Studies on Synthesis of Polycyclic Aromatic Hydrocarbons Based on Difluorocarbocation Generation

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CHAPTER 1

General Introduction

1-1. Polycyclic Aromatic Hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) consist of fused benzene rings in various configurations.[1] For example, acenes, phenacenes, and helicenes exhibit linear, zig-zag, and helical arrangements of the benzene rings, respectively. It is noteworthy that [n]helicenes ($n \geq 5$) have helical chirality (Figure 1-1).

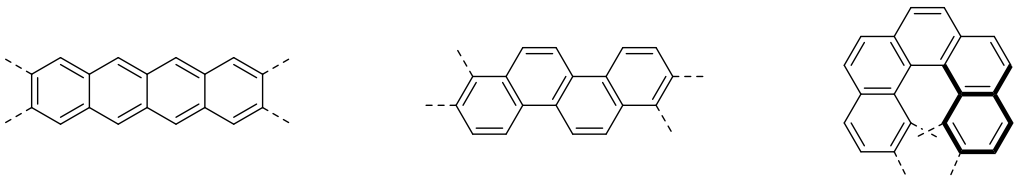
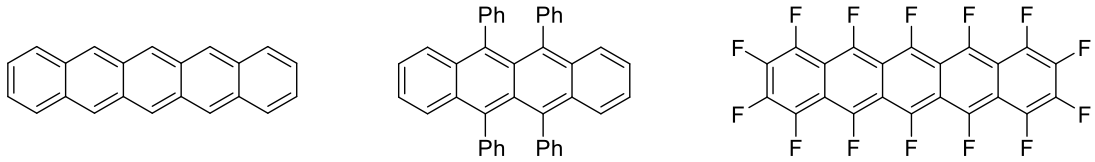


Figure 1-1. Major Families of Polycyclic Aromatic Hydrocarbons
(n Represents the Number of Benzene Rings).

During the past decades, PAHs have attracted considerable attention, mainly because of their viability as materials for organic electronic devices.[2] Acenes are already known as one of the most representative organic semiconducting materials (Figure 1-2).[3] Moreover, phenacenes are emerging as a new semiconducting PAH subfamily, partly due to their oxidation resistance and O_2 sensing behavior; thus, the synthesis and physical properties such as solubility in organic solvents of higher-order phenacenes have been extensively investigated (Figures 1-3).[4,5] Helicenes also appeared quite recently as organic chiral inducers with unique chirality-derived characteristics (eq. 1-1, 1-2).[6,7] Therefore, efficient method for the synthesis of PAHs have been developed to date. In the next section, general PAH syntheses using C–C bond formations are described.

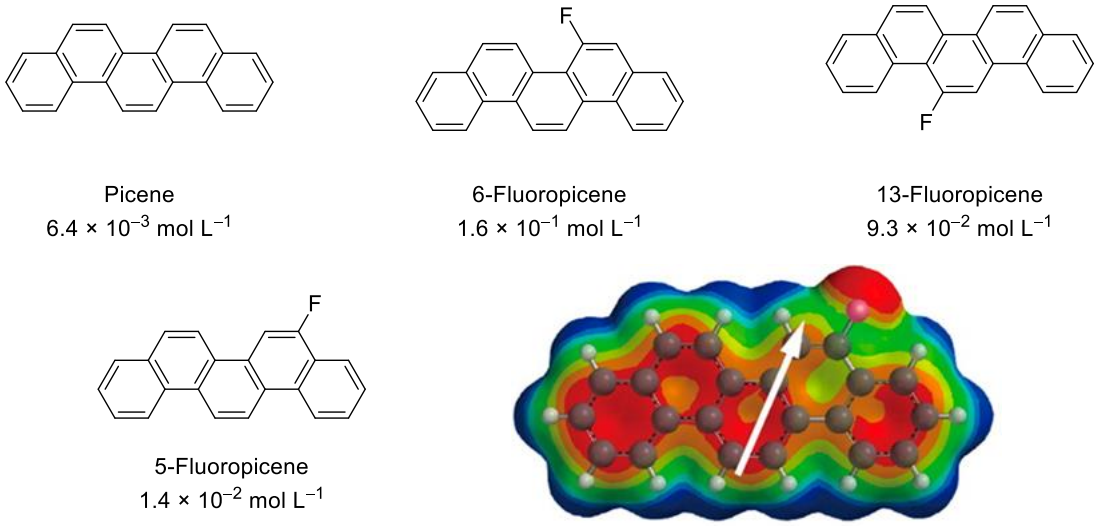


μ = 1.5 cm^2/VS
P-Type

μ = 15 cm^2/VS
P-Type

μ = 0.1 cm^2/VS
N-Type

Figure 1-2. Properties of Acenes as Semiconductors.



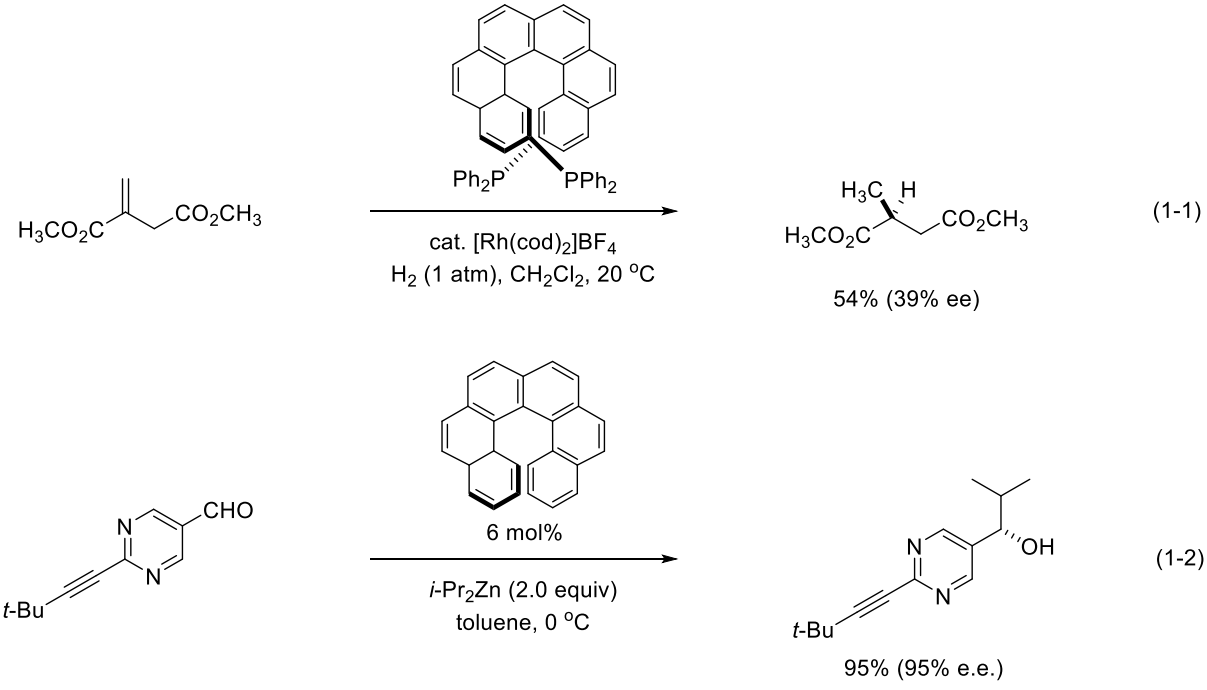
Picene
6.4×10^{-3} mol L^{-1}

6-Fluoropicene
1.6×10^{-1} mol L^{-1}

13-Fluoropicene
9.3×10^{-2} mol L^{-1}

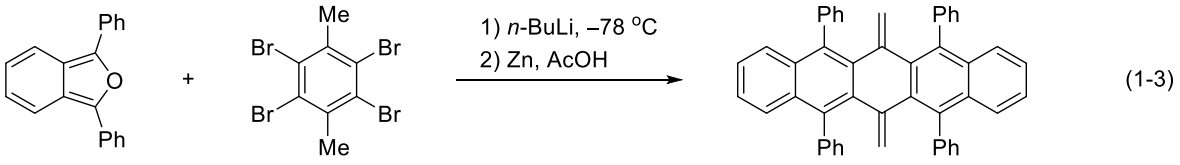
5-Fluoropicene
1.4×10^{-2} mol L^{-1}

Figure 1-3. Solubility of (Fluoro)phenacenes in THF and Electrostatic Potential Map of Fluoro[5]phenacene.

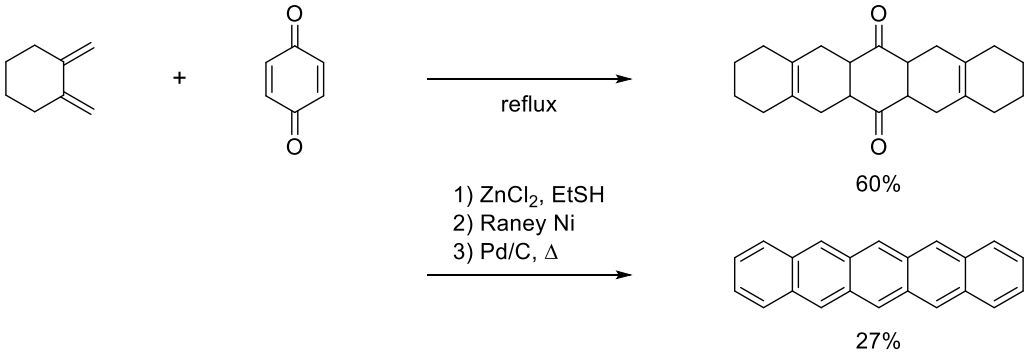


1-2. General Synthesis of Polycyclic Aromatic Hydrocarbons (Single Ring Constructions)

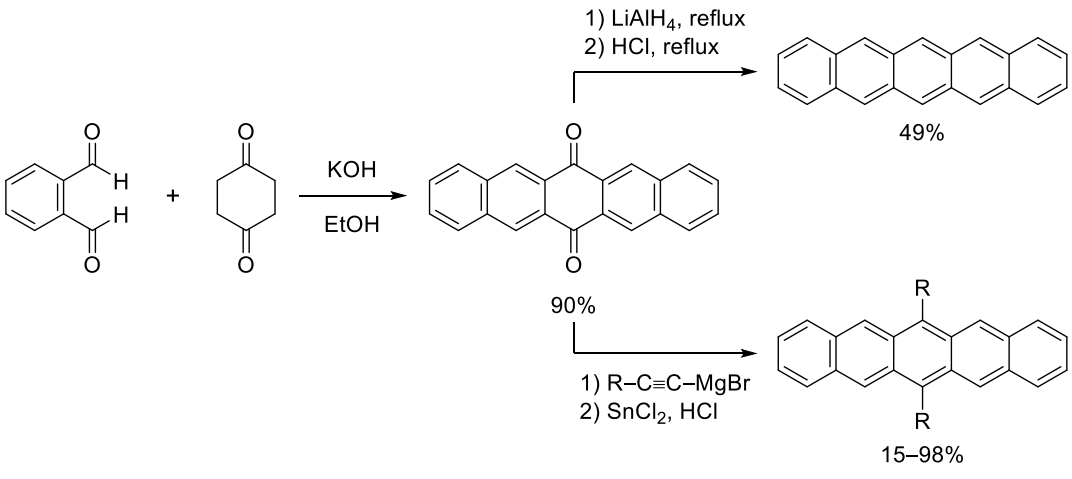
The advantages of PAHs have made them fascinating synthetic targets. Besides the frequently used [4 + 2] reaction of dienes with arynes or quinones as dienophiles (Diels–Alder reaction, eq. 1-3, 1-4),[8] there have been many powerful methods for the synthesis of [n]acenes, such as dehydration condensation reactions of aldehydes with ketones (Aldol reaction, eq. 1-5, 1-6)[9] and electrophilic aromatic substitution between acyl cation equivalents and arenes (Friedel–Crafts reaction, eq. 1-7, 1-8).[10]



(1-3)

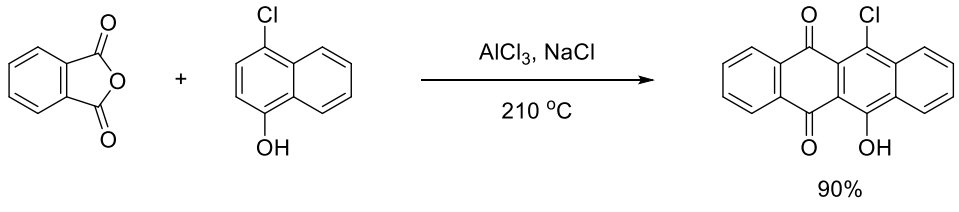


(1-4)

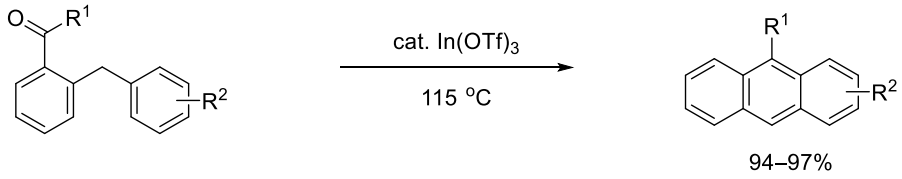


(1-5)

(1-6)



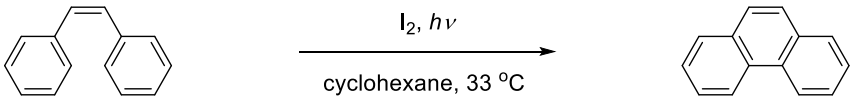
(1-7)



(1-8)

Methods for the synthesis of non-linear PAHs, such as [n]phenacenes (zig-zag PAHs) and [n]helicenes (helical PAHs), have also been developed, which are basically similar to these for phenanthrenes. The general synthesis of these PAHs has been developed based on oxidative photocyclization of *cis*-stilbene derivatives (Mallory reaction, eq. 1-9, 1-10),[11] ring closing metathesis (eq. 1-11),[12] and alkynylbiaryl cyclization (eq. 1-12).[13]

It is noteworthy that these reactions are the method of *single ring construction*. Thus, tandem reaction (eq. 1-3−1-6) or repetition of single ring construction (Scheme 1-1)[14] have been used for the synthesis of higher order PAHs. Given the wide diversity of the PAH structures, a systematic *multiple ring construction* approached on highly required.



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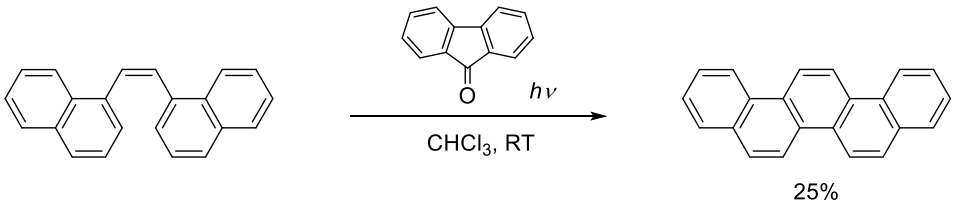

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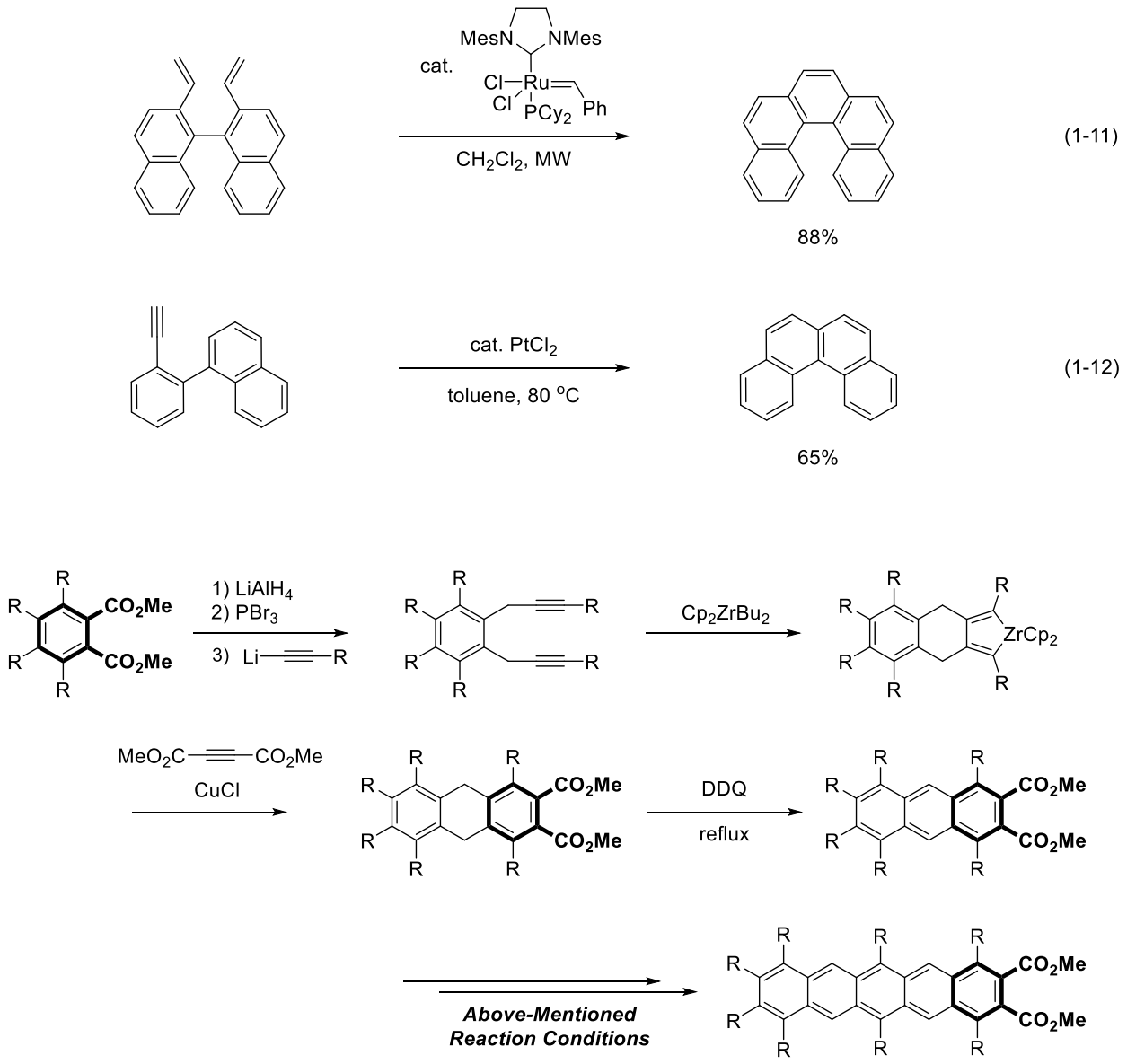
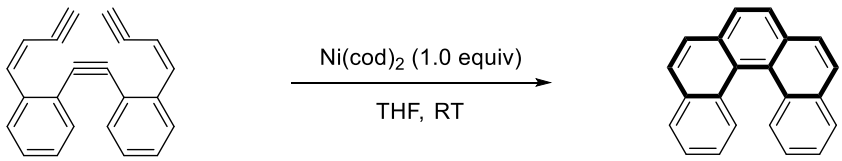


Scheme 1-1. Repetitive Extension of Acene Substructures

1-3. General Synthesis of Polycyclic Aromatic Hydrocarbons (Multiple Ring Constructions)

In contrast to the example shown above, nickel(0)-catalyzed intramolecular [2+2+2] cycloisomerization of triynes affords fused aromatic compounds through formation of three C–C bonds (eq. 1-13).[15] This reaction provides a highly efficient method of three-ring constructions in one operation. However, only a few examples of efficient PAH syntheses using *multiple ring constructions* have been reported.

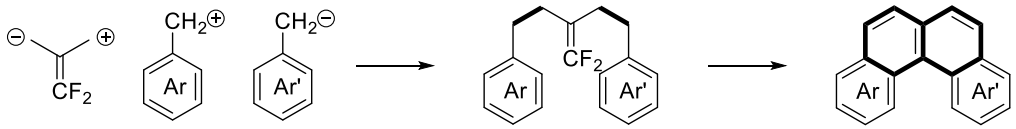


83%

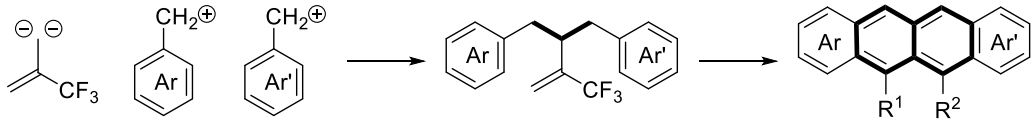
(1-13)

Thus, in this study I tried to establish methods for PAH synthesis via *multiple ring constructions,* starting from (i) 1,1-difluoro-1-alkenes by domino cyclizatios, which construct [4]helicene substructures (Scheme 1-2, top) and (ii) 2-trifluoromethyl-1-alkenes by domino or stepwise cyclizations which construct [4]acene substructures, followed by introduction of substituents (R^1, R^2) into the internal positions of acenes (Scheme 1-2, bottom).

[Chapter 2] Synthesis of [4]Helicene Derivatives (Helical)



[Chapter 3] Synthesis of Internal by Substituted Acene Derivatives (Linear)



Scheme 1-2. Plans for PAH Synthesis via Multiple Ring Constructions

1-4. Fundamentals and Outlines of This Thesis

1-4-1. Difluorocarbocation Generation from Fluoroalkenes

For more than decades, our laboratory has studied up on generation of fluorinated carbocations (especially CF_2 cations) and their synthetic use.[16] Fluorine substituents (i) stabilize the α-carbocations by donating their unshared electron pair to the vacant p-orbital of the cationic center and (ii) act as leaving groups because of their high electronegativity (Figure 1-4).[17] Based on the CF_2 cations, our laboratory have reported several reports on the synthesis of cyclic/acyclic and fluorinated/fluorine-free compounds.

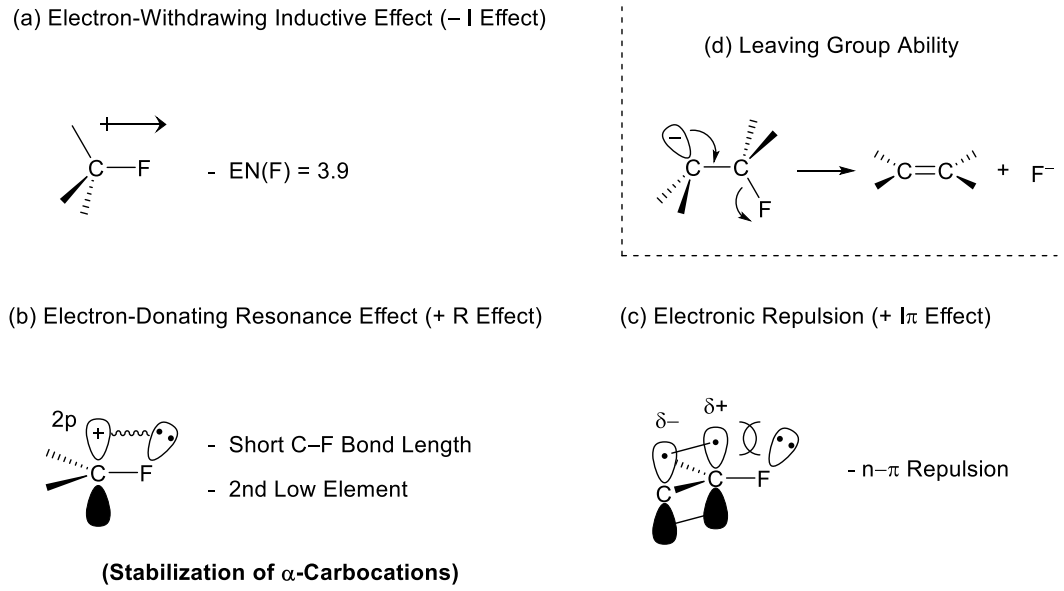
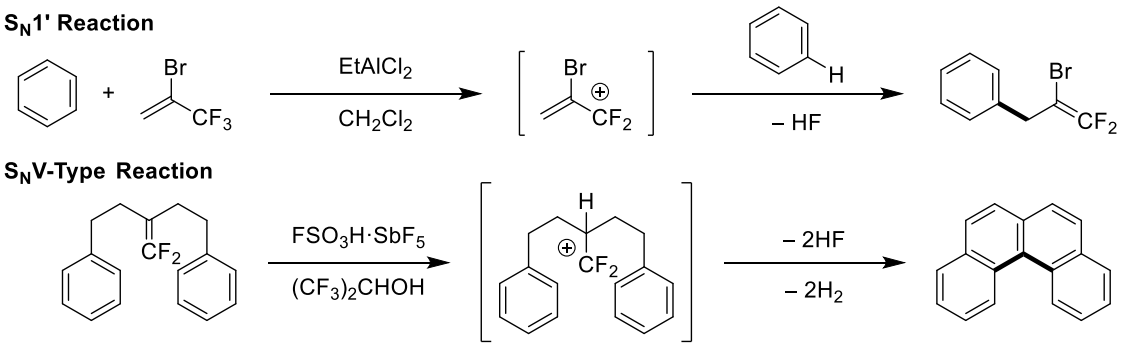


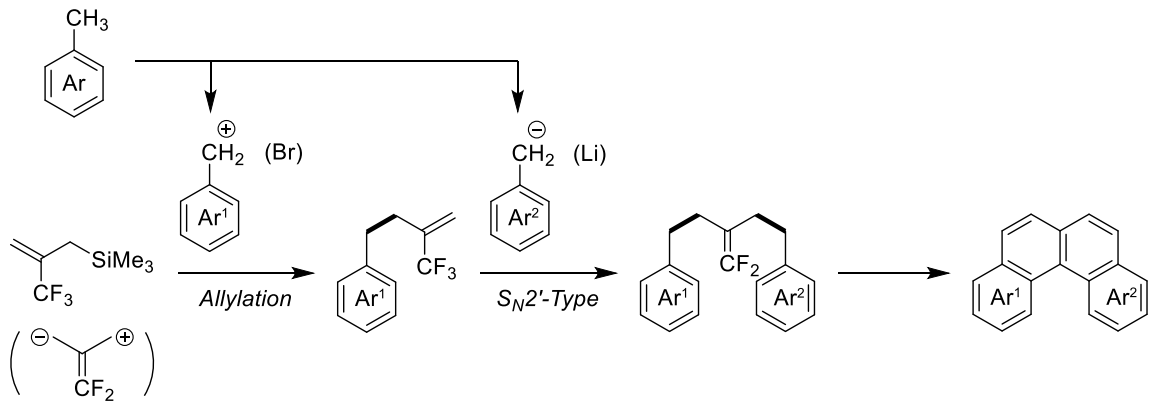
Figure 1-4. Properties of Fluorine Substituents.

Our group has already reported two reactions based on the stabilized CF_2 cations (Scheme 1-3). Elimination of a fluoride ion from trifluoromethylated alkenes was promoted with aluminium Lewis acids (Scheme 1-3, top).[16e] The generated CF_2 cations underwent Friedel–Crafts-type arylation at the position γ to the fluorine substituents with arenes to afford 3,3-difluoroallylated arenes. It is noteworthy that the two C–F bonds remain unreacted (single C–F bond activation of CF_3 groups was accomplished). Treatment of 1,1-difluoroalkenes with super acids caused regioselective protonation (Figure 1-3, bottom).[18] Thus-generated CF_2 cations underwent domino Friedel–Crafts-type ring closure to afford [4]helicenes and their π-extended variants.



Scheme 1-3. Catalytic C–F Bond Activations of Fluoroalkenes via Fluorine Elimination

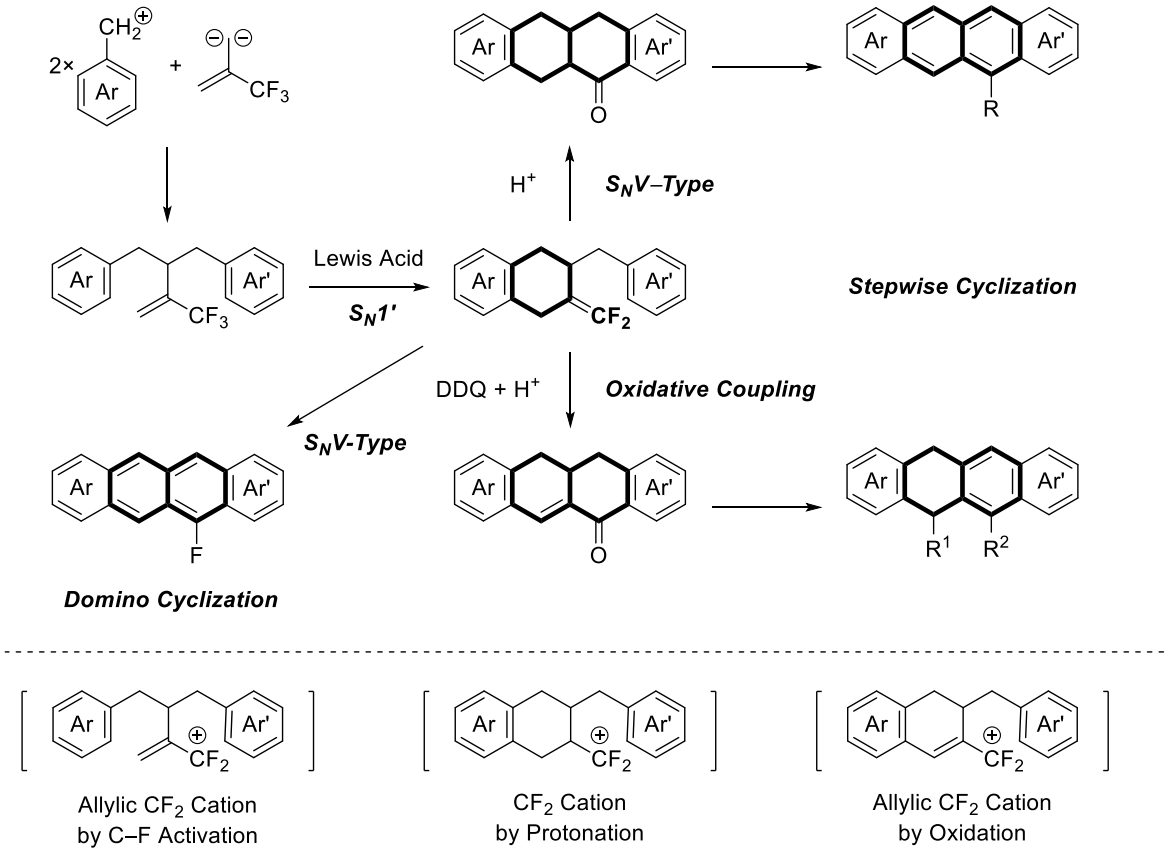
In chapter 2, PAHs were synthesized via a methylarene-based protocol (Scheme 1-4). Trimethyl[2-(trifluoromethyl)allyl]silane was electrophilically benzylated with Ar^1CH_2Br (prepared from Ar^1CH_3) to afford 2-trifluoromethyl-1-alkenes that were in turn nucleophilically benzylated with Ar^2CH_2Li (prepared from Ar^2CH_3) through S_N2'-type reaction to produce 1,1-difluoroethylenes, which are cyclization precursors bearing two 2-arylethyl groups. Magic acid efficiently promoted the domino Friedel–Crafts-type cyclization of these precursors, followed by dehydrogenation that enabled the connection among two aryl groups (Ar^1 and Ar^2) by forming two benzene rings between them, facilitating the synthesis of the desired higher-order PAHs. With the proposed protocol, the combination of even a limited number of methylarenes can yield a variety of PAHs in diverse configurations.



Scheme 1-4. Strategy: Allylation and S_N2'-Type Reaction of Two Methylarenes Followed by Domino Cyclization

In chapter 3, (trifluoromethyl)alkenes bearing two aryl groups were treated with $AlMe_2Cl$ to afford fluorinated dihydrotetracenes through a domino two-ring construction followed by dehydrogenation, leading to the synthesis of 5-fluorotetracenes (Scheme 1-5). In addition, treatment of the same (trifluoromethyl)alkenes with both $AlMe_2Cl$ (1.2 equiv) and Me_3Al (1.0 equiv) resulted in selective one-ring construction, affording bicyclic difluoroalkenes. (i) Treatment of the bicyclic difluoroalkenes with TfOH allowed regioselective protonation to generate the CF_2 cations, whose

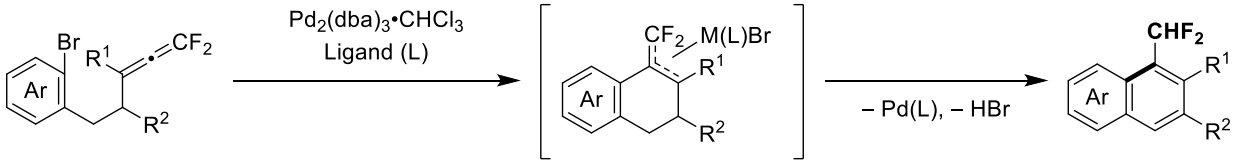
Friedel–Crafts-type cyclization afforded tetracyclic ketones. The obtained ketones were useful intermediates for the introduction of substituents (R), providing 5-substituted tetracenes. Furthermore, I found new CF_2 cation generation via *oxidation*. (ii) Treatment of the bicyclic difluoroalkenes with DDQ/TfOH generated allylic CF_2 cations, whose Friedel–Crafts-type cyclization afforded tetracyclic enones. The enones facilitated introduction of two substituents (R^1 and R^2) to the tetracene skeletons, followed by dehydrogenation to afford 5,6-disubstituted tetracene derivatives. The oxidative CF_2 cation generation was extended to the system of (Difluoromethyl)naphthalenes, which provides a novel synthetic utility of the difluoromethyl groups (not shown).



Scheme 1-5. Synthesis of Substituted Acenes via S_N1' / S_NV-Type Domino or Stepwise Cyclizations

In chapter 4, synthesis of (difluoromethyl)naphthalenes is described. *o*-Bromophenyl-bearing 1,1-difluoroallenes underwent intramolecular insertion in the presence of a palladium catalyst.

Regioselective C–C bond formation occurred to form six-membered carbocycles, leading to aforementioned promising difluoromethylated naphthalenes (Scheme 1-6).



Scheme 1-6. (Difluoromethyl)naphthalene Synthesis from 1,1-Difluoroallenes

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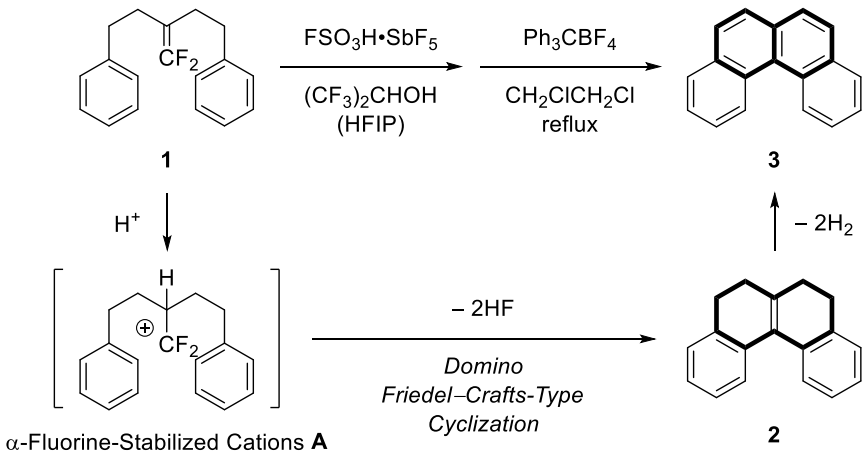
CHAPTER 2

Synthesis of PAHs Based on Methylarenes via Domino Cyclization of 1,1-Difluoroalkenes

2-1. Introduction

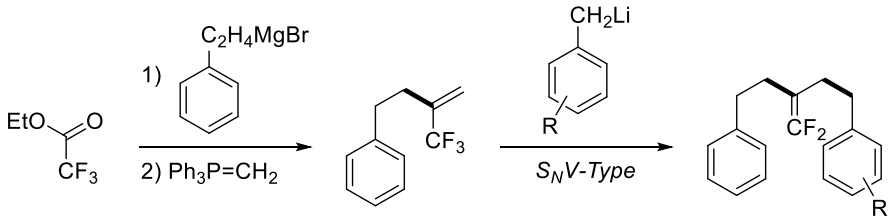
Our laboratory has reported the domino Friedel–Crafts-type cyclization of 1,1-difluoro-1-alkenes **1** (Scheme 2-1), which efficiently yielded a [4]helicene structure by forming two benzene rings between two aryl groups (Ar^1 and Ar^2).[1] Upon the treatment of **1** bearing two 2-arylethyl groups [CF_2=C($CH_2CH_2Ar^1$)($CH_2CH_2Ar^2$)] with magic acid ($FSO_3H{\cdot}SbF_5$) in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP),[2] the protonation proceeded regioselectively, generating α-fluorine-stabilized cations **A**.[3] These, in turn, underwent the domino Friedel–Crafts-type cyclization followed by dehydrogenation of the resulting tetracyclic products **2**, forming [4]helicenes and their π-extended variants **3**.[4,5]



Scheme 2-1. S_NV-Type Reaction Followed by Domino Cyclization

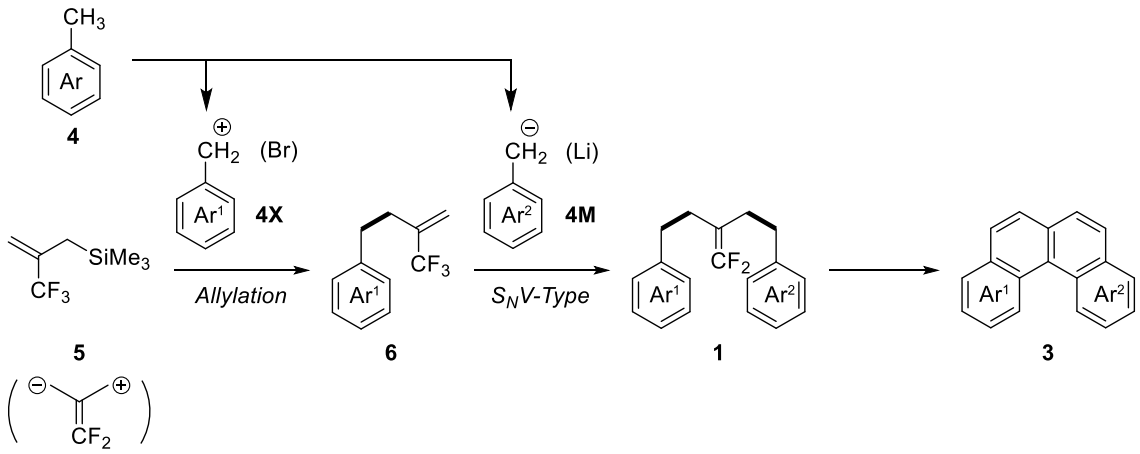
Despite the utility of the domino cyclization, the preparation of the starting **1** has been less examined. Bromine-mediated coupling was employed for the symmetrical difluoroalkenes

[CF_2=C(CH_2CH_2Ar)$_2$],[6] while the S_N2'-type reaction of 2-trifluoromethyl-1-alkenes was adopted (eq. 2-1) for the unsymmetrical ones [CF_2=C($CH_2CH_2Ar^1$)($CH_2CH_2Ar^2$)].[7]

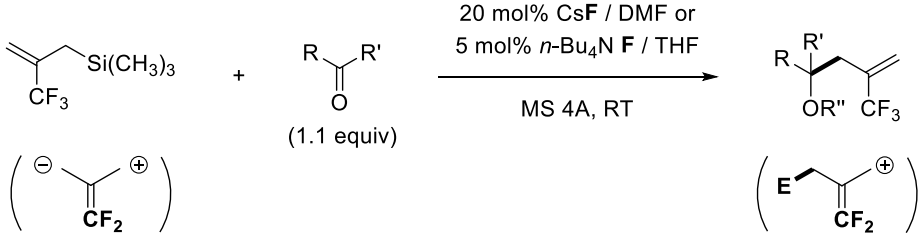


(2-1)

For the systematic synthesis of PAHs, I adopted methylarenes **4** as starting materials for the preparation of **1** (Scheme 2-2). Allylsilane **5**, originally developed as a (trifluoromethyl)allylating agent for aldehydes or ketones (eq. 2-2),[8] would react with the benzyl halides **4X** (Ar^1CH_2X) derived from **4** (Ar^1CH_3). Then, the resulting (trifluoromethyl)alkenes **6** would undergo an S_N2'-type reaction with the benzyl metals **4M** (Ar^2CH_2M) derived from **4** (Ar^2CH_3), forming the desired unsymmetrical difluoroalkenes **1**.



Scheme 2-2. Strategy and Overview of the Tetracene Synthesis



(2-2)

Theoretically, the number of 1,1-difluoro-alkenes, *N*, synthesized from methylarenes **1** whose

number is *n* can be expressed as follows:

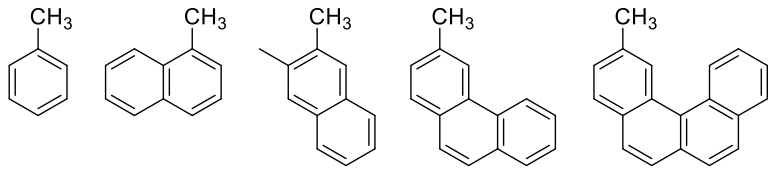
$$N = n + (n^2 - n)/2 = (n^2 + n)/2$$

Thus, the combination of even a limited number of **4** could facilitate the production of a variety of **1**, whose domino cyclization might lead to the corresponding PAHs.

2-2. Preparation of Cyclization Precursors: 1,1-Difluoroalkenes

2-2-1. Preparation of Methylarenes 4

Five methylarenes (Figure 2-1) were selected for this study. Toluene (**4a**) and methylnaphthalenes **4b,c** are commercially available, while methylphenanthrene **4d**[5] and methyl[4]helicene **4e**[1] were prepared by our cation cyclization methods as described below.



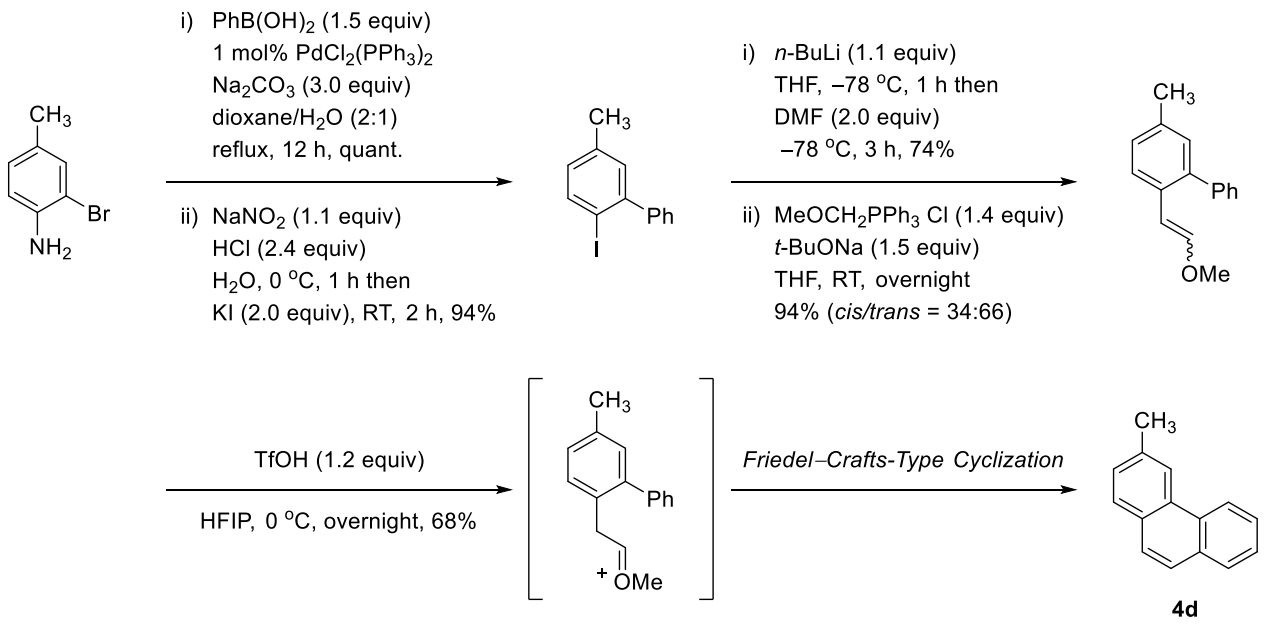
4a **4b** **4c** **4d** **4e**

Methylarene	Aryl Group	# of Benzene Ring(s)
4a	Phenyl	1
4b	Naphthalen-1-yl	2
4c	3-Methylnaphthalen-2-yl	2
3d	Phenanthren-3-yl	3
4e	[4]Helicen-2-yl	4

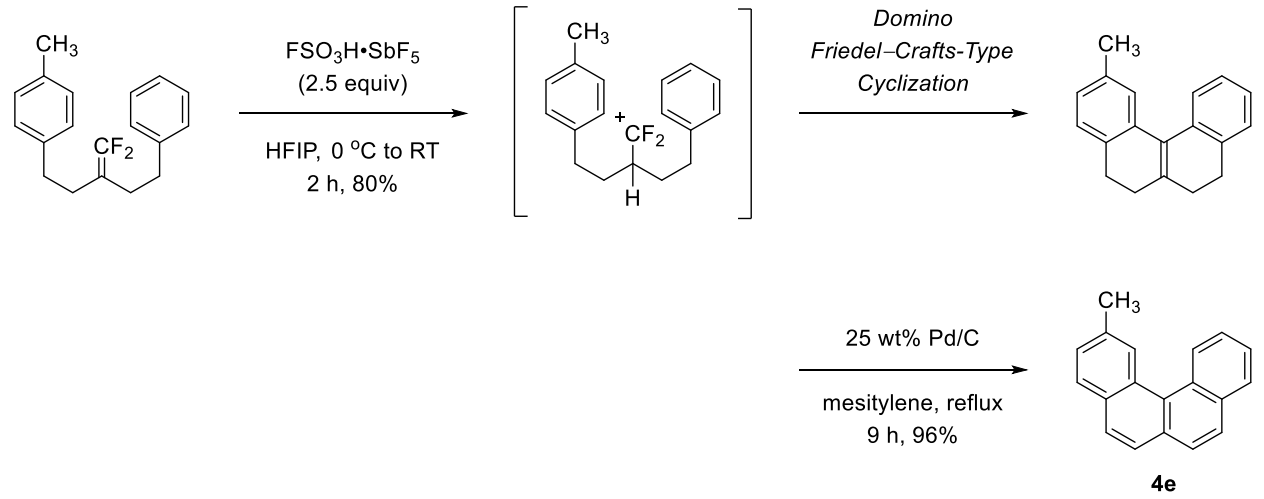
Figure 2-1. List of Starting Methylarenes

For the preparation of **4d**, commercially available 2-bromotoluidine was subjected to Suzuki–Miyaura coupling with phenylboronic acid (Scheme 2-3). The subsequent diazotization and iodination resulted in the corresponding biphenyl iodide in a 94% yield (two steps); the formylation of this iodide with dimethylformamide (DMF, 74% yield) followed by methoxymethylidenation gave the corresponding vinyl ether (94% yield, *cis*/*trans* = 34:66). Upon treatment with trifluoromethanesulfonic acid (TfOH, 1.2 equiv), the vinyl ether underwent Friedel–Crafts-type

cyclization via the in situ generated oxocarbenium ion, forming the desired **4d** in a 68% yield. **4e** was prepared via the method shown in Scheme 2-4. Thus, 1,1-difluoroalkene bearing a phenyl group and a *p*-tolyl group was treated with magic acid (2.5 equiv) in HFIP (80% yield for domino cyclization); the subsequent dehydrogenation of the product with Pd/C gave **4e** (96% yield).



Scheme 2-3. Preparation of Methyphenanthrene **4d**

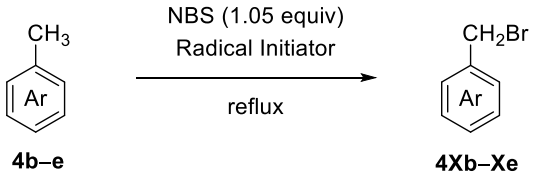


Scheme 2-4. Preparation of Methyl[4]helicene **4e**

2-2-2. Preparation of Benzyl Bromides 4X and 2-Trifluoromethyl-1-alkenes 6 (Electrophilic Benzylation)

The electrophilic benzyl components ($ArCH_2Br$ **4X**) were prepared by the bromination of **4** (Table 2-1). The bromination of **4b** and **4c** with *N*-bromosuccinimide (NBS)/benzoyl peroxide (BPO) in refluxing tetrachloromethane (77 °C) gave the corresponding benzyl bromides **4Xb** and **4Xc** in 78% and 72% yields, respectively (Entries 1 and 2). However, **4d** formed the corresponding bromide **4Xd** only in a 56% yield under similar conditions (Entry 3) partly because of the formation of (dibromomethyl)phenanthrene; to suppress such dibromination, the process was examined at a lower temperature. Unlike BPO and azobis(isobutyronitrile) (AIBN) that operate at 80 and 70 °C, respectively, 2,2'-azobis(2,4-dimethyl-4-methoxy)valeronitrile (V-70) acts as a radical initiator at 25 °C.[9] Thus, **4d** was treated with NBS/V-70 in refluxing dichloromethane (40 °C) to undergo monobromination and the desired **4Xd** was obtained in an 80% yield (Entry 4); NBS/V-70 also allowed a good yield (84%) of (bromomethyl)[4]helicene **4Xe** (Entry 5).

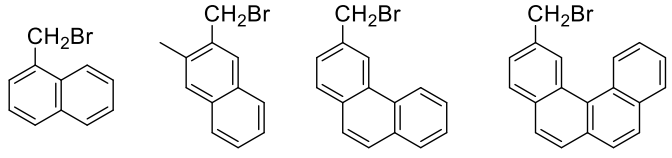
Table 2-1. Preparation of Benzyl Bromides **4Xb–Xe**



4b–e **4Xb–Xe**

Entry	**4**	Solvent, Initiator /mol%	*t* /h	**4X**	Yield /%
1	**4b**	CCl_4, BPO (3)	3	**4Xb**	78
2	**4c**	CCl_4, BPO (3)	3	**4Xc**	72[a]
3	**4d**	CCl_4, BPO (3)	13	**4Xd**	56
4	**4d**	CH_2Cl_2, V-70 (5)	3	**4Xd**	80
5[b]	**4e**	CH_2Cl_2, V-70 (5)	2	**4Xe**	84

a) ^1H NMR yield based on an internal standard CH_2Br_2; b) NBS (1.5 equiv); BPO = Dibenzoyl peroxide; V-70 = 2,2'-azobis(2,4-dimethyl-4-methoxy)valeronitrile

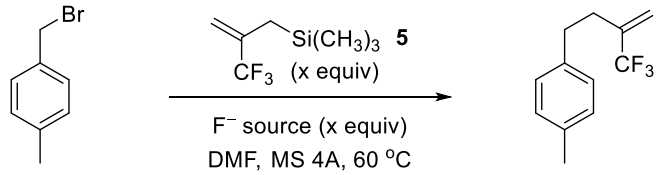


4Xb **4Xc** **4Xd** **4Xe**

With benzyl bromide ($PhCH_2Br$, **4Xa**) and the prepared bromides **4Xb**,**Xe**, the benzylation of trimethyl[2-(trifluoromethyl)allyl)silane (**5**) was examined. The allylsilane was prepared from the commercially available ethyl trifluoroacetate via a reported procedure.[8]

Silane **5** readily reacted with the benzyl bromides in the presence of a stoichiometric amount of cesium fluoride (Table 2-2). α-Bromo-*p*-xylene (**4Xf**) was adopted as a model compound and treated with **5** (1.1 equiv) and cesium fluoride (1.1 equiv; Kanto Chemical Co., Inc., cesium fluoride 4N) in DMF at 60 °C (Entry 1); the desired CF_3-allylation product (2-trifluoromethyl-1-alkene **6f**) was obtained in a 56% yield. Attempts to perform the reaction in dimethyl sulfoxide (DMSO) or with sodium fluoride as the fluoride ion source failed (Entries 2 and 3). Among the other fluoride ion sources examined, namely, *n*-Bu_4NF, $(Me_2N)_3SSiF_2Me_3$ (TASF), and *n*-$Bu_4NSnF_2Ph_3$, TASF formed **6f** in a 57% yield (Entries 4–6). The use of 2.1 equiv of **5** and 2.1 equiv of cesium fluoride improved this yield up to 67% (Entry 7).

Table 2-2. Benzylation of [(Trifluoromethyl)allyl]silane **5**



4Xf **6f**

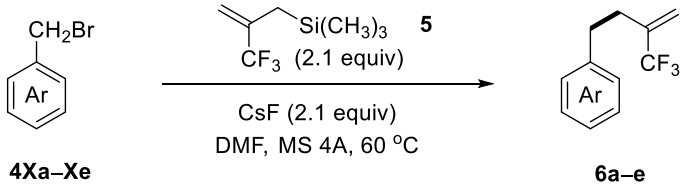
Entry	F^- source	x /equiv	*t* /h	Yield /%
1	CsF	1.1	5	56
2[a]	CsF	1.1	7	11
3	NaF	1.1	7	–
4	*n*-Bu_4N F[b]	1.1	1	Trace
5	$(Me_2N)_3S$ SiF_2Me_3[c]	1.1	4	57
6	*n*-Bu_4N SnF_2Ph_3	1.1	4	–
7	CsF	2.1	4	67

a) The reaction was conducted in DMSO; b) TBAF; c) TASF.

Various (trifluoromethyl)alkenes **6** were synthesized by the CsF-promoted benzylation of **5** (Table 2-3). When using **4Xa** (1.1 equiv relative to **5**), phenylated (trifluoromethyl)alkene **6a** was obtained in a quantitative yield (Entry 1); the benzylation with the other bromides (**4Xb–Xe**) were effected

under the optimized conditions as summarized in Table 2-3, leading to the corresponding **6b–e** in 46–89% yields (Entries 2–5).[10]

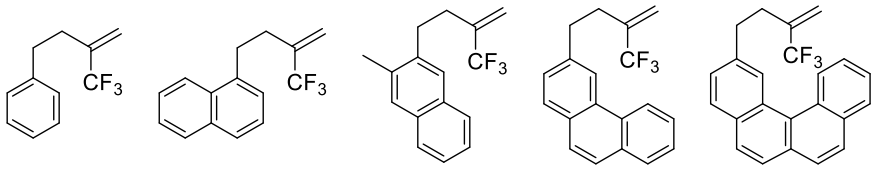
Table 2-3. Preparation of 2-Trifluoromethyl-1-alkenes **6** with Benzyl Bromides **4X**



4Xa–Xe **6a–e**

Entry	**4X**	*t* /h	**6**	Yield /%
1[a]	**4Xa**	7	**6a**	Quant[b]
2	**4Xb**	2	**6b**	84
3[c]	**4Xc**	7	**6c**	47
4	**4Xd**	1	**6d**	89
5	**4Xe**	5	**6e**	46

a) $PhCH_2Br$ (**4Xa**, 1.1 equiv), **5**, CsF (1.1 equiv); b) Yield based on **5**; c) **5** (1.1 equiv), CsF (1.1 equiv), 90 °C.



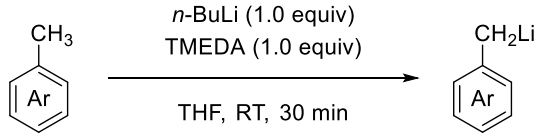
6a **6b** **6c** **6d** **6e**

2-2-3. Preparation of Difluoroalkenes 1 (S_N2'-Type Reaction)

The synthesized **6** were subjected to an S_N2'-type reaction to afford **1**, the domino cyclization precursor. The required benzyllithiums **4Ma–Mc** were generated by the deprotonation of **4a–c** (Scheme 2-5, Method A). **4a** was treated with an equimolar amount of butyllithium in the presence of *N,N,N′,N′*-tetramethylethylenediamine (1 equiv) to give **4Ma**, which in turn reacted with **6a**, producing the desired difluoroalkene **1a** as an S_N2'-type product in an 80% yield (Table 2-4, Entry 1).[1] The naphthylated difluoroalkenes **1b** and **1c** were similarly prepared using **4Mb** and **4Mc**, generated from **4b** and **4c** via Method A, in 80% and 96% yields, respectively (Table 2-4, Entries 2 and 3). The generation of **4Md** and **4Me** bearing an extended π-system (a phenanthrene or a [4]helicene moiety) was not simple; when **6a** was treated with a solution prepared from **4d** via Method

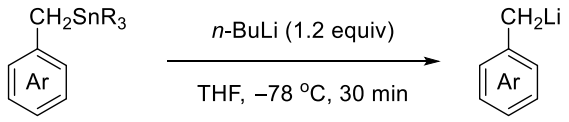
A, the desired product **1d** was obtained only in a 12% yield (Table 2-4, Entry 4). Replacing butyllithium with *sec*-butyllithium resulted in no change (12% yield; Table 2-4, Entry 5). Attempts to generate **4Md** through lithium–halogen exchange were also fruitless (eq. 2-3); **4Xd** was treated with butyllithium (1.0 equiv) in THF at –78 °C, followed by **6a** addition, to afford the undesired dimerization product [1,2-di(phenanthren-3-yl)ethane] in a quantitative yield. The treatment of (chloromethyl)phenanthrene **4Yd**, corresponding to **4Xd**, with lithium metal in THF at 0 °C to room temperature gave a complex mixture, not containing **1d** (eq. 2-4).

Method A (Deprotonation)



4a–c **4Ma–Mc**

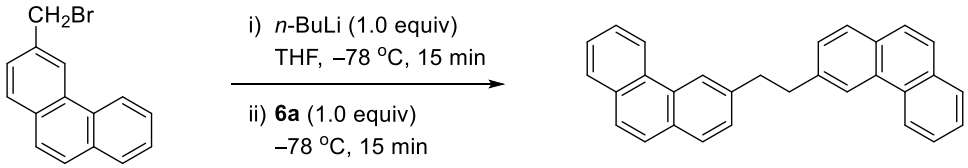
Method B (Sn–Li Exchange)



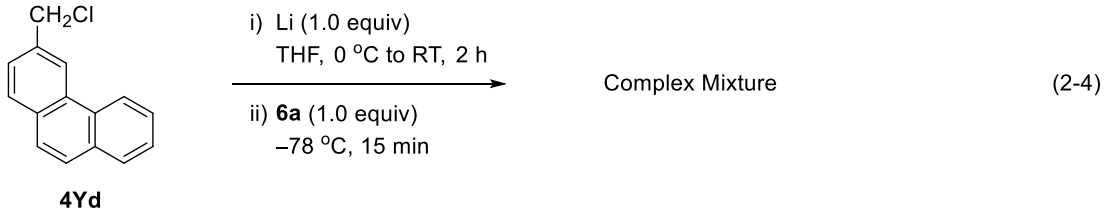
7d,e (R = *n*-Bu) **4Md,Me**

Benzyllithium	Aryl Group	# of Benzene Ring(s)
4Ma	Phenyl	1
4Mb	Naphthalen-1-yl	2
4Mc	3-Methylnaphthalen-2-yl	2
4Md	Phenanthren-3-yl	3
4Me	[4]Helicen-2-yl	4

Scheme 2-5. Generation of Benzyllithiums **4Ma–Me**

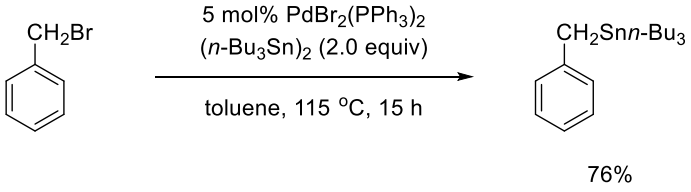


4Xd Quant (2-3)



(2-4)

Next, I tried lithiation by Sn–Li exchange (Scheme 2-5, Method B). The required benzylstannanes **7d** and **7e** were prepared according to the procedure reported for benzyl bromides ($PhCH_2Br$, eq. 2-5),[11] with some modifications.



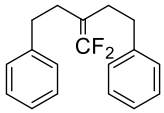
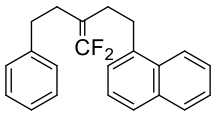
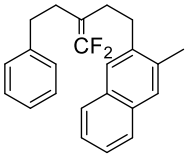
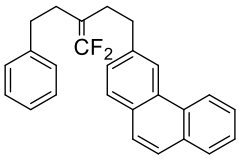
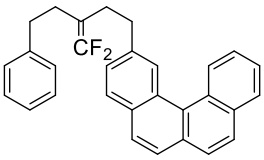
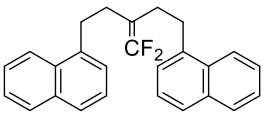
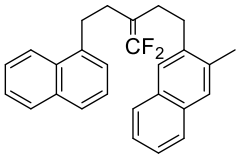
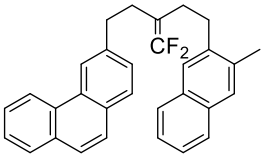
(2-5)

Although the sterically demanding **4Xd** did not form the desired **7d** with hexabutyldistannane and a $PdCl_2(MeCN)_2$ catalyst (Table 2-5, Entry 1), adding lithium chloride (5 equiv) probably promoted the transmetallation step, giving **7d** in 54% and 40% yields with a $PdCl_2(MeCN)_2$ and a $PdCl_2(PPh_3)_2$ catalyst, respectively (Table 2-5, Entries 2 and 3). The use of a benzonitrile complex [$PdCl_2(PhCN)_2$] and distannane (2 equiv) further increased this yield to 77% (Entries 4 and 5). Under the modified conditions, **7e** bearing a [4]helicenyl group was obtained in a 56% yield (Entry 6).

The Sn–Li exchange of **7d** and **7e** proceeded smoothly on treatment with butyllithium to generate (phenanthrylmethyl)lithium **4Md** and ([4]helicenylmethyl)lithium **4Me**, respectively, which were in turn subjected to the S_N2'-type reaction with (trifluoromethyl) alkene **6a** to afford difluoroalkenes **1d** and **1e** in 81% and 58% yields, respectively (Table 2-4, Entries 6 and 7). Thus, generation of benzyllithiums bearing an extended π-system was achieved by the Migita–Kosugi–Stille coupling, followed by Sn–Li exchange.

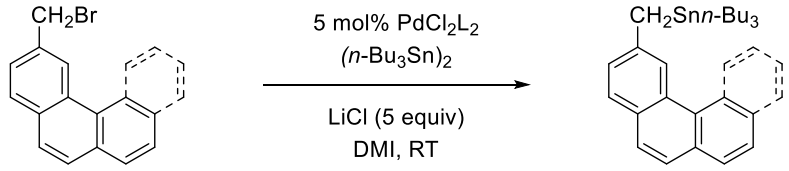
Table 2-4. Preparation of 1,1-Difluoro-1-alkene **1** from (Trifluoromethyl)alkenes **6** and Benzyllithiums **4M**

6a,b,d **4Ma–Mc** **1a–h**

Entry	**6**	**4M**	Generation of **4M**	t /h	**1**		Yield /%
1	**6a**	**4Ma**	A	2		**1a**	80
2	**6a**	**4Mb**	A	2		**1b**	80
3	**6a**	**4Mc**	A	1		**1c**	96
4	**6a**	**4Md**	A[a]	2		**1d**	12
5	**6a**	**4Md**	A[b]	2		**1d**	12
6	**6a**	**4Md**	B[c]	1		**1d**	81
7	**6a**	**4Me**	B	2		**1e**	58
8	**6b**	**4Mb**	A	2		**1f**	61
9	**6b**	**4Mc**	A	2		**1g**	76
10	**6d**	**4Mc**	A	9		**1h**	84

Generation of **4M**: Method A) **4a–c** (1.5 equiv vs. **6**), *n*-BuLi (1.5 equiv), TMEDA (1.5 equiv), THF, RT, 30 min; Method B) **7d**,**e** (1.2 equiv vs. **6**), *n*-BuLi (1.2 equiv), THF, –78 °C, 30 min; a) **4d** (0.9 equiv vs. **6a**), *n*-BuLi (0.9 equiv), TMEDA (0.9 equiv); b) **4d** (0.9 equiv vs. **6a**), *sec*-BuLi (0.9 equiv), TMEDA (0.9 equiv); c) The S_N2'-type reaction was carried out at –78 °C.

Table 2-5. Preparation of Benzylstannanes **7d,e**



4Xd,Xe

7d (Phenanthren-3-yl)
7e ([4]Helicen-2-yl)

Entry	**4X**	L	$(R_3Sn)_2$ /equiv	*t* /h	**7**	Yield /%
1[a]	**4Xd**	MeCN	1.2	1.5	**7d**	–
2	**4Xd**	MeCN	1.2	0.5	**7d**	54
3[b]	**4Xd**	PPh_3	1.2	2.3	**7d**	40
4	**4Xd**	PhCN	1.2	0.5	**7d**	64
5	**4Xd**	PhCN	2.0	0.5	**7d**	77
6	**4Xe**	PhCN	2.0	0.5	**7e**	56

a) No LiCl was used; b) Room temperature to 85 °C; DMI = 1,3-Dimethylimidazolidinone; R = Butyl.

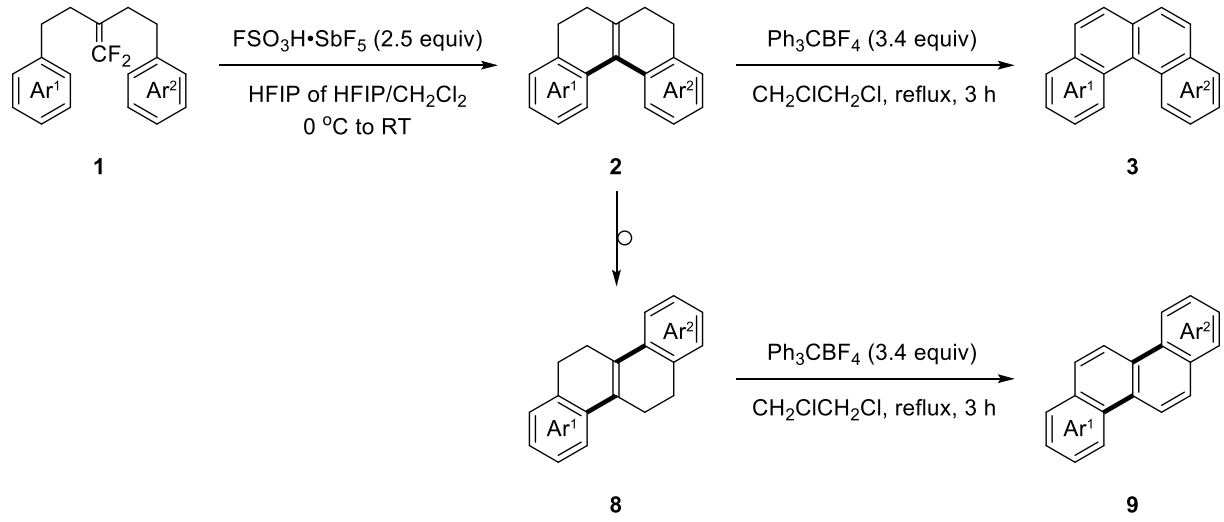
A series of difluoroalkenes **1a–e** (domino cyclization precursors), consisting of toluene (**4a**) as an electrophilic benzyl component, were synthesized. Other 1,1-difluoro-1-alkenes (**1f–h**) were also similarly obtained. **6b** underwent an S_N2'-type reaction with **4Mb** and **4Mc** to form the corresponding precursors **1f** and **1g** in 61% and 76% yields, respectively (Table 2-5, Entries 8 and 9), while **6d** reacted with **4Mc** to give **1h** in an 84% yield (Table 2-4, Entry 10).[12]

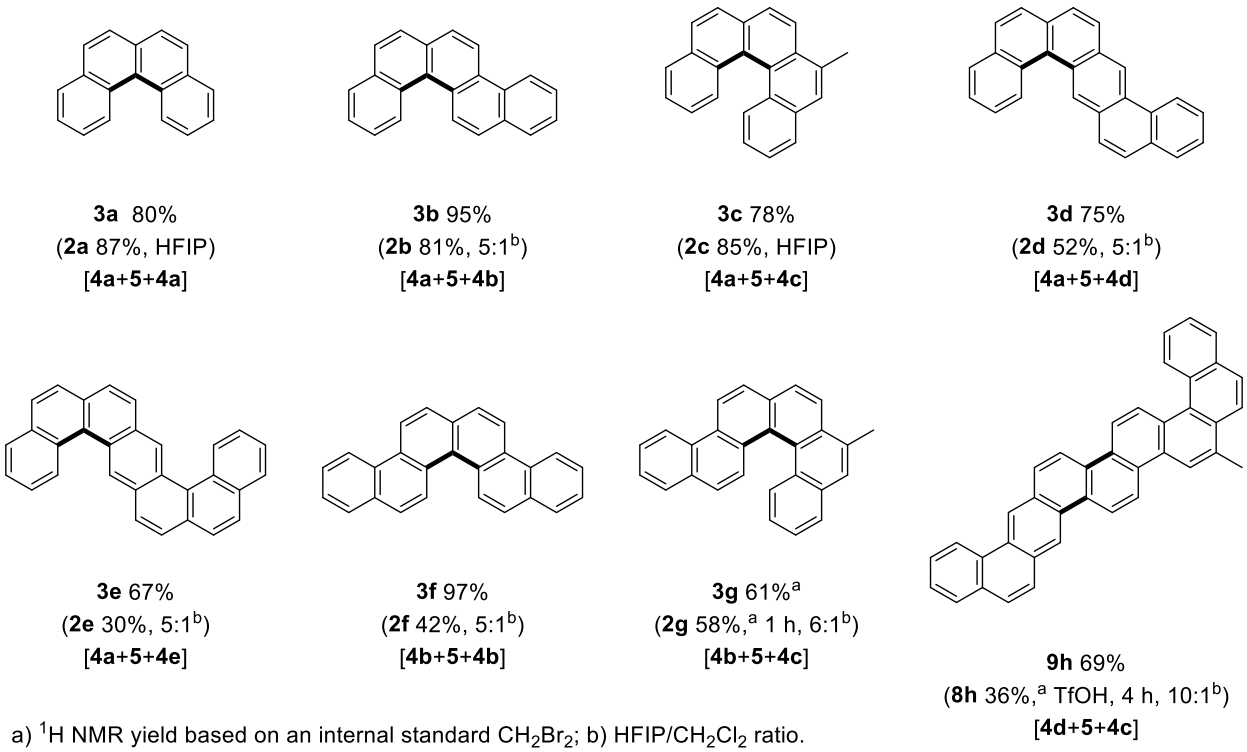
2-3. Domino Cyclization of 1 and Dehydrogenation (Synthesis of PAHs 3)

Having **1** in hand, the domino cyclization and dehydrogenation were performed (Figure 2-2). **1a** was treated with magic acid ($FSO_3H{\cdot}SbF_5$, 2.5 equiv) in HFIP at 0 °C to room temperature; the sequential cyclization proceeded smoothly and the tetracyclic product **2a** was obtained in an 87% yield. The cyclization of **1b** gave **2b** via cyclization on the ortho position (not *peri*-position) in an 81% yield. When the difluoroalkenes with extended π-systems such as **1b** were hardly dissolved in HFIP, the difluoroalkenes were dissolved in a minimum amount of dichloromethane and added to an HFIP solution of magic acid. The reaction of **1c** produced **2c** in an 85% yield. The cyclization of **1d**

and **1e**, respectively bearing a phenanthrene and a [4]helicene moiety, gave the corresponding products in 52% (**2d**) and 30% (**2e**) yields; in these cases, the C–C bonds were formed at the less hindered positions. The difluoroalkenes **1f** and **1g**, consisting of methylnaphthalenes **4b** and **4c**, produced **2f** and **2g** in 42% and 58% yields, respectively. In case of **1h**, consisting of methylnaphthalene **4c** and methylphenanthrene **4d**, the skeletal rearrangement previously described in our domino cyclization[1b] was observed to afford a hydrogenated chrysene ([4]phenacene) substructure (**8h**, 36% yield; Scheme 2-6) through spiro intermediates, probably due to the steric congestion in **2h**.

As shown in Scheme 2-4 (last step), the dehydrogenation of the cyclization products **2** with Pd/C required harsh reaction conditions (mesitylene, reflux, 9 h). The low reactivity of Pd/C might be attributed to the twisted structure of the hydrogenated [4]helicene moiety, which could have prevented the substrates **2** from being absorbed on the palladium surface. Thus, the dehydrogenation (aromatization) of **2** was conducted using Ph_3CBF_4.[13] **2a**, obtained from **1a**, was treated with Ph_3CBF_4 in refluxing 1,2-dichloroethane (85 °C); after chromatographic purification, the desired fully aromatized [4]helicene **3a**, consisting of the electrophilic benzyl component **4Ma**, CF_3-allylsilane **5**, and the nucleophilic benzyl component **4Ma** (i.e., **4a** + **5** + **4a**), was obtained in an 80% yield (Figure 2-2). The domino cyclization products **2b–g** and **8h**, produced from **1b–h**, underwent dehydrogenation with Ph_3CBF_4, forming the desired PAHs **3b–g** and **9h** with various benzene ring configurations in good to excellent yields.[14]





3a 80%
(**2a** 87%, HFIP)
[**4a+5+4a**]

3b 95%
(**2b** 81%, 5:1[b])
[**4a+5+4b**]

3c 78%
(**2c** 85%, HFIP)
[**4a+5+4c**]

3d 75%
(**2d** 52%, 5:1[b])
[**4a+5+4d**]

3e 67%
(**2e** 30%, 5:1[b])
[**4a+5+4e**]

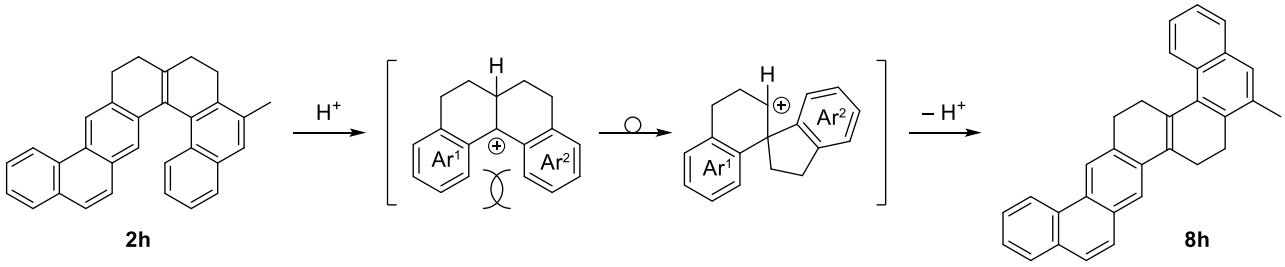
3f 97%
(**2f** 42%, 5:1[b])
[**4b+5+4b**]

3g 61%[a]
(**2g** 58%,[a] 1 h, 6:1[b])
[**4b+5+4c**]

9h 69%
(**8h** 36%,[a] TfOH, 4 h, 10:1[b])
[**4d+5+4c**]

a) ^{1}H NMR yield based on an internal standard CH_2Br_2; b) HFIP/CH_2Cl_2 ratio.

Figure 2-2. Synthesis of PAHs **3** and **9** by Domino Cyclization of 1,1-Difluoroalkenes **1** and Dehydrogenation



Scheme 2-6. Skeletal Rearrangement to **8h**

2-4. References

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4. For our publications on the synthesis based on stabilized CF_2 cations, see: (a) Ichikawa, J.; Jyono, H.; Kudo, T.; Fujiwara, M.; Yokota, M. *Synthesis* **2005**, *2005*, 39. (b) Ichikawa, J.; Kaneko, M.; Yokota, M.; Itonaga, M.; Yokoyama, T. *Org. Lett.* **2006**, *8*, 3167. (c) Yokota, M.; Fujita, D.; Ichikawa, J. *Org. Lett.* **2007**, *9*, 4639. (d) Fuchibe, K.; Takayama, R.; Yokoyama, T.; Ichikawa, J. *Chem. Eur. J.* **2017**, *23*, 2831. (e) Fuchibe, K.; Hatta, H.; Oh, K.; Oki, R.; Ichikawa, J. *Angew. Chem. Int. Ed.* **2017**, *56*, 5890. (f) Fuchibe, K.; Oki, R.; Hatta, H.; Ichikawa, J. *Chem. Eur. J.* **2018**, *24*, 17932. See also ref 1.
5. For our dehydrative PAH synthesis conducted in HFIP via fluorine-free carbocations, see: (a) Takahashi, I.; Hayashi, M.; Fujita, T.; Ichikawa, J. *Chem. Lett.* **2017**, *46*, 392. (b) Fujita, T.; Takahashi, I.; Hayashi, M.; Wang, J.; Fuchibe, K. Ichikawa, J. *Eur. J. Org. Chem.* **2017**, *2017*, 262.

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10. When the yields of benzylation were moderate, benzyl fluoride and benzyl formate were observed as byproducts in the crude mixtures.
11. Azizian, H.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1981**, *215*, 49.
12. Throughout the studeis of Table 2-4, sideproducts such as regioisomers and overreaction products were not isolated.
13. The use of DDQ as a dehydrogenating agent resulted in low product yields.
14. The structures of PAHs **3g** and **9h** were confirmed by single crystal X-ray analysis.

2-5. Experimental Section

Synthesis of Alkynes

General. 1,1,1,3,3,3-Hexafluoropropan-2-ol (HFIP) was distilled from activated molecular sieves 4A and stored over activated molecular sieves 4A. Dichloromethane, THF, and DMF were dried by passing through a column of activated alumina followed by a column of Q-5 scavenger (Engelhard). Magic acid was purchased from Merck KGaA and used as received. V-70 was purchased from Wako Pure Chemical Industries, Ltd. and used as received. CsF was purchased from Kanto Chemical Co., Inc. (Cesium fluoride 4N) and activated before use (*vide infra*). Molecular sieves 4A (powder) was purchased from Merck KGaA and activated before use (*vide infra*). [(Trifluoromethyl)allyl]silane **5** was prepared by the reported procedure.[23] HFIP can be purchased from commercial suppliers such as

Merck KGaA.

Column chromatography and preparative thin layer chromatography (PTLC) were conducted on silica gel (Silica Gel 60 N, Kanto Chemical Co., Inc. for column chromatography and Wakogel B-5F, Wako Pure Chemical Industries, Ltd. for PTLC). Purification of PAH **3g** was also performed by preparative HPLC (GPC), using a JAI LC-908 instrument (Jaigel-2H, $CHCl_3$).

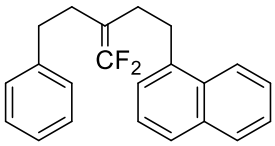
IR spectra were recorded on a Horiba FT-300S spectrometer by the attenuated total reflectance (ATR method). NMR spectra were recorded on Bruker Avance 500 or Jeol JNM ECS-400 spectrometers in $CDCl_3$ at 500 or 400 MHz (^{1}H NMR), at 126 or 101 MHz (^{13}C NMR), and at 470 or 376 MHz (^{19}F NMR). Chemical shifts were given in ppm relative to internal Me_4Si (for ^{1}H NMR: $\delta = 0.00$), $CDCl_3$ (for ^{13}C NMR: $\delta = 77.0$), and C_6F_6 (for ^{19}F NMR: $\delta = 0.0$).[31] High-resolution mass spectroscopy (HRMS) was conducted with a Jeol JMS-T100GCV spectrometer (EI, TOF) or a Jeol JMS-T100CS spectrometer (ESI^+, TOF or $APCI^+$, TOF). Elemental analysis was performed with a Yanako MT-3 CHN Corder apparatus. Single crystal X-ray structure analysis was performed on a Bruker APEXII ULTRA instrument equipped with a CCD diffractometer using Mo Kα (graphite monochromated, λ = 0.71069 Å) radiation.

Benzylation of [(trifluoromethyl)allyl]silane 5 [preparation of 2-trifluoromethyl-1-alkene 6b]. Molecular sieves 4A (99 mg) and CsF (314 mg, 2.06 mmol) were heated under vacuum (160 °C, 2 h, 0.5 Torr). To the activated MS 4A and CsF were added a DMF solution (10 mL) of benzyl bromide **4Xb** (215 mg, 0.973 mmol) and [(trifluoromethyl)allyl]silane **5** (0.38 mL, 2.0 mmol). The reaction mixture was heated for 1 h at 60 °C. Phosphate buffer (pH 7, 10 mL) was added to quench the reaction at room temperature. Organic materials were extracted with AcOEt three times. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane) to give (trifluoromethyl)alkene **6b** (206 mg, 84% yield) as a colorless liquid.

S_N2'-type reaction of 2-trifluoromethyl-1-alkenes 6 (preparation of 1,1-difluoro-1-alkene 1b, Method A). To a THF solution (4 mL) of TMEDA (0.21 mL, 1.4 mmol) and methylarene **4b** (201 mg, 1.42 mmol) was added butyllithium (1.0 mL, 1.4 mol/L in hexane, 1.4 mmol) at room temperature. The reaction mixture was stirred for 30 min at room temperature and cooled to –78 °C. To the THF solution of benzyllithium **4Mb** was added a THF solution (3 mL) of (trifluoromethyl)alkene **6a** (187 mg, 0.934 mmol). After stirring for 1 h at –78 °C, the reaction mixture was allowed to warm to room temperature and stirred for 30 min. Aqueous NH_4Cl (5 mL) was added to quench the reaction at room temperature. Organic materials were extracted with AcOEt three times. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane/AcOEt = 50:1) to give difluoroalkene **1b** as a colorless liquid (240 mg, 80% yield).

S_N2'-type reaction of 2-trifluoromethyl-1-alkenes 6 (preparation of 1,1-difluoro-1-alkene 1d, Method B). To a THF solution (4 mL) of benzylstannane **7d** (108 mg, 0.224 mmol) was added butyllithium (0.16 mL, 1.4 mol/L in hexane, 0.22 mmol) at –78 °C. The reaction mixture was stirred for 30 min at –78 °C. To the THF solution of benzyllithium **4Md** was added a THF solution (0.7 mL) of (trifluoromethyl)alkene **6a** (37 mg, 0.19 mmol). The reaction mixture was stirred for 1 h at –78 °C. Phosphate buffer (pH 7, 5 mL) was added to quench the reaction at –78 °C. Organic materials were extracted with AcOEt three times. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane/AcOEt = 10:1) to give difluoroalkene **1d** as a colorless liquid (57 mg, 81% yield).

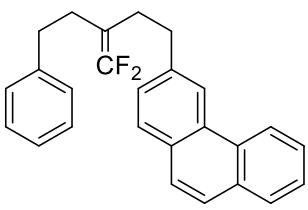
1-[3-Difluoromethylidene-5-phenylpent-1-yl]naphthalene (1b): ^{1}H NMR (500 MHz, $CDCl_3$): δ



1b

2.34 (tdd, J = 8.0 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.41 (tdd, J = 8.0 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.72 (t, J = 8.0 Hz, 2H), 3.16 (t, J = 8.0 Hz, 2H), 7.16 (d, J = 7.0 Hz, 2H), 7.20 (dd, J = 7.5, 7.5 Hz, 1H), 7.27–7.32 (m, 3H), 7.40 (dd, J = 8.0, 7.0 Hz, 1H), 7.49 (ddd, J = 8.1, 6.9, 1.5 Hz, 1H), 7.54 (ddd, J = 8.1, 6.9, 1.5 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.7 (d, J_{CF} = 2 Hz), 28.5 (d, J_{CF} = 2 Hz), 31.4 (dd, J_{CF} = 3, 3 Hz), 34.0 (dd, J_{CF} = 3, 3 Hz), 88.4 (dd, J_{CF} = 17, 17 Hz), 123.4, 125.52, 125.54, 125.97, 125.99, 126.1, 126.9, 128.3, 128.4, 128.9, 131.6, 133.9, 137.3, 141.1, 153.7 (dd, J_{CF} = 283, 283 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 66.9 (br d, J = 54 Hz, 1F), 67.2 (br d, J = 54 Hz, 1F); IR (neat): ν 3026, 2956, 1745, 1263, 1215, 775, 748 cm^{-1}; EA: calcd for $C_{22}H_{20}F_2$: C, 81.96; H 6.25%, found: C, 81.8; H 6.41%.

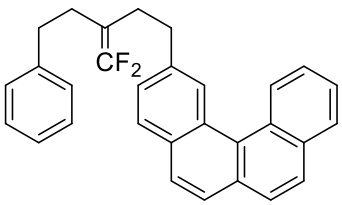
3-[3-Difluoromethylidene-5-phenylpent-1-yl]phenanthrene (1d): ^{1}H NMR (500 MHz, $CDCl_3$): δ



1d

2.34 (tdd, J = 8.0 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.43 (tdd, J = 8.0 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.75 (t, J = 8.0 Hz, 2H), 2.97 (t, J = 8.0 Hz, 2H), 7.18–7.23 (m, 3H), 7.29 (dd, J = 7.5, 7.5 Hz, 2H), 7.43 (dd, J = 8.0, 1.3 Hz, 1H), 7.59 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H), 7.66 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H), 7.70 (d, J = 9.3 Hz, 1H), 7.72 (d, J = 9.3 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.89 (dd, J = 7.5, 1.0 Hz, 1H), 8.46 (s, 1H), 8.69 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 28.2, 28.4, 34.0 (dd, J_{CF} = 3, 3 Hz), 34.6 (dd, J_{CF} = 3, 3 Hz), 88.1 (dd, J_{CF} = 17, 17 Hz), 121.7, 122.6, 126.1, 126.3, 126.4, 126.5, 126.7, 127.3, 128.3, 128.4, 128.6, 128.7, 130.1, 130.4, 130.5, 132.2, 139.6, 141.2, 153.8 (dd, J_{CF} = 283, 283 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 67.1 (br d, J = 53 Hz, 1F), 67.2 (br d, J = 53 Hz, 1F); IR (neat): ν 3064, 2927, 1747, 1603, 1219, 771 cm^{-1}; EA: calcd for $C_{26}H_{22}F_2$: C, 83.84; H, 5.95%, found: C, 83.44; H, 6.10%.

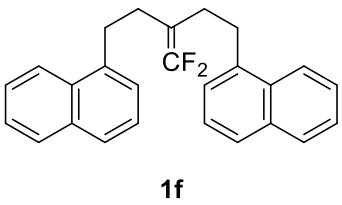
2-[3-Difluoromethylidene-5-phenylpent-1-yl][4]helicene (1e): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.36



1e

(tdd, J = 8.2 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.46 (tdd, J = 7.8 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.75 (t, J = 8.2 Hz, 2H), 3.00 (t, J = 7.8 Hz, 2H), 7.17 (d, J = 7 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 7.26–7.28 (m, 2H), 7.46 (dd, J = 7.0, 1.5 Hz, 1H), 7.63 (ddd, J = 7.3, 7.3, 1.2 Hz, 1H), 7.68 (ddd, J = 7.7, 7.7, 1.7 Hz, 1H), 7.79 (d, J = 8.5 Hz, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 8.03 (dd, J = 7.5, 1.5 Hz, 1H), 8.91 (s, 1H), 9.10 (d, J = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 28.3 (d, J_{CF} = 2 Hz), 28.4 (d, J_{CF} = 3 Hz), 34.0 (dd, J_{CF} = 3, 3 Hz), 34.5 (dd, J_{CF} = 3, 3 Hz), 88.0 (dd, J_{CF} = 13, 13 Hz), 125.8, 126.07, 126.11, 126.3, 126.7, 126.9, 127.05, 127.11, 127.2, 127.4, 127.7, 128.3, 128.4, 128.60, 128.63, 130.3, 130.4, 131.1, 132.0, 133.5, 139.0, 141.1, 153.8 (dd, J_{CF} = 284, 284 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 67.2 (br d, J = 55 Hz, 1F), 67.3 (br d, J = 55 Hz, 1F); IR (neat): v 3049, 2954, 2925, 2860, 1747, 1603, 1454, 1219, 843, 771 cm^{-1}; HRMS (EI, TOF, 60 eV) *m/z*: calcd for $C_{30}H_{24}F_2$ ($[M]^+$): 422.1853, found: 422.1846.

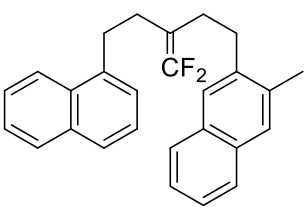
1-[3-Difluoromethylidene-5-(naphthalen-1-yl)pent-1-yl]-naphthalene (1f): ^{1}H NMR (500 MHz,



1f

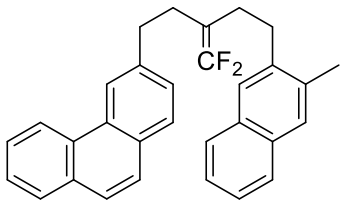
$CDCl_3$): δ 2.47 (tdd, J = 8.3 Hz, J_{HF} = 2.5, 2.5 Hz, 4H), 3.17 (t, J = 8.3 Hz, 4H), 7.30 (d, J = 6.5 Hz, 2H), 7.40 (dd, J = 7.5, 7.5 Hz, 2H), 7.46–7.54 (m, 4H), 7.73 (d, J = 8.0 Hz, 2H), 7.87 (dd, J = 8.0, 1.0 Hz, 2H), 7.99 (d, J = 8.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 28.0, 31.5 (t, J_{CF} = 3 Hz), 88.8 (t, J_{CF} = 17 Hz), 123.4, 125.5, 125.6, 126.0, 126.1, 127.0, 128.9, 131.6, 133.9, 137.3, 153.8 (t, J_{CF} = 284 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 67.3 (br s); IR (neat): v 3055, 2960, 1747, 1512, 1217, 775 cm^{-1}; EA: calcd for $C_{26}H_{22}F_2$: C, 83.84, H, 5.95%; found: C, 83.57; H, 6.10%.

2-[3-Difluoromethylidene-5-(naphthalen-1-yl)pent-1-yl]-3-methylnaphthalene (1g): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.35 (tdd, J = 8.4 Hz, J_{HF} = 2.0 Hz, 2.0 Hz, 2H), 2.45 (s, 3H), 2.48 (tdd, J = 8.4 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.82–2.87 (m, 2H), 3.17–3.23 (m, 2H), 7.32 (d, J = 9.0 Hz, 1H), 7.38–7.41 (m, 3H), 7.47–7.54 (m, 2H), 7.54 (s, 1H), 7.60 (s, 1H), 7.72–7.76 (m, 3H), 7.85–7.89 (m, 1H), 8.02 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.6, 27.6 (d, J_{CF} = 3 Hz), 27.9 (d, J_{CF} = 3 Hz), 31.5 (dd, J_{CF} = 3, 3 Hz), 31.9 (dd, J_{CF} = 3, 3 Hz), 88.7 (dd, J_{CF} = 17, 17 Hz), 123.4, 125.1, 125.3, 125.55, 125.56, 126.0, 126.1, 126.9, 126.9, 127.0, 127.1, 128.2, 128.9, 131.7, 132.3, 132.4, 133.9, 134.5, 137.3, 138.2, 153.8 (dd, J_{CF} = 283, 283 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 67.1 (br d, J = 54 Hz, 1F), 67.3 (br d, J = 54 Hz, 1F); IR (neat): ν 3055, 2954, 1745, 1597, 1261, 1215, 775, 746 cm^{-1}; EA: calcd for $C_{27}H_{24}F_2$: C, 83.91; H, 6.26%, found: C, 83.58; H, 6.44%.



1g

3-[3-Difluoromethylidene-5-(3-methylnaphthalen-2-yl)pent-1-yl]phenanthrene (1h): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.40 (tdd, J = 8.2 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.50 (s, 3H), 2.53 (t, J = 8.0 Hz, J_{HF} = 2.0, 2.0 Hz, 2H), 2.90 (t, J = 8.2 Hz, 2H), 3.04 (t, J = 8.0 Hz, 2H), 7.42 (t, J = 4.5 Hz, 2H), 7.46 (dd, J = 8.1, 1.5 Hz, 1H), 7.58 (s, 1H), 7.62 (t, J = 7.2 Hz, 1H), 7.63 (s, 1H), 7.68 (td, J = 8.3, 1.3 Hz, 1H), 7.70–7.78 (m, 2H), 7.730 (s, 1H), 7.734 (s, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 8.50 (s, 1H), 8.70 (d, J = 8.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.5, 27.2, 28.5, 31.7, 34.6, 88.4 (t, J_{CF} = 17 Hz), 121.8, 122.5, 125.1, 125.3, 126.3, 126.4, 126.5, 126.6, 126.7, 126.8, 127.0, 127.3, 128.2, 128.5, 128.6, 130.0, 130.3, 130.5 132.2, 132.3, 132.4 134.5, 138.2, 139.4, 153.7 (t, J_{CF} = 283 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 67.3 (s); IR (neat): ν 3053, 2929, 1747, 1454, 1207, 839, 744 cm^{-1}; HRMS (ESI$^+$, TOF) *m/z*: calcd for $C_{31}H_{26}F_2Na$ ($[M+Na]^+$): 459.1900, found: 459.1894.



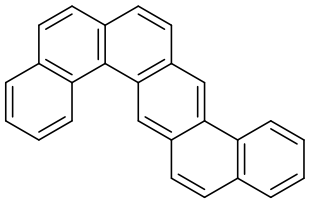
1h

Domino cyclization of 1,1-difluoro-1-alkenes 1 (preparation of tetracyclic product 2b). To an HFIP solution (3 mL) of magic acid ($FSO_3H \cdot SbF_5$, 387 mg, 1.22 mmol) was added an HFIP solution (3 mL) of difluoroalkene **1b** (152 mg, 0.471 mmol) at 0 °C. After stirring for 1 h at 0 °C, the reaction mixture was allowed to warm to room temperature and stirred for 30 min. Aqueous $NaHCO_3$ was added to quench the reaction at room temperature. Organic materials were extracted with $CHCl_3$ three times. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane/AcOEt = 20:1) to give tetracyclic product **2b** as a colorless liquid (108 mg, 81% yield).

Dehydrogenation of tetracyclic products 2 (Synthesis of PAH 3b). To a 1,2-dichloroethane solution (2 mL) of Ph_3CBF_4 (161 mg, 0.488 mmol) was added a 1,2-dichloroethane solution (2 mL) of tetracyclic product **2b** (40 mg, 0.14 mmol). The reaction mixture was refluxed for 3 h. After removal of the solvent under reduced pressure, the residue was passed through a short plug of silica gel (hexane/AcOEt = 10:1). The resulting crude mixture was purified by column chromatography on silica gel (hexane/AcOEt = 10:1) to give PAH **3b** as colorless crystals (38 mg, 95% yield).

Spectral data of difluoroalkenes **1a** and **1c**, tetracyclic product **2a**, and PAHs **3a** and **3c** were described in our previous paper.[16] Spectral data of **3b** were in complete agreement with those reported in literature.[32] Spectral data of methylarene **4d** were in complete agreement with those reported in literature.[33] Spectral data of methylarene **4e** and (trifluoromethyl)alkene **6a** were described in our previous paper.[16]

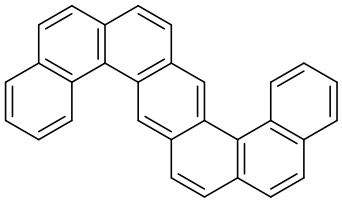
Benzo[*a*]naphtho[1,2-*h*]anthracene (3d): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.0 Hz, 1H),



3d

7.67 (d, *J* = 8.0 Hz, 1H), 7.73–7.80 (m, 3H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 1H), 7.96–7.99 (m, 2H), 8.08 (d, *J* = 7.0 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 8.92 (d, *J* = 8.0 Hz, 1H), 9.28 (s, 1H), 9.34 (d, *J* = 9.0 Hz, 1H), 9.64 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 122.1, 123.1, 125.8, 126.5, 126.8, 127.0, 127.11, 127.14, 127.2, 127.62, 127.65, 127.7, 127.8, 128.0, 128.5, 128.6, 128.7, 129.0, 130.3, 130.5, 130.6, 131.0, 132.13, 132.15, 133.6; IR (neat): *v* 1510, 1223, 906, 831, 746 cm^{-1}; HRMS (ESI^+, TOF) *m/z*: calcd for $C_{26}H_{17}$ ($[M+H]^+$): 329.1330, found: 329.1335.

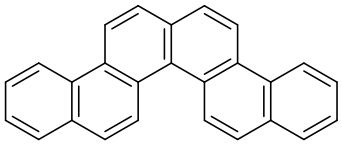
Dinaphtho[1,2-*a*:1',2'-*h*]anthracene (3e): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (ddd, *J* = 8.5, 6.8,



3e

1.4 Hz, 2H), 7.80 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 2H), 7.87 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 8.5 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H), 8.10 (dd, *J* = 7.0, 1.4 Hz, 2H), 8.11 (d, *J* = 9.0 Hz, 2H), 9.40 (d, *J* = 8.0 Hz, 2H), 9.67 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 125.8, 126.7, 126.8, 127.14, 127.19, 127.5, 127.7, 127.9, 128.2, 128.6, 128.7, 130.4, 130.9, 131.7, 133.5.; IR (neat): *v* 904, 829, 750, 733, 521 cm^{-1}; HRMS (ESI^+, TOF) *m/z*: calcd for $C_{30}H_{19}$ ($[M+H]^+$): 379.1487, found: 379.1469.

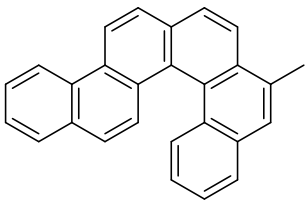
Naphtho[1,2-*c*]chrysene (3f): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (ddd, *J* = 8.0, 7.0, 1.4 Hz, 2H),



3f

7.76 (ddd, *J* = 7.0, 7.0, 1.4 Hz, 2H), 7.99 (d, *J* = 9.8 Hz, 2H), 8.04 (d, *J* = 7.0 Hz, 2H), 8.14 (d, *J* = 6.3 Hz, 2H), 8.865 (d, *J* = 8.2 Hz, 2H), 8.87 (d, *J* = 6.3 Hz, 2H), 9.01 (d, *J* = 9.8 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 121.9, 123.4, 125.9, 126.59, 126.61, 126.9, 126.9, 128.2, 128.3, 128.6, 130.1, 130.5, 130.9, 131.7; IR (neat): *v* 1595, 1259, 831, 737, 688 cm^{-1}; HRMS (ESI^+, TOF) *m/z*: calcd for $C_{26}H_{17}$ ($[M+H]^+$): 329.1330, found: 329.1343.

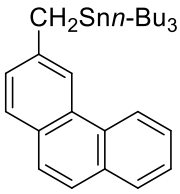
9-Methylnaphtho[2,1-*c*]chrysene (3g): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.90 (s, 3H), 7.19 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.49 (dd, *J* = 7.1, 7.1 Hz, 1H), 7.53 (d, *J* = 9.2 Hz, 1H), 7.64 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.72 (ddd, *J* = 7.6, 7.6, 1.1 Hz, 1H), 7.82 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 4.4 Hz, 1H), 8.14 (d, *J* = 4.6 Hz, 1H), 8.20 (d, *J* = 9.2 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.85 (d, *J* = 7.9 Hz, 1H), 8.87 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 20.3, 122.0, 123.1, 123.4, 124.0, 124.4, 126.2, 126.4, 126.50, 126.52, 126.92, 126.93, 127.2, 127.3, 127.6, 128.2, 128.4, 129.0, 129.3, 129.4, 130.1, 130.4, 131.6, 131.9, 132.0, 132.1, 132.3; IR (neat): *v* 2922, 1255, 1034, 835, 750, 733 cm^{-1}; HRMS (ESI$^+$, TOF) *m/z*: calcd for $C_{27}H_{19}$ ([M+H]$^+$): 343.1487, found: 343.1485; CCDC 1948090.



3g

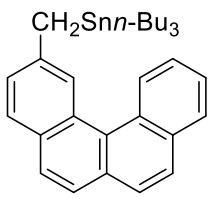
Benzylstannanes **7d** and **7e** were prepared according to the reported procedure,[27] using a $PdCl_2(PhCN)_2$ catalyst, LiCl (5 equiv), and $(n\text{-}Bu_3Sn)_2$ (2 equiv).

3-[(Tributylstannyl)methyl]phenanthrene (7d): ^{1}H NMR (500 MHz, $CDCl_3$): □ 0.80–0.89 (m, 15H), 1.21–1.29 (m, 6H), 1.41–1.48 (m, 6H), 2.59 (s, 2H*0.84), 2.59 (d, J_{HSn} = 55.0 Hz, 2H*0.16), 7.26 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.56 (ddd, *J* = 8.5, 6.8, 1.4 Hz, 1H), 7.59 (d, *J* = 8.5 Hz, 1H), 7.61 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.66 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.85 (dd, *J* = 7.8, 1.4, 1H), 8.28 (s, 1H), 8.62 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 10.2, 14.4, 19.9, 28.0, 29.8, 120.2, 123.2, 125.4, 126.7, 126.9, 127.5, 127.7, 129.08, 129.12, 129.12, 130.6, 131.3, 133.0, 143.2; IR (neat): *v* 2966, 1427, 1205, 881, 758 cm^{-1}; EA: calcd for $C_{27}H_{38}Sn$: C, 67.38; H, 7.96%, found: C, 67.41; H 7.88%.



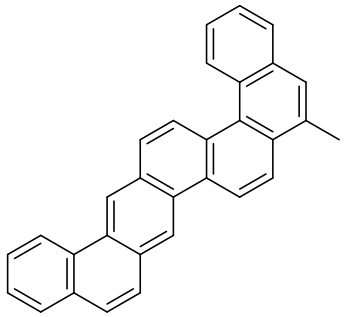
7d

2-[(Tributylstannyl)methyl][4]helicene (7e): ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.82 (t, *J* = 7.3 Hz, 9H), 0.86–0.91 (m, 6H), 1.21–1.29 (m, 6H), 1.42–1.50 (m, 6H), 2.60 (s, 2H*0.86), 2.60 (d, J_{HSn} = 55.0 Hz, 2H*0.16), 7.29 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.60 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.65 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 9.3 Hz, 1H), 7.81 (d, *J* = 9.3 Hz, 1H), 7.84 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 7.5 Hz, 1H), 8.75 (s, 1H), 9.14 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 9.53, 13.6, 19.3, 27.3, 29.0, 124.4, 124.8, 125.5, 125.7, 126.5, 126.6, 127.0, 127.1, 127.3, 127.8, 128.4, 128.5, 130.2, 130.5, 130.8, 131.2, 133.6, 142.2; IR (neat): *v* 2954, 2922, 1606, 1456, 839, 742 cm^{-1}; EA: calcd for $C_{31}H_{40}Sn$: C, 70.07; H, 7.59%, found: C, 70.04; H 7.56%.



7e

1-Methylbenzo[*l*]naphtho[1,2-*b*]chrysene (9h) ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.86 (s, 3H), 7.05 (dd, *J* = 7.1, 7.1 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 1H), 7.46 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.62 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.70 (dd, *J* = 7.0, 7.0 Hz, 1H), 7.77 (s, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 8.87 (d, *J* = 8.1 Hz, 1H), 9.04 (s, 1H), 9.17 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 20.3, 121.2, 122.9, 123.4, 123.5, 126.5, 126.6, 126.7, 126.8, 126.9, 127.01, 127.04, 127.1, 127.4, 127.6, 127.7, 128.0, 128.5, 128.7, 128.8, 128.9, 129.2, 129.6, 130.0, 130.2, 131.4, 131.8, 131.9, 132.2, 132.48, 132.50; IR (neat): *v* 2922, 1437, 1095, 1032, 906, 731 cm^{-1}; HRMS ($APCI^+$, TOF) *m/z*: calcd for $C_{31}H_{21}$ ($[M+H]^+$): 393.1643, found: 393.1648; CCDC 1945281.


9h

CHAPTER 3

Synthesis of Substituted Acenes via Domino or Stepwise Cyclizations of CF_3-Alkenes

3-1. Introduction

As previously described, PAHs have attracted considerable attention, because of their potentiality as organic electronic materials.[1] Acenes, having a linear benzene ring configuration, are of special importance and have long been used as organic semiconducting materials (Figure 3-1).[2–3] Among them, substituted acenes such as TIPS-pentacene[4] and rubrene[5] have exhibited remarkable semiconducting property, and thus development of synthetic methods for these compounds have been highly desirable.

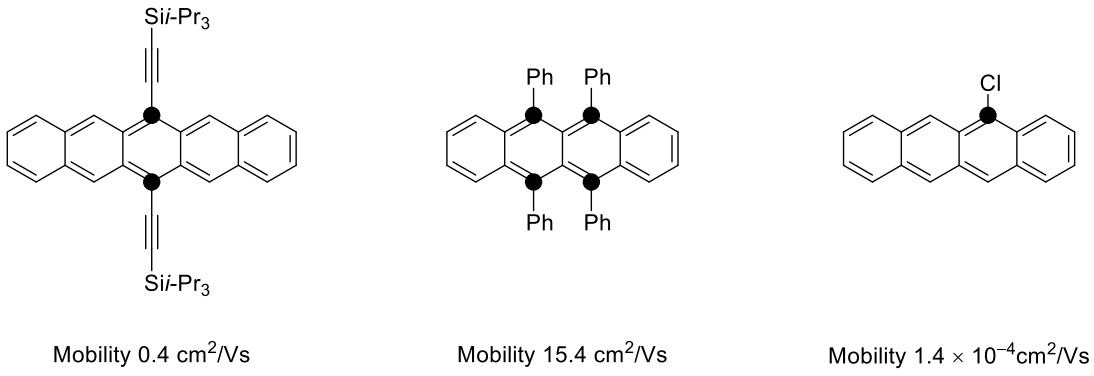
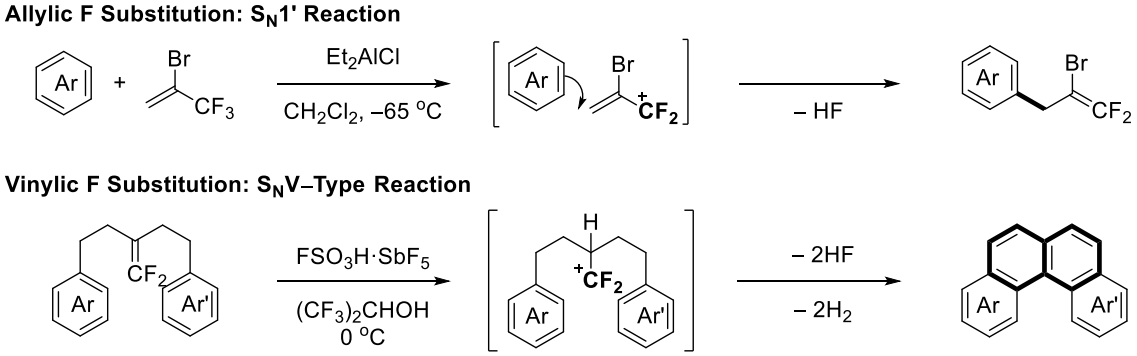


Figure 3-1. Structures and Properties of Substituted Acenes

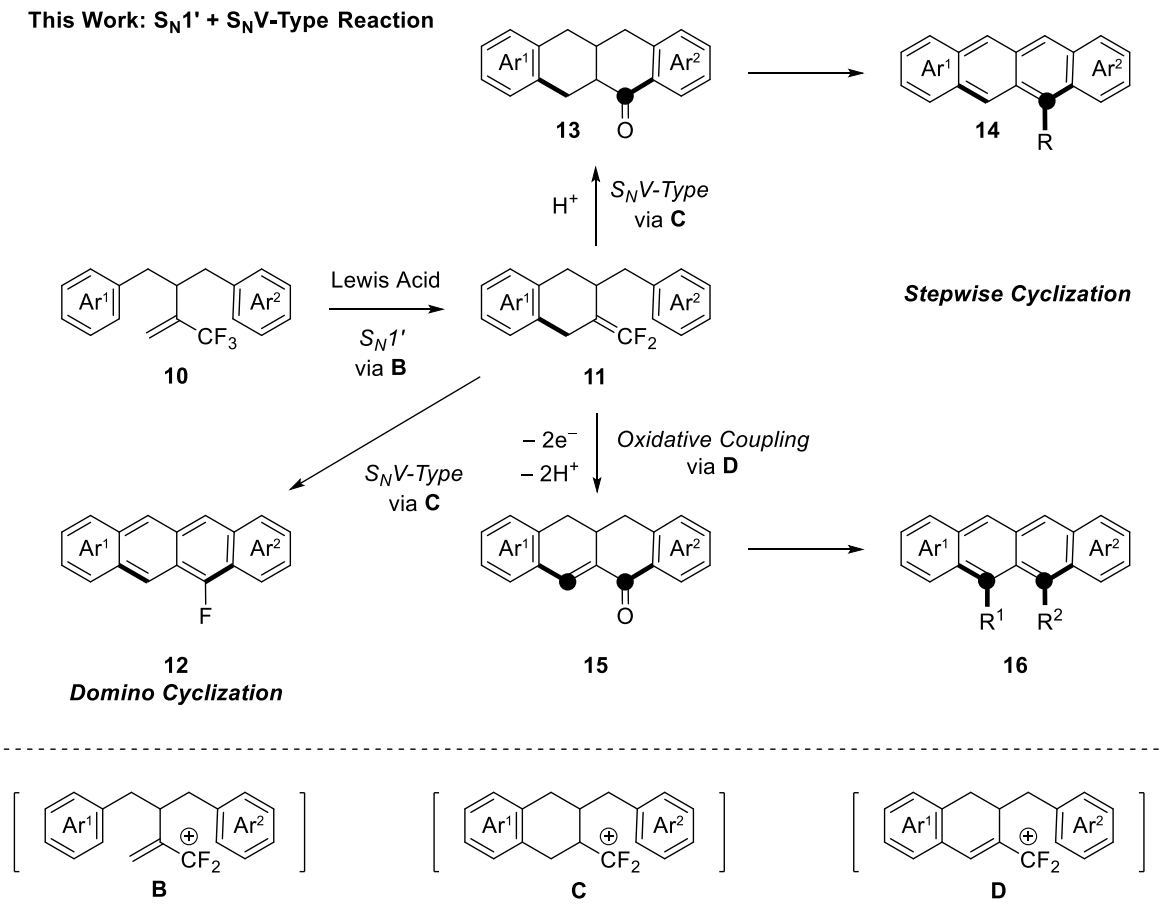
Our laboratory has reported two types of cationic C–C bond formations using fluoroalkenes [*i.e.* 2-trifluoromethyl-1-alkenes and 1,1-difluoro-1-alkenes]. Thus, when 3,3,3-trifluoro-1-propenes were treated with aluminium Lewis acids (S_N1' reaction, Scheme 3-1, top),[6] the generated allylic CF_2 cations in turn underwent intermolecular Friedel–Crafts-type arylation to afford aryl-bearing 1,1-difluoro-1-alkenes. When 1,1-difluoroalkenes were treated with super acid, $FSO_3H{\cdot}SbF_5$ (S_NV-type

reaction, Scheme 3-1, bottom),[7] protonation proceeded regioselectively, as mentioned in Chapter 2, and the generated CF_2 cations underwent double intramolecular Friedel–Crafts-type ring formation, followed by dehydrogenation, to afford [4]helicenes.

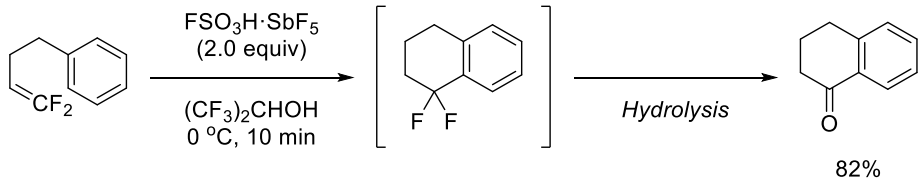
In order to construct an acene (tetracene) substructure, I combined these reactions (S_N1' + S_NV-type reaction, Scheme 3-2). Thus, CF_3-alkenes **10**, bearing two aryl groups are subjected to aluminium Lewis acids. The generated allylic CF_2 cations **B** would undergo intramolecular arylation to afford bicyclic 1,1-difluoroalkenes **11** (1st ring construction). Subsequent Friedel–Crafts-type ring formation (2nd ring construction) would be promoted by the acid liberated during the first cyclization, via CF_2 cations **C**, followed by dehydrogenation to afford fluorinated [4]acenes **12** as domino cyclization products. For introduction of carbon substituents (R) into tetracenes **14**, stepwise cyclization is adopted. Previously, our laboratory reported α-tetralone synthesis through Friedel–Crafts-type cyclization of 1,1-difluoroalkenes (eq. 3-1).[8] Thus, treatment of 1,1-difluoroalkenes **11** with appropriate acids would afford the corresponding α-tetralone derivatives **13**, whose ketone moiety can be utilized for introduction of substituents R. Finally, a new approach to CF_2 cations through oxidation was examined. Thus, oxidative CF_2 generation would give *allylic* CF_2 cations **D** from **11**, whose cyclization would facilitate synthesis of enones **15**. By using **15**, introduction of two carbon substituents (R^1 and R^2) to internal positions would be realized.



Scheme 3-1. Catalytic C–F Bond Activation of Fluoroalkenes via Fluorine Elimination



Scheme 3-2. Synthesis of Substituted Acenes via S_N1' / S_NV-Type Domino or Stepwise Cyclizations



(3-1)

From the perspective of the CF_2 cation generation, aforementioned methods can be classified into three categories, as follows (Types A–C, Figure 3-2). In Type A generation, elimination of F^- leads to CF_2 cations ("$– F^-$").[6, 9] In Type B generation, addition of H^+ or metal cations leads to CF_2 cations ("$+ H^+$" or "$+ M^{n+}$").[7,10–12] By developing the Type C generation, which can be expressed as "$– e^-$," I have added new entry to CF_2 cations generation.

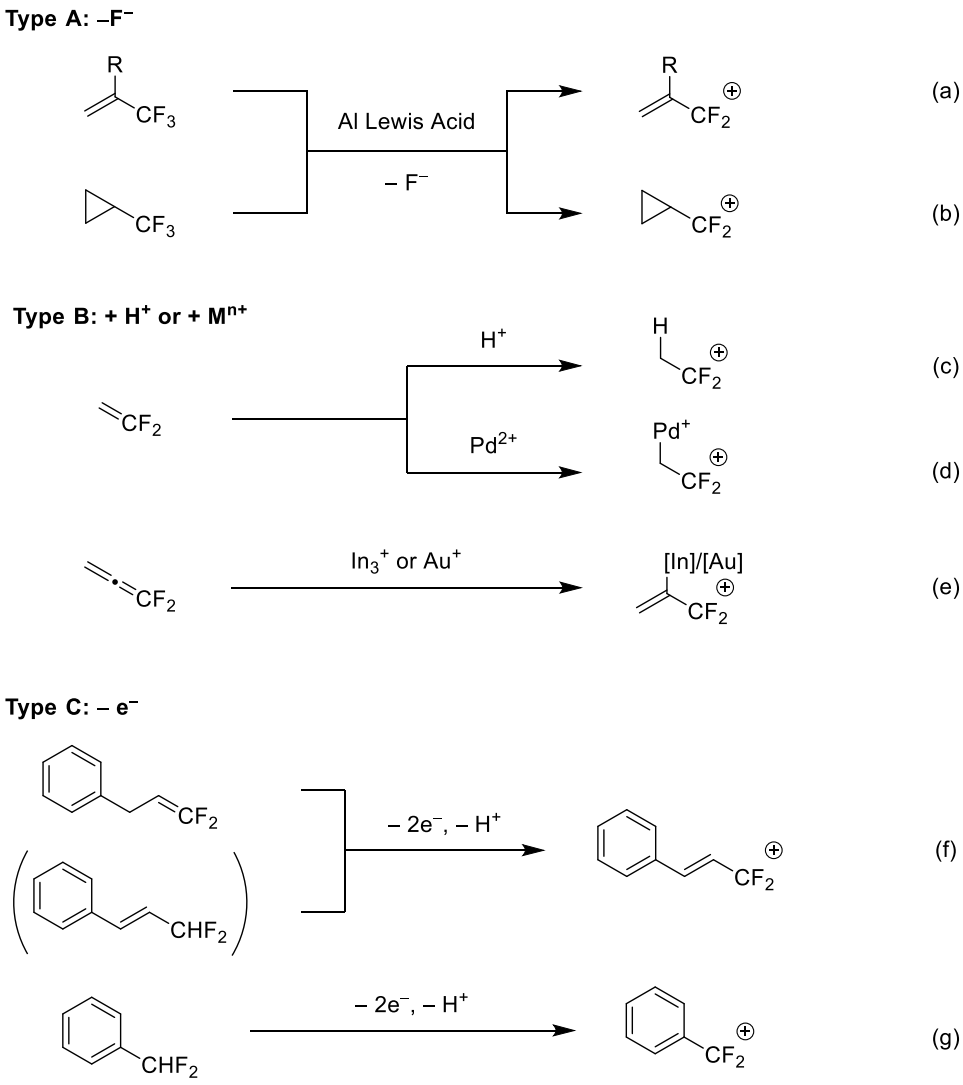
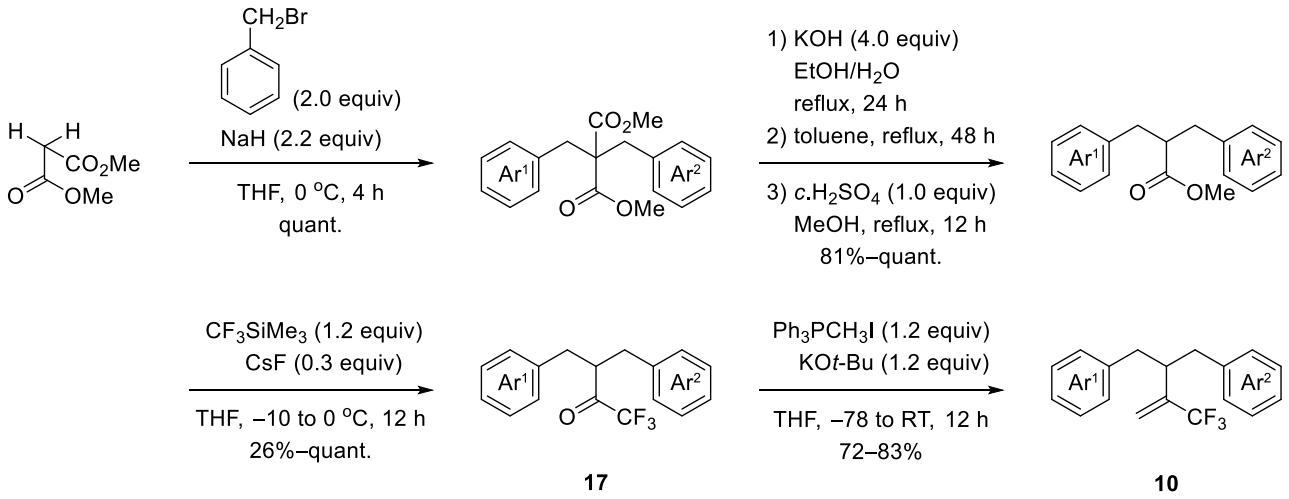


Figure 3-2. Methods for Generation of CF_2 Cations

3-2. Preparation of Cyclization Precursors: CF_3-Alkenes

The starting (trifluoromethyl)alkenes were prepared from malonic diesters (Scheme 3-3). Dimethyl malonate was benzylated with two molecules of benzyl bromides under basic conditions. The formed diesters were decarboxylated under standard conditions and again esterified with methanol. Trifluoromethylation of the ester moiety with trimethyl(trifluoromethyl)silane (Rupert reagent)/CsF was performed under the reported conditions. Wittig methylenation of the resulting ketones successfully afforded the desired (trifluoromethyl)alkenes **10**.

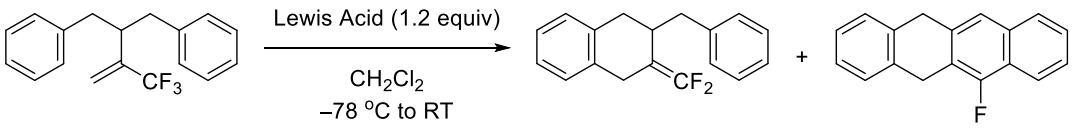


Scheme 3-3. Preparation of (Trifluoromethyl)alkenes.

3-3. Synthesis of Fluorinated Acenes from CF_3-Alkenes via Domino Cyclization and Dehydrogenation

Lewis-acid promoted intramolecular arylation of (trifluoromethyl)alkenes **10** was investigated, using diphenylated substrate **10a** as a model substrate (Table 3-1). Trimethylaluminium was less effective for the arylation and bicyclic difluoroalkene **11a** was obtained in an 11% yield (Entry 1). Among the chlorinated aluminium Lewis acids examined (entries 2–4), dimethylaluminium chloride (Entry 2) and ethylaluminium dichloride (Entry 4), which were effective for our previous arylations (Sheme 3-1, top), gave favorable results ($AlMe_2Cl$, a 34% yield of the desired domino product **18a** and a 49% yield of bicyclic difluoroalkene **11a**; $AlEtCl_2$, a 23% yield of **18a** and a 47% yield of **11a**). Trichloroaluminium, which was insoluble in dichloromethane, was not effective for the arylation (Entry 5). Thus, the domino fluorinated tetracene derivative **18a** was obtained with $AlMe_2Cl$ in a 34% yield.

Table 3-1. Optimization of Lewis Acids

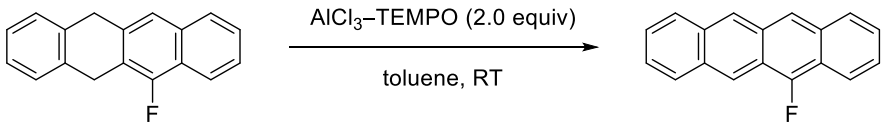


10a **11a** **18a**

Entry	Lewis Acid	*t* /h	**11a** /%	**18a** /%	**10a** /%
1	$AlMe_3$	1	11	–	86
2	$AlMe_2Cl$	0.25	49	34	4
3	$AlEtCl_2$	0.25	38	13	10
4	$AlMeCl_2$	0.5	47	23	2
5	$AlCl_3$	1	12	5	–

a) ^{19}F NMR yield based on an internal standard *p*-$Tol_2C(CF_3)_2$; b) recovery; c) –50 °C

Although dehydrogenation of the obtained **18a** resulted in failure (not shown), treatment with TEMPO–$AlCl_3$ complex (2.0 equiv) was effective and the desired 5-fluorotetracene **12a** was obtained in a 32% yield (Scheme 3-4).



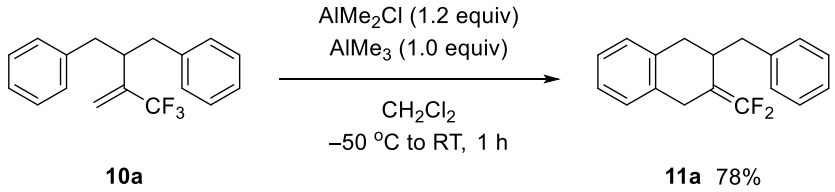
18a **12a** 32%

Scheme 3-4. Dehydrogenation of Fluorodihydrotetracene.

3-4. Synthesis of Substituted Acenes from CF_3-Alkenes via Stepwise Cyclization and Dehydrogenation: First Cyclization through S_N1' Reaction

Bicyclic difluoroalkene **11a** is a potential precursor for the preparation of tetracyclic ketone **13a**, which allows introduction of substituents at the L-region. Although less reactive, trimethylaluminium afforded **11a** in a selective manner, suppressing the generation of domino product **18a** (an 11% yield, Entry 1, Table 3-1). Assuming that the methyl ligand behaved as a base to remove a proton liberated in the first ring construction (S_N1' reaction), the intramolecular arylation with $AlMe_2Cl$ was performed in the presence of a stoichiometric amount of $AlMe_3$ (Scheme 3-5). As expected, formation of the

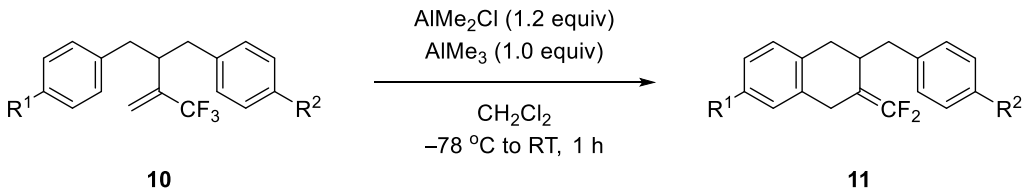
domino product **18a** was completely suppressed and the desired, bicyclic difluoroalkene **11a** was obtained in a 78% yield.



Scheme 3-5. Selective Synthesis of Bicyclic Difluoroalkene **11a**.

Having the procedure to synthesize bicyclic 1,1-difluoroalkenes **11** in hand, scope of the first ring construction was examined (Table 3-2). Not only non-substituted **10a** but also electron-rich and -deficient **10b**–**f** afforded the corresponding product **11b**–**f** in 55–87% yields. It is noteworthy that arylation of less nucleophilic **10e** and **10f** proceeded in the presence of zirconium tetrachloride (Entries 5 and 6).[6] Friedel–Crafts-type reaction of electron-deficient halobenzenes has been less explored to date.

Table 3-2. Synthesis of 1,1-Difluoroalkenes **11** by Intramolecular Arylation of (Trifluoromethyl)alkenes **10** (The First Ring Construction).

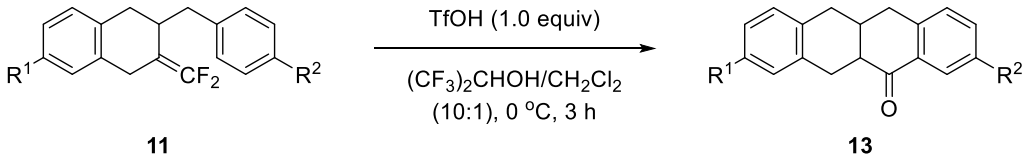


Entry	R^1	R^2	Lewis Acid /equiv	Yield /%	**11**
1	H	H	$AlMe_2Cl$ (1.2)	87	**11a**
2	Me	Me	$AlMe_2Cl$ (1.2)	87	**11b**
3	Ph	Ph	$AlMe_2Cl$ (1.2)	83	**11c**
4	Me	Cl	$AlMe_2Cl$ (1.2)	77	**11d**
5	Br	Br	$ZrCl_4$ (1.0)	55	**11e**
6	Cl	Cl	$ZrCl_4$ (1.0)	58	**11f**

3-5 Synthesis of Substituted Acenes from CF_3-Alkenes via Stepwise Cyclization and Dehydrogenation: Second Cyclization through S_NV-Type Reaction

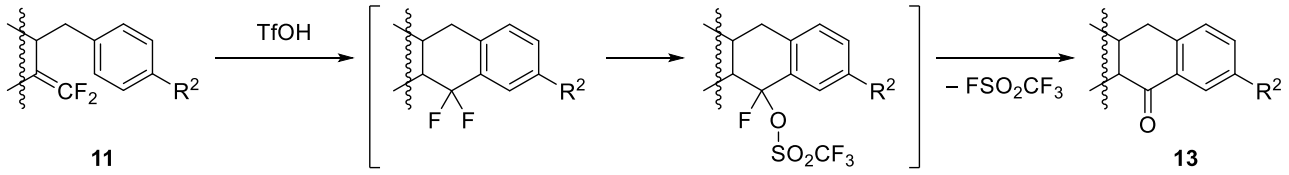
The Friedel–Crafts-type cyclization of bicyclic difluoroalkenes **11** (the second ring construction) was performed with a stoichiometric amount of trifluoromethanesulfonic acid (TfOH, Table 3-3). Thus, difluoroalkenes **11** were treated with 1.0 equiv of TfOH in $(CF_3)_2CHOH$ (HFIP)/CH_2Cl_2 (10:1) at room temperature. The desired ketones **13** were obtained in 31–81% yields. ^{19}F NMR analysis of the reaction mixture revealed that the ketones were generated in the reaction medium. The generation of the ketone **13** before quenching the reaction can be ascribed to elimination of sulfonyl fluoride from *F*,*O*-acetal-like intermediates, generated in situ (Scheme 3-6).[18]

Table 3-3. Acid-promoted synthesis of tetracyclic ketones **13** by intramolecular cyclization of bicyclic difluoroalkenes **11** (the second ring construction)



11 **13**

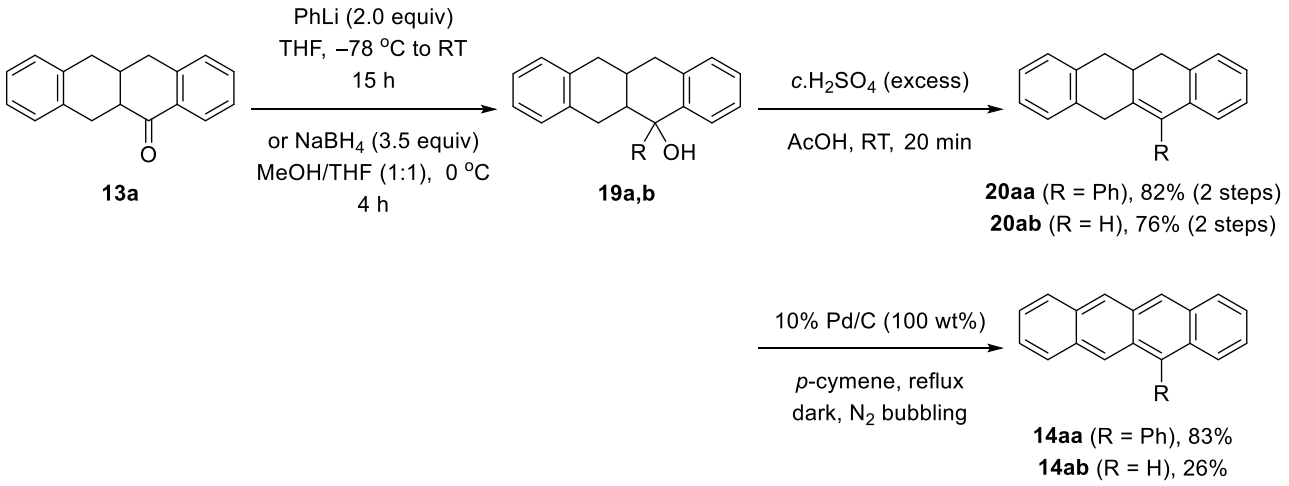
Entry	R^1	R^2	Yield /%	**13**
1	H	H	81	**13a**
2	Me	Me	81	**13b**
3	Ph	Ph	81	**13c**
4	Me	Cl	31	**13d**
5	Br	Br	52	**13e**
6	Cl	Cl	62	**13f**



11 **13**

Scheme 3-6. Plausible Mechanism for Generation of Ketone **13**

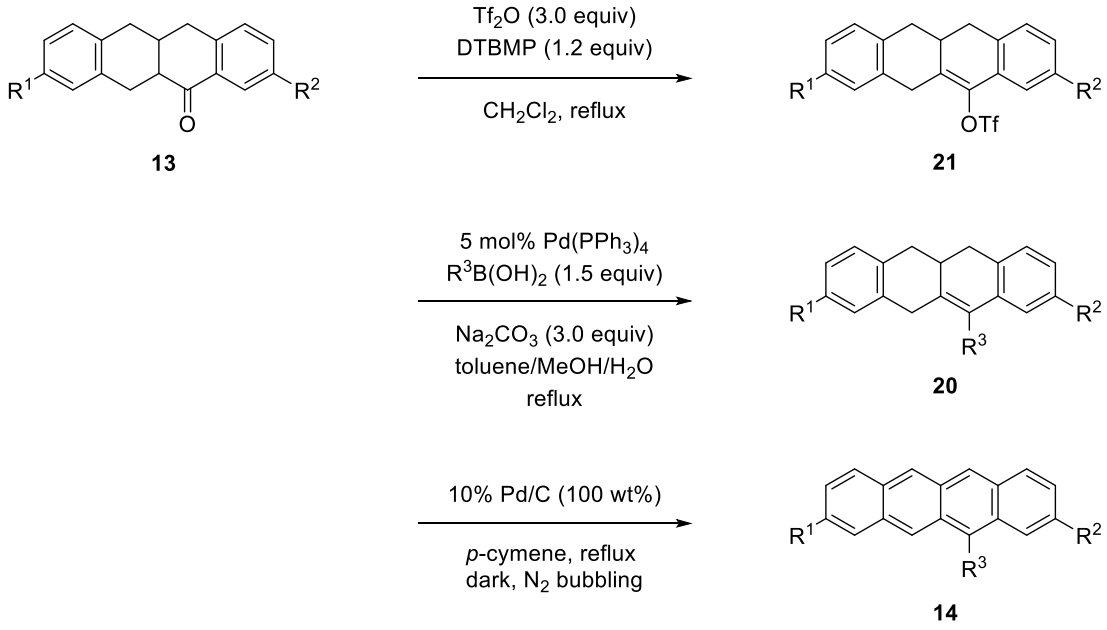
Then, tetracyclic ketones **13** were utilized for introduction of substituents (Scheme 3-7). Treatment of ketone **13a** with phenyllithium or sodium borohydride followed by acidic dehydration (H_2SO_4) afforded the corresponding cyclohexenes **20aa** and **20ab** in 82% and 76% yields, respectively (two-step yields). Dehydrogenation of **20aa** and **20ab** with Pd/C under N_2 stream successfully afforded the desired 5-phenyltetracene **14a** and tetracene **14b** in 82% and 26% yield, respectively.



Scheme 3-7. Synthesis of Substituted and Parent Tetracenes **14**.

Pd-catalyzed cross coupling reaction successfully widened the scope of the substituent introduction (Table 3-4). Tetracyclic ketones **13** were treated with trifluoromethanesulfonic anhydride in the presence of 2,6-di*t*-butyl-4-methylpyridine (DTBMP). Thus formed vinyl triflates **21** were subjected to the Suzuki–Miyaura coupling with boronic acids to afford substituted cyclohexenes **20**. Cyclohexenes **20aa–ca** were finally dehydrogenated under the above-mentioned conditions (Pd/C, under N_2 stream) to afford the desired substituted tetracenes **14**. Chlorinated **20da** underwent dehalogenation by Pd/C.[19] Dihalogenated **20ea** and **20fa** were dehydrogenated with trityl cation, generated from triphenylmethyl alcohol and triflic acid to afford the desired halogen-disubstituted tetracenes **14ea** and **14fa**.

Table 3-4. Synthesis of Internally Substituted Tetracenes **14**



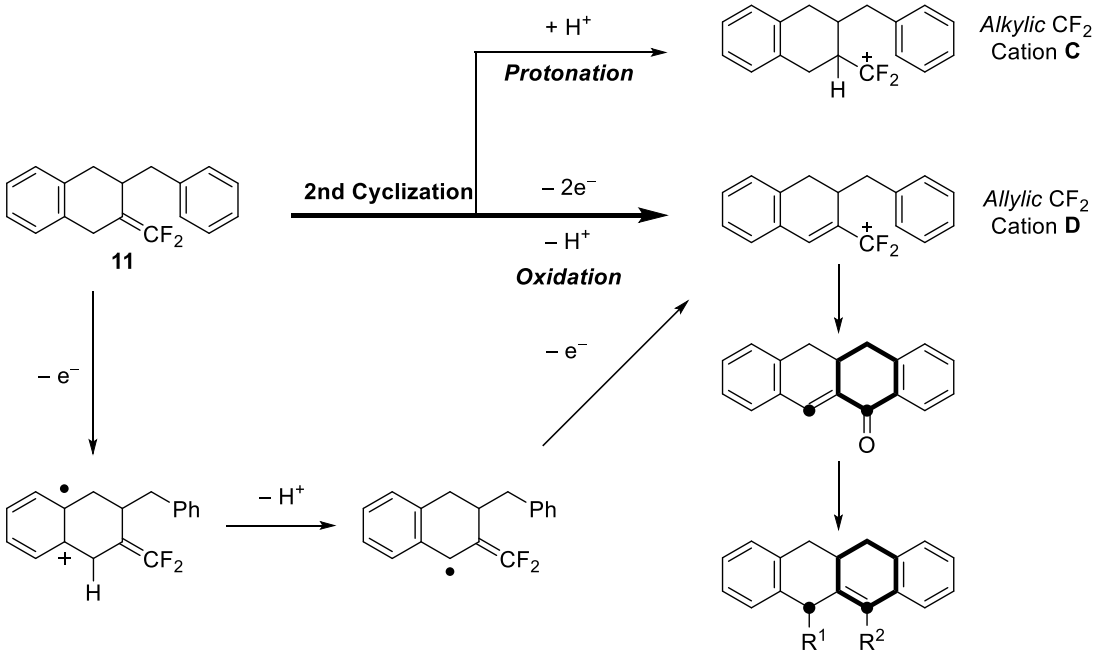
Entry	R^1	R^2	**13**	Yield /%		
				Triflation	Coupling (R^3)	Dehydrogenation
1	H	H	**13a**	87, 4 h	61 (Ph, **20aa**), 2 h	83, **14aa**, 14 h
2	H	H	**13a**	"	94 (*p*-$CH_3C_6H_4$, **20ac**), 5 h	55, **14ac**,12 h
3	H	H	**13a**	"	86 (*p*-$CF_3C_6H_4$, **20ad**), 5 h	60, **14ad**,18 h
4	H	H	**13a**	"	88 (*trans*-Styryl, **20ae**)	41, **14ae**,24 h
5	Me	Me	**13b**	77, 4 h	93 (Ph, **20ba**), 5 h	67, **14ba**,12 h
6	Ph	Ph	**13c**	Quant, 4 h	80 (Ph, **20ca**), 3 h	83, **14ca**,24 h
7	Me	Cl	**13d**	61, 12 h	83 (Ph, **20da**), 2 h	62, (R^2 = H), 24 h[b]
8	Br	Br	**13e**	68, 1 h	70 (Ph, **20ea**), 14 h[a]	30, **14ea**, 12 h[c]
9	Cl	Cl	**13f**	59, 15 h	89 (Ph, **20fa**), 3 h	23, **14fa**, 12 h[c]

a) 4 mol% $PdCl_2$(dppp), PhMgBr (1.4 equiv), LiBr (1.0 equiv), Et_2O, reflux; b) Pd/C (199 wt%); c) Ph_3COH (2.0 equiv), CF_3SO_3H, reflux, dark.

3-6 Synthesis of Substituted Acenes from CF_3-Alkenes via Stepwise Cyclization and Dehydrogenation: Second Cyclization by Oxidation

As described in the previous section, protonation (Type B CF_2 cation generation, Scheme 3-2) of bicyclic difluoroalkenes **11** facilitated the second ring construction, leading to monosubstituted tetracenes. In this section, for the synthesis of disubstituted tetracenes, I turned my attention to *oxidative* CF_2 cation generation (Type C generation): thus, bicyclic difluoroalkenes **11**, having an electron-rich benzo moiety, would be oxidized with agents such as 2,3-dichloro-5,6-dicyano-*p*-

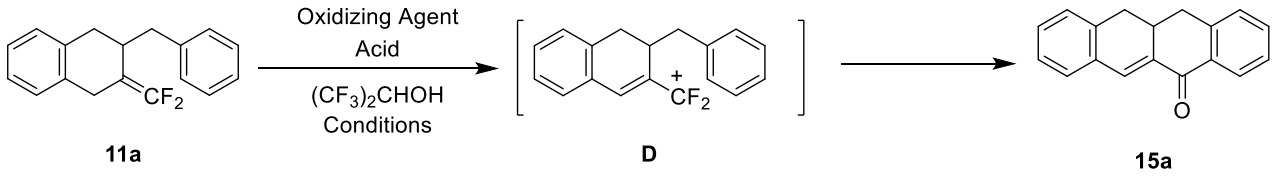
benzoquinone (DDQ).[20] The cation radical intermediates thus generated would then undergo deprotonation, followed by the second one-electron oxidation to generate *allylic* CF_2 cations **D**, which is dehydrogenated versions of **C**. The newly introduced unsaturated moiety would allow introduction of an additional substituent (scheme 3-8).



Scheme 3-8. Synthesis of Disubstituted Acenes via Oxidative Cyclizations

Using bicyclic difluoroalkene **11a** as a model substrate, reaction conditions were optimized (Table 3-5). On treatment with iodobenzene diacetate (1.0 equiv) or iodobenzene bis(trifluoroacetate) (1.1 equiv) in HFIP at 0 °C, **11a** underwent the Friedel–Crafts-type cyclization to afford the desired α,β-unsaturated ketone **15a** albeit in 2% and 9% yields, respectively (second-ring construction, Entries 1 and 2). Whereas enone **15a** was not obtained with triphenylmethylium tetrafluoroborate (Ph_3CBF_4) or DDQ at 60 °C (Entries 3 and 4), addition of trifluoromethanesulfonic acid to DDQ promoted the cyclization even at 0 °C to afford **15a** in an 83% yield (Entry 6).[21] Trifluoroacetic acid, aluminium chloride, *tert*-butyl(chloro)dimethylsilane were not effective as activating agents for DDQ to afford **15a** in 0%, 51% and 21% yields, respectively (Entries 7–9).

Table 3-5. Optimization of Oxidative Generation of CF_2 Cations.

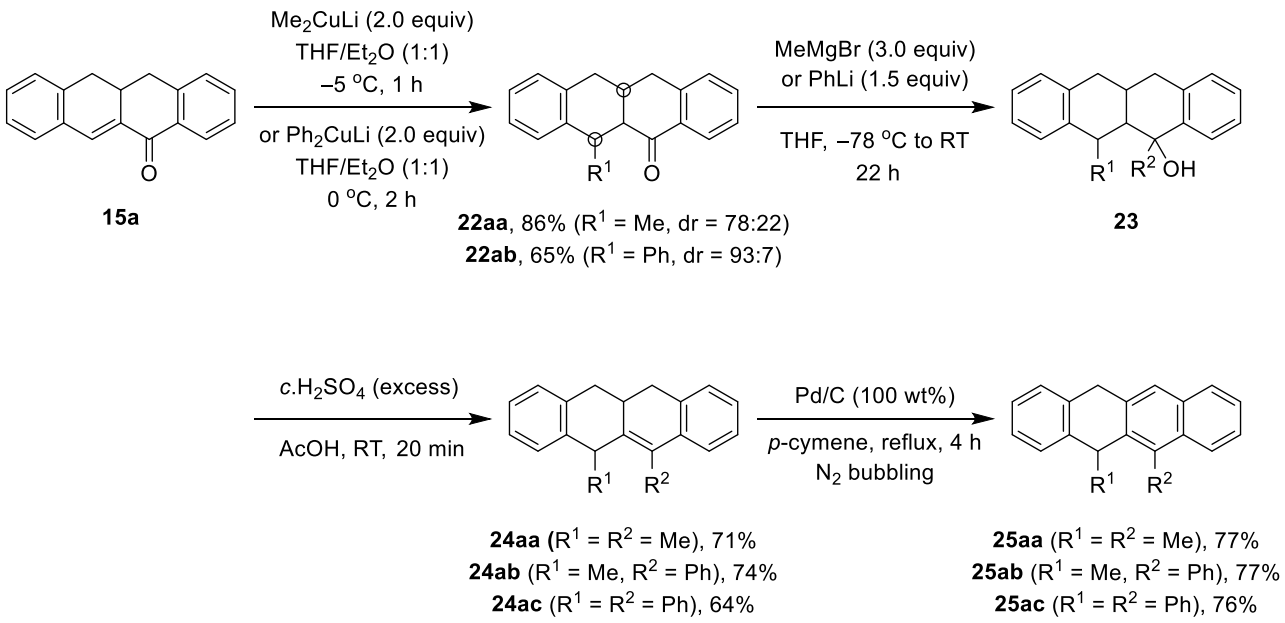


11a **D** **15a**

Entry	Oxidizing Agent /eq.	Acid /eq.	Conditions	Yield /%[a]
1	$PhI(OCOCH_3)_2$ (1.0)	–	0 °C, 3 h	2
2	$PhI(OCOCF_3)_2$ (1.1)	–	0 °C, 4 h	9
3	Ph_3CBF_4 (1.0)	–	60 °C, 3 h	0
4	DDQ (1.0)	–	60 °C, 1 h	0
5	DDQ (1.0)	CF_3SO_3H (1.1)	60 °C, 5 h	72
6	DDQ (1.0)	CF_3SO_3H (1.0)	0 °C, 3 h	83[b]
7	DDQ (1.0)	CF_3CO_2H (1.0)	0 °C, 5 h	0
8	DDQ (1.0)	$AlCl_3$ (1.7)	0 °C, 3 h	51
9	DDQ (1.0)	TBSCl (1.0)	0 °C, 3 h	20

a) Yield was determined by ^1H NMR spectroscopy based on an internal standard CH_2Br_2; b) Isolated yield; DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone.

The tetracyclic enones **15** thus obtained are useful intermediates for double introduction of substituents (R^1 and R^2, Scheme 3-9). Firstly, 1,4-addition of organocuprate ($R^1{}_2CuLi$) to **15** was conducted. The desired conjugate addition products (tetracyclic ketones) **22aa** and **22ab** were obtained in 86% (dr =78:22) and 65% (dr = 93:7) yields, respectively (introduction of the first substituents). Secondly, addition of carbanions to the tetracyclic ketones **22aa** or **22ab** was performed with MeMgBr or PhLi (introduction of the second substituents). The addition products (tertiary alcohols, **23**) were subjected to dehydration with concentrated sulfuric acid to afford tetrahydrotetracenes **24aa**–**ac** in 64–74% yields. Finally, dehydrogenation of **24aa**–**ac** with Pd/C under N_2 stream afforded 5,6-disubstituted dihydrotetracenes **25aa**–**ac** in 76–77% yields.[22]

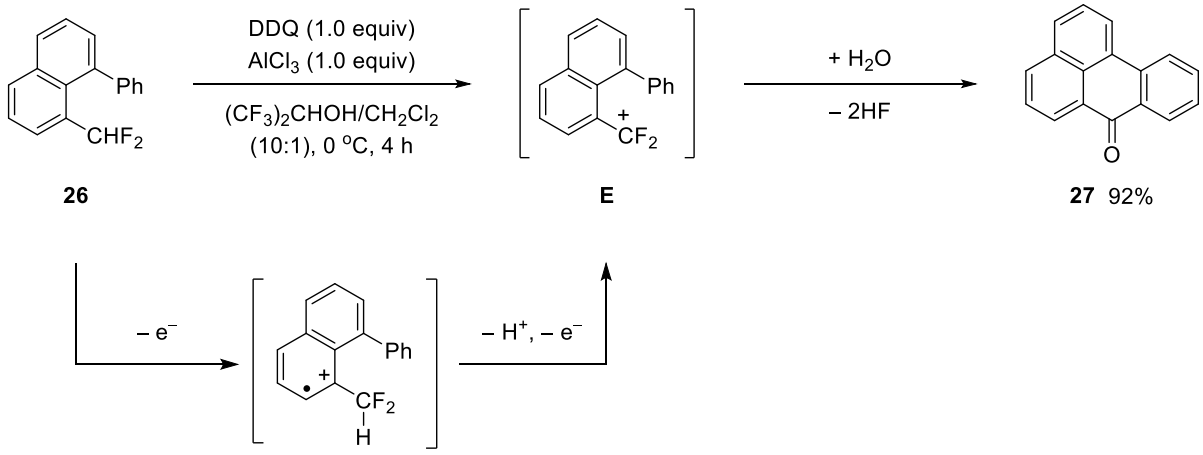


Scheme 3-9. Synthesis of Substituted Tetracenes **25**

3-7 Oxidative Generation of Difluorocarbocations from (Difluoromethyl)arenes and Their Cyclization

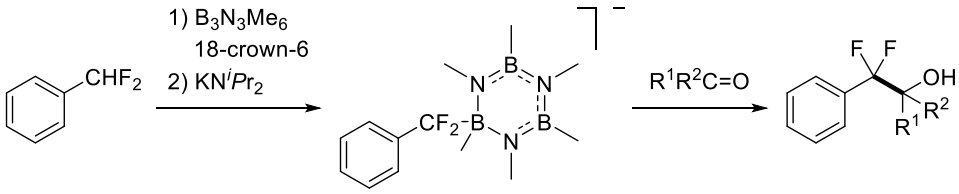
Oxidative generation of allylic CF_2 cations, triggered by one-electron removal from electron-rich benzo moiety, might be extended to generation of benzylic CF_2 cations from (difluoromethyl)arenes (Scheme 3-10). Thus, (difluoromethyl)naphthalene **26** bearing a phenyl group was treated with DDQ (1.0 equiv) and aluminium trichloride (1.0 equiv) in HFIP/dichloromethane (10:1), which led successfully to the formation of benzanthrone **27** in a 92% yield. Formation of **27** can be ascribed to one-electron oxidation of **26**, followed by deprotonation/one-electron oxidation, which facilitated generation of benzylic CF_2 cations **E**. The Friedel–Crafts-type cyclization of **E** afforded **27**.

Scheme 3-10. Synthesis of Benzanthrone via Oxidative Benzylic CF_2 Cation Generation



26 **E** **27** 92%

Difluoromethyl groups can be isosteric to hydroxy groups and behave as hydrogen bond donor.[23] Thus, difluoromethyl groups have been utilized in pharmaceutical and agrochemical applications.[24–26] In contrast to these advantages, synthetic utility of the difluoromethyl groups has been unexplored to date. Quite recently, C–C bond formation using the C–H bond in the benzylic difluoromethyl groups was conducted under basic conditions (eq. 3-2).[27] The oxidative CF_2 cation generation described above has disclosed another potential of difluoromethyl groups in organic synthesis.



(3-2)

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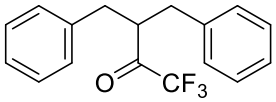
3-9. Experimental section

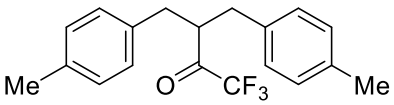
General statements: IR spectra were recorded on a Horiba FT-300S spectrometer. NMR spectra were recorded on a Bruker Avance 500 spectrometer in $CDCl_3$ at 500 MHz (^{1}H NMR), at 126 MHz (^{13}C NMR), and at 470 MHz (^{19}F NMR) or JEOL JNM-ECS 400 spectrometer in $CDCl_3$ at 400 MHz (^{1}H NMR) and at 101 MHz (^{13}C NMR). Chemical shifts were given in ppm relative to internal Me_4Si (for ^{1}H and ^{13}C NMR: $\delta = 0.00$) and C_6F_6 (for ^{19}F NMR: $\delta = 0.0$). High resolution mass spectroscopy (HRMS) was conducted with a JEOL JMS-T100GCV (EI^+) and a JEOL JMS-T100CS ($APCI^+$) spectrometer. Elemental analyses were performed with a YANAKO MT-3 CHN Corder apparatus. Column chromatography was conducted on silica gel (Silica Gel 60 N, Kanto Chemical Co., Inc.). Purification by preparative HPLC was performed by LC-908-C60 instrument (Japan Analytical Industry Co., $CHCl_3$). Cesium fluoride (4*N,* Kanto Chemical Co., Inc.) was activated by heating at 170 °C for 4 h under 1.0 torr pressure. Dimethylaluminum chloride, trimethylaluminum and ethylaluminium dichloride were purchased from Kanto Chemical Co., Inc. as a hexane solution (ca. 1.0 M). 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) was purchased from Tokyo Chemical Industry Co., Ltd. 10% Pd/C was purchased from Wako Pure Chemical Industries, Ltd. Trifluoromethyl(trimethyl)silane was supplied by Toso F-Tech, Inc. Trifluoromethanesulfonic acid (TfOH) and trifluoromethanesulfonic anhydride (Tf_2O) were supplied by Central Glass Co., Ltd. 1,1,1,3,3,3-Hexafluoropropan-2-ol (HFIP) supplied by Central Glass Co., Ltd (purity 99.9%) was distilled from CaH_2 and stored over molecular sieves 4A. *p*-Cymene was distilled from CaH_2 and stored over molecular sieves 4A. Tetrahydrofuran (THF), diethyl ether, dichloromethane, and toluene were dried by passing over a column of activated alumina followed by a column of Q-5 scavenger (Engelhard). All the reactions were performed using standard glassware apparatus under argon.

Trifluoromethylation of ester moiety [Preparation of Trifluoromethylketones 17]. To a THF solution (45 mL) of ester moiety (24.1 g, 91.6 mmol) and cesium fluoride (3.04 g, 20.0 mmol) was added trifluoromethyl(trimethyl)silane (16.5 mL, 112 mmol) dropwise (2 h) at –5 °C. After being stirred for 12 h, phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with AcOEt three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane/AcOEt = 20 : 1) to give **10a** (21.7 g, 74.2 mmol, 81%) as a colorless liquid.



17a

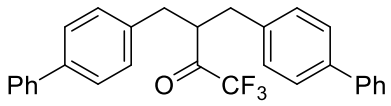
3-Benzyl-1,1,1-trifluoro-4-phenylbutan-2-one (10a): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.77 (dd, J = 13.8, 6.7 Hz, 2H), 3.06 (dd, J = 13.8, 7.6 Hz, 2H), 3.56 (tt, J = 7.6, 6.7 Hz, 1H), 7.11 (d, J = 7.2 Hz, 4H), 7.24 (t, J = 7.0 Hz, 2H), 7.30 (dd, J = 7.2, 7.0 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 37.2, 50.7, 115.3 (q, J_{CF} = 294 Hz), 126.9, 128.7, 128.9, 137.6, 194.1 (q, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 82.8 (s); IR (neat): ν 3030, 1757, 1496, 1147, 912, 742 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{17}H_{15}F_3O$ [M]$^+$: 292.1075; Found: 292.1065.



17b

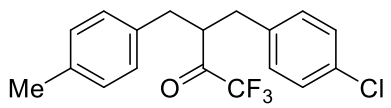
4-(4-Methylphenyl)-3-(4-methylphenyl)methyl-1,1,1-trifluorobutan-2-one (10b): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.31 (s, 6H), 2.71 (dd, J = 13.8, 6.7 Hz, 2H), 3.00 (dd, J = 13.8, 7.4 Hz, 2H), 3.51 (tt, J = 7.4, 6.7 Hz, 1H), 6.98 (d, J = 7.9 Hz, 4H), 7.08 (d, J = 7.9 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): d 21.0, 36.7, 50.7, 115.4 (q, J_{CF} = 294 Hz), 128.8, 129.3, 134.5, 136.4, 194.3 (q, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 82.6 (s); IR ($CHCl_3$): ν 2925, 1757, 1516, 1211, 1147, 808 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{19}H_{19}F_3O$ [M]$^+$: 320.1388; Found: 320.1389.

4-(Biphenyl-4-yl)-3-(biphenyl-4-yl)methyl-1,1,1-trifluorobutan-2-one (10c): ^{1}H NMR (500 MHz, $CDCl_3$): δ2.84 (dd, J = 13.8, 6.8 Hz, 2H), 3.13 (dd, J = 13.8, 7.6 Hz, 2H), 3.63 (tt, J = 7.6, 6.8 Hz, 1H), 7.20 (d, J = 8.2 Hz, 4H), 7.34 (tt, J = 7.4, 1.0 Hz, 2H), 7.43 (dd, J = 8.1, 7.4 Hz, 4H), 7.52 (d, J = 8.2 Hz, 4H), 7.57 (d, J = 8.1 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ36.7, 50.5, 115.4 (q, J_{CF} = 293 Hz), 127.0, 127.3, 127.4, 128.8, 129.4, 136.6, 139.8, 140.6, 194.1 (q, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 82.8 (s); IR ($CHCl_3$): ν 3032, 1753, 1487, 1167, 1153, 764 cm^{-1}; HRMS (EI$^+$): Calcd. for $C_{29}H_{23}F_3O$ $[M]^+$: 444.1701; Found: 444.1704.



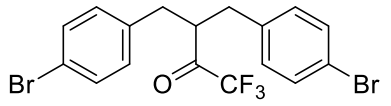
17c

4-(4-Chlorophenyl)-3-[(4-methylphenyl)methyl]-1,1,1-trifluorobutan-2-one (17d): ^{1}H NMR (500 MHz, $CDCl_3$): δ2.32 (s, 3H), 2.70 (dd, J = 13.8, 7.0 Hz, 1H), 2.74 (dd, J = 13.8, 6.2 Hz, 1H), 2.99 (dd, J = 13.8, 7.4 Hz, 1H), 3.03 (dd, J = 13.8, 7.4 Hz, 1H), 3.49 (dddd, J = 7.4, 7.4, 7.0, 6.2 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 7.01 (d, J = 9.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0, 36.2, 36.9, 50.6, 115.3 (q, J_{CF} = 293 Hz), 128.8 (4C), 129.4, 130.3, 132.8, 134.1, 136.2, 136.7, 193.9 (q, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ82.6 (s); IR ($CHCl_3$): ν 3024, 1757, 1493, 1213, 1146, 806 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{18}H_{16}ClF_3O$ $[M]^+$: 340.0842; Found: 340.0844.



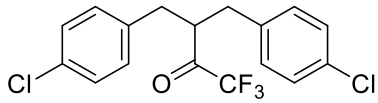
17d

4-(4-Bromophenyl)-3-(4-bromophenyl)methyl-1,1,1-trifluorobutan-2-one (17e): ^{1}H NMR (500 MHz, $CDCl_3$): δ2.70 (dd, J = 13.8, 6.7 Hz, 2H), 3.00 (dd, J = 13.8, 7.7 Hz, 2H), 3.47 (tt, J = 7.7, 6.7 Hz, 1H), 6.97 (d, J = 8.2 Hz, 4H), 7.41 (d, J = 8.2 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ36.5, 50.2, 115.3 (q, J_{CF} = 293 Hz), 121.1, 130.6, 131.9, 136.3, 193.5 (q, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ82.6 (s); IR ($CHCl_3$): ν2931, 1757, 1489, 1147, 1072, 1011 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{17}H_{13}Br_2F_3O$ $[M]^+$: 449.9265; Found: 449.9267.



17e

4-(4-Chlorophenyl)-3-(4-chlorophenyl)methyl-1,1,1-trifluorobutan-2-one (17f): ^{1}H NMR

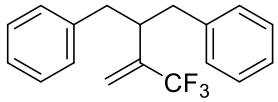


17f

(500 MHz, $CDCl_3$): δ 2.72 (dd, J = 13.8, 6.7 Hz, 2H), 3.02 (dd, J = 13.8, 7.7 Hz, 2H), 3.47 (tt, J = 7.7, 6.7 Hz, 1H), 7.03 (d, J = 8.6 Hz, 4H), 7.26 (d, J = 8.6 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 36.4, 50.4, 115.3 (q, J_{CF} = 293 Hz), 128.9, 130.3, 133.0, 135.7, 193.6 (q, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 83.7 (s); IR ($CHCl_3$): ν 2931, 1759, 1493, 1217, 1149, 1093 cm^{-1}.; HRMS (EI$^+$): Calcd for $C_{17}H_{13}Cl_2F_3O$ $[M]^+$: 360.0296; Found: 360.0295.

Wittig reaction of Trifluoromethylketones 17 [Preparation of Trifluoromethylalkenes 10]. To a THF solution (110 mL) of methyl(triphenyl)phosphonium iodide (10.7 g, 26.5 mmol) was added potassium *tert*-butoxide (2.9 g, 25.8 mmol) at –78 °C. The reaction mixture stirred for 10 min at that temperature. To the mixture was added trifluoromethylketone **38a** (6.4 g, 21.9 mmol) at –78 °C. After being stirred for 12 h at room temperature, saturated aqueous NH_4Cl was added to the mixture. Organic materials were extracted with Et_2O three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give **11a** (5.4 g, 18.5 mmol, 87%) as a colorless liquid.

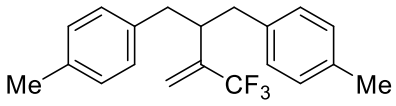
3-Benzyl-4-phenyl-2-(trifluoromethyl)but-1-ene (10a): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.79 (dd,



10a

J = 13.8, 7.1 Hz, 2H) , 2.85 (dd, J = 13.8, 7.3 Hz, 2H), 2.96 (tt, J = 7.3, 7.1 Hz, 1H), 5.26 (s, 1H), 5.75 (s, 1H), 7.12 (d, J = 7.2 Hz, 4H), 7.19 (t, J = 7.6 Hz, 2H), 7.27 (dd, J = 7.6, 7.2 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 40.1, 42.9, 119.5 (q, JCF = 6 Hz), 123.9 (q, J_{CF} = 275 Hz), 126.2, 128.2, 129.2, 139.2, 140.0 (q, J_{CF} = 28 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 94.3 (s); IR ($CHCl_3$): ν 3028, 1757, 1496, 1119, 752, 698 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{18}H_{17}F_3$ $[M]^+$: 290.1282; Found: 290.1273.

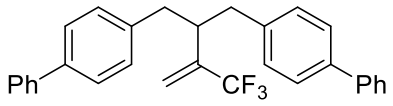
4-(4-Methylphenyl)-3-(4-methylphenyl)methyl-2-(trifluoromethyl)but-1-ene (10b): ^{1}H NMR



10b

(500 MHz, $CDCl_3$): δ 2.30 (s, 6H), 2.72 (dd, J = 13.9, 7.2 Hz, 2H), 2.78 (dd, J = 13.9, 7.2 Hz, 2H), 2.92 (tt, J = 7.2, 7.2 Hz, 1H), 5.21 (s, 1H), 5.72 (d, J = 1.1 Hz, 1H), 6.99 (d, J = 7.9 Hz, 4H), 7.06 (d, J = 7.9 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0, 39.6, 42.8, 119.3 (q, JCF = 6 Hz), 123.9 (q, J_{CF} = 275 Hz), 128.9, 129.1, 135.6, 136.1, 140.2 (q, J_{CF} = 28 Hz).; ^{19}F NMR (470 MHz, $CDCl_3$): δ 94.3 (s); IR ($CHCl_3$): ν 2925, 1516, 1163, 1117, 804 cm^{-1}; HRMS (EI$^+$): Calcd. for $C_{20}H_{21}F_3$ [M]$^+$: 318.1595; Found: 318.1598.

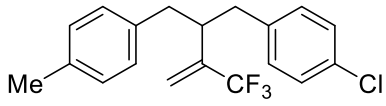
4-(Biphenyl-4-yl)-3-(biphenyl-4-yl)methyl-2-(trifluoromethyl)but-1-ene (10c): ^{1}H NMR (500



10c

MHz, $CDCl_3$): δ 2.85 (dd, J = 13.9, 7.0 Hz, 2H), 2.92 (dd, J = 13.9, 7.2 Hz, 2H), 3.04 (tt, J = 7.2, 7.0 Hz, 1H), 5.30 (s, 1H), 5.79 (s, 1H), 7.20 (d, J = 8.3 Hz, 4H), 7.32 (tt, J = 7.4, 1.2 Hz, 2H), 7.42 (dd, J = 8.2, 7.4 Hz, 4H), 7.50 (dd, J = 8.3, 1.8 Hz, 4H), 7.58 (dd, J = 8.2, 1.2 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.7, 42.7, 119.6 (q, J_{CF} = 6 Hz), 123.9 (q, J_{CF} = 275 Hz), 127.0 (2C), 127.1, 128.7, 129.6, 138.3, 139.1, 140.1 (q, J_{CF} = 28 Hz), 140.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ 94.4 (s); IR ($CHCl_3$): ν 3028, 1487, 1165, 1117, 912, 735 cm^{-1}; HRMS (EI$^+$): Calcd. for $C_{30}H_{25}F_3$ [M]$^+$: 442.1908; Found: 442.1907.

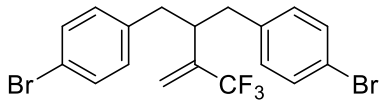
3-(4-Chlorophenyl)methyl-4-(4-methylphenyl)-2-(trifluoromethyl)but-1-ene (10d): ^{1}H NMR



10d

(500 MHz, $CDCl_3$): δ 2.31 (s, 3H), 2.70 (dd, J = 13.8, 7.2 Hz, 1H), 2.73–2.78 (m, 2H), 2.82 (dd, J = 13.8, 7.0 Hz, 1H), 2.88 (dd, J = 14.2, 7.2 Hz, 1H), 5.22 (s, 1H), 5.74 (s, 1H), 7.00 (d, J = 7.7 Hz, 2H), 7.01 (d, J = 8.3 Hz, 2H), 7.08 (d, J = 7.7 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0, 39.2, 39.9, 43.0, 119.6 (q, JC–F = 6 Hz), 123.9 (q, JC–F = 275 Hz), 128.4, 129.0 (2C), 130.5, 132.1, 135.9, 137.7, 140.1 (q, JCF = 29 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 94.3 (s); IR ($CHCl_3$): ν 2927, 1493, 1165, 1119, 806 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{19}H_{18}ClF_3$ [M]$^+$: 338.1049; Found: 338.1047.

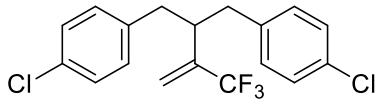
4-(4-Bromophenyl)-3-(4-bromophenyl)methyl-2-(trifluoromethyl)but-1-ene (10e): ^{1}H NMR



10e

(500 MHz, $CDCl_3$): δ 2.71 (dd, J = 13.8, 6.9 Hz, 2H), 2.78 (dd, J = 13.8, 7.3 Hz, 2H), 2.87 (tt, J = 7.3, 6.9 Hz, 1H), 5.21 (s, 1H), 5.75 (s, 1H), 6.96 (d, J = 8.2 Hz, 4H), 7.39 (d, J = 8.2 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.5, 42.9, 119.9 (q, J_{CF} = 6 Hz), 120.3, 123.7 (q, J_{CF} = 275 Hz), 130.9, 131.5, 137.9, 139.7 (q, JCF = 28 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): δ 94.3 (s); IR ($CHCl_3$): ν 3026, 1487, 1163, 1113, 1072, 1011 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{18}H_{15}Br_2F_3$ [M]$^+$: 447.9472; Found: 447.9478.

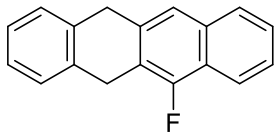
4-(4-Chlorophenyl)-3-(4-chlorophenyl)methyl-2-(trifluoromethyl)but-1-ene (10f): ^{1}H NMR



10f

(500 MHz, $CDCl_3$): δ 2.73 (dd, J = 13.8, 6.9 Hz, 2H), 2.79 (dd, J = 13.8, 7.3 Hz, 2H), 2.87 (tt, J = 7.3, 6.9 Hz, 1H), 5.22 (s, 1H), 5.76 (d, J = 1.2 Hz, 1H), 7.03 (d, J = 8.4 Hz, 4H), 7.24 (d, J = 8.4 Hz, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 39.4, 42.9, 119.9 (q, J_{CF} = 6 Hz), 123.7 (q, J_{CF} = 275 Hz), 128.5, 130.5, 132.2, 137.4, 139.5 (q, JCF = 29 Hz); ^{19}F NMR: δ 94.3 (s); IR ($CHCl_3$): ν 2935, 1493, 1163, 1117, 1014, 808 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{18}H_{15}Cl_2F_3$ [M]$^+$: 358.0503; Found: 358.0505.

5-Fluoro-6,11-dihydrotetracene (18a): ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.10 (s, 2H), 4.15 (s, 2H),



18a

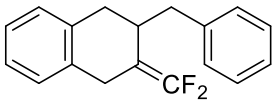
7.21−7.25 (m, 2H), 7.32−7.34 (m, 1H), 7.37-7.38 (m, 1H), 7.46 (m, 2H), 7.56 (s, 1H), 7.44−7.49 (m, 2H), 7.77−7.89 (m, 1H), 8.05−8.07 (m, 1H); ^{13}C NMR (126 MHz, CDC1$_3$): δ 28.4 (d, J_{CF} = 4 Hz), 36.3 (d, J_{CF} = 2 Hz), 119.0 (d, J_{CF} = 17, 34 Hz), 120.3 (dd, J_{CF} = 29, 4 Hz), 122.0 (d, J_{CF} = 18 Hz), 125.4 (d, J_{CF} = 1 Hz), 126.1, 126.4 (d, $_JCF$ = 3 Hz), 126.8 (d, J_{CF} = 3 Hz), 127.3, 127.7, 133.0, 133.1, 135.4, 136.4, 136.45, 136.49, 154.8 (d, J_{CF} = 249 Hz); ^{19}F NMR (470 MHz, CDCl3): δ 31.6 (s, 1F); IR (neat): ν 1456, 1329, 1279, 1036, 775, 746 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{18}H_{13}F$ [M]$^+$: 248.1001; Found 248.1005.

S_N1' Reaction of Trifluoromethylalkenes 10 with Aluminium Lewis Acid (1st cyclization): To a CH_2Cl_2 solution (13 mL) of trifluoromethylalkene **10a** (1.9 g, 6.5 mmol) was added a hexane

solution of trimethylaluminium (6.0 mL, 1.09 M, 6.5 mmol) and a hexane solution of dimethylaluminium chloride (7.3 mL, 1.07 M, 7.8 mmol) at –78 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give a mixture of **11a** and **18a'** (**11a** : **18a'** = 97 : 3. 90% yield by ^{19}F NMR).

S_N1' Reaction of Trifluoromethylalkenes 10 with Zirconium Lewis Acid (1st cyclization): To a CH_2Cl_2 solution (20 mL) of trifluoromethylalkene **11b** (1.0 g, 2.3 mmol) was added a hexane solution of trimethylaluminium (2.1 mL, 1.06 M, 2.2 mmol) and a hexane solution of zirconium(IV) chloride (525 mg, 2.3 mmol) at –78 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give a mixture of **11d** and **18d'** (**11d** : **18d'** = 78 : 22. 72% yield by ^{19}F NMR).

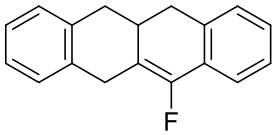
2-Benzyl-3-difluoromethylidene-1,2,3,4-tetrahydronaphthalene (11a): ^1H NMR (500 MHz, $CDCl_3$): δ 2.49 (dd, J = 13.5, 9.0 Hz, 1H), 2.60 (dt, J = 15.6, 2.9 Hz, 1H), 2.65 (dd, J = 13.5, 6.8 Hz, 1H), 2.77 (dd, J = 10.6, 5.4 Hz, 1H), 3.04–3.11 (m, 1H), 3.38 (dt, J = 18.8, 3.8 Hz, 1H), 3.46 (dd, J = 18.8, 2.4 Hz, 1H), 7.03 (d, J = 7.3 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H), 7.10–7.15 (m, 3H), 7.18 (t, J = 7.5 Hz, 1H), 7.25 (dd, J = 7.5, 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.3, 33.2 (brs), 33.5–34.0 (m), 38.7 (dd, J_{CF} = 2, 2 Hz), 87.8 (q, J_{CF} = 17, 17 Hz), 126.2, 126.3, 126.4, 128.2, 128.4, 129.1, 129.4, 134.0, 135.2, 139.8, 152.0 (t, J_{CF} = 284 Hz); ^{19}F NMR (126 MHz, $CDCl_3$): δ 66.5 (d, J_{FF} = 56 Hz, 1F), 67.9 (d, J_{FF} = 56 Hz, 1F);



11a

IR ($CHCl_3$): ν 1749, 1225, 995, 741, 698 cm^{-1}; HRMS (EI^+): Calcd for $C_{18}H_{16}F_2$ $[M]^+$: 270.1220; Found: 270.1224.

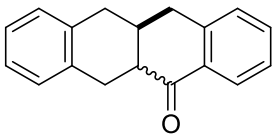
5-Fluoro-6,11,11a,12-tetrahydrotetracene (18a'): ^1H NMR (500 MHz, $CDCl_3$): δ 2.65–2.72 (m, 1H), 2.75–2.93 (m, 4H), 3.74 (d, J = 20.0 Hz, 1H), 3.82 (d, J = 20.0 Hz, 1H), 7.05–7.23 (m, 6H), 7.28 (dd, J = 6.4, 5.4 Hz, 1H), 7.34 (d, J = 7.2 Hz, 1H); ^{19}F NMR (470 MHz, $CDCl_3$): δ 28.5 (s)



18a'

Brönsted Acid-Promoted Cyclization of 1,1-Difluoroalkenes 11 (Preparation of Cyclic Ketone 13a, SNV-type Reaction): To a HFIP (10 mL) and CH_2Cl_2 (1.0 mL) solution of difluoroalkene **11a** and monofluoroalkene **18a'** (1.6 g, 5.7 mmol, **11a**:**18a'** = 97:3) was added a TfOH (1.0 mL, 11 mmol) at 0 °C. The reaction mixture was stirred for 3 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by recrystallization (Hexane/AcOEt = 10:1) to give **13a** (1.0 g, *cis/trans* = 85:15, 73%) as a yellow solid.

6,11,11a,12-Tetrahydro-5(5a*H*)-tetracenone (13a):



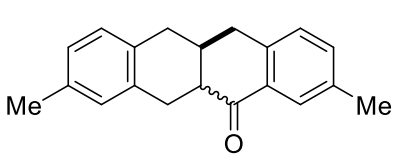
13a

[*Cis Diastereomer*]: ^1H NMR (500 MHz, $CDCl_3$): δ 2.75 (dd, J = 16.7, 7.1 Hz, 1H), 2.81–2.89 (m, 1H), 2.94 (dd, J = 16.7, 5.9 Hz, 2H), 3.01 (dd, J = 17.0, 7.3 Hz, 1H), 3.08 (ddd, J = 6.7, 6.7, 4.8 Hz, 1H), 3.14 (dd, J = 17.0, 4.7 Hz, 1H), 3.33 (dd, J = 16.0, 7.1 Hz, 1H), 7.03 (d, J = 6.3 Hz, 1H), 7.07–7.17 (m, 3H), 7.25 (d, J = 7.1 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 8.04 (d, J = 7.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.4, 32.1, 32.6, 32.9, 45.9, 125.85, 125.88, 126.7, 127.4, 129.1, 129.27, 129.30, 131.2, 133.5, 134.1, 134.3, 142.3, 199.2; IR ($CHCl_3$, *cis*,*trans* mixture): ν 1685, 1560, 1541, 1508, 771, 669 cm^{-1}; HRMS (EI^+, *cis*,*trans* mixture): Calcd for $C_{18}H_{16}O$ $[M]^+$: 248.1201; Found 248.1205, 248.1207.

[*Trans* Diastereomer]: ^1H NMR (500 MHz, $CDCl_3$): δ 2.38 (dddd, J = 22.7, 11.9, 4.7, 4.7 Hz, 1H),

2.61 (ddd, *J* = 12.6, 12.6, 5.7 Hz, 1H), 2.81–2.97 (m, 3H), 3.09 (dd, *J* = 16.5, 5.1 Hz, 1H), 3.13 (dd, *J* = 16.5, 4.2 Hz, 1H), 3.49 (ddd, *J* = 10.8, 5.8, 5.8 Hz, 1H), 7.09–7.19 (m, 3H), 7.22 (d, *J* = 6.2 Hz, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.51 (t, *J* = 7.4 Hz, 1H), 8.09 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 29.7, 36.1, 36.5, 37.2, 48.0, 125.8, 126.0, 126.8, 127.4, 128.4, 128.5, 129.3, 132.1, 133.5, 134.6, 135.3, 142.9, 199.2.

2,9-Dimethyl-5,5a,6,11,11a,12-hexahydro-11-tetracenone (13b):

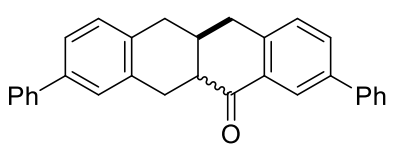


13b

[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.27 (s, 3H), 2.35 (s, 3H), 2.69 (dd, *J* = 16.6, 6.8 Hz, 1H), 2.77-2.84 (m, 1H), 2.88 (dt, *J* = 16.8, 5.1 Hz, 2H), 2.95 (dd, *J* = 16.8, 7.4 Hz, 1H), 3.01-3.09 (m, 2H), 3.25 (dd, *J* = 16.8, 7.4 Hz, 1H), 6.91 (s, 2H), 6.96 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.84 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 20.9, 27.4, 31.8, 32.2, 33.1, 46.0, 126.8, 127.5, 129.2, 129.3, 129.6, 131.0, 131.1, 134.2, 134.5, 135.3, 136.3, 139.6, 199.7; IR ($CHCl_3$, *cis*,*trans* mixture): ν 2916, 1680, 1496, 1284, 814 cm^{-1}; HRMS (EI$^+$, *cis*,*trans* mixture): Calcd for $C_{20}H_{20}O$ $[M]^+$: 276.1514; Found 276.1512, 276.1517.

[*Trans* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.31 (s, 3H), 2.38 (s, 3H), 2.57 (ddd, *J* = 12.7, 11.4, 5.7 Hz, 1H), 2.77-2.84 (m, 2H), 2.85-2.92 (m, 1H), 3.01-3.09 (m, 2H), 3.44 (dd, *J* = 17.5, 5.7 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 7.03 (s, 1H), 7.17 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 9.0 Hz, 1H), 7.89 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0, 29.8, 36.2, 36.4, 36.9, 48.2, 126.7, 128.3, 128.5, 129.8, 131.6, 131.9, 135.2, 135.6, 136.5, 140.2, 199.6.

2,9-Diphenyl-5,5a,6,11,11a,12-hexahydro-11-tetracenone (13c):



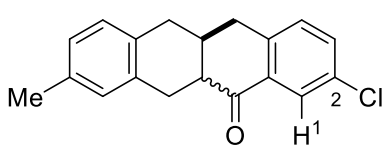
13c

[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.82 (dd, *J* = 16.7, 7.2 Hz, 1H), 2.86-2.94 (m, 1H), 2.99 (dd, *J* = 16.0, 5.6 Hz, 1H), 3.03–3.11 (m, 2H), 3.12–3.18 (m, 1H), 3.21 (dd, *J* = 17.1, 4,7 Hz, 1H), 3.43 (dd, *J* = 11.9, 6.8 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.28–7.48 (m, 9H), 7.56 (d,

J = 7.7 Hz, 2H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.74 (dd, *J* = 7.9, 1.9 Hz, 1H), 8.29 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.7, 31.9, 32.5, 33.0, 46.1, 124.9, 125.8, 126.96, 126.99, 127.03, 127.6, 127.8, 128.7, 128.8, 129.8, 130.0, 131.5, 132.2, 133.4, 134.7, 139.0, 139.8, 140.0, 141.0, 141.2, 199.2; IR ($CHCl_3$, *cis*,*trans* mixture): ν 2910, 1680, 1481, 758, 696 cm^{-1}; HRMS (APCI$^+$, *cis*,*trans* mixture): Calcd for $C_{30}H_{25}O$ $[M+H]^+$: 401.1905; Found 401.1906.

[*Trans* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.40–2.49 (m, 1H), 2.69 (ddd, *J* = 12.6, 11.4, 5.7 Hz, 1H), 2.86–3.24 (m, 5H), 3.59 (dd, *J* = 17.5, 5.5 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.30–7.59 (m, 11H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.75 (dd, *J* = 7.9, 2.0 Hz, 1H), 8.32 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 29.9, 36.2, 36.3, 37.0, 48.2, 124.6, 124.8, 127.1, 127.6, 128.0, 128.7, 128.9, 129.2, 132.4, 133.8, 135.7, 139.2, 140.0, 141.0, 141.9, 199.1.

2-Chloro-9-methyl-5,5a,6,11,11a,12-hexahydro-12-tetracenone (13d):



13d

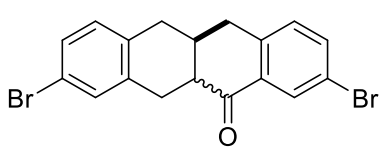
[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.28 (s, 3H), 2.67 (dd, *J* = 16.7, 7.1 Hz, 1H), 2.78–2.86 (m, 1H), 2.89 (dd, *J* = 16.9, 6.0 Hz, 2H), 2.96 (dd, *J* = 17.2, 7.2 Hz, 1H), 3.03–3.13 (m, 2H), 3.24 (dd, *J* = 16,7, 7.0 Hz, 1H), 6.92 (s, 2H), 6.96 (s, 1H), 7.19 (d, *J* = 8.3 Hz, 1H), 7.44 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.99 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 20.9, 27.3, 31.6, 32.1, 32.9, 45.8, 127.0, 127.2, 129.2, 129.6, 130.8, 130.9, 132.5, 132.9, 133.4, 133.8, 135.5, 140.6, 198.2

[*Trans* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.31 (s, 3H), 2.24–2.39 (m, 1H), 2.55–2.62 (m, 1H), 2.78–2.86 (m, 2H), 2.87–2.95 (m, 1H), 3.03–3.13 (m, 2H), 3.43 (dd, *J* = 17.3, 5.8 Hz, 1H), 7.01 (s, 1H), 7.03 (s, 2H), 7.23 (d, *J* = 8.3 Hz, 1H), 7.45 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.04 (d, *J* = 2.2 Hz, 1H).

In order to determine the regiochemistry of the cyclizations, HMBC analysis by a 400 MHz instrument for *cis* isomer was performed. A cross-peak between C^2 (δ 140.6, α to a chlorine substituent) and H^1 (δ 7.9, peri to a carbonyl group) was observed, suggesting that the first

cyclization took place on the electron-rich methylphenyl group and the second one took place on the remaining chlorophenyl group.

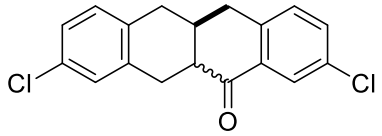
2,9-Dibromo-5,5a,6,11,11a,12-hexahydro-11-tetracenone (13e)



13e

[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.64 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.79–2.87 (m, 2H), 2.91(dd, *J* = 17.1, 6.0 Hz, 1H), 2.92 (dd, *J* = 17.1, 6.0 Hz, 1H), 3.07 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.15 (dd, *J* = 17.2, 4.5 Hz, 1H), 3.33 (dd, *J* = 17.2, 6.4 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.31 (s, 1H), 7.60 (dd, *J* = 8.2, 2.2 Hz, 1H), 8.13 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.3, 31.2, 32.4, 32.7, 45.4, 119.6, 120.9, 129.1, 130.2, 130.9, 131.3, 131.8, 132.7, 133.0, 136.3, 136.5, 140.6, 197.3.; IR ($CHCl_3$): ν 2906, 1684, 1473, 1404, 1194, 752 cm^{-1}; HRMS (EI^+): Calcd for $C_{18}H_{14}Br_2O$ $[M]^+$: 405.9391; Found 405.9395.

2,9-Dichloro-5,5a,6,11,11a,12-hexahydro-11-tetracenone (13f)



13f

[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.65–2.71 (m, 1H), 2.81–2.90 (m, 3H), 2.90–2.98 (m, 1H), 3.03–3.08 (m, 1H), 3.17 (dd, *J* = 17.0, 4.2 Hz, 1H), 3.34 (dd, *J* = 17.0, 6.0 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 7.15 (s, 1H), 7.21(d, *J* = 8.2 Hz, 1H), 7.45 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 27.4, 31.2, 32.4, 32.8, 45.4, 126.2, 127.2, 128.9, 130.5, 131.0, 131.5, 132.4, 132.5, 133.1, 133.6, 135.9, 140.2, 197.5; IR ($CHCl_3$, *cis*,*trans* mixture): ν 2918, 1685, 1477, 1410, 1234 $cm^{-1;}$ HRMS (EI^+, *cis*,*trans* mixture): Calcd for $C_{18}H_{14}Cl_2O$ $[M]^+$: 316.0422; Found 316.0422.

[*Trans* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.28–2.38 (m, 1H), 2.59 (ddd, *J* = 12.9, 11.2, 5.8 Hz, 1H), 2.74–2.79 (m, 1H), 2.90–2.98 (m, 2H), 3.03–3.08 (m, 1H), 3.11 (dd, *J* = 16.5, 4.2 Hz, 1H), 3.44 (dd, *J* = 17.7, 5.8 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.19 (s, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.47 (dd, *J* = 8.2, 2.4 Hz, 1H), 8.04 (d, *J* = 2.3 Hz, 1H); ^{13}C NMR

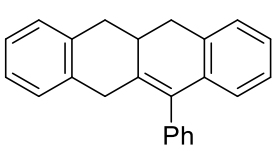
(126 MHz, $CDCl_3$): δ 29.5, 35.8, 35.9, 36.5, 47.5, 126.2, 127.3, 129.0, 129.7, 130.2, 131.7, 132.8, 133.17, 133.21, 133.6, 136.9, 141.0, 197.7.

Introduction of a Substituent to a Cyclic Ketone 13a (Preparation of Substituted Tetrahydro Tetracene derivative 20a, Introduction with Carbanions: Method A): To a THF (10 mL) solution of a bromobenzene (0.32 mL, 3.0 mmol) was added a hexane solution of *n*-butyllithium (1.6 M, 2.0 mL, 3.2 mmol) at –78 °C. **13a** (495 mg, 2.0 mmol) was added at –78 °C. The reaction mixture was warmed to room temperature and stirred for 15 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was added an acetic acid (1.0 mL) solution of sulfuric acid (0.1 mL) at room temperature. The reaction mixture was stirred for 20 min. Water was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give **20aa** (504 mg, 82%) as a yellow solid.

Introduction of a Substituent to a Cyclic Ketone 13a (Preparation of Tetrahydrotetracene 20ab, Introduction with Hydride: Method A): To a THF (3.0 mL) and MeOH (3.0 mL) solution of **14a** (82 mg, 0.33 mmol) was added $NaBH_4$ (46 mg, 1.2 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 4 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was added an acetic acid (1.0 mL) solution of sulfuric acid (0.1 mL) at room temperature. The reaction mixture was stirred for 20 min. Water was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column

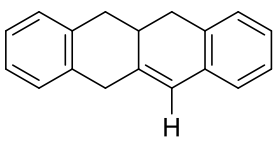
chromatography on silica gel (Hexane) to give **20ab** and 20ab**'** (**20ab**:**20ab'** = 86:14. 76% yield by ^{1}H NMR).

5-Phenyl-6,11,11a,12-tetrahydrotetracene (20aa): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.72–2.85 (m, 2H), 2.85–2.95 (m, 2H), 3.00 (dd, J = 13.6, 4.2 Hz, 1H), 3.41 (d, J = 18.5 Hz, 1H), 3.46 (d, J = 18.5 Hz, 1H), 6.62 (d, J = 7.6 Hz, 1H), 6.98 (d, J = 7.0 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 7.07 (ddd, J = 7.4, 7.4, 0.8 Hz, 1H), 7.10–7.26 (m, 6H), 7.38 (dddd, J = 7.4, 7.4, 1.3, 1.3 Hz, 1H), 7.43–7.49 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 34.1, 35.6, 35.8, 36.0, 125.3, 126.0, 126.1, 126.29, 126.34, 126.8, 127.1, 127.3 (2C), 128.7, 130.0, 133.2, 134.8, 137.0, 137.6, 138.1, 139.7; IR ($CHCl_3$): ν 3018, 2927, 1483, 750, 702 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{24}H_{20}$ [M]$^+$: 308.1565; Found 308.1560.

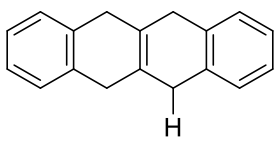


20aa

5,5a,6,12-Tetrahydrotetracene (20ab) and 5,6,11,12-Tetrahydrotetracene (20ab'):



20ab



20ab'

20ab: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.62–2.81 (m, 3H), 2.86–2.94 (m, 2H), 3.63 (d, J = 18.1 Hz, 1H), 3.71 (d, J = 18.1 Hz, 1H), 6.36 (s, 1H), 6.99 (d, J = 7.2 Hz, 1H), 7.04–7.19 (m, 7H).

20ab' ^{1}H NMR spectral data met complete agreement with those in the literature.[1)]

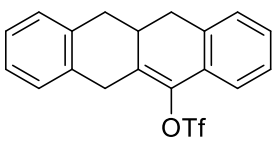
20ab, 20ab' mixture

^{13}C NMR (126 MHz, $CDCl_3$): δ 34.6, 35.1, 35.6, 35.7, 36.4, 121.5, 125.4, 125.8, 126.0, 126.2, 126.4, 126.5, 127.3, 127.4, 127.6, 128.0, 134.41, 134.42, 134.9, 136.7, 138.0, 141.5; IR ($CHCl_3$): ν 3026, 2833, 1483, 1456, 1219, 771, 748 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{18}H_{16}$ [M]$^+$: 232.1252; Found 232.1247.

Triflation of a Cyclic Ketone 14a (Preparation of Vinyl Triflate 21, Method B): To a CH_2Cl_2 (5.0 mL) solution of **14a** (245 mg, 0.99 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 241 mg, 1.2 mmol) was added Tf_2O (0.50 mL, 3.0 mmol). The reaction mixture was warmed to reflux and

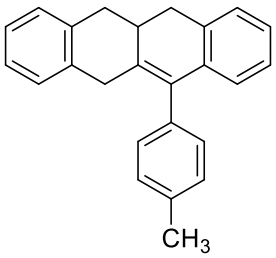
stirred for 4 h. Hexane was added to the mixture and filtered. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane/Toluene = 10:1) to give **31a** (335 mg, 89%) as a yellow liquid.

5-Trifluoromethanesulfonyloxy-6,11,11a,12-tetrahydrotetracene (21a): ^{1}H NMR (500 MHz, $CDCl_3$): δ2.72–2.82 (m, 2H), 2.85–2.96 (m, 3H), 3.83 (d, J = 19.5Hz, 1H), 3.88 (d, J = 19.5 Hz, 1H), 7.14–7.28 (m, 7H), 7.33 (d, J = 7.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 30.6, 34.2, 34.9, 37.0, 118.5 (q, JCF = 321 Hz), 121.1, 126.6, 126.9,127.0, 127.4, 127.5, 127.9, 128.3, 129.7, 133.2,133.8, 134.9, 137.1, 139.8; ^{19}F NMR (470 MHz, $CDCl_3$): δ88.1 (s); IR ($CHCl_3$): ν2935, 1415, 1207, 1138, 972, 744 cm^{-1}; HRMS (APCI$^+$): Calcd for $C_{18}H_{15}O$ $[M–CF_3SO_2]^+$: 247.1123; Found 247.1120.



21a

Introduction of Substituents with Vinyl Triflate 21 (Coupling Reaction, Method B): To a toluene (5.0 mL), MeOH (2.0 mL), and water (3.0 mL) solution of **21a** (533 mg, 1.4 mmol) were added 4-methylphenyl boronic acid (255 mg, 1.9 mmol), $Pd(PPh_3)_4$ (80 mg, 0.07 mmol), and sodium carbonate (445 mg, 4.2 mmol). The reaction mixture was warmed to reflux and stirred for 5 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give **20ac** (425 mg, 94%) as a yellow solid.

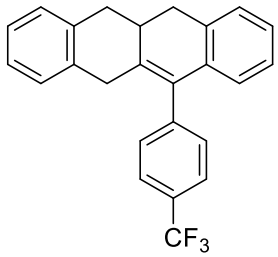


20ac

5-(4-Methylphenyl)-6,11,11a,12-tetrahydrotetracene (20ac): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.43 (s, 3H), 2.70–2.82 (m, 2H), 2.85–2.92 (m, 2H), 2.98 (dd, J = 13.2, 3.6 Hz, 1H), 3.41 (d, J = 18.6 Hz, 1H), 3.47 (d, J = 18.6 Hz, 1H), 6.64 (d, J = 7.5 Hz, 1H), 6.98 (d, J = 6.3 Hz, 1H), 7.01 (d, J = 7.5 Hz, 1H), 7.03–7.19 (m, 7H), 7.26 (d, J = 7.2 Hz, 2H).; ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.3, 34.1, 35.6, 35.9, 36.0, 125.3, 125.96, 126.04, 126.26, 126.31, 127.0, 127.3 (2C), 129.4, 129.9, 133.1,

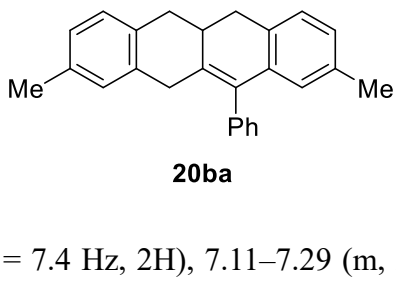
134.9, 136.3, 136.6, 137.06, 137.14, 137.4, 138.1; IR ($CHCl_3$): ν 3018, 2924, 1483, 910, 766, 729 cm^{-1}; HRMS (EI^+): Calcd for $C_{25}H_{22}$ $[M]^+$: 322.1722; Found 322.1726.

5-(4-Trifluoromethylphenyl)-6,11,11a,12-tetrahydrotetracene (20ad): ^1H NMR (500 MHz, $CDCl_3$): δ 2.75 (dd, J = 13.6, 9.6 Hz, 1H), 2.78–2.85 (m, 1H), 2.87 (d, J = 14.2 Hz, 1H), 2.93 (dd, J = 14.2, 6.6 Hz, 1H), 3.01 (dd, J = 13.6, 4.2 Hz, 1H), 3.37 (d, J = 19.9 Hz, 1H), 3.41 (d, J = 19.9 Hz, 1H), 6.53 (d, J = 7.5 Hz, 1H), 6.98 (d, J = 6.8 Hz, 1H), 7.02 (dd, J = 7.2, 7.2 Hz, 1H), 7.09 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 7.13–7.21 (m, 4H), 7.27–7.38 (m, 2H), 7.72 (d, J = 7.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 34.1, 35.4, 35.6, 36.0, 124.3 (q, J_{CF} = 273 Hz), 125.1, 125.7 (q, J = 2 Hz), 126.2, 126.4, 126.47, 126.50, 127.3, 127.4, 129.1 (q, J_{CF} = 32 Hz), 130.5, 132.1, 134.8, 136.3, 136.5, 137.9, 138.5, 143.6; ^{19}F NMR(470 MHz, $CDCl_3$): δ 99.4 (s); IR ($CHCl_3$): ν 2931, 1323, 1122, 1066, 739 cm^{-1}; HRMS (EI^+): Calcd for $C_{25}H_{19}F_3$ $[M]^+$: 376.1439; Found 376.1438.



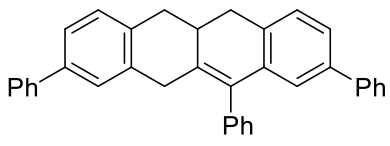
20ac

2,9-Dimethyl-11-phenyl-5,5a,6,12-tetrahydrotetracene (20ba): ^1H NMR (500 MHz, $CDCl_3$): δ 2.15 (s, 3H), 2.26 (s, 3H), 2.67–2.80 (m, 2H), 2.81–2.88 (m, 2H), 2.94 (dd, J = 13.4, 3.8 Hz, 1H), 3.38 (s, 2H), 6.43 (s, 1H), 6.80 (s, 1H), 6.89 (d, J = 7.4 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H), 7.06 (d, J = 7.4 Hz, 2H), 7.11–7.29 (m, 2H), 7.38 (dd, J = 7.4, 7.4 Hz, 1H), 7.42-7.48 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0, 21.2, 34.1, 35.3, 35.4, 36.3, 126.0, 126.6, 126.7 (2C), 126.9, 127.2, 128.1, 128.6, 130.0, 131.9, 133.2, 135.0, 135.7, 135.8, 136.8, 137.8, 139.8; IR ($CHCl_3$): ν 2922, 1491, 1441, 908, 810 cm^{-1}; HRMS (EI^+): Calcd. for $C_{26}H_{24}$ $[M]^+$: 336.1878; Found: 336.1878.



20ba

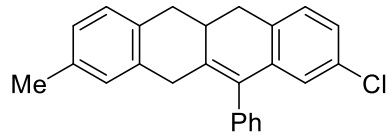
2,9,11-Triphenyl-5,5a,6,12-tetrahydrotetracene (20ca): ^1H NMR (500 MHz, $CDCl_3$): δ 2.81 (dd, J = 13.6, 9.9 Hz, 1H), 2.83–2.91 (m, 1H), 2.93 (d, J = 14.4 Hz, 1H), 2.98 (dd, J = 14.1, 6.0 Hz, 1H), 3.06 (dd, J = 13.6, 4.0 Hz, 1H), 3.50 (d, J = 19.0 Hz, 1H), 3.55 (d, J = 19.0 Hz, 1H), 6.87 (d,



20ca

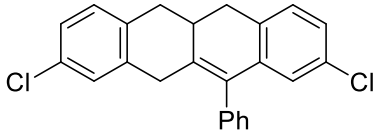
J = 1.6 Hz, 1H), 7.20–7.28 (m, 6H), 7.28–7.34 (m, 4H), 7.35–7.42 (m, 6H), 7.43–7.49 (m, 2H), 7.54 (d, J = 7.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 34.4, 35.3, 35.6, 36.1, 124.2, 124.8, 124.9, 126.2, 126.8, 126.96, 127.00, 127.5, 127.8, 128.55, 128.65, 128.8 (2C), 130.0 (2C), 133.4, 134.0, 137.2, 137.3, 137.9, 139.39, 139.43, 139.5, 141.1, 141.4; IR ($CHCl_3$): ν 3028, 1481, 908, 760, 698 cm^{-1}; HRMS ($APCI^+$): Calcd. for $C_{36}H_{29}$ $[M+H]^+$: 461.2269; Found: 461.2269.

2-Chloro-9-methyl-12-phenyl-5,5a,6,11-tetrahydrotetracene (20da): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.27 (s, 3H), 2.66–2.80 (m, 2H), 2.80–2.91 (m, 2H), 2.95 (dd, J = 13.4, 3.6 Hz, 1H), 3.37 (d, J = 19.9 Hz, 1H), 3.41 (d, J = 19.9 Hz), 6.58 (d, J = 1.9 Hz, 1H), 6.81 (s, 1H), 6.96 (d, J = 7.8 Hz, 1H), 7.03 (dd, J = 7.8, 2.0 Hz, 1H), 7.06 (d, J = 8.2 Hz, 1H), 7.08 (d, J = 8.2 Hz, 1H), 7.12–7.23 (m, 2H), 7.39 (dd, J = 7.8, 7.8 Hz, 1H), 7.43–7.51 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0, 34.2, 34.9, 35.3, 36.2, 125.2, 125.9, 126.7, 127.1, 127.2, 128.1, 128.2, 128.9, 129.9, 132.0, 132.5, 133.2, 134.7, 136.0, 136.5, 138.7, 138.9, 139.5; IR ($CHCl_3$): ν 2925, 1477, 1441, 808, 702 cm^{-1}; HRMS (EI^+): Calcd. for $C_{25}H_{21}Cl$ $[M]^+$: 356.1332; Found: 356.1333.



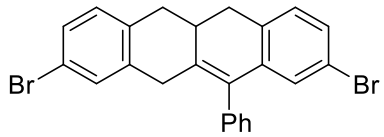
20da

2,9-Dichloro-11-phenyl-5,5a,6,12-tetrahydrotetracene (20fa): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.68 (dd, J = 13.8, 9.8 Hz, 1H), 2.71–2.80 (m, 1H), 2.80 (dd, J = 13.8, 13.8 Hz, 1H), 2.88 (dd, J = 13.8, 4.8 Hz, 1H), 2.96 (dd, J = 13.5, 3.8 Hz, 1H), 3.35 (d, J = 18.7 Hz, 1H), 3.40 (d, J = 18.7 Hz, 1H), 6.59 (d, J = 1.9 Hz, 1H), 6.97 (s, 1H), 7.04 (dd, J = 7.9, 1.9 Hz, 1H), 7.06–7.23 (m, 5H), 7.40 (dd, J = 7.1, 7.1 Hz, 1H), 7.44–7.53 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 34.0, 34.8, 35.0, 35.8, 125.3, 126.0, 126.1, 127.3, 128.2, 128.6, 129.0, 129.8, 131.8, 132.1, 133.0, 136.2, 138.1, 138.4, 138.48, 138.52.; IR ($CHCl_3$): ν 2931, 1477, 904, 727, 700 cm^{-1}; HRMS ($APCI^+$): Calcd for $C_{24}H_{19}Cl_2$ $[M+H]^+$: 377.0864; Found 377.0867.



20fa

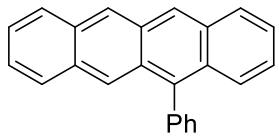
2,9-Dibromo-11-phenyl-5,6,6a,12-tetrahydrotetracene (20ea): To an Et_2O (5.0 mL) solution of **21e** (228 mg, 0.42 mmol), $PdCl_2$dppp (10.7 mg, 0.02 mmol), and LiBr (37.8 mg, 0.44 mmol) was added an Et_2O solution of phenylmagnesiumbromide (2.0 M 0.30 mL, 0.60 mmol). The reaction mixture was warmed to reflux and stirred for 14 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane/Toluene = 10:1) to give **20ea** (137 mg, 70%) as a white solid.



20ea

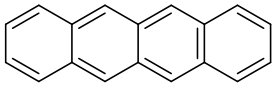
^{1}H NMR (500 MHz, $CDCl_3$): δ 2.65 (dd, J = 13.8, 9.6 Hz, 1H), 2.69–2.81 (m, 2H), 2.85 (dd, J = 13.4, 4.4 Hz, 1H), 2.93 (dd, J = 13.8, 4.0 Hz, 1H), 3.34 (d, J = 19.6 Hz, 1H), 3.39 (d, J = 19.6 Hz, 1H), 6.73 (d, J = 1.7 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 7.03 (d, J = 6.2 Hz, 1H), 7.08–7.21 (m, 2H), 7.12 (s, 1H), 7.19 (dd, J = 7.9, 1.9 Hz, 1H), 7.26 (dd, J = 8.0, 1.8 Hz, 1H), 7.40 (dd, J = 7.2, 7.2 Hz, 1H), 7.43–7.51 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 34.0, 34.9, 35.1, 35.7, 119.9, 120.2, 127.3, 128.1, 128.6, 128.9, 129.0, 129.05, 129.07, 129.8, 130.2, 132.9, 133.5, 136.7, 138.1, 138.5, 138.8, 138.9; IR ($CHCl_3$): ν 2929, 1473, 1074, 806, 702 cm^{-1}; HRMS (APCI$^+$): Calcd. for $C_{24}H_{19}Br_2$ $[M+H]^+$: 466.9833; Found: 466.9831.

5-Phenyltetracene (14aa): Spectral data met complete agreement with those in the literature.[2)]



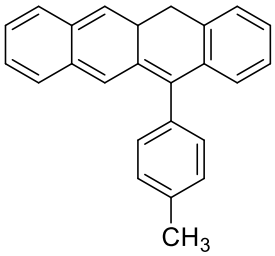
14aa

5-Phenyltetracene (14ab): Spectral data met complete agreement with those in the literature.[2)]



14ab

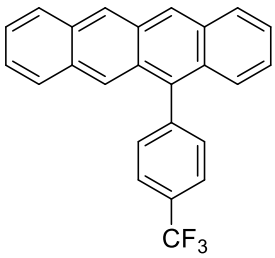
5-(4-Methylphenyl)tetracene (14ac): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.58 (s, 3H), 7.27–7.48 (m, 8H), 7.68 (d, J = 9.1 Hz, 1H), 7.81 (d, J = 8.6 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 8.32 (s, 1H), 8.70 (s, 1H), 8.72 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.4, 124.8, 124.9, 125.0, 125.2, 125.7, 126.3, 126.5, 126.9, 127.9, 128.5, 128.7, 129.2, 129.5, 129.7, 130.0, 131.1, 131.2, 131.29, 131.32, 135.9, 137.0, 137.1.; IR ($CHCl_3$): ν 3043, 3020, 1672, 1217, 893 cm^{-1}; HRMS (APCI^{+}): Calcd for $C_{25}H_{19}$ $[M+H]^{+}$: 319.1487; Found 319.1486.



14ac

Dehydrogenative Synthesis of Substituted Tetracenes 20 (Synthesis of 14, Aromatization with Pd/C): To a *p*-cymene (5.0 mL) solution of **20a** (50.9 mg, 0.165 mmol) was added 10% Pd/C (49.7 mg, 100 wt% to **20a**). Nitrogen was introduced to the reaction mixture (60 mL / min) through a bubbler of glass filter and warmed to reflux under dark condition. After being stirred for 14 h, the mixture was filtered using $CHCl_3$ as an eluent. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give **14a** (41.1 mg, 83%) as a red solid.

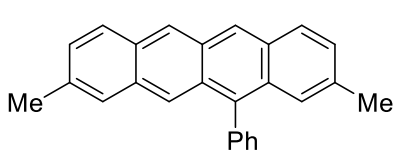
5-[4-(Trifluoromethyl)phenyl]tetracene (15c): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (dd, J = 8.6, 6.6 Hz, 1H), 7.34 (dd, J = 8.1, 6.7 Hz, 1H), 7.36–7.43 (m, 2H), 7.54 (d, J = 8.9 Hz, 1H), 7.63 (d, J = 7.6 Hz, 2H), 7.81 (d, J = 8.6 Hz, 1H), 7.91 (d, J = 7.6 Hz, 2H), 7.99 (d, J = 8.6 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 8.16 (s, 1H), 8.70 (s, 1H), 8.75 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 122.3 (q, J = 272 Hz), 124.9, 125.3, 125.50, 125.53 (q, J = 4 Hz), 125.7, 126.2, 126.7, 127.4, 128.0, 128.62,



14ac

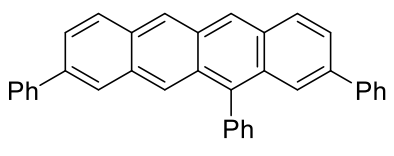
128.64, 129.0, 129.5, 129.8, 129.9 (q, J = 32 Hz), 131.0, 131.2, 131.6, 131.9, 134.9, 143.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ 99.4 (s); IR ($CHCl_3$): ν 2925, 1321, 1122, 1065, 744 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{25}H_{15}F_3$ [M]$^+$: 372.1126; Found 372.1122.

2,9-Dimethyl-11-phenyltetracene (15h): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.44 (s, 3H), 7.20 (dd, J = 8.4, 7.4 Hz, 2H), 7.35 (s, 1H), 7.48 (d, J = 6.8 Hz, 2H), 7.56 (s, 1H), 7.58 (d, J = 7.0 Hz, 1H), 7.60–7.65 (m, 2H), 7.88 (d, J = 8.8 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 8.10 (s, 1H), 8.60 (s, 1H), 8.64 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.9, 22.3, 124.1, 124.5, 126.1, 126.5, 126.6, 127.4, 127.68, 127.75, 128.2, 128.38, 128.45, 129.4, 129.81, 129.84, 131.5, 131.7, 134.4, 134.6, 135.4, 139.4; IR ($CHCl_3$): ν 2914, 1626, 895, 731, 700 cm^{-1}; HRMS (APCI$^+$): Calcd for $C_{26}H_{21}$ [M+H]$^+$: 333.1643; Found 333.1642.



14ba

2,9,11-Triphenyltetracene (14ca): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (dd, J = 7.3, 7.3 Hz, 1H), 7.36 (dd, J = 7.3, 7.3 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.55 (d, J = 6.7 Hz, 2H), 7.58–7.62 (m, 3H), 7.64 (d, J = 7.5 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 7.2 Hz, 2H), 7.85 (s, 1H), 8.02 (s, 1H), 8.06 (dd, J = 8.4, 8.4 Hz, 1H), 8.11 (dd, J = 8.4, 8.4 Hz, 1H), 8.32 (s, 1H), 8.69 (d, J = 7.2 Hz, 1H), 8.73 (d, J = 6.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 124.3, 125.2, 125.6, 126.0, 126.1, 126.3, 126.5, 127.1, 127.28, 127.33, 127.4, 127.7, 128.6, 128.79, 128.81, 129.2, 129.9, 130.0, 130.2, 130.37, 130.42, 131.5, 131.6, 137.2, 137.3, 137.4, 138.9, 140.8, 141.2; IR ($CHCl_3$): ν 3026, 1466, 899, 756, 694 cm^{-1}; HRMS (APCI$^+$): Calcd for $C_{36}H_{25}$ [M+H]$^+$: 457.1956; Found 457.1957.

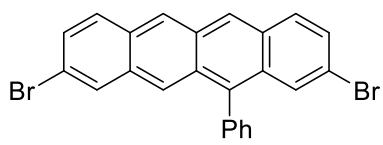


14ca

Dehydrogenative Synthesis of Halogen-Substituted Tetracenes 20 (Synthesis of 14, Aromatization with In Situ-Generated Trityl Cation): To a trifluoroacetic acid (1.0 mL) solution of **20ea** (23.6 mg, 0.051 mmol) was added triphenylmethanol (29.2 mg, 0.112 mmol). The

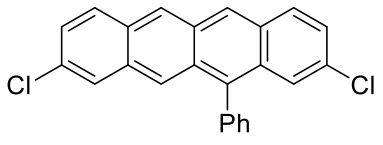
reaction mixture was warmed to reflux under dark condition. After being stirred for 12 h, the mixture was filtered using $CHCl_3$ as an eluent. After removal of the solvent under reduced pressure, the residue was purified by recrystallization (Hexane : Toluene = 10 : 1) to give **14ea** (7.1 mg, 30%) as a brown solid.

2,9-Dibromo-11-phenyltetracene (14ea): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39–7.48 (m, 4H), 7.59–7.68 (m, 3H), 7.81 (s, 1H), 7.85 (d, J = 9.0 Hz, 1H), 7.89 (d, J = 9.0 Hz, 1H), 8.00 (s, 1H), 8.14 (s, 1H), 8.63 (s, 1H), 8.66 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 119.6, 120.1, 125.0, 127.1, 127.3, 128.0, 128.5, 128.70, 128.74, 129.1, 129.3, 129.4, 129.6, 129.8, 129.9, 130.2, 130.3, 130.6, 131.2, 132.2, 136.4, 137.9; IR ($CHCl_3$): ν 1593, 914, 887, 742, 702 cm^{-1}; HRMS (APCI$^+$): Calcd for $C_{24}H_{15}Br_2$ $[M+H]^+$: 462.9520; Found 462.9525.



14ea

2,9-Dichloro-11-phenyltetracene (15g): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (dd, J = 7.2, 2.0 Hz, 1H), 7.32 (dd, J = 7.2, 2.0 Hz, 1H), 7.45 (d, J = 6.4 Hz, 1H), 7.46 (d, J = 6.4 Hz, 1H), 7.61–7.68 (m, 4H), 7.80 (s, 1H), 7.93 (d, J = 9.1 Hz, 1H), 7.97 (d, J = 9.1 Hz, 1H), 8.14 (s, 1H), 8.66 (s, 1H), 8.68 (s, 1H).; ^{13}C NMR (126 MHz, $CDCl_3$): δ 124.9, 125.0, 126.5, 126.8, 126.9, 127.1, 127.2, 128.0, 128.7, 129.3, 129.4, 129.7, 129.8, 130.0, 130.1, 130.3, 131.1, 131.2, 131.4, 131.6, 136.4, 138.0.; IR ($CHCl_3$): ν 3057, 1608, 1456, 912, 742 cm^{-1}; HRMS (APCI$^+$): Calcd for $C_{24}H_{15}Cl_2$ $[M+H]^+$: 373.0551; Found 373.0551.

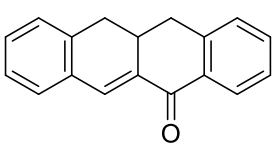


14fa

Oxidative Cation Cyclization of 1,1-Difluoroalkenes 11 (Preparation of Cyclic α,β-Unsaturated Ketone 14): To a HFIP (50 mL) solution of DDQ (1.2 g, 5.3 mmol) and TfOH (0.47 mL, 5.3 mmol) was added a HFIP (3.0 mL) solution of difluoroalkene **11a** (1.4 g, 5.3 mmol) at 0 °C. The reaction mixture was stirred for 3 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over

anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane/AcOEt = 20:1) to give **14a** (1.1 g, 83%) as a yellow solid.

5,11,11a,12-Tetrahydro-5-tetracenone (15a): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.89–2.92 (m, 2H), 3.02–3.18 (m, 3H), 7.21–7.33 (m, 4H), 7.36 (d, J = 6.7 Hz, 1H), 7.39 (d, J = 7.4 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.86 (d, J = 3.9 Hz, 1H), 8.11 (d, J = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 32.3, 34.9, 35.8, 127.1, 127.2, 127.4, 127.9, 128.1, 129.4, 129.8, 132.8, 133.2, 133.8, 134.7, 135.3, 136.4, 142.0, 186.1; IR ($CHCl_3$): ν 1655, 1560, 1458, 1281, 760, 669 cm^{-1}; HRMS (EI^+): Calcd for $C_{18}H_{14}O$ $[M]^+$: 246.1045; Found 246.1039.



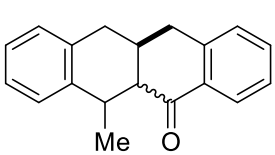
15a

Introduction of Substituents to a Tetracene Skeleton 14a (Introduction to β Carbon):

To an Et_2O (5.0 mL) solution of CuI (384 mg, 2.0 mmol) was added an Et_2O solution of methyllithium (1.2 M, 3.5 mL, 4.1 mmol) at –5 °C. The reaction mixture was stirred for 1 h. The reaction mixture was added a THF (5.0 mL) solution of **14a** (244 mg, 1.0 mmol) at –5 °C. After being stirred for 2 h, saturated ammonium chloride solution was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane/AcOEt = 20:1) to give **22aa** (225 mg, *cis*/*trans* = 78:22, 86%) as a yellow solid.

5-Methyl-5,5a,6,11,11a,12-hexahydro-6-tetracenone (22aa)

[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.48 (d, J = 7.0 Hz, 3H), 2.18–2.28 (m, 1H), 2.35 (dd, J = 13.8, 7.8 Hz, 1H), 2.77–2.89 (m, 2H), 2.91–2.98 (m, 1H), 3.13 (dd, J = 16.5, 4.1 Hz, 1H), 3.65 (qd, J = 7.1, 7.0 Hz, 1H), 7.10 (d, J = 6.4 Hz, 2H), 7.18–7.22 (m, 1H), 7.25 (d, J = 8.5 Hz, 1H), 7.31 (d, J = 8.5 Hz,

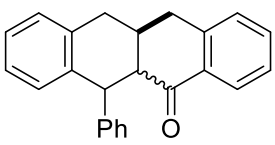


22aa

1H), 7.33 (d, J = 8.0 Hz, 1H), 7.48 (ddd, J = 7.8, 7.8, 1.3 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 26.5, 32.2, 37.1, 37.4, 37.8, 57.2, 125.3, 126.6, 126.7, 127.4, 128.0, 128.5, 128.6, 133.3, 134.8, 141.5, 142.7, 198.9; IR ($CHCl_3$, *cis*, *trans* mixture): ν 2922, 1680, 1603, 1282, 744 cm^{-1}.

[*Trans* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.54 (d, J = 7.4 Hz, 3H), 2.78–2.90 (m, 3H), 3.00 (dd, J = 6.1, 6.1 Hz, 1H), 3.08 (dd, J = 4.8, 4.8 Hz, 1H), 3.24–3.31 (m, 2H), 6.99 (d, J = 7.5 Hz, 1H), 7.07–7.12 (m, 1H), 7.14–7.23 (m, 2H), 7.24–7.28 (m, 1H), 7.29–7.34 (m, 1H), 7.46–7.50 (m, 1H), 7.94 (d, J = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 19.2, 32.5, 34.5, 34.6, 35.6, 51.0, 125.8, 126.1, 126.6, 126.7, 126.9, 128.9, 129.3, 132.6, 133.9, 140.2, 141.7, 199.7.

5-Phenyl-5,5a,6,11,11a,12-hexahydro-6-tetracenone (22ab)



22ab

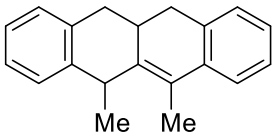
[*Cis* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.87–2.97 (m, 4H), 3.12–3.19 (m, 1H), 3.37 (dd, J = 6.1, 4.8 Hz, 1H), 4.72 (d, J = 6.3 Hz, 1H), 6.97–7.05 (m, 4H), 7.10 (d, J = 7.9 Hz, 2H), 7.12–7.21 (m, 5H), 7.31 (t, J = 7.4 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 33.3, 33.4, 33.8, 46.7, 51.5, 126.0, 126.3, 126.7, 127.0, 127.5, 128.5, 129.1, 129.6, 130.4 (2C), 133.0, 135.3, 137.9, 141.8, 142.2, 199.9; IR ($CHCl_3$, *cis*, *trans* mixture): ν 2906, 1684, 1601, 1284, 750 cm^{-1}; HRMS (EI$^+$, *cis*, *trans* mixture): Calcd for $C_{24}H_{20}O$ [M]$^+$: 324.1514; Found 324.1514.

[*Trans* Diastereomer]: ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.37–2.47 (m, 1H), 2.86–3.04 (m, 4H), 3.21 (d, J = 4.2 Hz, 1H), 4.94 (d, J = 8.0 Hz, 1H), 6.97–7.05 (m, 3H), 7.08–7.23 (m, 5H), 7.28 (d, J = 8.5 Hz, 1H), 7.29–7.33 (m, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 37.3, 37.80, 37.83, 43.8, 58.2, 125.7, 125.8, 126.7, 126.8, 127.9, 128.4, 128.5, 129.0, 130.7, 133.3, 139.6, 142.4, 148.8, 198.3.

Introduction to Carbonyl Carbon (Preparation of *peri*-Disubstituted Tetrahydrotetracene 24a): To a THF (5.0 mL) solution of **22aa** (211 mg, 0.80 mmol) was added an Et_2O solution of

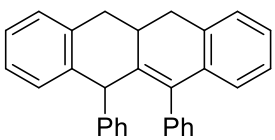
methylmagnesiumbromide (3.0 M, 0.80 mL, 2.4 mmol) at –78 °C. The reaction mixture was warmed to room temperature and stirred for 22 h. Phosphate buffer (pH 7) was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was added an acetic acid (1.0 mL) solution of sulfuric acid (0.1 mL) at room temperature. The reaction mixture was stirred for 20 min. Water was added to the mixture. Organic materials were extracted with CH_2Cl_2 three times. The combined extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane) to give **24aa** (149 mg, 71%) as a yellow solid.

5,6-Dimethyl-5,11,11a,12-tetrahydrotetracene (24aa): ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.36 (d, J = 7.4 Hz, 3H), 2.16 (d, J = 2.5 Hz, 3H), 2.43–2.53 (m, 1H), 2.70 (t, J = 15.0 Hz, 1H), 2.77 (d, J = 5.3 Hz, 1H), 2.78–2.84 (m, 2H), 4.01 (q, J = 7.4 Hz, 1H), 7.10 (dd, J = 7.2, 1.2 Hz, 1H), 7.12–7.17 (m, 4H), 7.17–7.22 (m, 2H), 7.29 (d, J = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.1, 24.5, 34.7, 36.7, 36.9, 38.5, 122.6, 125.2, 125.8, 126.0, 126.4, 126.7, 126.8, 127.4, 127.6, 135.7, 137.2, 137.5, 141.1, 142.1; IR ($CHCl_3$): ν 2922, 1485, 1450, 756, 729 cm^{-1}; HRMS (EI$^+$): Calcd for $C_{20}H_{20}$ [M]$^+$: 260.1565; Found 260.1566.



24aa

5,6-Diphenyl-5,11,11a,12-tetrahydrotetracene (24ac): ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.57 (dd, J = 13.2, 13.2 Hz, 1H), 2.76 (dd, J = 13.5, 4.8 Hz, 1H), 2.82 (dd, J = 12.5, 4.8 Hz, 1H), 2.91 (dd, J = 9.9, 5.0 Hz, 1H), 3.10 (dd, J = 15.6, 15.6 Hz, 1H), 5.02 (s, 1H), 6.63 (d, J = 7.2 Hz, 1H), 6.98 (brs, 1H), 7.01–7.06 (m, 2H), 7.10 (t, J = 7.2 Hz, 2H), 7.12–7.17 (m, 4H), 7.19 (ddd, J = 7.1, 7.1, 1.6 Hz, 1H), 7.21–7.33 (m, 6H), 7.43 (brs, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 34.3, 35.9, 37.3, 48.6, 125.7, 126.1, 126.4, 126.5, 126.6, 126.7, 126.8, 127.0, 127.78 (3C), 127.83, 128.4, 130.1, 136.1, 136.3, 137.6, 138.3,

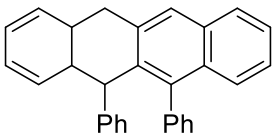


24ac

139.1, 139.3, 139.8, 143.5; IR ($CHCl_3$): ν 3020, 1491, 908, 729, 698 cm^{-1}.

Dehydrogenative Synthesis of Substituted Dihydrotetracenes 25a: To a *p*-cymene (5.0 mL) solution of **24aa** (52.5 mg, 0.137 mmol) was added 10% Pd/C (54.8 mg, 100 wt% to **28c**). Nitrogen was introduced to the reaction mixture (60 mL / min) through a bubbler of glass filter warmed to reflux. After being stirred for 4 h, the mixture was filtered using $CHCl_3$ as an eluent. After removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (Hexane/Toluene = 10:1) to give **25aa** (39.7 mg, 76%) as a white solid.

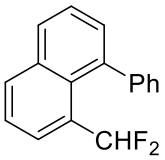
5,6-Diphenyl-5, 12-dihydrotetracene (25ac): ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.97 (s, 2H), 5.27



25ac

(s, 1H), 6.86 (d, J = 7.0 Hz, 2H), 7.03–7.09 (m, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.15–7.22 (m, 3H), 7.23–7.34 (m, 5H), 7.34 (d, J = 6.4 Hz, 1H), 7.37–7.42 (m, 2H), 7.43 (td, J = 8.2, 1.8 Hz, 1H), 7.49 (td, J = 8.2, 2.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 2H).

1-(Difluoromethyl)-8-phenylnaphthalene (26): ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.31 (t, J_{HF} = 55.3



26

Hz, 1H), 7.38-7.42 (m, 3H), 7.46 (d, J = 5.0 Hz, 2H), 7.47 (d, J = 5.3 Hz, 1H), 7.53 (dd, J = 8.1, 7.1 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.92 (dd, J = 8.3, 1.4 Hz, 1H), 7.95 (dd, J = 7.3, 1.0 Hz), 8.04 (dd, J = 8.2, 1.1 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ 111.6 (t, J_{CF} = 237 Hz), 125.1, 125.9 (t, J_{CF} = 9 Hz), 127.8, 128.4, 128.9 (t, J_{CF} = 5 Hz), 129.0, 129.4, 130.8, 131.2 (t, J_{CF} = 21 Hz), 132.0, 134.6, 138.4, 143.2, 198.6; ^{19}F NMR (470 MHz, $CDCl_3$): δ 53.7 (d, J_{HF} = 53.7 Hz, 2F); IR (neat): ν 3055, 1599, 1510, 1462, 1444, 1362, 1336, 1261, 1240, 1107, 1090, 1016, 835, 806, 769, 700 cm^{-1} ; HRMS (EI^+): calcd for $C_{17}H_{12}F_2$ [M^+]: 254.0907, found: 254.0909.

1) Thummel, P. R.; Cravey, E. W.; Nutakul, W. *J. Org. Chem.* **1978**, *43*, 2473.

2) Ming, C.; Yifeng, C.; Yuanhong, L. *Chem. Commun.* **2012**, *48*, 12189.

3) Luo, J.; Hart, H. *J. Org. Chem.* **1987**, *52*, 4833.

CHAPTER 4

Synthesis of (Difluoromethyl)naphthalenes from 1,1-Difluoroallenes via Palladium-Catalyzed Insertion

4-1. Introduction

The difluoromethyl (CHF_2) group as a fluorinated functional group has attracted considerable attention. Its unique properties are attributed to the steric and electronic characteristics of fluorine.[1] The CHF_2 group is a bioisostere of a hydroxyl group and serves as a hydrogen donor for hydrogen bonding while simultaneously exhibiting hydrophobicity (Figure 4-1, 4-2).[2–4] On the basis of these facts, the number of difluoromethylated biologically active substances is definitely increasing.

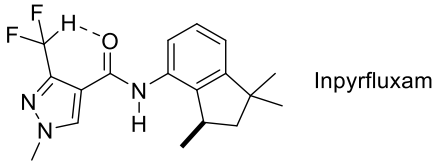


Figure 4-1. Hydrogen Donor for Hydrogen Bonding

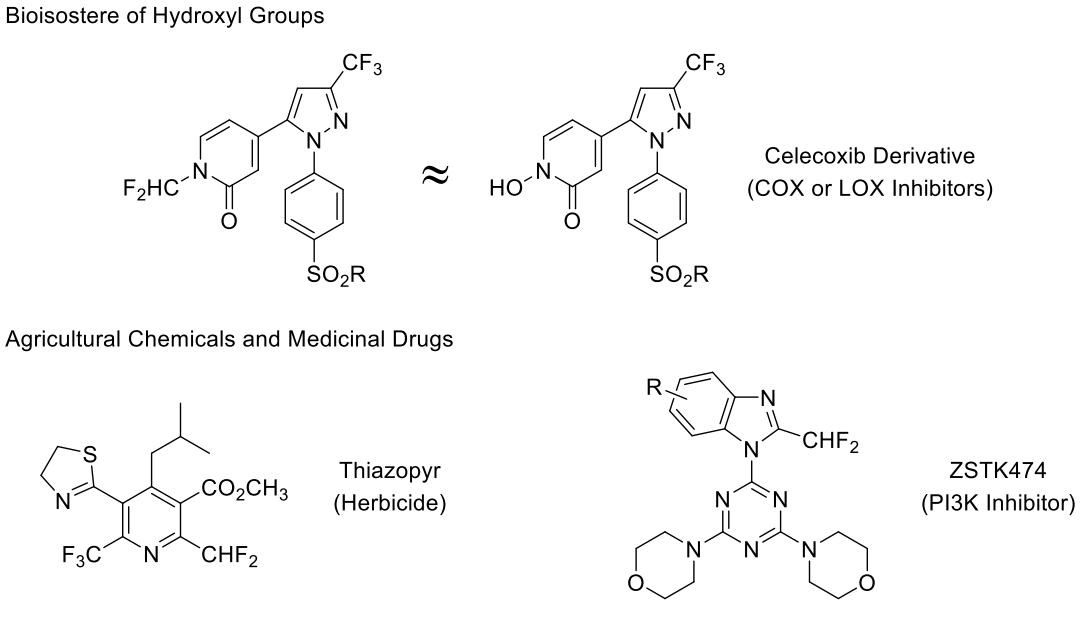
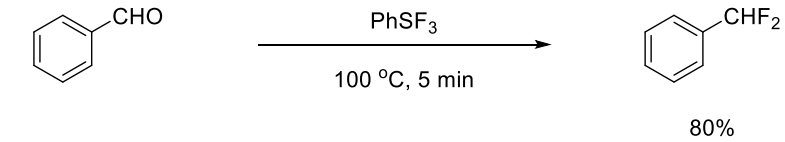
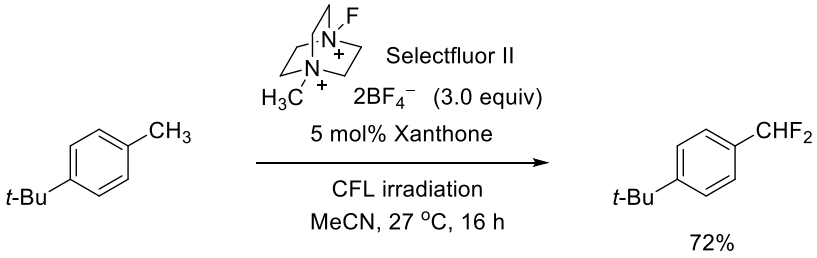


Figure 4-2. Properties of (Difluoromethyl)arenes

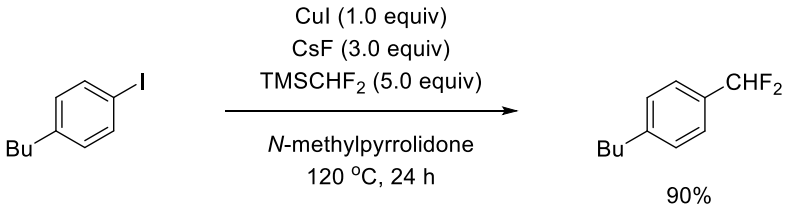
Among the difluoromethylated compounds, (difluoromethyl)arenes have been extensively investigated in terms of their synthesis, due to their abundance in bioactive compounds.[5] Typical methods to synthesize (difluoromethyl)arenes include the (i) deoxyfluorination of aromatic aldehydes or their derivatives (eq. 4-1),[6] (ii) double C–H fluorination of methylarenes (eq. 4-2),[7] and (iii) difluoromethylation of (pseudo)haloarenes (eq. 4-3)[8] or arylmetals (eq. 4-4)[9] by cross coupling reaction.[10] However, all these methods require aromatic rings in the starting materials. From a synthetic point of view, a process for simultaneous formation of an aromatic ring and installation of a difluoromethyl group is desirable.



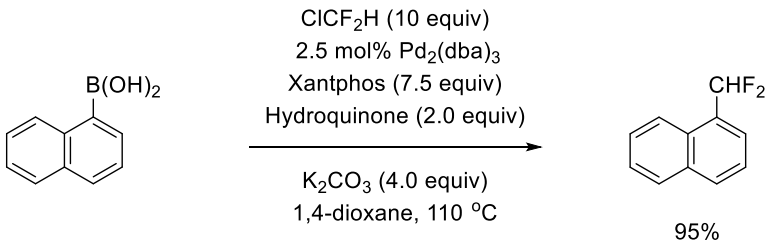
(4-1)



(4-2)



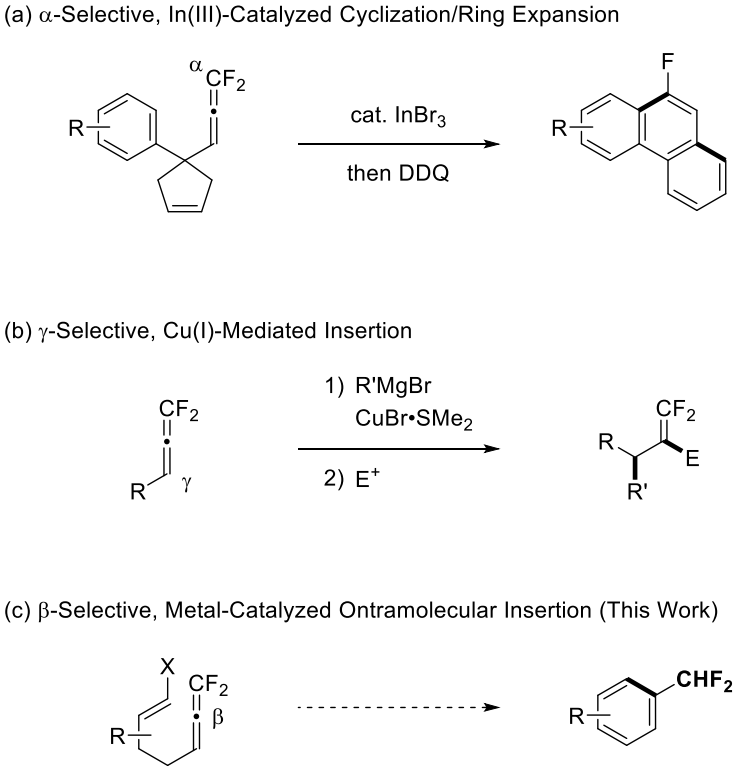
(4-3)



(4-4)

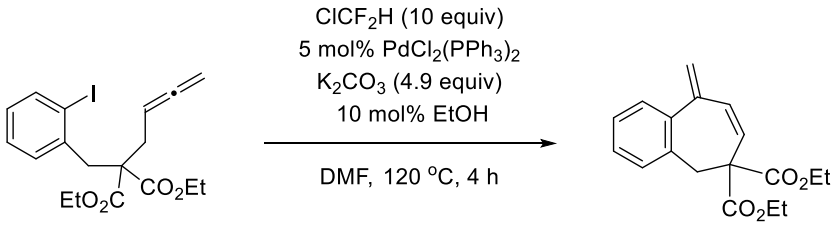
Over the past few years, our group has developed metalcatalyzed or -mediated reactions of 1,1-difluoroallenes,[11] involving the C–C bond formation at the positions α and γ to the fluorine substituents, respectively (Scheme 4-1): (a) with respect to the regioselective C–C bond formation at

the α position, 1,1-difluoroallenes were treated with an indium(III) catalyst.[12–14] Metallated allylic CF_2 cations, stabilized by the α-fluorine substituents,[1] were generated and subsequently underwent domino Friedel–Crafts-type cyclization/ring expansion, affording regioselectively monofluorinated PAHs (pinpoint fluorinated PAHs), which are soluble p-type semiconducting materials.[15] Notably, the fluorination and construction of aromatic rings were simultaneously achieved during the synthesis of fluoroarenes. (b) The formation of a C–C bond at the γ position was achieved using a stoichiometric amount of organocopper(I) reagents.[16] 1,1-Difluoroallenes underwent regioselective insertion, forming a C–C bond at the position γ to the fluorine substituents to afford γ-branched 1,1-difluoroalkenes.[17] On the basis of the above-mentioned two reactions, (a) ring construction of arenes and (b) insertion with organometallics, the intramolecular insertion of 1,1-difluoroallenes was envisioned to facilitate the synthesis of (difluoromethyl)arenes via ring construction,[18] which permits the rare formation of C–C bonds at the position β to the fluorine substituents.[19]

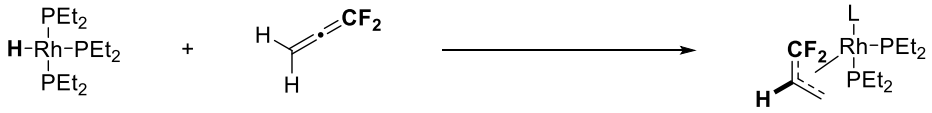


Scheme 4-1. α-, γ-, and γ-Selective C–C Bond Formations of 1,1-Difluoroallenes by Metal Complexes (DDQ = 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone)

In this study, (difluoromethyl)naphthalenes were synthesized by the palladium(0)-catalyzed regioselective insertion of *o*-bromophenyl-bearing 1,1-difluoroallenes. Since the Pd-catalyzed intramolecular insertion of fluorine-free allenes (eq. 4-5)[20,21] and β-selective insertion of 1,1-difluoroallen into Rh–H bond has been previously reported (eq 4-6),[14c] the insertion of 1,1-difluoroallenes into Pd–C bond was envisioned to occur, leading to the construction of naphthalene ring with the CHF_2 group. Thus, through the study on the synthesis of (difluoromethyl)naphthalenes, the unexplored C–C bond formation via insertion of difluoroallenes was achieved.



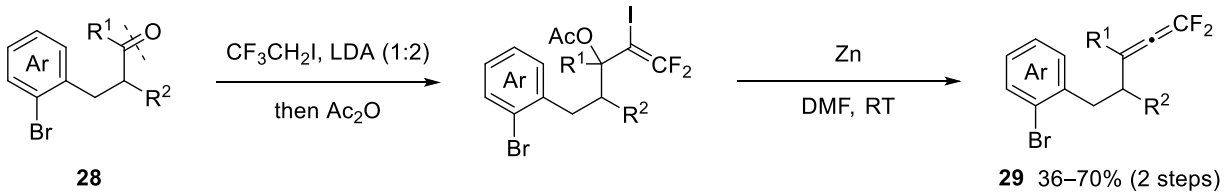
(4-5)



(4-6)

4-2. Synthesis of (Difluoromethyl)naphthalenes

For the difluorovinylidenation of carbonyl compounds, Ichikawa's protocol was adopted to prepare 1,1-difluoroallenes **29** (Scheme 4-2).[22] *o*-Bromophenyl-bearing aldehydes or ketones **28** were treated with 2,2-difluoro-1-iodovinyllithium, which was generated from commercially available 1,1,1-trifluoro-2-iodoethane and LDA in a ratio of 1 : 2, followed by acetic anhydride, generating the corresponding iodoacetates. These acetates were subsequently treated with zinc metal, and IZnOAc was eliminated, affording the desired mono- or disubstituted 1,1-difluoroallenes **29**.

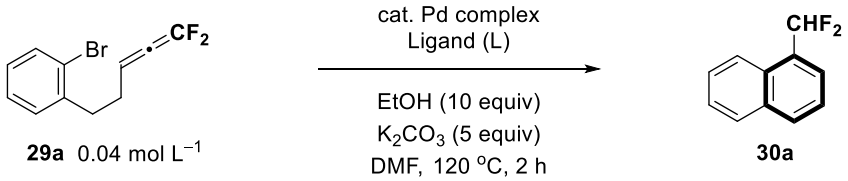


Scheme 4-2. Preparation of 1,1-Difluoroallenes

By using the model substrate **29a** (Ar = C_6H_4, R^1, R^2 = H), the catalyst system was investigated in the presence of ethanol[21] (Table 4-1). Although palladium(II) acetate gave a complex mixture (entry 1), $Pd_2(dba)_3{\cdot}CHCl_3$ afforded the desired 1-(difluoromethyl)naphthalene **30a**, albeit in 5% yield (entry 2). Triphenylphosphine-ligated $PdCl_2(PPh_3)_2$ and $Pd(PPh_3)_4$ afforded **30a** in 21% and 32% yields (entries 3 and 4), respectively. Thus, ring construction via insertion proceeded as expected and the insertion exhibited similar regioselectivity to that reported in the corresponding fluorine-free system, generating stable π-allylpalladium(II) intermediates (vide infra).

The yields of **30a** varied depending on the steric bulk of ligands L and the Pd/L ratio. By using triarylphosphines with $Pd_2(dba)_3{\cdot}CHCl_3$, the yields of **30a** exhibited a correlation with the Tolman cone angle θ (Pd/L = 1/1, entries 5–10, Table 4-1). Thus, P*m*-Tol_3 with a large θ (184°) afforded **30a** in the highest yields (42%, entry 10), whereas extremely bulky ligands resulted in poor yields (entries 13–15). In addition, trialkylphosphines and phosphites afforded **30a** in 14–24% yields (entries 16–19). Notably, the yields of **30a** were also affected by the Pd/L ratio. The use of P*m*-Tol_3 with a Pd/L ratio of 1/1 afforded **30a** in the highest yield (42%, entry 10), whereas higher ligand loadings (Pd/L = 1/2 and 1/4) led to lower yields of **30a** (24% and 25% yields in entries 11 and 12), respectively. Relatedly, the use of bidentate ligands [3 mol% $Pd_2(dba)_3{\cdot}CHCl_3$, 6 mol% $Ph_2P(CH_2)_nPPh_2$ (n = 1–4) or 6 mol% dppf, Pd/P = 1/2] also afforded poor yields of **30a** (9–16% yields, not shown).

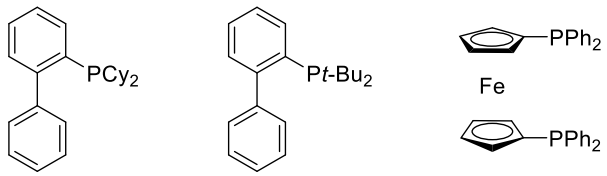
Table 4-1. Effect of Catalyst[a]



29a 0.04 mol L^{-1} — **30a**

Entry	Pd complex /mol%	Ligand (L), mol%	Pd/L ratio	Tolman cone angle (θ)	**30a** /%
1[b]	$Pd(OAc)_2$, 5	None	–	–	Complex Mixture
2	$Pd_2(dba)_3$•$CHCl_3$, 3	None	–	–	5
3[c]	$PdCl_2(PPh_3)_2$, 5	None	–	–	21
4	$Pd(PPh_3)_4$, 5	None	–	–	32
5	$Pd_2(dba)_3$•$CHCl_3$, 3	PPh_3, 6	1/1	145[d]	23
6	$Pd_2(dba)_3$•$CHCl_3$, 3	P*p*-Tol_3, 6	1/1	145[d]	23
7	$Pd_2(dba)_3$•$CHCl_3$, 3	$P(C_6H_4p\text{-}OMe)_3$,6	1/1	145	30
8	$Pd_2(dba)_3$•$CHCl_3$, 3	$P(C_6H_4p\text{-}CF_3)_3$, 6	1/1	149	25
9	$Pd_2(dba)_3$•$CHCl_3$, 3	$P(C_6H_3 3,5\text{-}Me_2)_3$, 6	1/1	175	38
10	$Pd_2(dba)_3$•$CHCl_3$, 3	P*m*-Tol_3, 6	1/1	184	42
11	$Pd_2(dba)_3$•$CHCl_3$, 3	P*m*-Tol_3, 12	1/2	184	24
12	$Pd_2(dba)_3$•$CHCl_3$, 3	P*m*-Tol_3, 24	1/4	184	25
13	$Pd_2(dba)_3$•$CHCl_3$, 3	Po-Tol_3, 6	1/1	193	12
14	$Pd_2(dba)_3$•$CHCl_3$, 3	Cy-JohnPhos, 6	1/1	–	12
15	$Pd_2(dba)_3$•$CHCl_3$, 3	*t*-Bu-JohnPhos, 6	1/1	–	0
16	$Pd_2(dba)_3$•$CHCl_3$, 3	PCy_3, 6	1/1	170	24
17	$Pd_2(dba)_3$•$CHCl_3$, 3	Pt-Bu_3, 6	1/1	182	18
18	$Pd_2(dba)_3$•$CHCl_3$, 3	$P(OEt)_3$, 6	1/1	109	14
19	$Pd_2(dba)_3$•$CHCl_3$, 3	$P(OPh)_3$, 6	1/1	130	14

a) ^{19}F NMR yield based on the internal standard $PhCF_3$; b) 7 h; c) 80 °C, 15 h; d) Value of PPh_3; Tol = tolyl.

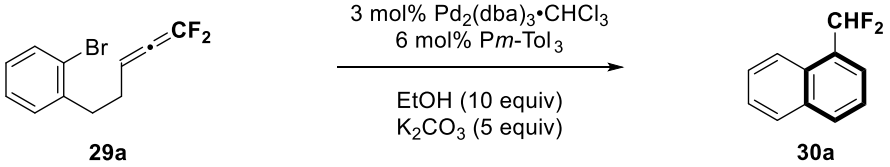


Cy-JohnPhos — *t*-Bu-JohnPhos — dppf

The concentration of **29a** strongly affected the product yield (Table 4-2). Higher concentrations (0.5 and 0.1 mol L^{-1}, entries 1 and 2) led to decreased yields of **30a** (4% and 19%, respectively), affording a complex reaction mixture. The reactions using higher concentrations presumably caused undesired intermolecular reactions. On the other hand, the reactions conducted using lower concentration (0.01 mol L^{-1}) led to an increased yield of **30a** (49%, entry 4), whereas highly diluted conditions (0.001 mol L^{-1}) afforded a lower yield (10%, entry 5). The survey of solvents revealed

that DMF is the most suitable solvent for this insertion reaction (entries 6–9). Use of 50 equiv. of ethanol led to the generation of **30a** in the highest yield (76%, entry 10).

Table 4-2. Effect of Substrate Concentration and Solvent[a]



29a **30a**

Entry	Conditions	**29a** /mol L^{-1}	**30a** /%	**29a**[b] /%
1	DMF, 120 °C, 2 h	0.5	4	–
2	DMF, 120 °C, 2 h	0.1	19	–
3[c]	DMF, 120 °C, 2 h	0.04	42	–
4	DMF, 120 °C, 2 h	0.01	49	–
5	DMF, 120 °C, 2 h	0.001	10	–
6	DMA, 110 °C, 2 h	0.04	12	–
7	DMSO, 110 °C, 2 h	0.04	31	–
8	1,4-dioxane, 100 °C, 1 h	0.04	–	75
9	toluene, 110 °C, 2 h	0.04	–	–
10[d]	DMF, 120 °C, 2 h	0.01	76	–

a) ^{19}F NMR yield based on the internal standard $PhCF_3$; b) Recovery; c) Table 4-1, entry 10; d) EtOH 50 equiv; DMA = *N*,*N*-dimethylacetamide.

(Difluoromethyl)naphthalenes were synthesized under the optimized conditions (Fig. 4-2). Electron-withdrawing and -donating groups on the tethered benzene ring did not affect the reaction. Thus, (difluoromethyl)naphthalenes **30a–f** were isolated in 48–67% yields. In addition, disubstituted difluoroallenes participated in the reaction, affording naphthalene **30g** in a decreased yield (52% by ^{19}F NMR). 1,1-Difluoroallenes bearing a methyl or phenyl group at the position δ to the fluorine substituents afforded the corresponding products **30h** and **30i** in 57% and 43% yields, respectively. This intramolecular insertion was applicable not only to six-membered ring construction but also to five-membered ring construction. 1,1-Difluoroallene, having a CMe_2 tether instead of an ethylene tether, afforded the corresponding product **30j** in 83% yield.[23]

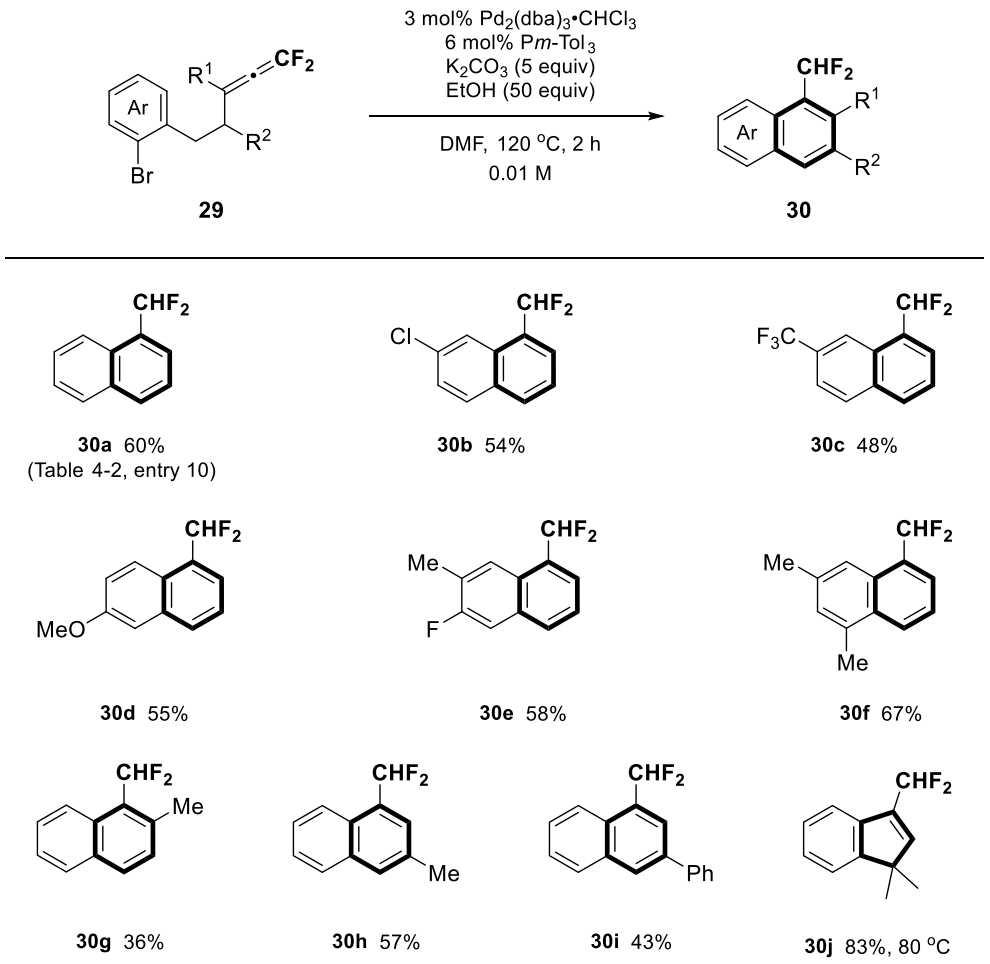
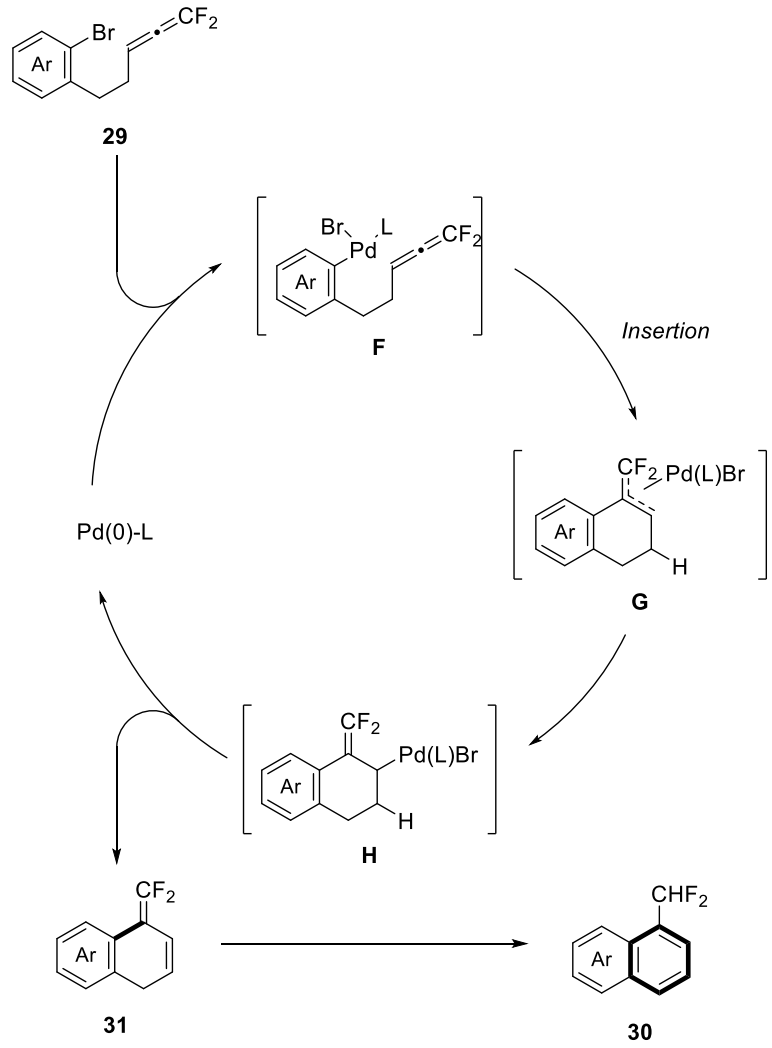


Figure 4-3. Synthesis of (Difluoromethyl)naphthalenes

[^{19}F NMR yield based on the internal standard $PhCF_3$].

The plausible mechanism is described in Scheme 4-3. Bromoallenes **29** underwent oxidative addition to palladium(0), affording arylpalladium(II) bromides **F**. Intermediates **F** underwent regioselective insertion to generate more stable π-allylpalladium(II) intermediates **G**, forming a C–C bond at the position β to the fluorine substituents.[24] Taking the effects of the steric bulk of the ligand and the Pd/L ratio (1/1) into consideration (Table 4-1), it is supposed that the Pd(0)·L complex is the catalytically active species, and the steric bulk of the ligand can suppress the formation of Pd(0)·L_n complexes (n > 1), which must be less reactive for the coordination and insertion of the difluoroallene moiety in **F**. β-Hydrogen elimination from σ-allylpalladium(II) intermediates **H** affords cyclic 1,1-difluoro-1,3-dienes **31**, whose isomerization provides **30**. Shibasaki has reported that the use of

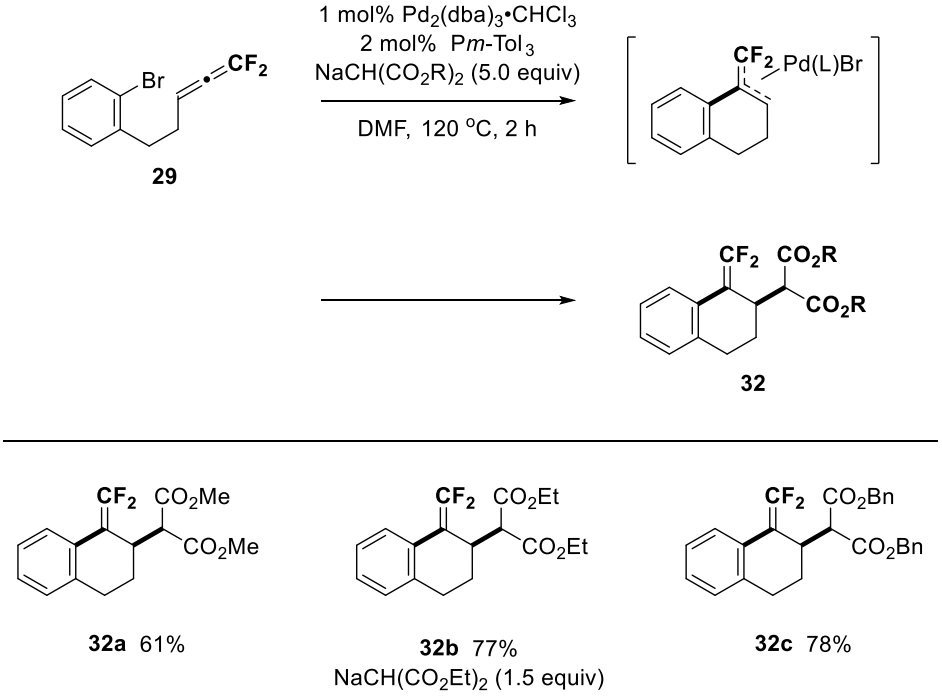
pinacol as an additive for the Heck reaction of alkenyl triflates leads to the stabilization of a reactive Pd(0)·L_2 complex.[25,26] In the present system, ethanol might stabilize the reactive Pd(0)·L complex via coordination.



Scheme 4-3. Proposed Catalytic Cycle.

4-3. Tsuji–Trost Reaction of Difluorinated π-Allyl-Palladium

This is the first example to generate terminally fluorinated π-allylpalladium(II) intermediates not through oxidative addition but through insertion.[27] The π-allylpalladium(II) intermediates thus-formed underwent the Tsuji–Trost reaction at the position γ to the fluorine substituents (Scheme 4-4) and the corresponding alkylation product **32a–c** was obtained in 61–78% yields.[27b]



Scheme 4-4. The Tsuji–Trost Reaction of The Difluorinated π-Allylpalladium(II) Intermediate

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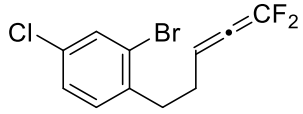
4-5. Experimental Section

Preparation of 1,1-difluoroallenes

1,1-Difluoroallenes **29a**–**j** were prepared by our reported method.[21]

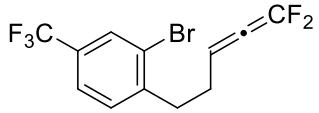
5-(2-Bromo-4-chlorophenyl)-1,1-difluoropenta-1,2-diene (**29b**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 2.51–2.59 (m, 2H), 2.87 (dd, J = 22.6, 7.6 Hz, 1H), 2.89 (t, J = 7.7 Hz, 1H), 6.48 (tt, J = 6.0 Hz, J_{HF} = 2.5 Hz, 1H), 7.14 (d, J = 8.0 Hz, 1H), 7.23 (dd, J = 8.0, 2.0 Hz, 1H), 7.56 (d, J = 2.0 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 31.9, 33.5, 120.6 (t, J_{CF} = 5 Hz), 124.5, 127.7, 131.0, 132.5, 132.8, 138.5,



29b

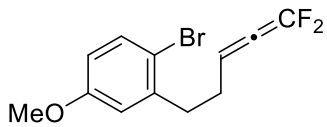
152.9 (t, J_{CF} = 260 Hz), 170.5 (t, J_{CF} = 36 Hz); ^{19}F NMR (470 MHz; $CDCl_3$; C_6F_6): δ 60.4 (br s); IR (neat): ν 2015, 1464, 1201, 818 cm^{-1}; HRMS (EI): *m/z* calcd. for $C_{11}H_8BrClF_2$ [M] $^+$: 291.9466; Found: 291.9453.

5-[2-Bromo-4-(trifluoromethyl)phenyl]-1,1-difluoropenta-1,2-diene (**29c**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 2.55–2.63 (m, 2H), 2.98 (t, J = 8.0 Hz, 2H), 6.49 (tt, J = 5.5 Hz, J_{HF} = 2.5 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.81 (s, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 31.7, 34.1, 120.3 (t, J_{CF} = 6 Hz), 123.2 (q, J_{CF} = 273 Hz), 124.4 (q, J_{CF} = 4 Hz), 124.5, 130.0 (q, J_{CF} = 6 Hz), 130.5 (q, J_{CF} = 33 Hz), 130.6, 144.1, 153.0 (t, J_{CF} = 262 Hz), 170.9 (t, J_{CF} = 36 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 60.6 (br s, 2F), 99.1 (s, 3F); IR (neat): ν 2941, 2011, 1462, 1321, 1122, 1171, 1078, 829 cm^{-1}; HRMS (EI): *m/z* calcd. for $C_{12}H_8BrF_5$ [M]$^+$: 325.9730; Found: 325.9731.



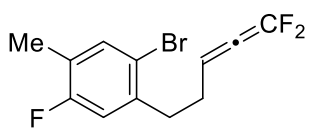
29c

5-(2-Bromo-5-methoxylphenyl)-1,1-difluoropenta-1,2-diene (**29d**): ^{1}H NMR (400 MHz; $CDCl_3$; $SiMe_4$): δ 2.55 (m, 2H), 2.86 (t, J = 7.8 Hz, 2H), 3.76 (s, 3H), 6.48 (tt, J = 6.0 Hz, J_{HF} = 2.4 Hz, 1H), 6.64 (dd, J = 8.8, 3.0 Hz, 1H), 6.75 (d, J = 3.0 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 32.0, 34.3, 55.3, 113.6, 114.7, 116.1, 121.0 (t, J_{CF} = 5 Hz), 133.4, 140.8, 152.8 (t, J_{CF} = 260 Hz), 159.0, 170.2 (t, J_{CF} = 36 Hz); ^{19}F NMR (376 MHz, $CDCl_3$; C_6F_6): δ 60.3–60.4 (m); IR (neat): ν 2937, 2837, 2011, 1460, 1240, 1190, 1055, 802 cm^{-1}; HRMS (EI): *m/z* calcd. for $C_{12}H_{11}BrF_2O$ [M]$^+$: 287.9961; Found: 287.9949.



29d

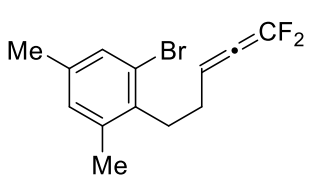
5-(2-Bromo-5-fluoro-4-methylphenyl)-1,1-difluoropenta-1,2-diene (**29e**): ^{1}H NMR (400 MHz; $CDCl_3$; $SiMe_4$): δ 2.22 (s, 3H), 2.50–2.59 (m, 2H), 2.86 (t, J = 7.8 Hz, 2H), 6.47 (tt, J = 6.0 Hz, J_{HF} = 2.6 Hz, 1H), 6.87 (d, J_{HF} = 10.0 Hz, 1H), 7.35 (d, J = 6.8 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 13.9 (d, J_{CF} = 3 Hz), 31.9, 33.8, 116.7 (d, J_{CF} = 24 Hz), 117.8 (d, J_{CF} = 3 Hz), 120.7 (t, J_{CF} = 5 Hz), 125.0 (d, J_{CF} =



29e

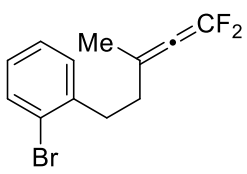
18 Hz), 135.1 (d, J_{CF} = 6 Hz), 139.0 (d, J_{CF} = 7 Hz), 152.9 (t, J_{CF} = 260 Hz), 160.4 (d, J_{CF} = 244 Hz), 170.5 (t, J_{CF} = 36 Hz); ^{19}F NMR (376 MHz, $CDCl_3$; C_6F_6): δ 42.5 (ddq, J_{HF} = 10, 7, 1 Hz, 1F), 60.4 (td, J_{FH} = 6, 3 Hz, 2F); IR (neat): ν 2931, 2866, 2011, 1485, 1460, 1192, 1134, 881 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{12}H_{10}BrF_3$ $[M]^+$: 289.9918; Found: 289.9922.

5-(2-Bromo-4,6-dimethylphenyl)-1,1-difluoropenta-1,2-diene (**29f**): ^{1}H NMR (400 MHz; $CDCl_3$; $SiMe_4$): δ 2.25 (s, 3H), 2.31 (s, 3H), 2.37–2.49 (m, 2H), 2.92 (t, J = 8.0 Hz, 2H), 6.48–6.55 (m, 1H), 6.91 (s, 1H), 7.23 (s, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 20.4, 20.5, 30.7, 31.1, 121.4 (t, J_{CF} = 5 Hz), 125.1, 130.5, 131.2, 135.2, 137.5, 137.7, 152.8 (t, J_{CF} = 259 Hz), 169.9 (t, J_{CF} = 36 Hz); ^{19}F NMR (376 MHz, $CDCl_3$; C_6F_6): δ 60.2–60.3 (m); IR (neat): ν 2951, 2920, 2009, 1460, 1190, 955, 850 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{13}H_{13}BrF_2$ $[M]^+$: 286.0169; Found: 286.0181.



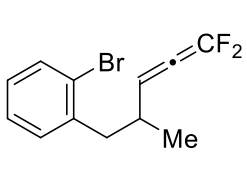
29f

5-(2-Bromophenyl)-3-methyl-1,1-difluoropenta-1,2-diene (**29g**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 1.98 (t, J_{HF} = 5.0 Hz, 3H), 2.48 (tt, J = 8.0 Hz, J_{HF} = 5.5 Hz, 2H), 2.89 (t, J = 8.0 Hz, 2H), 7.07 (ddd, J = 7.8, 7.0, 2.1 Hz, 1H), 7.18–7.25 (m, 2H), 7.53 (dd, J = 7.0, 1.2 Hz, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 22.9, 33.9, 37.0, 124.3, 127.5, 127.9, 130.3, 132.0 (t, J_{CF} = 6 Hz), 132.9, 140.3, 150.4 (t, J_{CF} = 260 Hz), 163.2 (t, J_{CF} = 35 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 61.6 (tq, J_{FH} = 5.5, 5.0 Hz); IR (neat): ν 2993, 2922, 2004, 1479, 1176, 1159, 748 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{12}H_{11}BrF_2$ $[M]^+$: 272.0012; Found: 272.0005.



29g

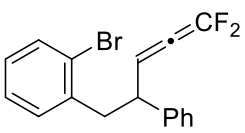
5-(2-Bromophenyl)-4-methyl-1,1-difluoropenta-1,2-diene (**29h**): ^{1}H NMR (400 MHz; $CDCl_3$; $SiMe_4$): δ 1.06–1.14 (m, 3H), 2.65–2.88 (m, 2H), 2.88–3.00 (m, 1H), 6.45 (ddd, J = 7.6, 5.2, 2.4 Hz, 1H), 7.02–7.13 (m, 1H), 7.13–7.20 (m, 1H), 7.20–7.32 (m, 1H), 7.54 (dd, J = 8.4, 3.6 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 18.5, 36.7, 42.0, 124.7, 126.5 (dd, J_{CF} = 5, 5 Hz), 127.3, 128.1, 131.4, 133.0, 138.9, 153.4 (dd, J_{CF} = 259,



29h

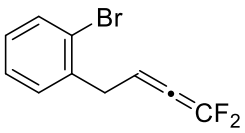
259 Hz), 168.9 (dd, J_{CF} = 36, 36 Hz); ^{19}F NMR (376 MHz, $CDCl_3$; C_6F_6): δ 60.1 (dm, J = 121 Hz, 1F), 60.5 (dm, J = 121 Hz, 1F); IR (neat): ν 2968, 2931, 2009, 1446, 1238, 1194, 746 cm^{-1}; HRMS (EI): m/z calcd. for $C_{12}H_{11}BrF_2$ $[M]^+$: 272.0012; Found: 272.0005.

5-(2-Bromophenyl)-4-phenyl-1,1-difluoropenta-1,2-diene (**29i**): ^{1}H NMR (500 MHz; $CDCl_3$; SiMe$_4$): δ 3.03 (dd, J = 14.0, 7.5 Hz, 1H), 3.32 (dd, J = 14.0, 7.5 Hz, 1H), 3.91–3.99 (m, 1H) 6.62 (ddd, J = 6.5 Hz, J_{HF} = 2.5, 2.5 Hz, 1H), 6.86 (d, J = 7.5 Hz, 1H), 7.03 (dd, J = 7.5, 7.5 Hz, 1H), 7.08 (dd, J = 7.5, 7.5 Hz, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.23 (dd, J = 7.5, 7.5 Hz, 1H), 7.29 (dd, J = 7.5, 7.5 Hz, 2H), 7.52 (d, J = 7.5 Hz, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; SiMe$_4$): δ 41.7, 48.0, 123.9 (dd, J_{CF} = 6, 6 Hz), 124.6, 127.1, 127.2, 128.0, 128.1, 128.6, 131.6, 132.8, 138.3, 140.6, 153.4 (dd, J_{CF} = 263, 263 Hz), 170.4 (dd, J_{CF} = 37, 37 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 60.7 (ddd, J = 119 Hz, J_{FH} = 4, 3 Hz, 1F), 61.5 (ddd, J = 119 Hz, J_{FH} = 5, 3 Hz, 1F); IR (neat): ν 3030, 2925, 2009, 1450, 1194, 744, 698 cm^{-1}; HRMS (EI): m/z calcd. for $C_{17}H_{13}BrF_2$ $[M]^+$: 334.0169; Found: 334.0173.



29i

4-(2-Bromophenyl)-4-methyl-1,1-difluoropenta-1,2-diene (**29j**): ^{1}H NMR (500 MHz; $CDCl_3$; SiMe$_4$): δ 1.62 (s, 6H), 6.75 (t, J_{HF} = 2.4 Hz, 1H) 7.11 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 7.30 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 7.43 (dd, J = 7.6, 1.6 Hz, 1H), 7.61 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; SiMe$_4$): δ 28.1, 43.8, 123.2, 127.4, 128.0, 128.5, 130.7 (t, J_{CF} = 6 Hz), 135.5, 144.5, 153.2 (t, J_{CF} = 260 Hz), 167.6 (t, J_{FC} = 36 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 60.9 (d, J_{FH} = 2 Hz); IR (neat): ν 2974, 2009, 1435, 1192, 752 cm^{-1}; HRMS (EI): m/z calcd. for $C_{12}H_{11}BrF_2$ $[M]^+$: 272.0012; Found: 272.0018.



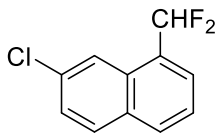
29j

Synthesis of (difluoromethyl)naphthalenes and (difluoromethyl)indenes

Synthesis of **30a** is described as a typical procedure. The mixture of $Pd_2(dba)_3{\cdot}CHCl_3$ (4.0 mg, 3.9 mol%), Pm-Tol_3 (2.4 mg, 7.8 mol%), K_2CO_3 (89.9 mg, 0.650 mmol), ethanol (0.380 ml, 6.50 mmol) in DMF (10 mL) was stirred for 15 min at room temperature under argon. A solution of **29a** (33.6 mg,

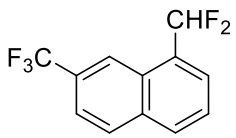
0.130 mmol) in DMF (3 mL) was added to the mixture, and then heated to 120 °C. After stirring for 2 h at the same temperature, the mixture was cooled to room temperature, and then $PhCF_3$ (16.2 mg, 0.111 mmol) was added as an internal standard. (Difluoromethyl)naphthalene **30a** was obtained in 76% yield that determined by ^{19}F NMR. The reaction was quenched with aq. NaOH (2 mol/L, 15 mL), and the organic products were extracted with Et_2O. The combined organic layers were washed with water, brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (pentane). 1-(Difluoromethyl)naphthalene **30a** was obtained as a colorless liquid (14.0 mg, 60%). The spectral data of **29a** met complete agreement with those in literature.[8b]

7-Chloro-1-(difluoromethyl)naphthalene (**30b**): ^1H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 7.06 (t, J_{HF} = 55.0 Hz, 1H), 7.47–7.53 (m, 2H), 7.70 (dd, J = 7.1, 1.0 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.94 (d, J = 8.3 Hz, 1H), 8.16 (s, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 115.2 (t, J_{CF} = 239 Hz), 122,88, 122.90, 124.9, 125.9 (t, J_{CF} = 9 Hz), 127.4, 128.9 (t, J_{CF} = 21 Hz), 130.2, 131.3, 132.0, 133.3; ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 51.0 (d, J_{FH} = 55 Hz); IR (neat): ν 3059, 2974, 1583, 1502, 1176, 1113, 1092, 1020, 829, 750 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{11}H_7ClF_2$ $[M]^+$: 212.0204; Found: 212.0199.



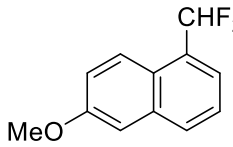
30b

1-Difluoromethyl-7-(trifluoromethyl)naphthalene (**30c**): ^1H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 7.13 (t, J_{HF} = 54.8 Hz, 1H), 7.64 (dd, J = 7.7 Hz, 1H), 7.74 (dd, J = 8.7, 1.4 Hz, 1H), 7.78 (d, J = 7.0 Hz, 1H), 8.03 (d, J = 8.7 Hz, 2H) 8.49 (s, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 115.1 (t, J_{CF} = 240 Hz), 121.6 (q, J_{CF} = 5 Hz), 122.2 (q, J_{CF} = 3 Hz), 124.1 (q, J_{CF} = 273 Hz), 126.2 (t, J_{CF} = 9 Hz), 126.9, 128.7, 129.1 (q, J_{CF} = 32 Hz), 129.8, 130.7 (t, J_{CF} = 21 Hz), 131.4, 135.0; ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 51.4 (d, J_{FH} = 55 Hz, 2F), 99.3 (s, 3F); IR (neat): ν 1315, 1165, 1122, 1076, 1028, 839 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{12}H_7F_5$ $[M]^+$: 246.0468; Found: 246.0477.



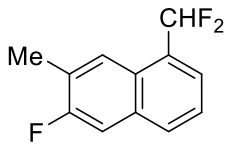
30c

1-Difluoromethyl-6-methoxynaphthalene (**30d**): ^{1}H NMR (400 MHz; $CDCl_3$; $SiMe_4$): δ 3.91 (s, 3H), 7.05 (t, J_{HF} = 55.2 Hz, 1H), 7.18 (d, J = 2.6 Hz, 1H), 7.24 (dd, J = 9.2, 2.6 Hz, 1H), 7.43 (dd, J = 7.6, 7.6 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.6 Hz, 1H), 8.07 (d, J = 9.2 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 55.3, 106.7, 115.6 (t, J_{CF} = 237 Hz), 119.8, 122.6 (t, J_{CF} = 9 Hz), 125.0, 125.15, 125.23, 129.6 (t, J_{CF} = 21 Hz), 130.3, 135.3, 157.8; ^{19}F NMR (376 MHz, $CDCl_3$; C_6F_6): δ 51.5 (d, J_{FH} = 55 Hz); IR (neat): ν 2960, 2933, 1630, 1518, 1261, 1105, 1022 cm^{-1}; HRMS (EI): m/z calcd. for $C_{12}H_{10}F_2O$ $[M]^+$: 208.0700; Found: 208.0697.



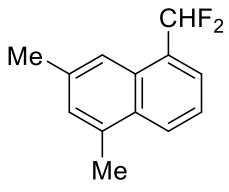
30d

1-Difluoromethyl-6-fluoro-7-methylnaphthalene (**30e**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 2.48 (s, 3H), 7.05 (t, J_{HF} = 55.1 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.46 (d, J = 9.0, 1H), 7.59 (d, J = 7.5 Hz, 1H), 7.84 (d, J = 9.0 Hz, 1H), 7.98 (d, J = 7.5 Hz, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 15.6 (d, J_{CF} = 4 Hz), 111.4 (d, J_{CF} = 22 Hz), 115.6 (t, J_{CF} = 239 Hz), 124.2 (td, J_{CF} = 9, 2 Hz), 124.8, 126.0 (d, J_{CF} = 6 Hz), 127.4 (d, J_{CF} = 21 Hz), 128.0 (d, J_{CF} = 10 Hz), 129.1 (t, J_{CF} = 21 Hz), 130.5 (d, J_{CF} = 5 Hz), 133.7 (d, J_{CF} = 10 Hz), 160.2 (d, J_{CF} = 249 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 44.1 (dd, J = 9, 9 Hz, 1F), 51.5 (d, J_{FH} = 55 Hz, 2F); IR (neat): ν 2966, 1514, 1250, 1095, 1026, 870 cm^{-1}; HRMS (EI): m/z calcd. for $C_{12}H_9F_3$ $[M]^+$: 210.0656; Found: 210.0663.



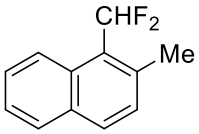
30e

1-Difluoromethyl-5,7-dimethylnaphthalene (**30f**): ^{1}H NMR (400 MHz; $CDCl_3$; $SiMe_4$): δ 2.51 (s, 3H), 2.68 (s, 3H), 7.13 (t, J_{HF} = 55.2 Hz, 1H), 7.24 (s, 1H), 7.46 (dd, J = 7.8, 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.77 (s, 1H), 8.08 (d, J = 7.8 Hz, 1H); ^{13}C NMR (101 MHz; $CDCl_3$; $SiMe_4$): δ 19.7, 22.1, 115.4 (t, J_{CF} = 237 Hz), 120.6, 123.6, 124.4 (t, J_{CF} = 9 Hz), 127.3, 129.2 (t, J_{CF} = 21 Hz), 129.5, 130.3, 131.2, 134.8, 136.7; ^{19}F NMR (376 MHz, $CDCl_3$; C_6F_6): δ 50.7 (d, J_{FH} = 55 Hz); IR (neat): ν 2974, 1383, 1134, 1016, 810, 758, 748 cm^{-1}; HRMS (EI): m/z calcd. for $C_{13}H_{12}F_2$ $[M]^+$: 206.0907; Found: 206.0912.



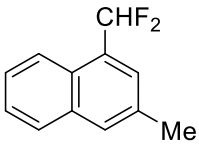
30f

1-Difluoromethyl-2-methylnaphthalene (**30g**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 2.64 (t, J = 1.9 Hz, 3H), 7.29 (d, J = 8.5 Hz, 1H), 7.37 (t, J_{HF} = 54.0 Hz, 1H), 7.47 (dd, J = 7.2 Hz, 1H), 7.55 (ddd, J = 8.4, 7.2, 1.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 2H), 8.34 (d, J = 8.5 Hz, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 19.5, 114.7 (t, J_{CF} = 236 Hz), 124.3 (t, J_{CF} = 3 Hz), 125.5, 126.2, 127.0, 128.5, 129.0, 130.4, 131.2, 132.7, 135.4 (t, J_{CF} = 7 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 52.6 (d, J = 54 Hz); IR (neat): ν 2927, 1818, 1512, 1186, 1099, 1036, 1011, 814, 742 cm^{-1}; HRMS (EI): m/z calcd. for $C_{12}H_{10}F_2$ $[M]^+$: 192.0751; Found: 192.0730.



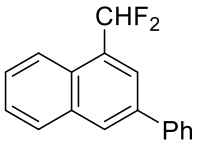
30g

1-Difluoromethyl-3-methylnaphthalene (**30h**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 2.53 (s, 3H), 7.10 (t, J_{HF} = 55.3 Hz, 1H), 7.50–7.55 (m, 3H), 7.72 (s, 1H), 7.80–7.84 (m, 1H), 8.08–8.13 (m, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 21.5, 115.4 (t, J_{CF} = 239 Hz), 123.3, 126.2, 126.4, 127.0 (t, J_{CF} = 9 Hz), 127.9, 128.1 (t, J_{CF} = 13 Hz), 129.3 (t, J_{CF} = 21 Hz), 130.3, 134.1, 134.4; ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 50.8 (d, J_{FH} = 55 Hz); IR (neat): ν: 2966, 1514, 1346, 1111, 1018, 877, 748 cm^{-1}; HRMS (EI): m/z calcd. for $C_{12}H_{10}F_2$ $[M]^+$: 192.0751; Found: 192.0758.



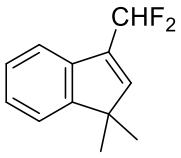
30h

1-Difluoromethyl-3-phenylnaphthalene (**30i**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 2.51 (s, 3H), 2.68 (s, 3H), 7.13 (t, J_{HF} = 55.2 Hz, 1H), 7.24 (s, 1H), 7.46 (dd, J = 7.8, 7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.77 (s, 1H), 8.08 (d, J = 7.8 Hz, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 115.4 (t, J_{CF} = 239 Hz), 123.4, 124.6 (t, J_{CF} = 9 Hz), 126.8, 127.2, 127.3, 127.8, 128.8, 129.0, 129.1, 130.1 (t, J_{CF} = 21 Hz), 134.2, 137.6, 140.1; ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 50.7 (d, J_{FH} = 55 Hz); IR (neat): ν 3060, 2924, 1603, 1346, 1246, 1113, 1022, 889 cm^{-1}; HRMS (EI): m/z calcd. for $C_{17}H_{12}F_2$ $[M]^+$: 254.0907; Found: 254.0919.



30i

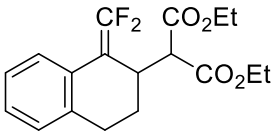
3-Difluoromethyl-1,1-dimethylindene (**30j**): ^{1}H NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 1.35 (s, 6H),



30j

6.60 (t, J_{HF} = 3.0 Hz, 1H), 6.62 (t, J_{HF} = 55.3 Hz, 1H), 7.21–7.30 (m, 2H), 7.32–7.37 (m, 1H), 7.43–7.48 (m, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 24.0, 49.0, 112.8 (t, J_{CF} = 234 Hz), 120.9, 121.5, 126.2, 126.7, 134.5 (t, J_{CF} = 23 Hz), 137.8, 147.1 (t, J_{CF} = 9 Hz), 153.5; ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 47.2 (dd, J_{FH} = 55, 3 Hz); IR (neat): ν 2962, 2925, 2856, 1469, 1375, 1022, 818, 771 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{12}H_{12}F_2$ $[M]^+$: 194.0907; Found: 194.0905.

1-Difluoromethylidene-2-di(ethoxycarbonyl)methyl-1,2,3,4-tetrahydronaphthalene (**32b**): ^{1}H



32b

NMR (500 MHz; $CDCl_3$; $SiMe_4$): δ 1.22 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.97–2.09 (m, 2H), 2.81 (ddd, *J* = 17.7, 5.9, 3.8 Hz, 1H), 2.88 (ddd, *J* = 17.7, 10.7, 6.9 Hz, 1H), 3.43 (d, *J* = 11.1 Hz, 1H), 3.61–3.67 (m, 1H), 4.13 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.17 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 7.11–7.15 (m, 1H), 7.18 (dd, *J* = 3.5, 3.5 Hz, 1H), 7.19 (dd, *J* = 3.5, 3.5 Hz, 1H), 7.43 (ddd, *J* = 5.7, 3.5, 3.5 Hz, 1H); ^{13}C NMR (126 MHz; $CDCl_3$; $SiMe_4$): δ 13.9, 14.0, 25.1, 25.3, 32.7, 52.9, 61.4, 61.5, 90.0 (dd, J_{CF} = 22, 11 Hz), 126.3, 127.2, 127.4 (dd, J_{CF} = 4, 4 Hz), 128.0, 128.1, 129.0, 135.49, 135.53, 152.9 (dd, J_{CF} = 293, 286 Hz); ^{19}F NMR (470 MHz, $CDCl_3$; C_6F_6): δ 73.5 (d, *J* = 36 Hz, 1F), 76.8 (d, *J* = 36 Hz, 1F); IR (neat): ν 2981, 2937, 1755, 1728, 1240, 1032, 766 cm^{-1}; HRMS (EI): *m*/*z* calcd. for $C_{18}H_{20}F_2O_4$ $[M]^+$: 338.1330; Found: 338.1325.

CHAPTER 5

Conclusions

In this thesis, I have developed a systematic *multiple ring construction* approach for PAHs synthesis via domino or stepwise cyclizations of fluoroalkenes.

In chapter 2, PAHs were synthesized via a methylarene-based protocol. First, trimethyl[2-(trifluoromethyl)allyl]silane was electrophilically benzylated to afford 2-trifluoromethyl-1-alkenes. Second, the 2-trifluoromethyl-1-alkenes were in turn nucleophilically benzylated through S_NV-type reaction to produce 1,1-difluoro-1-alkenes (cyclization precursors). Finally, I succeeded in [4]helicene and [4]chrysene synthesis via domino Friedel–Crafts-type cyclization of these precursors and subsequent dehydrogenation.

In chapter 3, the synthesis of internally substituted [4]acenes via a domino or stepwise two-ring construction, starting from 2-trifluoromethyl-1-alkenes bearing two aryl groups, was achieved. The synthesis involves introduction of internally substituent(s), followed by dehydrogenation. For the domino synthesis of fluorinated [4]acenes, the (trifluoromethyl)alkenes was treated with $AlMe_2Cl$. Lewis acid-promoted S_N1' reaction, followed by intramolecular S_NV-type reaction afforded fluorinated dihydrotetracenes. Subsequent dehydrogenation afforded fully aromatized fluoro[4]acenes. For the stepwise synthesis of internally substituted [4]acenes, the (trifluoromethyl)alkenes bearing two aryl groups were treated with $AlMe_2Cl$ in the presence of a stoichiometric amount of $AlMe_3$. The domino reaction was suppressed by $AlMe_3$ to afford bycyclic difluoroalkenes bearing a pendant aryl group. Protonation or oxidation of the bicyclic difluoroalkenes generated aliphatic or allylic CF_2 cations, whose Friedel–Crafts-type cyclization gave tetracyclic ketones or enones respectively. The subsequent introduction of substituents into the ketones or enones provided mono- or disubstituted tetracene derivatives. The oxidative CF_2 cation generation was also applied for the cyclization of (difluoromethyl)naphthalenes, leading to benzanthrone synthesis.

In chapter 4, the synthesis of (difluoromethyl)naphthalene derivatives by the palladium-catalyzed C–C bond formation via intramolecular insertion of 1,1-difluoroallenes was accomplished. When *o*-bromophenyl-bearing 1,1-difluoroallenes were treated with a Pd(0) complex, C–C bond formation at the position β to the fluorine substituents occurred, affording pharmaceutically and agrochemically promising (difluoromethyl)naphthalenes.

Notably, the key CF_2 cation generations used in these syntheses are classified into three categories: Type A, Type B, and Type C generations. Protonation of difluoroalkenes with super-acid (as in Chapter 2) is presented as "+ H^+-type" CF_2 cation generation (Type A). Elimination of a fluoride ion from trifluoromethylated alkenes with Lewis acids (as in Chapter 3) is presented as "– F^--type" CF_2 cation generation (Type B). Oxidation of difluoroalkenes or (difluoromethyl)naphthalenes (as in Chapter 3) is presented as "– e^--type" CF_2 cation generation (Type C). Especially, the type C method is the new finding achieved in this thesis, leading to the completion of the set of CF_2 cation generations.

LIST OF PUBLICATIONS

(1) Fuchibe, K.; Takao, G.; Takahashi, H.; Ijima, S.; Ichikawa, J.

Methylarene-Based PAH Synthesis via Domino Cyclization of 1,1-Difluoro-1-alkenes

Bull. Chem. Soc. Jpn. **2019**, *92*, 2019.

(2) Fuchibe, K.; Watanabe, S.; Takao, G.; Ichikawa, J.

Synthesis of (difluoromethyl)naphthalenes using the ring construction strategy: C–C bond formation on the central carbon of 1,1-difluoroallenes via Pd-catalyzed insertion

Org. Biomol. Chem. **2019**, *17*, 5047.

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February 2020

Go Takao