主論文

Annulative π-Extension of Arenes and Alkynes

芳香環およびアルキンのπ拡張反応

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Preface

The studies presented in this thesis have been carried out under the direction of Professor Kenichiro Itami at Department of Chemistry, Graduate School of Science, Nagoya University between April 2011 and March 2016. The studies are concerned with annulative π-extension of arenes and alkynes.

I would like to express my sincerest gratitude to Professor Kenichiro Itami for great support, valuable suggestions and hearty encouragement throughout this work. I was so lucky to have a chance to hear his MLBA award lecture at Kyushu University in 2008, which was absolutely turning point in my carrier. I would like to greatly appreciate everything Lecturer Hideto Ito provided me during the course of this study. I appreciate to Associate Professor Yasutomo Segawa for his helpful suggestions and the measurement of X-ray crystallography. I also appreciate Associate Professor Junichiro Yamaguchi, Associate Professor Shinya Hagihara and Assistant Professor Kei Murakami for their helpful discussions, and encouragements.

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Contents

List of Abbreviations

Å	angström unit	Et	ethyl
Ac	acetyl	ECP	effective core potential
acac	acetylacetonate	EDG	electron donating group
AFM	atomic force microscope	ESI	electrospray ionization
Alk	alkyl	EWG	electron withdrawing group
APEX	annulative π-extension	GC	gas chromatography
Ar	aryl	GNR	graphene nanoribbon
bipy	2,2'-bipyridyl	h	hour(s)
Bn	benzyl	HOMO	highest occupied molecular orbital
BQ	1,4-benzoquinone	^{i}Pr	1-methyl-1-ethyl
Bz	benzoyl	J	coupling constant (NMR)
cat	catalytic	IRC	intrinsic reaction coordinate
CNT	carbon nanotube	LUMO	lowest unoccupied molecular orbital
cod	1,5-cyclooctadiene		
Cp	cyclopentadienyl	m	meta
Cp*	pentamethylcyclopentadienyl	MALDI-TOF MS	matrix assisted laser desorption/ionization time of flight mass spectrometry
δ	chemical shift (NMR)		
DART	direct analysis in real time		
dba	dibenzylideneacetone	Me	methyl
DCE	1,2-dichloroethane	Mes	2,4,6-trimethylphenyl
DDQ	2,3-dichloro-5-dicyano-p-benzoquinone	min	minute(s)
		MP2	Møller-Plesset second-order perturbation theory
DFT	density functional theory		
DMF	N,N-dimethylformamide	MS	molecular sieves
DMPU	N,N'-dimethylpropyleneurea	Ms	methanesulfonyl
DMSO	dimethyl sulfoxide	^{n}Bu	1-butyl
Dtbpm	bis(di-$tert$-butylphosphino)methane	NBS	N-bromosuccinimide
		NMR	nuclear magnetic resonance
dtbpy	4,4'-di-$tert$-butyl-2,2'-bipyridine	o	ortho
		o-chloranil	3,4,5,6-tetrachloro-1,2-benzoquinone
equiv	equivalent(s)		

o-DTBQ	3,5-di-*tert*-butyl-1,2-benzoquinone	STM	scanning tunneling microscope
p	para	^{t}Bu	1,1-dimethyl-1-ethyl
p-chloranil	2,3,5,6-tetrachloro-1,4-benzoquinone	TBAB	tetra-*n*-butylammonium bromide
p-DTBQ	2,5-di-*tert*-butyl-1,4-benzoquinone	TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
PAH	polycyclic aromatic hydrocarbon	Tf	trifluoromethanesulfonyl
		TfO	triflate
pin	pinacolato	THF	tetrahydrofuran
Ph	phenyl	TMS	trimethylsilyl
Ppy	2-phenylpyridinato	Ts	tosyl
R	an organic group	UV	ultraviolet
rt	room temperature	XPhos	2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl
SCS	spin-component-scaled		
SDD	Stuttgard-Dresden basis set		
S_EAr	electrophilic aromatic substitution		

General Introduction

1. Introduction

Fused π-conjugated system is a key component in material and pharmaceutical science due to their unique physical property as well as bioactivity. In particular, π-extended aromatics show superior physical and biological properties to small aromatics arisen from their extended π-conjugation, tunable HOMO–LUMO gap, absorption, and emission of longer wavelength light, lower oxidation and/or reduction potentials, strong π-π interactions, and higher mechanical strength.[1] With these attractive properties, π-extended aromatics are often employed as organic electronics materials. Therefore, development of efficient synthetic method for π-extended molecules is strongly demanded and regarded as one of the most important research fields.

One of the simplest and most intuitive methods for the construction of π-extended aromatics would be stepwise π-extension of abundant small aromatics (Scheme 1)[2-4]. For example, anthracene is classically synthesized in multi-steps from benzene by the sequence of Friedel–Crafts acylation with phthalic anhydride and reduction of anthraquinone (Scheme 1a).[2] In the synthesis of carbazoles and dibenzothiophenes, π-extension reactions are also effective by employing easily available indoles and benzothiophenes (Scheme 1b)[3]. However, most of these synthesis demands multi-step sequences including halogenation, cross-coupling reaction, oxidation, cyclization, and so on. For the synthesis of polycyclic aromatic hydrocarbons (PAHs), nanographenes, and graphene nanoribbons, cyclodehydrogenation has been frequently employed to polyarylated compounds which are derived from cross-coupling reaction between aryl halide and aryl metals and/or Diels–Alder reaction (Scheme 1c)[4]. As mentioned above, typical π-extension methods usually require multi-step reactions, lowering the yields and the efficiencies in synthesis.
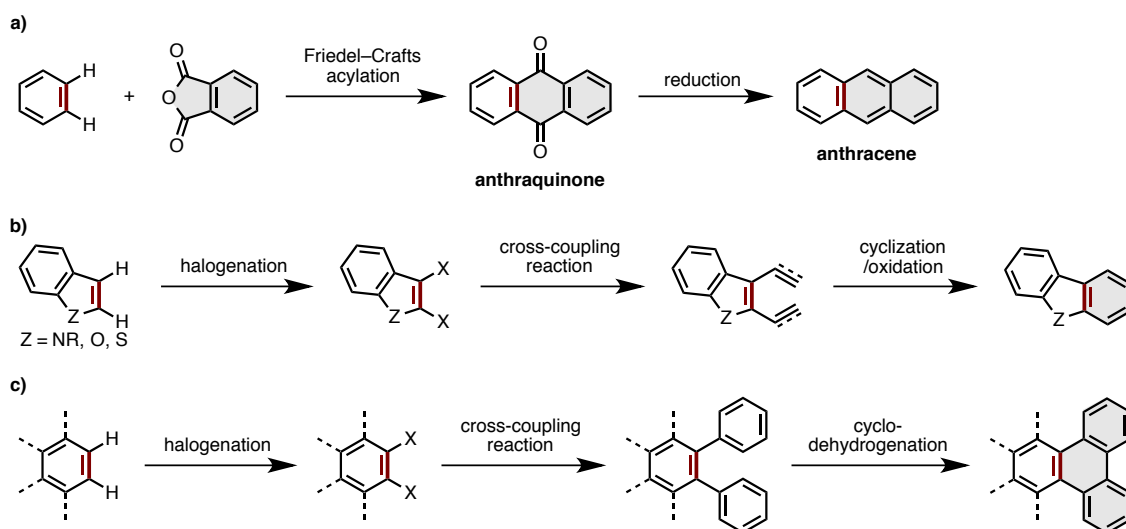
Scheme 1. General stepwise π-extension strategies for π-extended aromatics

Toward achieving more efficient and rapid access to π-extended aromatics from small π-components, single-step annulative π-extension (APEX) reaction has recently received significant attentions (Figure 1). APEX reaction can be defined as single step π-extension reaction from small template aromatics with π-extending reagent thereby constructing one or more new aromatic rings. These APEX technologies have been contributed to provide reliable ways for the synthesis of valuable π-extended materials. In particular, APEX reaction with unfunctionalized arenes and heteroarenes which dose not require any pre-functionalization such as halogenation is more ideal from view points of convenience, step- and atom-efficiency. Moreover, it has great potential for fine-tuning the structures and properties of π-systems at the late stage of synthesis.
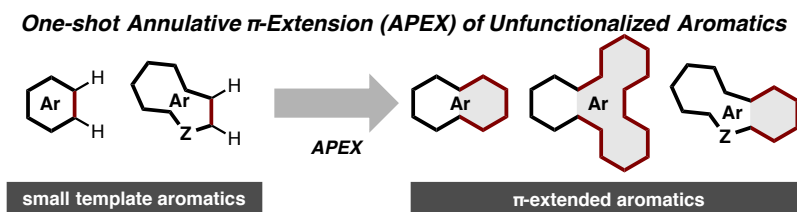
Figure 1. Concept of one-shot annulative π-extension (APEX) of unfunctionalized small template aromatics for synthesis of π-extended aromatics

In the general introduction, the existing APEX reactions of various aromatics such as PAHs and heteroarenes for the synthesis of π-extended aromatics are described. Furthermore, significance of the work described in this thesis is clarified by introducing the scope, limitation, characteristics and needs in the APEX methodology.

2. APEX Reaction of Aromatic Hydrocarbons

2-1. Bottom-up synthesis of π-extended PAHs from small template aromatics

Aromatic hydrocarbons are representative and fundamental skeletons that constitute the basis of life science and materials science. In particular, aromatic hydrocarbons having more than two fused rings are called as polycyclic aromatic hydrocarbons (PAHs).[5] In the field of materials science, PAHs are regarded as attractive molecules attributed from their high thermal stability, narrow HOMO-LUMO gap, strong π-π stacking ability, and so on.[4e,g,k] Additionally, larger PAHs such as nanographenes, graphenes, and graphene nanoribbons (GNRs) possess not only the above-mentioned attractive properties but also further outstanding electronic, optoelectronic, and spintronic properties.[4d,l,q,r,6] Because their properties are highly depended on their size, shape as well as structures, their preparation with atom-by-atom precision is critically important. Therefore, bottom-up synthetic approaches toward atomically precise synthesis of PAHs and nanographenes have received much attention in the synthetic chemistry and materials science.[4]

Scheme 2 shows the current mainstream of bottom-up synthesis of π-extended PAHs, nanographenes, and GNRs by using small aromatic components.[4] For example, hexabenzocoronene is synthesized by cyclodehydrogenation, so-called Scholl reaction[7], of hexaphenylbenzene which can be approached through metal-mediated [2+2+2] trimerization of diphenylacetylene, Diels–Alder reaction between diphenylacetylene and tetraphenylcyclopentadienone, or cross-coupling reaction between aryl halides and arylmetal species.[4b,d,e,j,l,n,q,r,s] In addition to them, there are a lot of synthetic variations such as intramolecular cyclization of arylacetylenes, ring-closing olefin metathesis of vinylarenes,[4e,i,o,q,r] and so on. Although these bottom-up syntheses provide chemically pure PAHs, nanographenes, and GNRs, stepwise protocols and annoying preparation of functionalized arene components make the synthetic efficiency, value, and overall yields of final products lowered. In this regards, "growth-from-template" method by one-shot APEX reaction of small PAH templates is considered as one of the most attractive, ideal, and straightforward methods for the bottom-up synthesis of π-extended PAHs, nanographenes, and GNRs.
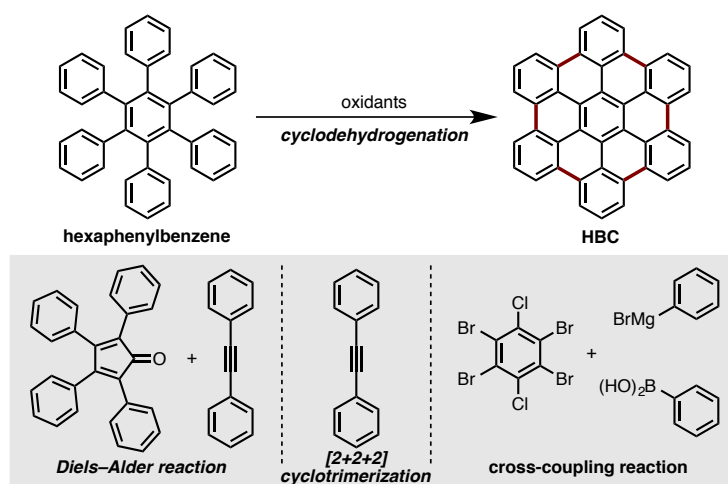
Scheme 2. Commonly employed stepwise synthesis of PAHs, nanographenes, and GNRs involving Diels–Alder reaction, cyclotrimerization, coupling reaction, and cyclodehydrogenation

2-2. Region-selective APEX reaction of PAHs for synthesis of structurally uniform π-extended nanocarbon

PAHs have various regions with different edge structures, as shown in Figure 2, which are referred to as bay-region (concave armchair edge), K-region (convex armchair edge), L-region (zigzag edge), and so on. If one could establish a method achieving region-selective one-shot APEX of an unfunctionalized PAH template, the synthesis of structurally well-defined π-extended PAHs, nanographenes, and GNRs can be significantly streamlined. Furthermore, APEX would allow the late-stage fine-tuning of properties of these nanocarbons.
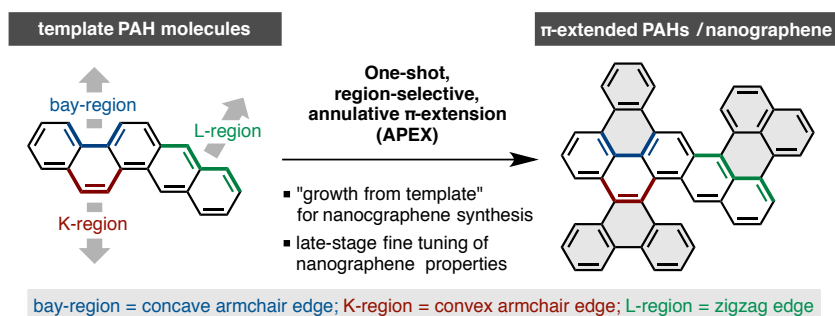
Figure 2. One-shot, region-selective annulative π-extension (APEX) reaction of PAHs for synthesis of π-extended PAHs, nanographenes, and GNRs

2-3. Discovery of bay-region selective APEX reactions of PAHs

Bay-region selective APEX reaction of PAHs would be one of the representative examples of APEX reaction.[8-13] Classical and pioneering bay-region APEX reaction would be represented by Clar's work in 1932, which performs Diels–Alder reaction at the bay-region of perylene with maleic anhydride in nitrobenzene followed by rearomatization.[8] About 20 years later, Clar and Zander improved their bay-region selective APEX reaction (Scheme 3).[9] In the molten maleic anhydride, perylene was smoothly converted to compound **1** in the presence of *p*-chloranil as an oxidant. Decarboxylation of **1** by soda-lime affords non-substituted benzoperylene **2** which would be further reactive for second bay-region APEX with maleic anhydride to afford Diels–Alder adduct **3** in good yield. Overall, coronene can be synthesized in 25% from perylene by iterative APEX reactions and decarboxylation reactions.
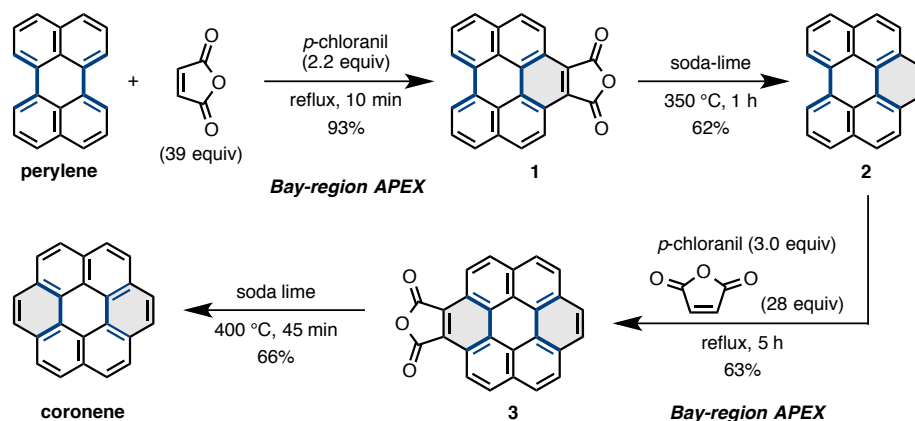
Scheme 3. Early bay-region selective Diels–Alder APEX reaction by Clar and Zander

2-4. Bay-region selective APEX reaction of PAHs through Diels–Alder reaction

While these bay-region selective APEX reactions are quite simple and clearly effective for the synthesis of π-extended PAHs, they had been forgotten over half a century until Scott and Fort reinvestigated in 2009.[10] They shed a spotlight again on the potential of Diels–Alder APEX at bay-regions, and calculated activation energies for Diels–Alder cycloaddition between acetylene and various PAHs having bay-regions (Scheme 4). Activation energies are estimated to be 44, 30, 24, and 22

kcal/mol for phenanthrene, perylene, bisanthene, and tetrabenzocoronene, respectively. These results indicate that the larger differences of aromatic stabilization energies between starting PAHs and cycloadducts are, the larger the activation energies become. This means that larger PAHs such as bisanthene and tetrabezocoronene are more feasible for Diels–Alder APEX than phenanthrene and perylene.

compound	activation energy (kcal/mol)
phenanthrene	43.9
perylene	30.0
bisanthene	24.2
tetrabenzocoronene	21.9
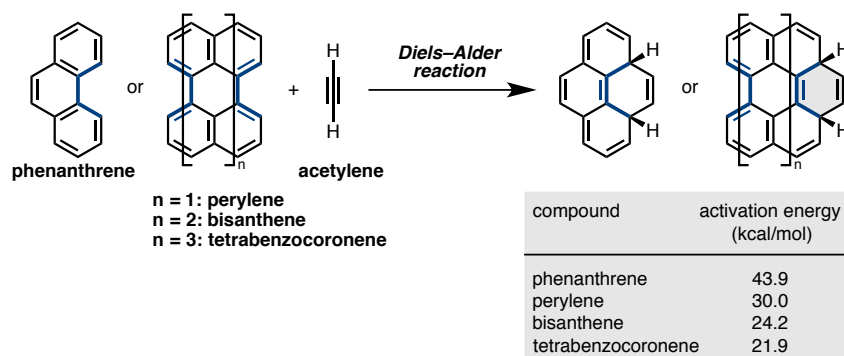
Scheme 4. Activation energies calculated for bay-region Diels–Alder reaction between acetylene and PAHs at B3LYP/6-31G(d) level of theory

Scott and Fort also proved their hypothesis by demonstrating bay-region selective Diels–Alder APEX of perylene and 7,14-dimesitylbisanthene with diethyl acetylenedicarboxylate **4** (Scheme 5).[10] In the reaction of perylene, mono-APEX product **5** was obtained in 25% yield after heating in toluene at 150 °C for 3 days. Significant amount of starting perylene remained unreacted, and double-APEX product **6** was not detected. Moreover, as expected and supported by their calculation results, no Diels–Alder adducts was obtained in the reaction between phenanthrene and **4**. On the other hand, Diels–Alder APEX proceeds more smoothly under milder reaction conditions in the case of using **7** as a substrate yielding mono- and double-APEX products **8** and **9** in the good combination yield.
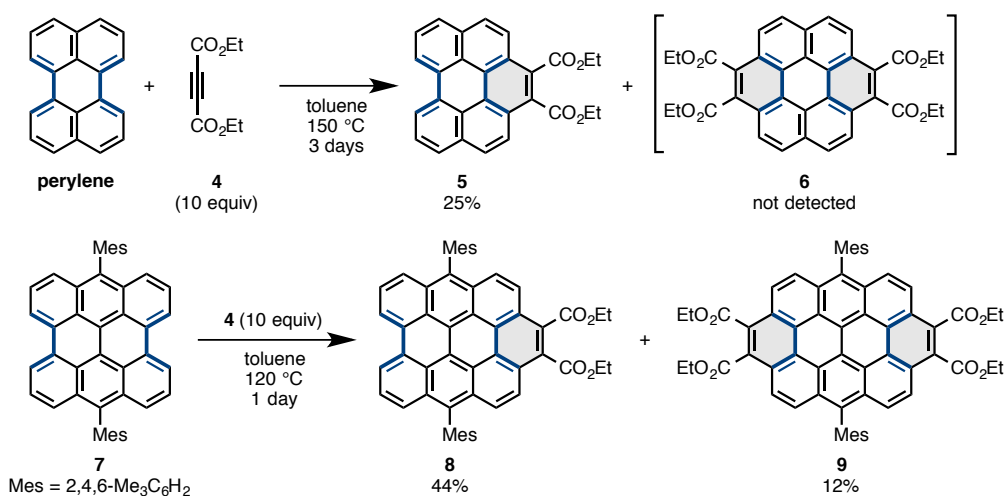
Scheme 5. Bay-region selective Diels–Alder APEX reaction with diethyl acetylenedicarboxylate

Since their groundbreaking discovery for bay-region selective APEX reaction of PAHs through Diels–Alder reaction, many researchers have challenged to discover the appropriate dienophiles, namely π-extending agents, as summarized in Scheme 6. For example, acetylenes,[10] nitroethylene,[11] vinyl phenyl sulfoxide[11], benzoquinones[12], and various aryne precursors[13] were found as suitable π-extending agents. It is noteworthy that acetylene is envisaged to act as 2-carbon π-extension unit for the sequential template growth of small carbon nanotube (CNT) fragments for the synthesis of structurally well-defined CNTs.[10a, b, 11, 13d, 14] Theoretical investigations on these Diels–Alder APEX for CNT synthesis have been also well studied by Scott and Fort.[10b]
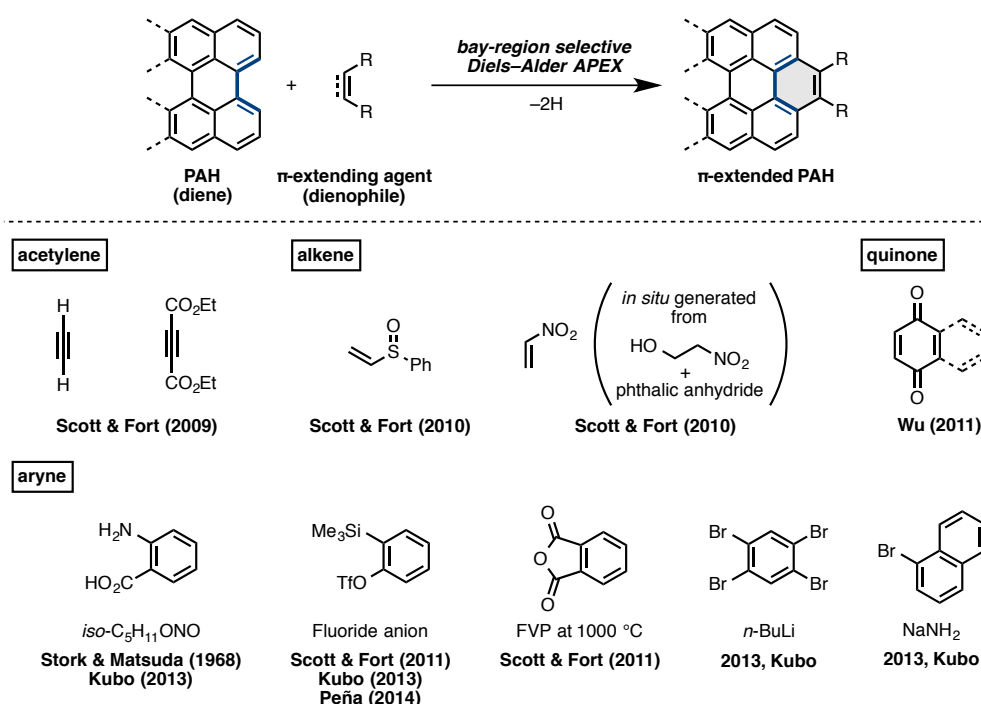
Scheme 6. Bay-region selective Diels–Alder APEX reactions with various dienophiles

The above-mentioned Diels–Alder APEX reaction was applied to nanographene synthesis by groups of Wu[12] and Peña[13e]. In 2011, Wu and co-workers achieved the synthesis of huge π-extended quinone **11** and **12** by sequential bay-region selective Diels–Alder APEX reactions of bisanthene **10** with naphthoquinone and benzoquinone (Scheme 7).[12]
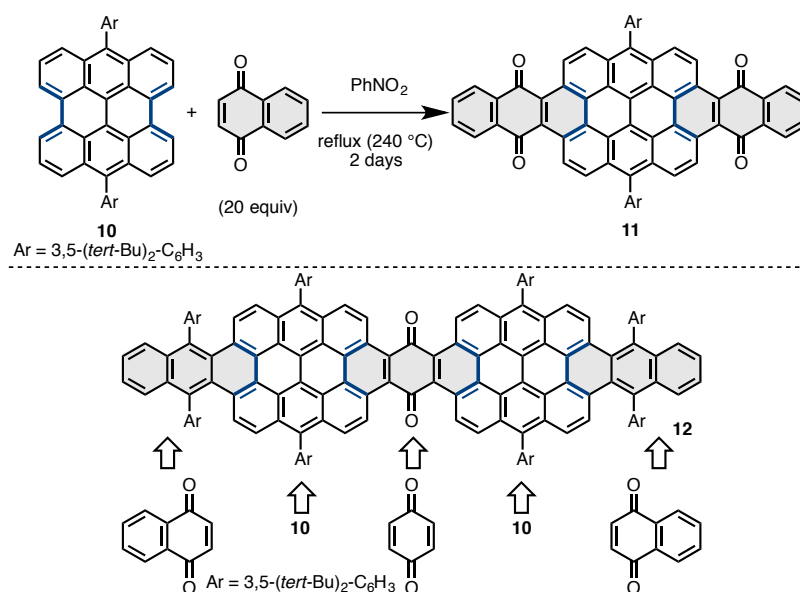
Scheme 7. Bay-region selective Diels–Alder APEX reaction with various quinones

Peña and co-workers employed the APEX product for the palladium-catalyzed [2+2+2] cyclotrimerization to obtain clover-shaped nanographene with 22 fused benzene rings (Scheme 8).[13e] They succeeded to visualize the molecular structure of **13** in the atomic resolution by AFM and STM. Surprisingly, this clover-shaped nanographene can be synthesized in only 2 steps from commercially available perylene in the acceptable total yield.
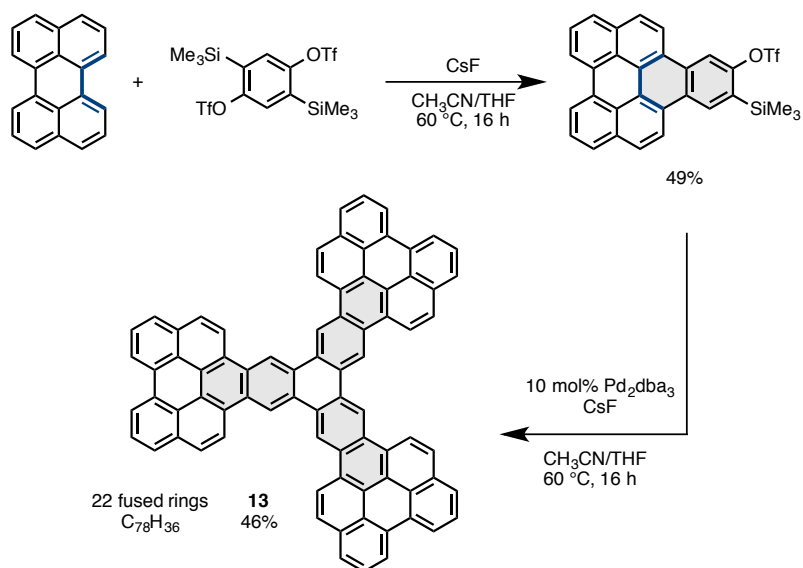
Scheme 8. Synthesis of clover-shaped nanographene having 22 fused benzene rings by Diels–Alder APEX reaction of perylene

2-5. APEX reaction of benzene and naphthalene

Compared to APEX of PAHs by Diels–Alder reaction described above, APEX reaction of more simple arene templates such as benzene and naphthalenes is not very common. Early work was reported in 1986 by Sakakibara and co-workers (Scheme 9).[15] Although the details are not clear, benzene was extended by addition of acetylene dicarboxylate with palladium catalyst and *N*-methyl-*p*-toluidine to give naphthalene derivative **14** in 43% yield.
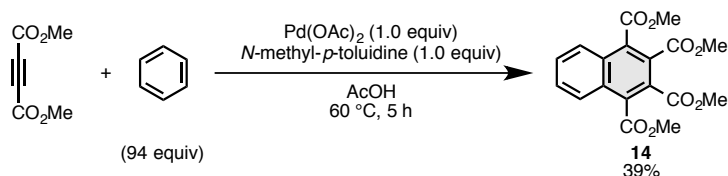
Scheme 9. Pioneering APEX reaction of simple arenes

Over 20 years later, several groups renovated the above reaction (Scheme 10). The group of Wu reported palladium-catalyzed APEX reaction of electron-rich benzene with diarylacetylenes, which provided corresponding tetraarylnaphthalenes.[16] Satoh and Miura found in the investigation on oxidative coupling/cyclization cascade of primary and secondary benzamide with alkynes that tertiary benzamides underwent the APEX reaction through rhodium catalysis.[17] Although they showed only two examples, the amount of arenes can be reduced to the stoichiometric one against alkyne. Recently, Cramer improved the rhodium-catalyzed APEX reaction by addition of copper di-2-ethylhexanoate and decabromodiphenyl ether as oxidants under microwave irradiation.[18] This catalytic system was widely applicable to a variety of arenes including substituted benzene, naphthalene, triphenylene, fluorene, heteroarenes, and so on. The above-mentioned APEX reactions of simple arenes are considered to proceed through C–H activation/metalation of arene by palladium or rhodium catalysis.
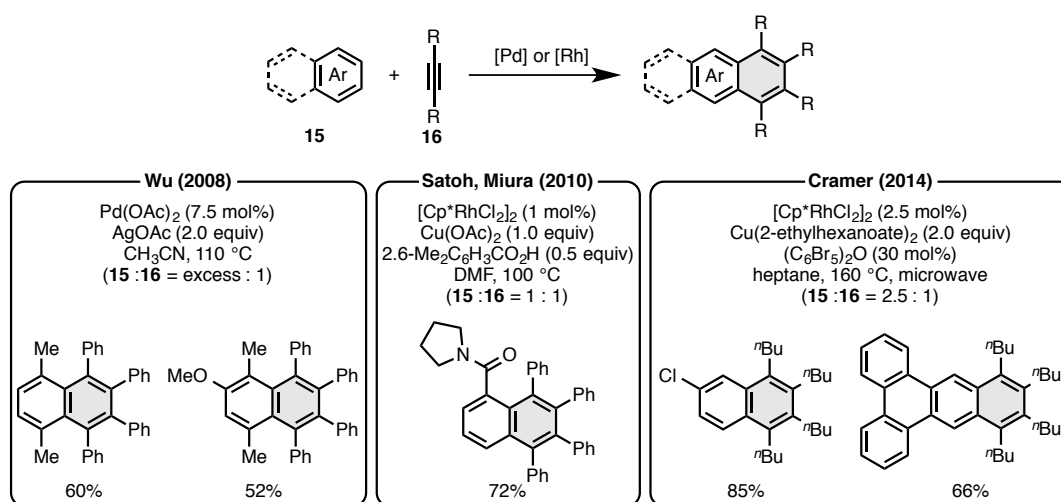
Scheme 10. APEX reactions of arenes with alkynes by C–H activation

3. APEX Reaction of Heteroarenes

3-1. APEX reaction of heteroarene *via* electrophilic aromatic substitution (S$_E$Ar)

Fused heteroaromatics are essential structural motifs and widely used not only in the field of materials science but also in pharmaceutical science.[19] Five membered heteroarenes such as pyrrole, thiophene, and furan are so abundant that these are often used as templates in one-shot APEX reaction for the synthesis of fused heteroaromatics such as carbazoles, dibenzothiophenes, and dibenzofurans. In particular, a number of one-shot APEX reactions on the basis of electrophilic aromatic substitution (S$_E$Ar) reaction have been established for these electron-rich arenes.

Early work of this kind was reported in 1954 by Dann and co-workers. They performed the condensation of 2,5-dimethylthiophene and 2,5-hexanedione in aqueous hydrofluoric acid media to provide 1,3,4,7-tetramethylbenzo[*c*]thiophene in 42% yield (Scheme 11).[20] Fletcher expanded similar APEX reaction to isoindoline synthesis in 1966.[21] In the presence of trichloroacetic acid, 2,5-diphenypyrrole was transformed to 1,3,4,7-tetraphenylisoindole in 39% yield by using 1,2-dibenzoylethane as a π-extending reagent.
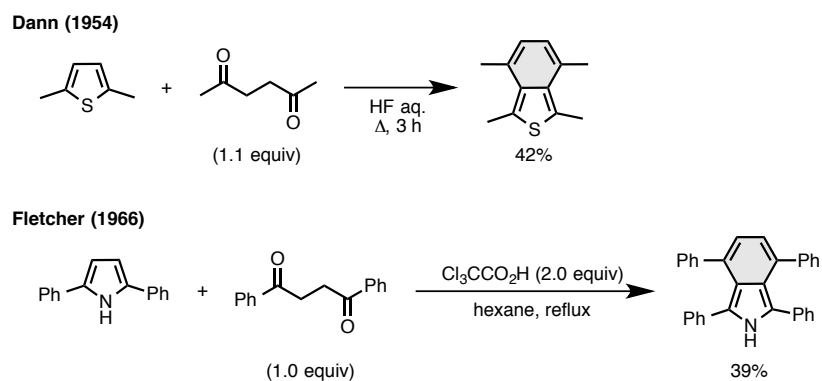
Scheme 11. Pioneering examples about APEX reaction of thiophene and pyrrole

After their pioneering discovery, 2,5-hexanedione has been commonly used for the synthesis and derivatization of elipticine, a naturally occurring alkaloid having *anti*-cancer properties isolated from *Ochrosia elliptica* Labill.[22] As shown in Scheme 12, Cranwell and Saxton succeeded the total synthesis of ellipticine in 1962 by one-shot APEX.[23] Indole can be transformed to 1,4-dimethylcarbazole in 36% yield by using 2,5-hexanedione as a π-extending reagent under gaseous dry hydrogen chloride

atmosphere in boiling ethanol. From this intermediate, 5-step sequential transformations furnished ellipticine. This achievement opened the door to novel synthetic methodologies of ellipticine and its analogues.
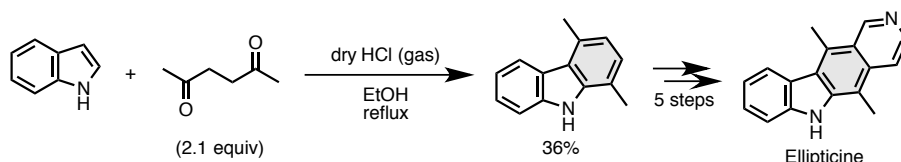
Scheme 12. Synthesis of ellipticine by APEX of indole with 2,5-hexanedione

This method can provide a chance to construct a key carbozole skeleton in one-shot, but it had not gained a lot of popularity due to its harsh reaction conditions and low yields. About half a century later, Török and co-workers overcame this dilemma by employing a strong solid acid montmorillonite K-10 as catalyst to the APEX reaction of indole with 2,5-hexanedione under microwave irradiation.[24] Since then, various π-extending agents, such as 2,5-hexanediol[25], γ-peroxyacetylacetonate[26], β-nitrostylenes[27], ethyl 2-ethynylbenzyl carbonate[28], 2-amidodihydrofurans[29], tetrahydropyridine[30], β-nitroacrylate[31], and *ortho*-[α-(hydroxyl)benzyl]benzaldehyde acetal[32] have been investigated for single-step conversion from indoles to carbazoles (Scheme 13).
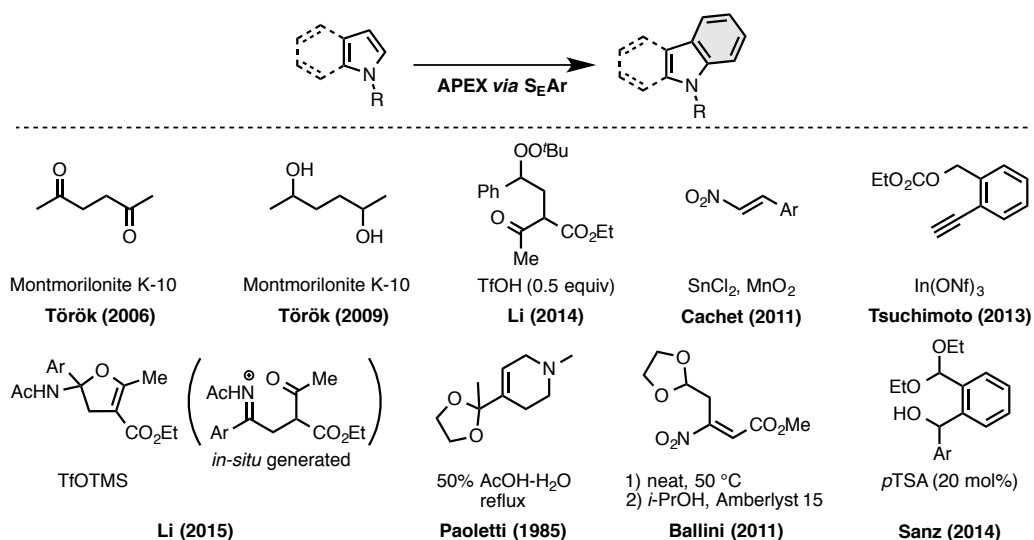
Scheme 13. π-extending agents for APEX of indole to carbazole

Among them, several π-extending agents were applied to the synthesis of biologically active compounds. Selected examples are described in Scheme 14. For example, the group of Paoletti applied tetrahydropyridine with indole under reflux condition in AcOH/H$_2$O for the synthesis of olivacine analogue isolated from *Aspidosperma olivaceum*.[30] Ballini and co-workers used β-nitroacrylate for APEX of pyrroles, which have potential to synthesize adipoxyte fatty-acid binding protein (A-FABP) inhibitors.[31] Recently, Li and co-workers demonstrated total synthesis of olivacine and asteropusazole A, isolated from a deep-water sponge of the genus *Asteropus*, by APEX of indoles with γ-peroxyketoesters.[26]
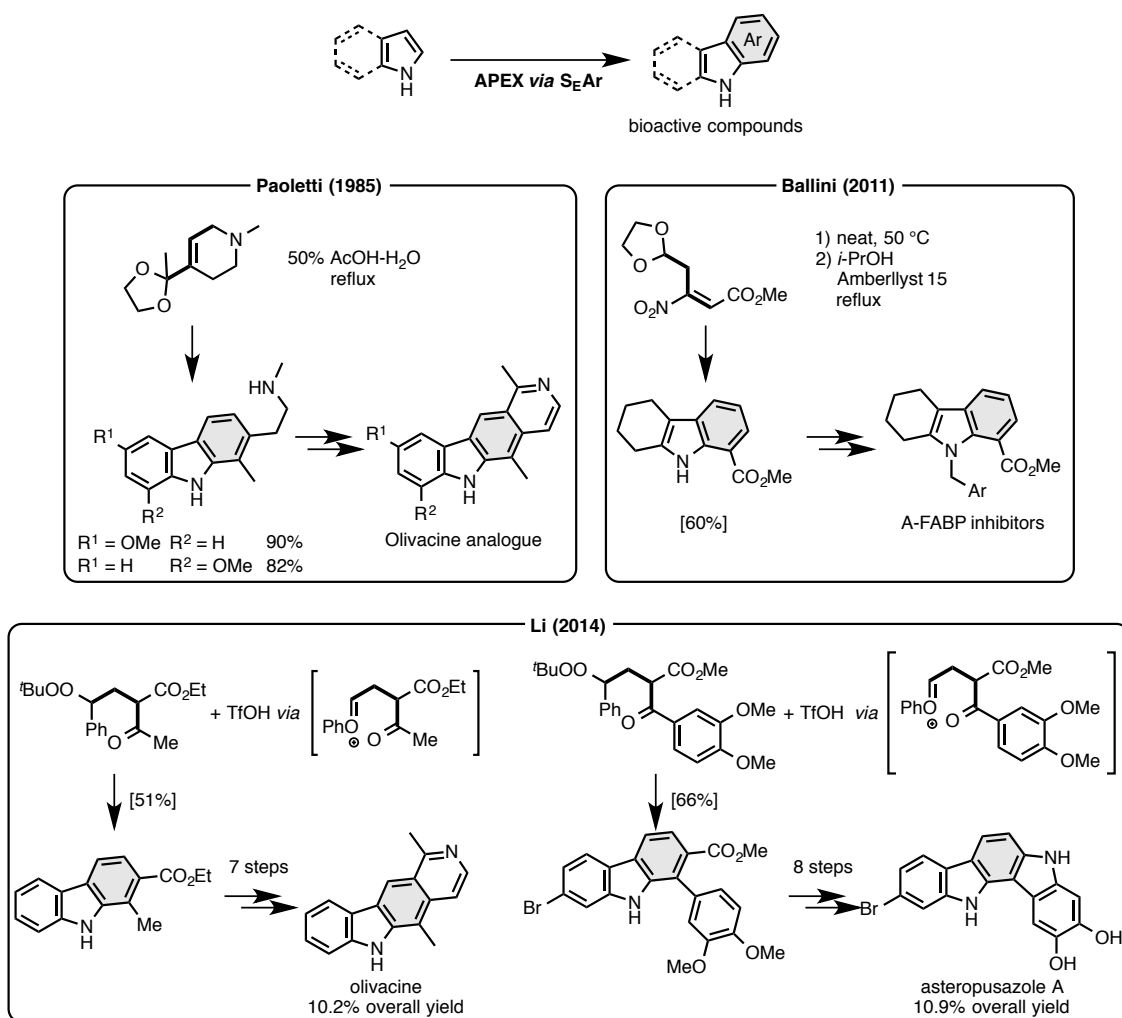
Scheme 14. APEX for synthesis of biologically active compound

In addition to newly discovered π-extending agent for carbozole synthesis by APEX as shown in Scheme 14, syntheses of other π-expanded heteroarenes have been also achieved (Scheme 15). For example, indolo[3,2-*b*]carbazole was synthesized by using aldehydes as a π-extending reagent. Bergman and Tholander employed simple aldehydes such as isobutylaldehyde for APEX of indole under reflux condition in H_2SO_4/MeOH media.[33] The same approach was also demonstrated by Jiang and co-workers in the synthesis of 4-(diphenylamino)benzaldehyde which works as hole-transporting materials in organic light-emitting diodes.[34] Indolo[2,3-*b*]carbazole, regioisomer of indolo[3,2-*b*]carbazole, was also obtained from indole and aldehyde catalyzed by molecular iodine, which was discovered by Bhuyan and co-workers.[35]
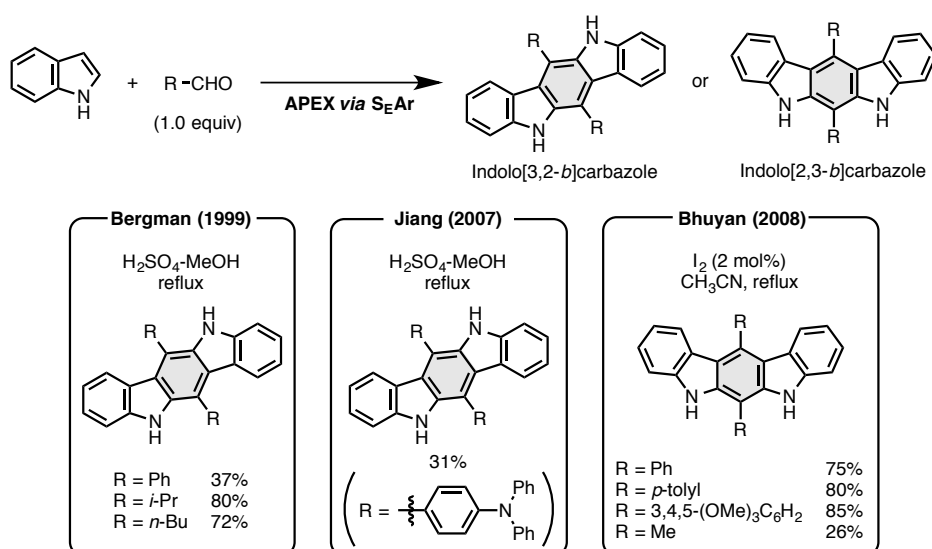
Scheme 15. APEX reaction of indoles with aldehydes

Mohanakrishnan and co-workers discovered a series of one-shot APEX reactions mediated/catalyzed by Lewis acid with benzylic bromide (Scheme 16).[36] They successfully applied not only indole as template but also thiophene and furan in the presence of catalytic amount of $ZnBr_2$ or $FeCl_3$.

71% (R = Br, condition A)   66% (R = Br, condition A)   70% (R = Br, condition A)
56% (R = OAc, condition B)

Condition A : ZnBr$_2$ (0.2 equiv), ClCH$_2$CH$_2$Cl, rt.
Condition B : FeCl$_3$ (0.2 equiv), ClCH$_2$CH$_2$Cl, reflux
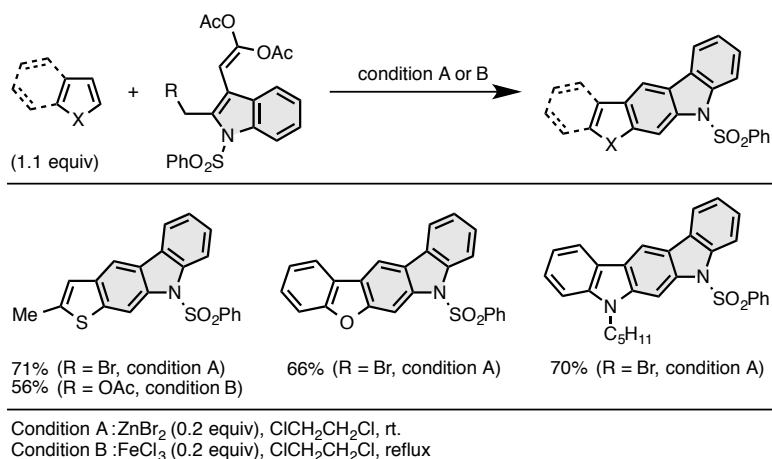
Scheme 16. APEX with benzylic bromide mediated/catalyzed by Lewis acid

They expanded their APEX chemistry with tetraacetate derived from phthalaldehyde catalyzed by BF$_3$·Et$_2$O, which furnished fused heteroarenes (Scheme 17).[37] Moreover, 2,5-dimethoxytetrahydrofuran also acted as a π-extending reagent with TfOH or ZnBr$_2$ for APEX of electron-rich aromatics (Scheme 18).[38]

58%   51%   56%
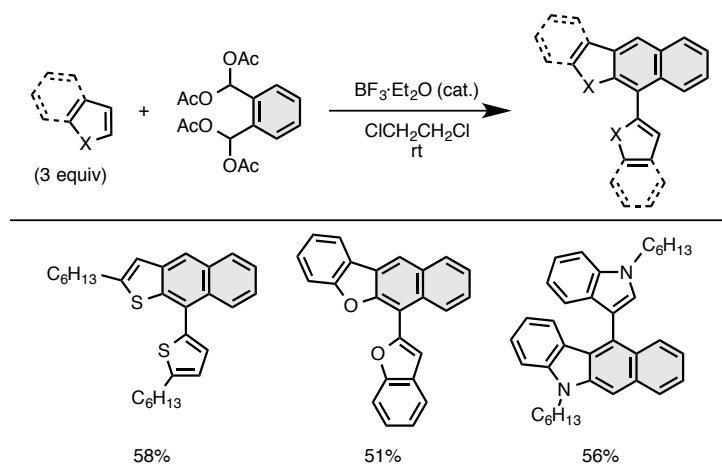
Scheme 17. Lewis acid mediated APEX reaction with tetraacetate

	condition A	condition B	condition C
X = S	88%	87%	–
X = Se	83%	81%	–
X = O	81%	35%	76%

condition A : 2,5-dimethoxytetrahydrofuran (2.0 equiv) and ZnBr$_2$ (1.0 equiv)
condition B : 2,5-dimethoxytetrahydrofuran (2.2 equiv) and TfOH (1.0 equiv)
condition C : 2,5-dimethoxytetrahydrofuran (4.4 equiv) and TfOH (2.0 equiv)
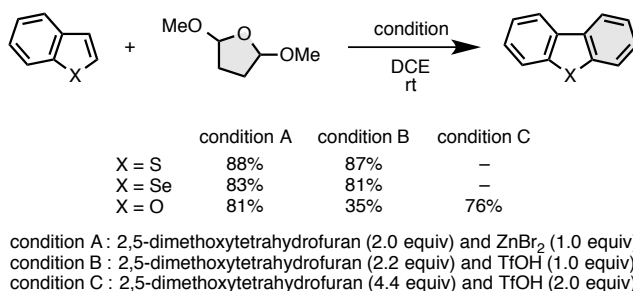
Scheme 18. Lewis acid mediated APEX reaction with 2,5-dimethoxytetrahydrofuran

3-2. APEX reaction of heteroarene *via* Diels–Alder reaction

[4+2] cycloaddition reaction, including Diels–Alder reaction, is efficient and well-known technique to obtain six-membered cyclic compounds. Thus, a sequence of Diels–Alder reaction and oxidation process is widely used in the synthesis of benzene derivatives over the past decades. Giomi and Cecchi employed 4,5-dicyanopyridazine as electron-deficient diene with *N*-methylpyrrole or *N*-methylindole for inverse electron-demand Diels–Alder reaction to afford 5,6-dicyano-*N*-methylindole or 2,3-dicyano- *N*-methylcarbazole with releasing nitrogen and hydrogen gas (Scheme 19).[39]
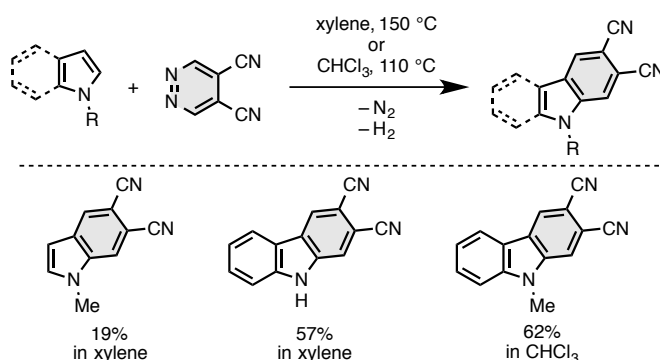
Scheme 19. APEX reaction of pyrrole and indole with 4,5-dicyanopyridazine

The combination of Michael addition and Diels–Alder reaction is also recognized as valuable APEX methodology. As exemplified in Scheme 20, 1,4-naphthoquinone and 2,5,8-quinolinetriones were used for APEX of indole by the group of Prota[40] and Menéndez[41], respectively.
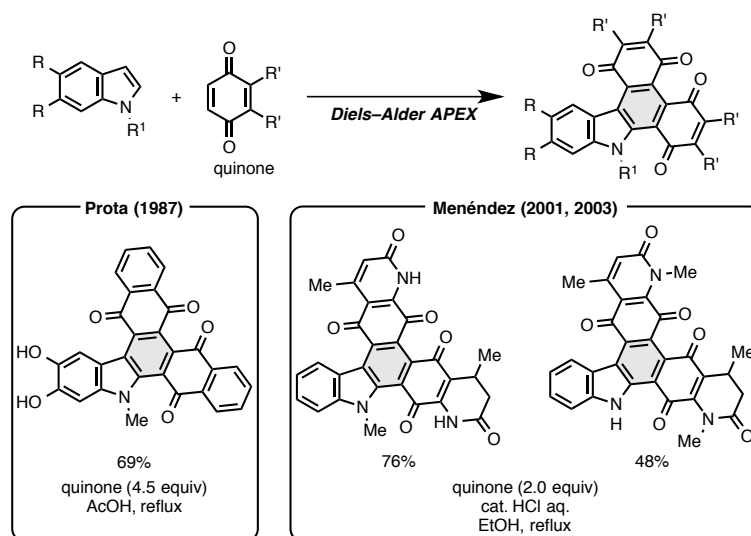
Scheme 20. APEX reaction of indole with 1,4-benzoquinone derivatives

Li and Tang developed APEX reaction of indoles with alkynylbenzaldehydes to obtain 5*H*-benzo[*b*]carbazol-6-yl ketones in one-shot (Scheme 21).[42] Formation of isobenzopyrylium cation derived from alkynylbenzaldehydes has a crucial role in the APEX reaction. From this intermediate **17**, electrophilic aromatic substitution (S$_E$Ar) would occur to give indolylisobenzopyrane **18**, followed by tandem ring-opening reaction catalyzed by palladium and Diels–Alder reaction or thermal electrocyclization yielded 5*H*-benzo[*b*]carbazol-6-yl ketones. Instead of palladium catalyst, copper(II) triflate is also applicable described by Nagarajan and Prakash.[43]
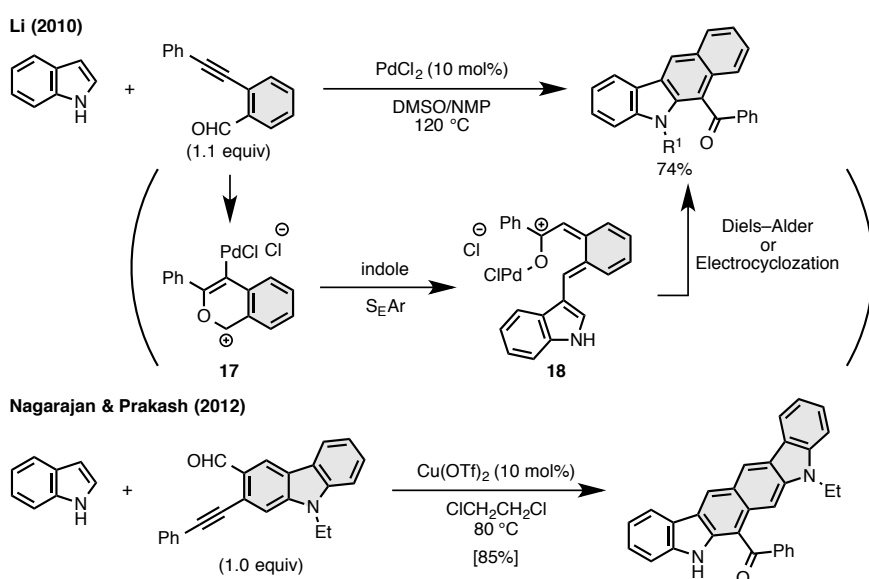
Scheme 21. APEX reaction with 2-alkynylarylaldehydes

3-3 APEX reaction of heteroarene through transition metal catalysis

C–H functionalization catalyzed by transition metals is one of the most potent methodologies for carbon–carbon and carbon–heteroatom bond forming reaction in recent organic synthesis. Thus, it should be no surprise that C–H functionalization was applied to synthesize fused π-conjugated systems. Palladium-catalyzed oxidative coupling of indole and alkynes was described in 2009 by Miura, Satoh, and co-workers, which was initiated by direct palladation at C3-position of indole (Scheme 22).[44]
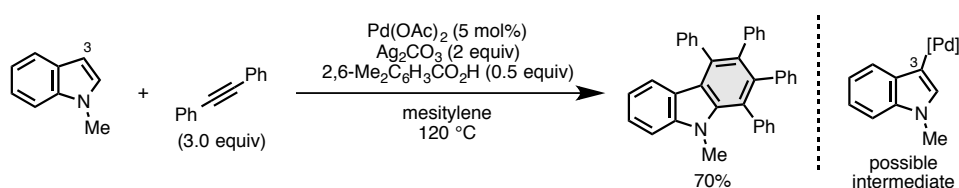
Scheme 22. Palladium-catalyzed APEX reaction of indole with alkynes

Li[45] and Shi[46] applied related APEX method to the synthesis of quinolone and isoquinoline through amide-directed C–H activation by rhodium(III) catalysis (Scheme 23).
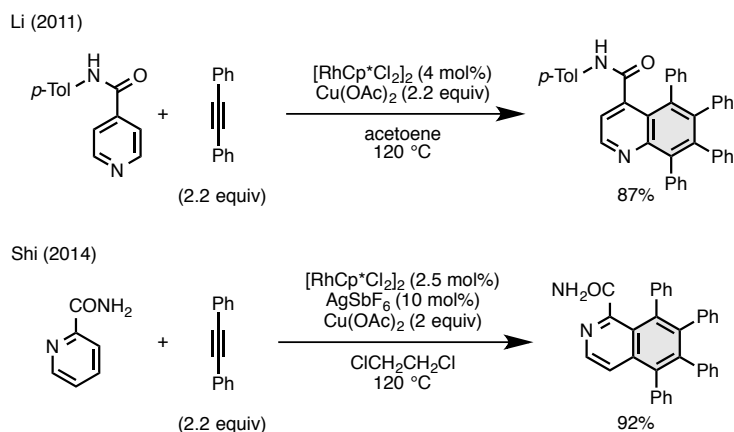
Scheme 23. Amide-directed, rhodium-catalyzed APEX reaction of pyridine derivatives with alkynes

The group of Ohno and Fujii applied 1,3-diynes as a π-extending agent in the one-shot synthesis of indole and carbozole *via* gold-catalyzed double hydroarylation with pyrrole and indole (Scheme 24).[47]

20
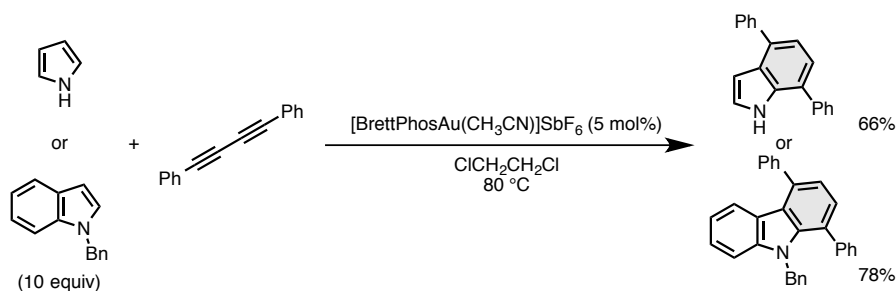
Scheme 24. Gold-catalyzed APEX reaction of pyrrole and indole with 1,3-diynes

Vinyl propargyl alcohol, a hybrid of alkene and alkyne, can be applied as a π-extending agent in the pyrrole-to-indole APEX reaction in the presence of ruthenium catalyst and trifluoroacetic acid (Scheme 25).[48]
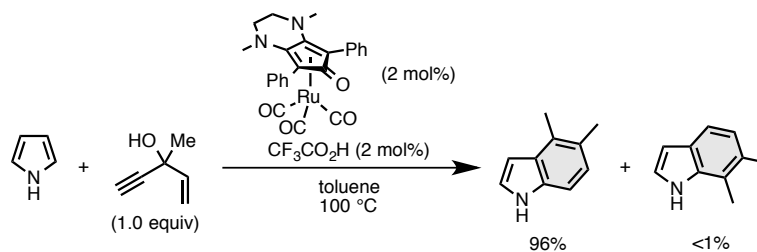
Scheme 25. APEX reaction of pyrrole with 1-vinyl propargyl alcohol through ruthenium catalysis

The group of Katukojvala envisioned to use electrophilic enalcarbenoids, which can be generated by rhodium-catalyzed decomposition of diazo compound, as a π-extending reagent in the heterocycle APEX reaction (Scheme 26).[49a] $Rh_2(OAc)_4$ is the best catalyst for the APEX of pyrrole to obtain corresponding 6-benzoxylindole in high yield. Furthermore, the indole-to-carbazole APEX reaction was also achieved under the influence of $Rh_2(OAc)_4$ catalyst and binaphthyl phosphoric acid.[49b] Similar approach was taken by Wang, Huang, and co-workers *via* pyrimidine-directed C–H rhodation at C2 position of indole followed by acid-catalyzed cyclization/dehydration sequence.[50]

Katukojvala (2014)

Wang, Huang (2015)
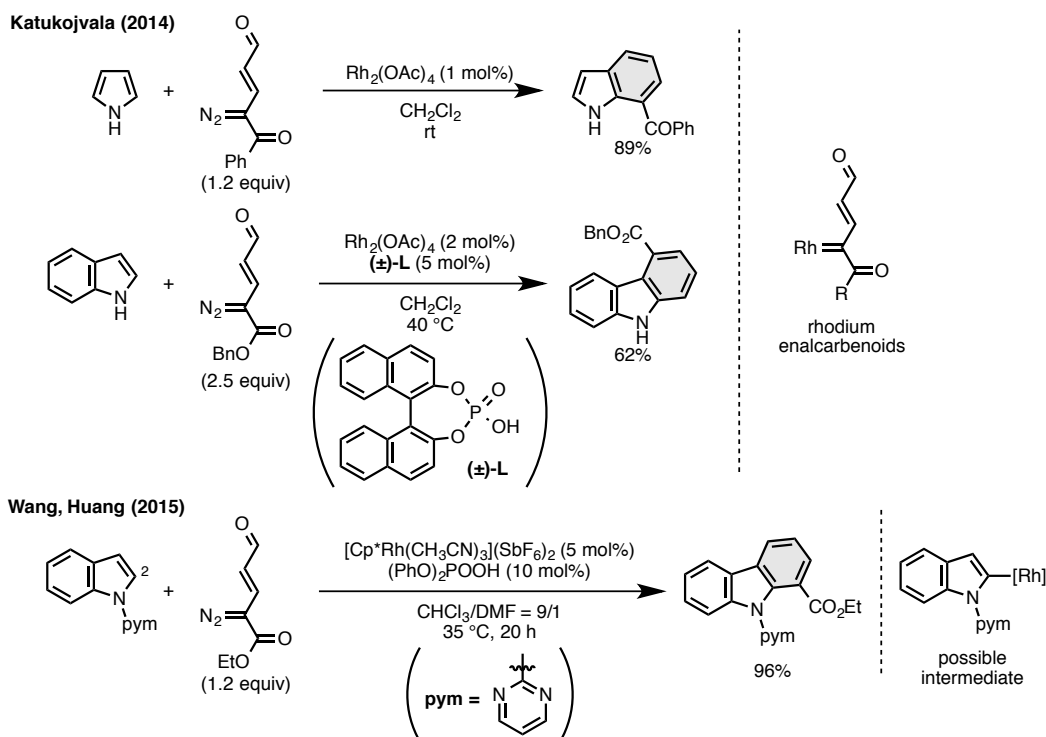
Scheme 26. APEX reaction of pyrrole and indoles *via* rhodium carbenoid

Visible light-induced photoredox catalysis has been paid much attention in recent organic synthesis, because it can activate the molecules under relatively mild conditions and enables unprecedented transformations that cannot be achieved by other conventional synthetic methods. Reiser and Paria applied photoredox iridium complex for APEX of pyrrole and furan with α-bromochalcone or α-bromocinnamate as shown in Scheme 27.[51]
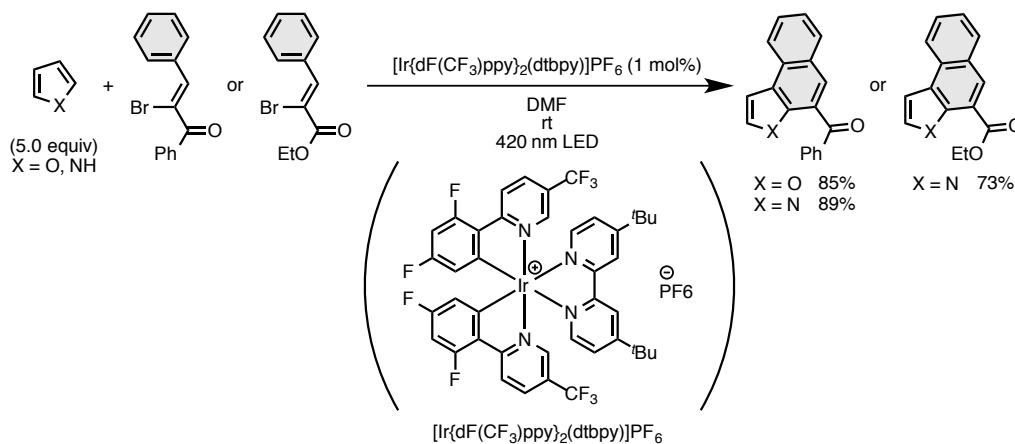
Scheme 27. APEX reaction of pyrrole and indoles by visible light-induced photoredox catalysis

4. Summary and perspective of existing APEX reactions

As described above, APEX reaction enables one-shot π-extension of various unfunctionalized aromatics to provide π-extended PAHs and heteroarenes which are classically synthesized by multi-step operations such as halogenation, cross-coupling reaction, Diels–Alder reaction, oxidation, and so on. APEX can make a substantial change in organic synthesis, but the examples are still limited. For example, APEX reaction of PAHs can potentially change the way we prepare nanographenes and grapahene nanoribbons. However, region-selective APEX of PAHs is limited to bay-region-selective APEX by Diels–Alder reaction. Therefore, the development of universal APEX reactions of PAHs, which enable K- and L-region-selective π-extensions, will make a breakthrough in the area of nanographene science. As π-extended fused heteroarenes are also privileged structural motifs in functional materials and pharmaceuticals, APEX of abundant small heteroarene templates can serve as an important tool in synthetic chemistry. Previously developed APEX reactions of heteroarenes can be categorized into three types: 1) electrophilic aromatic substitution reaction, 2) Diels–Alder reaction, and 3) C–H functionalization. Among them, C–H functionalization APEX is particularly attractive because it can reduce cumbersome multi-step synthetic operations. However, at the beginning of the author's research in 2011, transition metal-catalyzed C–H functionalization APEX was largely undeveloped and limited to a few examples using pyrroles or indoles.[44,52] Therefore, the development of convenient and user-friendly APEX reaction of diverse arene templates with a variety of π-extending reagents would allow rapid access to π-extended molecules in the desired substitution and aromatic patterns.

5. Overview of this thesis

In this thesis, the author has developed novel APEX reactions from several aromatic templates such as polycyclic aromatic hydrocarbons (PAHs), diarylacetylenes, thiophenes, benzofuran, and indoles for the synthesis of π-extended aromatics.

In Chapter 1, one-shot APEX reaction that occurs at the K-region of PAHs is described. Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$/o-chloranil catalytic system effectively promotes one-shot APEX reaction of PAHs with silicon-bridged aromatics as π-extending agents. DFT calculations suggest that the complete K-region selectivity stems from the olefinic (decreased aromatic) character of the K-region. This protocol is applicable to multiple APEX and sequential APEX reactions to construct various nanographene structures in a rapid and programmable manner.
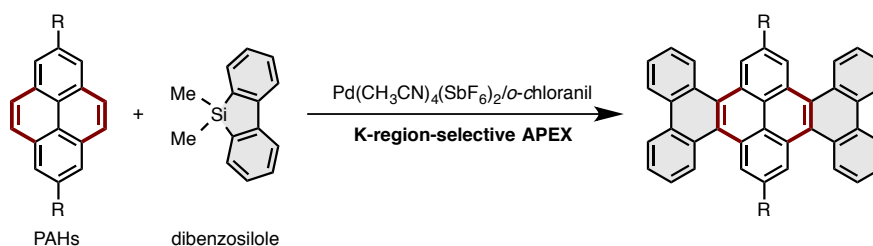
Scheme 28. One-shot, K-region-selective APEX of PAHs with Pd/o-chloranil catalyst and dibenzosiloles

In Chapter 2, the novel synthetic method for phenanthrene from alkynes has been developed. A variety of diarylacetylenes can be transformed to 9,10-diarylphenanthrenes through palladium catalysis with good functional group tolerances by using dibenzosiloles and dibenzogermoles as π-extending agents. Double π-extension of 1,4-bis(phenylethynyl)benzene is also possible, which shows enough potential for application to synthesis of larger polycyclic aromatic hydrocarbon, nanographenes, and graphene nanoribbon.
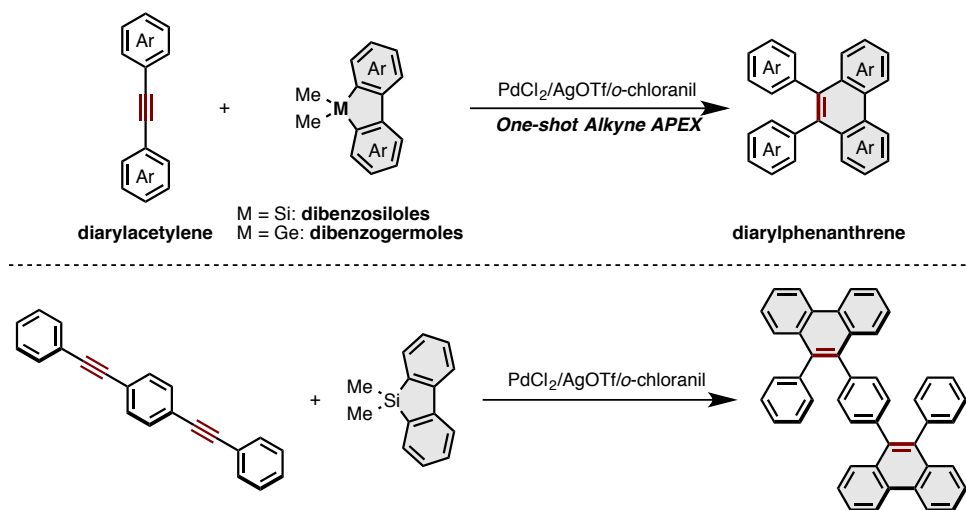
Scheme 29. Palladium-catalyzed annulative π-extension of alkynes with dibenzosiloles and dibenzogermoles for synthesis of diarylphenanthrenes

In Chapter 3, APEX reactions of heteroarenes including thiophenes, benzofuran, and *N*-tosylindole have been developed. Palladium/*o*-chloranil catalytic system enables to extend the π-system of benzo[*b*]thiophenes by using dimethyldibenzosiloles as π-extending agents. π-Extended dibenzofuran and carbazole can be also obtained from benzofuran and *N*-tosylindole, respectively with dimethyldibenzogermole as a germanium-based π-extending agent.
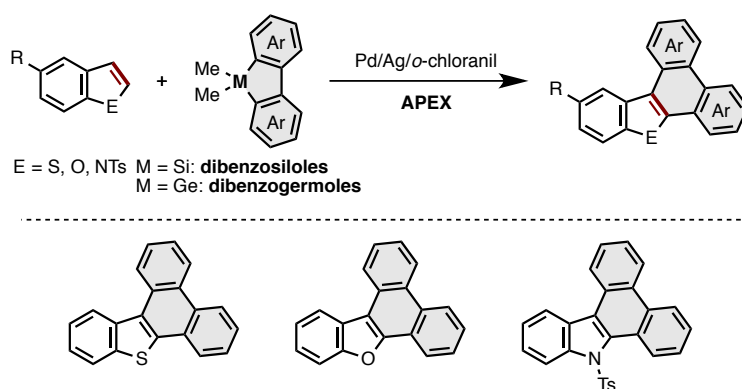
Scheme 30. One-shot APEX of heteroarenes with dibenzosilole and dibenzogermole

In Chapter 4, one-shot APEX of indole to carbazole by a Pd-Cu-Ag trimetallic system has been established. The unique trimetallic system can convert indoles to carbozoles using electron-deficient alkenes as two-carbon π-extending units. Investigation of reaction mechanism revealed that this one-shot APEX of indole is likely to proceed through the sequence of Pd/Cu-catalyzed indole C–H alkenylation, Ag-promoted Diels–Alder reaction, and dehydrogenative aromatization. The successful one-pot synthesis of granulatimide derivative, an interesting class of Chk1 kinase inhibitor, highlights the potential of the present reaction for further development and applications.
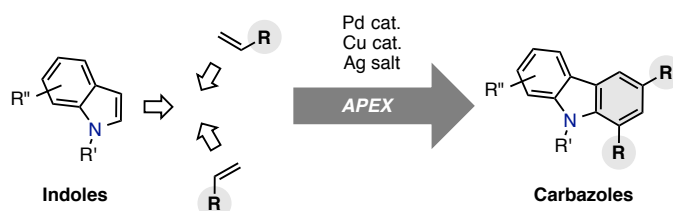
Scheme 31. One-shot APEX of indole to carbazole by Pd-Cu-Ag trimetallic system

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One-shot, K-region-selective Annulative π-Extension of Polycyclic Aromatic Hydrocarbons

Abstract

One-shot annulative π-extension (APEX) reactions that occur at the K-region (convex armchair edge) of polycyclic aromatic hydrocarbons (PAHs) are described. $Pd(CH_3CN)_4(SbF_6)_2$/o-chloranil catalytic system effectively promotes one-shot APEX reaction of PAHs with silicon-bridged aromatics as π-extending agents. DFT calculations suggest that the complete K-region selectivity stems from the olefinic (decreased aromatic) character of the K-region. The protocol is applicable to multiple APEX and sequential APEX reactions to construct various nanographene structures in a rapid and programmable manner.

1. Introduction

Nanographenes, which are nanometer-size subunits of graphenes (single-layer two-dimensional sp^2-hybridized carbon sheets)[1] with a tunable bandgap, have become hot molecular entities in the field of nanocarbon materials science.[2] As the properties of nanographenes depend heavily on the degree of π-extension, shape, width, and edge topology, a novel bottom-up methodology for the precisely controlled synthesis of structurally uniform nanographenes is highly desirable. Among various approaches to synthesize nanographenes with atom-by-atom precision[2], one-shot annulative π-extension (APEX) reactions of polycyclic aromatic hydrocarbons (PAHs) hold significant potential not only to achieve a "growth from template" synthesis of nanographenes, but also to fine-tune the properties of nanographenes.

In the last two decades, various bottom-up organic synthesis methods have been established for the controlled synthesis of large π-extended PAHs and nanographenes, as exemplified by the groundbreaking achievements of Müllen[3], Scott[4], Fasel[5], and others[6] (Figure 1). In essence, most of the reported nanographene syntheses rely on a two-step sequence of (i) *component assembly* of small π-components, using reactions such as Diels–Alder reactions, Suzuki–Miyaura couplings, and C–H activation reactions, to synthesize soluble nanographene precursors, followed by (ii) *stitching* (graphenization[2]) of soluble polyphenylene precursors by cyclodehydrogenation, flash-vacuum pyrolysis, or photocyclization, to yield the target nanographenes (Figure 1).[2,7] Although this state-of-the-art methodology has contributed significantly to the rapid progress of nanographene materials science, it has been well documented that the final and vital step of stitching (graphenization) is usually problematic.[7] For example, intramolecular oxidative cyclohydrogenations by Lewis acids and oxidants (Scholl-type reactions) often suffer from problems such as incomplete stitching, lack of regioselectivity, and undesirable rearrangements.
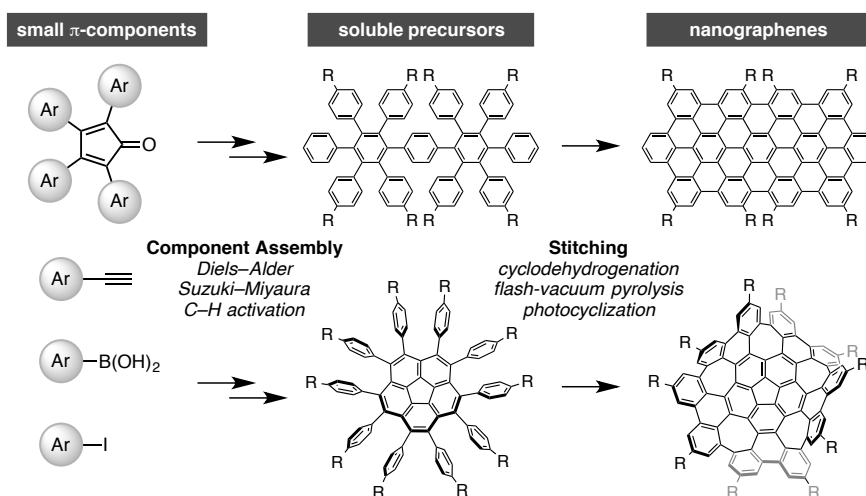
Figure 1. The well-established two-step synthesis of nanographene through π-component-assembling reaction and stitching (graphenization)

The continuing evolution of nanographene science is heavily dependent on the discovery of new reactions and strategies that allow rapid and predictable synthesis, and functionalization of nanographenes. Here, the significant potential of one-shot annulative π-extension (APEX) reactions of template PAH molecules with π-extending agents is illustrated (Figure 2), as an enabling concept that is complementary to the aforementioned two-step methodology. By devising APEX reactions that are selective to the specific regions of PAH structures (bay-region, K-region, and L-region; see Figure 2)[8], the direction-controlled growth or polymerization of a template PAH producing structurally uniform nanographenes would become possible. These regions correspond to the concave armchair edge (bay-region), convex armchair edge (K-region), and zigzag edge (L-region) in graphene nomenclature. APEX technology should also be useful for the late-stage fine-tuning of nanographene properties by subtly modifying their edge structures. Moreover, as a result of significant recent progress in surface-catalyzed cyclodehydrogenation and subsequent epitaxial elongation reactions of PAHs by the group of Fasel and Amsharov[9], a number of π-extended PAHs provided by the APEX technology could also be converted into structurally uniform carbon nanotubes.[9,10]

template PAH molecules → **nanographenes**

bay-region = concave armchair edge; K-region = convex armchair edge; L-region = zigzag edge
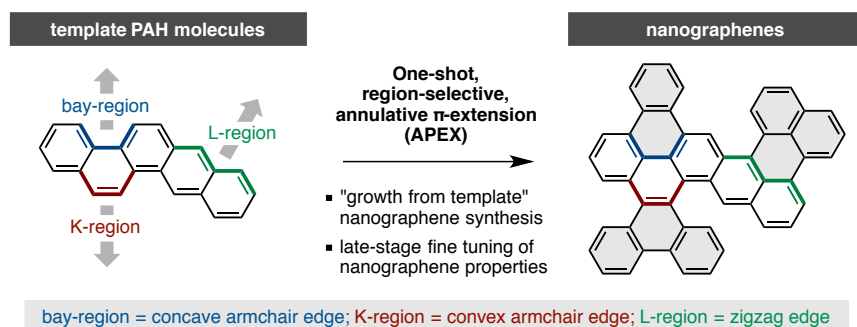
Figure 2. One-shot, region-selective APEX as alternative synthesis and functionalization of nanographenes through 'growth from template'

Although the full potential of APEX reactions in nanographene chemistry is yet to be realized partly because the concept had not been formulated, significant experimental[11] and theoretical[12] advances have appeared describing methods for bay-region-specific π-extension in PAHs. For example, Scott has revisited Clar's finding of the Diels–Alder reactivity at the PAH bay-regions[13] and proposed its use for metal-free growth of single-chirality carbon nanotubes[11,12] (Figure 3). This represents a bay-region-selective APEX reaction in our definition. However, no APEX reactions at other PAH regions (L-region and K-region) have been developed up until now. Although the dimerization of perylene under Scholl-type coupling to furnish quaterrylene represents the closest example of an L-region-selective APEX reaction, this can be categorized as the two-step method having a serious problem at the stitching (cyclodehydrogenation) stage.[14] The reactions at K-regions (convex armchair edges) are considered to be particularly difficult, as K-region bonds tend to have relatively high bond orders, and most aromatic substitution reactions occur preferentially at other aromatic C–H bonds.[8]
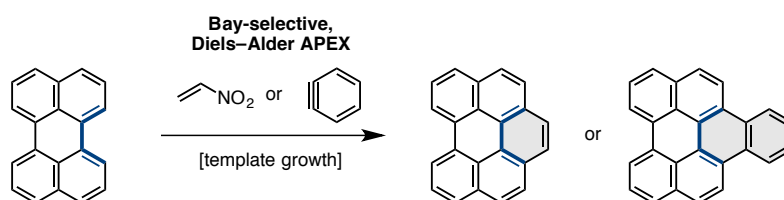
Figure 3. One-shot, bay-region-selective APEX by Diels–Alder reaction

In 2011, Itami and co-workers discovered Pd(OAc)$_2$/o-chloranil as the first-generation C–H activation catalyst for PAHs[15]. This catalyst uniquely and effectively promotes the C–H arylation of non-functionalized PAHs with arylboroxines with complete K-region selectivity. When coupled with the Scholl-type cyclodehydrogenation of the thus-formed arylated PAHs, a number of structurally intriguing nanographenes such as warped nanographenes[16] (Figure 1) have been synthesized. Although this was a two-step nanographene synthesis at the time, the observed C–H activation reactivity and selectivity might be translated into an APEX reaction when the K-region is activated and annulated with properly arranged 1,4-dimetal π-units in a [2+4] annulation fashion.

Herein, a one-shot APEX reaction that occurs selectively at the K-region of PAHs *via* double C–H activation is described[17] (Figure 4). This protocol is applicable to multiple APEX and sequential APEX reactions to construct various nanographene structures in a rapid and programmable manner.
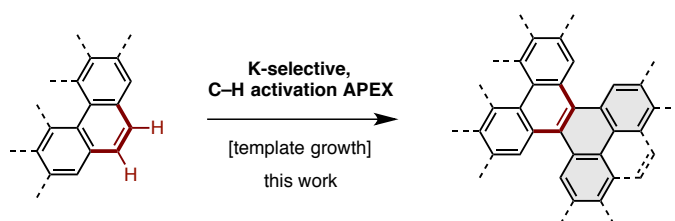
Figure 4. One-shot, K-region-selective APEX by double C–H activation

2. Results and Discussion

2-1. Working hypothesis

In 2011, the group of Itami reported K-region-selective direct arylation of polycyclic aromatic hydrocarbons with arylboroxines through $Pd(OAc)_2$/o-chloranil (3,4,5,6-tetrachloro-1,2-benzoquinone) catalysis (Scheme 1).[15a] In this report, they explain that the reaction is initiated by transmetalation of arylboroxine with palladium(II) to form aryl palladium species (ArPdX). After that, two possible reaction pathways are proposed: one of them involves electrophilic palladation mechanism, and the other is related to carbopalladation (π-coordination/insertion) mechanism (Figure 5).
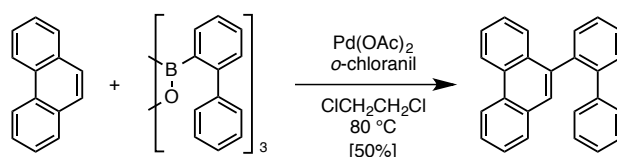
Scheme 1. K-region-selective direct arylation of PAHs with arylboroxines
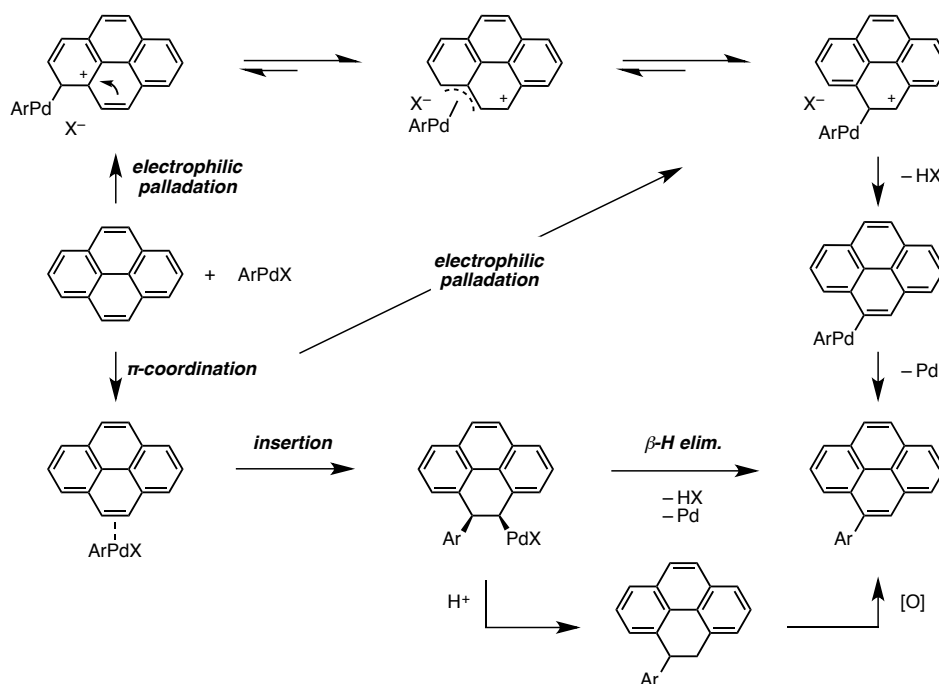
Figure 5. Proposed mechanism for K-region selective direct arylation of PAHs with arylboroxines[15a]

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Inspired by the above finding, one quite simple idea for novel APEX occurs to mind when an oraganometallic compound having two carbon-metal bonds at proper position is considered as a π-extending agent. One-shot APEX reaction *via* cascade C–H arylation of the PAH template with the π-extending agent might be feasible (Figure 6). Moreover, K-region specificity by palladium/*o*-chloranil catalytic system would enhance the desired region-selective APEX reaction of PAHs.
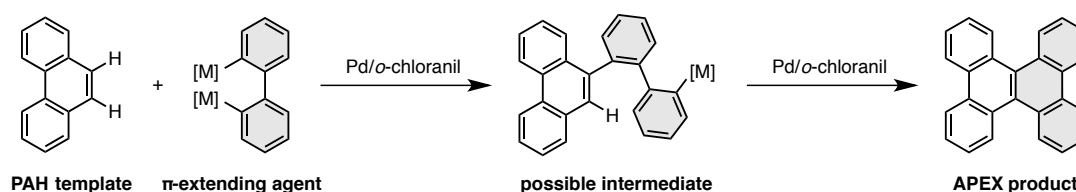
Figure 6. Working hypothesis for one-shot APEX of PAHs

2-2. Discovery of one-shot, K-region-selective APEX reaction of PAHs

To verify the working hypothesis described in Figure 6, suitable π-extending agent was thoroughly investigated with phenanthrene as a PAH template in the presence of Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ catalyst and *o*-chloranil in 1,2-dichloroethane at 80 °C. As listed in Table 1, the reaction with 2,2'-bis(trimethylsilyl)-1,1'-biphenyl having two carbon–silicon bonds provided dibenzo[*g*,*p*]chrysene (**3aa**) in 28% yield. Extensive screenings revealed that dimethyldibenzosilole[18] was proved to be the best π-extending agent affording **3aa** in 48% yield. The reaction with dimethyldibenzogermole also proceeded but led to the lower yield of desired APEX product. Dimethyldibenzostannole did not yield the product but generated a considerable amount of tetraphenylene and quaterphenyl by homo-dimerization.

Table 1. Discovery of suitable π-extending agent for APEX reaction[a]

1a
(0.20 mmol)

π-extending agent
(1.5 equiv)

5 mol% Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$
2.0 equiv o-chloranil

ClCH$_2$CH$_2$Cl (2.0 mL)
80 °C, 2 h

3aa

Me$_3$Si / SiMe$_3$ biphenyl	Me$_2$Si dibenzosilole	Me$_2$Ge dibenzogermole	Me$_2$Sn dibenzostannole
28%	48%	21%	0%
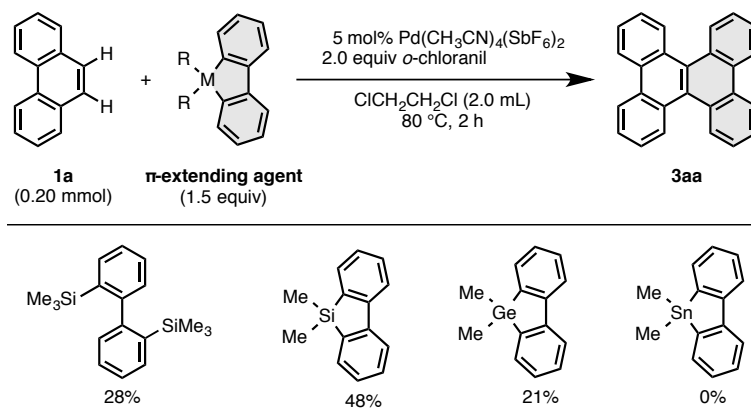
(a) Reaction conditions: phenanthrene (**1a**) (0.20 mmol), π-extending agent (1.5 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), o-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. GC yield was calculated using n-dodecane as an internal standard.

Dimethyldibenzosilole (**2a**) successfully reacted with 2,7-di-*tert*-butylphenanthrene to give **3aa** in 88% yield under the same conditions shown in Table 2. Changing the dimethyl groups of **2a** to diethyl, di-*iso*-propyl, and di-*n*-butyl groups only deteriorated the reaction efficiencies, which gave **3aa** in 53%, 41%, 56% yield, respectively.
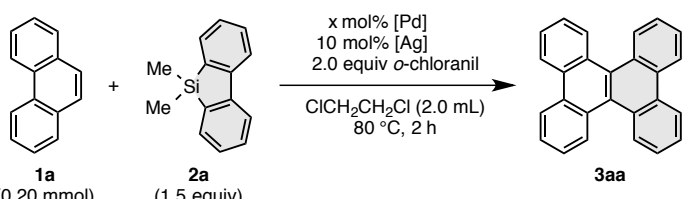
Table 2. Optimization of substituents on silicon atom[a]

1b
(0.20 mmol)

dibenzosilole
(1.5 equiv)

5 mol% Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$
2.0 equiv o-chloranil

ClCH$_2$CH$_2$Cl (2.0 mL)
80 °C, 2 h

3ba

Me$_2$Si	Et$_2$Si	^{i}Pr$_2$Si	^{n}Bu$_2$Si
88%	53%	41%	56%
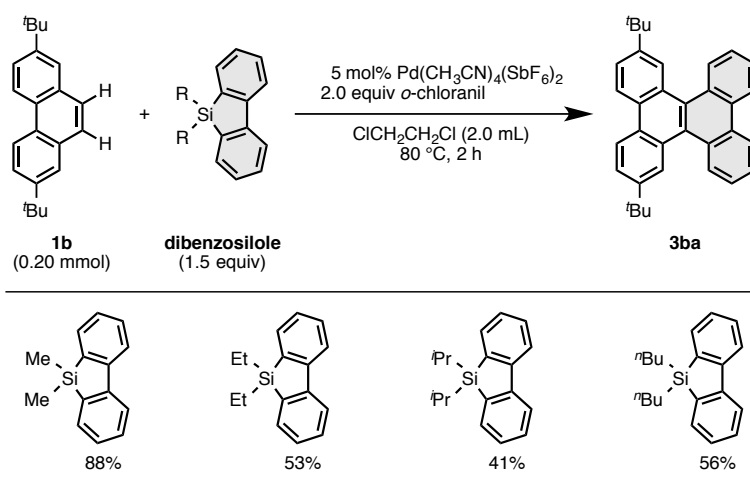
(a) Reaction conditions: phenanthrene **1b** (0.20 mmol), dibenzosiloles (1.5 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), o-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. GC yield was calculated using n-dodecane as an internal standard.

2-3. Screening of reaction conditions

Following the initial results described in Section 2-2, detail screening of reaction conditions with phenanthrene (**1a**) as a PAH template and dimethyldibenzosilole (**2a**) as a π-extending agent was performed in the presence of various catalysts and silver salts (Table 3). At first, neutral $Pd(OAc)_2$ catalyst, which shows a catalytic activity toward the previous K-region selective C–H arylation of PAHs with boroxines[15a], did not promote the APEX reaction at all (entry 1). However, the desired reaction proceeded when 10 mol% of AgOTf was used with $Pd(OAc)_2$ (entry 2). Then, various combinations of Pd sources and silver salts were tested for APEX (entries 3–7). As a result, the combination of $PdCl_2$ and AgOTf, $AgBF_4$, or $AgSbF_6$ gave the APEX product **3aa** in 36–41% yield (entries 4, 5, and 7). In these reactions, cationic Pd species are expected to form in situ, therefore, cationic palladium catalysts such as $Pd(CH_3CN)_4(BF_4)_2$ and $Pd(CH_3CN)_4(SbF_6)_2$ were employed without any silver salt (entries 8–12). Both $Pd(CH_3CN)_4(BF_4)_2$ and commercially available $Pd(CH_3CN)_4(SbF_6)_2$ showed good catalytic performance in this APEX reaction, and the latter catalyst was slightly superior to the former one in terms of the higher isolated yield (entries 8 and 9). Increasing the catalyst loading to 10, 20, and 30 mol% decreased rather than push up the yields (entries 10–12). Consequently, a cationic palladium species was found to be essential for the progress of APEX reaction, and the use of 5 mol% $Pd(CH_3CN)_4(SbF_6)_2$ gave the best result yielding **3aa** in 48% isolated yield (entry 9).

Table 3. Effects of palladium and silver catalysts[a]

1a	2a		3aa
(0.20 mmol)	(1.5 equiv)		

x mol% [Pd]
10 mol% [Ag]
2.0 equiv o-chloranil

ClCH₂CH₂Cl (2.0 mL)
80 °C, 2 h

entry	[Pd]	x	[Ag]	yield[b]
1	Pd(OAc)$_2$	5 mol%	none	nd
2	Pd(OAc)$_2$	5 mol%	AgOTf	12%
3	Pd(OCOCF$_3$)$_2$	5 mol%	AgOTf	23%
4	PdCl$_2$	5 mol%	AgOTf	36%
5	PdCl$_2$	5 mol%	AgBF$_4$	37%
6	PdCl$_2$	5 mol%	AgPF$_6$	2%
7	PdCl$_2$	5 mol%	AgSbF$_6$	41%
8	Pd(CH$_3$CN)$_4$(BF$_4$)$_2$	5 mol%	none	43% (43%)
9	Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$	5 mol%	none	48%
10	Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$	10 mol%	none	(33%)
11	Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$	20 mol%	none	(25%)
12	Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$	30 mol%	none	(19%)

(a) Reaction conditions: phenanthrene (**1a**) (0.20 mmol), dibenzosilole **2a** (1.5 equiv), Pd cat. (x mol%), silver salt (10 mol%), o-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. (b) Isolated yield. The numbers in the parentheses are GC yield calculated using *n*-dodecane as an internal standard.

Secondly, the effect of oxidants was investigated (Table 4). When commonly used oxidants such as DDQ, *p*-benzoquinone, and CuCl$_2$[19] were employed instead of *o*-chloranil, they displayed virtually no APEX activity. Interestingly, *p*-chloranil was also ineffective for APEX. It is assumed that the high reactivity of *o*-chloranil stems from not only its high oxidation ability but also its unique *o*-quinone structure which can potentially bind to palladium in a bidentate manner and modulate the redox property of a metal effectively[20].

Table 4. Effects of oxidants[a]
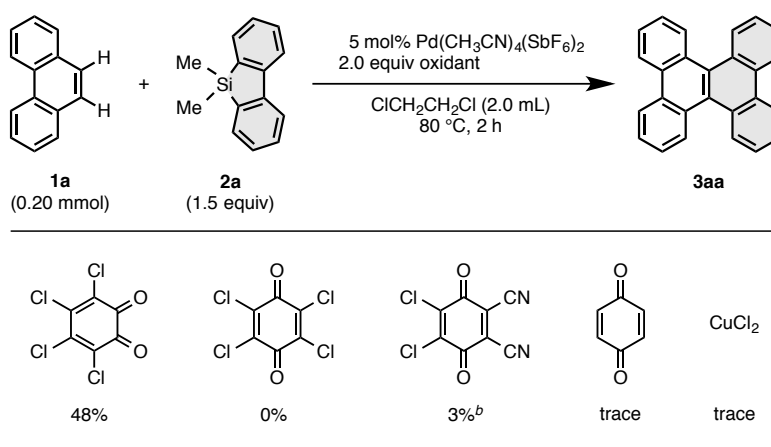
(a) Reaction conditions: phenanthrene (**1a**) (0.20 mmol), dibenzosilole **2a** (1.5 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), oxidant (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. (b) GC yield, which was calculated using n-dodecane as an internal standard.

Next, the effects of solvent, concentration, and reaction temperature were investigated (Table 5). It was found that 1,2-dichloroethane is appropriate as solvent in this APEX reaction (entry 1). Aromatic solvents such as toluene, chlorobenzene, 1,2-dichlorobenzene, fluorobenzene, and trifluoromethylbenzene are also applicable for the present APEX reactions (entries 2–5 and 7), while hexafluorobenzene was not effective (entry 6). The change in the volume of 1,2-dichloroethane had no effect to improve the yield (entries 8–11). The reactions at higher temperature than 80 °C did not elevate the yield due to the faster decomposition or homocoupling of dibenzosilole (entries 12–14). On the other hand, the reaction at lower temperature made the reaction progress slower, and the significant amount of silole remained unreacted after the reactions (entries15–17).

Table 5. Effect of solvent, concentration, and reaction temperature[a]
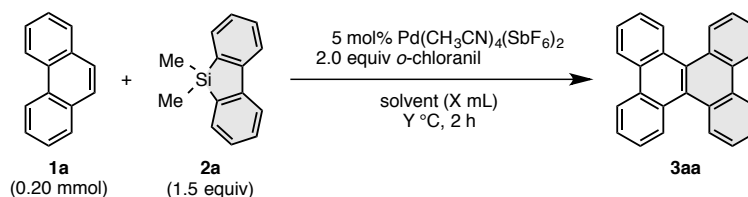
entry	solvent	X mL	Y °C	GC yield[b]
1	ClCH$_2$CH$_2$Cl	2.0 mL	80 °C	48%[c]
2	o-Cl$_2$C$_6$H$_4$	2.0 mL	80 °C	23%
3	PhCl	2.0 mL	80 °C	28%
4	PhCF$_3$	2.0 mL	80 °C	41%
5	PhF	2.0 mL	80 °C	31%
6	C$_6$F$_6$	2.0 mL	80 °C	3%
7	toluene	2.0 mL	80 °C	23%
8	ClCH$_2$CH$_2$Cl	1.0 mL	80 °C	38%
9	ClCH$_2$CH$_2$Cl	4.0 mL	80 °C	40%
10	ClCH$_2$CH$_2$Cl	8.0 mL	80 °C	40%
11	ClCH$_2$CH$_2$Cl	10 mL	80 °C	35%
12	ClCH$_2$CH$_2$Cl	2.0 mL	140 °C	40%
13	ClCH$_2$CH$_2$Cl	2.0 mL	120 °C	38%
14	ClCH$_2$CH$_2$Cl	2.0 mL	100 °C	47%
15	ClCH$_2$CH$_2$Cl	2.0 mL	60 °C	37%
16	ClCH$_2$CH$_2$Cl	2.0 mL	40 °C	12%
17	ClCH$_2$CH$_2$Cl	2.0 mL	rt	5%

(a) Reaction conditions: phenanthrene (**1a**) (0.20 mmol), dibenzosilole **2a** (1.5 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), o-chloranil (2.0 equiv), solvent (X mL), 2 h. (b) GC yield was calculated using *n*-dodecane as an internal standard. (c) Isolated yield.

At last, the amount of π-extending agent and *o*-chloranil was tuned (Table 6). Addition of small excess amount of dibenzosilole gradually enhanced the reaction, but the use of 1.5 equivalent of silole was enough to gain a desired product **3aa** in high yield (entries 1–5). Meanwhile, reducing the amount of *o*-chloranil from 2.0 equivalent decreased the yield (entries 6 and 7), but the addition of excess amount of *o*-chloranil had almost no effect compared to the standard conditions (entries 3 and 8).

Table 6. Effect of amount of dibenzosilole and *o*-chloranil[a]
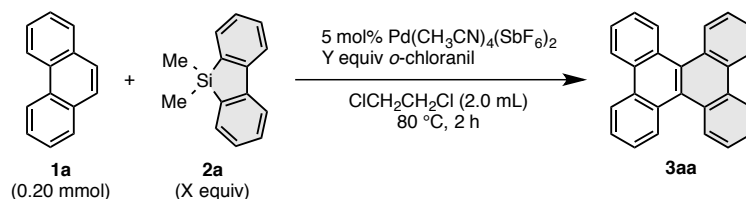
entry	X equiv	Y equiv	GC yield[b]
1	1.0	2.0	18%
2	1.25	2.0	25%
3	1.5	2.0	48%[c]
4	2.0	2.0	38%
5	2.5	2.0	44%
6	1.5	1.0	21%
7	1.5	1.5	27%
8	1.5	3.0	39%

(a) Reaction conditions: phenanthrene (**1a**) (0.20 mmol), dibenzosilole **2a** (X equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), *o*-chloranil (Y equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. (b) GC yield was calculated using *n*-dodecane as an internal standard. (c) Isolated yield.

As a result of extensive optimization of reaction conditions, the APEX reaction of phenanthrene (**1a**) was effectively promoted with dimethyldibenzosilole (**2a**) (1.5 equiv) in the presence of Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL/0.20 mmol of phenanthrene) at 80 °C for 2 h (Scheme 2).
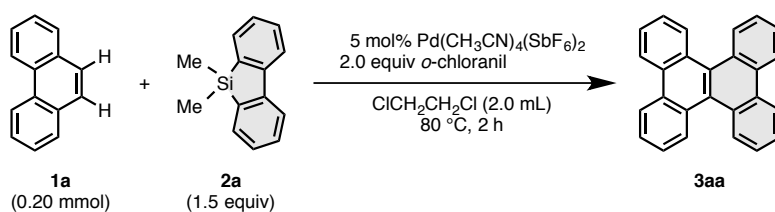
Scheme 2. Optimal reaction conditions for the APEX reaction of phenanthrene (**1a**) with dimethyldibenzosilole (**2a**)

2-4. Substrate Scope

As shown in Table 7, various structurally and electronically diverse silicon-bridged aromatics **2** were found to react with 2,7-di-*tert*-butylphenanthrene (**1b**), providing the corresponding dibenzo[*g,p*]chrysenes (**3bb–3bj**) in good to excellent yield with virtually complete K-region selectivity. In particular, dibenzosiloles having electron-deficient substituents **2b–2e**[18,21] showed excellent reactivity. The tribenzo[*a,c,f*]tetraphene framework **3bj** can be readily constructed by the APEX reaction of **1b** and benzonaphthosilole **2j**[21]. Notably, dichloro- and diboryl-substituted dibenzosiloles **2d–2f** underwent the APEX reactions smoothly, leaving C–Cl and C–B bonds intact (**3bd**, **3be**, and **3bf**). The tolerance of the reaction for these bonds makes it attractive for further π-extension and functionalization using well-established cross-coupling chemistry. Furthermore, methylene-bridged phenanthrene **1c** reacted with **2a** to afford benzoindenochrysene **3ca**, which can potentially lead to soluble nanographenes by facile substitution at the methylene moiety. Ease of post-functionalization is particularly advantageous for controlled surface alignment of nanographenes for device applications.

Table 7. Scope of one-shot, K-region-selective APEX reaction of PAHs[a]

Reaction scheme showing compound **1** (0.20 mmol) with Ar substituents and two H positions reacting with compound **2** (1.5 equiv) a dimethyldibenzosilole bearing Me, Me, Si and Ar groups, under conditions: 5 mol% Pd(CH₃CN)₄(SbF₆)₂, 2.0 equiv *o*-chloranil, ClCH₂CH₂Cl (2.0 mL), 80 °C, 2 h, to give product **3**.

3bb (89%)   **3bc** (93%)   **3bd** (88%)   **3be** (70%)   **3bj** (47%)

3bf (25%)   **3bg** (63%)   **3bh** (74%)   **3bi** (57%)   **3ca** (51%)[b]

Substrate definitions:

2b: R¹ = H, R² = CF₃, R³ = H
2c: R¹ = H, R² = F, R³ = H
2d: R¹ = H, R² = Cl, R³ = H
2e: R¹ = R² = Cl, R³ = H
2f: R¹ = R² = Bpin, R³ = H
2g: R¹ = R² = *t*Bu, R³ = H
2h: R¹ = H, R² = OMe, R³ = H
2i: R¹ = R² = H, R³ = OMe

2b-2i   **2j**   **1c**

(a) Reaction conditions: phenanthrene **1** (0.20 mmol), dimethyldibenzosilole **2** (1.5 equiv), Pd(CH₃CN)₄(SbF₆)₂ (5 mol%), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. (b) 0.10 mmol scale. 1.0 mL of 1,2-dichloroethane was used.

2-5. Multiple APEX and sequential APEX

To showcase the utility of the new APEX methodology in accessing a variety of nanographene (π-extended PAH) structures in a rapid and programmable manner, several types of multiple APEX reactions were examined (Scheme 3a-c).

For example, a 2:1 APEX reaction occurs when treating ladder-type *bis*-silicon-bridged *p*-terphenyl **4**[21] with an excess of 2,7-di-*tert*-butylphenanthrene (**1b**) in the presence of $Pd(CH_3CN)_4(SbF_6)_2$/*o*-chloranil to construct the dibenzodiphenanthroanthracene framework **5** in 69% yield (Scheme 3a). Other isomers were not observed in the reaction, highlighting the fidelity of the present method to specific reaction sites. An alternative mode of the double APEX reaction (1:2 APEX) was also possible by the reaction of 2,7-di-*tert*-butylpyrene (**6**) (1.6 g, 1.0 equiv) and dibenzosilole **2a** (3.2 g, 3.0 equiv) in the presence of $Pd(CH_3CN)_4(SbF_6)_2$ (5 mol%) and *o*-chloranil (4.0 equiv) (Scheme 3b). Notably, the reaction could be conducted on a gram scale to yield di-*tert*-butylhexabenzotetracene (**7**) in 2.6 g (83% yield). The gram-scale synthesis clearly underscores the high capability of the present reaction conditions for multiple APEX reactions. Furthermore, the $Pd(CH_3CN)_4(SbF_6)_2$/*o*-chloranil system effectively promoted the one-shot fourfold APEX reaction of 7,7'-di-*tert*-butyl-2,2'-bipyrene (**8**) (1.0 equiv) with dibenzosilole **2a** (10 equiv) to provide bihexabenzotetracene **9** in 31% yield (Scheme 3c).
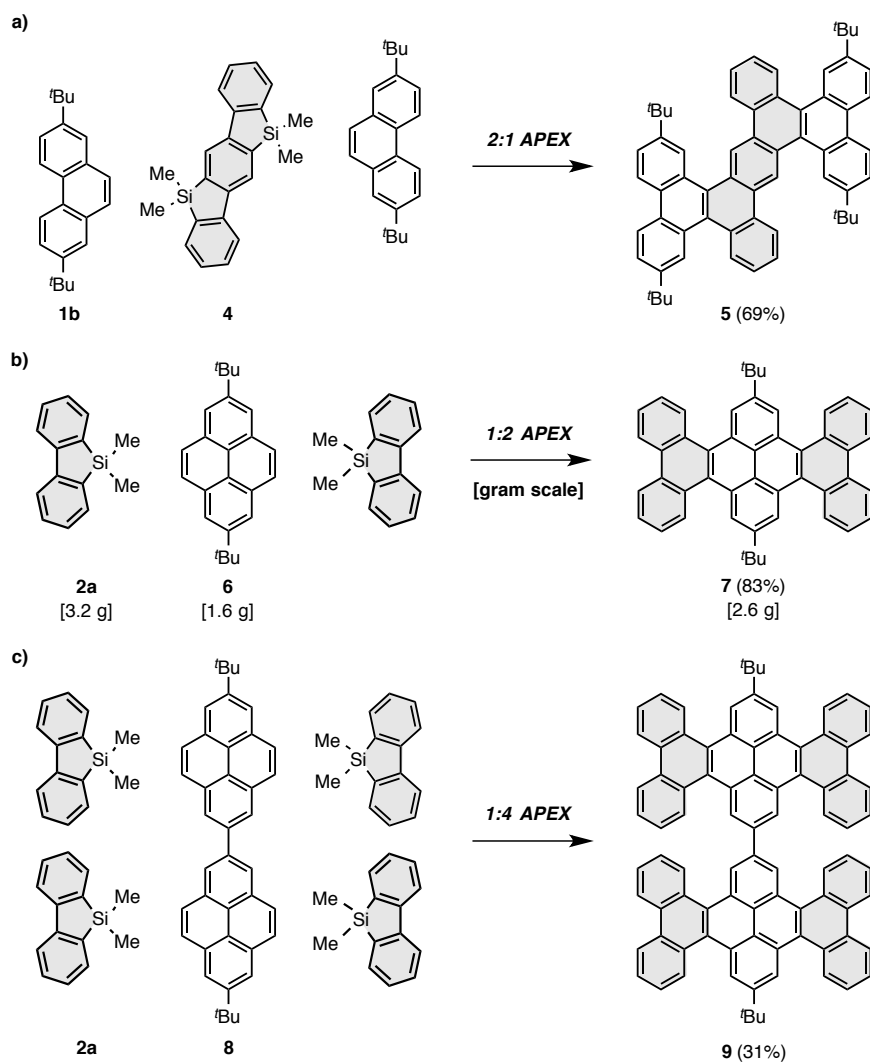
Scheme 3. Multiple APEX reaction

(a) 2:1 APEX. Reaction conditions: **4** (0.10 mmol), **1b** (5.0 equiv), Pd(CH₃CN)₄(SbF₆)₂ (5 mol%), *o*-chloranil (4.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 2 h. (b) 1:2 APEX. Reaction conditions: **6** (5.0 mmol), **2a** (3.0 equiv), Pd(CH₃CN)₄(SbF₆)₂ (5 mol%), *o*-chloranil (4.0 equiv), 1,2-dichloroethane (50 mL), 80 °C, 8 h. (c) Reaction conditions: **8** (0.10 mmol), **2a** (10 equiv), Pd(CH₃CN)₄(SbF₆)₂ (15 mol%), *o*-chloranil (10 equiv), 1,2-dichloroethane (4.0 mL), 80 °C, 1 h.

To further examine the applicability of APEX technology for the construction of larger molecules, sequential APEX reactions were investigated (Scheme 4). Pleasingly, the 2:1 APEX reaction of 2,7-di-*tert*-butylpyrene (**6**) (3.0 equiv) with *bis*-silicon bridged biphenyl **10**[22] (1.0 equiv) under Pd(CH₃CN)₄(SbF₆)₂/*o*-chloranil conditions afforded tetra-*tert*-butylhexabenzohexacene (**11**) in 53% yield. The follow-up 1:2

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APEX reaction of **11** (1.0 equiv) with dibenzosilole **2a** (4.0 equiv) also took place to furnish the target decabenzooctacene framework **12** in 17% yield. In this particular reaction, a considerable amount of starting material likely to be attributed to poor solubility in the reaction media was recovered. It should also be mentioned that the first sign of the possibility of employing APEX in an oligomerization/polymerization manifold was observed when oligomers were detected by MALDI-TOF MS analysis in the first 2:1 APEX reaction shown in Scheme 4. Although this possible mode of reaction has not been investigated extensively yet, it is envisaged that the present APEX reaction could be applied to even larger molecules through judicious choice of solubilizing substituents on the substrates. Thus, the present result bodes well for the potential application of the new APEX methodology to the bottom-up synthesis of graphene nanoribbons with controlled edge structures.
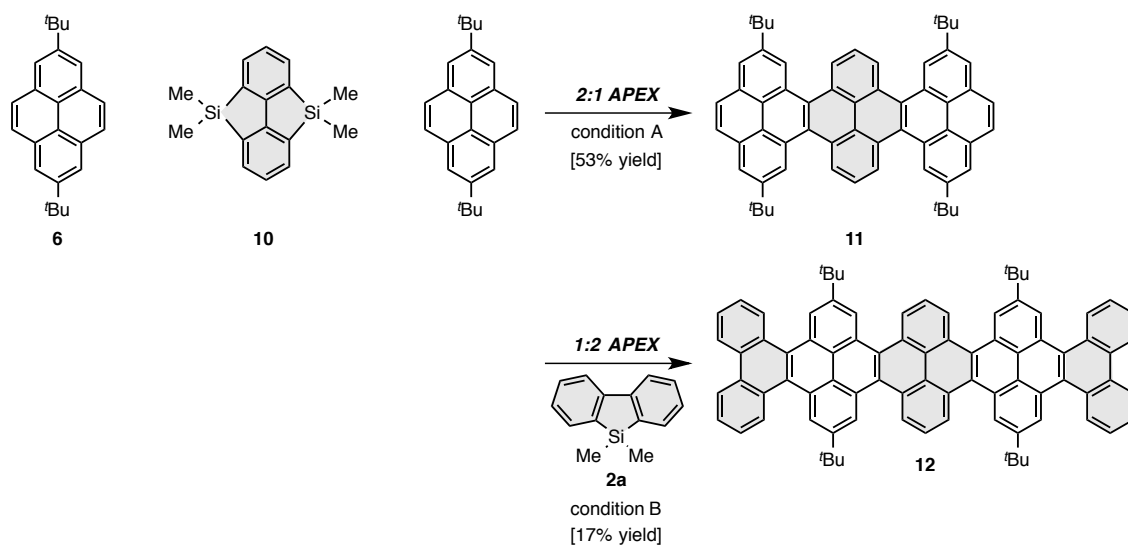
Scheme 4. Sequential APEX reaction

Condition (A): **6** (3.0 equiv), **10** (50 μmol), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (5 mol%), *o*-chloranil (4.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 6 h. Condition (B): **11** (22.8 μmol), **2a** (4.0 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (15 mol%), *o*-chloranil (5.0 equiv), 1,2-dichloroethane (0.50 mL), 80 °C, 4 h.

2-6. Mechanistic consideration of K-region-selective APEX

Although the exact mechanism of the present APEX reaction remains unclear, current assumption is shown in Figure 7. A palladium(II) species undergoes the first transmetalation with silicon-bridged aromatic **2a**, followed by coordination of phenanthrene (**1a**) to arylpalladium intermediate **A** at the K-region yielding π-complex **B**. Coordination-induced insertion at the K-region C=C bond, followed by the second transmetalation forms palladacycle intermediate **D**. Reductive elimination and oxidative aromatization yields APEX product **3ab** and palladium(0), the latter of which is oxidized to the active palladium(II) species by the action of *o*-chloranil.
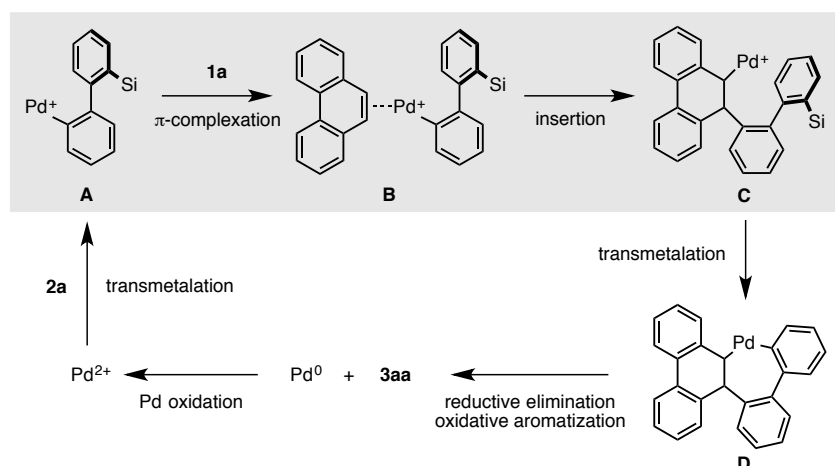
Figure 7. A possible mechanism of K-region-selective C–H activation APEX

It is assumed that the K-region selectivity in the present APEX reaction stems from the preferential palladium π-complexation at the K-region of PAHs prior to the insertion step, as depicted in Figure 7. To prove this hypothesis, DFT[23] calculations (using B3PW91 hybrid functional[24]) was conducted for the π-complexation and insertion steps on a model reaction of *o*-chloranil-bound cationic phenylpalladium species with phenanthrene yielding the alkylpalladium species shown in Figure 8 (a model reaction relevant to **A→B→C** in Figure 7). Reaction pathways were followed by intrinsic reaction coordinate (IRC[25]) computations, and high-accuracy, single-point energy calculations of DFT-optimized structures were performed with Møller–Plesset perturbation theory (MP2[26]). Among possible π-coordination complexes at C1–C2, C2–C3, C3–C4, and C9–C10 bonds, the π-complex at C9–C10 (K-region) was found

to be most stable (**9, 10Pd**). This may be due to the tendency of this bond to have the most olefinic (less aromatic) character[8,27]. It was also calculated all possible transition states of insertion from these π-complexes to give alkylpalladium complexes (Figure 8). The formation of C9–Pd complex (**9Pd-10Ph**), which leads to APEX at the K-region, was found to be most favorable both kinetically and thermodynamically. Thus, the basis of K-region selectivity in the new APEX reaction has been supported by computational theory. Based on these calculations, the most olefinic (least aromatic) K-region π-bond is predicted to be the first APEX reaction site in future functionalizations of related π-extended PAHs and nanographenes.
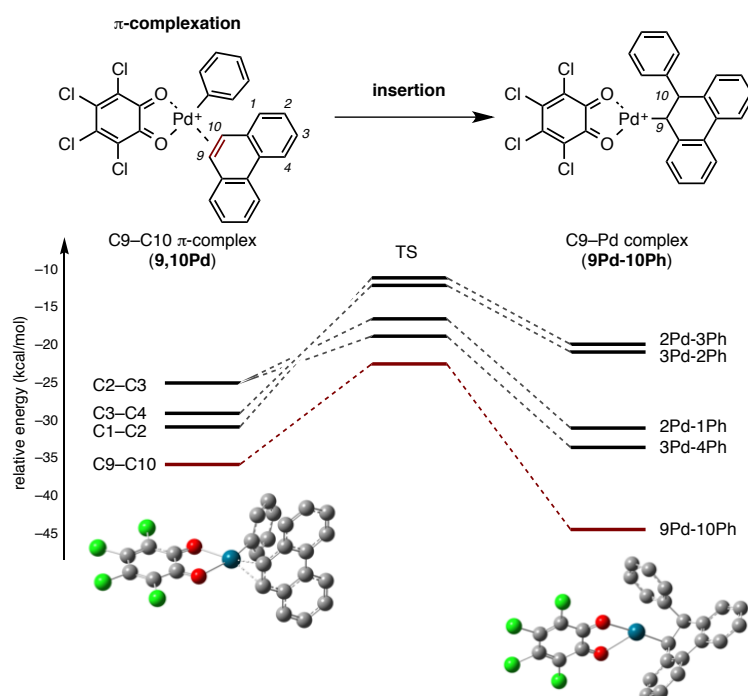
Figure 8. Theoretical calculations of π-complexation and insertion steps

Structures were optimized by the density functional theory (DFT) calculations using B3PW91 hybrid functional (hydrogen atoms are omitted for clarity). Reaction pathways were followed by intrinsic reaction coordinate (IRC) computations, and high-accuracy, single-point energy calculations of DFT-optimized structures were performed with Møller–Plesset perturbation theory (MP2). Energies are relative to that of *o*-chloranil-bound cationic phenylpalladium species.

3. Conclusions

The present APEX methodology is complementary to the state-of-the-art two-step nanographene synthetic methods, thereby finding significant use in the "growth from template" nanographene synthesis and in the late-stage fine-tuning of nanographene properties. Moreover, APEX technology is not limited to the synthesis and functionalization of π-extended PAHs and nanographenes. One of most significant features of the present APEX reaction is that unfunctionalized PAHs can be directly used for π-component assembly and π-extension without any pre-functionalization. Thus, various π-conjugated molecules made by many research groups (for many different purposes) will be suitable substrates for this APEX reaction, furnishing even more exciting classes of π-conjugated systems.

4. Experimental Section
4-1. General

Unless otherwise noted, all materials including dry solvents were obtained from commercial suppliers and used without further purification. $PdCl_2$ was purchased from Wako. $AgSbF_6$ was purchased from Aldrich. *o*-Chloranil was purchased from TCI and recrystallized from benzene before use. Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of nitrogen or argon in oven-dried glassware with standard vacuum-line techniques. All work-up and purification procedures were carried out with reagent-grade solvents in air

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} precoated plates (0.25 mm). Preparative thin-layer chromatography (PTLC) was performed using Wako-gel® B5-F silica coated plates (0.75 mm) prepared in our laboratory. Flash column chromatography was performed with KANTO Silica Gel 60N (spherical, neutral, 40-100 μm). Preparative gel permeation chromatography (GPC) was performed with a JAI LC-9204 instrument equipped with JAIGEL-1H/JAIGEL-2H columns using chloroform as an eluent. Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). The developed chromatogram was analyzed by UV lamp (254 nm and 365 nm). High-resolution mass spectra (HRMS) were obtained from a JMS-T100TD instrument (DART), Bruker Daltonics Ultraflex III TOF/TOF (MALDI-TOF-MS) and Thermo Fisher Scientific Exactive (ESI, APCI). Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECS-600 (^{1}H 600 MHz, ^{13}C 150 MHz, ^{19}F 565 MHz) spectrometer and a JEOL ECA 600II with Ultra COOL™ probe (^{1}H 600 MHz, ^{13}C 150 MHz). Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm). Chemical shifts for ^{19}F NMR are expressed in parts per million (ppm) relative to hexafluorobenzene (δ –162.00 ppm) as an external standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad signal), coupling constant (Hz), and integration.

4-2. Preparation of Substrates

4-2-1. Preparation of Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$

$$PdCl_2 + 2\ AgSbF_6 \xrightarrow[\text{overnight}]{CH_3CN,\ rt} Pd(CH_3CN)_4(SbF_6)_2$$
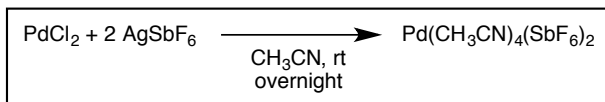
To a suspension of PdCl$_2$ (177 mg, 1.0 mmol) in CH$_3$CN (10 mL) was added AgSbF$_6$ (687 mg, 2.0 mmol), and the resultant mixture was stirred at room temperature overnight. The reaction mixture was filtrated, then Et$_2$O was added into the filtrate to recrystallize Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$. The complex was collected by filtration (710 mg, 96%).

4-2-2. Preparation of 2,7-di-*tert*-butylphenanthrene (1b)
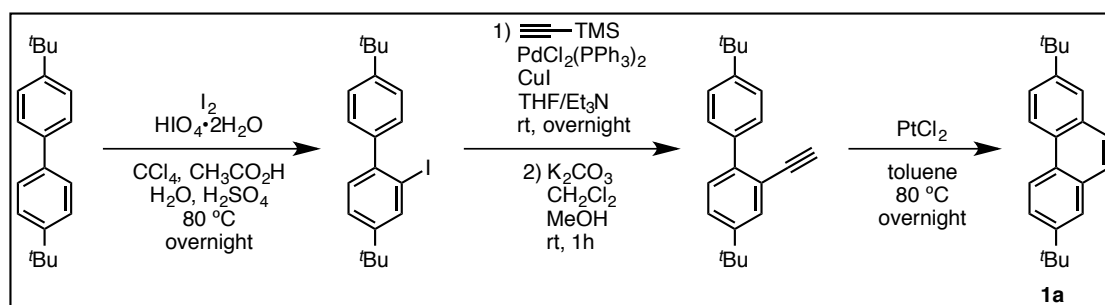
Synthesis of 4,4'-di-*tert*-butyl-2-ethynyl-1,1'-biphenyl[28]

To a solution of 4,4'-di-*tert*-butylbiphenyl (13.3 g 50 mmol) in CCl$_4$/CH$_3$CO$_2$H/ H$_2$O/H$_2$SO$_4$ (20 mL/25 mL/5.0 mL/1.0 mL) were added iodine (12.7 g, 50 mmol) and HIO$_4$·2H$_2$O (5.7 g, 25 mmol), and the resulting reaction mixture was stirred at 80 °C overnight. After cooled to room temperature, sat. NaHCO$_3$ aq. was added to the reaction mixture and it was extracted with CH$_2$Cl$_2$. Combined organic layer was dried over Na$_2$SO$_4$, filtrated and concentrated under reduced pressure to give 4,4'-di-*tert*-butyl-2-iodo-1,1'-biphenyl. This crude product was used for the next step without purification.

A solution of 4,4'-di-*tert*-butyl-2-iodo-1,1'-biphenyl, trimethylsilylacetylene (7.4 g, 75 mmol), PdCl$_2$(PPh$_3$)$_2$ (1.75 g, 2.5 mmol), and CuI (476 mg, 2.5 mmol) in THF/triethylamine (100 mL/100 mL) was stirred at room temperature overnight. 1N HCl aq. was added to the reaction mixture and it was extracted with CH$_2$Cl$_2$.

Combined organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. The crude mixture was dissolved in MeOH/CH_2Cl_2 (50 mL/50 mL), and K_2CO_3 (6.9 g, 50 mmol) was added. Resulting suspension was stirred at room temperature for 1 h. Water was added and the organic layer was extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$, filtrated and concentrated under reduced pressure. Obtained crude 4,4'-di-*tert*-butyl-2-ethynyl-1,1'-biphenyl was used for the next step without purification.

PtCl$_2$-catalyzed synthesis of 2,7-di-*tert*-butylphenanthrene (1b)[29]

A solution of 4,4'-di-*tert*-butyl-2-ethynyl-1,1'-biphenyl and $PtCl_2$ (664 mg 2.5 mmol) in toluene (100 mL) was stirred at 80 °C overnight. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (eluent: hexane), and further purified by recrystallization from CH_2Cl_2/MeOH to obtain 2,7-di-*tert*-butylphenanthrene (**1b**) (5.0 g, 17 mmol, total 34% yield in 4 steps).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (d, $J = 9.0$ Hz, 2H), 7,82 (d, $J = 2.4$ Hz, 2H), 7.71 (dd, $J = 9.0$, 2.4 Hz, 2H), 7.70 (s, 2H), 1.45 (s, 18H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 148.9, 131.7, 128.1, 127.0, 124.8, 124.1, 122.3, 34.7, 31.4.

HRMS (DRAT, ESI$^+$) *m/z* calcd for $C_{22}H_{27}$ [M+H]$^+$: 291.2113, found: 291.2112.

4-2-3. Preparation of silicon-bridged aromatics

Silicon-bridged aromatics **2a**[18], **2b**[21], **2c**[21], **2d**[21], **2e**[21], **2f**[21], **2g**[18], **2h**[21], **2i**[21], **2j**[21], **2k**[21], **2l**[21], **2m**[21], **4**[21], and **10**[22] were prepared from the corresponding biphenyls according to reported method.

Synthesis of 5,5-dimethyl-3,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5*H*-dibenzo[*b,d*]siloles (2f)[30]
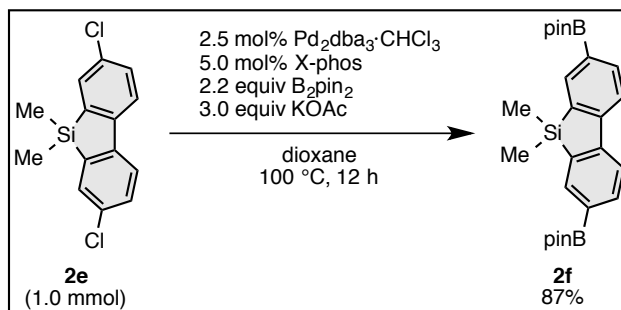
A solution of **2e** (279mg, 1.0 mmol), bis(pinacolate)diboron (559 mg, 2.2 mmol), Pd$_2$(dba)$_3$·CHCl$_3$ (tris(dibenzylideneacetone)dipalladium·CHCl$_3$, 26 mg, 0.025 mmol), XPhos (2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl, 24 mg, 0.05 mmol), potassium acetate (294 mg, 3 mmol) in dry 1,4-dioxane (10 mL) was heated with stirring at 80 °C for 16 h. After the reaction mixture was cooled down to room temperature, the reaction was quenched with water. Then the mixture was extracted with EtOAc. The combined organic phases was dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude product was passed through a short pad of silica gel (eluent: EtOAc). After the organic solvent was removed under reduced pressure, the residue was purified by recrystallization from EtOH to yield **2f** (400 mg, 87%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.10 (s, 2H), 7.90 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.86 (d, *J* = 7.2 Hz, 2H), 1.37 (s, 24H), 0.42 (s, 6H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 150.3, 139.2, 138.6, 136.9, 127.9 (br), 120.5, 83.7, 24.8, –3.2.

HRMS (ESI$^+$) *m/z* calcd for C$_{26}$H$_{37}$O$_4$B$_2$Si [M+H]$^+$: 463.2642, found: 463.2626.

4-3. APEX Reaction of PAHs with Siloles

4-3-1. General procedure
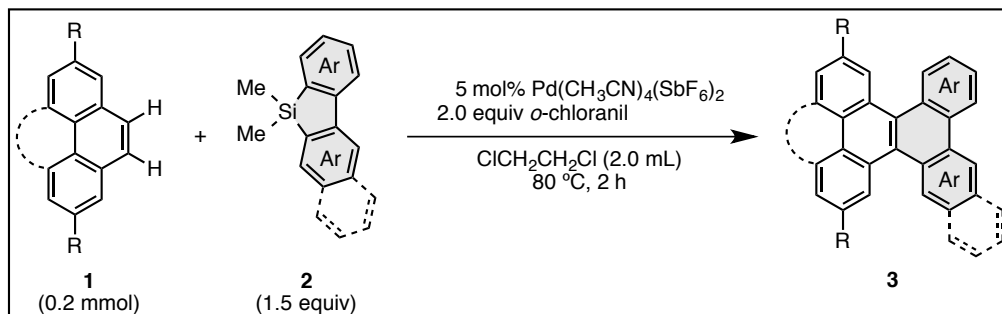
A solution of phenanthrene derivative **1** (0.20 mmol, 1.0 equiv), silicon-bridged aromatics **2** (0.30 mmol, 1.5 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (7.4 mg, 10 μmol, 5 mol%), and *o*-chloranil (98 mg, 0.40 mmol, 2.0 equiv) in DCE (2.0 mL) was stirred at 80 °C in the screw cap glass tube. After 2 hours, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH$_2$Cl$_2$). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC or silica gel column chromatography to yield π-extended PAH.

Dibenzo[*g*,*p*]chrysene (3aa)[31] CAS:191-68-4
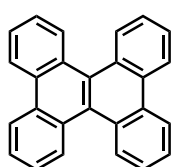
 PTLC: hexane only, Yield: 31.3 mg, 48%

3,14-Di-*tert*-butyldibenzo[*g*,*p*]chrysene (3ba)

PTLC: hexane only, Yield: 77.0 mg, 88%.
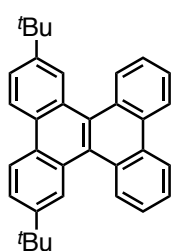
 ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.693 (dd, *J* = 10.4, 1.2 Hz, 4H), 8.687 (s, 2H), 8.58 (d, *J* = 9.0 Hz, 2H), 7.70 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.65 (t, *J* = 6.9 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 2H), 1.44 (s, 18H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 148.8, 130.8, 129.5, 128.7, 128.6, 127.9, 126.40, 126.37, 125.2, 124.4, 123.6, 123.1, 35.0, 31.4. One

aromatic carbon signal can be overlapped.

HRMS (DART, ESI$^+$) m/z calcd for C$_{34}$H$_{33}$ [M+H]$^+$: 441.2582, found: 441.2579.

6,11-Di-*tert*-butyl-3-(trifluoromethyl)dibenzo[*g,p*]chrysene (3bb)

PTLC: hexane only, Yield: 90.5 mg, 89%.
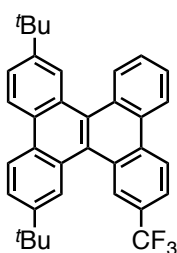
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.03 (s, 1H), 8.78 (d, J = 8.4 Hz, 1H), 8.75–8.69 (m, 2H), 8.68 (d, J = 1.8 Hz, 1H), 8.62–8.57 (m, 3H), 7.86 (dd, J = 8.7, 1.5 Hz, 1H), 7.74 (dd, J = 8.4, 1.8 Hz, 1H), 7.73 (dd, J = 8.7, 2.1 Hz, 1H), 7.71–7.67 (m, 2H), 1.442 (s, 9H), 1.440 (s, 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 149.5, 149.1, 132.8, 130.2, 129.9, 129.0, 128.9, 128.8 (2C), 128.7, 128.4, 128.20 ($^2J_{C-F}$ = 32.1 Hz), 128.17, 127.4, 127.3, 126.7, 126.3 ($^3J_{C-F}$ = 4.3 Hz),125.2, 125.02, 124.96, 124.8, 124.6 ($^1J_{C-F}$ = 271 Hz), 124.3, 124.0, 123.25, 123.22, 122.2 ($^3J_{C-F}$ = 4.4 Hz), 35.04, 35.02, 31.4, 31.3.

^{19}F NMR (565 MHz, CDCl$_3$) δ –62.25 (s).

HRMS (DART, ESI$^+$) m/z calcd for C$_{35}$H$_{32}$F$_3$ [M+H]$^+$: 509.2456, found: 509.2456.

6,11-Di-*tert*-butyl-3-fluorodibenzo[g,p]chrysene (3bc)

PTLC: hexane only, Yield: 84.9 mg, 93%.
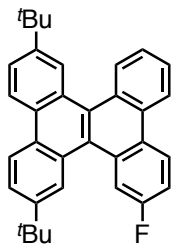
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.70–8.65 (m, 3H), 8.65 (d, J = 2.4 Hz, 1H), 8.63 (dd, J = 8.4, 1.2 Hz, 1H), 8.60 (dd, J = 9.0, 1.2 Hz, 2H), 8.38 (dd, J = 11.7, 2.7 Hz, 1H), 7.74 (dt, J = 8.4, 2.3 Hz, 2H), 7.67 (td, J = 7.8, 1.2 Hz, 1H), 7.62 (td, J = 7.5, 1.2 Hz, 1H), 7.40 (ddd, J = 9.0, 7.8, 3.0 Hz, 1H), 1.46 (s, 9H), 1.45 (s 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 161.5 ($^1J_{C-F}$ = 242.9 Hz), 149.2, 149.0, 131.0 ($^3J_{C-F}$ = 8.6 Hz), 130.5, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5 (2C), 127.3, 127.2 ($^4J_{C-F}$ = 2.8 Hz), 126.7, 126.2, 125.8 ($^3J_{C-F}$ = 8.6 Hz), 125.4, 124.8, 124.7, 124.5, 123.5, 123.2, 123.1, 114.7 ($^2J_{C-F}$ = 23.1 Hz), 113.7 ($^2J_{C-F}$ = 23.0 Hz), 35.0, 31.4.

^{19}F NMR (565 MHz, CDCl$_3$) d –114.87 (t, J = 13.0 Hz).

HRMS (DART, ESI$^+$) m/z calcd for C$_{34}$H$_{32}$F [M+H]$^+$: 459.2488, found: 459.2484.

6,11-Di-*tert*-butyl-3-chlorodibenzo[*g,p*]chrysene (3bd)

PTLC: hexane only, Yield: 84.0 mg, 88%.
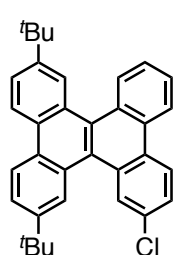
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.76 (s, 1H), 8.74–8.70 (m, 2H), 8.68–8.65 (m, 2H), 8.64 (d, J = 8.4 Hz, 1H), 8.61 (d, J = 8.4 Hz, 2H), 7.75 (dt, J = 9.0, 2.1 Hz, 2H), 7.71–7.65 (m, 2H), 7.63 (dd, J = 8.7, 2.1 Hz, 1H), 1.50 (s, 9H), 1.48 (s, 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 149.2, 149.0, 132.4, 130.6, 130.2, 129.5, 129.0, 128.9 (2C), 128.7, 128.6, 128.5, 128.3, 128.1, 126.8, 126.7, 126.6, 126.5, 125.3, 125.2, 124.9, 124.8, 124.6, 123.5, 123.2 (2C), 35.04, 35.02, 31.42, 31.39.

HRMS (DART, ESI$^+$) m/z calcd for C$_{34}$H$_{32}$Cl [M+H]$^+$: 475.2193, found: 475.2179.

3,14-Di-*tert*-butyl-6,11-dichlorodibenzo[*g,p*]chrysene (3be)

Silica gel column chromatography: hexane/EtOAc = 10:1 to 5:1, Yield: 71.4 mg, 70%.
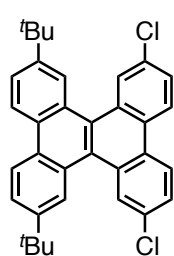
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.72 (d, J = 1.8 Hz, 2H), 8.64 (d, J = 1.8 Hz, 2H), 8.62 (d, J = 9.0 Hz, 2H), 8.58 (d, J = 9.0 Hz, 2H), 7.77 (dd, J = 9.0, 1.8 Hz, 2H), 7.63 (dd, J = 9.0, 2.4 Hz, 2H), 1.48 (s, 18H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 149.3, 132.7, 130.5, 128.7, 128.5, 128.3, 128.1, 127.7, 126.8, 125.0 (2C), 124.9, 123.2, 35.0, 31.4.

HRMS (DART, ESI$^+$) m/z calcd for C$_{34}$H$_{31}$Cl$_2$ [M+H]$^+$: 509.1803, found: 509.1805.

2,2'-(6,11-Di-*tert*-butyldibenzo[*g*,*p*]chrysene-3,14-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3bf)

Silica gel column chromatography: hexane/EtOAc = 10:1 to 6:1, Yield: 34.1 mg, 25%.
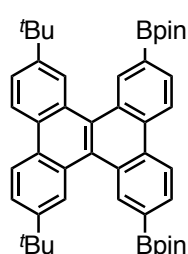
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.31 (s, 2H), 8.78 (d, *J* = 1.8 Hz, 2H), 8.74 (d, *J* = 8.0 Hz, 2H), 8.61 (d, *J* = 9.0 Hz, 2H), 8.05 (dd, *J* = 7.8, 0.6 Hz, 2H), 7.73 (dd, *J* = 8.4, 1.8 Hz, 2H), 1.49 (s, 18H), 1.37 (s, 24H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 148.7, 136.9, 132.6, 131.4, 129.1, 128.7, 128.6, 127.9, 126.6 (br), 126.1, 124.2, 122.9, 122.8, 83.9, 35.1, 31.5, 25.0.

HRMS (ESI$^+$) *m/z* calcd for C$_{46}$H$_{55}$O$_4$B$_2$ [M+H]$^+$: 693.4281, found: 693.4282.

3,6,11,14-Tetra-*tert*-butyldibenzo[*g*,*p*]chrysene (3bg)

PTLC: hexane only, Yield: 69.0 mg, 63%.
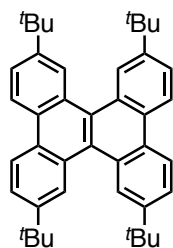
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.65 (d, *J* = 1.8 Hz, 4H), 8.59 (d, *J* = 8.4 Hz, 4H), 7.71 (dd, *J* = 8.7, 1.5 Hz, 4H), 1.44 (s, 36H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 148.8, 129.1, 128.5, 128.4, 124.9, 124.3, 123.2, 35.1, 31.6.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{42}$H$_{49}$ [M+H]$^+$: 553.3834, found: 553.3854.

6,11-Di-*tert*-butyl-3-methoxydibenzo[*g*,*p*]chrysene (3bh)

PTLC: hexane/CH$_2$Cl$_2$ = 4:1, Yield: 69.6 mg, 74%.
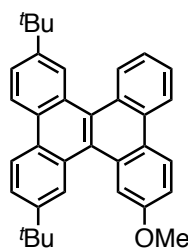
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.77 (d, *J* = 1.2 Hz, 1H), 8.69 (d, *J* = 1.2 Hz, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.63–8.58 (m, 4H), 8.17 (d, *J* = 3.0 Hz, 1H), 7.75–7.71 (m, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.30 (dd, *J* = 9.0, 2.4 Hz, 1H), 3.94 (s, 3H) 1.46 (s, 9H), 1.45 (s, 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 158.3, 148.9, 148.8, 130.9, 130.7, 128.9, 128.8 (3C), 128.7, 128.6, 128.5, 127.7, 126.5, 125.5, 125.4, 125.2, 124.9, 124.50, 124.48, 124.39, 123.3, 123.11, 123.06, 116.4, 109.9, 55.4, 35.1, 35.0, 31.6, 31.4.

HRMS (DART, ESI$^+$) m/z calcd for C$_{35}$H$_{35}$O [M+H]$^+$: 471.2688, found: 471.2681.

6,11-Di-*tert*-butyl-1-methoxydibenzo[g,p]chrysene (3bi)

PTLC: hexane only, Yield: 53.4 mg, 57%.
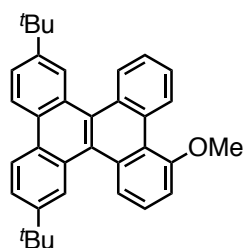
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.43–9.39 (m, 1H), 8.67–8.64 (m, 2H), 8.63–8.60 (m, 1H), 8.55 (dd, J = 9.0, 1.2 Hz, 2H), 8.29 (d, J = 8.4 Hz, 1H), 7.69 (t, J = 7.8 Hz, 2H), 7.60–7.56 (m, 2H), 7.53 (t, J = 8.1 Hz, 1H), 7.15 (d, J = 7.8 Hz, 1H), 4.10 (s, 3H), 1.43 (s, 18H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 157.8, 148.8, 148.6, 132.0, 130.3, 129.2, 128.8, 128.75, 128.69 (2C), 128.6, 128.4, 127.9 (2C), 126.7, 126.2, 125.5, 125.2 (2C), 124.4, 124.2, 123.04, 123.02, 121.2, 120.7, 108.5, 55.9, 34.9 (2C), 31.4 (2C).

HRMS (DART, ESI$^+$) m/z calcd for C$_{35}$H$_{35}$O [M+H]$^+$: 471.2688, found: 471.2679.

3,16-Di-*tert*-butyltribenzo[*a,c,f*]tetraphene (3bj)

PTLC: hexane only, Yield: 46.4 mg, 47%.
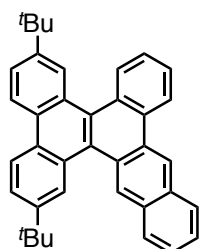
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.15 (s, 1H), 9.12 (s, 1H), 8.89 (s, 1H), 8.80 (d, J = 7.8 Hz, 1H), 8.69 (s, 1H), 8.63–8.57 (m, 3H), 8.12 (d, J = 7.8 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.72 (dd, J = 8.4, 1.8 Hz, 1H), 7.70 (dd, J = 8.7, 1.5 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.5 Hz, 1H), 7.58–7.50 (m, 2H), 1.45 (s, 9H), 1.44 (s, 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 148.9, 148.8, 132.0, 131.6, 131.3, 130.2, 129.9, 128.9, 128.8, 128.7, 128.6, 128.42, 128.39, 128.2, 128.1, 128.0, 127.9 (2C), 126.8, 126.7, 126.0, 125.9, 125.1, 124.9, 124.5, 124.4, 124.3, 123.1, 122.2, 35.0 (2C), 31.44, 31.42.

One aromatic carbon signal can be overlapped.

HRMS (DART, ESI$^+$) m/z calcd for C$_{38}$H$_{35}$ [M+H]$^+$: 491.2739, found: 491.2722.

4*H*-Benzo[*p*]indeno[7,1,2-*ghi*]chrysene (3ca)

A solution of 4*H*-Cyclopenta[*def*]phenanthrene **1c** (19 mg, 0.10 mmol, 1.0 equiv), **2a** (32 mg, 0.15 mmol, 1.5 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (3.7 mg, 5 μmol, 5 mol%), and *o*-chloranil (49 mg, 0.20 mmol, 2.0 equiv) in DCE (1.0 mL) was stirred at 80 °C in the screw cap glass tube. After 2 hours, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH$_2$Cl$_2$). After the organic solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (eluent: hexane/CH$_2$Cl$_2$ = 7:1) to give **3ca** (17.3 mg, 51%).
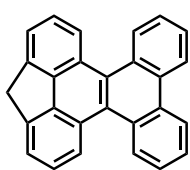
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.10 (dd, J = 7.8, 1.2 Hz, 2H), 8.79 (dd, J = 7.8, 1.2 Hz, 2H), 8.72 (d, J = 7.8 Hz, 2H), 7.81–7.76 (m, 4H), 7.75–7.68 (m, 4H), 4.45 (s, 2H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 141.6, 138.4, 130.8, 130.4, 128.5, 128.2, 127.1, 126.68, 126.66, 125.7, 124.7, 123.5, 121.6, 37.4.

HRMS (DART, ESI$^+$) m/z calcd for C$_{27}$H$_{17}$ [M+H]$^+$: 341.1330, found: 341.1331.

4-3-2. 2:1 APEX reaction of 1b with 4
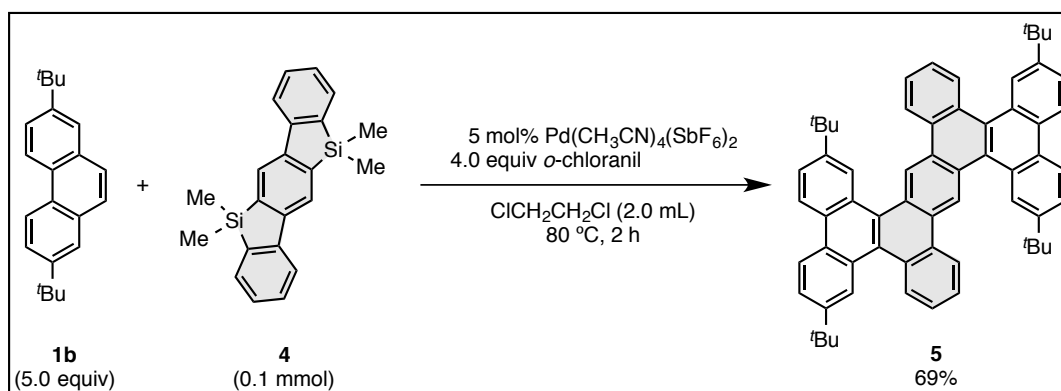
A solution of 2,7-di-*tert*-butylphenanthrene (**1b**) (145 mg, 0.5 mmol, 5.0 equiv), **4** (34.3 mg, 0.1 mmol, 1.0 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (7.4 mg, 10 μmol, 5 mol%), and

o-chloranil (98 mg, 0.4 mmol, 4.0 equiv) in DCE (2.0 mL) was stirred at 80 °C for 2 h in the screw cap glass tube. After the reaction mixture was cooled to room temperature, the mixture was passed through a short pad of silica gel (eluent: CH_2Cl_2). After the organic solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (eluent: hexane/CH_2Cl_2 = 19:1) to give **5** (55.3 mg, 69% yield).

^{1}H NMR (600 MHz, CDCl$_3$/CS$_2$) δ 9.90 (s, 2H), 9.07 (s, 2H), 8.85 (d, *J* = 7.8 Hz, 2H), 8.72–8.68 (m, 4H), 8.66 (d, *J* = 8.4 Hz 2H), 8.62 (d, *J* = 9.0 Hz, 2H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.71 (d, *J* = 9.0 Hz, 2H), 7.66–7.61 (m, 4H), 1.56 (s, 18H), 1.44 (s, 18H).

^{13}C NMR (150 MHz, CDCl$_3$/CS$_2$) δ 149.1, 148.7, 131.1, 130.0, 129.4, 129.1, 129.0, 128.8, 128.7, 128.6, 128.3, 128.2, 128.0, 126.53, 126.49, 125.1 (2C), 124.6, 124.4, 123.8, 123.7, 123.3, 123.1, 35.0, 34.9, 31.6, 31.4.

HRMS (APCI) *m/z* calcd for C$_{62}$H$_{59}$ [M+H]$^+$: 803.4611, found: 803.4576.

4-3-3. 1:2 APEX reaction of 6 with 2a (gram-scale synthesis of 10,21-di-*tert*-butylhexabenzo[*a,c,fg,j,l,op*]tetracene (7))
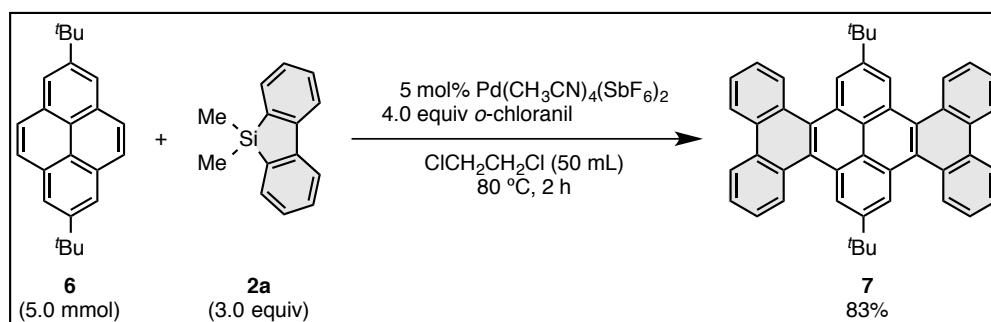
A solution of 2,7-di-*tert*-butylpyrene (**6**, 1.57 g, 5.0 mmol, 1.0 equiv), **2a** (3.15 g, 15 mmol, 3.0 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (185.5 mg, 0.25 mmol, 5 mol%), and *o*-chloranil (4.92 g, 20 mmol, 4.0 equiv) in DCE (50 mL) was stirred at 80 °C in the screw cap glass tube. After 8 h, the reaction mixture was cooled to room temperature, and then the organic solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (eluent: hexane/CH_2Cl_2 = 9:1) to give 10,21-di-*tert*-butylhexabenzo[*a,c,fg,j,l,op*]tetracene (**7**) (2.6 g, 83% yield).

^{1}H NMR (CDCl$_3$, 600 MHz) δ 9.05 (s, 4H), 8.90 (d, *J* = 8.2 Hz, 4H), 8.82 (d, *J* = 8.2 Hz, 4H), 7.76 (t, *J* = 8.2 Hz, 4H), 7.70 (t, *J* = 8.2 Hz, 4H), 1.61 (s, 18H).

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^{13}C NMR (CDCl$_3$, 100 MHz) δ 147.7, 131.0, 129.9, 128.5, 128.3, 127.9, 126.7, 126.6, 123.8, 123.4, 122.8, 35.7, 31.8.

HRMS (DART, ESI$^+$) m/z calcd for C$_{48}$H$_{39}$ [M+H]$^+$: 615.3052, found: 615.3067.

4-3-4. Preparation of 7,7'-di-*tert*-butyl-2,2'-bipyrene (**8**)
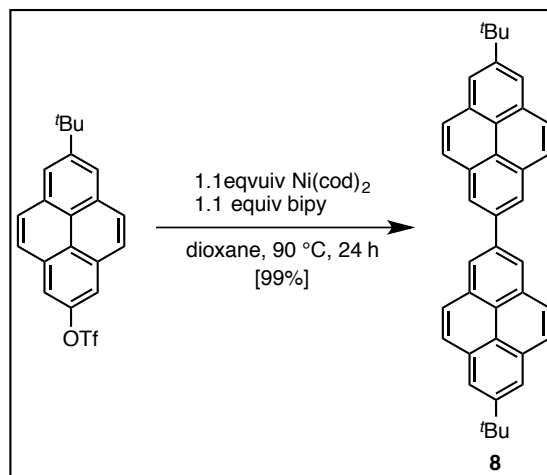
A solution of 7-(*tert*-butyl)pyren-2-yl trifluoromethanesulfonate (81 mg, 0.20 mmol, 1.0 equiv), bis(1,5-cyclooctadiene)nickel (60 mg, 0.22 mmol, 1.1 equiv), and 2,2'-bipyridyl (34 mg, 0.22 mmol) in dry 1,4-dioxane (2.0 mL) was stirred at 90 °C in 20-mL glass vessel tubes equipped with J. Young$^®$ O-ring tap containing a magnetic stirring bar. After 14 h, the reaction mixture was cooled to room temperature, passed through a short pad of silica gel (eluent: CH$_2$Cl$_2$). After cooled down to room temperature, the mixture was concentrated under reduced pressure. The mixture was extracted with CHCl$_3$. The combined organic phase was dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: hexane/CH$_2$Cl$_2$ = 6:1) to give **8** (102.6 mg, 99% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.64 (s, 4H), 8.26 (s, 4H), 8.18 (d, J = 9.0 Hz, 4H), 8.12 (d, J = 9.0 Hz, 4H), 1.61 (s, 18H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 149.2, 139.0, 131.6, 131.1, 128.1, 127.5, 124.4, 123.9, 122.9, 122.5, 35.3, 32.0.

HRMS (APCI) m/z calcd for C$_{40}$H$_{35}$ [M+H]$^+$: 515.2733, found: 515.2727.

4-3-5. 1:4 APEX reaction of 8 with 2a
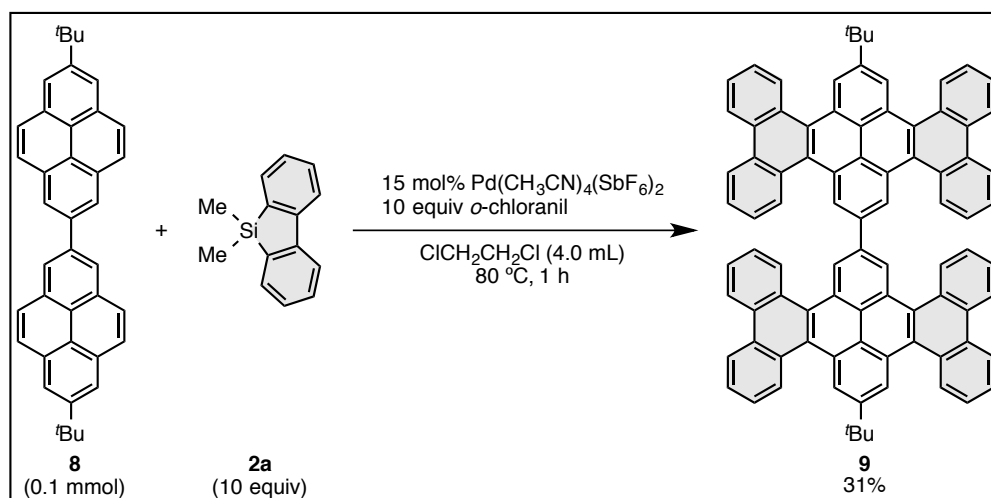
A solution of 7,7'-di-*tert*-butyl-2,2'-bipyrene (**8**) (51 mg, 0.10 mmol, 1.0 equiv), **2a** (210 mg, 1.0 mmol, 10 equiv), $Pd(CH_3CN)_4(SbF_6)_2$ (11 mg, 15 μmol, 15 mol%), and *o*-chloranil (245 mg, 1.0 mmol, 10 equiv) in DCE (4.0 mL) was stirred at 80 °C in the screw cap glass tube. After 1 h, the reaction mixture was cooled to room temperature, and the residue was subjected to silica gel column chromatography (eluent: hexane/CH_2Cl_2 = 4:1), and then purified by PTLC (eluent: $CHCl_3$) to give 21,21'-di-*tert*-butyl-10,10'-bihexabenzo[*a,c,fg,j,l,op*]tetracene (**9**) (34.3 mg, 31% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.65 (s, 4H), 9.11 (s, 4H), 9.08 (d, *J* = 8.4 Hz, 4H), 8.94 (d, *J* = 7.2 Hz, 4H), 8.85 (d, *J* = 7.2 Hz, 8H), 7.80–7.76 (m, 8H), 7.73 (t, *J* = 7.5 Hz, 4H), 7.49 (t, *J* = 7.8 Hz, 4H), 1.64 (s, 18H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 137.9, 131.2, 131.0, 129.83, 129.76, 129.0, 128.7, 128.6, 128.4, 128.2, 127.3, 126.9, 126.74, 126.68, 125.2, 123.9, 123.7, 122.7, 35.8, 31.8.

HRMS (APCI) *m/z* calcd for $C_{88}H_{59}$ [M+H]$^+$: 1115.4611, found: 1115.4556.

4-3-6. 2:1 APEX reaction of 6 with 10
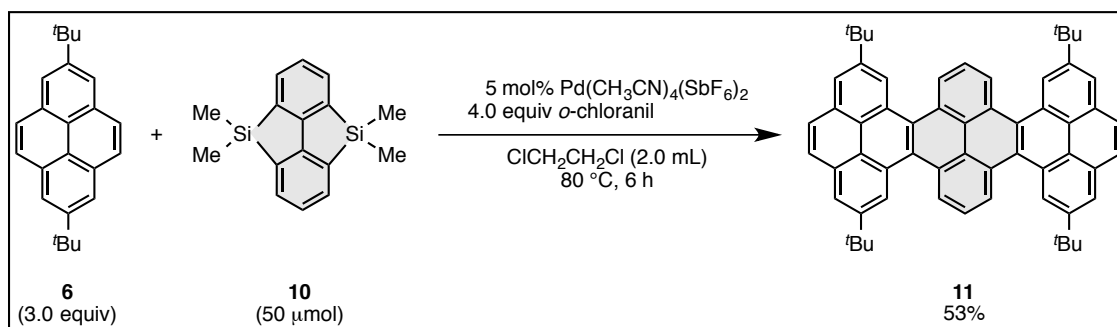
A solution of 2,7-di-*tert*-butylpyrene (**6**) (47 mg, 0.15 mmol, 3.0 equiv), 4,4,8,8-tetramethyl-4,8-dihydro-4,8-disilacyclopenta[*def*]fluorene (**10**) (13 mg, 50 μmol, 1.0 equiv), Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$ (2 mg, 2.5 mmol, 5 mol%), and *o*-chloranil (49 mg, 0.2 mmol, 4.0 equiv) in DCE (2.0 mL) was stirred at 80 °C in the screw cap glass tube. After 6 h, the reaction mixture was cooled to room temperature, and the residue was subjected to silica gel column chromatography (eluent: hexane/CH$_2$Cl$_2$ = 4:1), and then purified by preparative recycling gel permeation chromatography (CHCl$_3$) to give 2,7,13,18-tetra-*tert*- butylhexabenzo[*de,hi,lm,qr,uv,yz*]hexacene (**11**) (20.6 mg, 53% yield).

^{1}H NMR (600 MHz, CDCl$_3$) δ 9.31 (d, J = 1.8 Hz, 4H), 9.26 (d, J = 8.4 Hz, 4H), 8.28 (d, J = 1.8 Hz, 4H), 8.18–8.14 (m, 6H), 1.64 (s, 36H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 148.2, 131.0, 129.3, 128.8, 128.4, 127.5, 125.4 (2C), 124.7, 123.9, 123.2, 122.1, 35.5, 31.9.

HRMS (APCI) *m/z* calcd for C$_{60}$H$_{55}$ [M+H]$^+$: 775.4298, found: 775.4269.

4-3-7. 1:2 APEX reaction of 11 with 2a
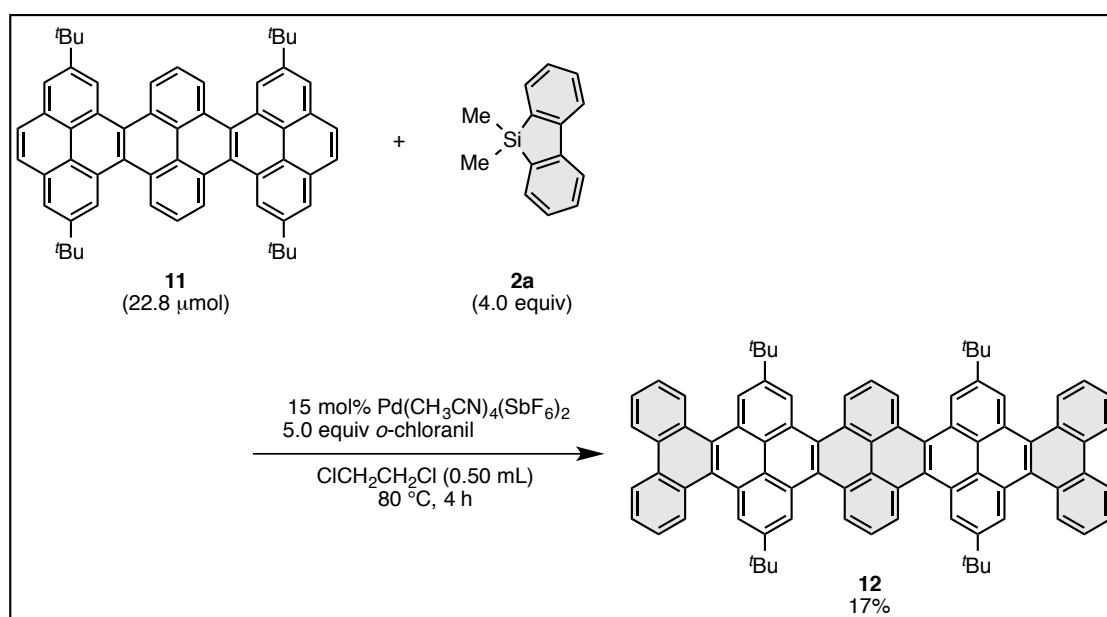
A solution of **11** (18 mg, 22.8 μmol, 1.0 equiv), **2a** (19 mg, 91.3 μmol, 4.0 equiv), $Pd(CH_3CN)_4(SbF_6)_2$ (2.0 mg, 3.4 μmol, 15 mol%), and *o*-chloranil (28 mg, 114 μmol, 5.0 equiv) in DCE (0.50 mL) was stirred at 80 °C in the screw cap glass tube. After 4 h, the reaction mixture was cooled to room temperature, and the residue was subjected to silica gel column chromatography (eluent: hexane/CH_2Cl_2 = 6:1), and then purified by preparative recycling gel permeation chromatography (eluent: $CHCl_3$) to give 10,16,27,33-tetra-*tert*-butyldecabenzo[$a,a_1b_1,c,e_1f_1,fg,jk,no,r,t,wx$]octacene (**12**) (4.1 mg, 17% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.33 (d, *J* = 1.2 Hz, 4H), 9.28 (d, *J* = 7.8 Hz, 4H), 9.15 (d, *J* = 1.2 Hz, 4H), 8.98 (d, *J* = 7.8 Hz, 4H), 8.85 (d, *J* = 7.2 Hz, 4H), 8.22 (t, *J* = 8.1 Hz, 2H), 7.79 (td, *J* = 7.2, 1.8 Hz, 4H), 7.74 (td, *J* = 7.8, 1.2 Hz, 4H), 1.67 (s, 36H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 147.9, 131.1, 129.9, 129.2, 128.8, 128.6, 128.4 (2C), 128.0, 126.8, 126.7, 125.6, 125.5, 125.0, 123.8, 123.7, 123.25, 123.15, 35.8, 31.9.

HRMS (APCI) *m/z* calcd for $C_{84}H_{67}$ [M+H]$^+$: 1075.5237, found: 1075.5209.

4-4. Computational Study
Computational methodology

All the calculations were carried out using the Gaussian 09 program package[23]. Geometry optimizations were performed at the density functional theory (DFT) level using the Becke's three-parameter hybrid functional[24a], PW91 non-local correlation functional[24b] (B3PW91) in conjunction with following basis sets; LanL2DZ[25] with effective core potential (ECP) for Pd, 6-31+G*[32] for O, C on phenanthrene and phenyl group due to the necessity of diffuse function to describe the extra electron placed far from the nuclei in the atoms, 6-31G* for Cl and other C atoms, 6-31G** for H on phenanthrene and 6-31G for other H atoms (called BS1). All structures were optimized without any symmetry assumptions and verified to be minima (no imaginary frequencies) or transition states (one imaginary frequency) on the free energy surface with analytical frequency calculations with B3PW91/BS1 level of theory. The transition states were confirmed by full intrinsic reaction coordinate[25] (IRC) calculations at the B3PW91/BS1 level. Full IRC calculations allowed displaying the direct connection between transition states and their corresponding reactants and products. For single-point energy calculations the spin-component-scaled Møller-Plesset second-order perturbation theory[26] (SCS-MP2) was employed to obtain more reliable energy because it usually gives results close to the experimental value. With SCS-MP2 theory larger basis sets were used; Stuttgard-Dresden basis set[33] (SDD) with ECP for Pd, 6-311+G* for O, C on phenanthrene and phenyl group, 6-311G* for Cl and other C atoms, 6-311G** for H (called BS2). Zero-point energy, enthalpy, and Gibbs free energy at 353.15 K and 1 atm were estimated from the gas-phase studies.
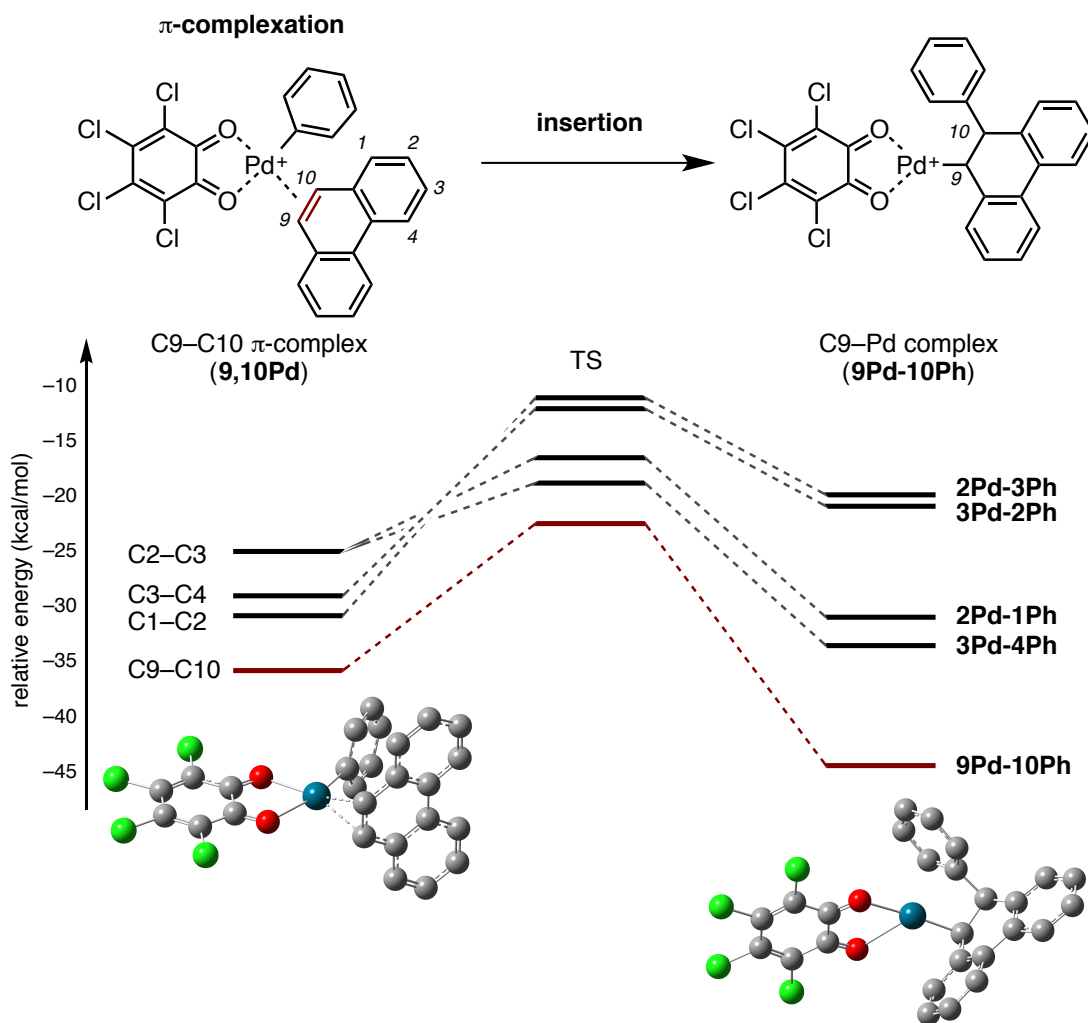
Figure 9. Energy surface of π-complexation and insertion

Table 8. Uncorrected and zero-point/thermal-corrected (353.15K) energies of stationary points (Hartree) and their Cartesian coordinates[a]

Compound	SCS-MP2	ZPE-corrected	H	G
9,10Pd	-3112.28758017	-3111.952546	-3111.911379	-3112.037355
TS_9Pd-10Ph	-3112.26739205	-3111.932653	-3111.892403	-3112.015648
9Pd-10Ph	-3112.30257031	-3111.965748	-3111.925322	-3112.049677
1,2Pd	-3112.27922752	-3111.944296	-3111.903161	-3112.029096
TS_2Pd-3Ph	-3112.25061561	-3111.916266	-3111.876115	-3111.998444
2Pd-3Ph	-3112.26477025	-3111.928666	-3111.888330	-3112.011000
2,3Pd_1	-3112.27230942	-3111.937552	-3111.896336	-3112.022723
TS_2Pd-1Ph	-3112.25914851	-3111.924700	-3111.884439	-3112.007596
2Pd-1Ph	-3112.28180495	-3111.945207	-3111.904938	-3112.027455
2,3Pd_2	-3112.27249533	-3111.937763	-3111.896527	-3112.023023
TS_3Pd-4Ph	-3112.26270610	-3111.928156	-3111.887933	-3112.010646
3Pd-4Ph	-3112.28587841	-3111.949187	-3111.908972	-3112.031041
3-4Pd	-3112.28066663	-3111.945701	-3111.904573	-3112.030501
TS_3Pd-2Ph	-3112.25108298	-3111.916719	-3111.876578	-3111.998839
3Pd-2Ph	-3112.26532032	-3111.929213	-3111.888909	-3112.011259

(a) E: electronic energy; ZPE: zero-point energy; H (=E+ZPE+E_{vib}+E_{rot}+E_{trans}+RT): sum of electronic and thermal enthalpies; G (=H–TS): sum of electronic and thermal free energies

9,10Pd

O	-1.16586400	1.12955600	0.42833200
O	-1.26581600	-1.15066900	-0.94787600
C	-2.26847900	0.76384300	0.01020200
C	-3.48903000	1.50768100	0.23094600
C	-2.32588500	-0.54633800	-0.78043200
C	-4.66599800	1.01829200	-0.27448900
C	-3.60468000	-1.00147100	-1.28366100
C	-4.72417200	-0.24914100	-1.03932600
Cl	-3.37591400	2.96050900	1.11644400
Cl	-6.11381600	1.87233700	-0.02944200
Cl	-6.23535300	-0.76399800	-1.62032100
Cl	-3.62685900	-2.46587300	-2.15939100
Pd	0.58425000	-0.13359000	-0.00600600
C	1.92831300	-1.95620200	-0.01490400
C	2.14484500	-1.24904000	-1.20763800
C	2.96690900	-2.05302000	0.98095900
H	1.09629700	-2.65692800	0.05433200
C	1.82794500	1.06431600	0.93363700
C	3.41089900	-0.60645400	-1.46128500
H	1.48028700	-1.40625900	-2.05720500
C	2.75164900	-2.80781500	2.15141000
C	4.22201600	-1.42115200	0.75275400
C	2.36382200	2.14000400	0.23568700
C	1.98014000	0.91230100	2.30665600
C	4.44792700	-0.68598500	-0.48923100
C	3.63091900	0.05668400	-2.68510700
C	3.74694000	-2.93360600	3.10259700
H	1.79117300	-3.29725700	2.29454900
C	5.21405300	-1.56343200	1.74415600
C	3.07448000	3.10928700	0.95430500
H	2.24810900	2.23912800	-0.84067500
C	2.69413700	1.89203800	3.00751700
H	1.56660700	0.05855100	2.83759100
C	5.67571900	-0.06319800	-0.79243300
H	2.82991200	0.08799900	-3.41992000
C	4.84858200	0.65297600	-2.95530200
C	4.98255400	-2.29954100	2.89432900
H	3.57841500	-3.52138300	3.99980000
H	6.18406400	-1.09687100	1.61634900
C	3.23829500	2.98573600	2.33404500
H	3.49909600	3.95837200	0.42415800
H	2.82147800	1.78945900	4.08248600
C	5.87217500	0.59406700	-1.99568200
H	6.49364600	-0.09450500	-0.08183200
H	5.01534700	1.15711200	-3.90234600
H	5.76942000	-2.39301500	3.63710200
H	3.79194800	3.74158000	2.88469400
H	6.83157200	1.06027300	-2.20017100

TS_9Pd-10Ph

O	-1.14624800	1.36928500	0.15064300
O	-1.18847000	-1.12728600	-0.75391200
C	-2.23689700	0.80330700	0.11671200
C	-3.48394800	1.42284000	0.52504500
C	-2.25993300	-0.64074700	-0.38768000
C	-4.64122800	0.69328300	0.46885700
C	-3.51970400	-1.35190400	-0.41586700
C	-4.65901700	-0.70858300	-0.00746900
Cl	-3.41481000	3.03881200	1.06664700
Cl	-6.11365000	1.39350500	0.95438300
Cl	-6.15128900	-1.52242900	-0.04186000
Cl	-3.50233800	-2.96485100	-0.97818200
Pd	0.65716500	0.17094600	-0.59880600
C	2.18382300	-1.03121800	-1.33312400
C	3.14785800	0.03285400	-1.33709900
C	2.27975900	-2.08406800	-0.32886500
H	1.72055500	-1.29054300	-2.28947200
C	2.03884300	1.66383100	-0.56373000
C	4.30144000	-0.03454000	-0.45656300
H	3.28816400	0.56411100	-2.27299900
C	1.34657300	-3.14190200	-0.33284100
C	3.32162000	-2.05559200	0.63896200
C	1.84236900	2.63490400	-1.55686700
C	2.39739900	2.03222600	0.74086000
C	4.37637700	-1.03989700	0.54024700
C	5.34568600	0.89557200	-0.61180900
C	1.39931900	-4.13601000	0.62880900
H	0.57793200	-3.16306800	-1.10014300
C	3.33467100	-3.06721400	1.61700200
C	1.96207200	3.98593300	-1.22384500
H	1.59948600	2.34707300	-2.57734000
C	2.50358700	3.38384100	1.06115200
H	2.60284300	1.27464900	1.49346000
C	5.51687900	-1.05484900	1.36828700
H	5.26406300	1.65639800	-1.38407900
C	6.45848300	0.85190000	0.20836600
C	2.39020700	-4.08404000	1.61837800
H	0.67954300	-4.94871600	0.61628900
H	4.09918100	-3.07274000	2.38564200
C	2.28868600	4.35865800	0.08103000
H	1.80721100	4.74350900	-1.98791300
H	2.76713100	3.67696500	2.07420900
C	6.53514200	-0.12771400	1.20943900
H	5.62378900	-1.81172500	2.13693100
H	7.26513500	1.56666500	0.07793800
H	2.43322200	-4.85274500	2.38439800
H	2.39093000	5.41070200	0.33360400
H	7.40403300	-0.17087200	1.85964000

9Pd-10Ph

O	-0.82511600	0.73880900	0.61766600
O	-1.24056000	-0.97207000	-1.38524100
C	-1.98862100	0.43082200	0.35883100
C	-3.13346000	0.97017400	1.06478000
C	-2.22214100	-0.58454200	-0.76303200
C	-4.38930500	0.52393600	0.74724900
C	-3.58413900	-1.02536200	-1.02560900
C	-4.61723300	-0.48671500	-0.30838200
Cl	-2.83112200	2.12737900	2.28550800
Cl	-5.74363900	1.13070600	1.58089900
Cl	-6.21945100	-0.97355900	-0.62063400
Cl	-3.80149800	-2.18981800	-2.25569200
Pd	0.93600300	-0.02782200	-0.54084200
C	2.57988800	-0.87579600	-1.39764000
C	3.58572400	0.25300300	-1.28798300
C	2.46475800	-1.83246300	-0.32106000
H	2.26977400	-1.19118700	-2.39577000
C	2.67441500	1.44405100	-0.87617700
C	4.70174200	-0.01006500	-0.30831800
H	4.02006400	0.48123500	-2.26739000
C	1.38332800	-2.75772600	-0.34897600
C	3.35213500	-1.79614700	0.80083200
C	1.68554300	1.88319600	-1.80470600
C	2.85326300	2.18756700	0.31545100
C	4.56125400	-0.95749200	0.72655000
C	5.87695300	0.73805300	-0.41211800
C	1.13862200	-3.58893900	0.73917000
H	0.77886100	-2.83393900	-1.24931200
C	3.06110300	-2.63287500	1.88060300
C	0.94060800	3.05179500	-1.55210900
H	1.62030900	1.41589700	-2.78592800
C	2.10782200	3.33356800	0.54634800
H	3.60464500	1.87247300	1.03297200
C	5.62557500	-1.12270400	1.63180500
H	5.97727900	1.46234600	-1.21727200
C	6.91778900	0.56829600	0.49714100
C	1.97190400	-3.50836400	1.85510500
H	0.31757700	-4.29828300	0.71241200
H	3.69037400	-2.61936100	2.76378100
C	1.15340600	3.77211700	-0.38691200
H	0.22082000	3.39399000	-2.29088900
H	2.27541000	3.90511700	1.45530200
C	6.78669400	-0.36715700	1.52514200
H	5.56224000	-1.86889600	2.41657000
H	7.82824900	1.15158300	0.39746300
H	1.78916700	-4.14905600	2.71307600
H	0.59197600	4.68314600	-0.19864900
H	7.59557300	-0.51922700	2.23334100

1,2Pd

O	1.69889300	0.50507000	-0.30945400
O	0.96746500	-1.85102300	0.69278900
C	2.53996400	-0.40504800	-0.31209700
C	3.87651900	-0.24447100	-0.83314400
C	2.12236300	-1.75205500	0.26747400
C	4.74158100	-1.30892100	-0.78523200
C	3.08521700	-2.83071600	0.28691300
C	4.34170300	-2.61479900	-0.21927700
Cl	4.29518100	1.27924600	-1.47650000
Cl	6.32236400	-1.14465900	-1.38718200
Cl	5.48866600	-3.86925700	-0.20730400
Cl	2.58085200	-4.32171200	0.94753400
Pd	-0.26671000	0.07839600	0.49870800
C	-2.51980700	0.54943200	2.74043500
C	-1.84977400	-0.50462500	2.06703900
C	-3.60018100	1.16817300	2.15426400
C	-2.29845600	-0.89684800	0.78421200
C	-4.08348000	0.80180100	0.86948900
H	-4.10135100	1.95389700	2.70825700
C	-3.42564100	-0.25438000	0.17841900
H	-1.97537200	-1.84985100	0.36554400
C	-5.23128200	1.44018500	0.25752400
C	-3.91215700	-0.70053400	-1.08235200
C	-5.68513500	0.96936700	-1.01105100
C	-5.93003600	2.51254900	0.85769400
C	-5.00475600	-0.11068300	-1.65165500
H	-3.40805100	-1.52444400	-1.58077900
C	-6.80923600	1.57142000	-1.62148100
C	-7.02594900	3.08631500	0.24048400
H	-5.61306700	2.90679400	1.81686800
H	-5.37824800	-0.46275200	-2.60987500
H	-7.14533500	1.19765100	-2.58514200
C	-7.47283000	2.61421200	-1.00740000
H	-7.54538300	3.90806800	0.72449900
H	-8.33627300	3.06940400	-1.48313100
H	-1.15863600	-1.13776700	2.62075300
H	-2.19690600	0.84131300	3.73478200
C	-0.90875800	1.89729500	0.12084100
C	-1.47458700	2.16458500	-1.11958300
C	-0.61322400	2.89852800	1.03910800
C	-1.75749000	3.49672200	-1.44751600
H	-1.70314000	1.37197300	-1.82746200
C	-0.90378800	4.22385200	0.69309600
H	-0.16258200	2.67565000	2.00282200
C	-1.47536200	4.52117400	-0.54447700
H	-2.20210700	3.72266000	-2.41371400
H	-0.67568200	5.01947300	1.39841700

H	-1.69837300	5.55215500	-0.80576900

TS_2Pd-3Ph

O	-0.64776800	-0.25098400	-2.86963000
O	1.22236800	-2.45802500	-1.49569900
C	0.13715100	-1.20430400	-2.95767200
C	1.38370900	-1.15558000	-3.68792300
C	-0.26270200	-2.49937600	-2.27813700
C	2.09718000	-2.31363800	-3.86925800
C	0.49835500	-3.69426000	-2.55618100
C	1.64679300	-3.59684800	-3.30229800
Cl	1.85374300	0.34873500	-4.34734000
Cl	3.53618000	-2.29434600	-4.78085000
Cl	2.59917100	-4.98059400	-3.58175400
Cl	-0.04655500	-5.15804100	-1.86043800
Pd	-2.38396200	-0.51474200	-1.47442800
C	-4.63870000	0.53213800	-0.42759700
C	-4.03157100	-0.78192900	-0.22204900
C	-5.73395900	0.64482900	-1.32573200
C	-4.41860900	-1.82945800	-1.09740200
C	-6.11142300	-0.38553300	-2.17548200
H	-6.23874900	1.60372200	-1.36560000
C	-5.40903200	-1.64644800	-2.08145300
H	-4.01684200	-2.82672600	-0.93958700
C	-7.19740800	-0.25154300	-3.14667300
C	-5.77119500	-2.72566200	-2.94318000
C	-7.51713300	-1.36252600	-3.97728000
C	-7.94583800	0.93104100	-3.30166200
C	-6.78047100	-2.58678200	-3.84788700
H	-5.23376400	-3.66572900	-2.85573400
C	-8.56048200	-1.25611900	-4.92075100
C	-8.96856100	1.01526100	-4.23388400
H	-7.73770900	1.80015400	-2.68665600
H	-7.05152200	-3.41969400	-4.49162500
H	-8.79330100	-2.11463900	-5.54517700
C	-9.28031500	-0.08269600	-5.05065000
H	-9.53239900	1.93849200	-4.32905300
H	-10.08314700	-0.01040500	-5.77800900
H	-3.57674400	-1.01536100	0.74041200
H	-4.61367100	1.23283800	0.40064300
C	-3.07130800	1.41189000	-1.38797900
C	-3.33737800	1.97154100	-2.65106900
C	-2.25846700	2.08826300	-0.45985500
C	-2.74257600	3.17900700	-2.99495800
H	-3.99460500	1.46169200	-3.35081800
C	-1.66956300	3.30311900	-0.82338400
H	-2.09742500	1.68387500	0.53671400
C	-1.91152800	3.84628200	-2.08349600
H	2.92992500	3.60877500	-3.97569100
H	-1.03415900	3.82469400	-0.11234100
H	-1.46553200	4.79846800	-2.35760600

2Pd-3Ph

O	1.51798300	0.83758900	-0.31378100
O	0.93359700	-1.31012900	1.14305500
C	2.30110100	-0.12838000	-0.35812800
C	3.56299200	-0.11192500	-1.05500800
C	1.86743900	-1.39609200	0.32306500
C	4.23419000	-1.29596700	-1.24847900
C	2.56161800	-2.62010500	0.01797000
C	3.72479400	-2.56316500	-0.71355700
Cl	4.09960500	1.38210900	-1.69298100
Cl	5.68494700	-1.31755400	-2.14627300
Cl	4.62137300	-3.98565400	-1.00077100
Cl	1.94808900	-4.07124000	0.68829700
Pd	-0.18544800	0.63790400	1.09828300

C	-2.45873700	1.73354200	2.09138600
C	-1.82827400	0.37710800	2.33812900
C	-3.62245100	1.71225200	1.16657500
C	-2.20492900	-0.70664900	1.51080500
C	-3.97515000	0.64354900	0.39805300
H	-4.17143700	2.64613400	1.08895900
C	-3.19360000	-0.58887800	0.51819500
H	-1.77533900	-1.68693800	1.70008300
C	-5.10131800	0.67924800	-0.55270800
C	-3.49830800	-1.69386600	-0.32182600
C	-5.34880000	-0.46248100	-1.36295600
C	-5.94454300	1.78991200	-0.70069800
C	-4.52351500	-1.62807400	-1.22274300
H	-2.90696900	-2.60007600	-0.22793900
C	-6.41016600	-0.45379200	-2.29001300
C	-6.98957500	1.78123500	-1.61799100
H	-5.80467400	2.67681300	-0.09138900
H	-4.74247600	-2.48745600	-1.85179800
H	-6.58326500	-1.33625300	-2.90025800
C	-7.22517800	0.65792100	-2.42076100
H	-7.62904000	2.65445300	-1.70698800
H	-8.04273800	0.65798100	-3.13487400
H	-1.41369100	0.16826200	3.32367500
H	-2.75750500	2.22000700	3.02912400
C	-1.26785300	2.56045400	1.48381300
C	-1.34815700	3.23650100	0.23871300
C	-0.13055000	2.79877700	2.30740400
C	-0.34361400	4.10691900	-0.15448100
H	-2.20861600	3.08044300	-0.40551300
C	0.87192300	3.69103100	1.89500100
H	-0.09250100	2.38548400	3.31278400
C	0.76454400	4.34303700	0.67419000
H	-0.42348500	4.61901700	-1.10947300
H	1.71912100	3.87911100	2.54864800
H	1.53404200	5.04324600	0.36156400

2,3Pd_1

O	-1.46856800	1.00530700	0.38066500
O	-1.57184200	-1.27980300	-0.97716700
C	-2.57674500	0.45946300	0.25887600
C	-3.79079800	1.00786500	0.81199600
C	-2.63294000	-0.85222800	-0.50958900
C	-4.96898900	0.32508500	0.63743500
C	-3.90567400	-1.52281200	-0.65008400
C	-5.02640200	-0.95299900	-0.10068200
Cl	-3.67717000	2.48470200	1.65943900
Cl	-6.41374500	0.94779300	1.28140500
Cl	-6.53478500	-1.72112300	-0.26098800
Cl	-3.92619800	-2.99685700	-1.51116700
Pd	0.23685200	0.05543200	-0.51780700
C	2.80657300	-0.13432600	-2.23177500
C	1.68985900	-0.93495400	-1.93450600
C	3.96036700	-0.16127800	-1.43757600
H	2.79256400	0.49453700	-3.11795000
C	1.74765400	-1.78919800	-0.78998500
C	5.09242000	0.64598400	-1.78193100
C	4.01507500	-1.01870300	-0.28583500
C	2.89056900	-1.80825500	0.01031600
H	0.97042000	-2.53198500	-0.62655500
C	6.22641500	0.60680600	-1.03193800
C	5.02824100	1.28717200	-2.65648200
C	5.22861300	-1.05104500	0.51366100
H	2.90790300	-2.48705100	0.85554100
C	6.32998200	-0.23212600	0.12563900
H	7.08279300	1.21859500	-1.30305400
C	5.37263000	-1.86217000	1.66056400

C	7.51981500	-0.25501700	0.88553500
C	6.54768800	-1.86825300	2.39003300
H	4.55928900	-2.50060100	1.98848800
C	8.35160500	0.37201400	0.57567700
C	7.63131100	-1.05987900	2.00209700
H	6.63348300	-2.50380800	3.26640900
H	8.55150600	-1.07135400	2.57847700
H	0.92933000	-1.08916700	-2.69929600
C	1.43053300	1.50392700	0.06707700
C	2.10547100	1.38604700	1.27492200
C	1.42101800	2.68017600	-0.67434300
C	2.80201700	2.50184700	1.75653400
H	2.09288600	0.46358900	1.84891600
C	2.12461100	3.78390800	-0.17680300
H	0.88538200	2.75832600	-1.61728100
C	2.81360700	3.69392400	1.03285100
H	3.32832000	2.42983300	2.70529500
H	2.12910500	4.71115100	-0.74477600
H	3.35681400	4.55478200	1.41329900

TS_2Pd-1Ph

O	-1.48557900	1.14979800	0.27640600
O	-1.56477800	-1.11452600	-1.11761600
C	-2.55179000	0.53410200	0.25714300
C	-3.76447700	0.99746500	0.90253000
C	-2.57609500	-0.80068800	-0.48443500
C	-4.87193000	0.19108700	0.89993200
C	-3.77042600	-1.61402100	-0.42033300
C	-4.87363800	-1.12961700	0.23416400
Cl	-3.71266500	2.52207400	1.66735600
Cl	-6.29562600	0.69717700	1.68285500
Cl	-6.30078700	-2.05308300	0.28958800
Cl	-3.73671600	-3.12681100	-1.21282500
Pd	0.21810600	0.26681000	-0.95459100
C	2.72794600	0.34218300	-1.82311100
C	1.70041600	-0.64005900	-2.09632100
C	3.81520700	0.01519900	-0.93152100
H	2.95184700	1.05916500	-2.60650700
C	1.71141300	-1.85547000	-1.32941200
C	4.91258400	0.90898000	-0.80628900
C	3.77685700	-1.18344100	-0.18039100
C	2.68789500	-2.08461300	-0.38996800
H	0.95824400	-2.61125800	-1.52973800
C	5.94510200	0.62521000	0.04316900
H	4.92069300	1.82094700	-1.39713600
C	4.85755100	-1.48034100	0.73628100
H	2.64893700	-3.01286600	0.16878400
C	5.94620800	-0.56041200	0.83625400
H	6.78782900	1.30658900	0.12579200
C	4.89282100	-2.64279100	1.54259400
C	7.01691000	-0.83443400	1.71974100
C	5.94866200	-2.88575100	2.39901600
H	4.08572000	-3.36594100	1.50128200
H	7.83938400	-0.12657800	1.78035800
H	7.02166900	-1.97758900	2.49003500
H	5.95145800	-3.78630500	3.00600200
H	7.84809000	-2.18005000	3.16464600
H	1.22419300	-0.63313000	-3.07874400
C	1.58026600	1.77142300	-0.80525900
C	1.99772500	2.03017200	0.50923500
C	1.23592600	2.82279800	-1.67114000
C	2.01191000	3.34358500	0.96994600
H	2.31038700	1.21746700	1.16008200
C	1.25818500	4.13593700	-1.19425000
H	0.96081500	2.62542300	-2.70479700
C	1.64339000	4.39451000	0.12121700

H	2.31999700	3.55044000	1.99170500
H	0.98604900	4.95300400	-1.85750000
H	1.67314200	5.41805500	0.48511700

2Pd-1Ph

O	-1.39063100	1.29368000	0.36852800
O	-1.37342800	-0.90912700	-1.11970300
C	-2.43740300	0.64157900	0.30088200
C	-3.68719100	1.04992200	0.90616400
C	-2.38690700	-0.67850300	-0.44491400
C	-4.74286000	0.17440000	0.91514200
C	-3.51192400	-1.57779900	-0.35153800
C	-4.65249500	-1.15528600	0.28489800
Cl	-3.73950400	2.58996200	1.64390000
Cl	-6.20279600	0.60698700	1.67903200
Cl	-6.01669900	-2.17207200	0.34893400
Cl	-3.37370500	-3.10105900	-1.11547300
Pd	0.34292400	0.51244000	-0.90388600
C	2.94644600	0.60827000	-1.69173700
C	1.82673100	-0.36444900	-2.02653500
C	4.04497300	0.05976500	-0.81804200
H	3.39479600	1.01590600	-2.60555300
C	1.78353000	-1.61831500	-1.33228100
C	5.21532800	0.82493800	-0.66280500
C	3.89825800	-1.15862900	-0.13614500
C	2.72840900	-1.95324500	-0.39280900
H	0.99936800	-2.32679500	-1.58307000
C	6.22913600	0.39832800	0.16720300
H	5.31946200	1.75916100	-1.20906700
C	4.94332900	-1.61398400	0.75301500
H	2.61553100	-2.90351500	0.11743800
C	6.12117500	-0.81291000	0.89503700
H	7.13364600	0.99249300	0.26974200
C	4.86914000	-2.81651000	1.49682900
C	7.16556900	-1.23760400	1.75529700
C	5.89957300	-3.20464400	2.32966600
H	3.99582700	-3.45559100	1.42783500
H	8.05312400	-0.61689000	1.84545800
C	7.05961200	-2.41342500	2.46245600
H	5.81502800	-4.13196100	2.88874600
H	7.86243100	-2.73383400	3.11937600
H	1.42611400	-0.33488800	-3.04143900
C	2.15796600	1.76755700	-0.99683100
C	2.37312100	2.16541700	0.34963600
C	1.28343700	2.55714500	-1.80053300
C	1.76409000	3.30644200	0.85048200
H	3.04203200	1.58629300	0.97863600
C	0.68484200	3.71647700	-1.27633700
H	1.18704200	2.34290500	-2.86290700
C	0.92667700	4.08858900	0.03847100
H	1.94880600	3.60267500	1.87947700
H	0.05117900	4.32508600	-1.91540300
H	0.47387400	4.99070400	0.44033700

2,3Pd_2

O	-1.42463200	1.07619600	0.21561800
O	-1.66370500	-1.50272000	-0.39052800
C	-2.57111500	0.62379800	0.07723000
C	-3.76032800	1.42846400	0.22139300
C	-2.70710700	-0.85518400	-0.25737800
C	-4.98789800	0.83422200	0.06703400
C	-4.03115700	-1.41779300	-0.40101200
C	-5.12420300	-0.60323800	-0.24692800
Cl	-3.55580900	3.08276600	0.58617200
Cl	-6.40488800	1.75740000	0.23891600
Cl	-6.69014700	-1.24268000	-0.41818800

Cl	-4.14234200	-3.08169300	-0.76620800
Pd	0.24137100	-0.26137200	-0.06468800
C	2.95508200	-1.22328600	-1.15954300
C	1.70766300	-1.78358400	-0.81277200
C	3.99946500	-1.10868900	-0.23685600
H	3.09984600	-0.91315300	-2.18842800
C	1.50099800	-2.25725000	0.52060200
C	3.77360800	-1.58443300	1.10006400
C	5.29923100	-0.55193500	-0.58609000
C	2.52609400	-2.13628400	1.45157100
H	0.60620000	-2.82369000	0.76657900
C	4.82724500	-1.51614400	2.06339400
C	6.31736600	-0.51246200	0.41025100
C	5.60449700	-0.05090800	-1.86851800
H	2.38425000	-2.51122900	2.46172200
C	6.04489100	-1.00607700	1.72677200
H	4.64218700	-1.88735600	3.06756400
C	7.58969000	0.01251900	0.09381600
C	6.85792100	0.45947600	-2.15722100
H	4.85670600	-0.05644300	-2.65426800
H	6.84151700	-0.96740300	2.46548600
H	8.35573600	0.03151800	0.86452600
C	7.86071100	0.49232800	-1.17214000
H	7.06728300	0.83668500	-3.15389800
H	8.84209900	0.89255600	-1.40801200
H	1.04440000	-2.10575900	-1.61557100
C	1.54180600	1.18176700	0.23744200
C	2.04267600	1.38426100	1.51679800
C	1.77993700	2.06668100	-0.80846500
C	2.81472000	2.52872800	1.75350600
H	1.83858500	0.68853600	2.32636200
C	2.55596700	3.20380500	-0.55232400
H	1.37973200	1.89606100	-1.80490300
C	3.07236700	3.43255100	0.72309100
H	3.20507000	2.70874200	2.75230200
H	2.75387600	3.90504400	-1.35945000
H	3.67368900	4.31720200	0.91452800

TS_3Pd-4Ph

O	-1.38083700	1.10179200	0.11692000
O	-1.72858000	-1.40282400	-0.70688000
C	-2.52986900	0.66272600	0.11567700
C	-3.69400200	1.44088700	0.49435100
C	-2.72253800	-0.79497000	-0.30460600
C	-4.92077600	0.83310500	0.52857700
C	-4.04448200	-1.37784400	-0.22199100
C	-5.09217700	-0.59173100	0.16878400
Cl	-3.44216600	3.07665800	0.90920400
Cl	-6.29613800	1.71738600	0.99905300
Cl	-6.66392100	-1.24835200	0.24471000
Cl	-4.20858400	-3.02148200	-0.65573000
Pd	0.25291600	-0.30563100	-0.65438400
C	2.81587900	-0.83876000	-1.14941300
C	1.65051400	-1.68059500	-1.34551900
C	3.72434800	-1.10094700	-0.05958000
H	3.23570600	-0.39595500	-2.04495800
C	1.34518800	-2.68033500	-0.35753400
C	3.36975000	-2.08843400	0.88910500
C	4.96620000	-0.38499800	0.08071200
C	2.16323400	-2.83972600	0.73067700
H	0.48561300	-3.32636800	-0.50643400
C	4.24360000	-2.37233500	1.98055600
C	5.82581700	-0.70780200	1.17589700
C	5.37786400	0.63290400	-0.81369000
H	1.92648400	-3.59317900	1.47761500
C	5.42893000	-1.70820100	2.11308100

H	3.95523700	-3.13582300	2.69773300
C	7.05877500	-0.02991900	1.32064600
C	6.58545700	1.28082600	-0.64790000
H	4.74114600	0.92536900	-1.64204500
H	6.09434900	-1.93698700	2.94150400
H	7.70585400	-0.29256000	2.15342300
C	7.43738400	0.94658000	0.42379100
H	6.88065400	2.05581700	-1.34922900
H	8.38727000	1.45934800	0.54173900
H	1.29388600	-1.82338000	-2.36783700
C	1.84067200	0.96334300	-0.69490600
C	2.17682800	1.50012600	0.55680900
C	1.76267600	1.78548300	-1.83211500
C	2.37017900	2.87388800	0.67667500
H	2.28871400	0.85280100	1.42299800
C	1.96167200	3.16166800	-1.69565700
H	1.55182000	1.36203300	-2.81173700
C	2.26074400	3.70339900	-0.44516800
H	2.61753700	3.29807800	1.64645700
H	1.89228900	3.80393100	-2.56998300
H	2.42740800	4.77255700	-0.34446400

3Pd-4Ph

O	-1.26965100	1.34727900	0.15154700
O	-1.50738500	-1.15403400	-0.71529100
C	-2.40041900	0.85635000	0.13551700
C	-3.60535300	1.58198500	0.48326100
C	-2.51882000	-0.60807700	-0.25696500
C	-4.79257300	0.90270700	0.57237600
C	-3.78972700	-1.27545300	-0.09735100
C	-4.88487500	-0.54205900	0.28395400
Cl	-3.44896100	3.24771100	0.82621900
Cl	-6.21117500	1.72279800	1.03599600
Cl	-6.40491400	-1.29472700	0.42380200
Cl	-3.85809100	-2.94407200	-0.46086600
Pd	0.41246400	-0.00117200	-0.67218600
C	3.04632400	-0.52808300	-1.11644000
C	1.79368800	-1.36415200	-1.35221600
C	3.95431700	-1.00212800	-0.00898200
H	3.62170500	-0.45348100	-2.04646900
C	1.46689800	-2.41480300	-0.42930100
C	3.52693500	-2.00996400	0.86535800
C	5.23360200	-0.40320100	0.17097300
C	2.26572100	-2.67060700	0.65280000
H	0.58856600	-3.02459700	-0.61926800
C	4.36145500	-2.42690500	1.94337200
C	6.06143300	-0.83959800	1.25992700
C	5.73336400	0.62109700	-0.68243700
H	1.98172400	-3.45405500	1.35164700
C	5.58930900	-1.85679800	2.13475100
H	4.00796900	-3.21093700	2.60752300
C	7.33587000	-0.25238100	1.44285600
C	6.97718000	1.17447400	-0.47512900
H	5.13444600	0.97726400	-1.51433600
H	6.22368600	-2.17801100	2.95639200
H	7.95657000	-0.59608500	2.26607300
C	7.78794700	0.73539500	0.59495400
H	7.34036400	1.95155300	-1.14122300
H	8.76905600	1.17615600	0.74470400
H	1.49305400	-1.50486800	-2.39263700
C	2.42353400	0.87725400	-0.82785200
C	2.57853700	1.55958000	0.40843500
C	1.78589100	1.56711000	-1.90172900
C	2.14219500	2.86929700	0.54811200
H	3.07039200	1.05874500	1.23652000
C	1.36276900	2.89837500	-1.74322500

H	1.74868900	1.11092000	-2.88887900
C	1.54275300	3.54389100	-0.52722600
H	2.28074100	3.38011300	1.49703800
H	0.91319500	3.41920800	-2.58405800
H	1.22581400	4.57621800	-0.40794900

3,4Pd

O	-1.27399200	-1.06967000	0.42837700
O	-1.08925800	0.90227900	-1.35147100
C	-2.31543700	-0.47225800	0.12613800
C	-3.60513600	-0.79518600	0.69017800
C	-2.20914500	0.65712500	-0.89497100
C	-4.70392300	-0.07666200	0.29126300
C	-3.40909800	1.37227800	-1.27006500
C	-4.60458300	1.01783200	-0.69893400
Cl	-3.67330300	-2.06457200	1.82760400
Cl	-6.23310700	-0.43631300	0.93901600
Cl	-6.02677300	1.84475900	-1.12505500
Cl	-3.24923000	2.62763700	-2.41552900
Pd	0.57760700	-0.45974800	-0.53141500
C	2.05083100	-0.06345500	-2.24564800
C	2.96810100	-1.09745300	-2.57367000
C	2.34183100	0.82963900	-1.18503700
C	4.14145400	-1.20353500	-1.86953800
C	3.55720500	0.71388400	-0.43779400
H	1.77364500	1.75472100	-1.12090300
C	4.46398800	-0.31865400	-0.80318300
H	4.86087700	-1.97542300	-2.13040500
C	3.90250900	1.62757000	0.62615200
C	5.70847600	-0.44602400	-0.11661000
C	5.16142100	1.47214000	1.28054100
C	3.05043700	2.67273400	1.05728700
C	6.04294000	0.41953100	0.88252500
H	6.38766000	-1.24184800	-0.40889000
C	5.52478800	2.36351600	2.31588400
C	3.42875100	3.53106700	2.07149800
H	2.07909700	2.81423600	0.59437500
H	6.99601400	0.32088100	1.39557700
H	6.48908400	2.23689300	2.80092100
C	4.67618800	3.37940400	2.70673200
H	2.75916400	4.32840600	2.38047900
H	4.96700400	4.05981200	3.50141800
H	1.25712300	0.18227300	-2.94952400
H	2.75269900	-1.76737400	-3.40001600
C	1.62642500	-1.80633400	0.44282500
C	1.67613100	-3.09953900	-0.06451100
C	2.12973100	-1.47303400	1.69431300
C	2.26005500	-4.09896900	0.72351900
H	1.27139000	-3.34649100	-1.04246700
C	2.70885200	-2.48732700	2.46759100
H	2.08787000	-0.45643700	2.07715200
C	2.77549400	-3.79353100	1.98350900

H	2.30387200	-5.11703800	0.34391400
H	3.10839300	-2.24348300	3.44900700
H	3.22711000	-4.57477000	2.58901800

TS_3Pd-2Ph

O	-1.10448600	-1.36787200	0.42608700
O	-0.88060100	0.54924000	-1.40752700
C	-2.09452400	-0.65766500	0.21444700
C	-3.38261500	-0.86451900	0.83930800
C	-1.92206500	0.51058300	-0.73888500
C	-4.36701600	0.07517600	0.66698200
C	-2.97674600	1.49223000	-0.83299000
C	-4.15985600	1.26827400	-0.17385200
Cl	-3.56890400	-2.24930200	1.82147500
Cl	-5.87110100	-0.11324900	1.44378500
Cl	-5.44187700	2.37801600	-0.32734200
Cl	-2.70584400	2.84948100	-1.83782000
Pd	0.70326200	-0.97612300	-0.85574800
C	2.40099800	-0.55936300	-1.99153400
C	3.26861600	-1.59143200	-1.42373100
C	2.39939200	0.72915800	-1.39010500
C	4.22673000	-1.19271500	-0.45671700
C	3.24529000	1.05556400	-0.31533000
H	1.79799200	1.50023100	-1.85876400
C	4.21326600	0.07261200	0.11736000
H	4.96014300	-1.92085100	-0.12025700
C	3.23046700	2.36168300	0.31783500
C	5.17762600	0.42584100	1.12516600
C	4.21478600	2.66045200	1.30450800
C	2.28023700	3.35628200	-0.00292600
C	5.18036400	1.66307400	1.68131000
H	5.90813400	-0.31998000	1.42587500
C	4.22998600	3.93260700	1.90952100
C	2.31402000	4.59921000	0.60393800
H	1.49963600	3.15412100	-0.72873700
H	5.91781800	1.92192800	2.43648400
H	4.98909700	4.15023600	2.65610900
C	3.29680400	4.89388100	1.56388200
H	1.57481600	5.34898100	0.33807500
H	3.32009600	5.87149100	2.03598900
H	2.04635900	-0.67120400	-3.01620200
H	3.52397800	-2.43807200	-2.05270000
C	1.84498900	-2.61295300	-0.39917700
C	1.35172900	-3.67133000	-1.18467500
C	2.05501800	-2.78115200	0.98182600
C	1.01951900	-4.88242700	-0.57005900
H	1.24310300	-3.56122000	-2.26108300
C	1.71854600	-3.99146900	1.57483600
H	2.47058000	-1.97217200	1.57708800
C	1.20360900	-5.04218900	0.80175400
H	0.63121300	-5.69996800	-1.17187900
H	1.86324900	-4.12317500	2.64409500

H	0.96075300	-5.99018400	1.27400000

3Pd-2Ph

O	-0.98775100	-1.39428000	0.54612000
O	-0.73080800	0.43751500	-1.36624200
C	-1.97642400	-0.68868700	0.27828200
C	-3.28335400	-0.87936100	0.85748700
C	-1.76640600	0.45587500	-0.67362800
C	-4.23893800	0.09338500	0.68430400
C	-2.77066500	1.48402200	-0.75312900
C	-3.97761400	1.29009000	-0.12293000
Cl	-3.53066100	-2.27212000	1.81897900
Cl	-5.76398400	-0.06515500	1.43233900
Cl	-5.22004900	2.44688200	-0.28661200
Cl	-2.43677700	2.84904800	-1.73308100
Pd	0.80303200	-1.07794500	-0.73287400
C	2.49227500	-0.67716800	-1.86522700
C	3.39401200	-1.71563900	-1.22650700
C	2.46767700	0.64091300	-1.34314300
C	4.37619700	-1.14475500	-0.27306500
C	3.28384500	1.05091400	-0.27661200
H	1.85195800	1.36977800	-1.85872900
C	4.32192100	0.13578600	0.19802600
H	5.15503500	-1.81028600	0.09428300
C	3.20424100	2.37536700	0.29872200
C	5.29633200	0.60948100	1.15766500
C	4.19649400	2.78515800	1.23981300
C	2.17748700	3.28712100	-0.03818400
C	5.23962200	1.87072300	1.64037100
H	6.07617600	-0.07578000	1.47782200
C	4.14502200	4.08221500	1.77677500
C	2.14569400	4.55898400	0.50517800
H	1.38729200	2.99099100	-0.71977700
H	5.97904000	2.21923200	2.35611000
H	4.90811900	4.38934500	2.48668700
C	3.13782800	4.96314800	1.41296900
H	1.34848200	5.24354600	0.23223500
H	3.11181300	5.96290100	1.83624400
H	2.18734200	-0.82752600	-2.90038900
H	3.92422800	-2.31406300	-1.97859600
C	2.36724900	-2.66098700	-0.50278400
C	1.44628800	-3.38869800	-1.30992200
C	2.43941700	-2.97013800	0.88013200
C	0.64459100	-4.39308900	-0.74367500
H	1.44958900	-3.25771800	-2.38972500
C	1.63292800	-3.95882100	1.42132000
H	3.14188600	-2.43815400	1.51524000
C	0.73941700	-4.67785200	0.61143100
H	-0.03253600	-4.95588700	-1.38015100
H	1.70471200	-4.18651300	2.48134700
H	0.12889100	-5.46420600	1.04628400

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Palladium-catalyzed One-shot Annulative π-Extension of Alkynes with Dibenzosiloles and Dibenzogermoles

Abstract

A novel synthetic method for diarylphenanthrene by annulative π-extension (APEX) of alkynes has been developed. In the presence of cationic palladium/*o*-chloranil catalyst, a variety of diarylacetylenes were transformed to 9,10-diarylphenanthrenes in one-shot with good functional group tolerances by using dibenzosiloles or dibenzogermoles as π-extending agents. Furthermore, double π-extension of 1,4-bis(phenylethynyl)-benzene is also possible to afford an oligoarylene product, which shows potential for application to the synthesis of larger polycyclic aromatic hydrocarbons and nanographenes.

1. Introduction

Nanographenes have recently received considerable attention in synthetic chemistry, nanocarbon science as well as organic electronics.[1] Chemical and physical properties of nanographenes highly depend on its size, shape, and peripheral structure.[2] Therefore, the precise synthesis of structurally uniform nanographene is strongly demanded. For the synthesis of nanographenes, cyclodehydrogenation (also called as graphitization or graphenization) by $FeCl_3$-mediated Scholl reaction, photocyclization, and oxidative coupling has been frequently applied to the oligo- and polyarylene precursors (Figure 1).[3] Among various synthetic ways for oligo- and polyarylene precursors, annulative π-extension (APEX) of alkyne such as Diels–Alder cycloaddition is regarded as one of the most powerful and reliable method for the construction of not only small oligophenylene derivatives but also ladder polyphenylenes that are precursors for graphene nanoribbons (GNRs).[4] From the viewpoint of a π-extension unit for alkyne, for example, tetraarylcyclopentadienone[5], tetraarylthiophene *S*-oxide[6], and *ortho-* alkynylformylarenes[7] are known to show good reactivity in Diels–Alder cycloaddition to give hexaarylbenzene derivatives, oligo- and polyphenylene products in good yields. These π-extension units have been widely used in the synthesis of π-extended PAHs, nanographenes and GNRs. Therefore, the development of efficient one-shot APEX reaction of alkynes would be an important concern for the nanocarbon sciences.
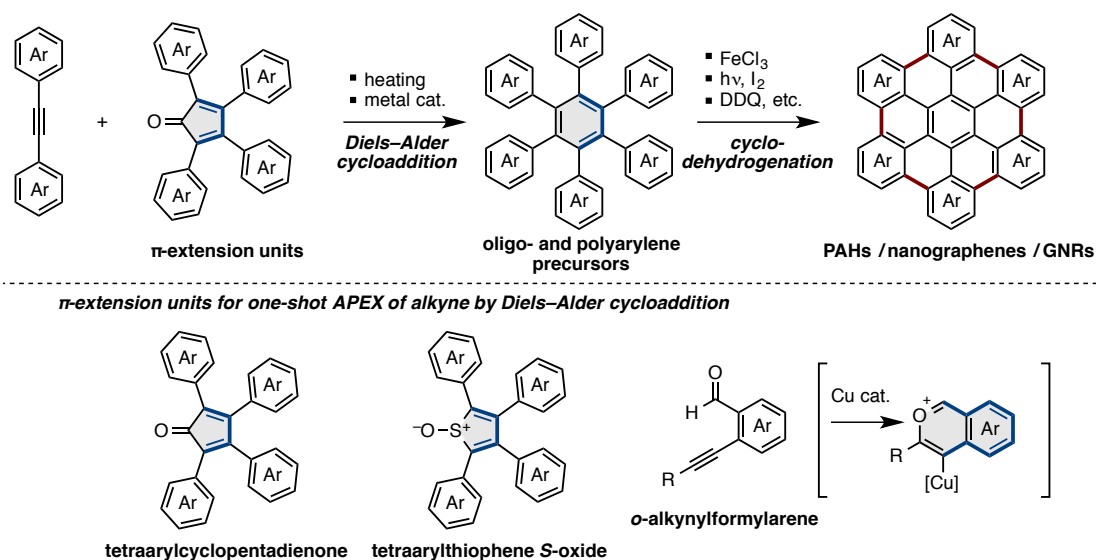
Figure 1. One-shot annulative π-extension of alkyne by Diels–Alder cycloaddition with various π-extension units for the synthesis of PAHs, nanographenes and GNRs

Recently, we have reported palladium/*o*-chloranil-catalyzed one-shot APEX reaction of PAHs with dibenzosiloles for the synthesis of structurally uniform nanographenes (Figure 2).[8] In this reaction, dibenzosilole derivatives work as a π-extension unit to enable one-shot APEX at various K-regions on PAHs such as phenanthrene and pyrene derivatives. Although dibenzosiloles and other silicon-bridged aromatics had been considered as relatively stable silicon-containing aromatics in the organic chemistry[9], they play unprecedented and unique roles as a π-extension unit by the synergistic effects of cationic palladium catalyst and *o*-chloranil[8]. These results prompted us to apply this new π-extension unit toward metal-catalyzed one-shot APEX reaction of alkynes[10] for the synthesis of oligoarylenes and nanographenes. Chapter 2 describes the novel one-shot annulative π-extension reaction of diarylacetylenes with dibenzosiloles catalyzed by palladium/*o*-chloranil system for the synthesis of diarylphenanthrene derivatives (Figure 3).
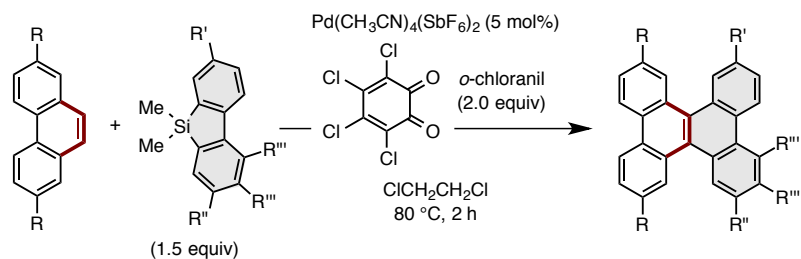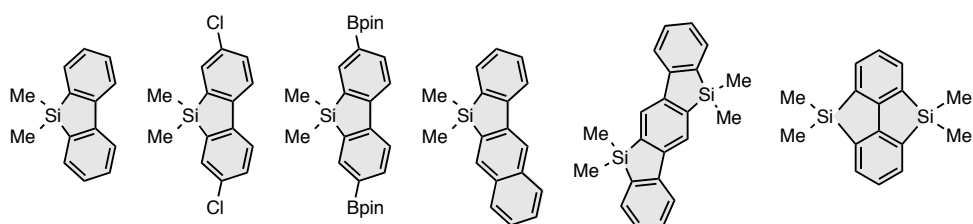
Figure 2. One-shot K-region-selective annulative π-extension for nanographene synthesis and functionalization
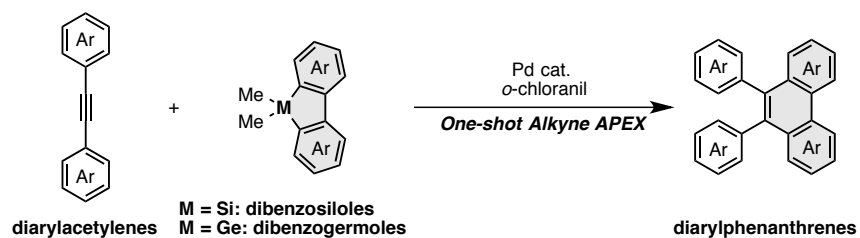
Figure 3. Outline of Chapter 2: palladium-catalyzed one-shot alkyne APEX with dibenzosiloles and dibenzogermoles

2. Results and Discussion

2-1. Discovery of one-shot APEX reaction of diphenylacetylene.

As described in Chapter 1, cationic palladium/*o*-chloranil system can catalyze annuulative π-extension at the K-region, the most olefinic carbon-carbon bond, of PAHs with dibenzosiloles. DFT calculation disclosed that the origin of K-region selectivity is likely attributed by the more favorable coordination of cationic palladium onto the carbon-carbon double bond at K-region prior to the carbometalation step. While the coordination of phenanthrene is considered to be even weak, an electron-deficient and cationic aryl palladium species would enables the coordination and following carbopalladation. Therefore, this catalytic APEX reaction with dibenzosiloles would be potentially applicable to the other substrates having C–C multiple bonds such as alkynes. Alkynes are known to show excellent reactivity toward metal-catalyzed carbometalation reactions.[10,11] Recently, there are some examples of transition-metal catalyzed one-shot APEX reaction of diphenylacetylene with various π-extension units for the synthesis of 9,10-diphenylphenanthrene (Scheme 1).[10,11] Thus alkynes are anticipated to be a good candidate as the substrate for the palladium-catalyzed APEX reaction with dibenzosilole. In fact, the initial investigation on APEX of diphenylacetylene (**1a**) with 1.2 equivalent of dibenzosilole (**2a**), 5 mol% of PdCl$_2$, 10 mol% of AgOTf, 2.0 equivalent of *o*-chloranil in 1,2-dichloroethane at 80 °C for 2 hours provided 9,10-diphenylphenanthrene (**3aa**) in 63% yield (Scheme 2).
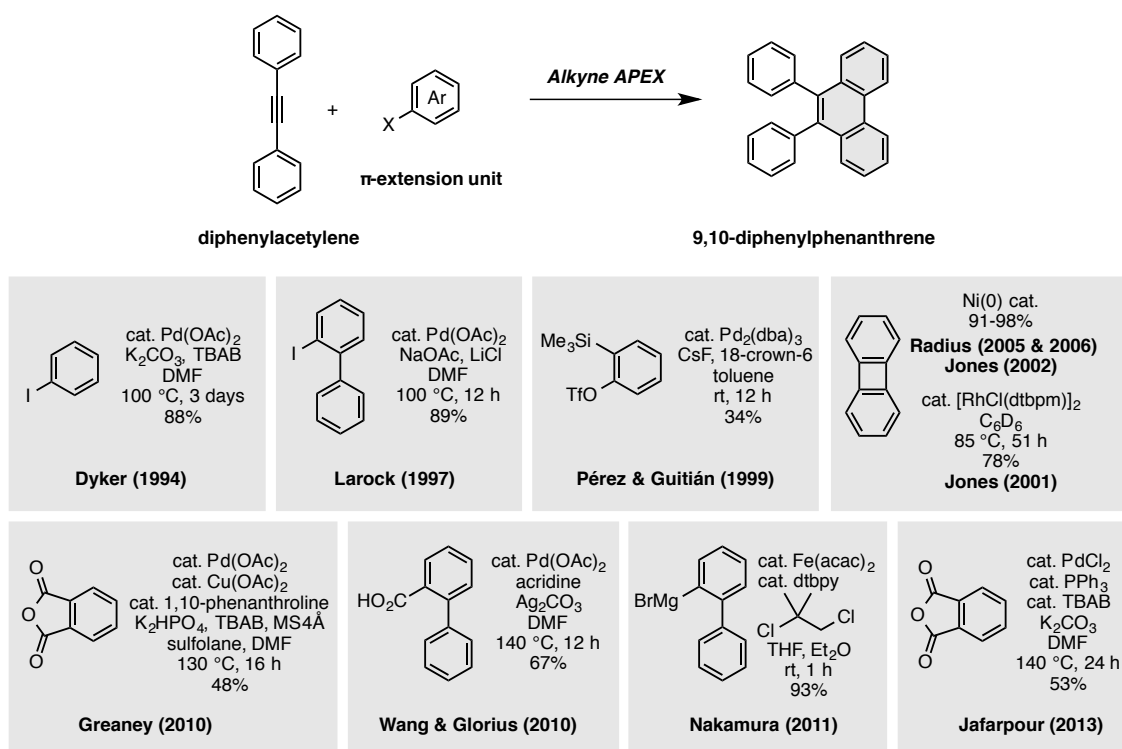
Scheme 1. Transition metal-catalyzed APEX reactions of diphenylacetylene with various π-extension units
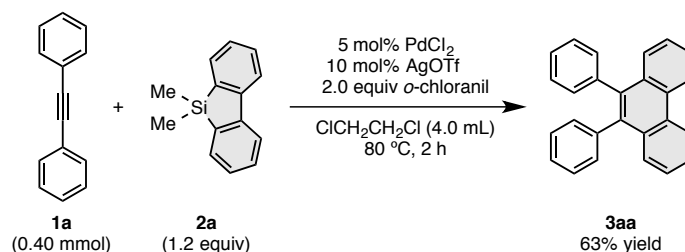
Scheme 2. Discovery of APEX reaction of diphenylacetylene with dibenzosilole

Encouraged by the aforementioned result, reaction conditions were further optimized with the screening of oxidants (Table 1). As in the case of APEX of PAHs, the reaction with *o*-chloranil also gave the best result for this alkyne APEX reaction to afford **3aa** in 70% yield. Although 3,5-di-*tert*-butyl-*o*-benzoquinone (*o*-DTBQ) provided the desired APEX product **3aa** in 25%, other common oxidants such as phenanthrenequinone, *p*-benzoquinone, *p*-chloranil, *p*-DTBQ, DDQ, $K_2S_2O_8$ and $CuCl_2$ were not effective at all.
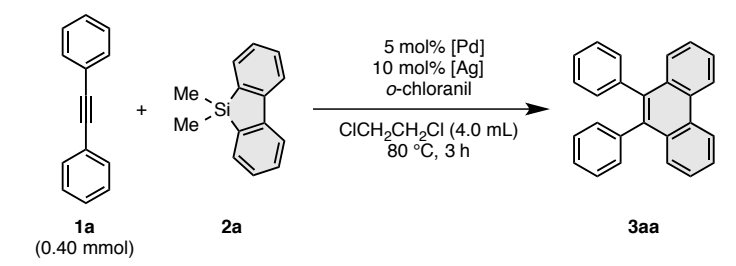
Table 1. Screening of oxidants[a]
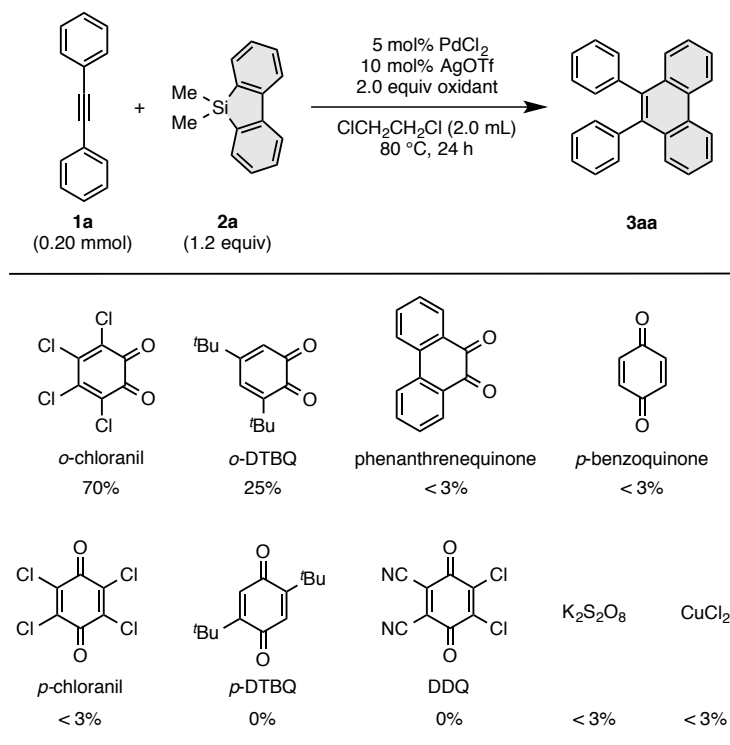
(a) Reaction conditions: diphenylacetylene **1a** (0.20 mmol), dibenzosilole **2a** (1.2 equiv), PdCl$_2$ (5 mol%), AgOTf (10 mol%), o-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 24 h. Yields were determined by ^{1}H NMR analysis calculated with dibromomethane as an internal standard.

Next, the effects of palladium catalysts, silver salt, and the equivalents of dibenzosilole and o-chloranil were investigated. Judging from the results listed in Table 2, the most critical parameter is the equivalent of dibenzosilole; 2.0 equivalent of dibenzosiloles dramatically increased the yield to 94% (entry 2). The absence of silver triflate or the use of neutral palladium acetate diminished the yields (entries 3 and 4). Therefore, the generation of cationic palladium seems to conduce to APEX reaction. The use of Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$, the optimal catalyst for APEX of PAHs, resulted in lower yield (entry 5). Decreasing the amount of o-chloranil to 1.5 equivalent gave the product in somewhat lower yield (87%, entry 6).

Table 2. Detail condition screening[a]

1a
(0.40 mmol)

2a

3aa

entry	[Si]	[Pd]	[Ag]	*o*-chloranil	NMR yield[b]
1[c]	1.2 equiv	PdCl$_2$	AgOTf	2.0 equiv	(63%)
2	2.0 equiv	PdCl$_2$	AgOTf	2.0 equiv	91% (94%)
3[c]	1.2 equiv	PdCl$_2$	none	2.0 equiv	2%
4	2.0 equiv	Pd(OAc)$_2$	none	2.0 equiv	15%
5[c]	2.0 equiv	Pd(CH$_3$CN)$_4$(SbF$_6$)$_2$	none	2.0 equiv	46%
6	2.0 equiv	PdCl$_2$	AgOTf	1.5 equiv	87%

(a) Reaction conditions: diphenylacetylene **1a** (0.40 mmol), dibenzosilole **2a** (1.2 equiv), PdCl$_2$ (5 mol%), AgOTf (10 mol%), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (4.0 mL), 80 °C, 3 h. (b) NMR yields were calculated with dibromomethane as an internal standard. The number in parenthesis is the isolated yield of the product. (c) Reaction time: 2 h.

Thus the best condition for APEX of diphenylacetylene (**1a**) with dibenzosilole **2a** was found to be PdCl$_2$ (5 mol%), AgOTf (10 mol%) and *o*-chloranil (2.0 equiv) in 1,2-dichloroethane at 80 °C, which can afford 9,10-diphenylphenanthrene (**3aa**) in 94% yield (Scheme 3).

1a
(0.40 mmol)

2a
(2.0 equiv)

3aa
94%
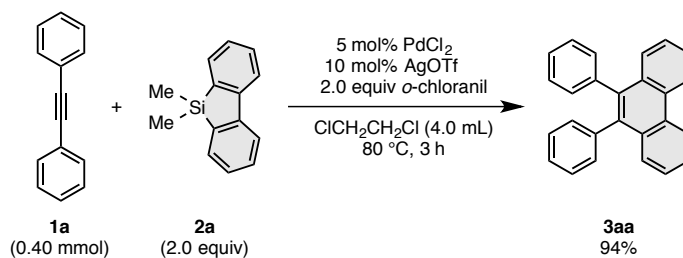
Scheme 3. Optimal reaction conditions for APEX reaction of diphenylacetylene with dibenzosilole

2-2. Substrate scope

With the optimal reaction conditions in hand, APEX reactions with various diphenylacetylenes were carried out to obtain diarylphenanthrenes **3** (Table 3). Interestingly, chloro, bromo, and boryl groups are tolerated to this reaction to give the corresponding products **3ba**, **3ca**, **3da**, **3ea**, and **3ia** in high yields, which means further functionalization or coupling reaction are possible. Diphenylacetylenes bearing trifluoromethyl groups (**1f** and **1g**) afford the products **3fa** and **3ga** in moderate yields. In the case of the reactions of substrate having methyl ester group (**1h**), the use of *o*-DTBQ instead of *o*-chloranil resulted in the better result, giving the products **3ha** in 43%. The reaction of dinaphtylacetylene **1j** also proceeded well to afford sterically congested 9,10-dinaphthylphenanthrene (**3ja**) as the 1:1 mixture of rotamers. However, *o*-methyl or *p-tert*-butyl functionalized diphenylacetylenes **3k** and **3l** did not react well, probably due to the steric hindrance or electron-donating characters of alkyl substituents.

Table 3. APEX with a variety of diarylacetylenes **1b**-**1l** and dibenzosilole **2a**[a]

1b-1l
(0.20 mmol)

2a
(2.0 equiv)

5 mol% PdCl$_2$
10 mol% AgOTf
2.0 equiv o-chloranil

ClCH$_2$CH$_2$Cl (2.0 mL)
80 °C

3ba-3la
[isolated yield]
(reaction time)

3ba
[64%]
(15 h)

3ca
[74%]
(24 h)

3da
[75%]
(15 h)

3ea
[73%]
(10 h)

3fa
[59%]
(24 h)

3ga
[52%]
(24 h)

3ha
[43%][b]
(24 h)

3ia
[75%]
(6 h)

3ja
[52%][c]
(24 h)

3ka
[20%][c]
(6 h)

3la
[18%]
(2 h)
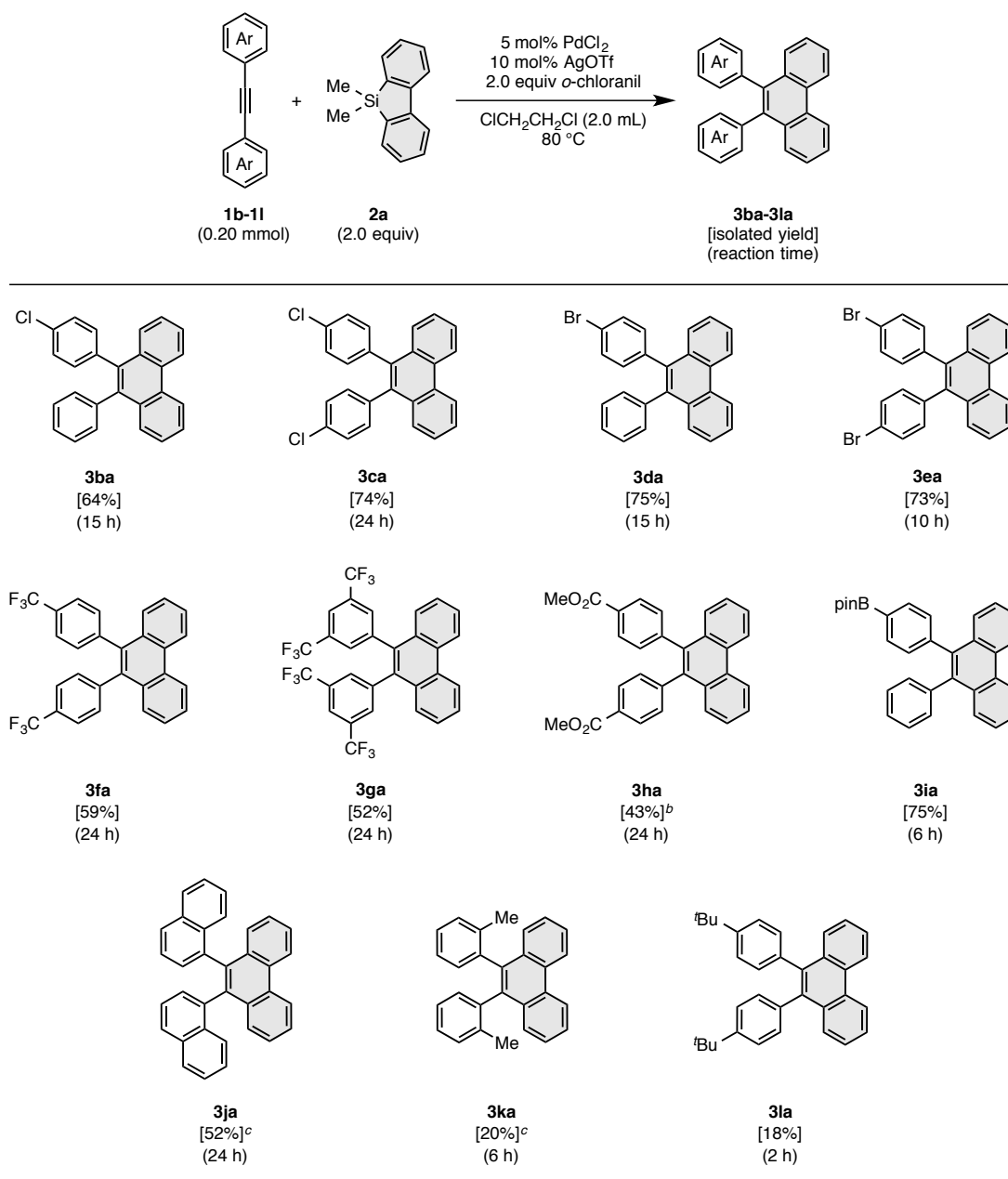
(a) Reaction conditions: diarylacetylenes **1** (0.20 mmol), dibenzosilole **2a** (2.0 equiv), PdCl$_2$ (5 mol%), AgOTf (10 mol%), o-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C.

(b) 3,5-di-*tert*-butyl-o-benzoquinone (o-DTBQ) (2.0 equiv) was used instead of o-chloranil.

(c) Products were obtained as the 1:1 mixture of rotamers.

A variety of π-extension units were tested for the current APEX reaction (Tables 4 and 5). In the APEX reactions with dibenzosiloles having electron-donating groups, 3,7-di-*tert*-butyldibenzosilole **2b** and 4-methyldibenzosilole **2c** effectively worked as a π-extending agent to afford the corresponding phenanthrenes **3ab** and **3ac** in 87% and 80% yields, respectively. Siloles bearing a methoxy group (**2d**) were also able to provide the corresponding APEX product **3ad** in 52% yield.

Table 4. APEX with dibenzosiloles having electron-donating group[a]
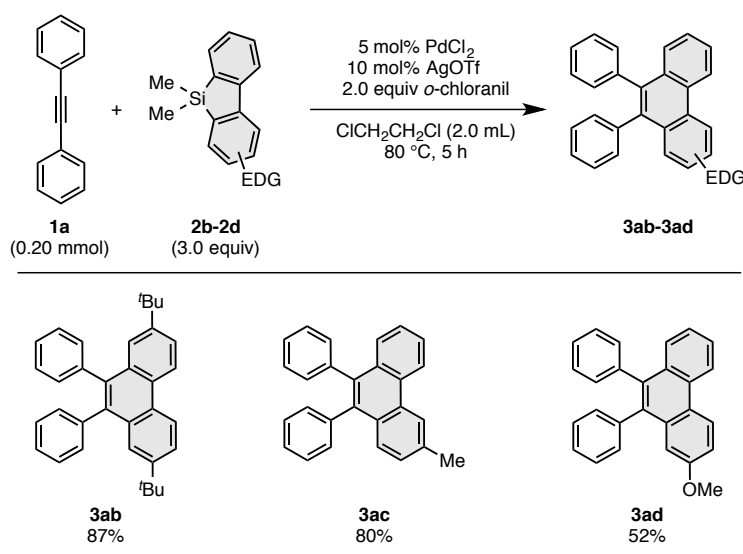
(a) Reaction conditions: diphenylacetylene **1a** (0.20 mmol), dibenzosiloles **2** (3.0 equiv), PdCl$_2$ (5 mol%), AgOTf (10 mol%), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 5 h.

In contrast to siloles bearing electron-donating groups, electron-deficient siloles such as 3-chlorodibenzosilole **2e** did not work enough to produce the desired product in high yield even with increased amounts of palladium catalyst and dibenzosiloles (Table 5, **3ae**, 46%). One possible reason is considered to be the less reactivity of electron-deficient dibenzosiloles because significant amount of siloles remained unreacted after the reactions. On the other hand, dibenzogermole **4e** showed the superior reactivity over silole, giving **3ae** in 84% yield. Furthermore, dibenzogermoles having a fluoro group **4f** and **4g** afforded APEX products **3af** and **3ag** in high yields.

Table 5. APEX with dibenzosiloles having electron-withdrawing group[a]

3ae Cl	
with **2e** : 46%	
with **4e** : 84%	

3af F
with **4f** : 93%

3ag F
with **4g** : 75%
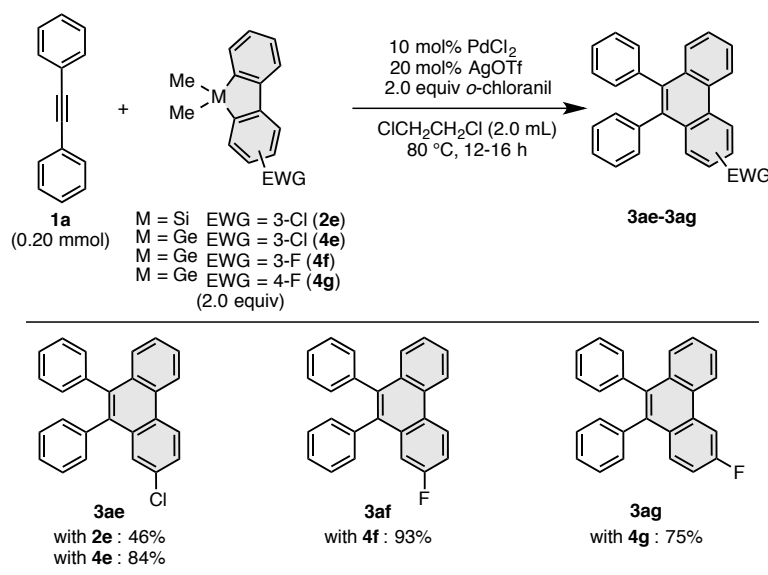
(a) Reaction conditions: diphenylacetylene **1a** (0.20 mmol), dibenzogermoles **4** (2.0 equiv), PdCl$_2$ (10 mol%), AgOTf (20 mol%), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 80 °C, 12 h.

Double π-extension of 1,4-bis(phenylethynyl)benzene (**1m**) with dibenzosilole **2a** was also demonstrated (Scheme 4). In this case, addition of extra dibenzosilole **2a** and *o*-chloranil was necessary after 8 h for producing the corresponding product **3ma** in reasonable yield because the consumption of dibenzosilole and *o*-chloranil by homo-dimerization, desilylation or decomposition occurred relatively faster than APEX of **1m**. The structure of **3ma** was confirmed by X-ray crystallographic analysis as shown in Figure 4.
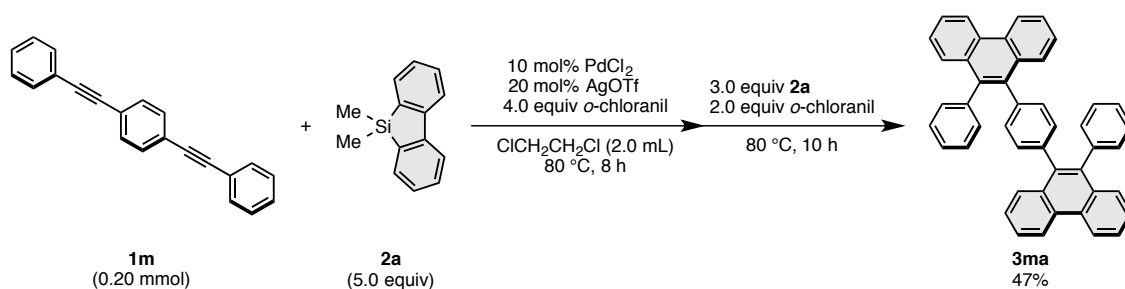
Scheme 4. Double APEX reaction of 1,4-bis(phenylethynyl)benzene (**1m**) with dibenzosilole **2a**

92
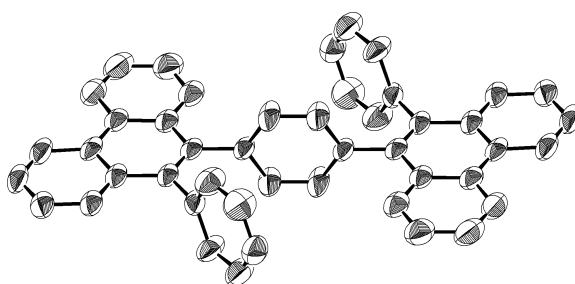
Figure 4. ORTEP drawing of **3ma** with 50% thermal ellipsoid

(Hydrogen atoms and solvent are omitted for clarity.)

2-3. Possible mechanism

Considering the APEX of PAHs, one possible reaction mechanism is described in Figure 5. The reaction can be initiated by the transmetalation of cationic palladium(II) with a dibenzosilole **2a** to give a biarylpalladium intermediate **A**. Subsequent coordination of an alkyne **1a** and carbopalladation would afford an alkenylpalladium intermediate which will induce intramolecular transmetalation event to generate palladacycle **C**. APEX product **3aa** would be obtained by reductive elimination from intermediate **C** along with Pd(0) species which can be oxidized by *o*-chloranil to regenerate Pd(II) species.
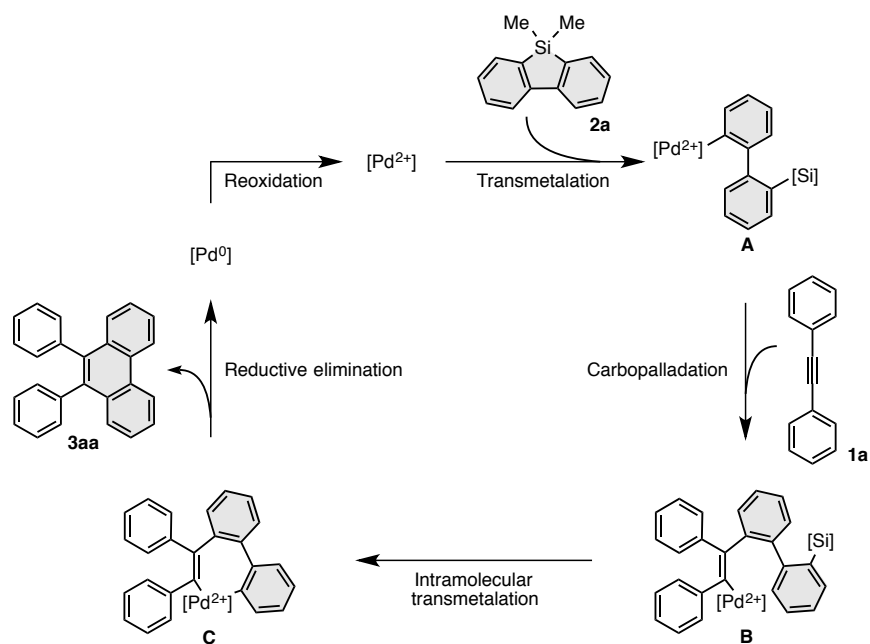
Figure 5. Possible mechanism of APEX reaction of diphenylacetylene

3. Conclusions

In summary, palladium-catalyzed annulative π-extension of alkynes with dibenzosiloles or dibenzogermoles has been demonstrated. $PdCl_2$/AgOTf/*o*-chloranil system enables to transform diarylacetylenes to diarylphenanthrenes in one-shot with good functional group tolerance. The use of dibenzogermoles having electron-deficient substituent significantly expanded the scope of this APEX reaction. Moreover, double π-extension of 1,4-bis(phenylethynyl)benzene was also applicable to form 1,4-bis(10-phenylphenanthren-9-yl)benzene. Looking ahead to application to polyphenyleneacetylene, this APEX technology has huge potential for precise synthesis of graphene nanoribbons.

4. Experimental Section

4-1. General

Unless otherwise noted, all materials including dry solvents were obtained from commercial suppliers and used without further purification. $PdCl_2$ and AgOTf were purchased from Wako and stored in glovebox filled by argon prior to use. *o*-Chloranil was purchased from TCI and recrystallized from benzene before use. *o*-DTBQ was purchased from TCI. Diarylacetylenes were purchased from Wako (**1a**, **1i**), Aldrich (**1b**), TCI (**1d**) or synthesized according to procedures reported in the literature (**1c**[12a], **1e**[12a], **1f**[12a], **1g**[12b], **1h**[12a], **1j**[12a], **1k**[12c], **1l**[12a]). Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of nitrogen or argon in oven-dried glassware with standard vacuum-line techniques. All work-up and purification procedures were carried out with reagent-grade solvents in air

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} precoated plates (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with KANTO Silica Gel 60N (spherical, neutral, 40-100 μm) or Biotage Isolera® equipped with Biotage SNAP Cartridge KP-Sil columns Preparative thin-layer chromatography (PTLC) was performed using Wako-gel® B5-F silica coated plates (0.75 mm) prepared in our laboratory. Preparative gel permeation chromatography (GPC) was performed with a JAI LC-9204 instrument equipped with JAIGEL-1H/JAIGEL-2H columns using chloroform as an eluent. Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). The developed chromatogram was analyzed by UV lamp (254 nm and 365 nm). High-resolution mass spectra (HRMS) were obtained from a JMS-T100TD instrument (DART). Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECS-600 (^{1}H 600 MHz, ^{13}C 150 MHz, ^{19}F 565 MHz) spectrometer and a JEOL ECA 600II with Ultra COOL™ probe (^{1}H 600 MHz, ^{13}C 150 MHz). Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm) or CD_2Cl_2 (δ 5.32 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm) or CD_2Cl_2 (δ 53.84 ppm). Chemical shifts for ^{19}F NMR are expressed in parts per million (ppm) relative to

hexafluorobenzene (δ –162.00 ppm) as an external standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, t = triplet, td = triplet of doublets, q = quartet, m = multiplet), coupling constant (Hz), and integration.

4-2. General procedure

Procedure A : APEX of diarylacetylenes (1a-1g, 1i-1l) with dibenzosilole (2a)
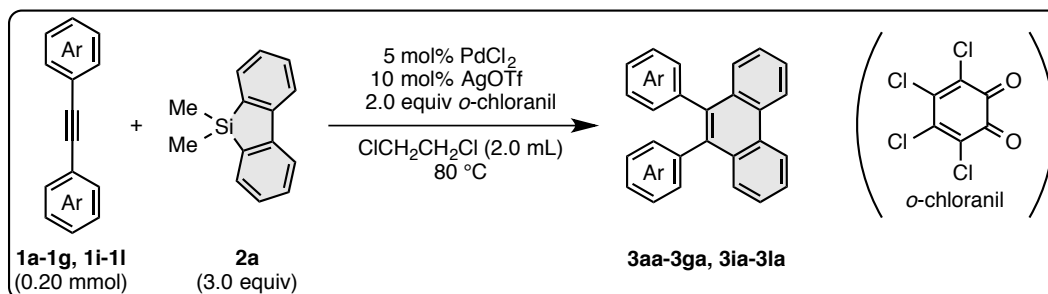
In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgOTf (5.1 mg, 20 μmol, 10 mol%). The vessel was taken out of the glovebox, then to this was added diarylacetylene **1a-1g, 1i-1l** (0.20 mmol, 1.0 equiv), dibenzosilole **2a** (0.40 mmol, 2.0 equiv), $PdCl_2$ (2.2 mg, 10 μmol, 5 mol%), and *o*-chloranil (98 mg, 0.40 mmol, 2.0 equiv), and 1,2-dichloroethane (2.0 mL) under a stream of nitrogen. After stirring at 80 °C, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH_2Cl_2). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC or silica gel column chromatography or Biotage Isolera® to yield diarylphenanthrene **3aa-3ga, 3ia-3la**.

Procedure B : APEX of diphenylacetylene (1a) with electron-rich dibenzosiloles (2b-2d)
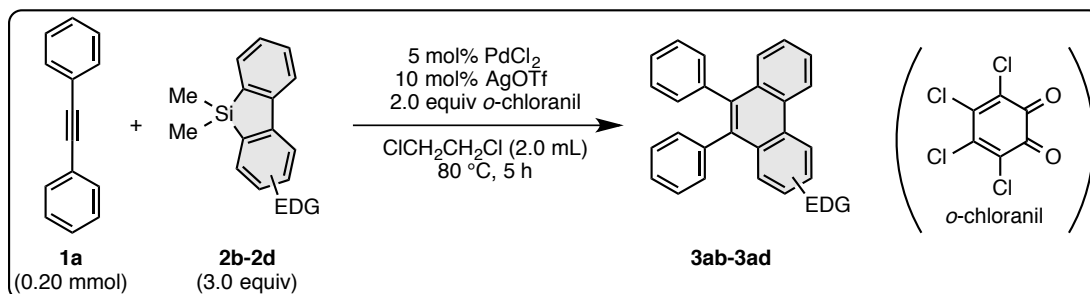
1a (0.20 mmol)   **2b-2d** (3.0 equiv)   **3ab-3ad**   *o*-chloranil

In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgOTf (5.1 mg, 20 μmol, 10 mol%). The vessel was taken out of the glovebox, then to this was added diarylacetylene **1a** (0.20 mmol, 1.0 equiv), dibenzosilole **2b-2d** (0.60 mmol, 3.0 equiv), PdCl$_2$ (2.2 mg, 10 μmol, 5 mol%), and *o*-chloranil (98 mg, 0.40 mmol, 2.0 equiv), and 1,2-dichloroethane (2.0 mL) under a stream of nitrogen. After stirring at 80 °C for 5 h, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH$_2$Cl$_2$). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC to yield diarylphenanthrene **3ab-3ad**.

Procedure C : APEX of diphenylacetylene (1a) with electron-deficient dibenzosiloles (4e-4g)
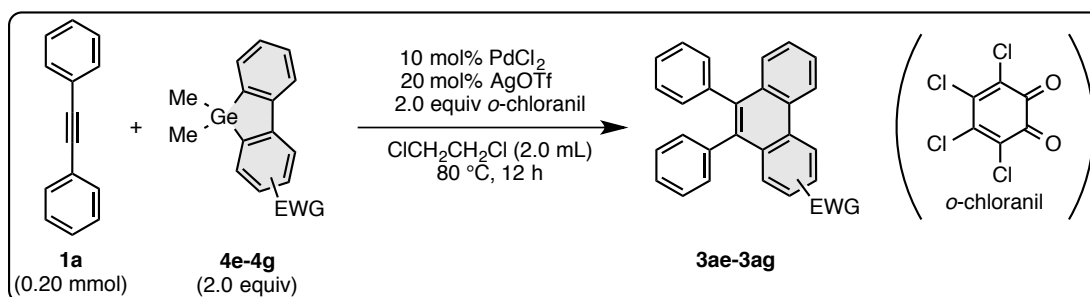
1a (0.20 mmol)   **4e-4g** (2.0 equiv)   **3ae-3ag**   *o*-chloranil

In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgOTf (10.3 mg, 40 μmol, 20 mol%). The vessel was taken out of the glovebox, then to this was added diarylacetylene **1a** (0.20 mmol, 1.0 equiv), dibenzogermole **4e-4g** (0.40 mmol, 2.0 equiv), PdCl$_2$ (3.7 mg, 20 μmol, 10 mol%), and *o*-chloranil (98 mg, 0.40 mmol, 2.0 equiv), and 1,2-dichloroethane (2.0 mL) under a stream of

nitrogen. After stirring at 80 °C for 12 h, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH_2Cl_2). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC or silica gel column chromatography to yield diarylphenanthrene **3ae-3ag**.

4-3. Compound data of APEX products

9,10-Diphenylphenanthrene (3aa)

Procedure A. 0.40 mmol scale (4.0 mL $ClCH_2CH_2Cl$), silica gel column chromatography: hexane:$CHCl_3$ = 9:1, Yield: 124.2 mg, 94%, white solid.
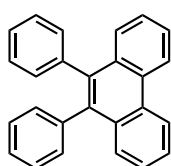
¹H NMR (600 MHz, CD_2Cl_2) δ 8.83 (d, *J* = 7.8 Hz, 2H), 7.70–7.66 (m, 2H), 7.52–7.47 (m, 4H), 7.29–7.24 (m, 4H), 7.24–7.20 (m, 2H), 7.20–7.17 (m, 4H).

¹³C NMR (150 MHz, $CDCl_3$) δ 139.6, 137.2, 131.9, 131.0, 130.0, 127.8, 127.6, 126.6, 126.5, 126.4, 122.5.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{26}H_{19}$ [M+H]⁺: 331.1487, found: 331.1481.

9-(4-Chlorophenyl)-10-phenylphenanthrene (3ba)

Procedure A. silica gel column chromatography: hexane:$CHCl_3$ = 9:1, Yield: 46.4 mg, 64%, white solid.
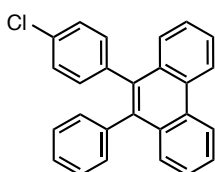
¹H NMR (600 MHz, CD_2Cl_2) δ 8.83 (dd, *J* = 8.4, 2.4 Hz, 2H), 7.71–7.67 (m, 2H), 7.53–7.47 (m, 4H), 7.31–7.23 (m, 5H), 7.18–7.15 (m, 2H), 7.13 (dt, *J* = 8.4, 2.1 Hz, 2H).

¹³C NMR (150 MHz, $CDCl_3$) δ 139.2, 138.1, 137.5, 135.8, 132.44, 132.36, 131.7, 131.6, 130.9, 130.04, 130.00, 127.9, 127.8, 127.5, 126.73, 126.71, 126.6, 126.5, 122.6, 122.5. Two carbon peaks are overlapped.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{26}H_{18}Cl$ [M+H]⁺: 365.1097, found: 365.1093.

9,10-Bis(4-chlorophenyl)phenanthrene (3ca)

Procedure A. PTLC: silica gel column chromatography: hexane:CHCl$_3$ = 9:1, Yield: 57.5 mg, 74%, white solid.
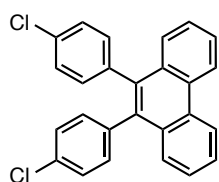
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.83 (d, J = 8.4 Hz, 2H), 7.70 (ddd, J = 8.4, 6.0, 1.2 Hz, 2H), 7.54–7.48 (m, 4H), 7.28 (d, J = 7.8 Hz, 4H), 7.12 (d, J = 8.4 Hz, 4H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 137.7, 136.1, 132.7, 132.2, 131.4, 130.1, 128.1, 127.5, 126.83, 126.75, 122.6.

HRMS (DART, ESI$^+$) m/z calcd for C$_{26}$H$_{17}$Cl$_2$ [M+H]$^+$: 399.0707, found: 399.0707.

9-(4-Bromophenyl)-10-phenylphenanthrene (3da)

Procedure A. silica gel column chromatography: hexane:CHCl$_3$ = 10:1, Yield: 61.4 mg, 75%, white solid.
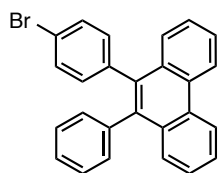
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.80 (dd, J = 7.8, 3.0 Hz, 2H), 7.67 (ddd, J = 8.4, 5.4, 2.4 Hz, 2H), 7.54 (dd, J = 8.4, 1.2 Hz, 1H), 7.52–7.46 (m, 3H), 7.37 (d, J = 8.4 Hz, 2H), 7.28–7.21 (m, 3H), 7.13 (dd, J = 7.8, 1.2 Hz, 2H), 7.03 (d, J = 8.4 Hz, 2H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 139.2, 138.6, 137.4, 135.8, 132.7, 131.7, 131.5, 130.9, 130.8, 130.1, 130.0, 127.9, 127.8, 127.5, 126.73, 126.72, 126.6, 126.5, 122.6, 122.5, 120.7. One carbon peak is overlapped.

HRMS (DART, ESI$^+$) m/z calcd for C$_{26}$H$_{18}$Br [M+H]$^+$: 409.0592, found: 409.0591.

9,10-Bis(4-bromophenyl)phenanthrene (3ea)

Procedure A. silica gel column chromatography: hexane, Yield: 71.1 mg, 73%.
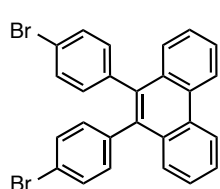
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.83 (d, J = 8.4 Hz, 2H), 7.70 (ddd, J = 8.4, 6.6, 1.2 Hz, 2H), 7.52 (ddd, J = 8.4, 7.2, 1.2 Hz, 2H), 7.48 (dd, J = 8.4, 1.2 Hz, 2H), 7.44 (dt, J = 8.4, 2.4 Hz, 4H), 7.06 (dt, J = 7.8, 2.4 Hz, 4H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 138.8, 136.4, 133.1, 131.8, 131.4, 130.5, 127.9, 127.3, 127.2, 123.0, 121.2.

HRMS (DART, ESI$^+$) m/z calcd for C$_{26}$H$_{17}$Br$_2$ [M+H]$^+$: 486.9697, found: 486.9691.

9,10-Bis[4-(trifluoromethyl)phenyl]phenanthrene (3fa)

Procedure A. silica gel column chromatography: hexane, Yield: 58.9 mg, 59%, white solid.
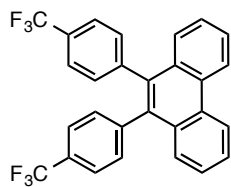
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.86 (d, J = 7.8 Hz, 2H), 7.73 (ddd, J = 7.8, 6.6, 1.2 Hz, 2H), 7.56–7.51 (m, 6H), 7.44 (dd, J = 8.4, 1.2 Hz, 2H), 7.33 (d, J = 7.8 Hz, 4H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 143.6, 136.4, 131.9, 131.5, 130.6, 129.3 (q, $^2J_{C–F}$ = 31.7 Hz), 127.8, 127.4, 125.20, 125.18, 124.7 (q, $^1J_{C–F}$ = 270.0 Hz), 123.1.

^{19}F NMR (564 MHz, CDCl$_3$) δ −62.8.

HRMS (DART, ESI$^+$) m/z calcd for C$_{28}$H$_{17}$F$_6$ [M+H]$^+$: 467.1234, found: 467.1236.

9,10-Bis[3,5-bis(trifluoromethyl)phenyl]phenanthrene (3ga)

Procedure A. silica gel column chromatography: hexane, Yield: 62.3 mg, 52%, white solid.
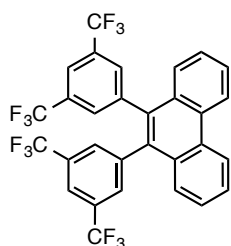
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.85 (d, J = 7.8 Hz, 2H), 7.79–7.73 (m, 4H), 7.62–7.56 (m, 6H), 7.46 (d, J = 8.4 Hz, 2H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 141.1, 135.3, 131.7 (q, $^2J_{C-F}$ = 33.0 Hz), 131.0, 130.5, 130.2, 127.8, 127.6, 127.1, 123.1, 122.9 (q, $^1J_{C-F}$ = 271.5 Hz), 121.0.

^{19}F NMR (564 MHz, CDCl$_3$) δ −63.5.

HRMS (DART, ESI$^+$) m/z calcd for C$_{30}$H$_{15}$F$_{12}$ [M+H]$^+$: 603.0982, found: 603.0975.

Dimethyl 4,4'-(phenanthrene-9,10-diyl)dibenzoate (3ha)
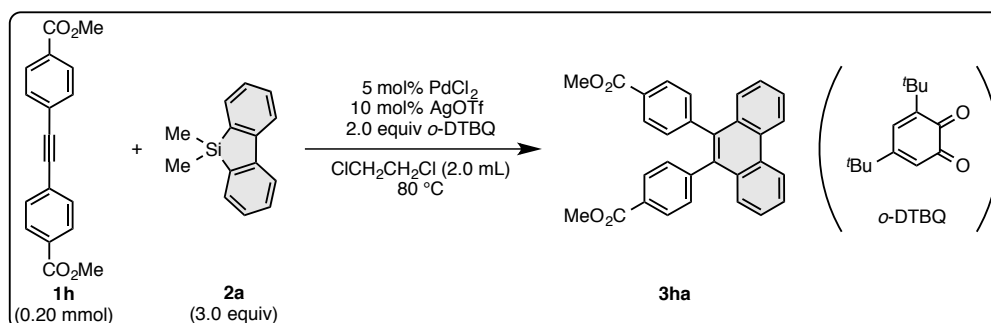
In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgOTf (5.1 mg, 20 μmol, 10 mol%). The vessel was taken out of the glovebox, then to this was added dimethyl 4,4'-(ethyne-1,2-diyl)dibenzoate **1h** (0.20 mmol, 1.0 equiv), dibenzosilole **2a** (0.40 mmol, 2.0 equiv), PdCl$_2$ (2.2 mg, 10 μmol, 5 mol%), and o-DTBQ (88 mg, 0.40 mmol, 2.0 equiv), and 1,2-dichloroethane (2.0 mL) under a stream of nitrogen. After stirring at 80 °C, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH$_2$Cl$_2$). After the organic solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (hexane:EtOAc = 4:1) then PTLC (hexane:EtOAc = 4:1) to yield diarylphenanthrene **3ha** in 43% (38.6 mg) as a white solid.

^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.85 (d, J = 8.4 Hz, 2H), 7.91 (d, J = 8.4 Hz, 4H), 7.72 (ddd, J = 7.8, 6.6, 1.2 Hz, 2H), 7.52 (t, J = 7.5 Hz, 2H), 7.47 (dd, J = 7.8, 1.2 Hz, 2H),

7.27 (d, J = 7.8 Hz, 4H), 3.88 (s, 6H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 167.1, 144.7, 136.7, 131.6, 130.6, 129.4, 129.2, 127.9, 127.35, 127.32, 123.1, 52.4. One carbon peak is overlapped.

HRMS (DART, ESI$^+$) m/z calcd for C$_{30}$H$_{23}$O$_4$ [M+H]$^+$: 447.1596, found: 447.1600.

4,4,5,5-Tetramethyl-2-[4-(10-phenylphenanthren-9-yl)phenyl]-1,3,2-dioxaborolane (3ia)

Procedure A. silica gel column chromatography: hexane:CHCl$_3$ = 1:1, Yield: 68.2 mg, 75%, white solid.
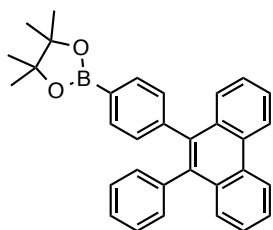
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.80 (d, J = 7.8 Hz, 2H), 7.68 (d, J = 7.2 Hz, 2H), 7.67–7.62 (m, 2H), 7.53 (d, J = 7.8 Hz, 1H), 7.50–7.43 (m, 3H), 7.23 (d, J = 7.8 Hz, 2H), 7.21–7.14 (m, 5H), 1.34 (s, 12H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 142.7, 139.4, 137.0, 136.9, 134.0 , 131.9, 131.7, 131.0, 130.5, 130.00, 129.96, 127.8, 127.7, 126.6, 126.5, 126.4, 122.4, 83.8, 24.9. One *ipso* carbon signal of C–B bond is not observed. Four tertiary carbon signals are overlapped.

HRMS (DART, ESI$^+$) m/z calcd for C$_{32}$H$_{30}$BO$_2$ [M+H]$^+$: 457.2339, found: 457.2331.

9,10-Di(naphthalen-1-yl)phenanthrene (3ja)

Procedure A. silica gel column chromatography: hexane:CHCl$_3$ = 19:1,, Yield: 44.8 mg, 52%, white solid. The compound was obtained as 1:1 mixture of rotamer.
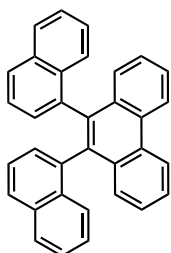
^{1}H NMR (600 MHz, CDCl$_3$, 60 °C) δ 8.88 (d, J = 8.4 Hz, 2H), 7.75 (d, J = 7.8 Hz, 1H), 7.67 (t, J = 8.4 Hz, 2H), 7.56 (d, J = 8.4 Hz, 3H), 7.49 (d, J = 8.4 Hz, 1H), 7.42–7.33 (m, 5H), 7.33–7.22 (m, 4H), 7.15 (t, J = 7.8 Hz, 1H), 7.02 (d, J = 6.6 Hz, 1H), 6.99–6.92 (m, 2H).

^{13}C NMR (150 MHz, CDCl$_3$, 60 °C) δ 137.3, 136.92, 136.86, 136.6, 133.3, 133.2, 132.6, 132.4, 130.4, 130.3, 129.7, 128.3, 128.2, 128.1, 127.7, 127.4,

127.3, 127.2, 127.1, 126.84, 126.81, 126.6, 125.8, 125.4, 125.3, 125.1, 125.0, 124.6, 122.64, 122.60. Four aromatic carbon signals are overlapped.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{34}H_{23}$ [M+H]⁺: 431.1794, found: 431.1799.

9,10-Di-*o*-tolylphenanthrene (3ka)

Procedure A. silica gel column chromatography: hexane, Yield: 14.5 mg, 20%, white solid. The compound was obtained as 1:1 mixture of rotamer.
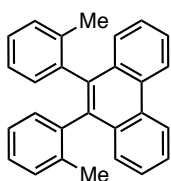
¹H NMR (600 MHz, CDCl₃, 60 °C) δ 8.77 (d, *J* = 9.0 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.13–7.08 (m, 2H), 7.00–6.92 (m, 6H), 2.25 (s, 3H), 2.24 (s, 3H).

¹³C NMR (150 MHz, CDCl₃, 60 °C) δ 139.6, 137.4 (0.5 C), 137.3 (0.5 C), 137.0 (0.5 C), 136.9 (0.5 C), 132.2, 132.0 (0.5 C), 131.9 (0.5 C), 130.1, 128.3 (0.5 C), 128.2 (0.5 C), 128.0, 127.4 (0.5 C), 127.3 (0.5 C), 127.13 (0.5 C), 127.11 (0.5 C), 126.5, 126.2, 122.5, 21.3.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{28}H_{23}$ [M+H]⁺: 359.1800, found: 359.1799.

9,10-Bis[4-(*tert*-butyl)phenyl]phenanthrene (3la)

Procedure A. silica gel column chromatography: hexane:CHCl₃ = 10:1, Yield: 15.9 mg, 18%, white solid.
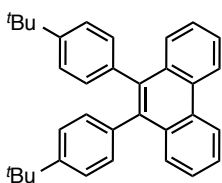
¹H NMR (600 MHz, CD₂Cl₂) δ 8.82 (d, *J* = 7.8 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 4H), 7.06 (d, *J* = 7.8 Hz, 4H), 1.29 (s, 18H).

¹³C NMR (150 MHz, CDCl₃) δ 148.9, 137.6, 136.5, 131.9, 130.7, 129.9, 128.0, 126.5, 126.2, 124.1, 122.4. 34.4, 31.3.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{34}H_{35}$ [M+H]⁺: 443.2739, found: 443.2733.

1,4-Bis(10-phenylphenanthren-9-yl)benzene (3ma)
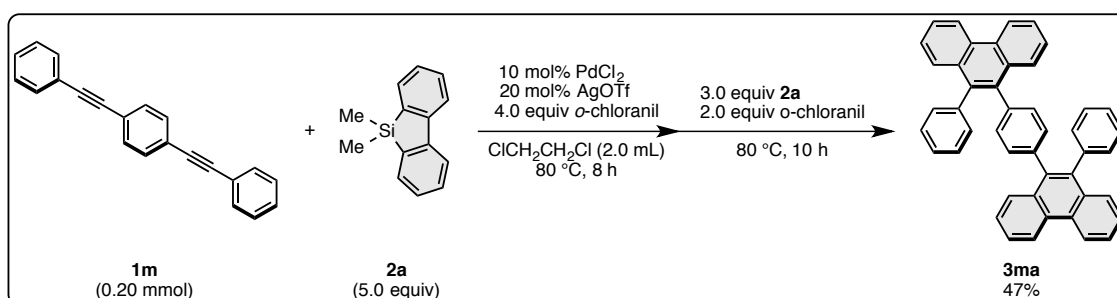
In the glovebox, to a 20 mL glass vessel equipped with J, Young® O-ring tap containing a magnetic stirrer bar was added AgOTf (10.3 mg, 40 μmol, 20 mol%). The vessel was taken out of the glovebox, then to this was added 1,4-bis(phenylethynyl)benzene **1m** (55.6 mg, 0.20 mmol, 1.0 equiv), dibenzosilole **2a** 210 mg, 1.0 mmol, 5.0 equiv), PdCl$_2$ (3.7 mg, 20 μmol, 10 mol%), and o-chloranil (196 mg, 0.80 mmol, 4.0 equiv), and 1,2-dichloroethane (2.0 mL) under a stream of nitrogen. After stirring at 80 °C for 8 h, dibenzosilole **2a** (126 mg, 0.6 mmol, 3.0 equiv) and o-chloranil (98 mg, 98 mg, 0.40 mmol, 2.0 equiv) were added under a stream of nitrogen at room temperature. After additional stirring for 10 h at 80 °C, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: CH$_2$Cl$_2$). After the organic solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (eluent: hexane). Further purification was performed by GPC to yield **3ma** (55.1 mg, 47%) as a pale yellow solid. The compound was obtained as 2:1 mixture of rotamer.

^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.83–8,79 (m, 4H), 7.71–7.55 (m, 6H), 7.52–7.45 (m, 4H), 7.36–7.28 (m, 4H + 0.33 × 2H), 7.28–7.19 (m, 6H), 7.08 (s, 0.33 × 4H), 7.08–7.04 (m, 0.67 × 2H), 7.01 (s, 0.67 × 4H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 140.1, 139.6, 138.3, 137.65, 137.62, 137.3, 132.5, 132.4, 132.3, 132.2, 131.7, 131.2, 130.8, 130.7, 130.38, 130.35, 130.3, 128.2, 128.11, 128.09, 128.0, 127.1, 127.0, 126.9, 126.8, 122.92, 122.89, 122.8.

HRMS (DART, ESI$^+$) m/z calcd for C$_{46}$H$_{31}$ [M+H]$^+$: 583.2420, found: 583.2411.

2,7-Di-*tert*-butyl-9,10-diphenylphenanthrene (3ab)

Procedure B. PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 77.4 mg, 87%, white solid.
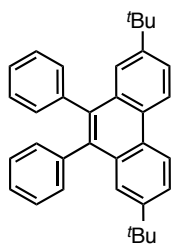
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.70 (d, *J* = 8.9 Hz, 2H), 7.73 (dd, *J* = 8.6, 2.0 Hz, 2H), 7.47 (d, *J* = 2.0 Hz, 2H), 7.28–7.25 (m, 4H), 7.23–7.17 (m, 6H), 1.26 (s, 18H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 149.4, 140.4, 137.6, 131.9, 131.5, 128.0, 127.9, 126.7, 124.9, 123.9, 122.4, 35.1, 31.3.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{34}$H$_{35}$ [M+H]$^+$: 443.2739, found: 443.2745.

3-Methyl-9,10-diphenylphenanthrene (3ac)

Procedure B. PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 54.9 mg, 80%, white solid.
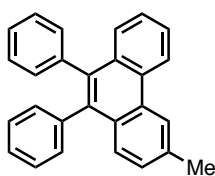
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.78 (d, *J* = 8.6 Hz, 1H), 8.59 (s, 1H), 7.62 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.54 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.47–7.43 (m, 2H), 7.30 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.24–7.20 (m, 4H), 7.19–7.12 (m, 6H), 2.62 (s, 3H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 139.7, 139.6, 137.1, 136.2, 136.1, 132.0, 131.1, 131.0, 130.0, 129.8, 129.7, 128.3, 127.8, 127.7, 127.52, 127.50, 126.45, 126.36, 126.1, 122.4, 122.2, 22.0. One tertiary carbon peak is overlapped.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{27}$H$_{21}$ [M+H]$^+$: 345.1643, found: 345.1650.

2-Methoxy-9,10-diphenylphenanthrene (3ad)

Procedure B. PTLC: hexane:CH$_2$Cl$_2$ = 6:1, Yield: 37.8 mg, 52%, white solid.
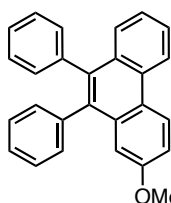
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.72 (d, *J* = 9.0 Hz, 1H), 8.71 (d, *J* = 8.4 Hz, 1H), 7.60 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.47 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.42 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.31 (dd, *J* = 9.0, 3.0 Hz, 1H), 7.28–7.24 (m, 4H), 7.24–7.20 (m, 2H), 7.20–7.17 (m, 4H), 6.88 (d, *J* = 3.0 Hz, 1H), 3.70 (s, 3H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 158.8, 140.2, 140.1, 138.1, 137.1, 133.8, 131.42, 131.38, 131.3, 130.5, 128.13, 128.07, 128.0, 126.91, 126.89, 126.8, 126.0, 124.7, 124.5, 122.3, 116.6, 109.2, 55.5.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{27}$H$_{21}$O [M+H]$^+$: 361.1592, found: 361.1587.

2-Chloro-9,10-diphenylphenanthrene (3ae)

Procedure C. Silica gel column chromatography: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 61.4 mg, 84%, white solid.
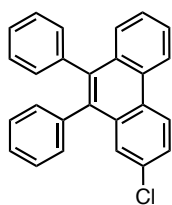
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.76 (d, *J* = 8.6 Hz, 2H), 7.71–7.67 (m, 1H), 7.63 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 2.4 Hz, 1H), 7.30–7.20 (m, 6H), 7.18–7.15 (m, 4H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 139.8, 139.4, 139.0, 136.8, 133.7, 133.1, 132.4, 131.5, 131.4, 130.0, 128.9, 128.4, 128.3, 128.1, 127.4, 127.3, 127.24, 127.22, 127.1, 124.8, 122.9. One tertiary carbon peak is overlapped.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{26}$H$_{18}$Cl [M+H]$^+$: 365.1097, found: 365.1090.

2-Fluoro-9,10-diphenylphenanthrene (3af)

Procedure C. PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 64.9 mg, 93%, white solid.
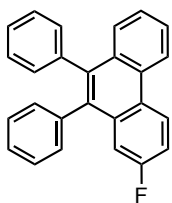
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.77 (dd, *J* = 9.3 Hz, $^4J_{H\text{-}F}$ = 5.9 Hz, 1H), 8.72 (d, *J* = 8.3 Hz, 1H), 7.66 (ddd, *J* = 8.3, 6.9, 1.0 Hz, 1H), 7.55 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.47 (ddd, *J* = 7.9, 6.8, 1.0 Hz, 1H), 7.41–7.37 (m, 1H), 7.25–7.21 (m, 4H), 7.21–7.17 (m, 3H), 7.15–7.12 (m, 4H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 161.4 (d, $^1J_{C\text{–}F}$ = 243.0 Hz), 139.2, 139.0, 138.4, 136.6 (d, $^4J_{C\text{–}F}$ = 4.2 Hz), 133.6 (d, $^3J_{C\text{–}F}$ = 7.2 Hz), 131.4, 130.9, 129.7, 128.0, 127.8, 127.6, 126.7, 126.6 (2C), 126.4, 124.8 (d, $^3J_{C\text{–}F}$ = 8.7 Hz), 122.3, 115.3 (d, $^2J_{C\text{–}F}$ = 23.0 Hz), 112.3 (d, $^2J_{C\text{–}F}$ = 21.6 Hz). Two tertiary carbon peaks are overlapped.

^{19}F NMR (564 MHz, CDCl$_3$) δ −114.2.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{26}H_{18}F$ [M+H]⁺: 349.1393, found: 349.1386.

3-Fluoro-9,10-diphenylphenanthrene (3ag)

Procedure C. PTLC: hexane:CH_2Cl_2 = 15:1, Yield: 52.4 mg, 75%, white solid.
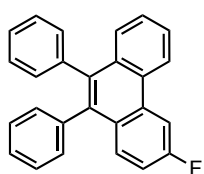
¹H NMR (600 MHz, CDCl₃) δ 8.65 (d, *J* = 8.4 Hz, 1H), 8.39 (dd, $^3J_{H-F}$ = 11.4 Hz, *J* = 2.4 Hz, 1H), 7.65 (ddd, *J* = 8.4, 6.6, 1.2 Hz, 1H), 7.57–7.48 (m, 3H), 7.25–7.17 (m, 7H), 7.15–7.11 (m, 4H).

¹³C NMR (150 MHz, CDCl₃) δ 161.5 (d, $^1J_{C-F}$ = 244.4 Hz), 139.32, 139.27, 136.8, 136.4 (d, $^4J_{C-F}$ = 2.9 Hz), 132.2, 131.6 (d, $^3J_{C-F}$ = 8.6 Hz), 131.0, 130.9, 130.2 (d, $^3J_{C-F}$ = 8.6 Hz), 129.3 (d, $^4J_{C-F}$ = 4.3 Hz), 128.6, 127.9, 127.64, 127.62, 127.2, 126.6, 126.5, 126.4, 122.7, 115.4 (d, $^2J_{C-F}$ = 23.0 Hz), 107.5 (d, $^2J_{C-F}$ = 21.6 Hz).

¹⁹F NMR (564 MHz, CDCl₃) δ −114.4.

HRMS (DART, ESI⁺) *m/z* calcd for $C_{26}H_{18}F$ [M+H]⁺: 349.1393, found: 349.1389.

4-4. X-ray Crystal Structure Analysis of 3ma

Details of the crystal data and a summary of the intensity data collection parameters for **3ma** are listed in Table 6. A suitable crystal was mounted with mineral oil on a glass fiber and transferred to the goniometer of a Rigaku Saturn CCD diffractometer. Graphite-monochromated Mo Ka radiation (*l* = 0.71070 Å) was used. The structures were solved by direct methods with (SIR-97)[13] or (SHELXS-97)[14] and refined by full-matrix least-squares techniques against F^2 (SHELXL-97)[14]. The intensities were corrected for Lorentz and polarization effects. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed using AFIX instructions.

Table 6. Crystallographic data and structure refinement details for **3ma**

	3ma·0.5MeOH
formula	$C_{46.50}H_{30}O_{0.50}$
fw	596.71
T (K)	103(2) K
l (Å)	0.71075 Å
cryst syst	Orthorhombic
space group	Pccn
a, (Å)	21.105(6)
b, (Å)	23.182(6)
c, (Å)	6.8933(16)
a, (deg)	90
b, (deg)	90
g, (deg)	90
V, (Å^3)	3372.6(15)
Z	4
D_{calc}, (g / cm^3)	1.175
m (mm^{-1})	0.068
F(000)	1252
cryst size (mm)	0.20 x 0.10 x 0.05
$2q$ range, (deg)	3.03 – 25.00°
reflns collected	22291
indep reflns/R_{int}	2964/0.1134
params	222
GOF on F^2	0.886
R_1, wR_2 [I>2s(I)]	0.0636, 0.1785
R_1, wR_2 (all data)	0.1538, 0.2224

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One-shot Annulative π-Extension of Heteroarenes

Abstract

One-shot annulative π-extension (APEX) reactions of heteroarenes are described. Cationic palladium/*o*-chloranil catalytic system enables extending the π-system of benzo[*b*]thiophenes by using dimethyldibenzosiloles as π-extending agents. π-Extended dibenzofuran and carbazole can be also obtained from benzofuran and *N*-tosylindole, respectively with dimethyldibenzogermole as a germanium-based π-extending agent.

1. Introduction

Over the past decades, fused π-conjugation systems containing heteroatoms have been recognized as quintessential structural motifs in the field of optoelectronics.[1] In contrast to carbon-based π-extended molecules, fused heteroarenes containing sulfur, nitrogen, and oxygen atoms are possible to control the electronic structure by intra- and intermolecular orbital interaction, thereby manifesting unique photophysical properties.[2] Historically, exploring the novel class of π-conjugated materials has been often supported by the development of novel synthetic strategies. Therefore, the practical and efficient synthetic methodology enables accessing new and distinctive electronic systems, which would promise to enhance and pioneer the research field dramatically.

Mainstreams to construct heteroatom-containing fused π-system represent (i) carbon-heteroatom (C–[E]) bond formation[3], (ii) carbon–carbon (C–C) bond formation of heteroethers[4], and (iii) functionalization including π-extension of heteroarenes (Figure 1). Although carbon–heteroatom and carbon–carbon bond formation is regarded as the well-established and reliable strategy, functionalization including π-extension reaction of heteroarene, in other words late-stage functionalization of heteroarenes, have not been established yet albeit this would be much more ideal than the others from the viewpoint of rapid synthesis and easy diversification of derivatives.

(i) Carbon-heteroatom bond forming reaction

[E]

metalation/ nucleophilic substitution/ C–[E] bond formation

X = H, halogene, heteroatom, etc.

(ii) C–C bond forming reaction of heteroether

C–C bond formation

X = H, halogene, etc.

(iii) Functionalization (π-Extension) of heteroarene

or

functionalization (π-extension)
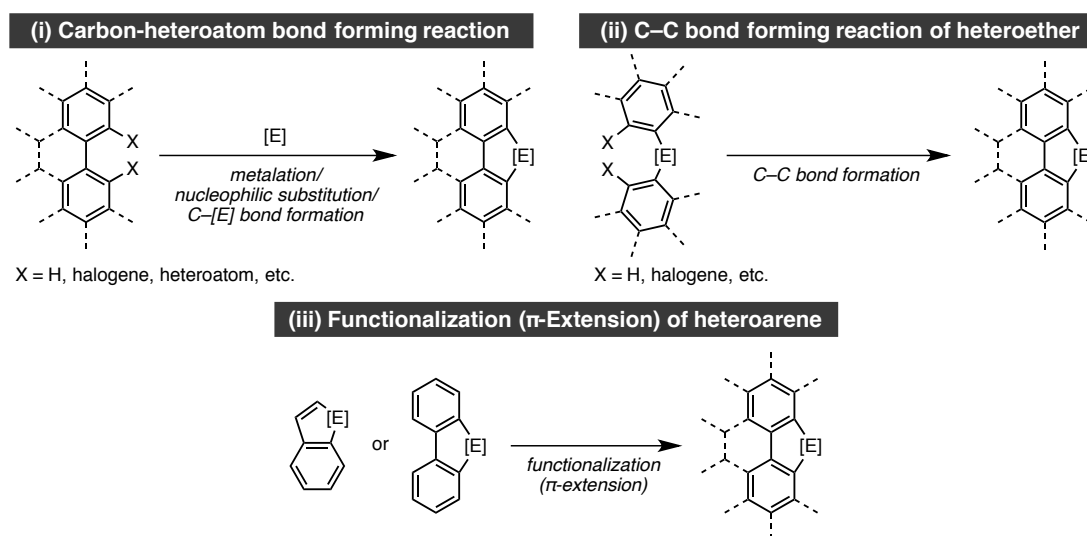
Figure 1. Ordinary synthetic methods for heteroatom-containing fused π-system

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Taking thiophene as an example to illustrate the recent progress of late-stage heteroarene functionalization[5-14], a variety of functional groups including aryl[6,7], alkynyl[5,8], alkenyl[5,9], alkyl[5,10], halo[5,11], carbonyl[5,12], nitrile[5,13], and boryl[5,14] can be introduce to thiophene in a regioselective manner (Figure 2). However, single-step π-extension of thiophene accompanied with construction of new benzene rings has been still undeveloped.[15]
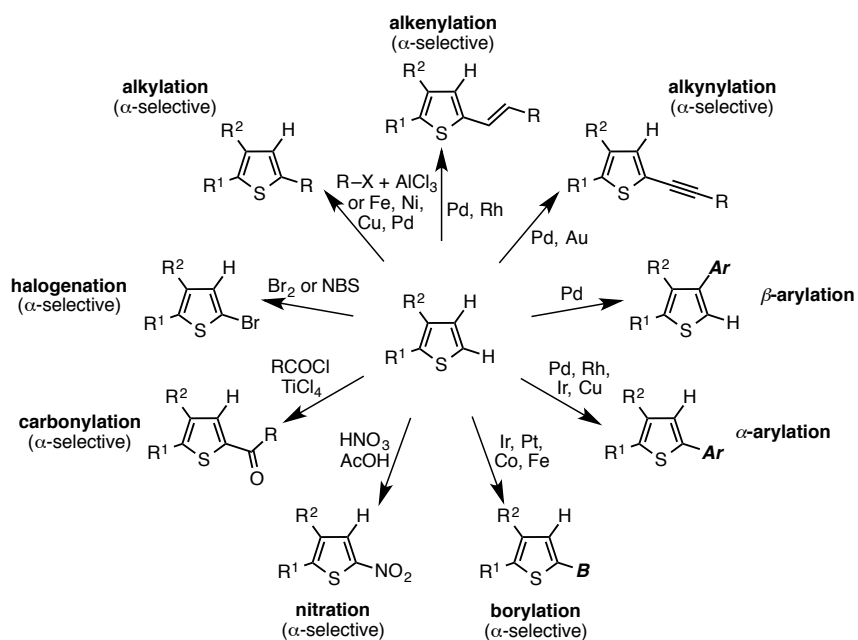
Figure 2. Regioselective functionalization of thiophene

One of the key reports on single-step π-extension of thiophene represents a copper mediated double cross-coupling of zirconacyclopentadienes with 2-iodo-3-bromothiophene pioneered by Takahashi and co-workers based on the double cross coupling strategy to expand the π-conjugation system.[15n-p] Since then, several π-extension reactions using arylmetals[15k,m-p] and alkenes[15l] with dihaloarene have been developed (Figure 3). Nevertheless, these reactions always require the pre-functionalization of substrates such as halogenation, rendering the multi-step process in nature. On the other hand, direct π-extension from unfunctionalized thiophene template is limited to Lewis acid-mediated benzannulation (Scheme 1).[15a-j]
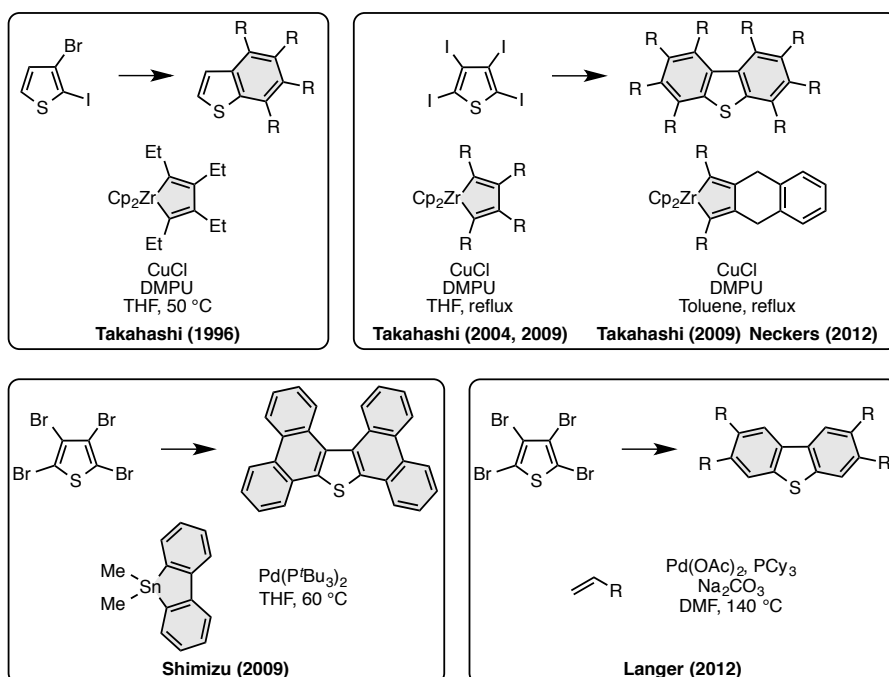
Figure 3. One-shot annulative π-extension of functionalized thiophenes by C–X/C–M

coupling
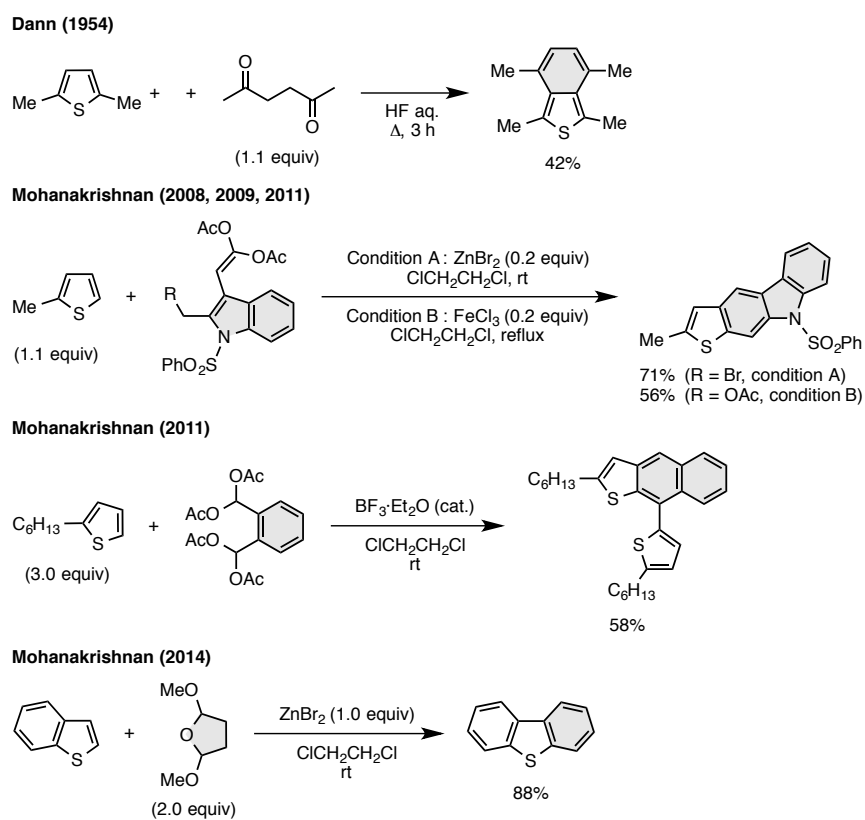
Scheme 1. One-shot annulative π-extension of unfunctionalized thiophenes through

Lewis acid-mediated benz- and naphtoannulation

In this chapter, the development of one-shot annulative π-extension (APEX) of heteroarenes, especially thiophenes, with dibenzosiloles as a π-extending agent is described (Scheme 2). A cationic palladium/*o*-chloranil system effectively promoted APEX reaction to afford phenanthro[9,10-*b*]thiophene in one-shot. Furthermore, other heteroarenes such as benzofuran and indole are also applicable as templates for APEX by using dibenzogermole instead of dibenzosilole as a π-extending agent.

E = S, O, NTs **M = Si: dibenzosiloles**
              M = Ge: dibenzogermoles
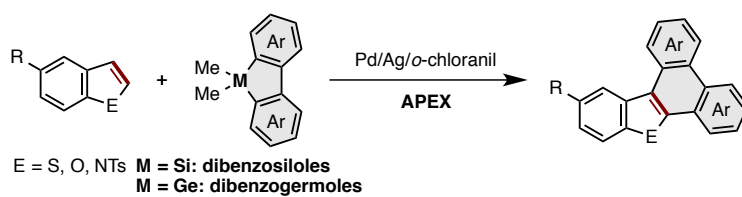
Scheme 2. Pd-catalyzed annulative π-extension of heteroarenes with dibenzosilole and dibenzogermole

2. Results and Discussion

2-1. Working hypothesis

During the course of studies on APEX reaction of PAHs and alkynes described in Chapters 1 and 2, it was found that palladium/*o*-chloranil catalytic system prefers to react at the most reactive carbon–carbon multiple bond such as K-region on PAHs or triple bond on alkynes (Scheme 3). Therefore, it was envisioned that other aromatic template having reactive C–C multiple bonds could be a suitable candidate for novel APEX reaction; benzo[*b*]thiophene as model substrate has enough potential to realize desired APEX reaction.
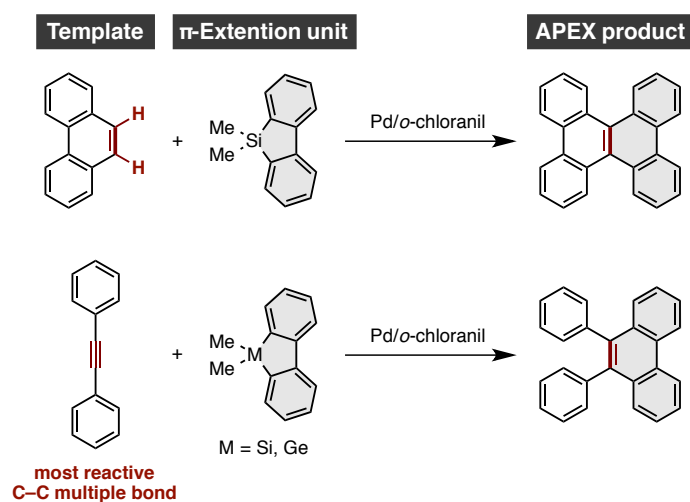
Scheme 3. Established APEX methodology for PAHs and alkynes with dibenzosilole and dibenzogermole

Except for limited examples of direct arylation of thiophenes[6d], oxidative coupling of benzo[*b*]thiophene with arylboronic acid[7a,d,f,i] and arylsilane[7g] usually provide *β*-substituted products selectively (Figure 4) Thus, *β*-arylation of benzo[*b*]thiophene with suitable π-extending agents such as dibenzosilole or dibenzogermole possibly trigger one-shot APEX reaction *via* the sequential intramolecular C–H arylation at *α*-position (Scheme 4).
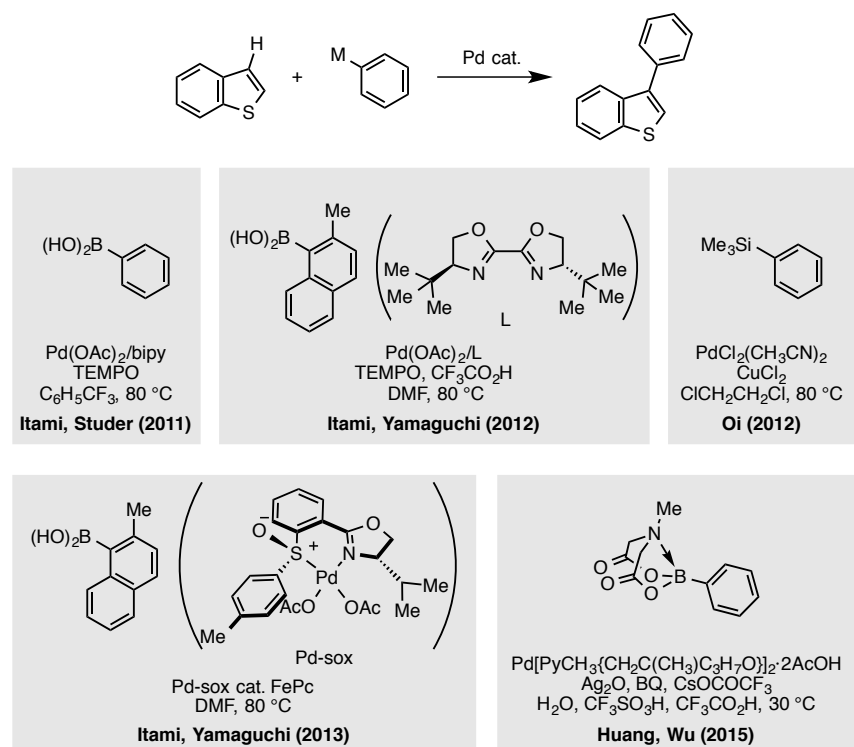
Figure 4. Recent examples of transition metal-catalyzed *β*-selective C–H arylation of benzothiophene with aryl metal species
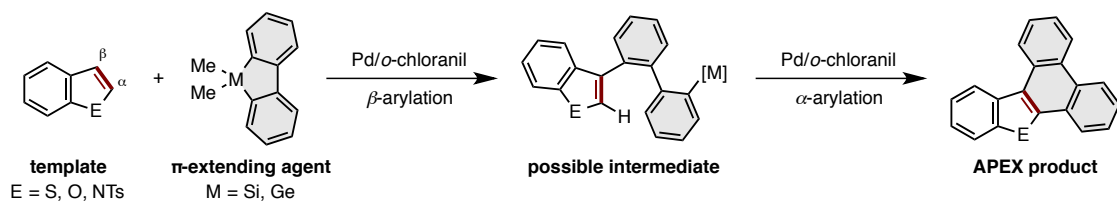
Scheme 4. Blueprint for one-shot APEX of heteroarenes initiated by Pd-catalyzed *β*-selective C–H arylation with dibenzosilole and dibenzogermole.

2-2. Optimization of reaction conditions for one-shot APEX reaction of benzo[b]thiophene

Optimal conditions for APEX of benzo[b]thiophene (**1a**) were established by using Pd(OAc)$_2$ as a catalyst and dimethyldibenzosilole (**2a**) as a π-extending agent in 1,2-dichloroethane at 70 °C (Table 1). Each parameter in Table 1 shows the difference from the standard conditions. As a result from the screening of silver salts, oxidants, and concentration, using 1.0 equivalent of AgPF$_6$, 3.0 equivalent of dibenzosilole **2a** and 2.0 equivalent of o-chloranil gave the best result affording APEX product **3aa** in 63% yield (Table 1, entry 1). Decreasing the amount of **2a** or AgPF$_6$ resulted in lower yields (entries 2 and 3). While the reactions with other silver salts such as AgOTf, AgBF$_4$, AgSbF$_6$, and AgNTf$_2$ also provided APEX product **3aa** to some extent, they did not exceed the yield with AgPF$_6$ (entries 4–7). Neutral palladium diacetate without any silver salt did not afford desired product at all, thus cationic palladium seems to be a key species for this APEX (entry 8). Although DDQ instead of o-chloranil afforded APEX product in 18% GC yield, DTBQ which was effective oxidant for APEX of alkynes only gave β-biphenylbenzo[b]thiophene **4** in 7% GC yield (entries 9 and 10). p-Benzoquinone was not effective as an oxidant (entry 11). The two-times diluted condition decelerated the reaction (entry 12). Finally, the best result was obtained with a marginally higher concentration (0.13 M), which gave **3aa** in 68% isolated yield (entry 13).

Table 1. Screening of reaction conditions for APEX reaction of benzothiophene with dibenzosilole[a]

entry	[Ag]	[oxidant]	yield[b]
1	AgPF$_6$	o-chloranil	63% (NMR)
2[c]	AgPF$_6$	o-chloranil	35% (NMR)
3	AgPF$_6$ (50 mol%)	o-chloranil	46% (GC)
4	AgOTf	o-chloranil	34% (GC)
5	AgBF$_4$	o-chloranil	27% (GC)
6	AgSbF$_6$	o-chloranil	38% (GC)
7	AgNTf$_2$	o-chloranil	40% (GC)

entry	[Ag]	[oxidant]	yield[b]
8	none	o-chloranil	0% (GC)
9	AgPF$_6$	DDQ	18% (GC)
10[d]	AgPF$_6$	DTBQ	0% (NMR)
11	AgPF$_6$	BQ	0% (NMR)
12[e]	AgPF$_6$	o-chloranil	48% (NMR)
13[f]	AgPF$_6$	o-chloranil	69% (NMR) 68% (isolated)

(a) Reaction conditions: benzo[b]thiophene (**1a**) (0.20 mmol), dimethyldibenzosilole (**2a**) (3.0 equiv), Pd(OAc)$_2$ (5 mol%), AgPF$_6$ (1.0 equiv), o-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 70 °C, 16 h. (b) GC yield was calculated using n-decane as an internal standard. NMR yield was calculated with CH$_2$Br$_2$ as an internal standard. (c) 2.0 equivalent of **2a** was used. (d) β-biphenylbenzo[b]thiophene **4** was obtained in 7% GC yield. (e) 4.0 mL of 1,2-dichloroethane was used. (f) 1.5 mL of 1,2-dichloroethane was used.

Hence, the reaction of benzo[b]thiophene (**1a**) (0.20 mmol) with dibenzosilole (**2a**) (3.0 equiv), Pd(OAc)$_2$ (5 mol%), AgPF$_6$ (1.0 equiv), and o-chloranil (2.0 equiv) in 1,2-dichloroethane (1.5 mL) at 70 °C was determined as the optimal conditions (Scheme 5).
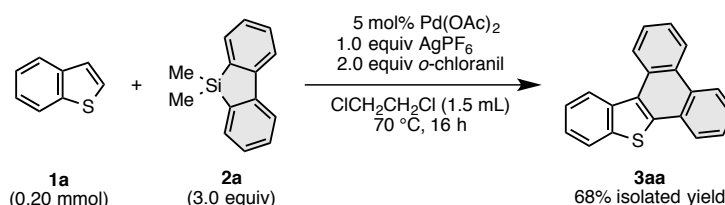
Scheme 5. Optimal conditions for APEX of heteroarene

2-3. Substrate scope in APEX of heteroarenes

With optimal conditions in hand, the substrate scope of benzo[*b*]thiophene derivatives **1** and dibenzosiloles **2** were investigated (Table 2). *tert*-Butyl and methyl substituted benzo[*b*]thiophenes **1b** and **1c** provided the desired APEX products **3ba** and **3ca** in moderate yields. Although electron-deficient benzo[*b*]thiophenes, for example 5-bromo, 5-chloro and 5-fluorobenzo[*b*]thiophenes **1d**, **1e**, and **1f** provided the desired products **3da**, **3ea**, and **3fa** in lower yields without loss of the halogen atoms, those results are attractive because these products are suitable substrates for further functionalization by classical cross-coupling protocols. The structure of **3da** was confirmed by X-ray crystallographic analysis as shown in Figure 5. Additionally, the reaction of benzo[*b*]thiophene (**1a**) with 3,7-di-*tert*-butyldibenzosilole **2b** afforded the corresponding APEX product in 28% yield.

Table 2. Substrate scope for APEX reaction of benzo[*b*]thiophenes[a]
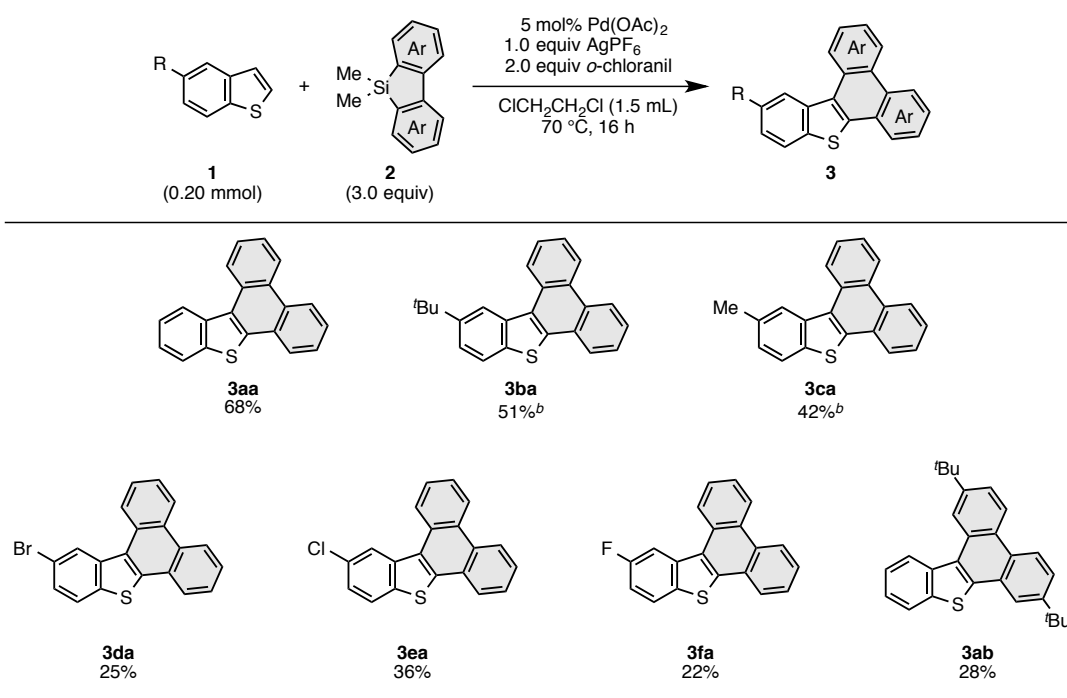
(a) Reaction conditions: benzo[*b*]thiophenes **1** (0.20 mmol), dimethyldibenzosiloles **2** (3.0 equiv), Pd(OAc)$_2$ (5 mol%), AgPF$_6$ (1.0 equiv), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (1.5 mL), 70 °C, 16 h. (b) Pd(OAc)$_2$ (10 mol%).

$R_1 = 0.0212$,
$wR_2 = 0.0544$
$GOF = 1.037$
Space Group $P2_1/n$
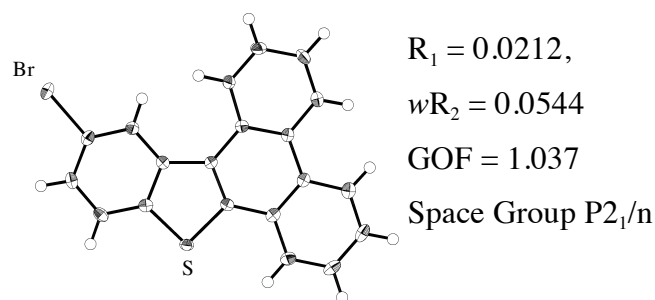
Figure 5. ORTEP drawing of 12-bromobenzo[*b*]phenanthro[9,10-*d*]thiophene (**3da**) with 50% thermal ellipsoid

When unsymmetrical dibenzosilole, for example 3-chlorodimethyldibenzosilole (**2c**), was used as a π-extending agent for APEX, two regioisomers **3ac** and **3ac'** were obtained in 38% combined yield as a 78:22 mixture (Scheme 6).
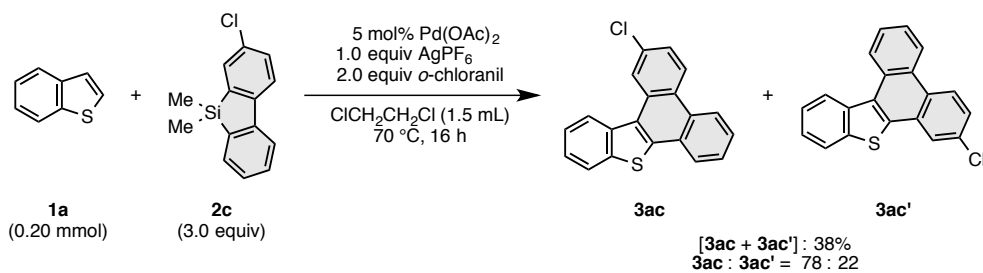
Scheme 6. APEX of **1a** with unsymmetrical dibenzosilole **2c**[*a*]

(a) Reaction conditions: benzo[*b*]thiophene (**1a**) (0.20 mmol), 3-chlorodimethyldibenzosilole (**2c**) (3.0 equiv), Pd(OAc)$_2$ (5 mol%), AgPF$_6$ (1.0 equiv), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (1.5 mL), 70 °C, 16 h. The ratio of regioisomer was determined by GC.

In addition to the above results, other heteroarene templates were also investigated (Scheme 7). Under the optimal conditions, 2,3-diphenylthiophene (**1g**) was transformed to 2,3-diphenylphenanthro[9,10-*b*]thiophene (**3ga**) in 50% yield. However this reaction conditions with dibenzosilole **2a** were not applicable to the APEX of benzofuran (**5**) and *N*-tosylindole (**7**). Further optimizations revealed that the combination of dimethyldibenzogermole (**2d**) as a suitable π-extension agent and AgOTf provided APEX products **6** and **8** in 33% and 30% yield, respectively.
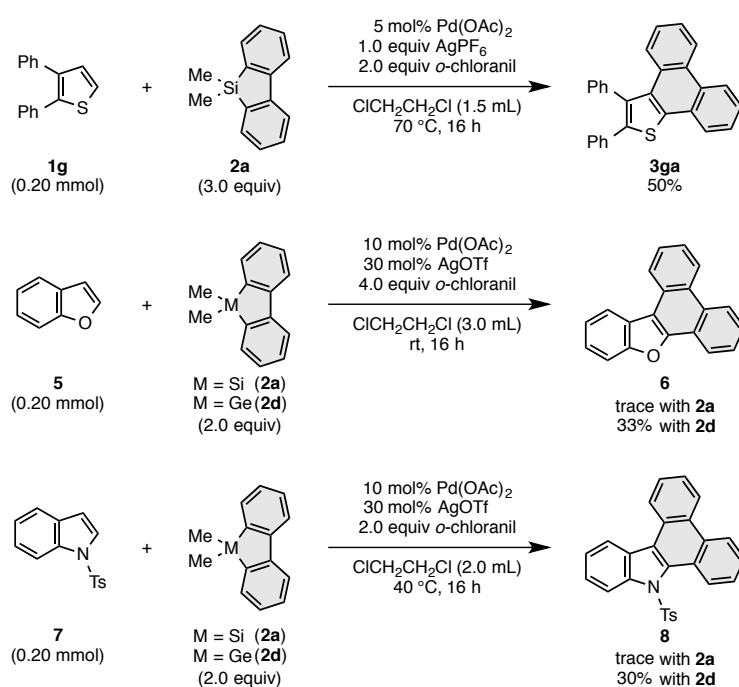
Scheme 7. APEX of thiophene, benzofuran, and *N*-tosylindole

2-4. Mechanistic consideration

In light of previous studies on APEX of PAHs [15a] and oxidative C–H arylation of thiophenes[7], the APEX reaction with benzo[*b*]thiophene (**1a**) is expected to be initiated by oxidative *β*-arylation of benzo[*b*]thiophene *via* carbopalladation mechanism (*vide infra*). In fact, C–H arylation of benzo[*b*]thiophene (**1a**) also proceeded to give arylated products **9-α** and **9-β** in 27% combined yield with 93% *β*-selectivity when trimethylphenylsilane was used as a coupling partner under the influence of

Pd(OAc)₂/AgOTf/*o*-chloranil system (Scheme 8). Thus, *β*-arylation of benzo[*b*]thiophene would happen at first in the APEX with dibenzosilole.
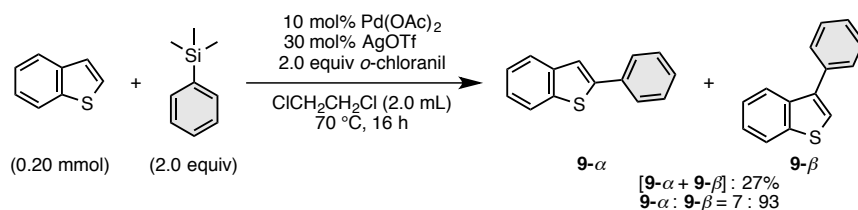
Scheme 8. Direct arylation of benzo[*b*]thiophene (**1a**) with trimethylphenylsilane[a]

(a) Reaction conditions: benzo[*b*]thiophene (**1a**) (0.20 mmol), trimethyl(phenyl)silane (2.0 equiv), Pd(OAc)₂ (10 mol%), AgOTf (30 mol%), *o*-chloranil (2.0 equiv), 1,2-dichloroethane (2.0 mL), 70 °C, 16 h. The ratio of **9-α** and **9-β** was determined by ¹H NMR.

Prior to *β*-arylation, transmetalation of dibenzosiloles with palladium(II) must occur. It is worth to note that a significant amount of hydrofluorinated by-product of dibenzosilole **10** was formed after the APEX of **1a** under the conditions shown in entry 13 of Table 1 (Scheme 9).[16] As well known in the transmetalation in Hiyama coupling with arylsilanes[17], the transmetalation of dibenzosilole could also occurred *via* (i) addition of anion such as F⁻ (PF₆⁻, OTf⁻, and AcO⁻ also have potential) to a silicon atom to provide a silicate intermediate, followed by (ii) electrophilic palladation (Scheme 10). Furthermore, by-product **10** is expected to form by the protonation of a silicate intermediate.
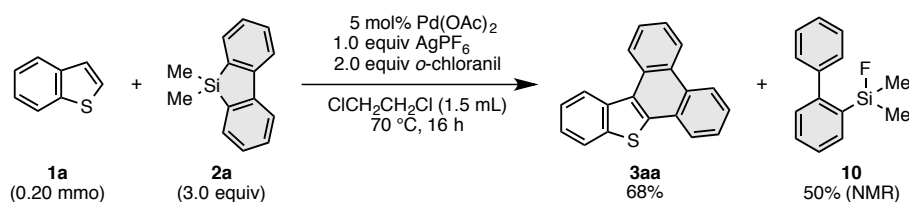
Scheme 9. APEX of benzo[*b*]thiophene accompanied with fluoride adduct **9**
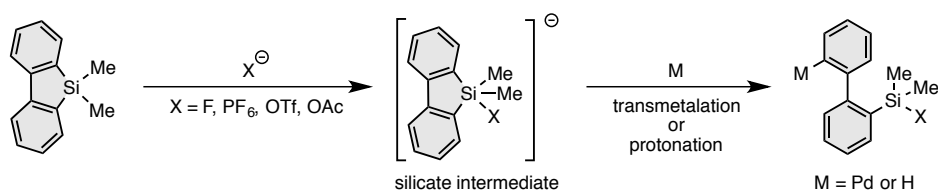
Scheme 10. Possible mechanism at transmetalation of dibenzosiloles

The result described in Scheme 6, which is the APEX of benzo[*b*]thiophene (**1a**) with 3-chlorodimethyldibenzosilole (**2c**), well supports the above mechanism. The selectivity of formation of regioisomers **3ac** and **3ac'** would be determined in the transmetalation of palladium and silicate intermediate. Preference of cleaving $C(sp^2)$– Si bond can be explained as follows; a sp^2-carbon on the chloro-substituted benzene ring more easily charges negatively due to an electron-withdrawing chloro substituent (**A**) than a sp^2-carbon on the other benzene ring (**B**). Thus transmetalation (palladation) could occur on the chloro-substituted benzene ring, which can lead to the selective formation of **3ac** through subsequent β-arylation and intramolecular α-arylation events (Scheme 11).
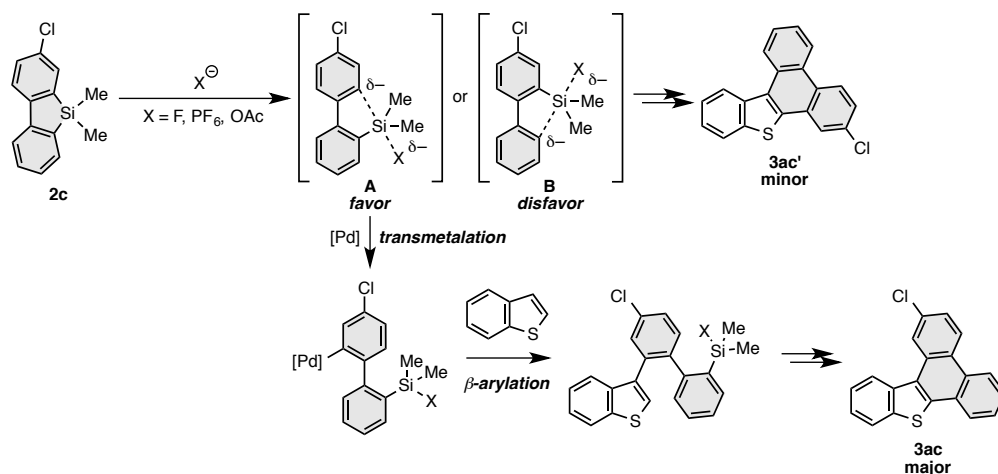
Scheme 11. Plausible mechanism of selective transmetalation/β-arylation in APEX of **2c**

On the premise that β-selective arylation of benzo[*b*]thiophene (**1a**) occurs at first, two possible pathways are assumable (Figure 6). Path A represents that intramoleculer transmatalation of intermediate **A** followed by reductive elimination would give the *cis*-dihydro adduct **C** which can be oxidized to provide APEX product **3aa**. Path B describes that β-H elimination in the carbopalladation intermediate **A** and sequential transmetalation/carbopalladation events to give the *trans*-fused precursor of APEX product **E** which can take place the second β-H elimination to produce the APEX product **3aa**.
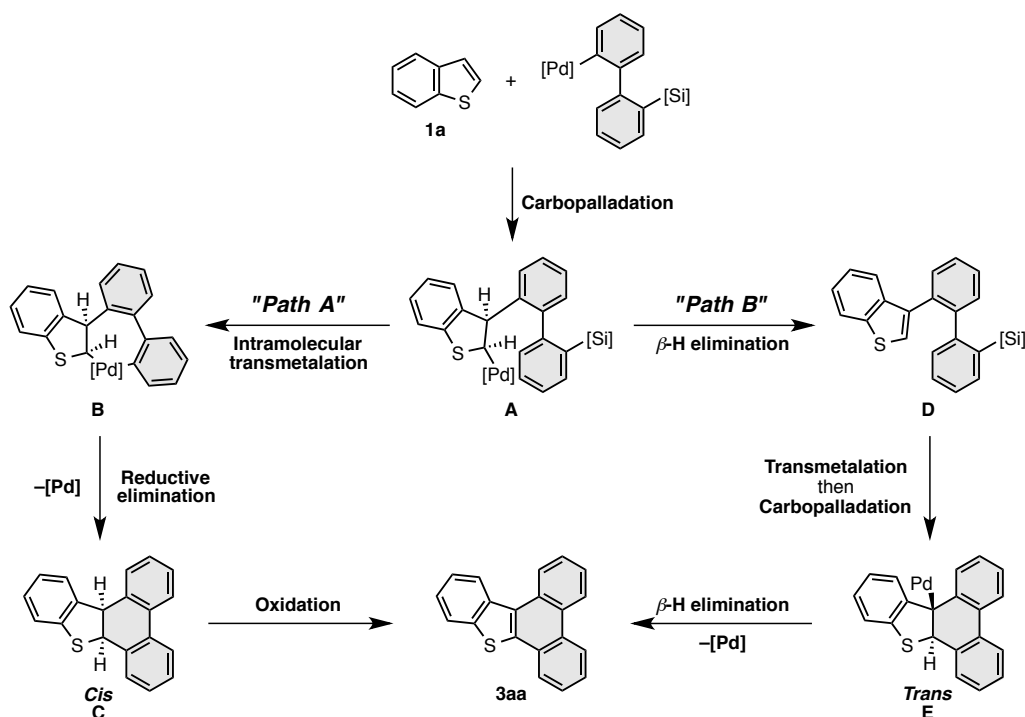
Figure 6. Plausible two reaction pathways in the carbopalladation-triggered APEX reaction of **1a**

In order to verify the both possible reaction pathways, several experiments on the mechanistic consideration were carried out (Schemes 12–15). It turned out that the APEX of benzofuran with dibenzogermole gave some useful insight about reaction mechanism (Scheme 12). When the reaction was conducted under the described condition in Scheme 12, *cis*-dihydro product **11** was obtained in 23% yield accompanied with 19% of APEX product **5**. The relative configuration of **11** was determined by X-ray crystallographic analysis (Figure 7), showing that two hydrogen atoms on the bridged position are located in *cis* position. This by-product **11** was readily oxidized by *o*-chloranil to afford APEX product **5** in 81% yield (Scheme 13). Although this phenomenon may be only the case of reaction with benzofuran, these results would support the existence of Path A.
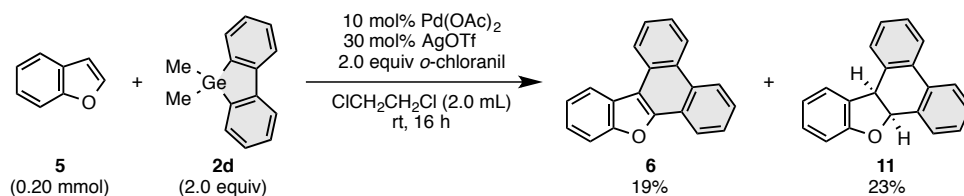
Scheme 12. Formation of APEX product **6** and *cis*-dihydro APEX product **11** in APEX of benzofuran **5** with dibenzogermole **2d**

$R_1 = 0.0321$,

$wR_2 = 0.0758$

$GOF = 1.034$

Space Group $P2_1/n$
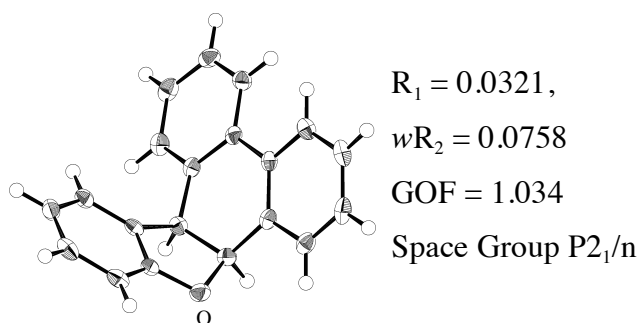
Figure 7. ORTEP drawing of intermediate **11** with 50% thermal ellipsoid
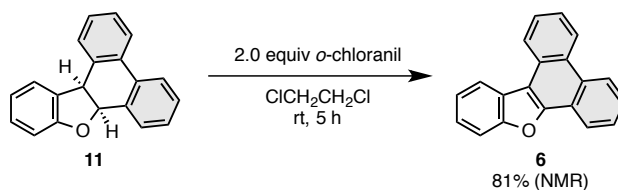
Scheme 13. Oxidation of *cis*-dihydro APEX product **11** with *o*-chloranil

To verify the existence of Path B, control experiments were carried out using trimethylsilylbiphenylbenzothiophene **12** as a model compound for intermediate **D** in Figure 6 (Scheme 14). The reaction of **12** under the standard reaction conditions for APEX proceeded well to give cyclized product **3aa** in 51% yield. This result indicates that Path B is also plausible.
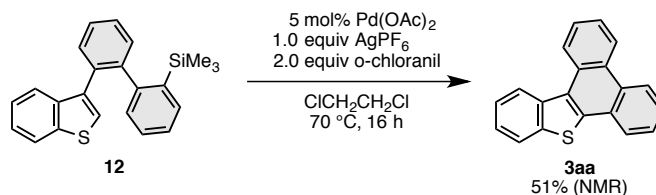
Scheme 14. Intramolecular C–H arylation of **12** under the standard reaction condition for APEX

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Encouraged by the result that β-biphenylbenzo[b]thiophene (4) was obtained in the APEX reaction of 1a with dibenzosilole 2a in the presence of DTBQ (Table 1, entry 10), experiments on another possible reaction pathways were also examined (Scheme 15). The both reactions of β- and α-biphenylbenzo[b]thiophene (4) and (13), which are potent by-products in the current APEX, gave the cyclodehydrogenation product 3aa only in 5% yields along with considerable decomposition of the starting material in the case of the reaction with 4. Hence these cyclodehydrogenations are possibly incorporated as alternative and minor pathways.
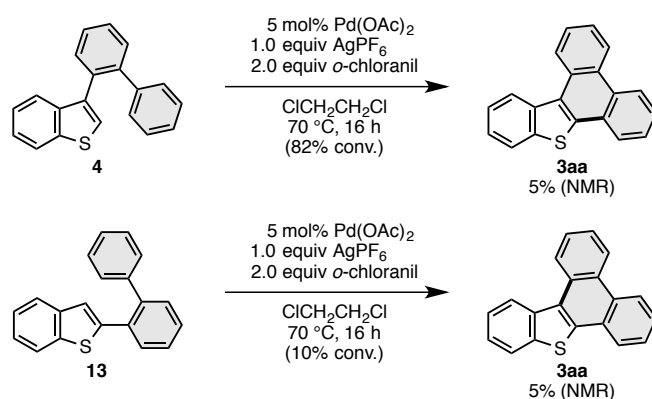
Scheme 15. Cylodehydrogenation of β- and α-biphenylbenzo[b]thiophene (4) and (13) for transformation to APEX product 3aa

As observed and considered above, plausible reaction mechanisms are summarized in Figure 8. At first, addition of anion species such as fluoride promotes the transmetalation of dibenzosilole 2a with palladium(II) to give arylpalladium species A that undergoes β-arylation *via* carbopalladation mechanism. Then the reaction proceeds through two pathways. Path A is involved in intramolecular transmetalation followed by reductive elimination to provide *cis*-dihydro APEX intermediate C that can be easily oxidized to APEX product 3aa. Path B is related to the double carbopalladation/β-H elimination sequence in inter- and intramolecular fashions. Additionally, cyclization from desilylated β-arylation product is maybe involved as a minor pathway.

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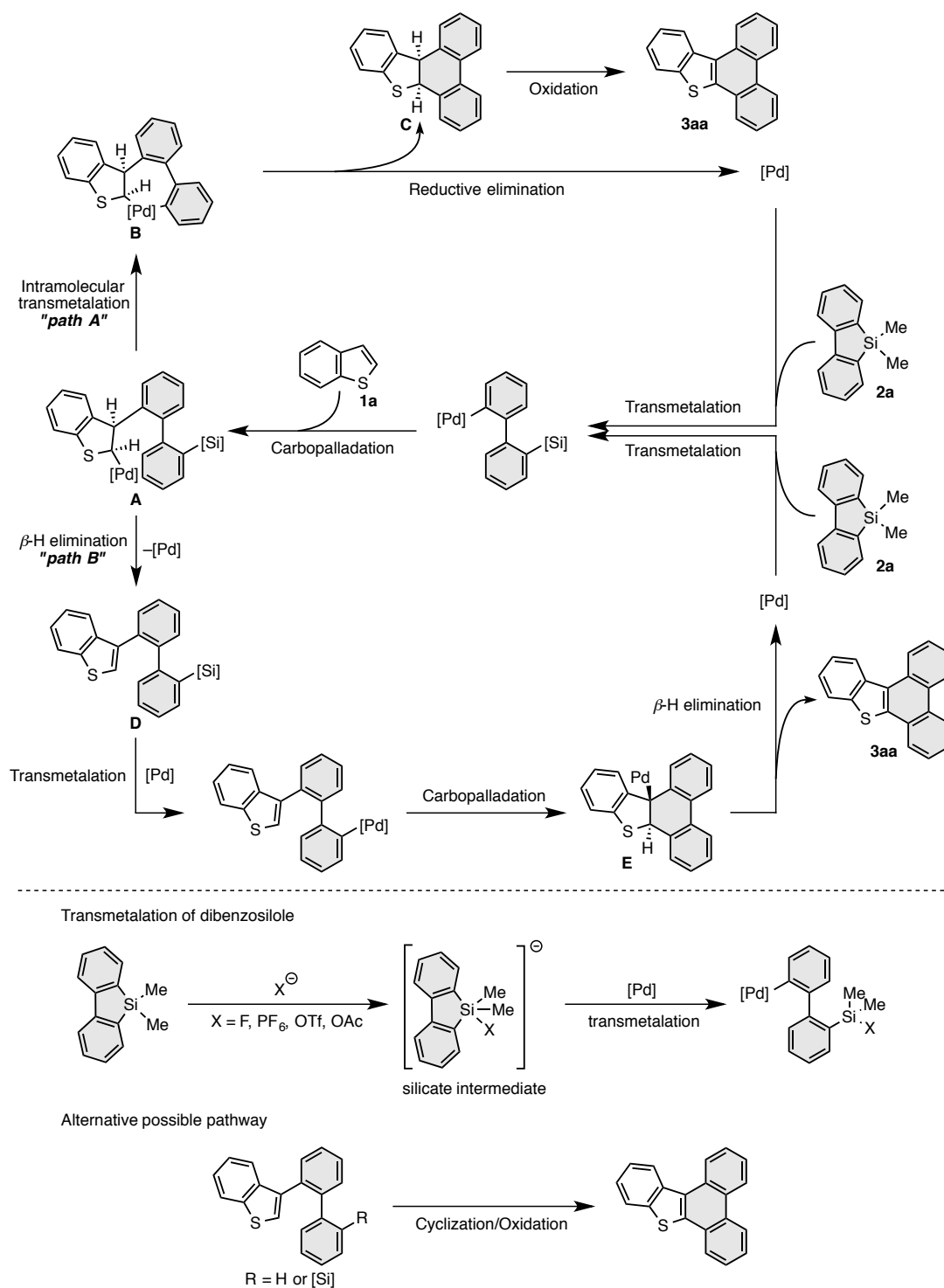
Figure 8. Overview of plausible reaction mechanisms

3. Conclusions

In summary, the annulative π-extension (APEX) reaction of heteroarenes such as thiophenes, benzofuran, and *N*-tosylindole as templates has been newly developed by using palladium catalyst, silver salts, and *o*-chloranil. The combination of π-extending agents such as dimethyldibenzosilole and dimethyldibenzogermole with silver hexafluorophosphate or silver triflate enables the synthesis of a variety of π-extended heteroarenes in one-shot. Investigation of reaction mechanism reveals that there are two possible pathways on the transmetalation/carbometalation sequence leading to APEX product. Current APEX methodology has obvious advantages over the existing stepwise π-extension methods in terms of step- and atom-economy.

4. Experimental Section

4-1. General

Unless otherwise noted, all materials including dry solvents were obtained from commercial suppliers and used without further purification. $Pd(OAc)_2$ was purchased from Wako. AgOTf was purchased from Wako and stored in glovebox filled by argon prior to use. $AgPF_6$ and $AgSbF_6$ were purchased from Aldrich and stored in glovebox filled by argon prior to use. *o*-Chloranil was purchased from TCI and recrystallized from benzene before use. Benzo[*b*]thiophene (**1a**) was purchased from Wako. 5-Bromobenzo[*b*]thiophene (**1d**) was purchased from TCI. 2,3-Benzofuran (**5**) was purchased from TCI and distilled before use. Benzo[*b*]thiophene derivatives (**1b**, **1c**, **1e**, **1f**)[18], 2,3-diphenylthiophene (**1g**)[19], and *N*-tosylindole (**7**)[20] were synthesized according to procedures reported in the literature. Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of nitrogen or argon in oven-dried glassware with standard vacuum-line techniques. All work-up and purification procedures were carried out with reagent-grade solvents in air

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} precoated plates (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with KANTO Silica Gel 60N (spherical, neutral, 40-100 μm). Preparative thin-layer chromatography (PTLC) was performed using Wako-gel® B5-F silica coated plates (0.75 mm) prepared in our laboratory. Preparative gel permeation chromatography (GPC) was performed with a JAI LC-9204 instrument equipped with JAIGEL-1H/JAIGEL-2H columns using chloroform as an eluent. Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). The developed chromatogram was analyzed by UV lamp (254 nm and 365 nm). High-resolution mass spectra (HRMS) were obtained from a JMS-T100TD instrument (DART). Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL ECS-600 (^{1}H 600 MHz, ^{13}C 150 MHz, ^{19}F 565 MHz) spectrometer and a JEOL ECA 600II with Ultra COOL™ probe (^{1}H 600 MHz, ^{13}C 150 MHz). Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm) or CD_2Cl_2 (δ 5.32 ppm). Chemical shifts for ^{13}C NMR

are expressed in ppm relative to CDCl$_3$ (δ 77.0 ppm) or CD$_2$Cl$_2$ (δ 53.84 ppm). Chemical shifts for ^{19}F NMR are expressed in parts per million (ppm) relative to hexafluorobenzene (δ −162.00 ppm) as an external standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration.

4-2. General procedure

In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgPF$_6$ (51 mg, 0.20 mmol, 1.0 equiv). The vessel was taken out of the glovebox, then to this was added benzo[*b*]thiophene **1** (0.20 mmol, 1.0 equiv), dibenzosilole **2** (0.60 mmol, 3.0 equiv), Pd(OAc)$_2$ (2.2 mg, 10 μmol, 5 mol%), and *o*-chloranil (98 mg, 0.40 mmol, 2.0 equiv), and 1,2-dichloroethane (1.5 mL) under a stream of nitrogen. After stirring for 16 h at 70 °C, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: hexane:CH$_2$Cl$_2$ = 1:1). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC to yield π-extended benzo[*b*]thiophenes.

Benzo[*b*]phenanthro[9,10-*d*]thiophene (3aa)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 39.0 mg, 68%, white solid.
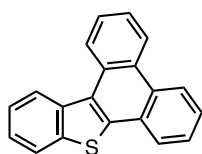
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.02 (d, *J* = 8.2 Hz, 1H), 8.81 (d, *J* = 8.9 Hz, 1H), 8.80 (d, *J* = 9.6 Hz, 1H), 8.71 (dd, *J* = 8.2, 0.8 Hz, 1H), 8.18 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.02 (d, *J* = 7.9 Hz, 1H), 7.76 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.70–7.64 (m, 3H), 7.58 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H),

7.49 (ddd, J = 7.8, 6.6, 1.2 Hz, 1H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 139.2, 138.3, 137.6, 129.9, 129.6, 129.4, 128.0 (2C), 127.32, 127.29 (2C), 125.6, 125.2, 125.1, 125.0, 124.7, 123.9, 123.8, 123.4, 123.2.

HRMS (DART, ESI$^+$) m/z calcd for C$_{20}$H$_{13}$S [M+H]$^+$: 285.0738, found: 285.0734.

12-(*tert*-Butyl)benzo[*b*]phenanthro[9,10-*d*]thiophene (3ba)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 34.6 mg, 51%, white solid.
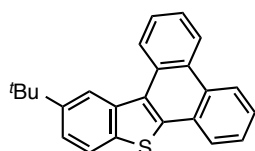
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.01 (d, J = 8.4 Hz, 1H), 8.82 (d, J = 1.8 Hz, 1H), 8.78 (d, J = 7.8 Hz, 1H), 8.69 (d, J = 8.4 Hz, 1H), 8.15 (dd, J = 7.2, 1.8 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.78 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 7.69–7.61 (m, 3H), 7.57 (dd, J = 8.4, 1.8 Hz, 1H), 1.53 (s, 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 148.0, 138.7, 137.7, 136.3, 130.0, 129.7, 129.3, 128.15, 128.12, 127.3, 127.2, 127.1, 125.4, 125.1, 123.85, 123.79, 123.4, 123.3, 122.6, 121.0, 35.1, 31.8.

HRMS (DART, ESI$^+$) m/z calcd for C$_{24}$H$_{21}$S [M+H]$^+$: 341.1364, found: 341.1353.

12-Methylbenzo[*b*]phenanthro[9,10-*d*]thiophene (3ca)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 25.1 mg, 42%, white solid.
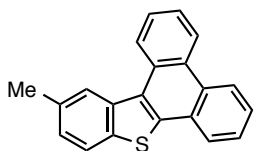
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.04 (d, J = 8.3 Hz, 1H), 8.81 (d, J = 8.3 Hz, 1H), 8.73 (d, J = 7.6 Hz, 1H), 8.63 (s, 1H), 8.18 (dd, J = 7.2, 1.0 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.79 (ddd, J = 8.4, 7.2, 1.8 Hz, 1H), 7.71–7.64 (m, 3H), 7.33 (dd, J = 7.8, 0.7 Hz, 1H), 2.64 (s, 3H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 138.7, 137.9, 136.3, 134.6, 130.0, 129.6, 129.4, 128.1, 127.8, 127.3, 127.23, 127.18, 126.7, 125.5, 125.1, 124.9, 124.0, 123.8, 123.4, 122.8, 22.1.

HRMS (DART, ESI$^+$) m/z calcd for C$_{21}$H$_{15}$S [M+H]$^+$: 299.0895, found: 299.0884.

**12-Bromobenzo[*b*]phenanthro[9,10-*d*]thiophene (3da)**

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 18.3 mg, 25%, white solid.
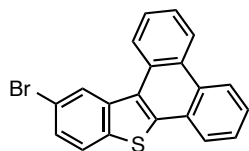
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.95 (d, *J* = 1.7 Hz, 1H), 8.91 (d, *J* = 7.6 Hz, 1H), 8.82 (d, *J* = 8.3 Hz, 1H), 8.74 (d, *J* = 8.3 Hz, 1H), 8.18 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.81 (ddd, *J* = 8.4, 6.6, 1.2 Hz, 1H), 7.75–7.67 (m, 3H), 7.60 (dd, *J* = 8.4, 1.8 Hz, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 139.6, 139.3, 137.8, 129.7 (2C), 129.6, 128.1, 127.8, 127.7, 127.6, 127.5, 127.4, 127.1, 126.0, 125.2, 124.4, 123.9, 123.7, 123.5, 119.1. HRMS (DART, ESI$^+$) *m/z* calcd for C$_{20}$H$_{12}$BrS [M+H]$^+$: 362.9843, found: 362.9830.

12-Chlorobenzo[*b*]phenanthro[9,10-*d*]thiophene (3ea)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 23.1 mg, 36%, white solid.
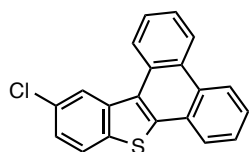
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.90 (d, *J* = 7.8 Hz, 1H), 8.81 (d, *J* = 8.4 Hz, 1H), 8.78 (s, 1H), 8.73 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.79 (t, *J* = 8.4 Hz, 1H), 7.74–7.66 (m, 3H), 7.47 (dd, *J* = 8.4, 1.8 Hz, 1H). ^{13}C NMR (150 MHz, CDCl$_3$) δ 139.7, 138.8, 137.3, 131.2, 129.64 (2C), 129.56, 127.7 (2C), 127.6, 127.5, 127.2, 125.9, 125.4, 125.2, 124.5, 124.0, 123.9, 123.7, 123.5. HRMS (DART, ESI$^+$) *m/z* calcd for C$_{20}$H$_{12}$ClS [M+H]$^+$: 319.0348, found: 319.0341.

12-Fluorobenzo[*b*]phenanthro[9,10-*d*]thiophene (3fa)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 13.5 mg, 22%, white solid.
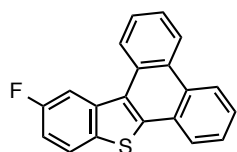
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.87 (d, *J* = 7.8 Hz, 1H), 8.81 (d, *J* = 8.2 Hz, 1H), 8.73 (d, *J* = 8.2 Hz, 1H), 8.48 (dd, $^3J_{H-F}$ = 11.4 Hz, *J* = 2.4 Hz, 1H), 8.17 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.94 (dd, *J* = 8.9 Hz, $^4J_{H-F}$ = 5.3 Hz, 1H), 7.78 (ddd, *J* = 7.8, 6.6, 0.6 Hz, 1H), 7.73–7.66 (m, 3H), 7.28–7.24 (m, 1H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 161.2 (d, $^1J_{\text{C–F}}$ = 240.0 Hz), 140.3, 138.6 (d, $^3J_{\text{C–F}}$ = 8.7 Hz), 134.4, 129.64, 129.58 (2C), 127.9, 127.7, 127.6, 127.5, 127.4, 125.8, 125.2, 124.0 (d, $^3J_{\text{C–F}}$ = 10.0 Hz), 123.9, 123.5, 123.4, 113.5 (d, $^2J_{\text{C–F}}$ = 24.5 Hz), 111.0 (d, $^2J_{\text{C–F}}$ = 24.5 Hz).

^{19}F NMR (564 MHz, CDCl$_3$) δ –117.3.

HRMS (DART, ESI$^+$) m/z calcd for C$_{20}$H$_{12}$FS [M+H]$^+$: 303.0644, found: 303.0640.

2,7-Di-*tert*-butylbenzo[*b*]phenanthro[9,10-*d*]thiophene (3ab)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 22.4 mg, 28%, white solid.
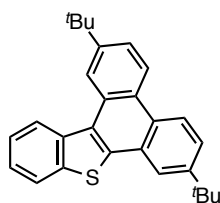
^{1}H NMR (600 MHz, CDCl$_3$) δ 9.02 (d, J = 1.7 Hz, 1H), 8.82 (d, J = 8.2 Hz, 1H), 8.71 (d, J = 8.9 Hz, 1H), 8.63 (d, J = 8.6 Hz, 1H), 8.12 (d, J = 2.0 Hz, 1H), 8.04 (d, J = 7.9 Hz, 1H), 7.75 (dd, J = 8.9, 2.0 Hz, 2H), 7.61 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 1.57 (s, 9H), 1.51 (s, 9H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 150.0, 149.7, 139.3, 138.6, 137.9, 129.6, 128.3, 127.5, 127.4, 127.2, 125.6, 125.0, 124.9, 124.5, 123.7, 123.4, 123.3, 123.1, 120.8, 120.0, 35.2, 35.0, 31.6, 31.4.

HRMS (DART, ESI$^+$) m/z calcd for C$_{28}$H$_{28}$S [M]$^+$: 396.1912, found: 396.1913.

2-Chlorobenzo[*b*]phenanthro[9,10-*d*]thiophene (3ac)

PTLC: hexane:CH$_2$Cl$_2$ = 15:1, Yield: 24.0 mg, 38% as a mixture of **3ac** and **3ac'** (78:22), white solid. **3ac** was isolated by recrystallization (CHCl$_3$/hexane), and identified by ^{1}H and ^{13}C NMR comparing with NMR spectra of the mixture of **3ac** and **3ac'**.
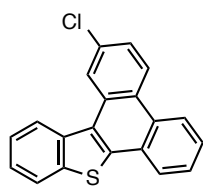

^{1}H NMR of **3ac** (600 MHz, CDCl$_3$) δ 8.98 (d, J = 2.4 Hz, 1H), 8.75 (d, J = 8.4 Hz, 1H), 8.73 (d, J = 8.4 Hz, 1H), 8.68–8.65 (m, 1H), 8.21–8.18 (m, 1H), 8.04 (dd, J = 7.8, 0.6 Hz, 1H), 7.73–7.67 (m, 2H), 7.67–7.61 (m, 2H), 7.53 (ddd, J = 8.4, 7.2, 1.2 Hz, 1H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 139.5, 139.1, 137.1, 133.4, 130.8, 128.8, 128.0, 127.9, 127.6 (2C), 126.9, 125.9, 125.4, 125.3, 125.2 (2C), 124.3, 123.4, 123.29, 123.28.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{20}$H$_{12}$ClS [M+H]$^+$: 319.0348, found: 319.0345.

2,3-Diphenylphenanthro[9,10-*b*]thiophene (3ga)

PTLC: hexane:CH$_2$Cl$_2$ = 10:1, Yield: 38.6 mg, 50%, white solid.
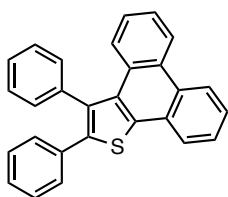
^{1}H NMR (600 MHz, CD$_2$Cl$_2$) δ 8.74–8.69 (m, 2H), 8.25–8.22 (m, 1H), 7.68–7.65 (m, 2H), 7.56 (dd, *J* = 8.4, 0.7 Hz, 1H), 7.53 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.49–7.46 (m, 3H), 7.43–7.41 (m, 2H), 7.34–7.31 (m, 2H), 7.26–7.23 (m, 3H), 7.22 (ddd, *J* = 9.0, 7.2, 1.8 Hz, 1H).

^{13}C NMR (150 MHz, CD$_2$Cl$_2$) δ 139.8, 138.8, 137.3, 136.8, 134.8, 133.9, 131.2, 130.3, 130.2, 129.9, 129.4, 128.8, 128.6, 128.32, 128.26, 127.9, 127.8, 127.0, 126.6, 126.0, 125.0, 124.4, 123.91, 123.87.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{28}$H$_{19}$S [M+H]$^+$: 387.1208, found: 387.1207.

Phenanthro[9,10-*b*]benzofuran (6)
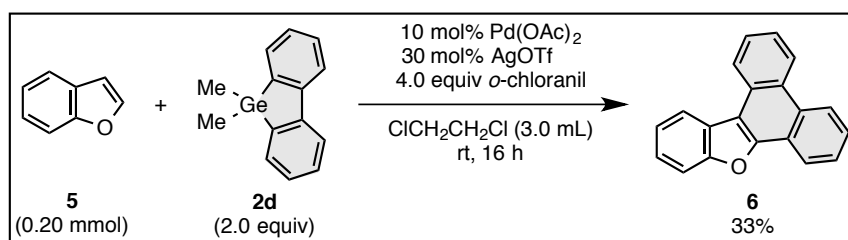
In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgOTf (15 mg, 60 μmol, 30 mol%). The vessel was taken out of the glovebox, then to this was added benzofuran **5** (24 mg, 0.20 mmol, 1.0 equiv), dimethyldibenzogermole **2d** (102 mg, 0.40 mmol, 2.0 equiv), Pd(OAc)$_2$ (4.5 mg, 20 μmol, 10 mol%), and 1,2-dichloroethane (1.0 mL) under a stream of nitrogen. Then, a 0.40 M solution of *o*-chloranil in 1,2-dichloroethane (2.0 mL, 0.80 mmol, 4.0 equiv) was slowly added by using syringe pump (rate: 0.50 mL/h) with stirring at room

temperature. After 16 h, the reaction mixture was passed through a short pad of silica gel (eluent: hexane:CH_2Cl_2 = 1:1). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC (hexane : CH_2Cl_2 = 15 : 1) to afford phenanthro[9,10-*b*]benzofuran (**6**) (17.8 mg, 33%) as a white solid.
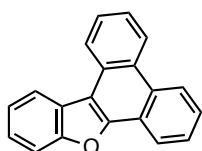
^{1}H NMR (600 MHz, CDCl$_3$) δ 8.79 (d, *J* = 7.8 Hz, 1H), 8.77–8.74 (m, 1H), 8.65 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.53–8.50 (m, 1H), 8.40–8.38 (m, 1H), 7.80–7.70 (m, 4H), 7.68 (ddd, *J* = 7.8, 6.6, 1.2 Hz, 1H), 7.52–7.46 (m, 2H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 155.8, 151.2, 130.5, 128.5, 128.2, 127.4, 127.15, 127.08, 125.6, 125.4, 125.1, 124.1, 123.8, 123.41, 123.35, 122.2, 121.74, 121.68, 114.3, 112.0.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{20}$H$_{13}$O [M+H]$^+$: 269.0966, found: 269.0959.
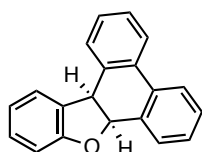

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.91–7.88 (m, 1H), 7.85 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.68 (dd, *J* = 7.3, 0.7 Hz, 1H), 7.49–7.47 (m, 1H), 7.39 (td, *J* = 7.1, 1.2 Hz, 1H), 7.36–7.32 (m, 3H), 7.25 (d, *J* = 6.2 Hz, 1H), 7.11 (t, *J* = 7.9 Hz, 1H), 6.86 (td, *J* = 7.6, 1.0 Hz, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 5.99 (d, *J* = 8.6 Hz, 1H), 4.74 (d, *J* = 8.9 Hz, 1H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 158.7, 132.6, 132.4, 131.8, 131.3, 130.5, 129.6 (2C), 129.3, 128.4, 128.23, 128.19, 127.7, 124.7, 123.6, 123.0, 120.9, 110.0, 81.9, 44.4.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{20}$H$_{15}$O [M+H]$^+$: 271.1123, found: 271.1115.

9-Tosyl-9*H*-dibenzo[*a,c*]carbazole (8)
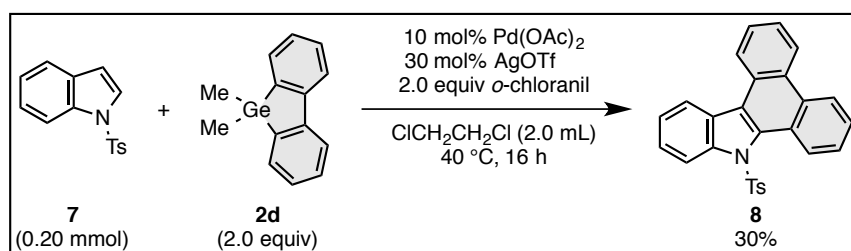
In the glovebox, to a screw cap glass tube containing a magnetic stirrer bar was added AgOTf (15 mg, 60 μmol, 30 mol%). The vessel was taken out of the glovebox,

then to this was added *N*-tosylindole **7** (54.3 mg, 0.20 mmol, 1.0 equiv), dimethyldibenzogermole **2d** (102 mg, 0.40 mmol, 2.0 equiv), Pd(OAc)$_2$ (4.5 mg, 20 μmol, 10 mol%), and *o*-chloranil (98 mg, 0.40 mmol, 2.0 equiv), and 1,2-dichloroethane (2.0 mL) under a stream of nitrogen. After stirring for 16 h at 40 °C, the reaction mixture was cooled to room temperature, and then passed through a short pad of silica gel (eluent: hexane:Et$_2$O = 1:1). After the organic solvent was removed under reduced pressure, the residue was purified by PTLC (hexane:Et$_2$O = 4:1) to afford 9-tosyl-9*H*-dibenzo[*a,c*]carbazole (**8**) (25.1 mg, 30%) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.98–8.95 (m, 1H), 8.82–8.78 (m, 1H), 8.74–8.72 (m, 1H), 8.55–8.53 (m, 1H), 8.41 (d, *J* = 8.2 Hz, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.76–7.66 (m, 4H), 7.46 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.41 (td, *J* = 7.1, 1.0 Hz, 1H), 6.83 (d, *J* = 8.2 Hz, 2H), 6.67 (d, *J* = 7.9 Hz, 2H), 2.07 (s, 3H).

^{13}C NMR (150 MHz, CDCl$_3$) δ 144.2, 142.0, 136.9, 131.0, 130.7, 130.6, 130.1, 128.7, 128.4, 127.6, 127.2, 127.0, 126.9, 126.3, 126.1, 125.91, 125.85, 125.6, 124.2, 124.0, 123.7, 122.8, 121.8, 119.9, 21.3.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{27}$H$_{19}$NO$_2$S [M]$^+$: 421.1137, found: 421.1152.

4-3. X-ray Crystal Structure Analysis of 3da and 11

Recrystallization of **3da** and **11** from CHCl$_3$/*n*-pentane yielded colorless crystals of **3da** and **11** suitable for X-ray crystal structure analysis. Details of the crystal data and a summary of the intensity data collection parameters for **3da** and **11** are listed in Table 3. A suitable crystal was mounted with mineral oil on a glass fiber and transferred to the goniometer of a Rigaku Saturn CCD diffractometer. Graphite-monochromated Mo Ka radiation ($l = 0.71070$ Å) was used. The structures were solved by direct methods with (SIR-97)[21] or (SHELXS-97)[22] and refined by full-matrix least-squares techniques against F^2 (SHELXL-97)[22]. The intensities were corrected for Lorentz and polarization effects. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed using AFIX instructions.

Table 3. Crystallographic data and structure refinement details for **3da** and **11**

	3da	11
formula	$C_{20}H_{11}BrS$	$C_{20}H_{14}O$
fw	363.26	270.31
T (K)	123(2)	123(2)
l (Å)	0.71075	0.71075
cryst syst	monoclinic	monoclinic
space group	$P2_1/n$	$P2_1/n$
a, (Å)	5.1414(5)	4.6243(8)
b, (Å)	15.2261(18)	15.592(3)
c, (Å)	18.358(2)	18.442(4)
a, (deg)	90	90
b, (deg)	97.590(3)	95.480(4)
g, (deg)	90	90
V, (Å^3)	1424.5(3)	1323.6(4)
Z	4	4
D_{calc}, (g / cm^3)	1.694	1.356
m (mm^{-1})	3.024	0.082
F(000)	728	568
cryst size (mm)	0.25 x 0.10 x 0.05	0.20 x 0.05 x 0.03
$2q$ range, (deg)	3.49 – 25.00°	3.43 – 25.00°
reflns collected	10270	9428
indep reflns/R_{int}	2479/0.0213	2337/0.0193
params	199	190
GOF on F^2	1.037	1.034
R_1, wR_2 [I>2s(I)]	0.0212, 0.0544	0.0321, 0.0758
R_1, wR_2 (all data)	0.0271, 0.0569	0.0439, 0.0820

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One-shot Indole-to-carbazole π-Extension by a Pd-Cu-Ag Trimetallic System

Abstract

A Pd-Cu-Ag trimetallic system that can convert indoles to carbozoles using electron-deficient alkenes as two-carbon units is described. Investigation of reaction mechanism revealed that this one-shot indole-to-carbozole π-extension is likely to proceed through the sequence of (i) Pd/Cu-catalyzed indole C–H alkenylation, (ii) Ag-promoted Diels–Alder reaction, and (iii) Ag-promoted dehydrogenative aromatization. The successful one-pot synthesis of granulatimide derivative, an interesting class of Chk1 kinase inhibitor, highlights the potential of the present reaction for further development and applications.

1. Introduction

Carbazole, which was first isolated in 1872 by Graebe and Glasere from coal tar, is the common structural motif found in numerous biologically active natural products (Figure 1).[1] Since the isolation of carbazole derivative ellipticine from the plant of *Ochrosia elliptica* Labill in 1959,[2] various naturally occurring carbazoles have attracted a great deal of attention in fields related to pharmaceuticals and agricultural chemicals due to their unique biological activity. In recent years, carbazole cores are also widely used in photorefractive materials and organic dyes for solar cells.[3]

Ellipticine
topoisomerase II inhibitor

Murrayanine
antimicrobial

Carbazomycin B
5-lipoxygenase inhibitor

Granulatimide
Chk1 kinase inhibitor

PVK
photorefractive material

MK-1 (n = 3), MK-2 (n = 4)
organic dye for DSSCs
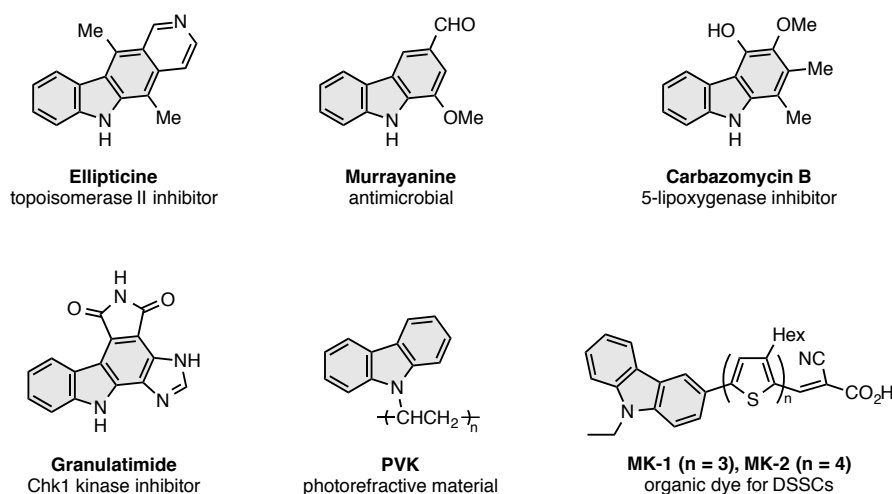
Figure 1. Carbazoles found in bioactive natural products and electronic materials

Therefore, various synthetic methodologies for making carbazoles have been developed such as C–C and C–N bond-forming coupling reaction, cyclization, Diels–Alder reaction, and so on (Figure 2).[4] However, those classical methods require multi-step sequences or pre-functionalization of reaction components to construct the carbazole backbones. Therefore more efficient and practical approaches are demanded from the view point of reducing overall steps and increasing yields.
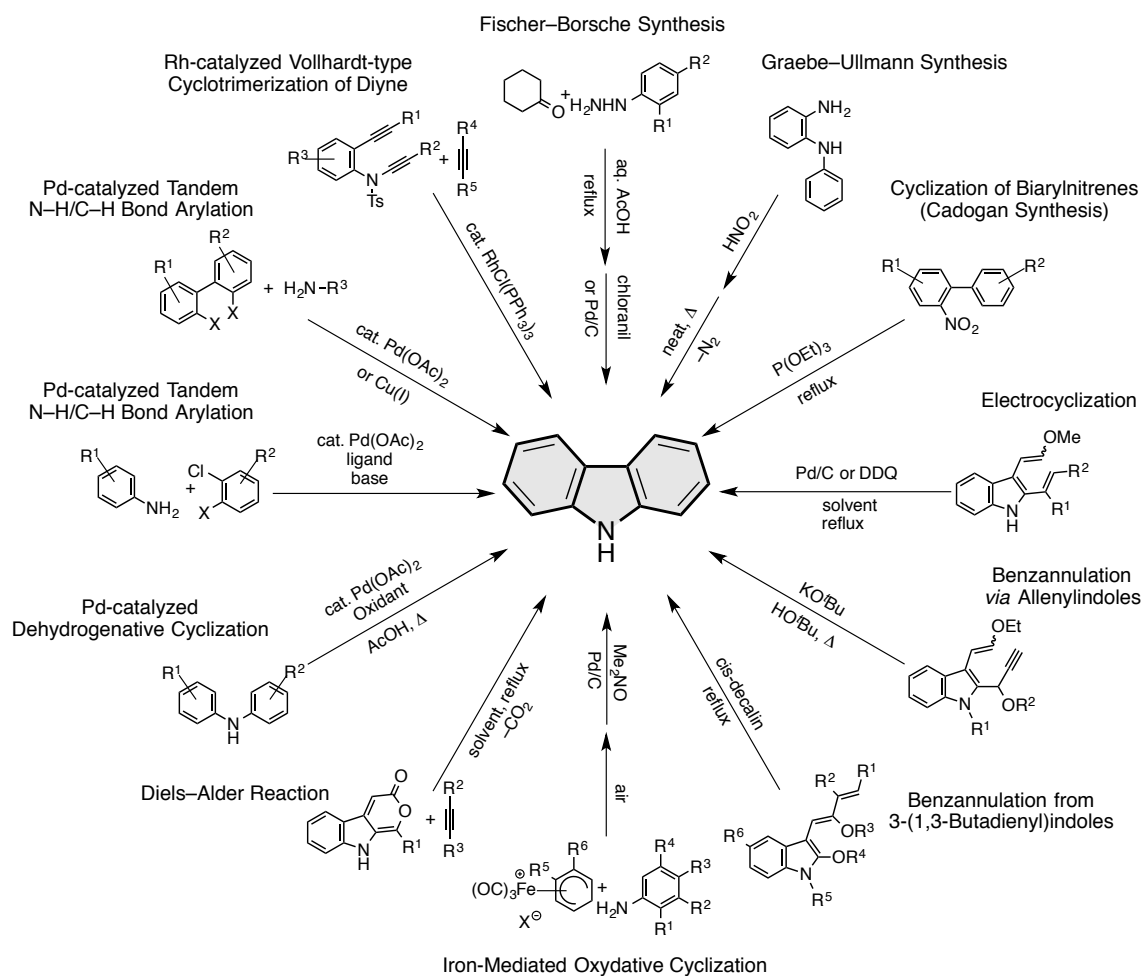
Figure 2. Methods to construct carbazoles

In recent years, indole-to-carbazole transformations, so-called one-shot annulative π-extension (APEX) of indole, have attracted much attention because of a ready availability of indoles. For example, Miura reported Pd-catalyzed formal [2+2+2] cycloaddition of indoles with diarylacetylenes to give tetraarylated carbazoles (Scheme 1).[5,6] Although there are other reports on the direct APEX of indoles to carbazoles,[7] the synthetic utility and the substrate scope remain relatively unexplored.
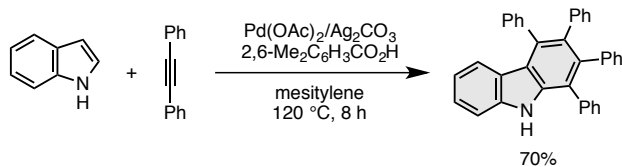
Scheme 1. Pd-catalyzed formal [2+2+2] cycloaddition of indoles with diarylacetylenes

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In this chapter, an indole-to-carbazole π-extension with vinyl compounds as two-carbon units is described. An interesting Pd-Cu-Ag trimetallic system allows to conduct this otherwise-difficult transformation in one-shot.

2. Results and Discussion

2-1. Working hypothesis

Toward the development of novel indole-to-carbazole APEX reaction, direct transformations of C–H bonds on C3- and C2-position of unfunctionalized indole should be needed albeit these are expected to be challenging. In 2005, Gaunt and co-workers reported C3-selective C–H alkenylation of indoles with acrylic esters by $Pd(OAc)_2/Cu(OAc)_2$ catalytic system.[8-10] The described possible reaction mechanism is based on Fujiwara–Moritani reaction ($Pd(OAc)_2$-catalyzed oxidative Heck reaction between benzene and styrene)[6] that demonstrates sequential (i) electrophilic palladation of indole to form (indol-3-yl)palladium(II), (ii) olefin insertion, (iii) β-H elimination to release the 3-alkenylindole and Pd(0), and (iv) reoxidation of Pd(0) to Pd(II) by stoichiometric amount of $Cu(OAc)_2$ (Figure 3). Gaunt also demonstrated the C2-selective alkenylation of indole just by simply changing the solvent.
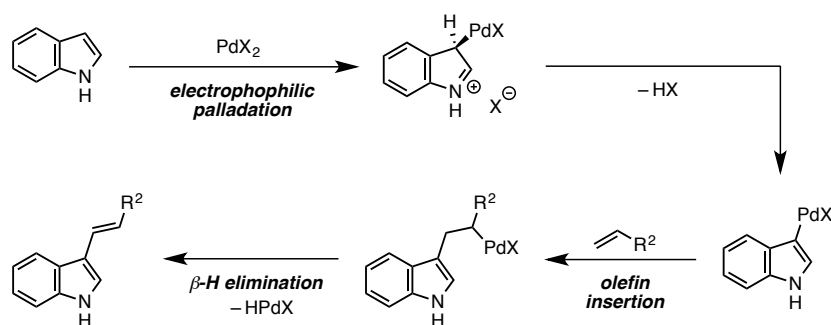
Figure 3. Proposed mechanism of C–H alkenylation of indole at C3 position

Taking these impressive works on C–H alkenylations into considerations, two possible APEX routes from indole to carbazole were envisioned as follows (Figure 4). Pathway A represents a sequential double C3 and C2 alkenylations of indole followed by cyclization and oxidation to furnish the 2,3-disubstituted carbazole. Pathway B is regarding to a successive C3 alkenylation of indole, Diels–Alder reaction with another alkene molecule, and oxidative aromatization to provide 1,3-disubstituted carbazole. Exploring various two-carbon π-extending units, palladium and copper catalysts, oxidants as well as the reaction conditions will lead to offer a novel indole-to-carbazole APEX reaction.
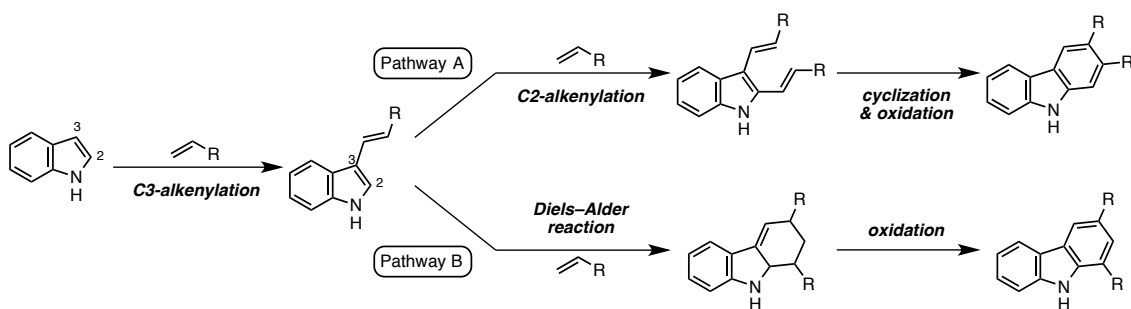
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Figure 4. Working hypothesis for one-shot APEX of indole

2-2. Discovery of Pd-Cu-Ag trimetallic system

Based on the working hypothesis, the author began exploring one-shot, indole-to-carbozole APEX reaction. Extensive screening revealed the combination of *N*-methylindole (**1a**, 0.20 mmol) as an arene template and methyl vinyl ketone (**2a**) (MVK, 10 equiv) as a two-carbon π-extending agent furnished 1,3-diacetylcarbazole (**3aa**) in 30% isolated yield without any regioisomers in the presence of catalytic amount of Pd(OAc)$_2$/Cu(OAc)$_2$ with AgOCOCF$_3$ (4.0 equiv) in toluene (1.0 mL) at 100 °C under air (Scheme 2). Both **1a** and **2a** were fully consumed after the reaction. The decomposed and/or oligomeric by-products derived from **1a** and **2a** were detected to some extent. The structure of **3aa** was confirmed by ^{1}H NMR, ^{13}C NMR and X-ray crystallographic analysis shown in Figure 5.[11]
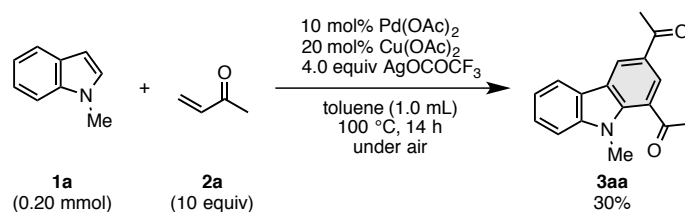
Scheme 2. One-shot APEX of *N*-methylindole (**1a**) with methyl vinyl ketone (**2a**)

R$_1$ = 0.0477

*w*R$_2$ = 0.0909

GOF = 1.113

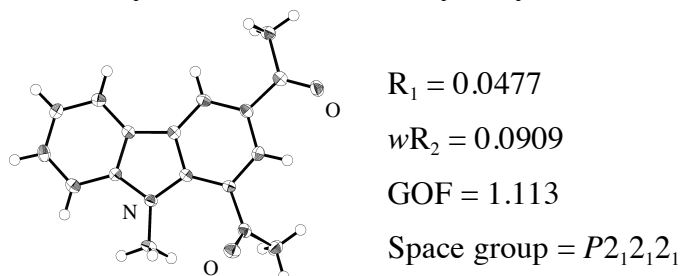Space group = *P*2$_1$2$_1$2$_1$

Figure 5. ORTEP drawing of 1,3-diacetylcarbazole (**3aa**) with 50% thermal ellipsoid

2-3. Screening of detail reaction conditions

Motivated by the above results, the optimization of detail reaction conditions regarding to the effects of solvent and reaction temperature was investigated (Table 1). Changing the solvent from toluene to DMSO and 1,4-dioxane increased the yields of **3aa** (entries 2 and 3). However, the use of DMF as solvent gave the product in lower yield (entry 4). Addition of small amount of DMSO (5% v/v) to 1,4-dioxane or toluene resulted in the higher yields of **3aa** than the reactions without DMSO (entries 5 and 6). In particular, the use of toluene/DMSO mixed solvent system was critical for high-yield production of desired carbazole **3aa** (70% isolated yield, entry 6). The reaction in toluene/DMSO at lower temperature (80 °C) resulted in significant decrease of yield (entry 7). On the other hand, considerable decomposition and polymerization of **1a** were observed at higher temperature (120 °C), resulting in decrease of yield (entry 8). As a result, the addition of small amount of DMSO plays a crucial role in this reaction. A polar solvent such as DMSO might prevent the deactivation of active Pd(0) and/or Pd(II) species.

Table 1. Effect of solvent and reaction temperature[a]

entry	solvent	volume	temperature	GC yield[b]
1	toluene	1.0 mL	100 °C	30%
2	DMSO	1.0 mL	100 °C	46%
3	1,4-dioxane	1.0 mL	100 °C	50%
4	DMF	1.0 mL	100 °C	18%
5	1,4-dioxane/DMSO	1.0 mL/50 μL	100 °C	49%
6	toluene/DMSO	1.0 mL/50 μL	100 °C	70%[c]
7	toluene/DMSO	1.0 mL/50 μL	80 °C	33%
8	toluene/DMSO	1.0 mL/50 μL	120 °C	40%

(a) Reaction conditions: *N*-methylindole (**1a**) (0.20 mmol), methyl vinyl ketone (**2a**) (10 equiv), Pd(OAc)$_2$ (10 mol%), Cu(OAc)$_2$ (20 mol%), AgOCOCF$_3$ (4.0 equiv), solvent, 14 h. (b) GC yield was calculated using *n*-dodecane as an internal standard. (c) Isolated yield.

The optimization results of palladium and copper catalysts are summarized in Table 2. Both Pd(0) and Pd(II) catalysts promoted the reaction (entries 1-4), and Pd(OAc)$_2$ showed the best performance for this reaction (entry 1). Very interestingly, **3aa** was obtained in 30% yield even in the absence of palladium catalyst (entry 5), of which details are discussed in Section 2-6. Addition of 1.0 equivalent of Cu(OAc)$_2$ or copper salts having a variety of other counter anions, for example trifluoroacetate, chloro, bromo, fluoro, and triflate anions, did not enhance the reaction well (entries 6-13). Although the APEX reaction proceeded without Cu(OAc)$_2$ in 27% yield (entry 14), addition of 20 mol% of Cu(OAc)$_2$ was beneficial to produce **3aa** in high yield.

Table 2. Investigation of Pd and Cu catalysts[a]
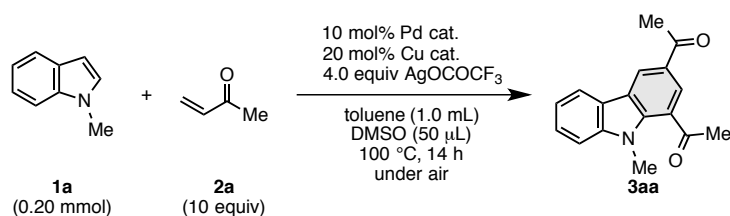
entry	Pd cat.	Cu cat.	GC yield[b]
1	Pd(OAc)$_2$	Cu(OAc)$_2$	70%[c]
2	Pd(OCOCF$_3$)$_2$	Cu(OAc)$_2$	47%
3	PdI$_2$	Cu(OAc)$_2$	39%
4	Pd$_2$(dba)$_3$·CHCl$_3$	Cu(OAc)$_2$	40%
5	none	Cu(OAc)$_2$	30%
6[d]	Pd(OAc)$_2$	Cu(OAc)$_2$	46%
7	Pd(OAc)$_2$	Cu(OCOCF$_3$)$_2$·H$_2$O	36%
8	Pd(OAc)$_2$	CuCl$_2$	31%
9	Pd(OAc)$_2$	CuBr$_2$	37%
10	Pd(OAc)$_2$	CuF$_2$	36%
11	Pd(OAc)$_2$	CuO	32%
12	Pd(OAc)$_2$	Cu(OTf)$_2$	25%
13	Pd(OAc)$_2$	Cu(acac)$_2$	39%
14	Pd(OAc)$_2$	none	27%

(a) Reaction conditions: *N*-methylindole (**1a**) (0.20 mmol), methyl vinyl ketone (**2a**) (10 equiv), Pd catalyst (10 mol%), Cu catalyst (20 mol%), AgOCOCF$_3$ (4.0 equiv), toluene (1.0 mL), DMSO (50 μL), 100 °C, 14 h. (b) GC yield was calculated using *n*-dodecane as an internal standard. (c) Isolated yield. (d) Cu(OAc)$_2$ (1.0 equiv).

The effect of silver salts is summarized in Table 3. The employment of 4.0 equivalent of AgOCOCF$_3$ presented most significant effect to give **3aa** in 70% yield (entry 1). However, decreasing the amount of AgOCOCF$_3$ to 2.0 equivalent and 0 equivalent resulted in 30% and 0% yields of **3aa**, respectively (entries 2 and 3). Although AgOAc slightly enhanced the reaction (entry 4), other silver salts did not show any acceleration effect of the reaction (entries 5–9).

Table 3. The effects of silver salt[a]

entry	Ag salt		GC yield[b]
1	AgOCOCF$_3$	(4.0 equiv)	70%[c]
2	AgOCOCF$_3$	(2.0 equiv)	31%
3	AgOCOCF$_3$	(5.0 equiv)	41%
4	AgOAc	(4.0 equiv)	35%
5	Ag$_2$CO$_3$	(4.0 equiv)	6%
6	AgBF$_4$	(4.0 equiv)	3%
7	AgPF$_6$	(4.0 equiv)	2%
8	AgSbF$_6$	(4.0 equiv)	1%
9	AgOTf	(4.0 equiv)	0%

(a) Reaction conditions: *N*-methylindole (**1a**) (0.20 mmol), methyl vinyl ketone (**2a**) (10 equiv), Pd(OAc)$_2$ (10 mol%), Cu(OAc)$_2$ (20 mol%), Ag salt (4.0 equiv), toluene (1.0 mL), DMSO (50 μL), 100 °C, 14 h. (b) GC yield was calculated using *n*-dodecane as an internal standard. (c) Isolated yield.

As explained above, the optimal reaction conditions to produce desired carbazole **3aa** was determined as the combination of Pd(OAc)$_2$ and Cu(OAc)$_2$ catalyst, AgOCOCF$_3$ (4.0 equiv) in toluene/DMSO (v/v = 20/1) at 100 °C under air (Scheme 3).
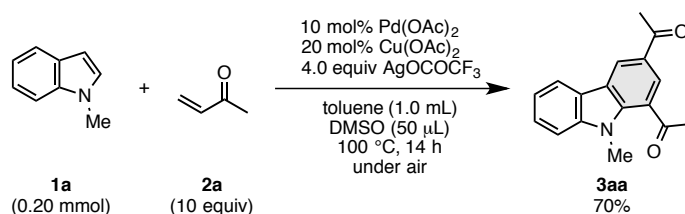

Scheme 3. Optimal reaction conditions for one-shot APEX of *N*-methylindole with methyl vinyl ketone

2-4. Substrate Scope

Next the substrate scope of vinyl compounds was investigated (Table 4). Other than methyl vinyl ketone, aryl or alkyl vinyl ketones were found to be applicable to the indole-to-carbazole π-extension reaction. Employing a series of phenyl vinyl ketones (**2b–2e**) gave the corresponding 1,3-dibenzoylcarbazoles (**3ab**, **3ac**, **3ad**, and **3ae**) in 37–61% isolated yields. The reaction with cyclohexyl vinyl ketone (**2f**) afforded the corresponding carbazole **3af** in somewhat lower yield (24% yield). Interestingly, it was found that the π-extension using methyl acrylate (**2g**) as a two-carbon unit proceeded well to give the carbazole **3ag** having two ester groups that are potentially transformable and removable.

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Table 4. APEX of *N*-methylindole (**1a**) with various aryl/alkyl vinyl ketones (**2b–2f**) and methyl acrylate (**2g**)[a]

1a
(0.20 mmol)

2b-2g
(10 equiv)

3

3ab
53%

3ac
50%

3ad
37%

3ae
61%

3af
24%

3ag
44%[b]
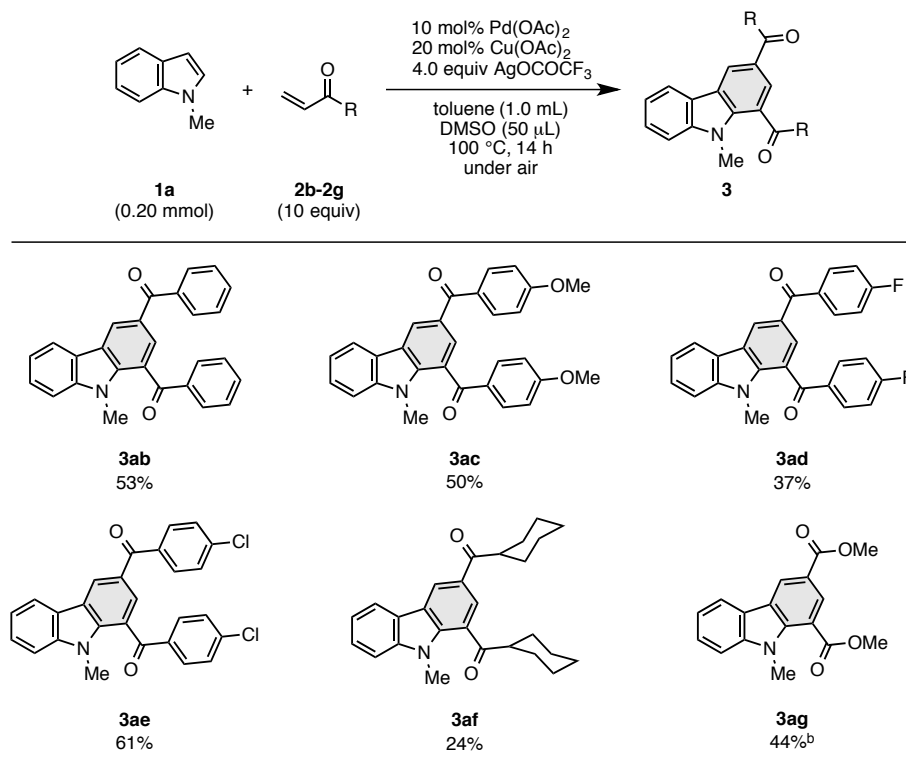
(a) Reaction conditions: *N*-methylindole (**1a**) (0.20 mmol), **2** (10 equiv), Pd(OAc)$_2$ (10 mol%), Cu(OAc)$_2$ (20 mol%), AgOCOCF$_3$ (4.0 equiv), toluene (1.0 mL), DMSO (50 μL), air, 100 °C, 14 h. Indicated yields are isolated yields. (b) DMSO (1.0 mL) was used as solvent.

The present one-shot indole-to-carbazole π-extension proved to be applicable to other indoles (Table 5). For example, the reactions of *N*-benzylindole (**1b**) and unsubstituted indole (**1c**) with **2a** furnished the corresponding carbazoles (**3ba** and **3ca**) in moderate yields. The reactions of indoles bearing electron-donating groups (**1d**, **1e**, and **1f**) proceeded smoothly to provide the APEX products (**3da**, **3ea**, and **3fa**). The tolerance for C–Cl and C–F bonds in the reactions makes it attractive for further transformations at these bonds of products (**3ga** and **3ha**). Similarly, reaction using *N*-methyl-7-azaindole (**1i**) provided the corresponding α-carboline **3ia** in 45% yield.
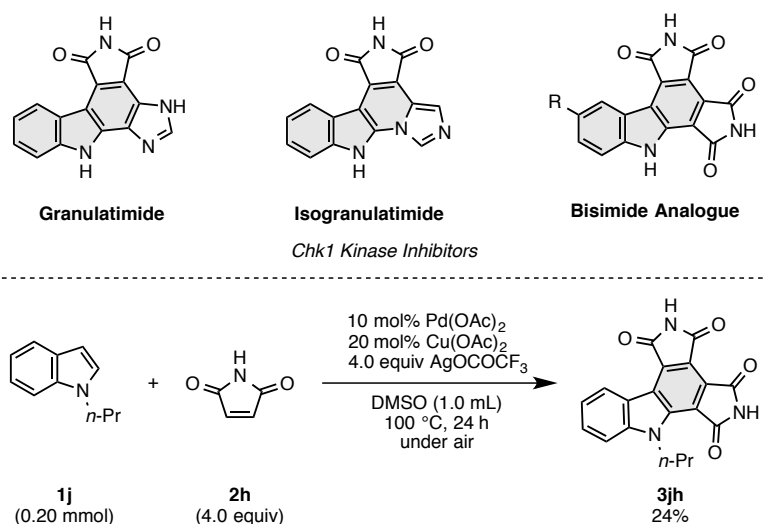
Table 5. π-Extension of indoles (**1b–1i**) with methyl vinyl ketone (**2a**)[a]
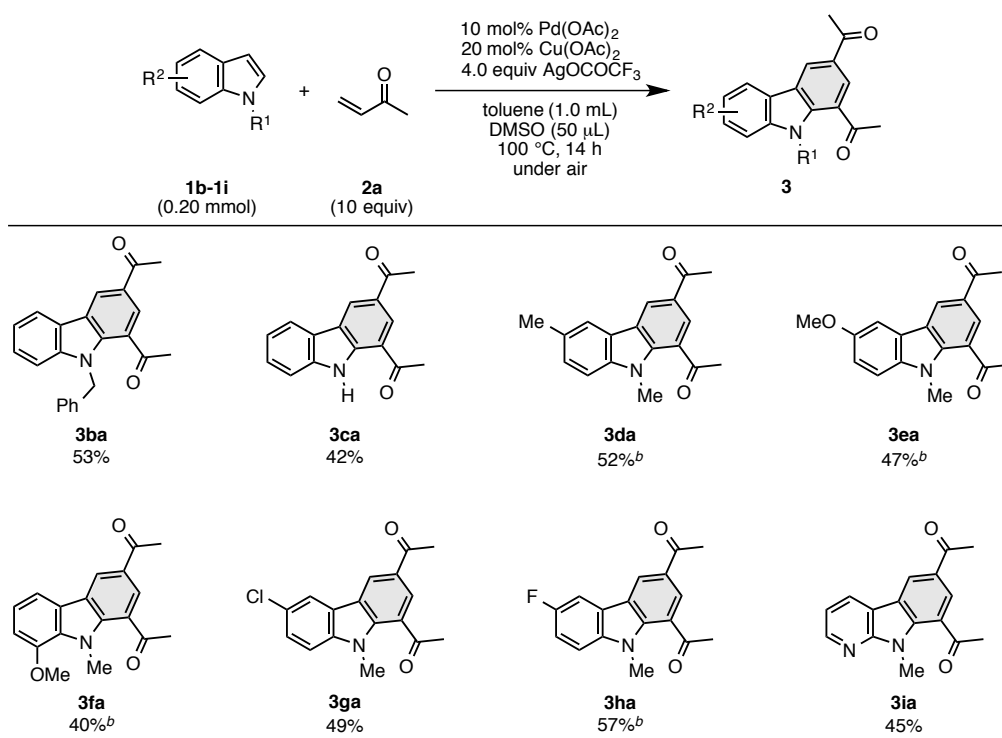
(a) Reaction conditions: **1** (0.20 mmol), methyl vinyl ketone (**2a**) (10 equiv), Pd(OAc)$_2$ (10 mol%), Cu(OAc)$_2$ (20 mol%), AgOCOCF$_3$ (4.0 equiv), toluene (1.0 mL), DMSO (50 μL), air, 100 °C, 14 h. Indicated yields are isolated yields. (b) Toluene (0.50 mL) and DMSO (0.50 mL) were used as solvent.

## 2-5. One-pot synthesis of granulatimide analogue

The present APEX reaction can be applied to the synthesis of biologically active molecules. Granulatimide and its analogues (carbazoles having one or two imide moieties) are well known as Chk1 kinase inhibitor (Scheme 4).[12] In particular, bisimide analogue shows much higher activity than other derivatives.[13] However, the previous four-step synthetic procedure provided these structures in less than 10% overall yield. Thus the one-pot synthesis of bisimide analogue by employing our APEX reaction was conducted. Gratifyingly, the reaction of *N-n*-propylindole (**1j**) with maleimide (**2h**) under the influence of Pd-Cu-Ag trimetallic system yielded the bisimide carbazole **3jh** in 24% yield in one-pot (Scheme 4).

Granulatimide **Isogranulatimide** **Bisimide Analogue**

Chk1 Kinase Inhibitors

1j
(0.20 mmol)

2h
(4.0 equiv)

10 mol% Pd(OAc)$_2$
20 mol% Cu(OAc)$_2$
4.0 equiv AgOCOCF$_3$

DMSO (1.0 mL)
100 °C, 24 h
under air

3jh
24%

*Scheme 4.* One-pot synthesis of bisimide analogue **3jh**

2-6. Mechanistic consideration

To investigate the reaction mechanism of the present π-extension reaction, the reactions of possible intermediates were conducted. Inspired by the elegant work of Gaunt,[8] the reaction of C3-alkenylated product **4** (Scheme 5) was investigated, which might be formed from **1a** and **2a** under Pd catalysis (oxidative Heck-like process). Indeed, compound **4** reacted with **2a** to give carbazole **3aa** in 56% GC yield under the standard conditions using Pd(OAc)$_2$, Cu(OAc)$_2$, and AgOCOCF$_3$. Taking the observed regioselectivity into account, it is assumed that **3aa** is produced by the Diels–Alder reaction of **4** and **2a**, and subsequent dehydrogenative aromatization (oxidation).[14] To further identify the real promoter for each elementary step, the reactions were carried out with omission of Pd, Cu, or Ag (Scheme 5). The reaction without Pd or Pd/Cu resulted in higher yield of **3aa** (77% and 80% GC yields, respectively). On the other hand, omission of all metals (Pd, Cu, Ag) led to dramatic decrease of **3aa** (4% GC yield), albeit the full consumption of **4**. These results not only indicate (i) the intermediacy of **4** in the APEX reaction and (ii) the C3-alkenylation/Diels–Alder/oxidation sequence as a possible mechanism of indole-to-carbazole π-extension, but also (iii) the role of metal promoters (Pd and Cu for C3-alkenylation, and Ag for Diels–Alder reaction and oxidation).

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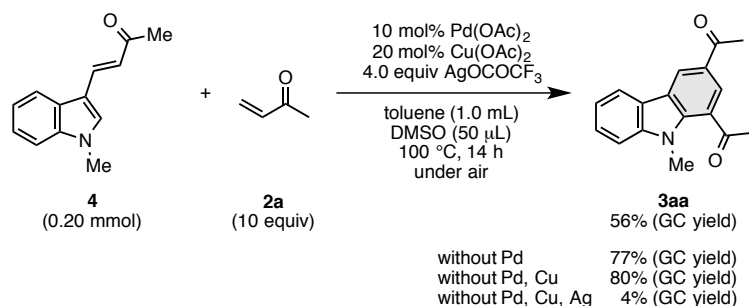
Scheme 5. Reactions of alkenylated indole **4** and **2a** under various conditions

The Michael addition product **5** of indole **1a** to **2a** could also be a possible intermediate.[15] Thus, alkylated indole **5** was treated with **2a** under the standard conditions (Scheme 6). While the both starting materials (**5** and **2a**) were consumed completely with or without Pd catalyst, carbazole **3aa** was produced in much lower yields (11% and 23% yield, respectively). Although it may be possible to assume that **5** is oxidized to **4** entering the above-mentioned sequence, other pathways could also be possible in the formation of **3aa**. Nevertheless, it is surmised that pathway through **5** is not the major one for the indole-to-carbazole π-extension under the current reaction conditions.
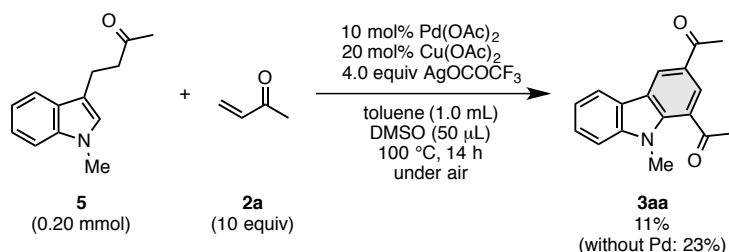
Scheme 6. Reactions from the Michael adduct **5**

Taking these results into consideration, the proposed major reaction pathway is depicted in Figure 6. An indole derivative **1** first reacts with Pd(II) to provide 3-indolylpalladium(II) species by C–H palladation. The thus-formed organopalladium species then undergoes Mizoroki–Heck-like reaction with an electron-deficient alkene **2** to produce a C3-alkenylated indole intermediate.[8] In this C–H alkenylation process, it is assumed that copper salt and silver salt are acting as a Pd(0)→Pd(II) oxidation catalyst and a terminal oxidant, respectively. The silver-promoted Diels–Alder reaction of a 3-alkenylindole with an alkene **2**, and the subsequent dehydrogenative

aromatization (oxidation) of a tetrahydrocarbazole intermediate produce a 1,3-disubstituted carbazole **3**.
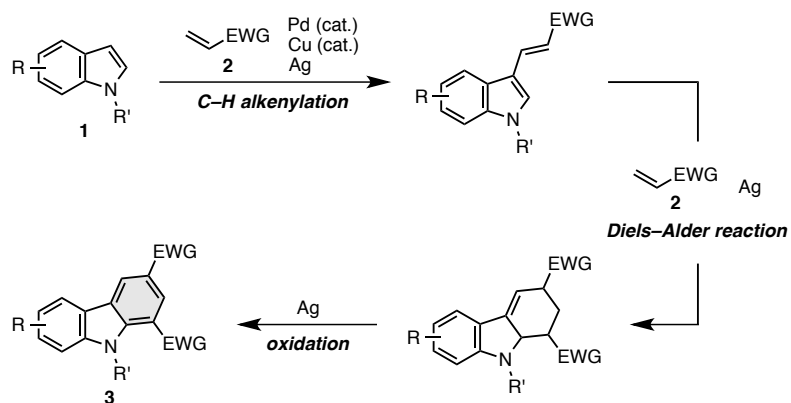

Figure 6. Possible major reaction pathway

Alternative reaction pathways are also described in Figures 7 and 8. One of them is Michael addition of indole to electron-deficient alkenes to form 3-alkyl indole which would be oxidized and provide C3-alkenylated indole intermediate in common with above major pathway (Figure 7). Thus, the common intermediate could be transformed to 1,3-disubstituted carbazole **3** in a same manner.
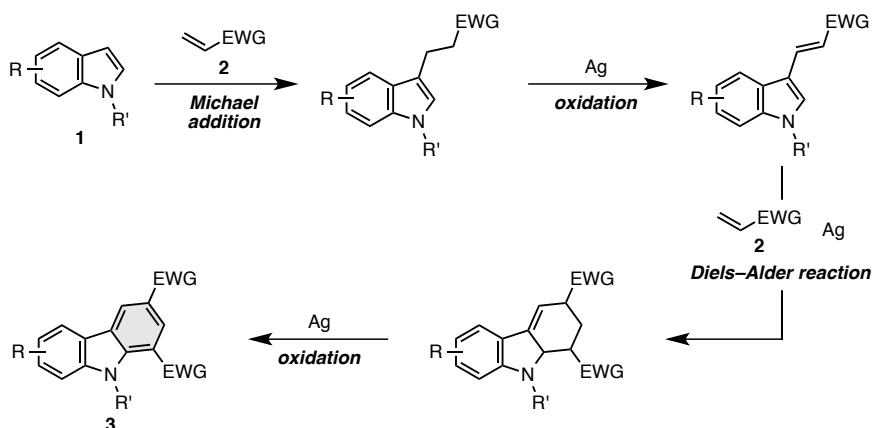
Figure 7. Possible minor reaction pathway involving Michael addition and Diels–Alder reaction

Furthermore, double Michael addition route should be also considered (Figure 8). The Michael addition of indole to conjugated alkenes easily undergoes, thus tandem double Michael addition, intramolecular Mannich reaction, and oxidation possibly provide 1,3-disubstituted carbozole **3**.
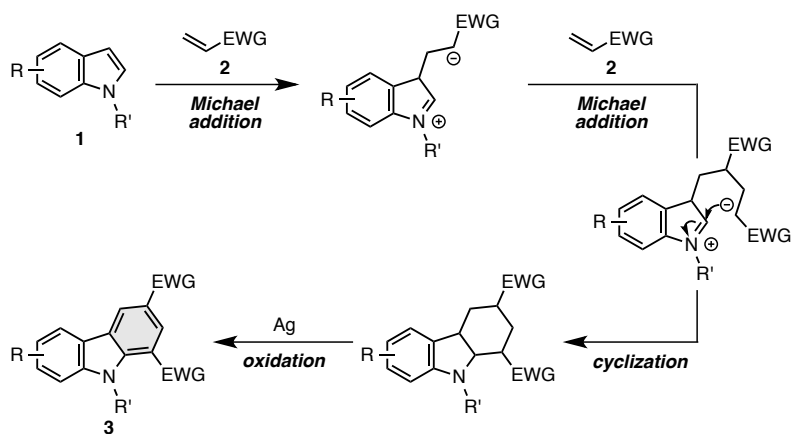

Figure 8. Alternative minor reaction pathway involving double Michael additions and Mannich reaction

3. Conclusions

In summary, a Pd-Cu-Ag trimetallic system that can convert indoles to carbazoles using electron-deficient alkenes as two-carbon units has been developed. Investigation of reaction mechanism revealed that this one-shot indole-to-carbozole π-extension is likely to proceed through the sequence of (i) Pd/Cu-catalyzed indole C–H alkenylation, (ii) Ag-promoted Diels–Alder reaction, and (iii) Ag-promoted dehydrogenative aromatization. The successful one-pot synthesis of granulatimide analogue highlights the potential of the present reaction for further development and applications.

After this study was published in *Chemical Science* in 2013, a number of related APEX reactions of indoles have been reported by other researchers. The group of Yu successfully applied same type of APEX reaction of indoles with enones that are *in situ*-generated from 3-chloropropiophenone derivatives (Scheme 7).[16] This reaction has broad substrate scope of both indoles and enones. Remarkably, one-pot APEX reactions for the synthesis of mixed aroyl-substituted carbazoles were also possible, which potentially provide a versatile method for the synthesis of highly functionalized carbazoles (Scheme 8).
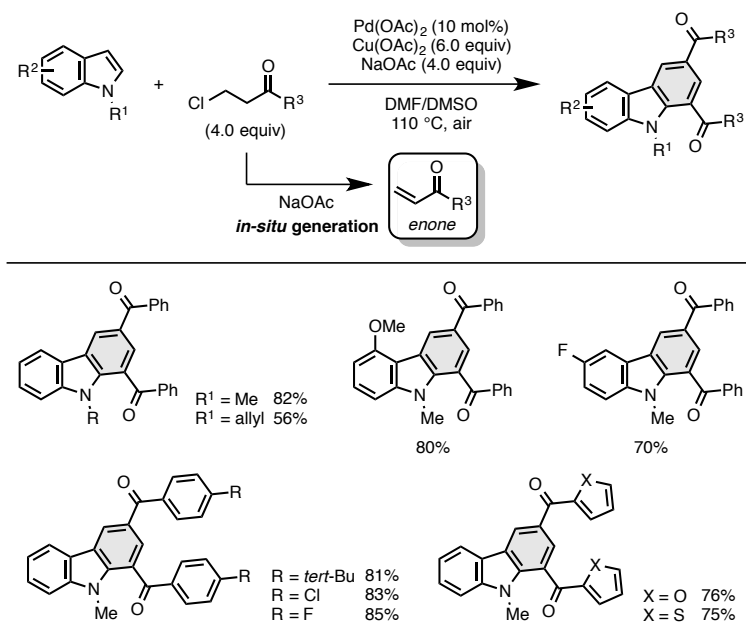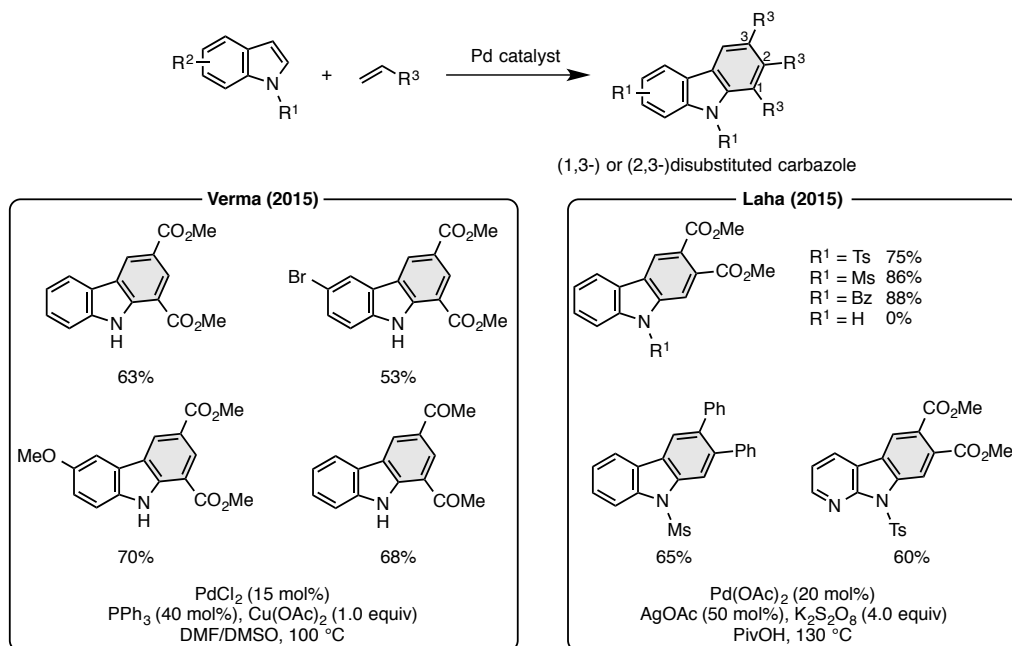

Scheme 7. Palladium-catalyzed APEX reaction of indoles with *in situ*-generated enones
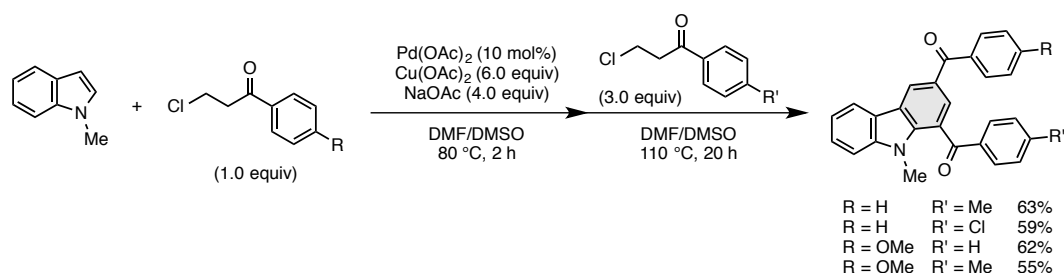
Scheme 8. One-pot sequential APEX reaction with *in situ*-generated enones

Recently, Verma and co-workers reinvestigated the synthetic utility and strategy of this Pd/Cu catalytic system which affords 1,3-disubstituted carbazoles from indoles and acrylic esters (Scheme 9).[17] The group of Laha developed a method for synthesis of 2,3-disubstituted carbazoles, different substitution pattern of above reports, from electron-deficient indole by Pd/Ag system.[18] In most cases, the reactions provide 2,3-disubstituted carbazoles.

Scheme 9. Recent examples of palladium-catalyzed APEX reactions of indoles with alkenes

These APEX reactions of indoles clearly show that our newly developed APEX is regarded as an important synthetic methodology in organic synthesis. Further development of APEX methodology and expansion of the substrate scopes will be expected in the near future.

4. Experimental Section

4-1. General

Unless otherwise noted, all materials including the dry solvent (dimethyl sulfoxide (DMSO)) were obtained from commercial suppliers and used as received. Toluene and 1,4-dioxane were purified by passing through a solvent purification system (Glass Contour). 1-Benzyl-1*H*-indole (**1b**)[19], 1,5-dimethyl-1*H*-indole (**1d**)[20], 5-methoxy-1-methyl-1*H*-indole (**1e**)[21], 5-fluoro-1-methyl-1*H*-indole (**1f**)[19], 5-chloro-1-methyl-1*H*-indole (**1g**)[20], 7-methoxy-1-methyl-1*H*-indole (**1h**)[22], 1-methyl-1*H*-pyrrolo[2,3-*b*]-pyridine (**1i**)[23], 1-propyl-1*H*-indole (**1j**)[24], 1-phenylprop-2-en-1-one (**2b**)[25], 1-(4-fluorophenyl)prop-2-en-1-one (**2c**)[26], 1-(4-chlorophenyl)prop-2-en-1-one (**2d**)[27], 1-(4-methoxyphenyl)prop-2-en-1-one (**2e**)[28], 1-(4-cyclohexyl-phenyl)prop-2-en-1-one (**2f**)[25], (*E*)-4-(1-methyl-1*H*-indol-3-yl)but-3-en-2-one (**4**)[29], 4-(1-methyl-1*H*-indol-3-yl)butan-2-one (**5**)[30] were synthesized according to procedures reported in the literature. Unless otherwise noted, all reactions were performed with dry solvents under air in flame-dried glassware. All π-extension reactions were performed in screw cap 7-mL glass vessel tubes and heated in a 10-well reaction block (heater + magnetic stirrer) unless otherwise noted. All work-up and purification procedures were carried out with reagent-grade solvents in air.

Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F_{254} precoated plates (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with KANTO Silica Gel 60N (spherical, neutral, 40-100 μm). Gas chromatography (GC) analysis was conducted on a Shimadzu GC-2010 instrument equipped with a HP-5 column (30 m × 0.25 mm, Hewlett-Packard). GC yields are expressed vs. *n*-dodecane as an internal standard. High-resolution mass spectra (HRMS) were obtained from JMS-T100TD (DART) or JMS-700 (FAB) instruments. Nuclear magnetic resonance (NMR) spectra were recorded on JEOL ECS-400 (^{1}H 400 MHz, ^{13}C 100 MHz), JEOL ECA-500 (^{1}H 500 MHz, ^{13}C 125 MHz), or JEOL ECA-600 (^{1}H 600 MHz, ^{13}C 150 MHz) spectrometer. Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm) or DMSO (δ 2.50 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to $CDCl_3$ (δ 77.16 ppm) or DMSO (δ

39.52 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, td = triplet of doublets, m = multiplet, br = broad signal), coupling constant (Hz), and integration.

4-2. General Procedure for Direct Indole-to-Carbazole π-Extension

1a-1i
(0.20 mmol)

2a-2g
(10 equiv)

3
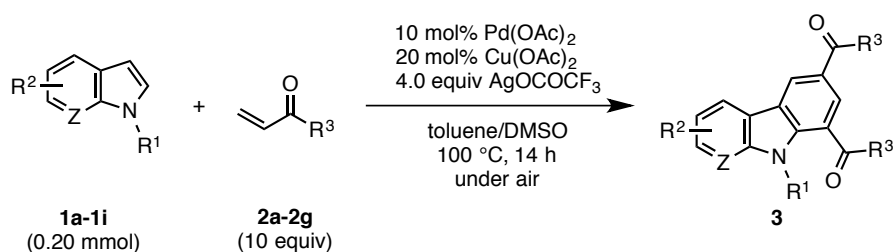
A 7-mL screw test tube containing a magnetic stirring bar was dried *in vacuo* with heating by heat-gun. After cooling, Pd(OAc)$_2$ (4.5 mg, 20 μmol), Cu(OAc)$_2$ (7.3 mg, 40 μmol), AgOCOCF$_3$ (176 mg, 0.80 mmol), alkene **2** (2.0 mmol), indole **1** (0.20 mmol), toluene and DMSO were added under air. The vessel was sealed with a cap and then the mixture was heated at 100 °C for 14 h with stirring. After cooling to room temperature, the reaction mixture was passed through a pad of Celite® and washed with EtOAc, then the filtrate was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel to afford carbazole **3**.

4-3. Compound Data of Coupling Products

1,3-Diacetyl-9-methyl-9*H*-carbazole (3aa)

1a
(0.20 mmol)

2a
(10 equiv)

3aa
70%
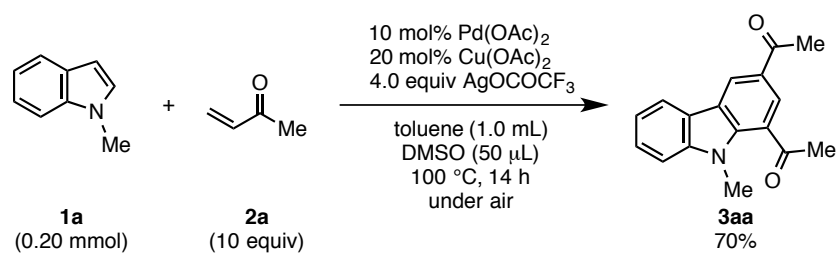
Following the general procedure with 1-methylindole (**1a**: 26 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was
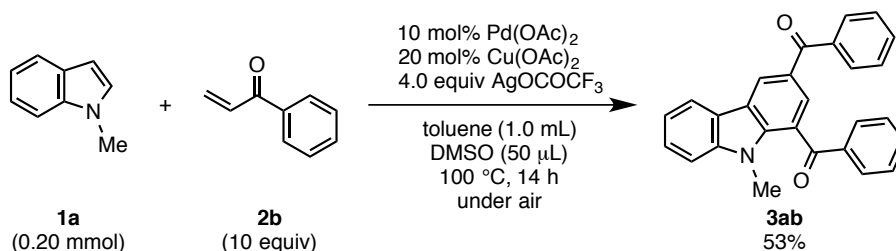
purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3aa** (37 mg, 70%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.77 (d, J = 1.8 Hz, 1H), 8.41 (d, J = 1.6 Hz, 1H), 8.12 (dd, J = 7.1, 0.8 Hz, 1H), 7.55 (td, J = 6.2, 1.1 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.34 (td, J = 7.1, 1.1 Hz, 1H), 3.78 (s, 3H), 2.83 (s, 3H), 2.74 (s, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) δ 200.1, 196.8, 143.1, 140.6, 127.6, 127.3, 127.2, 125.4, 124.6, 124.3, 122.6, 121.0, 120.2, 110.0, 34.1, 29.7, 26.6.

HRMS (DART, ESI$^+$) m/z calcd for C$_{17}$H$_{16}$NO$_2$ [M+H]$^+$: 266.1181, found: 266.1180.
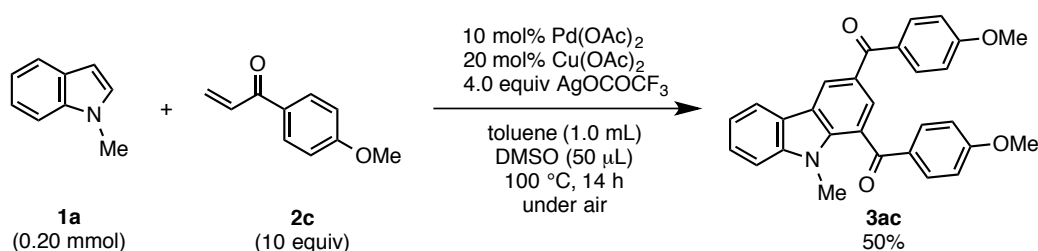
1,3-Dibenzoyl-9-methyl-9*H*-carbazole (3ab)

Following the general procedure with 1-methylindole (**1a**: 26 mg) and 1-phenyl-2-propen-1-one (**2b**: 264 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 15:1) to give **3ab** (41 mg, 53%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.75 (d, J = 1.6 Hz, 1H), 8.16 (d, J = 7.7 Hz, 1H), 8.04 (d, J = 1.8 Hz, 1H), 7.98–7.96 (m, 2H), 7.84–7.82 (m, 2H), 7.65 (m, 8H), 7.34 (td, J = 7.6, 0.9 Hz, 1H), 3.68 (s, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 195.93, 195.91, 142.7, 141.2, 138.4, 137.7, 133.9, 132.1, 130.8, 130.0, 129.9, 128.8, 128.4, 127.5, 127.3, 125.7, 124.8, 122.8, 122.4, 120.9, 120.7, 109.7, 33.3.

HRMS (DART, ESI$^+$) m/z calcd for C$_{27}$H$_{20}$NO$_2$ [M+H]$^+$: 390.1494, found: 390.1495.

1,3-Di(4-methoxybenzoyl)-9-methyl-9*H*-carbazole (3ac)

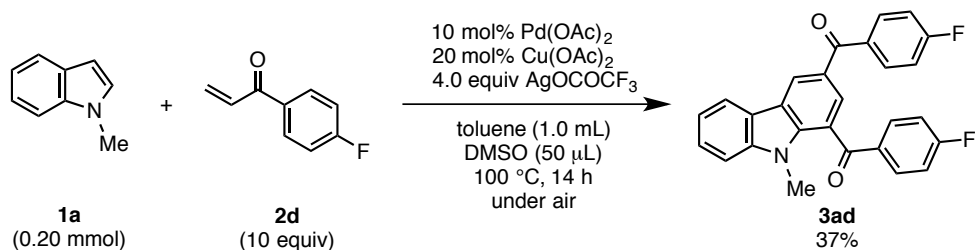|		
1a	**2c**	**3ac**
(0.20 mmol)	(10 equiv)	50%

Following the general procedure with 1-methylindole (**1a**: 26 mg) and 1-(4-methoxyphenyl)prop-2-en-1-one (**2c**: 324 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ac** (45 mg, 50%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.70 (d, J = 1.6 Hz, 1H), 8.15 (d, J = 7.8 Hz, 1H), 7.97–7.91 (m, 3H), 7.87–7.85 (m, 2H), 7.54 (td, J = 7.6, 1.1 Hz, 1H), 7.44 (d, J = 8.2 Hz, 1H), 7.33 (td, J = 7.6, 0.9 Hz, 1H), 6.99–6.94 (m, 4H), 3.88 (s, 3H), 3.87 (s, 3H), 3.67 (s, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 194.9, 194.8, 164.3, 163.0, 142.6, 140.7, 133.2, 132.5, 131.0, 129.2, 128.2, 127.2, 124.9, 124.6, 122.8, 122.7, 120.69, 120.67, 120.63, 114.1, 113.7, 109.5, 55.7, 55.6, 33.0.

HRMS (DART, ESI^{+}) m/z calcd for C$_{29}$H$_{24}$NO$_4$ [M+H]$^{+}$: 450.1705, found: 450.1709.

1,3-Di(4-fluorobenzoyl)-9-methyl-9*H*-carbazole (3ad)

1a	**2d**	**3ad**
(0.20 mmol)	(10 equiv)	37%

Following the general procedure with 1-methylindole (**1a**: 26 mg) and 1-(4-fluorophenyl)-2-propen-1-one (**2d**: 300 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 15:1) to give **3ad** (32 mg, 37%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.71 (d, J = 1.6 Hz, 1H), 8.16 (d, J = 7.7 Hz, 1H), 8.02–7.97 (m, 3H), 7.89–7.85 (m, 2H), 7.58 (td, J = 7.9, 1.1 Hz, 1H), 7.48 (d, J = 8.5

Hz, 1H), 7.36 (td, J = 7.5, 0.9 Hz, 1H), 7.21–7.16 (m, 4H), 3.68 (s, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) δ194.3, 194.2, 166.3 (d, J = 255 Hz), 165.3 (d, J = 253 Hz), 142.7, 141.0, 134.6 (d, J = 2.8 Hz), 134.1 (d, J = 2.8 Hz), 133.4 (d, J = 8.5 Hz), 132.5 (d, J = 8.7 Hz), 129.4, 127.5, 127.4, 125.5, 124.9, 122.7, 122.2, 121.0, 120.6, 116.1 (d, J = 25 Hz), 115.6 (d, J = 21 Hz), 109.7, 33.2.

HRMS (DART, ESI$^+$) m/z calcd for C$_{27}$H$_{18}$F$_2$NO$_2$ [M+H]$^+$: 426.1306, found: 426.1306.

## 1,3-Di(4-chlorobenzoyl)-9-methyl-9H-carbazole (3ae)
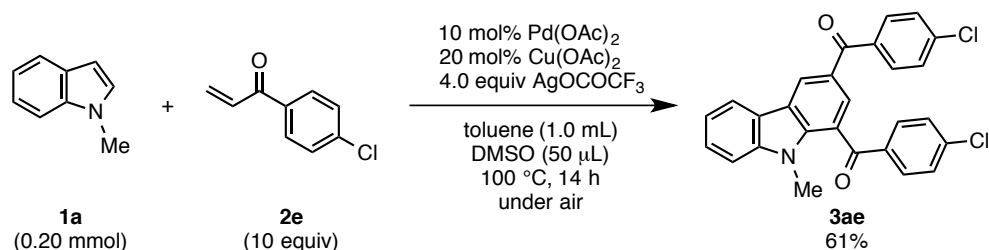
Following the general procedure with 1-methylindole (**1a**: 26 mg) and 1-(4-chlorophenyl)-2-propen-1-one (**2e**: 333 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 30:1) to give **3ae** (56 mg, 61%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.70 (d, J = 1.6 Hz, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 1.6 Hz, 1H), 7.92–7.89 (m, 2H), 7.79–7.76 (m, 2H), 7.59 (td, J = 7.6, 1.1 Hz, 1H), 7.56–7.47 (m, 5H), 7.36 (td, J = 7.6, 0.9 Hz, 1H), 3.68 (s, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 194.5, 194.4, 142.7, 141.1, 140.6, 138.6, 136.6, 136.0, 132.0, 131.4, 129.4, 129.2, 128.7, 127.5, 127.2, 125.7, 124.9, 122.6, 122.0, 121.0, 120.6, 109.7, 33.3.

HRMS (DART, ESI$^+$) m/z calcd for C$_{27}$H$_{18}$Cl$_2$NO$_2$ [M+H]$^+$: 458.0715, found: 458.0716.

1,3-Dicyclohexanecarbonyl-9-methyl-9*H*-carbazole (3af)

1a
(0.20 mmol)

2f
(10 equiv)

3af
24%
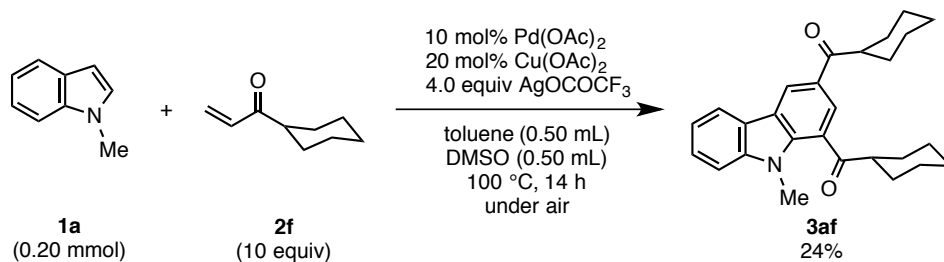
Following the general procedure with 1-methylindole (**1a**: 26 mg) and 1-(4-cyclohexylphenyl)prop-2-en-1-one (**2f**: 276 mg) in toluene (0.50 mL) and DMSO (0.50 mL), the crude product was purified by flash column chromatography (hexane:EtOAc = 25:1) to give **3af** (19 mg, 24%) as a pale yellow oil.

^{1}H NMR (CDCl$_3$, 600 MHz) δ 8.77 (d, *J* = 1.8 Hz, 1H), 8.34 (d, *J* = 1.2 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.55 (td, *J* = 7.2, 1.2 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.34 (t, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.46 (tt, *J* = 11.4, 3.6 Hz, 1H), 3.40 (tt, *J* = 11.4, 3.6 Hz, 1H), 2.06–1.75 (m, 10H), 1.65–1.25 (m, 10H).

^{13}C NMR (CDCl$_3$, 150 MHz) δ 206.7, 202.8, 142.9, 140.7, 127.2, 126.7, 126.4, 125.1, 124.5, 123.6, 122.7, 120.8, 120.3, 109.8, 49.2, 45.6, 33.5, 29.9, 29.5, 26.1, 26.09, 26.06, 25.9.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{27}$H$_{32}$NO$_2$ [M+H]$^+$: 402.2433, found: 402.2432.

Dimethyl 9-methyl-9*H*-carbazole-1,3-dicarboxylate (3ag)



1a
(0.20 mmol)

2g
(10 equiv)

3ag
44%
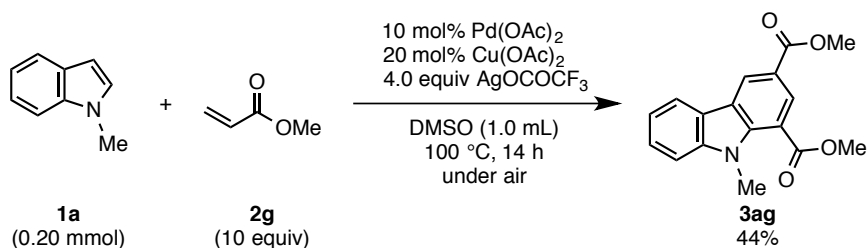
Following the general procedure with 1-methylindole (**1a**: 26 mg) and methyl acrylate (**2g**: 172 mg) in DMSO (1.0 mL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ag** (26 mg, 44%) as a pale yellow solid. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.91 (d, *J* = 1.6 Hz, 1H), 8.58 (d, *J* = 1.8 Hz, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 6.0 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.34 (t, *J* = 7.1 Hz, 1H), 4.04 (s, 3H), 3.99 (s, 3H), 3.93 (s, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 167.5, 167.1, 143.1, 141.4, 130.1, 127.3, 125.6, 125.5, 122.6, 120.9, 120.4, 120.2, 115.0, 109.8, 52.6, 52.2, 33.6.

HRMS (DART, ESI$^+$) m/z calcd for C$_{17}$H$_{16}$NO$_4$ [M+H]$^+$: 298.1079, found: 298.1080.
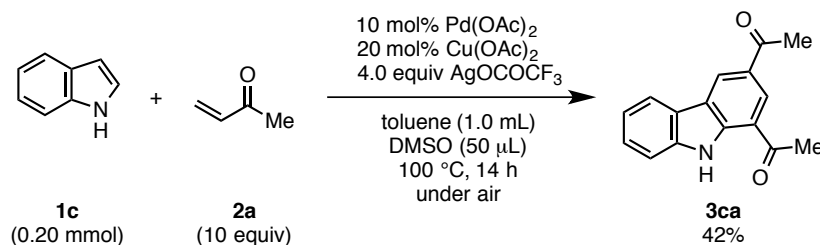
9-Benzyl-1,3-diacetyl-9*H*-carbazole (3ba)
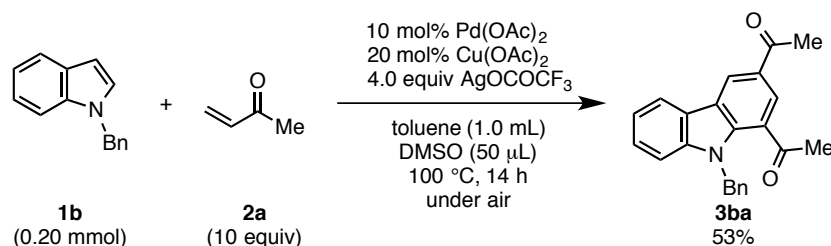
Following the general procedure with 1-benzyl-1*H*-indole (**1b**: 41 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ba** (36 mg, 53%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.85 (d, J = 1.6 Hz, 1H), 8.22 (d, J = 1.6 Hz, 1H), 8.22 (d, J = 7.3 Hz, 1H), 7.56–7.55 (m, 2H), 7.42–7.40 (m, 1H), 7.18– 7.17 (m, 3H), 6.75–6.74 (m, 2H), 5.66 (s, 2H), 2.76 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) δ 200.7, 196.8, 143.2, 138.7, 136.4, 128.8, 128.0, 127.54, 127.52, 126.8, 126.3, 125.9 (2C), 124.3, 122.7, 121.2, 120.4, 110.1, 48.5, 29.1, 26.6.

HRMS (DART, ESI$^+$) m/z calcd for C$_{23}$H$_{20}$NO$_2$ [M+H]$^+$: 342.1494, found: 342.1496.

1,3-Diacetyl-9*H*-carbazole (3ca)

Following the general procedure with 1*H*-indole (**1c**: 23 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ca** (21 mg,
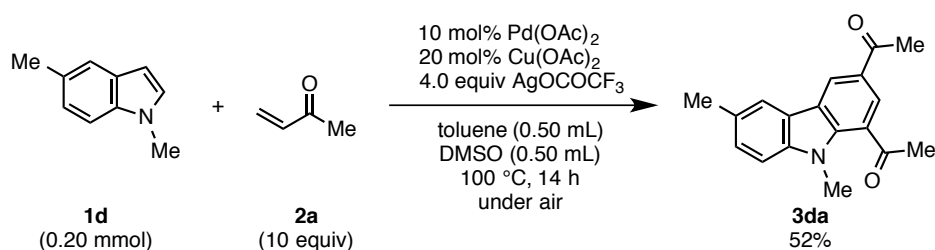
42%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 10.7 (br, 1H), 8.86 (d, J = 1.6 Hz, 1H), 8.64 (d, J = 1.6 Hz, 1H), 8.15 (dd, J = 7.6, 0.8 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.37 (td, J = 7.1, 1.6 Hz, 1H), 2.82 (s, 3H), 2.77 (s, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) δ 200.4, 197.0, 141.6, 140.6, 128.5, 128.4, 127.5, 126.5, 125.0, 122.4, 121.3, 120.7, 118.9, 111.9, 26.9, 26.7.

HRMS (DART, ESI$^+$) m/z calcd for C$_{16}$H$_{14}$NO$_2$ [M+H]$^+$: 252.1024, found: 252.1023.

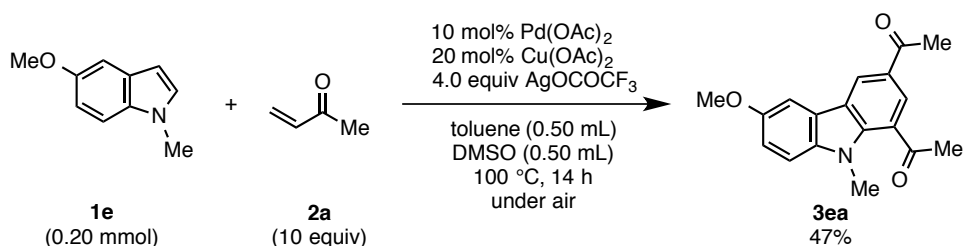### 1,3-Diacetyl-6,9-dimethyl-9H-carbazole (3da)

Following the general procedure with 1,5-dimethyl-1H-indole (**1d**: 29 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (0.50 mL) and DMSO (0.50 mL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3da** (29 mg, 52%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.76 (d, J = 1.6 Hz, 1H), 8.42 (d, J = 1.6 Hz, 1H), 7.93 (d, J = 0.7 Hz, 1H), 7.38 (d, J = 8.7 Hz, 1H), 7.37 (d, J = 7.2 Hz, 1H), 3.77 (s, 3H), 2.83 (s, 3H), 2.74 (s, 3H), 2.55 (s, 3H).

^{13}C NMR (CDCl$_3$, 125 MHz) δ 200.0, 196.8, 141.5, 140.8, 130.5, 128.6, 127.4, 127.1, 125.3, 124.6, 124.2, 122.8, 120.2, 109.7, 34.1, 29.6, 26.5, 21.4.

HRMS (DART, ESI$^+$) m/z calcd for C$_{18}$H$_{18}$NO$_2$ [M+H]$^+$: 280.1338, found: 280.1336.

1,3-Diacetyl-6-methoxy-9-methyl-9*H*-carbazole (3ea)

1e
(0.20 mmol)

2a
(10 equiv)

10 mol% Pd(OAc)$_2$
20 mol% Cu(OAc)$_2$
4.0 equiv AgOCOCF$_3$

toluene (0.50 mL)
DMSO (0.50 mL)
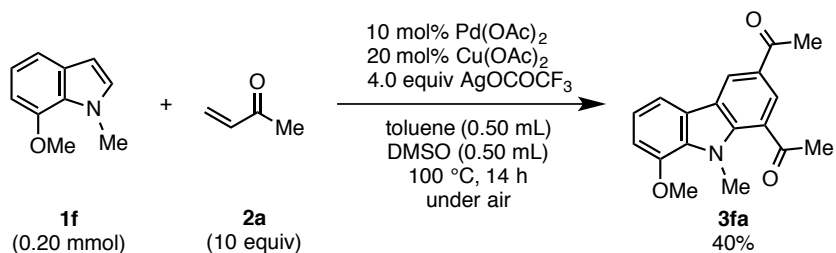100 °C, 14 h
under air

3ea
47%

Following the general procedure with 5-methoxy-1-methyl-1*H*-indole (**1e**: 32 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (0.50 mL) and DMSO (0.50 mL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ea** (28 mg, 47%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.74 (d, *J* = 1.6 Hz, 1H), 8.40 (d, *J* = 1.8 Hz, 1H), 7.58 (d, *J* = 2.5 Hz, 1H), 7.37 (d, *J* = 9.1 Hz, 1H), 7.17 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.94 (s, 3H), 3,75 (s, 3H), 2.83 (s, 3H), 2.74 (s, 3H).

^{13}C NMR (CDCl$_3$, 125 MHz) δ 199.9, 196.7, 155.1, 140.9, 138.0, 127.3, 127.2, 125.3, 124.7, 124.3, 123.2, 116.5, 110.8, 102.9, 56.1, 34.2, 29.6, 26.6.

HRMS (DART, ESI$^+$) *m/z* calcd for C$_{18}$H$_{18}$NO$_3$ [M+H]$^+$: 296.1286, found: 296.1285.

1,3-Diacetyl-8-methoxy-9-methyl-9*H*-carbazole (3fa)

1f
(0.20 mmol)

2a
(10 equiv)

10 mol% Pd(OAc)$_2$
20 mol% Cu(OAc)$_2$
4.0 equiv AgOCOCF$_3$

toluene (0.50 mL)
DMSO (0.50 mL)
100 °C, 14 h
under air

3fa
40%

Following the general procedure with 7-methoxy-1-methyl-1*H*-indole (**1f**: 32 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (0.50 mL) and DMSO (0.50 mL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3fa** (24 mg, 40%) as a pale yellow solid.
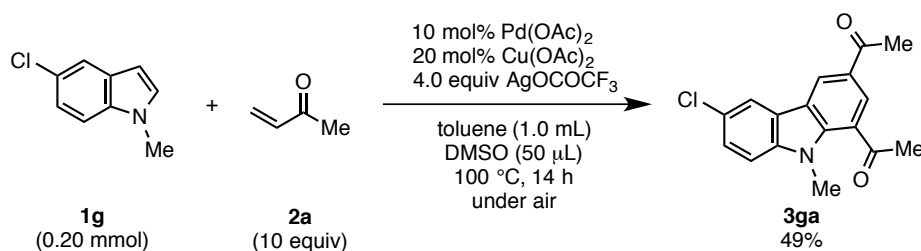
^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.75 (d, *J* = 1.6 Hz, 1H), 8.38 (d, *J* = 7.8, 0.7 Hz, 1H), 7.72 (dd, *J* = 2.5 Hz, 1H), 7.37 (d, *J* = 9.1 Hz, 1H), 7.17 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.94 (s, 3H), 3,75 (s, 3H), 2.83 (s, 3H), 2.74 (s, 3H).

^{13}C NMR (CDCl$_3$, 125 MHz) δ 200.0, 196.8, 147.7, 141.5, 132.6, 127.8, 127.0, 125.7,

125.0, 124.8, 124.6, 121.7, 112.7, 109.0, 56.0, 37.3, 29.8, 26.6.

HRMS (DART, ESI$^+$) m/z calcd for $C_{18}H_{18}NO_3$ [M+H]$^+$: 296.1286, found: 296.1286.

6-Chloro-1,3-diacetyl-9-methyl-9H-carbazole (3ga)

Following the general procedure with 5-chloro-1-methyl-1H-indole (**1g**: 33 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ga** (29 mg, 49%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.69 (d, J = 1.6 Hz, 1H), 8.43 (d, J = 1.8 Hz, 1H), 8.05 (d, J = 2.0 Hz, 1H), 7.48 (dd, J = 8.9, 2.0 Hz, 1H), 7.37 (d, J = 8.9 Hz, 1H), 3.75 (s, 3H), 2.83 (s, 3H), 2.74 (s, 3H).

^{13}C NMR (CDCl$_3$, 125 MHz) δ 199.8, 196.5, 141.4, 140.8, 128.0, 127.7, 127.3, 126.6, 124.8, 124.6, 124.3, 123.6, 119.9, 111.0, 34.2, 29.6, 26.5.

HRMS (DART, ESI$^+$) m/z calcd for $C_{17}H_{15}ClNO_2$ [M+H]$^+$: 300.0791, found: 300.0792.

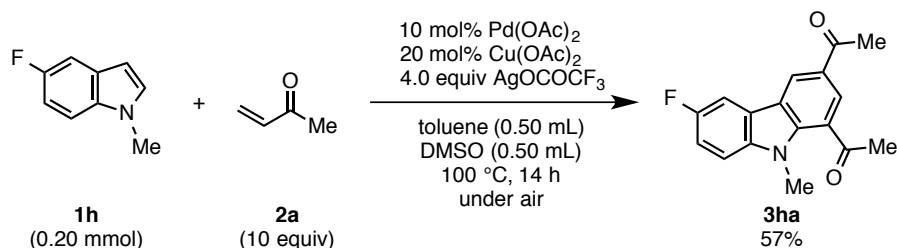### 6-Fluoro-1,3-diacetyl-9-methyl-9H-carbazole (3ha)

Following the general procedure with 5-fluoro-1-methyl-1H-indole (**1h**: 30 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (0.50 mL) and DMSO (0.50 mL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to

give **3ha** (32 mg, 57%) as a pale yellow solid.

^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.69 (d, J = 1.8 Hz, 1H), 8.43 (d, J = 1.8 Hz, 1H), 7.75 (dd, J = 8.9, 2.5 Hz, 1H), 7.38 (dd, J = 9.1, 4.1 Hz, 1H), 7.26 (td, J = 8.9, 2.5 Hz, 1H), 3.76 (s, 3H), 2.83 (s, 3H), 2.73 (s, 3H).

^{13}C NMR (CDCl$_3$, 150 MHz) δ 199.8, 196.6, 158.3 (d, J = 237 Hz), 141.3, 139.4, 127.74, 127.71, 125.0, 124.9 (d, J = 4.3 Hz), 124.6, 123.2 (d, J = 10 Hz), 115.2 (d, J = 24 Hz), 110.8 (d, J = 8.5 Hz), 106.1 (d, J = 24 Hz), 34.3, 29.6, 26.6.

HRMS (DART, ESI$^+$) m/z calcd for C$_{17}$H$_{15}$FNO$_2$ [M+H]$^+$: 284.1087, found: 284.1087.

1,3-Diacetyl-9-methyl-9*H*-8-azacarbazole (3ia)

1i (0.20 mmol) + **2a** (10 equiv)

10 mol% Pd(OAc)$_2$
20 mol% Cu(OAc)$_2$
4.0 equiv AgOCOCF$_3$
toluene (1.0 mL)
DMSO (50 μL)
100 °C, 14 h
under air

3ia 45%

Following the general procedure with 1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (**1i**: 26 mg) and methyl vinyl ketone (**2a**: 140 mg) in toluene (1.0 mL) and DMSO (50 μL), the crude product was purified by flash column chromatography (hexane:EtOAc = 3:1) to give **3ia** (24 mg, 45%) as a pale yellow solid.
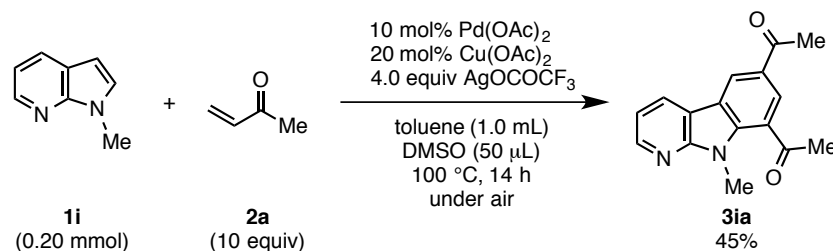
^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.71 (d, J = 1.6 Hz, 1H), 8.58 (dd, J = 4.8, 1.6 Hz, 1H), 8.39 (d, J = 1.6 Hz, 1H), 8.34 (dd, J = 7.8, 1.6 Hz, 1H), 7.27 (dd, J = 7.8, 4.8 Hz, 1H), 3.89 (s, 3H), 2.83 (s, 3H), 2.73 (s, 3H).

^{13}C NMR (CDCl$_3$, 100 MHz) δ 199.7, 196.5, 153.3, 147.4, 139.7, 128.4, 128.2, 127.4, 125.0, 124.8, 122.6, 116.8, 115.4, 32.2, 29.8, 26.6.

HRMS (DART, ESI$^+$) m/z calcd for C$_{16}$H$_{15}$N$_2$O$_2$ [M+H]$^+$: 267.1133, found: 267.1133.

7-Propyl-1*H*-dipyrrolo[3,4-*a*:3',4'-*c*]carbazole-1,3,4,6(2*H*,5*H*,7*H*)-tetraone (3jh)

1j
(0.20 mmol)

2h
(4.0 equiv)

3jh
24%
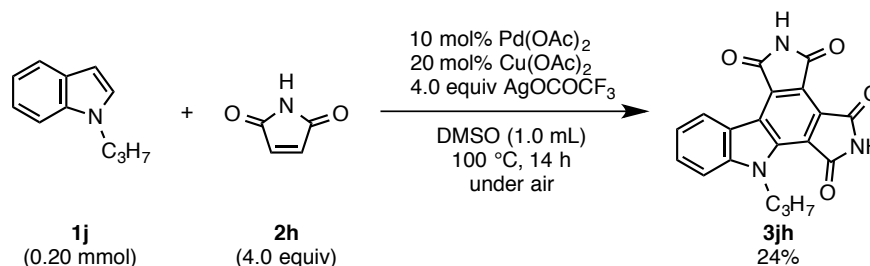
A 7-mL screw test tube containing a magnetic stirrindg bar was dried under in vacuum with heating by heat-gun. After cooling, Pd(OAc)$_2$ (4.5 mg, 20 μmol), Cu(OAc)$_2$ (7.3 mg, 40 μmol), AgOCOCF$_3$ (176 mg, 0.80 mmol), maleimide (**2h**: 77 mg, 0.80 mmol), *N*-propylindole (**1j**, 31 mg, 0.20 mmol), and DMSO (1.0 mL) were added under air. The vessel was sealed with a cap under air and then the mixture was heated at 100 °C for 14 h with stirring. After cooling to room temperature, the reaction mixture was directly purified by flash column chromatography on silica gel (CHCl$_3$:MeOH = 20:1), and the solvent was evaporated under reduced pressure. To this residue, water and EtOAc were added. The resulting solid at the interface between a organic and an aqueous phases was separated by filtration and washed with water then EtOAc to give pure compound **3jh** (17 mg, 24%) as an orange solid.

^{1}H NMR (DMSO-*d*$_6$, 600 MHz) δ 11.56 (br, 2H), 9.05–8.98 (m, 1H), 7.79–7.66 (m, 2H), 7.41–7.38 (m, 1H), 4.94–4.89 (m, 2H), 1.74–1.73 (br, 2H), 0.91–0.88 (br, 3H).

^{13}C NMR (DMSO–*d*$_6$, 150 MHz) δ 168.7, 167.8, 165.7, 165.6, 143.3, 138.6, 131.4, 130.0, 127.3, 125.7, 124.4, 121.7, 119.5, 119.3, 118.0, 110.8, 47.5, 22.7, 10.6.

HRMS (FAB, ESI$^+$) *m/z* calcd for C$_{19}$H$_{13}$N$_3$O$_4$Na [M+Na]$^+$: 370.0804, found: 370.0805.

4-4. X-ray Crystal Structure Analysis of 3aa

Details of the crystal data and a summary of the intensity data collection parameters for **3aa** are listed in Table 6. A suitable crystal was mounted with mineral oil on a glass fiber and transferred to the goniometer of a Rigaku Saturn CCD diffractometer. Graphite-monochromated Mo Ka radiation (l = 0.71070 Å) was used. The structures were solved by direct methods with (SIR-97)[31] or (SHELXS-97)[32] and refined by full-matrix least-squares techniques against F^2 (SHELXL-97)[32]. The intensities were corrected for Lorentz and polarization effects. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed using AFIX instructions.

Table 6. Crystallographic data and structure refinement details for **3aa**

	3aa
formula	$C_{17}H_{15}NO_2$
fw	265.3
T (K)	103(2)
l (Å)	0.7107
cryst syst	orthorhombic
space group	$P2_12_12_1$
a, (Å)	6.4112(19)
b, (Å)	12.077(4)
c, (Å)	16.676(5)
a, (deg)	90
b, (deg)	90
g, (deg)	90
V, (Å^3)	1291.4(7)
Z	4
D_{calc}, (g / cm^3)	1.365
m (mm^{-1})	0.09
F(000)	560
cryst size (mm)	$0.20 \times 0.10 \times 0.10$
$2q$ range, (deg)	3.37–24.99
reflns collected	8665
indep reflns/R_{int}	2272/0.0487
params	184
GOF on F^2	1.113
R_1, wR_2 [I>2s(I)]	0.0477, 0.0909
R_1, wR_2 (all data)	0.0538, 0.0942

5. References

(1) For recent reviews, see: (a) Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J.; *Chem. Rev.* **2012**, *112*, 3193. (b) Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303. (c) Maneerat, W.; Ritthiwigrom, T.; Cheenpracha, S.; Promgool, T.; Yossathera, K.; Deachathai, S.; Phakhodee, W.; Laphookhieo, S. *J. Nat. Prod.* **2012**, *75*, 741. (d) Deslandes, S.; Chassaing, S.; Delfourne, E. *Mar. Drugs* **2009**, *7*, 754. (e) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2003**, *20*, 216. (d) Blunt, J. W.; Copp, B. R.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2003**, *20*, 216.

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List of Publications

(副論文)

1. One-shot Indole-to-carbazole π-Extension by a Pd-Cu-Ag Trimetallic System
    <u>Kyohei Ozaki</u>, Hua Zhang, Hideto Ito, Aiwen Lei, Kenichiro Itami
    Chem. Sci. **2013**, *4*, 3416.

2. One-shot K-region-selective Annulative π-Extension for Nanographene Synthesis
    and Functionalization
    <u>Kyohei Ozaki</u>, Katsuaki Kawasumi, Mari Shibata, Hideto Ito, Kenichiro Itami
    Nat. Commun. **2015**, *6*: 6251.