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C–H Activation

Synthesis of Extended π-Systems through C–H Activation

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Activation of aromatic C–H bonds by a transition metal catalyst has received significant attention in the synthetic chemistry community. In recent years, rapid and site-selective extension of π-electron systems by C–H activation has emerged as an ideal methodology for preparing organic materials with extended π-systems. This Review focuses on recently reported π-extending C–H activation reactions directed toward new optoelectronic conjugated materials.

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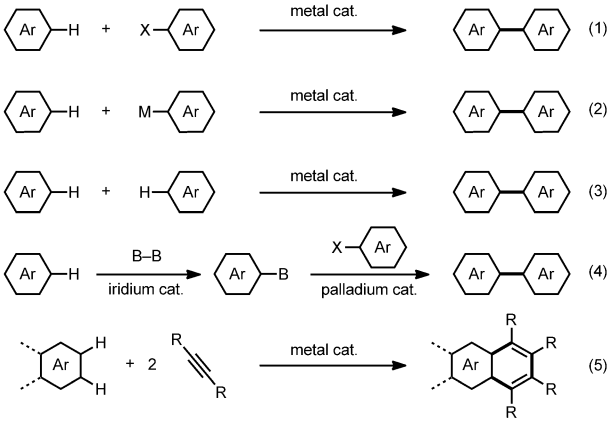
1. Introduction

Conjugated organic π-systems containing arenes and heteroarenes have received considerable attention because of their potential utility as organic electronic materials[1] (Figure 1). To advance organic materials science, improvements in synthetic methods for these compounds are critically important. The most efficient approach to synthesizing aryl–aryl conjugated systems is transition metal catalyzed cross-coupling reactions, e.g., the palladium-catalyzed Suzuki–Miyaura cross-coupling reaction.[2] The development of cross-coupling reactions enables the design of a number of new organic π-systems. However, there is still room for improvement of these reactions. For example, often the two substrates for cross-coupling, haloarenes and aryl metals, must be synthesized from simple molecules. From that standpoint, many chemists have been investigating direct C–H coupling reactions. Direct C–H arylation does not require the prefunctionalization of arenes so that concise synthesis of new organic molecules can be achieved. Currently, C–H activation reactions[3] are widely used for the synthesis of natural products and pharmaceuticals as well as for materials-directed compounds.[4] In this Review, we focus on the C–H bond activation reaction of arenes for the efficient extension of π-systems.

2. Overview

In this Review, we describe recent syntheses of materials-directed molecules utilizing C–H activation for the extension of arene π-systems (π-extension) and classify them according to the type of direct C–H arylation: C–H/C–X [Eq. (1) in Scheme 1], C–H/C–M [Eq. (2)], C–H/C–H [Eq. (3)], sequential C–H borylation and Suzuki–Miyaura cross-coupling [Eq. (4)], and the direct π-extension of arenes with alkynes through double C–H cleavage [Eq. (5)]. In this Review, classic Scholl-type reactions[5] and intramolecular C–H activation reactions[6] for π-extension are not addressed. As a general note to the reader, C–C bonds formed by C–H functionalization are indicated by bold lines.



Scheme 1. C–H activation methods for the extension of aromatic π-systems.

3. Extension of π-Systems by Intermolecular C–C Bond Formation

3.1. C–H/C–X Type π-Extension

Direct coupling reactions between C–H and C–X units where X is a halogen atom are described in this section (Scheme 2). Palladium complexes usually work nicely, but

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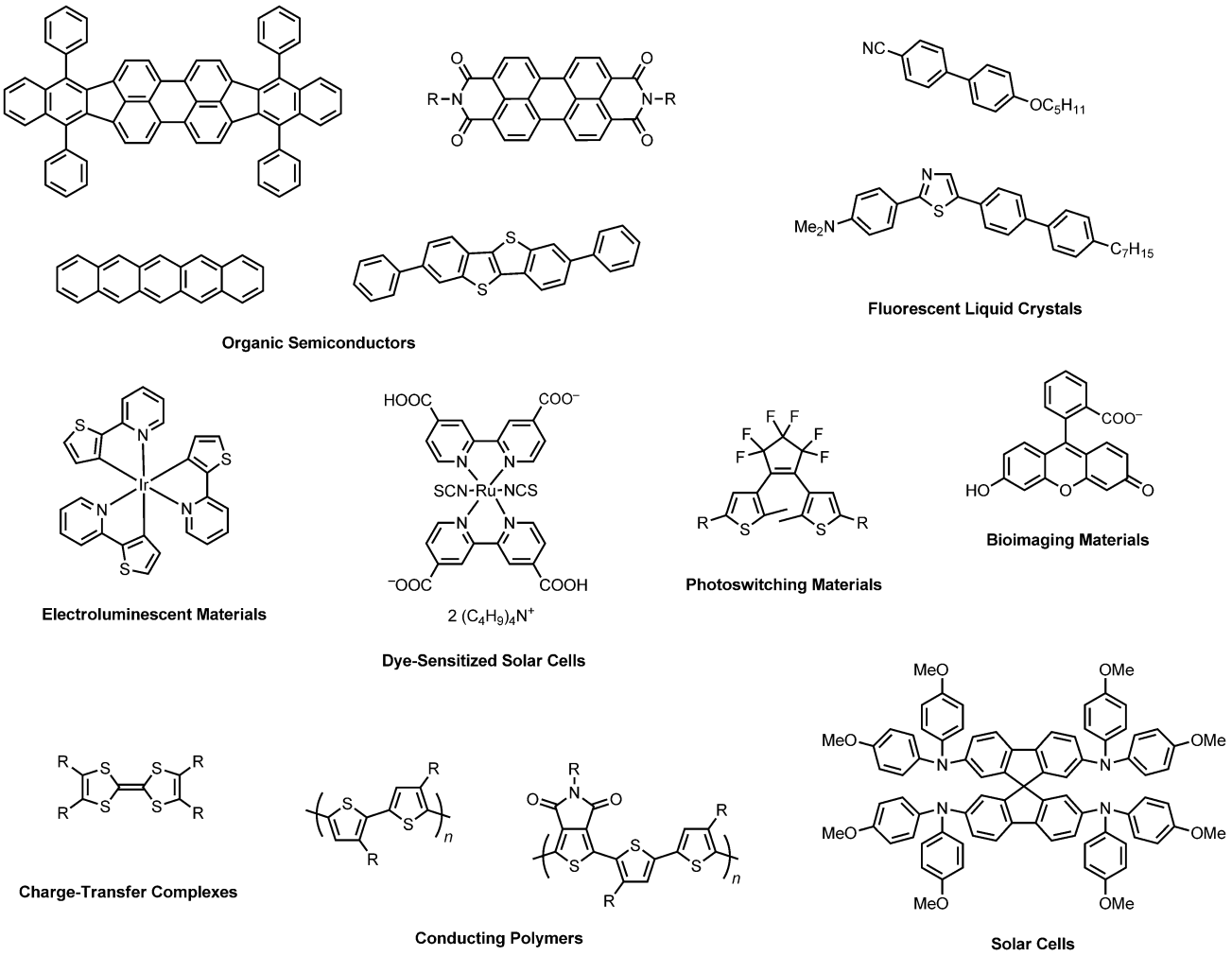
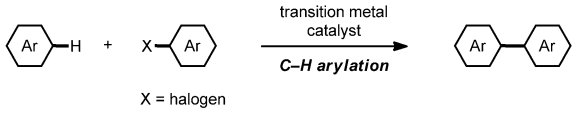


Figure 1. Representative organic materials with a conjugated π-system.



Scheme 2. C–H/C–X coupling reaction.

other transition metals are also known to catalyze these reactions. Bases are generally used to trap the acids that form (HX); some bifunctional bases such as carboxylates and carbonates also accelerate the C–H activation step through concerted metalation–deprotonation (CMD).[7] Reports on

Yasutomo Segawa was born in Chiba, Japan (1982). He studied chemistry at The University of Tokyo, Japan, and completed his PhD in 2009 with Prof. Kyoko Nozaki. He has been an Assistant Professor (with Prof. Kenichiro Itami) at Nagoya University since 2009, and became a Group Leader of JST-ERATO Itami Molecular Nanocarbon Project (Designated Associate Professor, Nagoya University) in 2013. His research focuses on the selective synthesis of curved aromatic hydrocarbons and the development of C–H functionalization reactions.

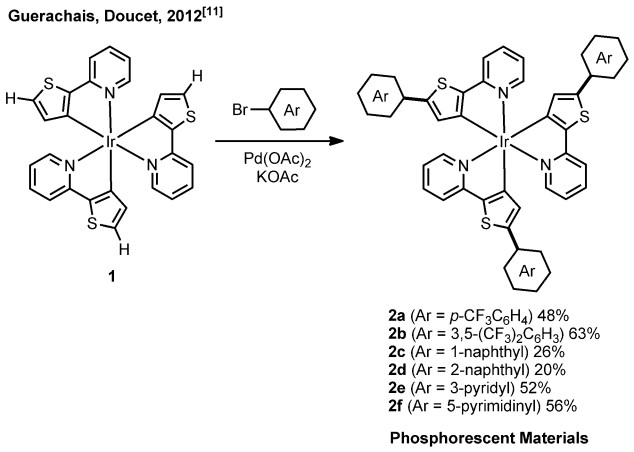
Takehisa Maekawa was born in Aichi, Japan (1988). He received a master's degree in chemistry from Nagoya University. Currently, he is a PhD student in the group of Prof. Kenichiro Itami. His research focuses on the rapid synthesis and extension of polycyclic aromatic hydrocarbons by C–H activation.

C–H/C–X coupling for π-extension are classified based on the substrate undergoing C–H activation, e.g., thiophenes, azoles (indole, imidazole, and thiazole), and other ring systems.

3.1.1. Thiophenes

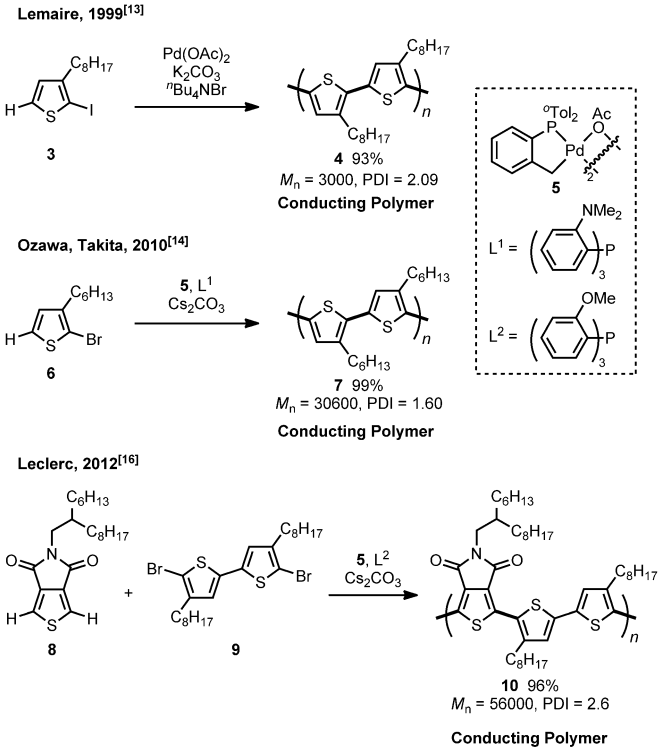
Since 1990 when Ohta and co-workers reported the first C–H arylation,[8] there have been many reports of palladium-catalyzed C–H arylation reactions of thiophenes.[9,10] Because thiophene is a widely used building block in organic electronic materials, C–H arylation reactions of thiophenes have great potential to accelerate developments in materials science. For example, in 2012 Doucet and Guerchais reported the C–H arylation of luminescent iridium complexes to tune photophysical properties at a late stage.[11] Pd-catalyzed C–H/C–Br type arylation was applied to 2-pyridylthiophenes on the iridium complex **1** to afford triarylated complexes **2a–f** in 20–63% yield (Scheme 3). The authors selected phosphine-free conditions[12] to avoid ligand-exchange reactions at the iridium center. Iridium complexes **2a–f** are nearly stable under the reaction conditions (130 °C, 48 h in dimethylacetamide (DMAc)). Both absorption and emission maxima of the arylated complexes **2a–f** were shifted to a high-wavenumber region. Late-stage arylation will accelerate the screening of luminescent compounds as materials for organic light-emitting diodes (OLEDs) and other devices.

The direct arylation of thiophene is a powerful method for synthesizing thiophene-containing π-conjugated polymers,[4b] which can be utilized for optoelectronic devices such as solar cells, LEDs, displays, and transistors. Scheme 4 shows three



Scheme 3. C–H arylation of a 2-(2-pyridyl)thien-3-yl ligand on iridium.

Kenichiro Itami was born in Pittsburgh, USA (1971) and raised in Tokyo. He studied chemistry at Kyoto University and completed his PhD in 1998 with Prof. Yoshihiko Ito. From 1997 to 1998, he was a predoctoral researcher in the group of Prof. Jan-E. Bäckvall at Uppsala University, Sweden. After his PhD, he became an Assistant Professor (with Prof. Jun-ichi Yoshida) at Kyoto University. He then moved to Nagoya University as an Associate Professor (with Prof. Ryoji Noyori) in 2005, and was promoted to Full Professor in 2008. He has also been Director of the Institute of Transformative Bio-Molecules (WPI-ITbM) since 2012 and Research Director of JST-ERATO Itami Molecular Nanocarbon Project since 2013. His research focuses on the development of new synthetic methods.



Scheme 4. Polymerization of thiophene by C–H/C–X coupling. PDI = polydispersion index.

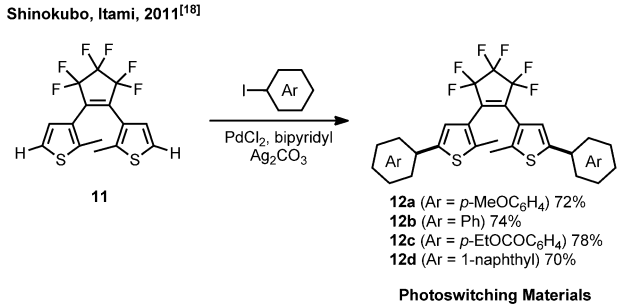
representative syntheses of polythiophenes by C–H arylation. The C–H/C–X cross-coupling of thiophene was first applied to polymer synthesis by Lemaire and co-workers.[13] 2-Iodo-3-alkylthiophenes (**3**) were converted into polythiophenes (**4**) in good yields with mainly head-to-tail structures, although the molecular weights were not high ($M_n = 3000$). In 2010 Takita and Ozawa reported an efficient method for the direct synthesis of regioregular polythiophenes.[14] Using Herrmann's palladacycle (**5**)[15] and $(2\text{-}Me_2NC_6H_4)_3P$ as catalyst precursors, they converted 2-bromo-3-hexylthiophene (**6**) into polythiophene (**7**) with high molecular weight and high regioregularity with up to quantitative yields. Leclerc synthesized an alternating copolymer of thienopyrrole-4,6-dione (**8**) and bithiophene (**9**) through a C–H/C–Br coupling reaction[16] using **5** and $(2\text{-}MeOC_6H_4)_3P$. Compared with the same copolymer synthesized under the Stille coupling conditions,[17] the copolymer **10** had a higher molecular weight ($M_n = 56000$) and higher yield (96%).

Dithienylethene, a photoswitching dye, has also been functionalized by C–H arylation of thiophenes. In 2011 Shinokubo and Itami reported the site-selective sequential multiarylation of dithienylethene **11**[18] through the α- and β-

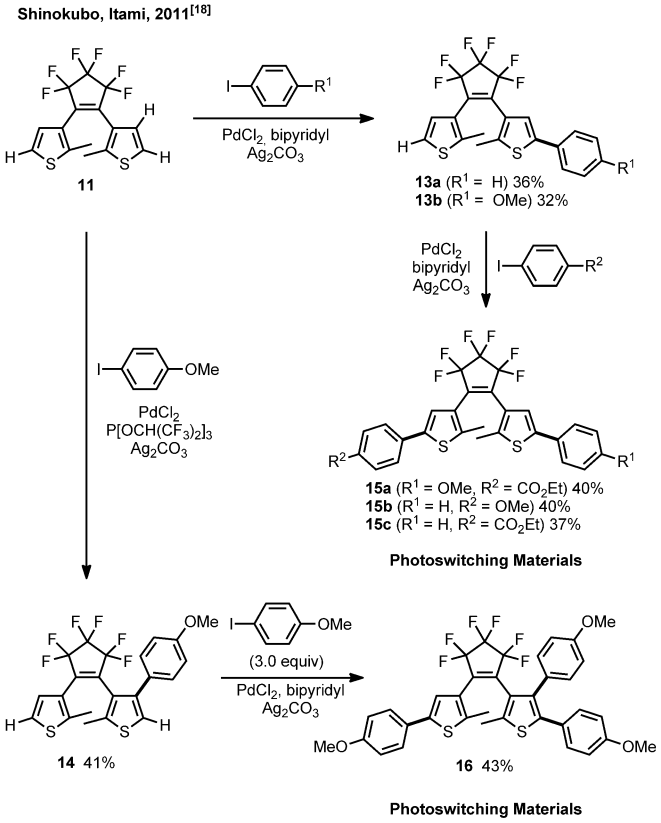
selective arylation[19] of thiophenes using catalysts developed by Itami. The starting material **11** was prepared by Suzuki–Miyaura cross-coupling of 2-methyl-3-thienylboronic acid with 1,2-dichlorohexafluorocyclopentene by a C–H/C–Cl coupling reaction.[20] Palladium-catalyzed C–H/C–I arylation of **11** was carried out to afford α,α′-diaryldithienylethenes **12a–d** (Scheme 5), α-aryldithienylethenes **13** (Scheme 6), and β-aryldithienylethene **14** by controlling the amount of iodoarenes (1.0 or 3.0 equiv) and the reaction conditions (2,2′-bipyridyl or $P[CH(CF_3)_2]_3$ as a ligand). Further α-arylation reactions of the α-aryldithienylethenes **13** and β-aryldithienylethene **14** were attempted to obtain unsymmetrical α,α′-diaryldithienylethenes **15** and α,α′,β-triaryldithienylethene **16**, respectively. Further development of the late-stage arylation of dithienylethenes will promote the rapid and simple fine-tuning of their photophysical properties.

In 2012 Guerchais and Doucet also applied a C–H/C–Br coupling reaction to dithienylethene **11**.[21] The authors reported that using potassium acetate (KOAc) as a base was critical to prevent decomposition of dithienylethene **11** and enhance the C–H palladation step via the CMD pathway. Several symmetrical and unsymmetrical α,α′-diaryldithienylethenes were synthesized in one or two steps, including donor–acceptor systems.

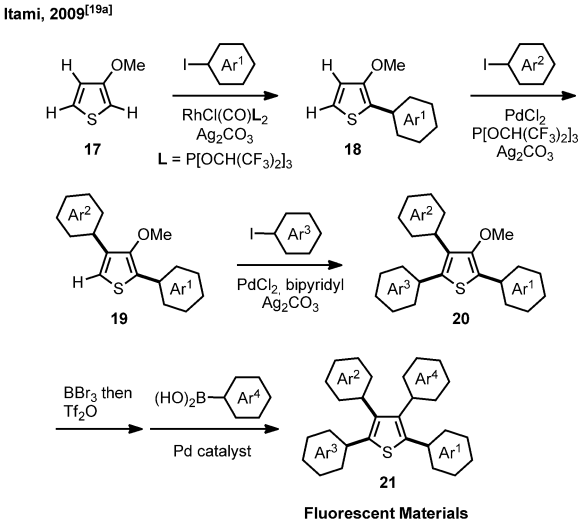
As exemplified by the above-mentioned examples, catalysts promoting the otherwise difficult β-selective arylation of thiophenes can be used for the π-extension of the thiophene core in various directions. In 2009 Itami reported the programmed synthesis of fluorescent tetraarylthiophenes by the sequential integration of α- and β-selective arylation reactions to 3-methoxythiophene **17** (Scheme 7).[19a] The C2-



Scheme 5. α-Selective C–H arylation of dithienylethene.



Scheme 6. Sequential α- and β-selective C–H arylation of dithienylethenes.



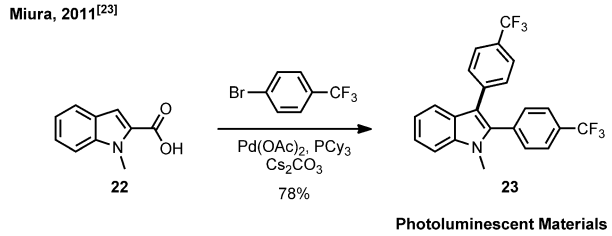
Scheme 7. Sequential C–H arylation for the synthesis of tetraarylthiophenes.

selective arylation of **17** was achieved by the action of the $RhCl(CO)\{P[OCH(CF_3)_2]_3\}_2$ catalyst, which can be followed by C4- and C5-selective arylation reactions catalyzed by $PdCl_2/P[OCH(CF_3)_2]_3$ and $PdCl_2$/bipyridyl, respectively. The thus-formed 2,4,5-triaryl-3-methoxythiophenes **20** can be converted to tetraarylthiophenes **21** by Suzuki–Miyaura coupling. In organic materials research, the properties of target molecules are often not easily predictable. Therefore, a programmable synthesis of π-conjugated molecules where one can access all possible derivatives and isomers like this example should find many applications in uses for combinatorial identification and optimization of lead structures.

3.1.2. Azoles

The C–H arylation of indoles[22] is an important reaction, as an indole core can be found in many natural products, pharmaceuticals, and synthetic materials. Miura and co-

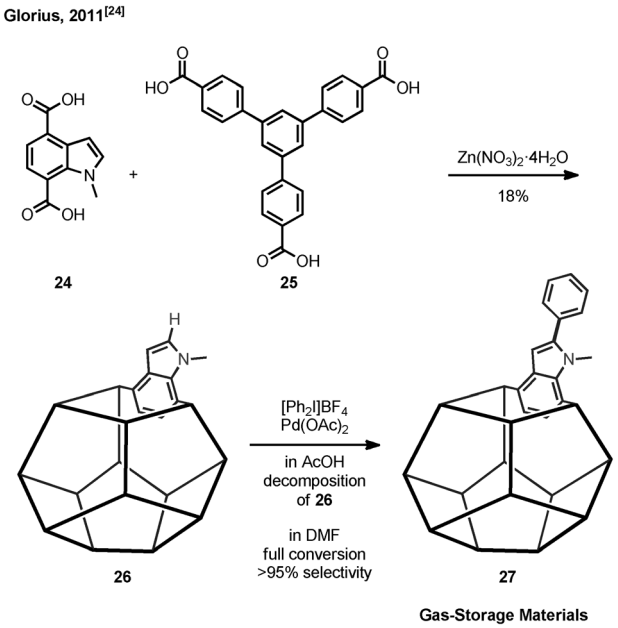
workers reported the direct and decarboxylative arylation of carboxyindoles.[23] The authors synthesized *N*-methyl-2,3-diarylindoles from *N*-methyl-2-carboxyindole (**22**) with bromoarenes and a palladium catalyst. For example, *N*-methyl-2,3-bis(4-trifluoromethylphenyl)indole (**23**) was obtained in 78% yield (Scheme 8). Some of the products had strong fluorescence even in the solid state. The absolute quantum yield of **23** was very high both in ethanol solution (0.90) and in the solid state (0.97). This reaction is a promising approach for the synthesis of a solid blue emitter for applications such as bioimaging.



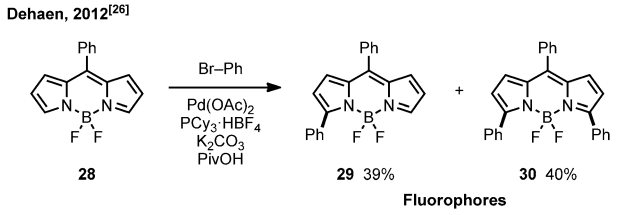
Scheme 8. One-step direct and decarboxylative C–H arylation of 1-methyl-2-carboxyindole.

Glorius reported the late-stage phenylation of *N*-methylindoles to modify a rod moiety of a metal–organic framework (MOF).[24] The Pd-catalyzed arylation of indoles[25] was applied to the MOF UMCM-1 (University of Michigan Crystalline Material-1; **26**) synthesized from *N*-methylindole-4,7-dicarboxylic acid (**24**), 1,3,5-tris(4-carboxyphenyl)-benzene (**25**), and zinc(II) nitrate. After evaluation of the reaction conditions, the authors found that dimethylformamide (DMF) was a good solvent for the C–H phenylation of *N*-methylindole moieties without decomposition of the MOF structure (Scheme 9). The regioselectivity was excellent (C2/C3 > 95:5) and moreover, the undesired Pd^{II}-mediated C–H/C–H dimerization of indoles was inhibited by the rigid framework. The cell parameters for MOF **26** ($P6_3/m$; $a = b =$ 40.633(11) Å; $c = 18.232(3)$ Å) and **27** ($P6_3/m$; $a = b =$ 41.09(2) Å; $c = 17.747(3)$ Å) imply that the C–H phenylation reaction took place in the cavity of the framework. The modified MOF **27** had four times larger N_2 uptake than **26**. Although the removal of palladium from **27** after the catalytic reaction was not complete, this report is at the forefront of research on the late-stage C–H functionalization of materials.

Boron complexes of dipyrromethenes (BODIPY) are useful fluorophore molecules because of their bright fluorescence in the visible region and robustness against light and chemicals. Deharn and co-workers reported the palladium-catalyzed C–H/C–Br coupling of BODIPY (**28**) with bromobenzene in 2012 (Scheme 10).[26] A mixture of monophenylated and diphenylated BODIPY (**29** and **30**) can be obtained in moderate yields. Other bromoarenes such as 4-bromoanisole, 3-bromothiophene, bromomesitylene, and 1-bromonaphthalene can be applied to yield mono- and diaryl BODIPYs. Although yields should be improved for efficient synthesis, the direct functionalization of BODIPY is important for fine-tuning its spectroscopic and electronic properties.



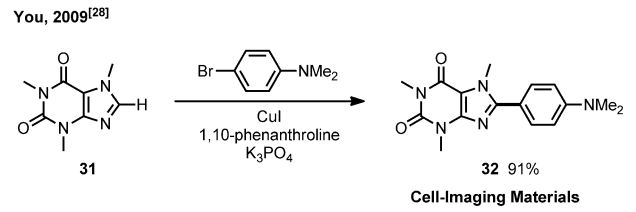
Scheme 9. Selective C–H arylation of an indole-containing MOF.



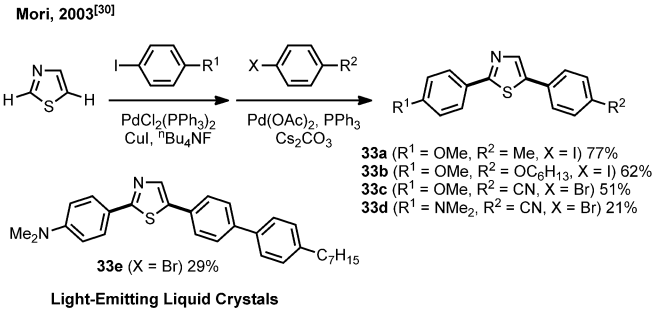
Scheme 10. Mono- and diphenylation of BODIPY (**28**).

1,3-Diazoles and other heteroarenes, such as 1,3-thiazoles and 1,3-oxazoles, have a relatively acidic hydrogen atom in the C2 position because of high π-donation from two heteroatoms. Xanthines (caffeine, theophylline, theobromine, etc.) are biologically active alkaloids, and the Pd- and Cu-catalyzed C–H arylation of caffeine (**31**) has been explored by Daugulis, You, and Ackermann.[27] You and co-workers found that 8-arylcaffeine had potential as a fluorescent material for cell imaging.[28] Scheme 11 depicts the Cu-catalyzed 4-(*N*,*N*-dimethylamino)phenylation of **31**. The product **32** has strong fluorescence even in the solid state; You and co-workers demonstrated cell imaging using **32** as a small biocompatible probe. The authors found that Lewis lung cancer cells and human embryo kidney 293 cells were successfully marked by **32**.

In the C–H activation of thiazoles, the regioselectivity at three nonequivalent C–H bonds at the 2-, 4-, and 5-positions is a current challenge. Many studies on the selective arylation of thiazoles[29] have been reported. Mori and co-workers applied the C–H arylation of thiazoles to the synthesis of light-emitting liquid crystals and prepared several 2,5-diarylthiazoles in a stepwise manner (Scheme 12).[30] The 2-position is more reactive than the other positions on thiazole; thus, C2-arylation was accomplished using a Pd/Cu catalyst system to afford 2-arylthiazoles with a small amount (ca. 6%) of 2,5-



Scheme 11. C–H arylation of caffeine at the C8-position.



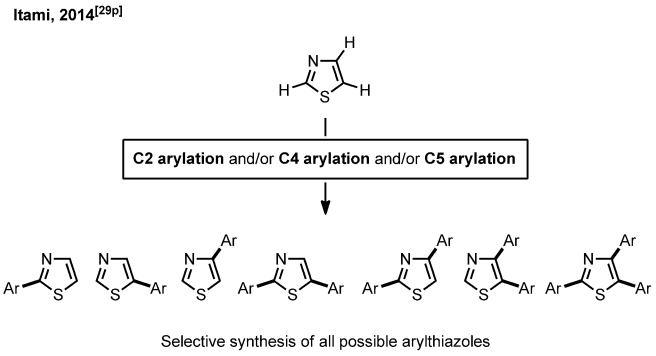
Scheme 12. Sequential C–H arylation of thiazole at the 2- and 5-positions.

diarylated side products. The 2-arylthiazoles were then converted into 2,5-diarylthiazoles **33a–e** via Pd-catalyzed C–H/C–X (X = Br, I) coupling reactions in 21–77% overall yield. The 2,5-diarylthiazoles **33a–e** have a nematic phase, which was identified by differential scanning calorimetry (DSC) and polarized microscopy, as well as high fluorescence quantum yields ($\Phi_F = 0.49$; **33e**). Mori and co-workers also synthesized donor–acceptor-type 2,5-diarylthiazoles and 2,5-diarylthiophenes by sequential C–H arylation reactions to evaluate the effect of the core structure (thiazole or thiophene) on photophysical and liquid-crystal characteristics.[31]

In 2014 Itami and co-workers established a programmed synthesis of photoluminescent arylthiazoles via sequential C–H couplings catalyzed by palladium or nickel complexes (Scheme 13).[29p] This versatile protocol can supply all possible arylthiazole substitution patterns (2-aryl, 4-aryl, 5-aryl, 2,4-diaryl, 2,5-diaryl, 4,5-diaryl, and 2,4,5-triaryl) from an unfunctionalized thiazole platform by 11 distinct synthetic routes. Over 150 arylthiazoles were synthesized by this unified synthesis platform. Like in the case of the programmed synthesis of tetraarylthiophenes shown in Scheme 7, the present method should find many uses for combinatorial lead-structure identification and optimization in optoelectronic arylthiazoles.

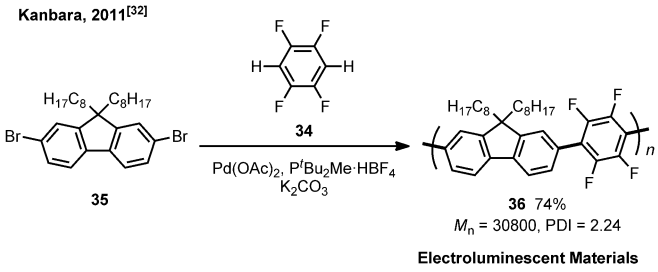
3.1.3. Benzene and Other Cyclic π-Systems

Compared with the research on the C–H/C–X coupling reactions of heteroarenes such as thiophenes and azoles, there have been few examples of C–H/C–X coupling reactions of benzene, because of the low reactivity of the C–H bonds of the benzene ring. Kanbara and co-workers synthesized a fluorene–tetrafluorophenylene copolymer[32] under the



Scheme 13. Sequential C–H arylation for the synthesis of all possible arylthiazoles.

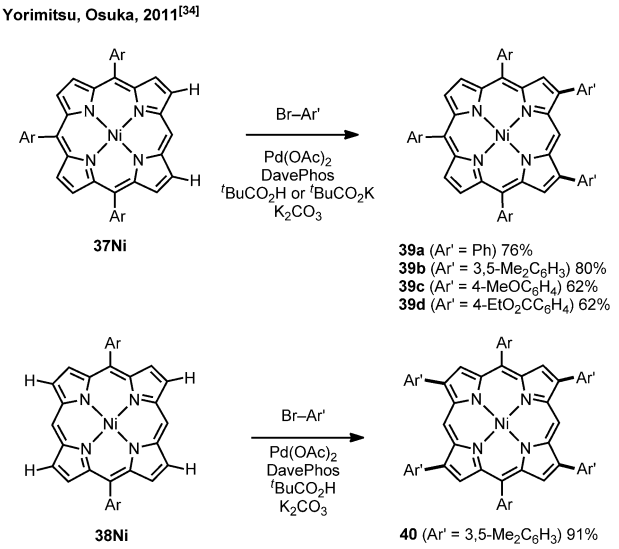
C–H/C–Br reaction conditions reported by Fagnou.[33] As the C–H moiety of fluorinated benzenes is relatively reactive to C–H metalation, 1,2,4,5-tetrafluorobenzene (**34**) was used as a coupling partner for bromoarenes. When 2,7-dibromo-9,9-dioctylfluorene (**35**) and **34** were reacted in the presence of $Pd(OAc)_2$ and $tBu_2MeP{\cdot}HBF_4$ as catalysts, a fluorene–tetrafluorophenylene copolymer (**36**) was obtained in good yield with a high degree of polymerization (57 on average, Scheme 14). Polymer **36** can be purified much more easily



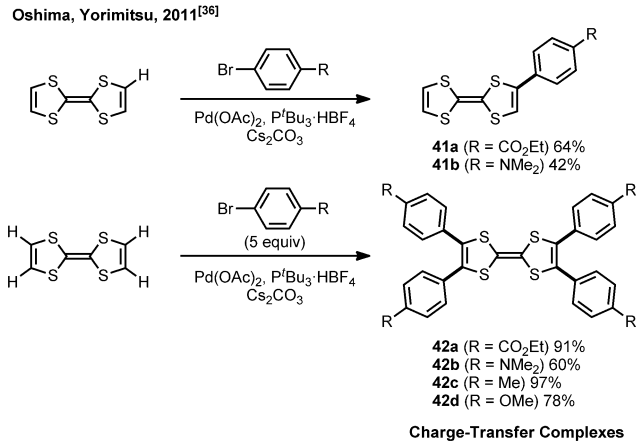
Scheme 14. Palladium-catalyzed C–H/C–Br type polycondensation of 2,7-dibromo-9,9-dioctylfluorene with 1,2,4,5-tetrafluorobenzene.

than the polymers synthesized using Stille or Suzuki–Miyaura cross-coupling, because C–H coupling is not subject to contamination with stoichiometric tin or boron salts. However, very high site-selectivity is needed for the reaction. Polycondensation of **34** with 3,6-dibromo-*N*-octyldibromocarbazole produces random copolymers with C–H/C–H coupling between carbazole and benzene; C–Br/B–Br coupling may also occur.

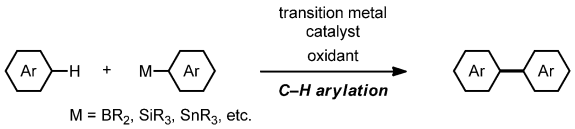
Porphyrins, a class of molecules with high aromaticity, have 18π-electrons, the ability to incorporate metal atoms, and high stability. The direct C–H functionalization of porphyrins is needed for the construction of π-extended porphyrin assemblies and hybrids between porphyrins and other aromatic molecules. In particular, the selective functionalization of porphyrins at the β-position is difficult compared with the *meso* position because of the comparatively low reactivity. Recently, Yorimitsu, Osuka, and co-workers reported the Pd-catalyzed β-selective C–H arylation of porphyrins (Scheme 15).[34] The direct arylation of 5,10,15-



Scheme 15. C–H arylation of di- or triarylporphyrins. DavePhos = 2-dicyclohexylphosphino-2′-dimethylamino-1,1′-biphenyl; Ar = 3,5-di-*tert*-butylphenyl.



Scheme 16. C–H arylation of TTF.



Scheme 17. C–H/C–M type coupling reaction.

triarylporphyrin (**37Ni**) and 5,15-diarylporphyrin (**38Ni**) was achieved by conducting C–H arylation[35] in the presence of pivalic acid. C–H arylation took place at the β-positions to generate diarylated products (**39a–d**) and a tetraarylated product (**40**). The authors found that the π-extension of porphyrins at the β-positions resulted in slightly red-shifted absorption spectra.

Tetrathiafulvalene (TTF), while not an aromatic compound, is an important organic π-molecule as a reversible oxidant, an electron donor, and a component of charge-transfer (CT) complexes. The ability to modify the electronic properties of TTF is important. However, the functionalization of TTF requires multistep syntheses consisting of, for example, metalation and cross-coupling. Oshima and Yorimitsu reported efficient palladium-catalyzed C–H/C–Br coupling reactions of TTF with aryl bromides (Scheme 16).[36] Monoarylated TTFs (**41a**,**b**) were obtained in moderate yields (42–64%) with di- or triarylated products when equal amounts of aryl bromide and TTF were reacted. When five equivalents of aryl bromides were used, tetraarylated TTF derivatives (**42a–d**) were produced in good yields. The authors converted the products (**41a**,**b** and **42a–d**) into 1:1 CT complexes using 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) or tetracyanoquinodimethane (TCNQ) and found that the CT complexes of **42b** (**42b**-DDQ and **42b**-TCNQ) had near-infrared absorptions of up to 1600 nm.

3.2. C–H/C–M- Type π-Extension

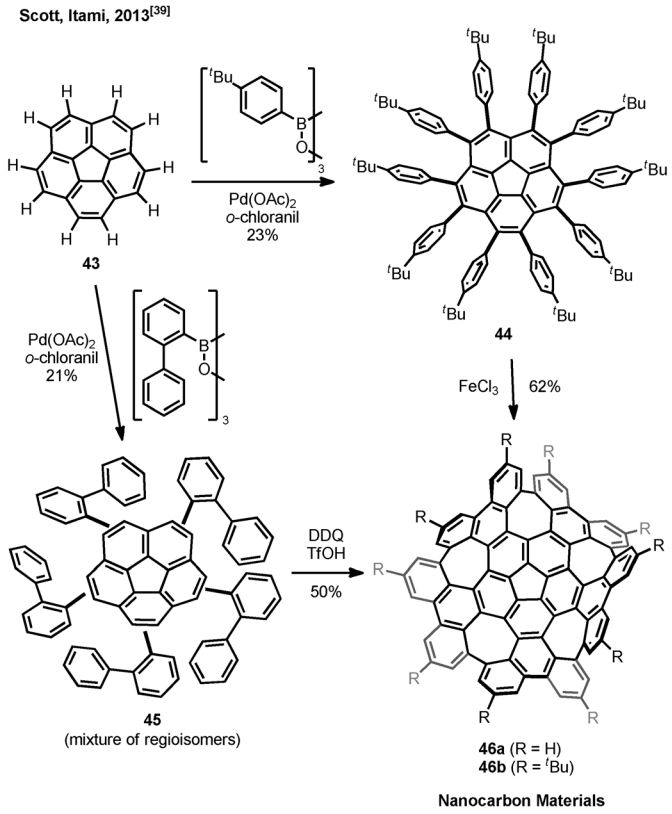
C–H/C–M coupling[37] proceeds in an oxidative manner (Scheme 17). Suitable oxidants are needed to reoxidize transition metal species in a catalytic cycle. In general, C–M/C–M homocoupling and C–H/C–H homocoupling compete with C–H/C–M coupling. Thus, high chemoselectivity is necessary to utilize C–H/C–M coupling as an efficient synthetic tool.

3.2.1. Polycyclic Aromatic Hydrocarbons

There are very few examples of the selective C–H arylation of polycyclic aromatic hydrocarbons (PAHs),[38] because of the low reactivity and small differences between the C–H bonds in PAHs. Itami and co-workers reported the Pd-catalyzed C–H/C–B coupling of PAHs, including phenanthroline, pyrene, fluoranthene, and perylene, using *o*-chloranil as an oxidant.[39] Through a sequence of C–H/C–B coupling and Scholl-type intramolecular C–H/C–H cyclization reactions, the authors demonstrated rapid π-extension of PAHs. Corannulene (**43**), a bowl-shaped PAH, was also arylated under these reaction conditions.[39d,e] For example, all 10 C–H bonds of **43** were arylated to form decaarylcorannulene **44**, in which the corannulene core is almost planar. Reaction of **43** with tris(*o*-biphenylyl)boroxin yielded pentabiphenylylcorannulene (**45**) as a mixture of regioisomers. Scholl reaction of both **44** and **45** produced a novel PAH, warped nanographene (**46a**,**b**; Scheme 18). Warped nanographene is a representative structure of a new family of nanocarbons having negative curvature.

3.2.2. Perylene Bisimides

The functionalization of perylene tetracarboxylic acid bisimides (PBIs)[40] has been widely explored to increase their solubility and modify their photophysical properties as multichromophores. Shinokubo and Osuka reported the direct arylation of PBIs[41] by applying a carbonyl-directed Ru-catalyzed C–H/C–B coupling reaction developed by Kakiuchi and co-workers.[42] In addition to the original reaction

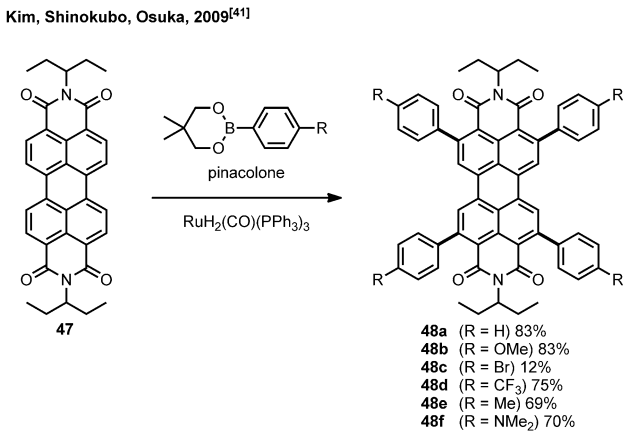


Scheme 18. Synthesis of warped nanographene (**46**) by C–H/C–B coupling and subsequent Scholl reaction. DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone; *o*-chloranil = 3,4,5,6-tetrachloro-*o*-benzoquinone; Tf = trifluoromethanesulfonyl.

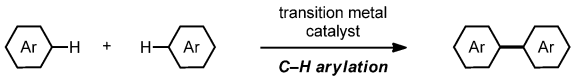
conditions (arylboronic acid neopentyl glycol esters, $RuH_2(CO)(PPh_3)_3$ as a catalyst, and pinacolone as an oxidant), the authors used mesitylene and increased the reaction temperature. Under these conditions, PBI **47** was successfully converted into tetraarylated PBIs **48a–f** in good yields (Scheme 19). The Ru-catalyzed carbonyl-directed C–H/C–B coupling has also been applied to synthesize picene and dibenzoanthracenes as candidates for organic field effect transistor (OFET) materials as well as for the synthesis of hexaarylanthracenes.[43]

3.3. C–H/C–H Type π-Extension

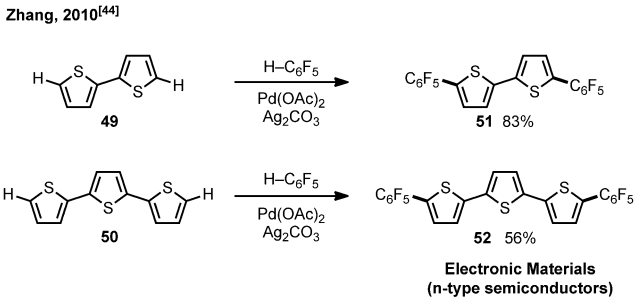
Reports of C–H/C–H cross-coupling reactions (Scheme 20) are much less common than those of other C–H coupling reactions. Since their seminal discovery by Fagnou and co-workers,[22a] C–H/C–H cross-coupling reactions have been widely explored as an ideal methodology for increasing the efficiency of syntheses. Zhang and co-workers reported the C–H/C–H cross-coupling of thiophenes and electron-deficient arenes[44] under previously reported reaction conditions.[45] This reaction was applied to bithiophene (**49**) and terthiophene (**50**) in order to introduce pentafluorophenyl groups at the α-positions, providing **51** and **52** in good yields (Scheme 21). The π-extended thiophenes **51** and **52** are known as *n*-type organic semiconductors.[46]



Scheme 19. Directed C–H arylation of perylene bisimide.



Scheme 20. C–H/C–H cross-coupling.



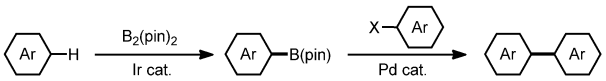
Scheme 21. C–H/C–H cross-coupling of bithiophene and terthiophene with pentafluorobenzene.

4. Sequential π-Extension by C–H Borylation

The iridium-catalyzed C–H borylation of arenes[47] changed the strategy for synthesizing π-extended molecules. The high yields and high selectivity of C–H borylation made this approach a key method for connecting π-systems in a programmable manner. Although the process requires two steps, C–H borylation followed by Suzuki–Miyaura coupling (Scheme 22), these reactions have many advantages, such as mild reaction conditions and the predictability of the borylation site. It has also been reported that the sequential reactions can be performed in one pot.[48]

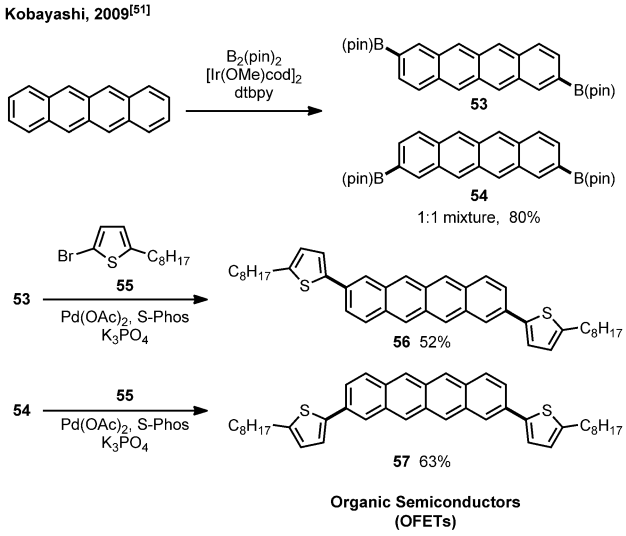
4.1. Acenes

The C–H borylation of PAHs such as pyrene, perylene,[49] and anthracene[50] has been reported. For pyrene and perylene, 2,7-diborylpyrene and 2,5,8,11-tetraborylperylene were obtained as the sole products, respectively, while anthracene was converted into a 1:1 mixture of 2,6- and 2,7-diborylanthracene. Kobayashi and co-workers reported the



Scheme 22. Sequential C–H borylation/Suzuki–Miyaura coupling for π-extension. B(pin) = 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl.

C–H borylation of tetracene and a subsequent Suzuki–Miyaura cross-coupling reaction (Scheme 23).[51] A mixture of 2,8- and 2,9-diboryltetracene (**53** and **54**) was obtained through the C–H borylation reaction. After separation by recrystallization, cross-coupling with bromothiophene (**55**) produced dithienotetracenes (**56** and **57**). These products demonstrated hole mobility ($3\times10^{-2}\,cm^2V^{-1}s^{-1}$ (**56**) and $2\times10^{-2}\,cm^2V^{-1}s^{-1}$ (**57**) in the saturation regime), suggesting potential application as OFETs.



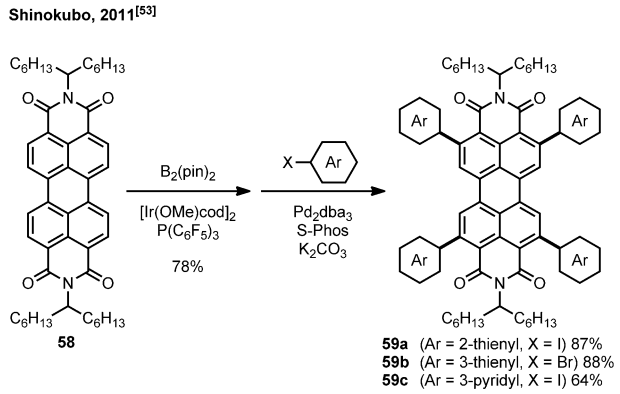
Scheme 23. C–H borylation and Suzuki–Miyaura coupling of tetracene. S-Phos = 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl; cod = 1,5-cyclooctadiene; dtbpy = 5,5′-di-*tert*-butyl-2,2′-bipyridine.

4.2. Perylenes

When phosphine is used as a ligand instead of 2,2′-bipyridine derivatives, C–H borylation takes place at the position *ortho* to the directing group.[52] Shinokubo and co-workers utilized *ortho*-borylation for the two-step functionalization of PBI (**58** in Scheme 24).[53] Four heteroaryl groups such as thienyl and pyridyl were introduced in two steps to yield **59a–c**. This is a complementary method for directing tetraarylation (Scheme 19) when the introduction of heteroarenes is difficult.

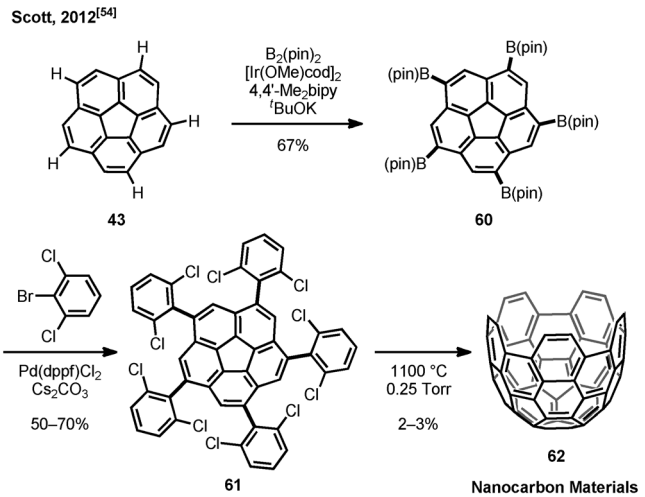
4.3. Corannulene

Scott and co-workers expanded the utility of aromatic C–H borylation by exploiting its reversibility.[54] The authors found that the C–H borylation of arenes becomes reversible in the presence of catalytic amounts of strong bases, such as *t*BuOK, Cs_2CO_3, K_2CO_3, and CsF. This is a very useful method

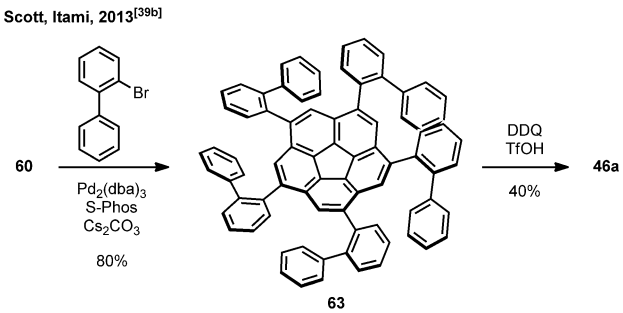


Scheme 24. Sequential C–H borylation/Suzuki–Miyaura coupling of perylene bisimide **58**.

for obtaining multiborylated PAHs in which the maximum number of boryl groups are introduced in a regioselective manner. Corannulene (**43**), a bowl-shaped C_5-symmetric PAH, was borylated C_5-symmetrically under these reaction conditions to furnish 1,3,5,7,9-pentaborylcorranulene (**60**), shown in Scheme 25. The product **60** can be converted into the hemispherical carbon nanotube end-cap **62**[55] and warped nanographene (**46a**, Scheme 26)[39e] by fivefold Suzuki–



Scheme 25. Sequential C–H borylation/Suzuki–Miyaura coupling route to nanotube endcap **62**. dppf = 1,1′-diphenylphosphinoferrocene.

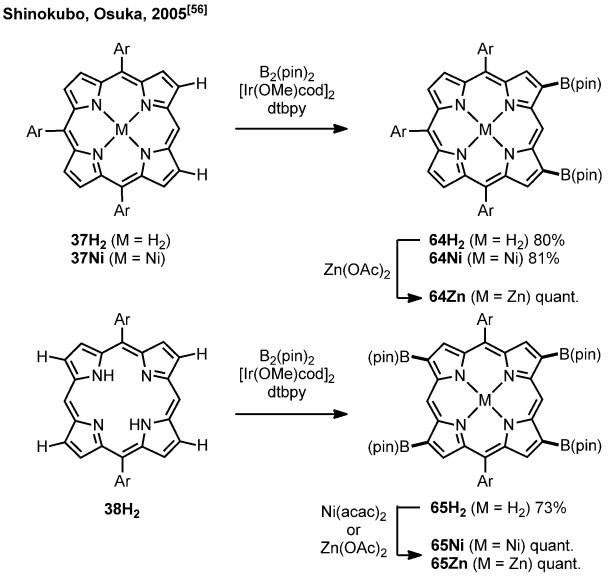


Scheme 26. Sequential C–H borylation/Suzuki–Miyaura coupling route to warped nanographene **46a**.

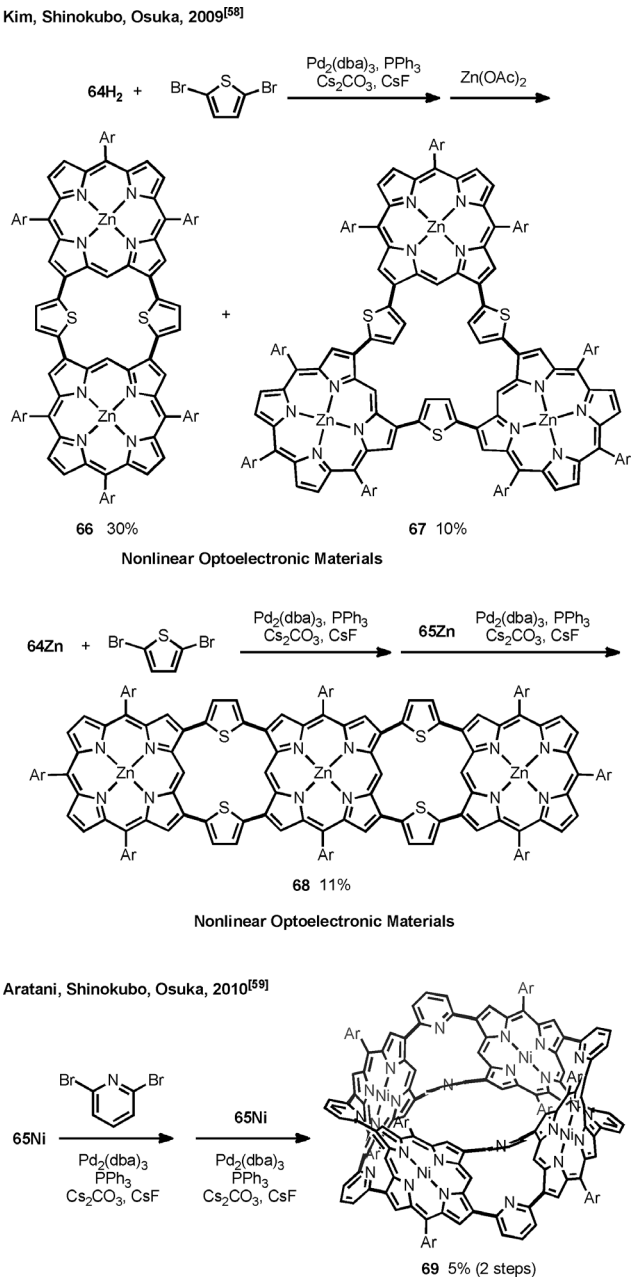
Miyaura cross-coupling and subsequent intramolecular C–C bond formation through flash vacuum pyrolysis or the Scholl reaction.

4.4. Porphyrins

Shinokubo and Osuka applied the C–H borylation reaction to porphyrins.[56] Porphyrins with very bulky aryl groups, such as 5,10,15-tris(3,5-di-*tert*-butylphenyl)porphyrin (**37H$_2$**), can be converted into the corresponding diborylporphyrin **64H$_2$** with high yield and perfect β-selectivity (Scheme 27). This method is also applicable to diarylporphyrin **38H$_2$** to yield the tetraborylated product **65H$_2$**. Free-base porphyrins **37H$_2$** and **38H$_2$** as well as the nickel(II) complex of tetraarylporphyrin (**37Ni**) were reacted in a similar manner to generate nickel(II) diborylporphyrin **64Ni**. Starting from these di- or tetraborylated porphyrins, several conjugated porphyrin arrays[57] were synthesized (Scheme 28). The Suzuki–Miyaura cross-coupling reaction of diborylporphyrin **64H$_2$** with 2,5-dibromothiophene produced a ladder-shaped dimer **66** and a triangular trimer **67**. A ladder-shaped trimer **68** was synthesized through sequential Suzuki–Miyaura cross-coupling reactions with **64Zn**, 2,5-dibromothiophene, and tetraborylporphyrin **65Zn**.[58] The porphyrin oligomers **66–68** showed high two-photon excitation (**66**: 7020 GM, **67**: 8060 GM, **68**: 17300 GM at 800 nm). Osuka and co-workers also synthesized the barrel-shaped porphyrin tetramer **69** from **65Ni** and 2,6-diborylpyridine through two cross-coupling reactions.[59] The "porphyrin nanobarrel" **69** can encapsulate fullerene C_{60} in its cavity.



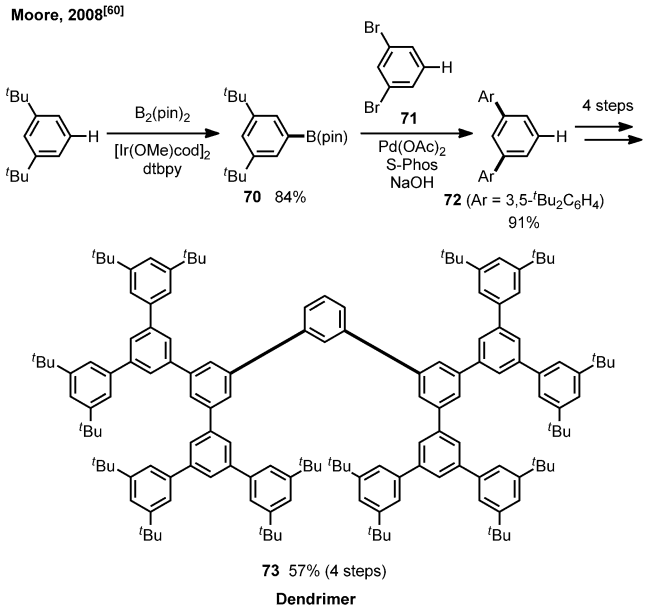
Scheme 27. C–H borylation of porphyrin. Ar = 3,5-di-*tert*-butylphenyl.



Scheme 28. Ladder-, triangular-, and barrel-shaped porphyrin oligomers. Ar = 3,5-di-*tert*-butylphenyl.

4.5. Dendrimers

Moore reported the synthesis of a dendrimer by sequential C–H borylation and cross-coupling reactions in 2008 (Scheme 29).[60] Two steps starting from 1,3-di-*tert*-butylbenzene and 1,3-dibromobenzene (**71**) produced the first-generation dendrimer **72**. Because **72** has suitable reactive sites for C–H borylation, the same reactions (1,3-diiodobenzene was used instead of **71**) were applied twice more to yield the third-generation dendrimer **73**. The overall yield of the six-step synthesis starting from 1,3-di-*tert*-butylbenzene was 44%, indicating the reliability of the two reactions. The dendrimer **73** had high thermal stability and a high melting

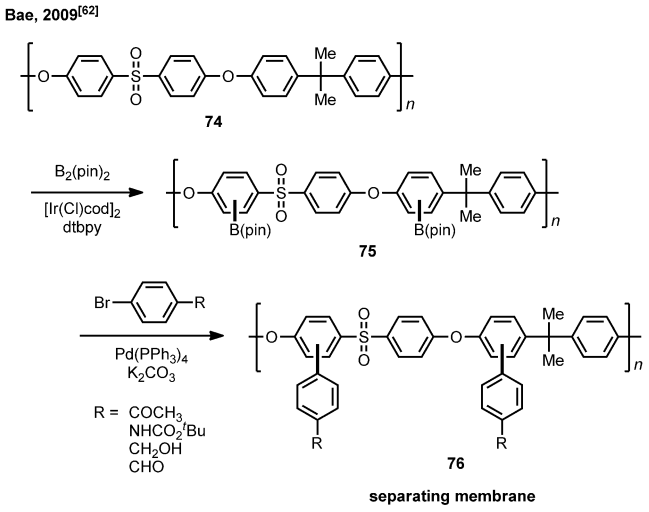


Scheme 29. Threefold sequential C–H borylation/Suzuki–Miyaura coupling to dendrimer **73**.

point (> 400 °C) with fluorescence ($\Phi = 0.15$), characteristic of rigid, conjugated dendrimers.[61]

4.5. Polymers

Post-synthesis functionalization of polymers is a powerful methodology for tuning the physical properties of polymers. However, very high reactivity and selectivity are required because reacted and unreacted moieties in a single polymer cannot be separated. Bae and co-workers demonstrated the functionalization of polysulfone,[62] a candidate membrane for the separation of small molecules and for fuel cells (Scheme 30).[63] The C–H borylation of polysulfone **74**

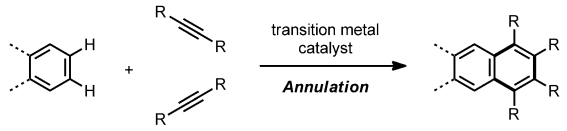


Scheme 30. Post-synthesis functionalization of polysulfone **74**.

occurred on both types of benzene rings, the -O-C_6H_4-SO_2- and -O-C_6H_4-CMe_2- moieties. After borylation with $B_2(pin)_2$, the Suzuki–Miyaura cross-coupling reaction with bromoarenes was carried out to introduce *para*-substituted aryl groups on the main chain (**76** in Scheme 30).

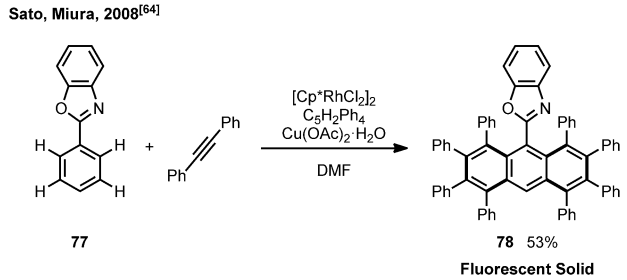
5. Aromatic Homologation

As an alternative methodology, alkynes can be used as building blocks for π-extension. Aromatic homologation through sequential C–H activation and cyclization can efficiently extend aromatic rings to π-extended molecules (Scheme 31).



Scheme 31. Aromatic homologation.

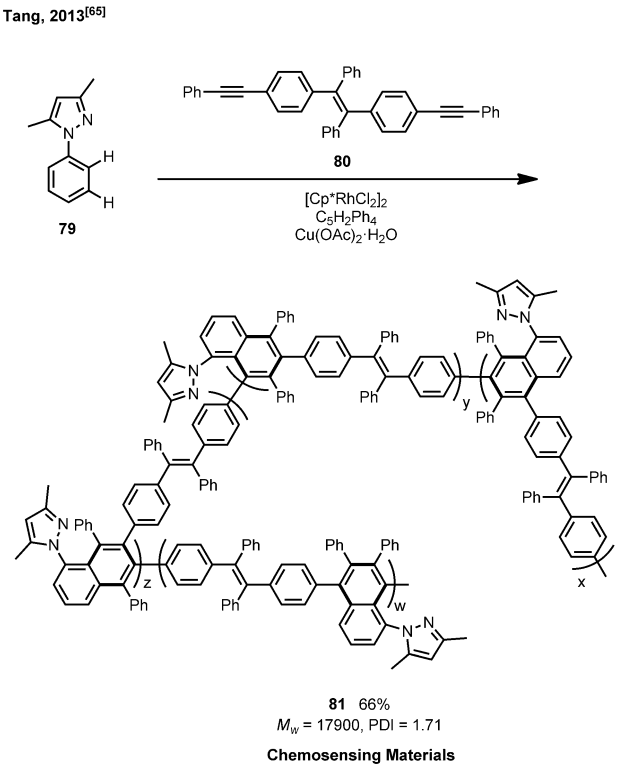
In 2008 Miura and co-workers reported the first azole-directed Rh-catalyzed aromatic homologation of a benzene ring[64] to give substituted naphthalene and anthracene. The authors developed the $[Cp^*RhCl_2]_2$ catalyst, which is now widely used in a range of directed C–H coupling reactions. Pyrazole and oxazoles can be used as directing groups for selective C−H bond cleavage and 1,2,3,4-tetraphenyl-1,3-cyclopentadiene is an effective ligand for enhancing yield in this catalytic system. The octaphenylated 2-(9-anthryl)benzoxazole **78** obtained from 2-phenylbenzoxazole (**77**) and diphenylacetylene exhibits solid state fluorescence over 470–530 nm (Scheme 32).



Scheme 32. Aromatic homologation of 2-phenylbenzoxazole (**77**).

Recently this type of reaction has been for polymer synthesis. In 2013 Tang and co-workers reported a new synthetic route to functional polymers by aromatic homologation with diyne substrates.[65] In the presence of $[Cp^*RhCl_2]_2$ and $Cu(OAc)_2$, as originally reported by Miura, homologation triggered the polymerization of 3,5-dimethyl-1-phenylpyrazole (**79**) with [4-(2-phenylethynyl)phenyl]-1,2-diphenylethane (**80**) to give poly(pyra-

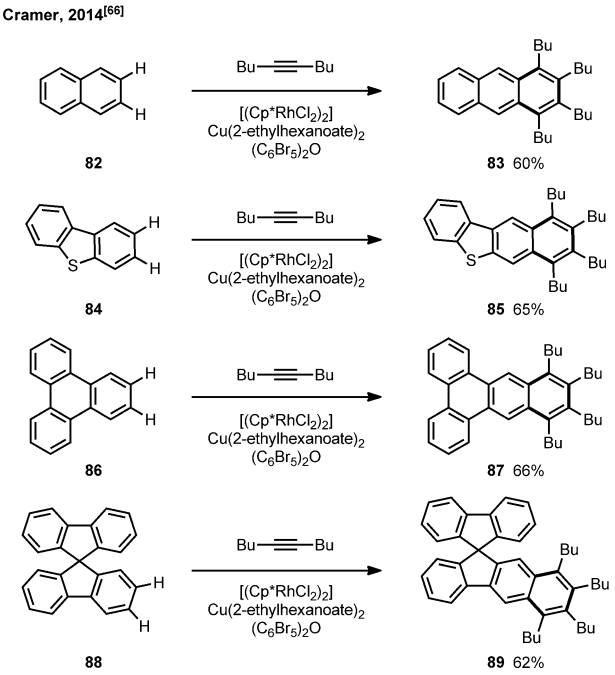
zolylnaphthalene) (**81**) as an atactic copolymer in good yield (Scheme 33). The copolymer obtained has high molecular weight ($M_w = 17900$) and aggregation-induced emission (AIE) activity. Thus, this copolymer is a potential material for chemosensors to detect explosive materials such as picric acid.



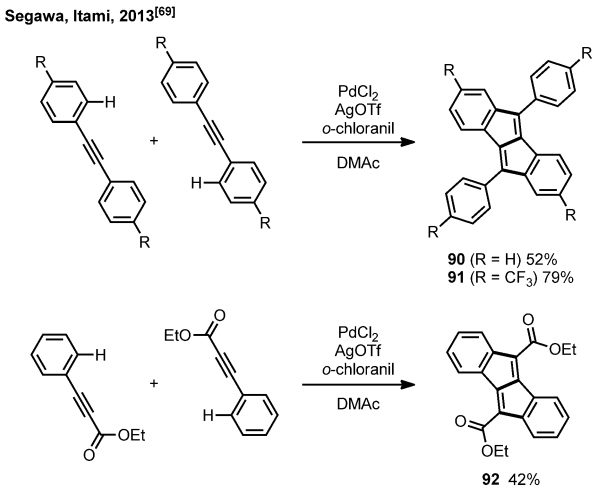
Scheme 33. Polymer synthesis by means of aromatic homologation.

Most of these π-extension methods make use of a directing group to cleave C–H bonds or reactive heteroarenes such as indoles and thiophenes. In 2014 Cramer and co-workers reported the Rh-catalyzed direct C–H activation of polycyclic hydrocarbons without a directing group (Scheme 34).[66] In addition to the previous catalytic system for aromatic homologation reaction, the authors used bis(pentabromophenyl) ether as a co-oxidant inspired by Glorius[67] to improve the yields. In this way PAHs can be regioselectively π-extended; e.g., from naphthalene (**82**) to anthracene (**83**), from dibenzothiophene (**84**) to benzonaphthothiophene (**85**), from triphenylene (**86**) to benzo[*f*]tetraphene (**87**), and from spirobifluorene (**88**) to the corresponding spiro[benzofluorene-fluorene] (**89**) in moderate yields.

Another type of aromatic homologation through C–H activation can be seen in the synthesis of dibenzo[*a*,*e*]pentalene (DBP). Because the 5-6-6-5 fused ring system of DBPs displays characteristic properties such as weak antiaromaticity, high reactivity, and high redox potentials, a synthetic route to DBPs has been developed.[68] In 2013 Segawa and Itami reported the palladium-catalyzed C–H/C–H dimerization of diarylacetylenes (Scheme 35).[69] For example, 5,10-diphenyldibenzo[*a*,*e*]pentalene (**90**) and its CF_3 derivative (**91**) were obtained in a single step from readily available diarylacetylenes. Similar to the C–H/C–B coupling reaction shown in Scheme 18, *o*-chloranil is essential to promote this DBP formation reaction. Not only symmetrical alkynes but also unsymmetrical alkynes such as ethyl 3-phenylpropiolate can be utilized in this reaction to afford DBP dicarboxylate **92**. Recently, Jin and Yamamoto reported the palladium-catalyzed C–H/C–Cl cross-dimerization of diarylacetylenes for the formation of DBPs, in which C–H activation took place as an intramolecular reaction.[70]



Scheme 34. Selective aromatic homologation without directing groups.



Scheme 35. Direct formation of dibenzo[*a*,*e*]pentalene from diphenylacetylene by means of double C–H activation.

6. Summary

In this Review we have summarized C–H functionalization reactions applied to π-systems for π-extension. Small aromatic molecules such as benzene, thiophene, indole, and thiazole can be effectively arylated to extend conjugation. Large and characteristic π-systems, such as tetracene, TTF, corannulene, and porphyrin, can also be functionalized directly or sequentially to produce materials with unique π-systems. Direct C–H arylation reactions as well as sequential C–H borylation and Suzuki–Miyaura cross-coupling approaches are very powerful methods for synthesizing π-extended molecules. The recent development of aromatic homologation reactions through double C–H cleavage for the rapid formation of π-extended molecules was also described. C–H functionalization has had a substantial impact on polymer science in terms of polymer synthesis as well as post-synthesis functionalization of polymers. We look forward to new discoveries and progress in C–H functionalization reactions to further contribute to the development of materials science.

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