heteroarylation of phenols through internal oxidative C–H activation: rapid screening of single-molecular white-light-emitting materials. *Angew. Chem. Int. Ed. Engl.* **54**, 14008–14012.
 49. Li, B., Zhou, L., Cheng, H., Huang, Q., Lan, J., Zhou, L., and You, J. (2018). Dual-emissive 2-(2'-hydroxyphenyl)oxazoles for high performance organic electroluminescent devices: discovery of a new equilibrium of excited state intramolecular proton transfer with a reverse intersystem crossing process. *Chem. Sci.* **9**, 1213–1220.
 50. Li, B., Tang, G., Zhou, L., Wu, D., Lan, J., Zhou, L., Lu, Z., and You, J. (2017). Unexpected sole enol-form emission of 2-(2'-hydroxyphenyl)oxazoles for highly efficient deep-blue-emitting organic electroluminescent devices. *Adv. Funct. Mater.* **27**, 1605245–1605253.
 51. Zhang, M., Cheng, R., Lan, J., Zhang, H., Yan, L., Pu, X., Huang, Z., Wu, D., and You, J. (2019). Oxidative C–H/C–H cross-coupling of [1,2,4]triazolo[1,5-a]pyrimidines with indoles and pyrroles: discovering excited-state intramolecular proton transfer (ESIPT) fluorophores. *Org. Lett.* **21**, 4058–4062.
 52. Huang, Q., Qin, X., Li, B., Lan, J., Guo, Q., and You, J. (2014). Cu-Catalyzed oxidative C–H/C–H coupling polymerisation of benzodiazoles: an efficient approach to regioregular polybenzodiazoles for blue-emitting materials. *Chem. Commun. (Camb.)* **50**, 13739–13741.
 53. Zhang, Q., Li, Y., Lu, Y., Zhang, H., Li, M., Yang, Y., Wang, J., Chen, Y., and Li, C. (2015). Pd-Catalyzed oxidative C–H/C–H coupling polymerization for polythiazole-based derivatives. *Polymer* **68**, 227–233.
 54. Aoki, H., Saito, H., Shimoyama, Y., Kuwabara, J., Yasuda, T., and Kanbara, T. (2018). Synthesis of conjugated polymers containing octafluorobiphenylene unit via Pd-catalyzed cross-dehydrogenative-coupling reaction. *ACS Macro Lett.* **7**, 90–94.
 55. Faradhiyani, A., Zhang, Q., Maruyama, K., Kuwabara, J., Yasuda, T., and Kanbara, T. (2018). Synthesis of bithiazole-based semiconducting polymers via Cu-catalyzed aerobic oxidative coupling. *Mater. Chem. Front.* **2**, 1306–1309.
 56. Liu, Z., Zeng, H., Zhang, W., Song, C., Yang, F., Liu, Y., and Zhu, J. (2019). Rh(III)-catalyzed N-nitroso-directed C–H olefination polymerization. *Polymer* **172**, 152–159.
 57. Ephritikhine, M. (1998). A new look at the McMurry reaction. *Chem. Commun (Camb.)* **1998**, 2549–2554.
 58. Maryanoff, B.E., and Reitz, A.B. (1989). The Wittig olefination reaction and modifications involving phosphoryl-stabilized carbanions. Stereochemistry, mechanism, and selected synthetic aspects. *Chem. Rev.* **89**, 863–927.
 59. Tan, G., Zhu, L., Liao, X., Lan, Y., and You, J. (2017). Rhodium/copper cocatalyzed highly trans-selective 1,2-diheteroarylation of alkynes with azoles via C–H addition/oxidative cross-coupling: a combined experimental and theoretical study. *J. Am. Chem. Soc.* **139**, 15724–15737.
 60. Zhao, D., Kim, J.H., Stegemann, L., Strassert, C.A., and Glorius, F. (2015). Cobalt(III)-catalyzed directed C–H coupling with diazo compounds: straightforward access towards extended π -systems. *Angew. Chem. Int. Ed. Engl.* **54**, 4508–4511.
 61. Kim, J.H., Gensch, T., Zhao, D., Stegemann, L., Strassert, C.A., and Glorius, F. (2015). Rh^{III}-Catalyzed C–H activation with pyridotriazoles: direct access to fluorophores for metal-ion detection. *Angew. Chem. Int. Ed. Engl.* **54**, 10975–10979.
 62. Matsuoka, W., Ito, H., and Itami, K. (2017). Rapid access to nanographenes and fused heteroaromatics by palladium-catalyzed annulative π -extension reaction of unfunctionalized aromatics with diiodobipyrals. *Angew. Chem. Int. Ed. Engl.* **56**, 12224–12228.
 63. Shimizu, M., Nagao, I., Tomioka, Y., and Hiyama, T. (2008). Palladium-catalyzed annulation of vic-bis(pinacolatoboryl)alkenes and -phenanthrenes with 2,2'-dibromobipyrals: facile synthesis of functionalized phenanthrenes and dibenzo[g,p]chrysenes. *Angew. Chem. Int. Ed. Engl.* **47**, 8096–8099.
 64. Koga, Y., Kaneda, T., Saito, Y., Murakami, K., and Itami, K. (2018). Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization. *Science* **359**, 435–439.
 65. Wu, X., Xiong, H., Sun, S., and Cheng, J. (2018). Rhodium-catalyzed relay carbenoid functionalization of aromatic C–H bonds toward fused heteroarenes. *Org. Lett.* **20**, 1396–1399.
 66. Yang, W., Qiao, R., Chen, J., Huang, X., Liu, M., Gao, W., Ding, J., and Wu, H. (2015). Palladium-catalyzed cascade reaction of 2-amino-N'-arylbenzohydrazides with triethyl orthobenzoates to construct indazolo[3,2-b]quinazolinones. *J. Org. Chem.* **80**, 482–489.
 67. Lévesque, É., Bechara, W.S., Constantineau-Forget, L., Pelletier, G., Rachel, N.M., Pelletier, J.N., and Charette, A.B. (2017). General C–H arylation strategy for the synthesis of tunable visible light-emitting benzo[a]imidazo[2,1,5-c,d]indolizine fluorophores. *J. Org. Chem.* **82**, 5046–5067.
 68. Sharma, K., Neog, K., and Gogoi, P. (2020). Pd(II)-catalyzed oxidative annulation via double C–H activations: synthesis and photophysical

- properties of bis-coumarins. *Org. Lett.* **22**, 73–77.
69. Pu, X., Zhang, M., Lan, J., Chen, S., Liu, Z., Liang, W., Yang, Y., Zhang, M., and You, J. (2019). Tandem Rh(III)-catalyzed C–H heteroarylation of indolyl ketones and Cu(II)-promoted intramolecular cyclization: one-pot access to blue-emitting phenanthrone-type polyheterocycles. *Org. Lett.* **21**, 1139–1143.
70. Flynn, A.B., and Ogilvie, W.W. (2007). Stereocontrolled synthesis of tetrasubstituted olefins. *Chem. Rev.* **107**, 4698–4745.
71. Nandakumar, A., and Perumal, P.T. (2013). Tetrasubstituted olefinic xanthene dyes: synthesis via Pd-catalyzed 6-exo-dig cyclization/ C–H activation of 2-bromobenzyl-N-propargylamines and solid state fluorescence properties. *Org. Lett.* **15**, 382–385.
72. Lian, Y., Bergman, R.G., Lavis, L.D., and Ellman, J.A. (2013). Rhodium(III)-catalyzed indazole synthesis by C–H bond functionalization and cyclative capture. *J. Am. Chem. Soc.* **135**, 7122–7125.
73. Prakash, S., Muralirajan, K., and Cheng, C.H. (2016). Cobalt-catalyzed oxidative annulation of nitrogen-containing arenes with alkynes: an atom-economical route to heterocyclic quaternary ammonium salts. *Angew. Chem. Int. Ed. Engl.* **55**, 1844–1848.
74. Ghorai, D., and Choudhury, J. (2015). Rhodium(III)–N-heterocyclic carbene-driven cascade C–H activation catalysis. *ACS Catal.* **5**, 2692–2696.
75. Thenarukandiyil, R., and Choudhury, J. (2015). Rhodium(III)-catalyzed activation and functionalization of pyridine C–H bond by exploring a unique double role of “N-heterocyclic carbene-pyridyl” ligand plat form. *Organometallics* **34**, 1890–1897.
76. Villar, J.M., Suárez, J., Varela, J.A., and Saá, C. (2017). N-Doped cationic PAHs by Rh(III)-catalyzed double C–H activation and annulation of 2-arylbenzimidazoles with alkynes. *Org. Lett.* **19**, 1702–1705.
77. Jayakumar, J., Parthasarathy, K., Chen, Y.H., Lee, T.H., Chuang, S.C., and Cheng, C.H. (2014). One-pot synthesis of highly substituted polyheteroaromatic compounds by rhodium(III)-catalyzed multiple C–H activation and annulation. *Angew. Chem. Int. Ed. Engl.* **53**, 9889–9892.
78. Zheng, L., and Hua, R. (2014). Modular assembly of ring-fused and π -extended phenanthroimidazoles via C–H activation and alkyne annulation. *J. Org. Chem.* **79**, 3930–3936.
79. Peng, S., Liu, S., Zhang, S., Cao, S., and Sun, J. (2015). Synthesis of polyheteroaromatic compounds via rhodium-catalyzed multiple C–H bond activation and oxidative annulation. *Org. Lett.* **17**, 5032–5035.
80. Mayakrishnan, S., Arun, Y., Balachandran, C., Awale, S., Maheswari, N.U., and Perumal, P.T. (2017). Ru(II)-Catalyzed regiospecific C–H/O–H oxidative annulation to access isochromeno[8,1-ab]phenazines: far-red fluorescence and live cancer cell imaging. *ACS Omega* **2**, 2694–2705.
81. Yang, X., Jiang, L., Yang, M., Zhang, H., Lan, J., Zhou, F., Chen, X., Wu, D., and You, J. (2018). Pd-Catalyzed direct C–H functionalization/annulation of BODIPYs with alkynes to access unsymmetrical benzo[*b*]Fused BODIPYs: discovery of lysosome-targeted turn-on fluorescent probes. *J. Org. Chem.* **83**, 9538–9546.
82. Li, J., Liu, J., Yin, J., Zhang, Y., Han, W., Lan, J., Wu, D., Bin, Z., and You, J. (2019). Double *Ortho*-C–H activation/annulation of benzamides with aryl alkynes: a route to double-helical polycyclic heteroaromatics. *J. Org. Chem.* **84**, 15697–15705.
83. Zhang, Q., Kawasumi, K., Segawa, Y., Itami, K., and Scott, L.T. (2012). Palladium-catalyzed C–H activation taken to the limit. Flattening an aromatic bowl by total arylation. *J. Am. Chem. Soc.* **134**, 15664–15667.
84. Wang, J., Bai, T.W., Chen, Y., Ye, C.B., Han, T., Qin, A.J., Ling, J., and Tang, B.Z. (2019). Palladium/benzoic acid-catalyzed regio- and stereoselective polymerization of internal diynes and diols through $C(sp^3)$ -H activation. *ACS Macro Lett.* **8**, 1068–1074.
85. Liu, D., Ding, Q., Fu, Y., Song, Z., and Peng, Y. (2019). Rh-catalyzed C–H amidation of 2-arylbenzo[*d*]thiazoles: a simple approach to single organic molecule white light-emitters in the solid state. *Org. Lett.* **21**, 2523–2527.
86. Jang, Y.-J., Hwang, S.-H., and Choi, T.-L. (2017). Iridium-catalyzed direct C–H amidation polymerization: step-growth polymerization by C–N bond formation via C–H activation to give fluorescent polysulfonamides. *Angew. Chem. Int. Ed. Engl.* **56**, 14474–14478.