24.1.1.3 1,1-Dihaloallenes (Update 2014)

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General Introduction

This update describes published methods for the synthesis and application of 1,1-dihaloallenes reported between 2005 and 2013. Publications on this product subclass that appeared prior to 2005 are included in the previous update compiled by Kostikov in 2005 (Section 24.1.1.1). Recently, reports on syntheses and applications of 1,1-dihaloallenes have been limited to difluorinated analogues.

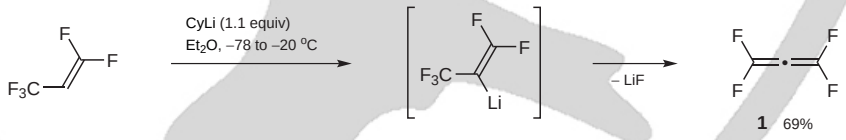
24.1.1.3.1 Synthesis of 1,1-Dihaloallenes

Generally, 1,1-difluoroallenes are synthesized via the formation of a second C=C bond in fluorinated alkenes or the rearrangement of the C≡C bonds in fluorinated alkynes. The former approach involves elimination reactions of (trifluoromethyl)alkenes and difluoroalkenes, while the latter approach involves substitution reactions of difluoropropargyl bromides. The latter method is further classified into two reaction types in which the propargyl moieties serve as nucleophiles or electrophiles.

24.1.1.3.1.1 Method 1: Eliminations from 1-(Trifluoromethyl)alk-1-enes and 1,1-Difluoroalk-1-enes

The most common method for synthesizing 1,1-difluoroallenes is the elimination of a fluoride ion or other leaving group from 1-(trifluoromethyl)alk-1-ene or 1,1-difluoroalkene substrates, respectively. Over the past few decades, the elimination of lithium fluoride from (3,3,3-trifluoroprop-1-en-2-yl)lithium or (1,1,3,3,3-pentafluoroprop-1-en-2-yl)lithium has been used for the preparation of difluoroallenes and tetrafluoroallenes, respectively.[1,2] Cyclohexyllithium is successfully employed as a base for the deprotonation of the vinylic proton in 1,1,3,3,3-pentafluoroprop-1-ene, leading to the formation of tetrafluoroallene (**1**) in 69% yield (Scheme 1). The lower volatility of the conjugate acid, cyclohexane, makes the purification of allene **1** by distillation easier.[3] Metal–halogen exchange is also useful for generating (3,3,3-trifluoroprop-1-en-2-yl)lithium to yield 1,1-difluoroallene.[4–6]

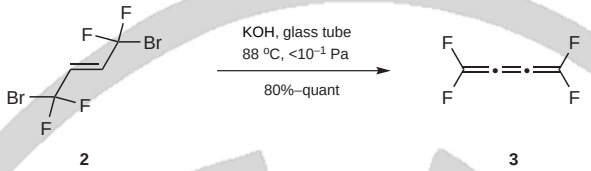
Scheme 1 Synthesis of Tetrafluoroallene by Lithium Fluoride Elimination[3]



Similar elimination in dibromotetrafluorobut-2-ene **2** affords tetrafluorobuta-1,2,3-triene (**3**) in high yield (Scheme 2).[7]

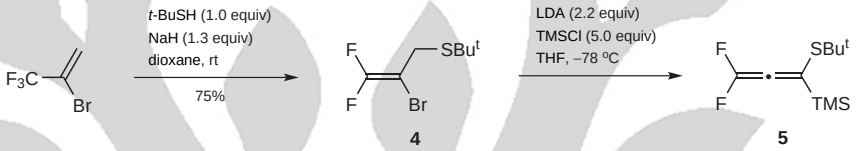
for references see p 231

Scheme 2 Synthesis of Tetrafluorobuta-1,2,3-triene by Double Dehydrobromination[7]



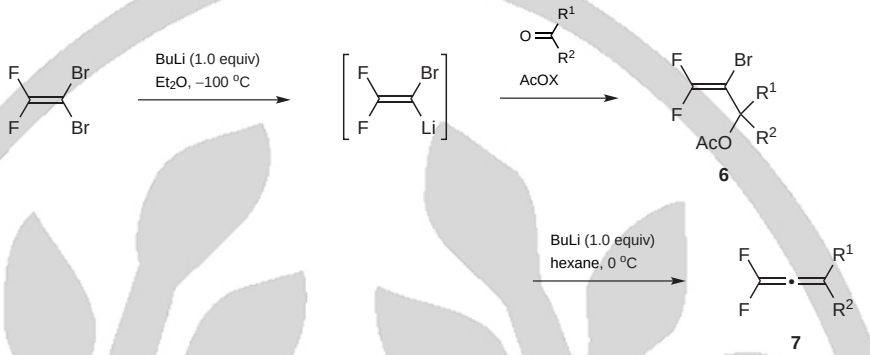
2-Bromo-3-(*tert*-butylsulfanyl)-1,1-difluoroprop-1-ene (**4**), prepared in 75% yield via an S_N2'-type reaction of 2-bromo-3,3,3-trifluoroprop-1-ene with a thiolate ion, undergoes dehydrobromination on treatment with lithium diisopropylamide (Scheme 3).[8] The initially formed allene is deprotonated and subsequent silylation with a chlorosilane affords 3-silyl-3-sulfanyl-substituted 1,1-difluoroallene **5** (yield not reported).

Scheme 3 Synthesis of a 3-Silyl-3-sulfanyl-substituted 1,1-Difluoroallene by Dehydrobromination[8]



1,1-Difluoroallenes are synthesized via the difluorovinylidenation of the carbonyl group in aldehydes and ketones (Scheme 4).[9–11] Carbonyl compounds are treated with (1-bromo-2,2-difluorovinyl)lithium or (1-iodo-2,2-difluorovinyl)lithium, which are prepared from 1,1-dibromo-2,2-difluoroethene or 1-iodo-2,2,2-trifluoroethane, respectively. The corresponding 2-halo-3,3-difluoroallyl acetates **6** and **8** are obtained after one-pot acetylation. Acetylated products **6** and **8** are then subjected to 1,2-elimination with butyllithium (for the bromides) or zinc metal (for the iodides) to afford 1,1-difluoroallenes **7** and **9**, respectively, in high yield.

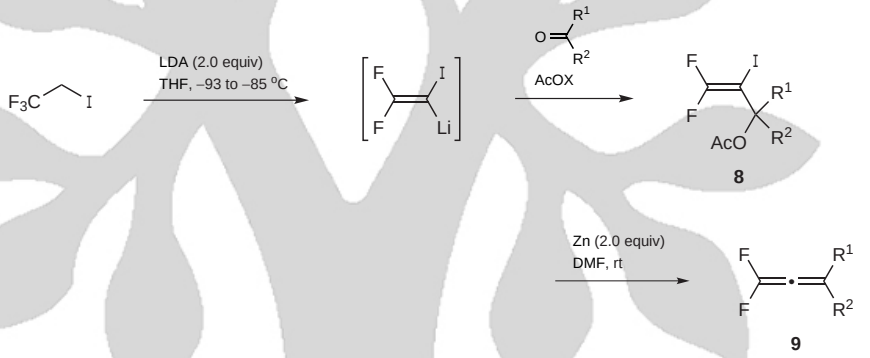
Scheme 4 Synthesis of 1,1-Difluoroallenes by Difluorovinylidenation of Carbonyl Compounds[9–11]



6 **7**

R^1	R^2	X	Yield (%)		Ref
			6	**7**	
$(CH_2)_2Ph$	H	Ac	93	87	[11]
Bu	Ph	$C(Me)=CH_2$	80	85[a]	[11]

[a] Acetylation (with 2 mol% TsOH) was performed after isolation of the allylic alcohol obtained from the ketone and (1-bromo-2,2-difluorovinyl)lithium.



8 **9**

R^1	R^2	X	Yield (%)		Ref
			8	**9**	
$(CH_2)_2Ph$	H	Ac	82	86	[11]
4-*t*-$BuC_6H_4CH_2CHMe$	H	Ac	87	92	[11]
CMe_2Ph	H	Ac	83	93	[11]
$(CH_2)_2Ph$	Me	$C(Me)=CH_2$	80	86[a]	[11]

[a] Acetylation (with 1 mol% TsOH) was performed after isolation of the allylic alcohol obtained from the ketone and (1-iodo-2,2-difluorovinyl)lithium.

Tetrafluoroallene (1):[3]

Cold Et_2O (500 mL) was added to cyclohexyllithium (4.52 g, 50.2 mmol) in a two-necked Schlenk flask at −80 °C. The mixture was cooled to −196 °C and degassed, and 1,1,3,3,3-

for references see p 231

pentafluoroprop-1-ene (6.06 g, 45.9 mmol) was condensed into the flask. After the mixture had been warmed to −100 °C, the flask was purged with argon and a thermometer was inserted into the suspension. The suspension was stirred at −75 °C for 3 h and subsequently warmed to −20 °C over 30 min. A fractionation column (50 cm) was fitted onto the flask and the head was cooled to −80 °C. Distillation gave a mixture of allene **1** and Et_2O (bp −39 to +15 °C), and fractional condensation of the distillate via two subsequent traps kept at −125 and −196 °C gave product **1** in the second trap; yield: 3.55 g (69%).

Tetrafluorobuta-1,2,3-triene (3):[7]
1,4-Dibromo-1,1,4,4-tetrafluorobut-2-ene (**2**; 1.0 g, 3.5 mmol) was passed over hot (88 °C) KOH packed in a U-shaped tube (diameter ≤1 cm) by evaporation under vacuum (10^{-1} Pa). The volatile materials were collected in traps kept at −78 °C (for H_2O) and −196 °C (for product **3**); yield: 0.43 g (100%).

1,1-Difluoro-2-iodo-5-phenylpent-1-en-3-yl Acetate [8, $R^1 = (CH_2)_2Ph$; $R^2 = H$]:[10,11]
LDA was freshly prepared by adding a 1.67 M soln of BuLi in hexane (12.0 mL, 20.0 mmol) to a soln of iPr_2NH (2.8 mL, 20 mmol) in THF (10 mL) over 10 min at 0 °C. The resulting soln was stirred for an additional 15 min and cooled to −93 °C. A soln of CF_3CH_2I (2.10 g, 10.0 mmol) in THF (5 mL) was added to the cold LDA soln over 10 min, keeping the bath temperature between −93 and −85 °C. After the mixture had been stirred for 20 min at the same temperature, a soln of 3-phenylpropanal (1.34 g, 10.0 mmol) in THF (5 mL) was added over 5 min, keeping the bath temperature between −93 and −85 °C. The mixture was stirred for an additional 30 min, and then warmed to −30 °C over 90 min. After Ac_2O (1.23 g, 12.0 mmol) had been added, the mixture was warmed to 0 °C over 2 h. The reaction was quenched with sat. aq NH_4Cl and the products were extracted with Et_2O. The combined organic layers were washed with brine and dried (Na_2SO_4). After the solvent had been removed under reduced pressure, the residue was purified by column chromatography (silica gel, hexane/EtOAc 20:1), giving a colorless liquid; yield: 3.01 g (82%).

(5,5-Difluoropenta-3,4-dien-1-yl)benzene [9, $R^1 = (CH_2)_2Ph$; $R^2 = H$]; Typical Procedure:[10,11]
A soln of the acetate **8** [$R^1 = (CH_2)_2Ph$; $R^2 = H$; 366 mg, 1.00 mmol] in DMF (2 mL) was added to a suspension of Zn powder (131 mg, 2.00 mmol) in DMF (3 mL) at rt, and the mixture was stirred for 3 h. After the resulting mixture had been filtered to remove the excess Zn and then diluted with Et_2O and brine, the products were extracted with Et_2O. The combined organic layers were washed with brine and dried (Na_2SO_4). After the solvent had been removed under reduced pressure, the residue was purified by column chromatography (silica gel, pentane), giving the product as a colorless liquid; yield: 155 mg (86%).

24.1.1.3.1.2 Method 2: Substitutions from 1,1-Difluoropropargyl Bromides

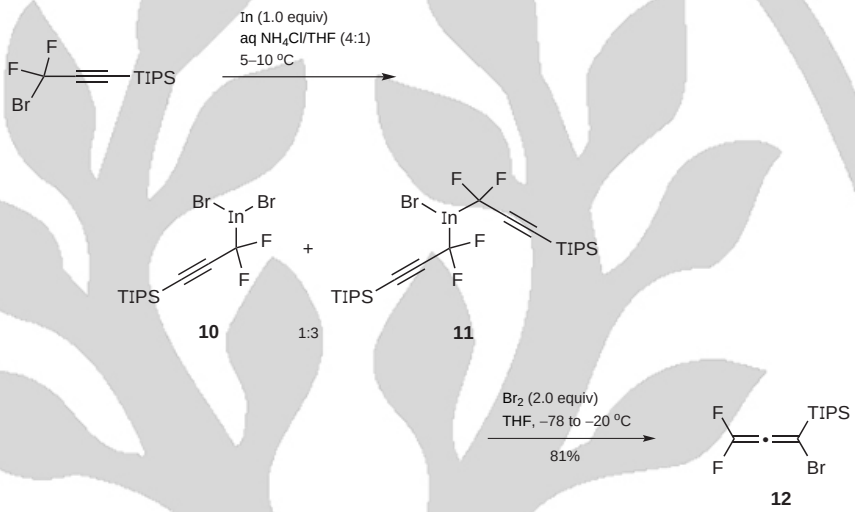
Substituted 1,1-difluoropropargyl bromides are also useful precursors for the synthesis of 1,1-difluoroallenes. The propargyl bromides can act as sources of both nucleophiles and electrophiles,[12] and undergo rearrangement of the C≡C bond to form the 1,2-diene structure.

24.1.1.3.1.2.1 Variation 1: Reactions with Electrophiles

On treatment with indium metal, 3-bromo-3,3-difluoro-1-(triisopropylsilyl)prop-1-yne forms the fluorinated propargylindium(III) species **10** and **11** (ca. 1:3), which can be isolated using silica gel column chromatography (Scheme 5).[13] The mixture of indium species **10** and **11** undergoes reaction with bromine at the position γ to the indium(III) center to

afford the triisopropylsilyl-substituted difluoroallene **12**.[14] Reaction of **10** and **11** with formaldehyde gives the corresponding difluoroallene in 67% yield.[15] Indium species **10** and **11** also react with *N*-chlorosuccinimide or glyoxylic acid to give the corresponding chlorination or hydroxyalkylation products, respectively; however, the yields of these products are not reported.[13] In contrast, other electrophiles, such as aromatic aldehydes, react with **10** and **11** at the position α to the metal center to afford propargylic compounds.[15]

Scheme 5 Synthesis of 1-Bromo-3,3-difluoro-1-(triisopropylsilyl)allene by Bromination of 1,1-Difluoropropargylindium(III) Species[14]



1-Bromo-3,3-difluoro-1-(triisopropylsilyl)allene (12):[14]

CAUTION: *Bromine is a severe irritant of the eyes, mucous membranes, lungs, and skin. Liquid bromine causes severe and painful burns on contact with eyes and skin.*

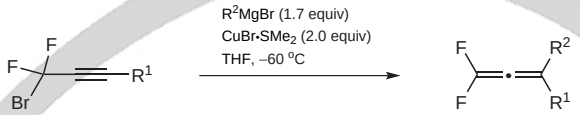
The organoindiums **10** and **11**, prepared from In powder (1.11 g, 9.71 mmol) and 3-bromo-3,3-difluoro-1-(triisopropylsilyl)prop-1-yne (3.20 g, 9.71 mmol, as reported) in 2% aq NH_4Cl/THF (4:1) at 5–10 °C under sonication, were dissolved in THF (50 mL), and the mixture was cooled to −78 °C. A soln of Br_2 (3.10 g, 19.4 mmol) in THF (10 mL) was added dropwise to the mixture. The mixture was warmed to −20 °C and stirred for an additional 0.5 h at this temperature. Sat. aq $Na_2S_2O_3$ was added to quench the reaction. After being stirred for 5 min at 0 °C, the products were extracted with Et_2O. The organic layers were washed with brine and dried (Na_2SO_4). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, hexane). The product was obtained as a colorless liquid; yield: 2.44 g (76%). As **12** is not very stable in soln, yields can vary from 67 to 81%.

24.1.1.3.1.2.2 Variation 2: Reactions with Nucleophiles

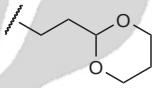
Nucleophilic attack on 1,1-difluoropropargyl bromides occurs at the C3 sp-hybridized carbon, and is accompanied by rearrangement of the C≡C bond and elimination of the bromide ion to yield 1,1-difluoroallenes. Difluoropropargyl bromides readily react with Grignard reagents in the presence of copper(I) bromide–dimethyl sulfide complex to afford 1,1-difluoroallenes **13**, which bear a nucleophile-derived substituent at the position γ to the fluorine substituents (Scheme 6).[16]

for references see p 231

Scheme 6 Synthesis of 1,1-Difluoroallenes by Copper(I)-Mediated S_N2'-Type Reaction of 1,1-Difluoropropargyl Bromides[16]



13

R^1	R^2	Yield[a] (%)	Ref
Ph	Et	70 (81)	[16]
$(CH_2)_5Me$	Et	91 (94)	[16]
$(CH_2)_2iPr$		68 (86)[b]	[16]
TMS	Bu	69 (73)	[16]

[a] Yield determined by ^{19}F NMR using (trifluoromethyl)benzene as internal standard is indicated in parentheses.
[b] Conditions: CuCl (4.0 equiv), R^2MgBr (2.2 equiv), −78 °C.

1,1-Difluoroallenes 13; General Procedure:[16]
A 1.0 M soln of the Grignard reagent in THF [2.2 mL, 2.2 mmol, as reported (1.7 equiv indicated in scheme)] was added to a soln of CuBr•SMe_2 (411 mg, 2.00 mmol) in THF (10 mL) at −60 °C. The resulting soln was stirred for 30 min and the 1,1-difluoropropargyl bromide (1.00 mmol) was added along the wall of the flask, keeping the temperature of the mixture at −60 °C. After being stirred for 1 h at −60 °C, the mixture was poured onto aq NH_4Cl and ice to quench the reaction. The products were extracted with cold hexane and dried (Na_2SO_4). The solvent was removed under reduced pressure to give the product.

24.1.1.3.2 Applications of 1,1-Dihaloallenes

1,1-Difluoroallenes possess both difluorinated alkene and cumulated diene structures. Because of these characteristics, 1,1-difluoroallenes enable the synthesis of fluorinated cyclic compounds via cycloaddition reactions.[1,17–19] Recently, an increasing number of reports on the nucleophilic reactions of 1,1-difluoroallenes have appeared and are described in the following sections.

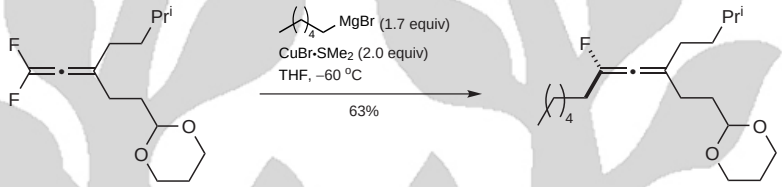
24.1.1.3.2.1 Method 1: Reactions with Nucleophiles

Because of their electrophilicity, 1,1-difluoroallenes can react with nucleophiles and numerous such reactions have been reported recently. Theoretical calculations suggest that the carbon α to the fluorine substituent is positively charged and the carbon γ to the fluorine substituent has a large LUMO coefficient.[16,18,20] In addition to these charge and orbital distributions, steric effects also influence the course of reactions with nucleophiles. Consequently, reactivity is observed at both the α and γ carbons of 1,1-difluoroallenes.

24.1.1.3.2.1.1 Variation 1: Substitutions at the α-Carbon

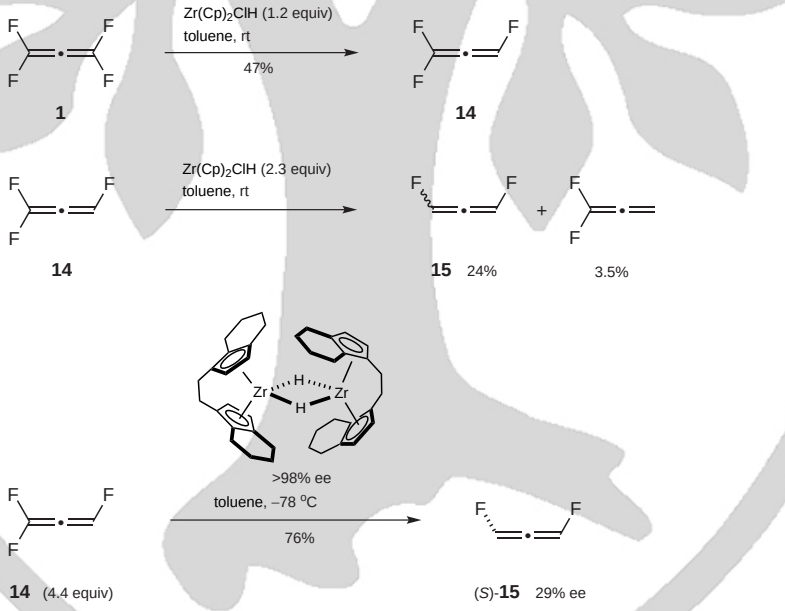
The reaction of 3,3-disubstituted 1,1-difluoroallenes with alkylcopper reagents occurs at the position α to the fluorine substituents and is followed by fluoride elimination, leading to overall replacement by the alkyl group. Alkylmagnesium bromides react with 1,1-difluoroallenes in the presence of copper(I) bromide–dimethyl sulfide complex to afford trisubstituted monofluoroallenes in good yield (Scheme 7).[16] Attack of an oxygen nucleophile can also occur at the position α to the fluorine substituents, albeit without the accompanying elimination of a fluoride ion (see Section 24.1.1.3.2.1.2, Scheme 12).

Scheme 7 Substitution of Fluorine in a 1,1-Difluoroallene with an Alkylcopper Reagent[16]



Reduction of the C—F bonds in fluoroallenes also proceeds upon treatment with metal hydrides, presumably via an addition–elimination process (Scheme 8). Tetrafluoroallene (**1**) undergoes reduction with chlorobis(η^5-cyclopentadienyl)hydridozirconium(IV) to give 1,1,3-trifluoroallene (**14**) in 47% yield.[21] Subsequently, 1,1,3-trifluoroallene (**14**) reacts again with the zirconium(IV) complex to preferentially afford 1,3-difluoroallene (**15**) over 1,1-difluoroallene. The hydrodefluorination of allene **14** has also been utilized for the synthesis of enantioenriched (*S*)-**15**.[21]

Scheme 8 Reductions of C—F Bonds in Fluoroallenes[21]



The substitution reaction involving 3-bromo-1,1-difluoroallene **12** and nucleophiles proceeds in an S_N2' fashion with bromide (not fluoride) elimination, providing a synthetic

for references see p 231

route to difluoropropargylic compounds **16** (Scheme 9).[14] A wide variety of O-, S-, N-, P-, and C-nucleophiles attack the carbon α to the fluorine substituents, and subsequent bromide elimination leads to formation of the product.

Scheme 9 S_N2'-Type Substitution Reaction of a 3-Bromo-1,1-difluoroallene[14]

12 **16**

Conditions	Nu	Yield (%)	Ref
MeOH, K_2CO_3, 0 °C	OMe	61	[14]
AcOH, AgOAc, rt	OAc	70	[14]
4-$MeOC_6H_4CH_2SH$, BuLi, THF, −78 to 0 °C	4-$MeOC_6H_4CH_2S$	53	[14]
Ph_3P, Et_2O, rt	$^+PPh_3Br^-$	92	[14]
$CH(Me)(CO_2Et)_2$, NaH, THF, 0 °C	$CMe(CO_2Et)_2$	70	[14]

3,3-Difluoro-3-methoxy-1-(triisopropylsilyl)prop-1-yne (16, Nu = OMe):[14]
A soln of bromoallene **12** (311 mg, 1.00 mmol) in THF (1 mL) was added to a mixture of K_2CO_3 (212 mg, 2.01 mmol, as reported) and MeOH (2 mL) at 0 °C. The mixture was stirred for 3 h at 0 °C. Sat. aq NH_4Cl (10 mL) was added to quench the reaction. After being stirred for 5 min at 0 °C, the products were extracted with Et_2O. The combined organic layers were washed with brine and dried (Na_2SO_4). After the solvent had been removed under reduced pressure, the residue was purified by column chromatography (silica gel, EtOAc/hexane 1:10), giving a colorless liquid; yield: 158 mg (61%).

24.1.1.3.2.1.2 Variation 2: Substitutions and Additions via Electrophilic Activation

In addition to the above-mentioned direct substitutions of fluorine with nucleophiles, 1,1-difluoroallenes can also be electrophilically activated by Lewis acids to enable bond formation. In this case, 1,1-difluoroallenes serve as a substrate for the construction of the phenanthrene framework via cationic C—C bond-forming processes.[22] 1,1-Difluoroallene **17**, bearing an aromatic ring and a cyclopentene moiety, undergoes sequential ring closure and ring expansion under indium(III) catalysis to afford the corresponding dihydrophenanthrene. The subsequent one-pot dehydrogenation with 2,3-dichloro-5,6-dicyanobenzo-1,4-quinone (DDQ) affords fluorinated phenanthrene **18** (Scheme 10). A series of regioselectively fluorinated polycyclic aromatic hydrocarbons can be readily synthesized using this sequence (Table 1).[22] Notably, combination of this domino sequence with halogenation/Suzuki–Miyaura cross coupling leads to a practical method for the synthesis of arylated fluorophenanthrenes (Scheme 11).[22]

Scheme 10 Domino Ring Closure and Ring Expansion of a 1,1-Difluoroallene[22]

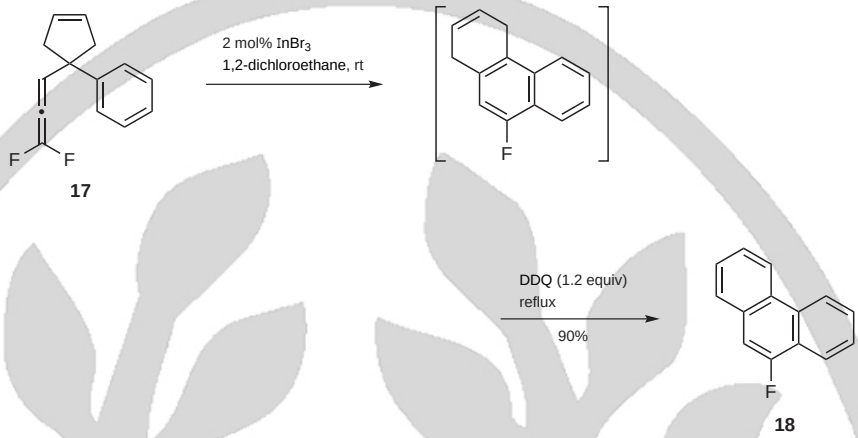
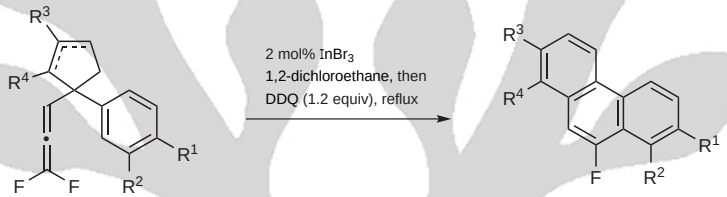
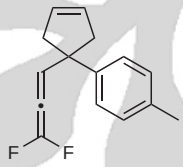
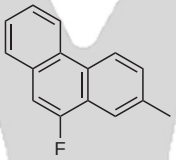
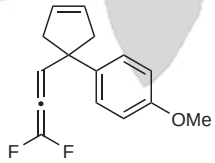
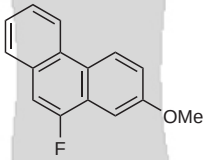
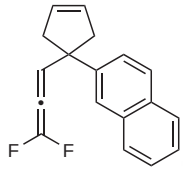
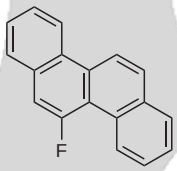
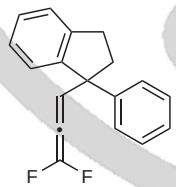
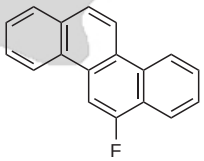


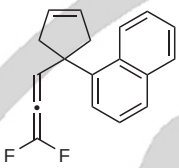
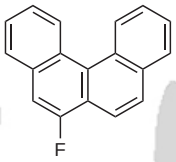
Table 1 Indium(III)-Catalyzed Synthesis of Regioselectively Fluorinated Polycyclic Aromatic Hydrocarbons from 1,1-Difluoroallenes[22]



Starting Material	Product	Yield (%)	Ref
		93	[22]
		66[a]	[22]
		85	[22]
		80	[22]

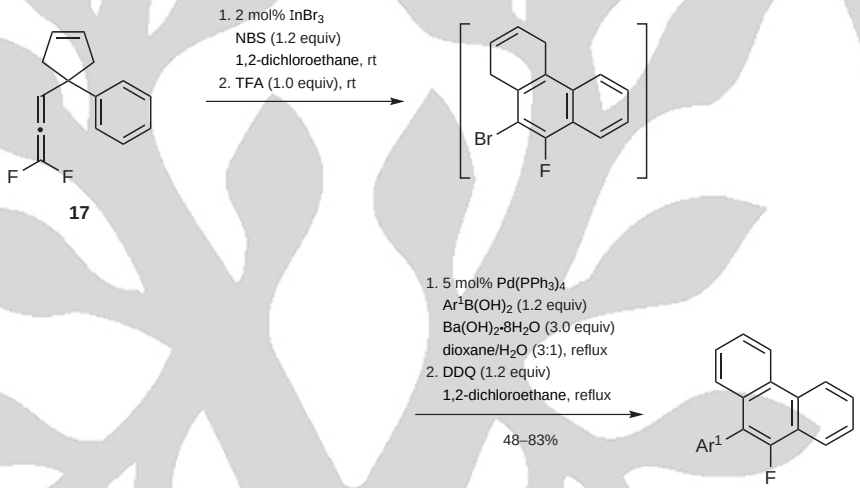
for references see p 231

Table 1 (cont.)

Starting Material	Product	Yield (%)	Ref
		80[b]	[22]

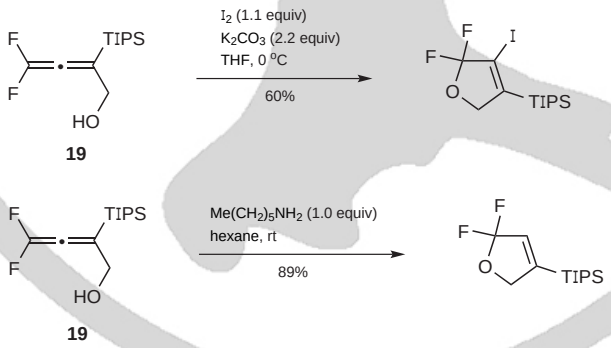
[a] $InBr_3$ (10 mol%) was used.
[b] 5-Fluorochrysene was obtained as a minor product (25:75).

Scheme 11 Sequential Processes for the Synthesis of Arylated Fluorophenanthrenes[22]



Homoallenyl alcohol **19**, prepared via indium-mediated reaction of a 1,1-difluoropropargyl bromide and formaldehyde (Section 24.1.1.3.1.2.1),[15] readily undergoes iodine-promoted 5-*endo* cyclization to afford an iodinated difluorodihydrofuran (Scheme 12).[23] An intramolecular addition of alcohol **19** also occurs in the presence of a primary amine (Scheme 12).[23] For substitution at the α-carbon, see Section 24.1.1.3.2.1.1, Scheme 7.

Scheme 12 Intramolecular Nucleophilic Additions of a 1,1-Difluorohomoallenyl Alcohol[23]



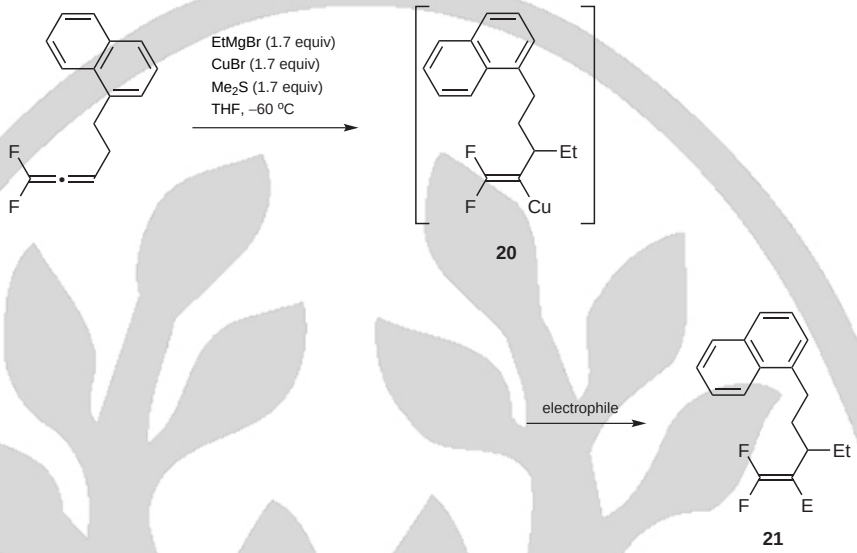
9-Fluorophenanthrene (18); Typical Procedure:[22]
Powdered $InBr_3$ (2 mg, 0.006 mmol) was added to a soln of 1,1-difluoroallene **17** (53 mg, 0.24 mmol) in 1,2-dichloroethane (6 mL) at rt. The resulting soln was stirred for 30 min at the same temperature. DDQ (65 mg, 0.29 mmol) was added as a solid, and the resulting mixture was refluxed for 1.5 h. After the solvent had been removed under reduced pressure, the residue was purified by column chromatography (silica gel, hexane) to give colorless crystals; yield: 42 mg (90%).

24.1.1.3.2.1.3 Variation 3: Carbo- and Hydrometalations

In contrast to the 3,3-disubstituted 1,1-difluoroallenes (Section 24.1.1.3.2.1.1, Scheme 7), 3-monosubstituted 1,1-difluoroallenes undergo carbometalation at the non-fluorinated double bond upon treatment with organocopper reagents (Scheme 13).[20] The formed (2,2-difluorovinyl)copper intermediates **20** can be utilized for sequential coupling with appropriate reagents to afford γ-branched, β-halogenated difluoroalkenes **21** (E = I) or β-stannylated difluoroalkenes **21** ($E = SnBu_3$) in good to high yield. Furthermore, cross-coupling reactions of intermediates **20** with aryl, benzyl, and allyl halides proceed under palladium(0) catalysis, allowing the introduction of carbon substituents on the vinylic carbon of 1,1-difluoroalk-1-enes.

for references see p 231

Scheme 13 Regioselective Carbocupration of 1,1-Difluoroallenes[20]

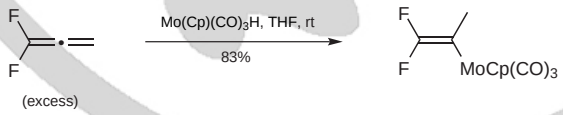


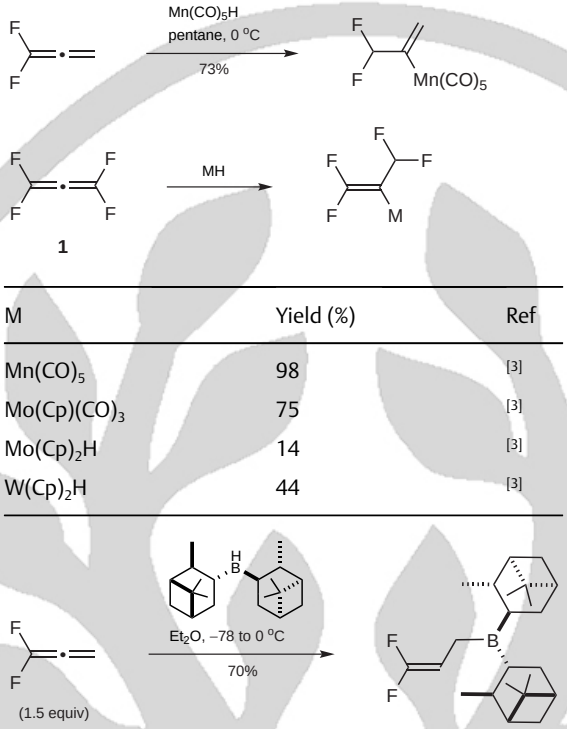
Electrophile	E	Conditions	Yield (%)	Ref
H_3O^+	H	THF, −60 °C	95	[20]
NIS (5.1 equiv)	I	THF, −60 °C	84	[20]
Bu_3SnCl (1.7 equiv)	$SnBu_3$	THF, −60 °C	66	[20]
PhI (1.0 equiv)	Ph	$Pd_2(dba)_3$ (5 mol%), Ph_3P (20 mol%), THF/HMPA (5:1), rt	90	[20]
BnBr (1.0 equiv)	Bn	$Pd_2(dba)_3$ (5 mol%), Ph_3P (20 mol%), THF/HMPA (5:1), rt	53[a]	[20]
(*E*)-MeCH=CHCH$_2$Br (1.0 equiv)	(*E*)-CH$_2$CH=CHMe	$Pd_2(dba)_3$ (5 mol%), Ph_3P (20 mol%), THF/HMPA (5:1), rt	85[b]	[20]

[a] ^{19}F NMR yield.
[b] Single regioisomer.

Hydrometalation of 1,1-difluoroallene and tetrafluoroallene (**1**) occurs on treatment with molybdenum, manganese, and tungsten hydrides to give the corresponding vinylmetal species (Scheme 14).[3,24] On the other hand, hydroboration of 1,1-difluoroallene with bis-(isopinocampheyl)borane shows a different regioselectivity, affording instead the (3,3-difluoroallyl)borane.[24]

Scheme 14 Regioselective Hydrometalations of 1,1-Difluoroallenes[3,24]





M	Yield (%)	Ref
$Mn(CO)_5$	98	[3]
$Mo(Cp)(CO)_3$	75	[3]
$Mo(Cp)_2H$	14	[3]
$W(Cp)_2H$	44	[3]

3-Ethyl-1,1-difluoro-5-(1-naphthyl)-2-phenylpent-1-ene (21, E = Ph); Typical Procedure:[20]

CAUTION: *Hexamethylphosphoric triamide is a possible human carcinogen and an eye and skin irritant.*

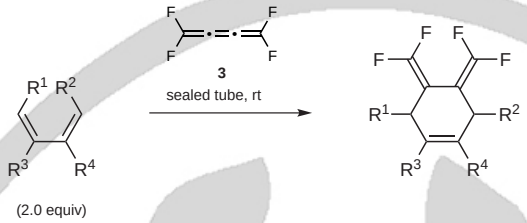
Me_2S (25 μL, 0.34 mmol) was added to a suspension of CuBr (49 mg, 0.35 mmol) in THF (2 mL) at rt. After the mixture had been stirred for 2 h, a 0.90 M soln of EtMgBr in THF (0.38 mL, 0.34 mmol) was added at −60 °C and the suspension was stirred for 30 min at the same temperature. A 0.46 M soln of 1-(5,5-difluoropenta-3,4-dien-1-yl)naphthalene in hexane (0.43 mL, 0.20 mmol) was added to the yellow suspension of the EtCu reagent at −60 °C, and the mixture was stirred for 1 h. HMPA (0.50 mL), $Pd_2(dba)_3$•$CHCl_3$ (10 mg, 0.0097 mmol), and Ph_3P (11 mg, 0.042 mmol) were added, and the resulting soln was stirred for 15 min. After iodobenzene (22 μL, 0.20 mmol) had been added, the mixture was warmed to rt and stirred for 8 h. Phosphate buffer (pH 7) was added to quench the reaction. The products were extracted with EtOAc, and the combined organic layers were washed with brine and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was purified by column chromatography (silica gel, hexane), giving the product as a colorless liquid; yield: 60 mg (90%).

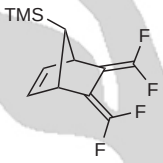
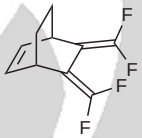
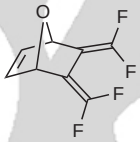
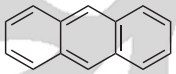
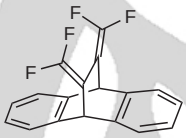
24.1.1.3.2.2 Method 2: Reactions with Unsaturated Compounds

Fluorinated allenes are reactive substrates for cycloadditions.[1,17–19] For example, the Diels–Alder reaction of tetrafluorobuta-1,2,3-triene (**3**) proceeds with dienes (Table 2).[25] In particular, cyclic dienes readily react to afford the corresponding cycloadducts, which bear two *exo*-difluoromethylene units, in high yield.

for references see p 231

Table 2 Cycloaddition Reactions of Tetrafluorobuta-1,2,3-triene with Dienes[25]



Starting Material	Solvent	Product	Yield (%)	Ref
	–		quant	[25]
	–		quant	[25]
	–		quant	[25]
	CH_2Cl_2		50	[25]

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Sample Chapter