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AIBN-initiated radical addition of *gem*-difluorinated alkyl iodides to alkynes and the Pd-catalyzed Sonogashira coupling reaction of *E*-phenyl difluoromethylene vinylic iodides with terminal alkynes

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Abstract—The addition of *gem*-difluorinated alkyl iodides to alkynes initiated by AIBN neatly gave the corresponding difluoromethylene vinyl iodides among which the stereoselectivity of aromatic acetylenes was high. The further coupling reaction of *E*-phenyl difluoromethylene vinyl iodides with terminal alkynes in the presence of catalytic palladium afforded the substituted difluorinated enynes.

1. Introduction

Organofluorine compounds have been widely applied in the areas of pharmaceuticals, agrochemicals, and other fields due to their unique properties arising from altered electron density, acidity or basicity, and hydrogen-bonding capability.[1] Indeed, recent reports have demonstrated that the CF_2 group has a steric profile similar to that of the CH_2 group, but since it has both a very different polarity and a very different reactivity, it can be regarded as an isopolar and isosteric replacement for oxygen.[2] Some potent antitumor agents, broad spectrum antibiotics, inhibitors of HIV-1 reverse transcriptase, and potent inhibitors of various proteolytic enzymes contain difluoromethylene group.[3]

Recently, much attention has been devoted to the synthesis of vinylic iodides and their derivatives since they emerged as highly valuable intermediates in a variety of synthetic applications, such as in palladium-catalyzed Sonogashira[4] and other coupling reactions,[5] particularly in the synthesis of biologically active compounds.[6] Although the addition of perfluoroalkyl iodides to terminal alkynes has been extensively investigated for the preparation of perfluorinated vinyl iodides,[7] few reports of difluoromethylene vinyl iodides have been documented. To the best of our knowledge, only Chen described the addition of diethyl iododifluoromethylphosphonate and difluorodiiodomethane derivatives to alkynes initiated by sodium dithionate.[8]

The importance of difluoromethylene vinylic iodides in the synthesis of biologically active compounds prompted us to explore new and convenient synthesis of the *gem*-difluorinated alkyl iodide reagents. Iododifluoroacetate **1** has been demonstrated to be a versatile *gem*-difluoromethylation reagent. Burton and Yang have developed a convenient methodology for the preparation of iododifluoroacetate from the commercially available bromodifluoroacetate.[9] 3-Phenyl-5-iododifluoromethyl-1,2,4-oxadiazole **2** bearing 1,2,4-oxadiazole moiety also could be prepared from 3-phenyl-5-bromodifluoro-1,2,4-oxadiazole using the same method.[10] Iododifluoromethyl phenyl thioether has been prepared by the nucleophilic reaction of phenylthiol and CF_2I_2 in a very low yield.[11] Herein, a convenient and efficient method for the synthesis of **3** has been achieved. Bromodifluoromethyl phenyl thioether and its derivatives[12] have been readily converted to compounds **3** via the halogen exchange process in the presence of sodium iodide (Scheme 1).

Keywords: Alkynes; Radical addition; Difluoromethylene vinylic iodides; Sonogashira coupling.
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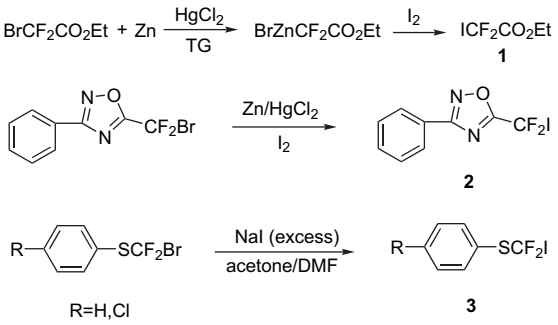
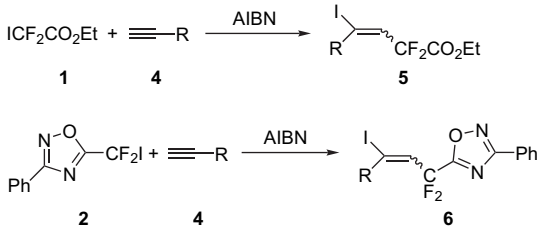


Scheme 1.

2. Results and discussion

Among radical addition of perfluoroalkyl iodides to alkynes initiated by UV light, AIBN, benzoyl peroxide, SmI_2, Et_3B, $Na_2S_2O_4$, etc.,[13] $Na_2S_2O_4$ is one of the most effective methods for the preparation of fluorinated vinylic iodides. However, when we treated iododifluoroacetate with phenylethyne in the presence of $Na_2S_2O_4/NaHCO_3$ in CH_3CN/H_2O (1:1), DMF/H_2O (1:1), or DMSO/H_2O (1:1), **5a** was formed in only 16–24% yields. When 1,4-dioxane/H_2O (1:1) was used as solvent, the yield raised to 32%. When the mixture was heated in copper powder at 60 °C for 8 h, no adduct was obtained. Fortunately, the addition of iododifluoroacetate to phenylethyne initiated by AIBN in the absence of solvent at 65 °C proceeded smoothly, and the addition reaction was completed in 16 h and the *E*-isomer adduct **5a** was isolated in 85% yield. The scope of the reaction was studied by the addition of iododifluoroacetate **1** and 3-phenyl-5-iododifluoro-1,2,4-oxadiazole **2** to a variety of other terminal alkynes. The results are summarized in Table 1. Unlike perfluoroalkyl iodides,[14] **1** and **2** reacted with phenylethyne **4a** to afford the corresponding adducts in good yields (entries 1 and 8). Other functional groups, including alkyl, ester, trimethylsilyl, on the alkynes gave moderate yields.

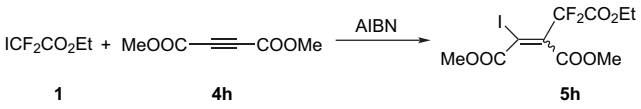
Table 1. AIBN-initiated addition of iododifluoroacetate **1** and 3-phenyl-5-iododifluoro-1,2,4-oxadiazole **2** to terminal alkynes **4**



Entry	Substance	Alkyne **4**	Product	Yield[a] (%)	*E*/*Z* ratio[b]
1	**1**	Ph (**4a**)	**5a**	85	100:0
2	**1**	COOMe (**4b**)	**5b**	30	3.2:1
3	**1**	C_4H_9 (**4c**)	**5c**	38	4.2:1
4	**1**	TMS (**4d**)	**5d**	35	1:2.3
5	**1**	CH_2OTs (**4e**)	**5e**	11	100:0
6	**1**	CH_2OCOPh (**4f**)	**5f**	13	100:0
7	**1**	CH_2OH (**4g**)	**5g**	Trace	
8	**2**	Ph (**4a**)	**6a**	95	100:0
9	**2**	C_4H_9 (**4c**)	**6c**	79	3:1
10	**2**	CH_2OH (**4g**)	**6g**	14	1:2.1

[a] Isolated yield.
[b] Determined by NMR spectra.

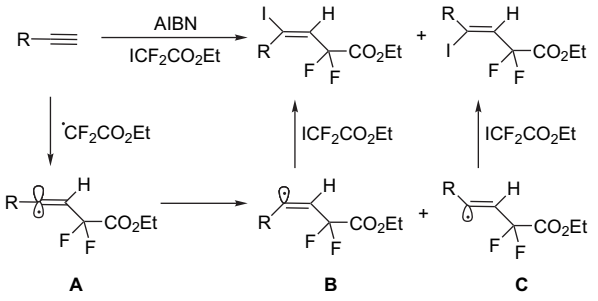
Unfortunately, the yields of propargyl alcohol and its derivatives were very low. Under the same reaction conditions, AIBN also initiated the addition of **1** to the internal alkyne such as but-2-ynedioic acid dimethyl ester **4h** (Scheme 2). However, the adduct **5h** was isolated in low yield (25%) with no geometric selectivity (*E*/*Z*=1:1).



Scheme 2.

The geometry of the double bond in **5** and **6** was established by comparing the chemical shift of the vinylic protons, which exhibited a typical triplets with coupling to the adjacent CF_2 group. The alkenyl hydrogen of *E*-isomer appeared lower field than that of *Z*-isomer.[15] The δ 6.89 (J_{H-F}=11.9 Hz) and δ 7.76 (J_{H-F}=11.4 Hz) chemical shifts on ^{1}H NMR spectra of **5b** were assigned to *E* and *Z* isomers while the δ 6.92 (J_{H-F}=11.1 Hz) and δ 7.37 (J_{H-F}=14.7 Hz) chemical shifts on ^{1}H NMR spectra of **5d** were assigned to *E* and *Z* isomers, respectively.

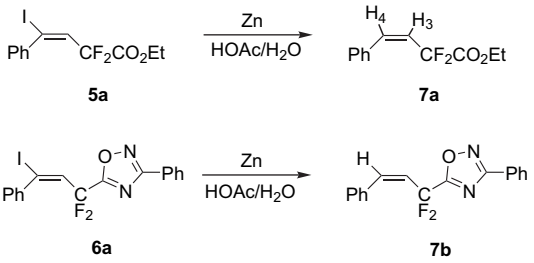
In the case of phenylethynes **4a**, **4e**, and **4f** (entries 1, 5, 6, and 8), the adducts gave single isomer. As for the influence of the substituent (*R*) in alkynes **4** on the geometric selectivity of the addition reactions, a possible explanation may be given as follows: when the $EtO_2CCF_2^{\bullet}$ adds to alkynes, they would form vinyl intermediates **B** and **C**.[16] A vinyl radical is known to have a low inversion barrier (6–9 kcal/mol), and π-conjugated substituents such as phenyl groups are usually thought to favor the linear form in order to ensure a better orbital overlap for resonance.[17] With such a linear vinyl radical, we can assume that the steric hindrance between the CF_2CO_2Et group and electron donor was unfavorable for the formation of the *E*-isomer (**C**) leading to the *Z*-isomer (**B**). Other substituents lead to a mixture of *E* and *Z* isomers (Scheme 3).



Scheme 3.

Reduction of 2,2-difluoro-4-iodo-4-phenyl-but-3-enoic acid ethyl ester **5a** and 5-(1,1-difluoro-3-iodo-3-phenyl-allyl)-3-phenyl-[1,2,4]oxadiazole **6a** was achieved by acidic reduction with zinc according to the literature method[18] and the products 2,2-difluoro-4-phenyl-but-3-enoic acid ethyl ester **7a** and 5-(1,1-difluoro-3-phenyl-allyl)-3-phenyl-[1,2,4]oxadiazole **7b** were obtained in 70% and 80% yield, respectively (Scheme 4). The products had *Z*-configuration implying retention of stereochemistry during zinc reduction.

The determination of the configuration was based on the coupling constant across the double bond on ^{1}H NMR spectra. It is well-known that in 1,2-substituted ethylenic compounds the $^3J_{trans}$ constant is always larger than the $^3J_{cis}$ constant. A doublet of triplet centered at 6.95 ppm (J_{H4-H3}=12.6 Hz, J_{H4-F}=1.7 Hz) of **7a** is observed for the H_4 proton, which shows the ^{1}H NMR features described by Chen and Long and Reglier et al.[19] Similarly, the $^3J_{H-H}$ constant of **7b** is 12.5 Hz, hence the configuration is ascertained as *Z*-isomer.



Scheme 4.

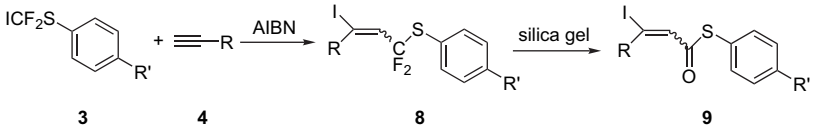
Previous reports showed that halogen exchange reaction of fluoroalkyl bromide in the presence of NaI usually proceeded easily in acetone[20] or butanone.[21] Unfortunately, the reaction of bromodifluoromethyl phenyl thioether with NaI did not occur when only acetone or butanone was used as solvent. In DMF solution, bromodifluoromethyl phenyl thioether was converted completely in several hours into a complicated mixture with less than 10% of **3** formed. When the reaction was carried out in the mixture of acetone and DMF (4.4:1, v/v), it went on smoothly yielding 56% of **3a** and 50% of **3b** after fractional distillation.

Different from **5** and **6**, adducts **8** prepared from iododifluoromethyl phenyl thioether analogues **3** and terminal alkynes **4** were not stable. The difluoromethylene moiety was hydrolyzed into carbonyl group in air or during column chromatography on silica gel except for strong electron-withdrawing ester **4b**. The detailed results are summarized in Table 2. In the case of **4b** (entries 3 and 4), a triplet of CF_2 group was observed on the ^{13}C NMR spectra of the final products. However, the conversions of **3** were only 36% and 30% to give adduct products **8** in 27% and 23% yields, respectively. In the case of **4a** (entries 1 and 2), the hydrolyzed products were obtained in 85% and 76% yields through a long time column chromatography on silica gel. In the case of electron-donating alkyl group and trimethylsilyl groups **4c** and **4d** (entries 5–8), intermediates **8** could convert to **9** easily during column chromatography. The O=C–S moiety could be identified by ^{13}C NMR spectroscopy, which could reach to δ 185 ppm. The possible explanation was that when oxygen, sulfur, and nitrogen in particular, adjacent to carbon–fluorine bonds, it greatly increased the reactivity toward nucleophiles.[22]

Difluoromethylene vinylic iodides are valuable intermediates in a variety of synthetic applications. The Sonogashira coupling reaction is one of the very useful methods for the synthesis of fluorinated conjugated enynes. Under the cocatalysis of $PdCl_2(PPh_3)_2$ (2 mol %) and CuI (5 mol %), the Sonogashira cross-coupling reaction of difluoromethylene vinyl iodide **5a** with phenylethyne was systematically examined first, especially with bases and solvents. We found that the base influenced the reaction drastically. When 1 equiv base (for example, Et_3N and DABCO) was used, the reaction did not occur or underwent very slowly even at reflux (Table 3, entries 2, 3, and 9). In contrast, the reactions were complicated while the base was excessively used (Table 3, entries 1 and 5). Using 1.5 equiv of 1,4-diazabicyclo[2,2,2]octane (DABCO) as a base in THF, the reaction proceeded very well to form difluorinated enyne **10a** in good yield (Table 3, entry 10). The results are summarized in Table 3.

The palladium/copper(I) iodide cocatalyzed coupling reaction of difluoromethylene vinyl iodides **5a** and **6a** with terminal alkynes **4** gave substituted difluorinated enynes **10** and **11**. The results are summarized in Table 4. Both aromatic (Table 4, entries 1 and 7) and aliphatic acetylenes (Table 4, entries 2–5) worked well. The low yields in entries 8 and 9 were due to incomplete reaction even at reflux for 48 h. Another reason was that it was difficult to isolate products by column chromatography because the polarity of the product was similar to that of the substrate.

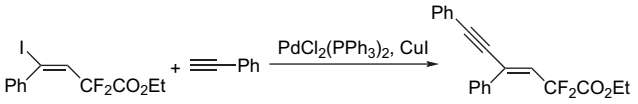
Table 2. AIBN-initiated addition of iododifluoromethyl phenyl thioether **3** to terminal alkynes **4**



Entry	R′	Alkyne **4**	Conversion[a] (%)	Yield of **8**[b] (%)	Yield of **9**[b] (%)	E/Z ratio[c]
1	H (**3a**)	Ph (**4a**)	89	—	85 (**9aa**)	100:0
2	Cl (**3b**)	Ph (**4a**)	85	—	76 (**9ab**)	7.6:1
3	H (**3a**)	COOMe (**4b**)	36	27 (**8ba**)	—	2.7:1
4	Cl (**3b**)	COOMe (**4b**)	30	23 (**8bb**)	—	1.4:1
5	H (**3a**)	C_4H_9 (**4c**)	71	—	64 (**9ca**)	1:3.4
6	Cl (**3b**)	C_4H_9 (**4c**)	68	—	50 (**9cb**)	1:1.8
7	H (**3a**)	TMS (**4d**)	92	—	36 (**9da**)	1:2.0
8	Cl (**3b**)	TMS (**4d**)	88	—	31 (**9db**)	1:2.2

[a] The conversion was determined by GC analysis.
[b] Isolated yield.
[c] Determined by NMR spectra.

Table 3. Optimization of reaction conditions for the $PdCl_2(PPh_3)_2$/CuI-cocatalyzed Sonogashira coupling reaction of **5a** with phenylethyne



5a **10a**

Entry	Base	Solvent	Temp	Conversion (%)	Yield[a] (%)
1	Et_3N	Et_3N	rt	Complicate	
2	Et_3N (1 equiv)	THF	rt	[b]	
3	Et_3N (1 equiv)	THF	Reflux	82[c]	
4	Et_3N (1.5 equiv)	CH_3CN	rt	100	63
5	Et_3N (4 equiv)	CH_3CN	rt	Complicate	
6	Pyridine (1.5 equiv)	CH_3CN	rt	Complicate	
7	Piperidine (4 equiv)	THF	rt	[d]	
8	K_2CO_3 (1.5 equiv)	THF	Reflux	100	46
9	DABCO (1 equiv)	THF	rt	83[c]	
10	**DABCO (1.5 equiv)**	**THF**	**rt**	**100**	**86**
11	DABCO (1.5 equiv)	CH_3CN	rt	100	75

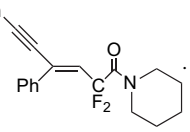
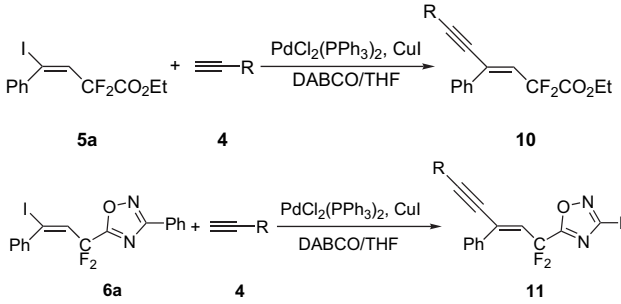
[a] Isolated yield.
[b] No reaction occurred.
[c] The conversion was determined by GC analysis.
[d] The product was  .

Table 4. $PdCl_2(PPh_3)_2$/CuI-cocatalyzed Sonogashira coupling reaction of difluoromethylene vinylic iodides **5a** and **6a** with terminal alkyne **4**



5a **4** **10**

6a **4** **11**

Entry	Substance	Alkyne	Product	Yield of **10** or **11**[a] (%)
1	**5a**	Ph (**4a**)	**10a**	86
2	**5a**	C_4H_9 (**4c**)	**10b**	72
3	**5a**	TMS (**4d**)	**10c**	72
4	**5a**	CH_2OCOPh (**4f**)	**10d**	66
5	**5a**	C_6H_{13} (**4h**)	**10e**	62
6	**5a**	*t*-C_4H_9 (**4i**)	**10f**	37[b]
7	**6a**	Ph (**4a**)	**11a**	72
8	**6a**	C_4H_9 (**4c**)	**11b**	31[c]
9	**6a**	TMS (**4d**)	**11c**	55[c]

[a] Isolated yield.
[b] The K_2CO_3 was used as base at reflux.
[c] The substance does not react completely at reflux the conversion was 40% and 63%, respectively.

3. Conclusions

In conclusion, we have developed a convenient procedure to prepare difluoromethylene vinyl iodides. By utilizing AIBN as an initiator, the difluoromethylene vinyl iodides were obtained from *gem*-difluorinated alkyl iodides and the geometric selectivity of aromatic acetylenes was high. The adducts **8**, except for strong electron-withdrawing ester **4b**, were not stable, therefore, the difluoromethylene moiety was hydrolyzed into carbonyl group on prolonged standing in air or during column chromatography on silica gel. We have also developed a facile method for the preparation of difluoromethylene enyenes via palladium-catalyzed cross-coupling of difluoromethylene vinyl iodides with terminal alkynes.

4. Experimental

4.1. General

Melting points were uncorrected. IR spectra were measured on a Nicolet Magna IR-550 spectrometer. High-resolution

mass spectra were carried out on a Finnigan GC–MS-4021 spectrometer. ^{1}H (500 MHz) and ^{13}C (125.8 MHz) NMR spectra were recorded on a Bruker AC-500 spectrometer with Me_4Si as an internal standard. ^{19}F NMR spectra were obtained on a Bruker AC-500 (470 MHz) spectrometer in $CDCl_3$ with $CFCl_3$ as an external standard, downfield shifts being designated as negative. All chemical shifts (δ) are expressed in parts per million, and coupling constants (J) are given in hertz.

4.2. General procedure for the addition of difluoromethylene iodides to terminal alkynes

Under nitrogen atmosphere, a mixture of difluoromethylene iodides (5.0 mmol), alkyne **4** (6.0 mmol), and AIBN (100 mg) was stirred at 65 °C for 16 h. The reaction mixture was directly purified by flash column chromatography (silica gel, eluting with petroleum ether/ethyl acetate=20:1) to give **5**.

4.2.1. 2,2-Difluoro-4-iodo-4-phenyl-but-3-enoic acid ethyl ester (5a). Light yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.31 (5H, s), 6.72 (1H, t, J_{H-F}=10.9 Hz), 3.97 (2H, q, J=7.2 Hz), 1.19 (3H, t, J=7.2 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −94.92 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.2 (t, J=33.3 Hz), 141.4, 133.7 (t, J=28.4 Hz), 130.1, 128.7, 128.4, 111.5 (t, J=250.3 Hz), 109.4 (t, J=10.1 Hz), 63.8, 14.3; EIMS (*m*/*z*) 352 (M^+, 1) 279 (15), 225 (37), 197 (52), 169 (100), 102 (29), 91 (46); IR (cm^{-1}, KBr) 2984, 1772, 1630, 697; HRMS calcd for $C_{12}H_{11}F_2IO_2$: 351.9772, found: 351.9771.

4.2.2. 4,4-Difluoro-2-iodo-pent-2-enedioic acid 5-ethyl ester 1-methyl ester (5b). Light yellow liquid; *E*/*Z*=3.2:1. *Z*-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 (1H, t, J_{H-F}=11.4 Hz), 4.40 (2H, q, J=7.1 Hz), 3.90 (3H, s), 1.38 (3H, t, J=7.1 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −101.45 (2F, d, J_{H-F}=9.4 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.0, 162.1 (t, J=33.3 Hz), 142.3 (t, J=29.9 Hz), 112.3 (t, J=249.4 Hz), 99.4 (t, J=9.6 Hz), 64.4, 55.1, 14.5.

E-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.89 (1H, t, J_{H-F}=11.9 Hz), 4.35 (2H, q, J=7.1 Hz), 3.81 (3H, s), 1.36 (3H, t, J=7.1 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −98.92 (2F, d, J_{H-F}=14.1 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 164.4, 162.6 (t, J=33.3 Hz), 141.1 (t, J=29.8 Hz), 111.5 (t, J=250.8 Hz), 95.1 (t, J=9.6 Hz), 64.0, 54.3, 14.5.

EIMS (*m*/*z*) 334 (M^+, 8), 262 (100), 207 (12); IR (cm^{-1}, KBr) 2986, 2957, 1777, 1738, 1625, 773; HRMS calcd for $C_8H_9F_2IO_4$: 333.9514, found: 333.9514.

4.2.3. 2,2-Difluoro-4-iodo-oct-3-enoic acid ethyl ester (5c). Colorless liquid; *E*/*Z*=4.2:1. *Z*-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.38 (1H, t, J_{H-F}=12.9 Hz), 4.36 (2H, q, J=7.1 Hz), 2.61 (2H, t, J=7.4 Hz), 1.59–1.49 (2H, m), 1.39–1.30 (5H, m), 0.93 (3H, t, J=7.3 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −98.81 (2F, d, J_{H-F}=11.3 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.2 (t, J=34.4 Hz), 128.8 (t, J=29.6 Hz), 115.5 (t, J=9.7 Hz), 112.7 (t, J=247.7 Hz), 63.8, 47.1, 31.6, 21.8, 14.5, 14.4.

E-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.40 (1H, t, J_{H-F}=13.3 Hz), 4.34 (2H, q, J=7.2 Hz), 2.61 (2H, t, J=7.4 Hz), 1.59–1.49 (2H, m), 1.39–1.30 (5H, m), 0.93 (3H, t, J=7.3 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −98.69 (2F, d, J_{H-F}=13.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.8 (t, J=34.4 Hz), 131.9 (t, J=27.0 Hz), 120.2 (t, J=7.5 Hz), 112.2 (t, J=252.4 Hz), 63.9, 41.2, 32.6, 22.2, 14.6, 14.5.

EIMS (*m*/*z*) 332 (M^+, 3), 259 (29), 205 (81), 177 (100); IR (cm^{-1}, KBr) 2961, 1769, 1631; HRMS calcd for $C_{10}H_{15}F_2IO_2$: 332.0085, found: 332.0079.

4.2.4. 2,2-Difluoro-4-iodo-4-trimethylsilanyl-but-3-enoic acid ethyl ester (5d). Light yellow liquid; *E*/*Z*=1:2.3. *Z*-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37 (1H, t, J_{H-F}=14.7 Hz), 4.34 (2H, q, J=7.1 Hz), 1.36 (3H, t, J=7.1 Hz), 0.32 (9H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −98.57 (2F, d, J_{H-F}=14.6 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.3 (t, J=34.3 Hz), 144.4 (t, J=25.9 Hz), 124.1 (t, J=7.0 Hz), 112.4 (t, J=252.1 Hz), 64.0, 14.5, 1.8.

E-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.92 (1H, t, J_{H-F}=11.1 Hz), 4.36 (2H, q, J=7.1 Hz), 1.36 (3H, t, J=7.1 Hz), 0.24 (9H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −99.82 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.1 (t, J=35.0 Hz), 139.0 (t, J=29.0 Hz), 120.0, 112.9 (t, J=252.1 Hz), 63.9, 14.5, −1.3.

EIMS (*m*/*z*) 348 (M^+, 3), 333 (10), 305 (27), 221 (75), 178 (100), 77 (31); IR (cm^{-1}, KBr) 2961, 1774, 848, 765; HRMS calcd for $C_9H_{15}F_2IO_2Si$: 347.9854, found: 347.9855.

4.2.5. 2,2-Difluoro-4-iodo-5-(toluene-4-sulfonyloxy)-pent-3-enoic acid ethyl ester (5e). Light yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73 (2H, d, J=8.3 Hz), 7.31 (2H, d, J=8.1 Hz), 6.64 (1H, tt, J_{H-F}=11.5 Hz, J_{H-H}=1.7 Hz), 4.62–4.60 (2H, m), 4.27 (2H, q, J=7.1 Hz), 2.39 (3H, s), 1.28 (3H, t, J=7.1 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ −100.42 (2F, dt, J_{H-F}=9.4, 2.4 Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 161.0 (t, J=33.7 Hz), 144.7, 131.4, 129.1, 128.5 (t, J=29.4 Hz), 127.0, 110.4 (t, J=249.8 Hz), 100.4 (t, J=8.7 Hz), 74.4, 62.5, 20.7, 12.9; EIMS (*m*/*z*) 460 (M^+, 1), 333 (86), 305 (27), 155 (100), 91 (65); IR (cm^{-1}, KBr) 3047, 2985, 1771, 1369, 1177, 667; HRMS calcd for $C_{14}H_{15}F_2IO_5S$: 459.9653, found: 459.9650.

4.2.6. Benzoic acid 4-ethoxycarbonyl-4,4-difluoro-2-iodo-but-2-enyl ester (5f). White solid; mp 124–125 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.10 (2H, d, J=8.1 Hz), 7.60 (1H, t, J=7.4 Hz), 7.47 (2H, t, J=7.7 Hz), 6.71 (1H, t, J_{H-F}=13.3 Hz), 5.13 (2H, s), 4.36 (2H, q, J=7.1 Hz), 1.35 (3H, t, J=7.1 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ −98.61 (2F, d, J_{H-F}=13.2 Hz); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 166.0, 163.4 (t, J=33.8 Hz), 135.0 (t, J=27.9 Hz), 134.1, 130.6, 130.0, 129.2, 112.2 (t, J=253.2 Hz), 110.7 (t, J=7.4 Hz), 66.3, 64.4, 14.5; EIMS (*m*/*z*) 410 (M^+, 1), 283 (100), 255 (28), 105 (86), 77 (15); IR (cm^{-1}, KBr) 3064, 2985, 1769, 1729, 1635, 712; HRMS calcd for $C_{14}H_{13}F_2IO_4$: 409.9827, found: 409.9833.

4.2.7. 4,4-Difluoro-2-iodo-3-methoxycarbonyl-pent-2-enedioic acid 5-ethyl ester 1-methyl ester (5h). Light yellow liquid; *E*/*Z*=1:1; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.40

(4H, q, J=7.2 Hz), 3.90–3.81 (12H, m), 1.38 (3H, t, J=7.2 Hz), 1.36 (3H, t, J=7.2 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −99.51 (2F, s), −101.51 (2F, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 165.0, 164.9, 162.8, 162.0, 161.1 (t, J=33.0 Hz), 160.9 (t, J=32.7 Hz), 138.3 (t, J=26.0 Hz), 137.2 (t, J=26.2 Hz), 110.9 (t, J=255.4 Hz), 110.4 (t, J=255.9 Hz), 101.0 (t, J=5.2 Hz), 98.5 (t, J=6.0 Hz), 63.9, 63.7, 54.0, 53.8, 53.3, 53.2, 13.8, 13.8; EIMS (m/z) 392 (M^+, 5), 288 (100), 265 (19); IR (cm^{-1}, KBr) 2957, 1779, 1741, 1613, 1259, 772; HRMS calcd for $C_{10}H_{11}F_2IO_6$: 391.9568, found: 391.9568.

4.2.8. 5-(1,1-Difluoro-3-iodo-3-phenyl-allyl)-3-phenyl-[1,2,4]oxadiazole (6a). Colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.95–7.93 (2H, m), 7.54–7.45 (3H, m), 7.22–7.11 (5H, m), 7.01 (1H, t, J_{H-F}=9.9 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −87.4 (2F, d, J_{H-F}=9.9 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 172.3 (t, J=35.2 Hz), 170.2, 142.0, 134.7 (t, J=29.0 Hz), 133.4, 131.1, 130.6, 129.8, 129.3, 129.0, 127.2, 112.8 (t, J=244.4 Hz), 112.4 (t, J=10.1 Hz); EIMS (m/z) 424 (M^+, 4), 297 (3), 269 (100), 167 (28), 77 (5); IR (cm^{-1}, KBr) 3059, 1629, 1445, 756, 697; HRMS calcd for $C_{17}H_{11}F_2IN_2O$: 423.9884, found: 423.9876.

4.2.9. 5-(1,1-Difluoro-3-iodo-hept-2-enyl)-3-phenyl-[1,2,4]oxadiazole (6c). Colorless liquid; E/Z=3:1. E-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12–8.09 (2H, m), 7.55–7.48 (3H, m), 6.73 (1H, t, J_{H-F}=12.8 Hz), 2.65 (2H, t, J=7.5 Hz), 1.58–1.51 (2H, m), 1.37–1.29 (2H, m), 0.90 (3H, t, J=7.4 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −89.9 (2F, d, J_{H-F}=12.7 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.3 (t, J=36.4 Hz), 168.9, 131.9, 130.9 (t, J=26.7 Hz), 129.0, 127.7, 125.5, 121.3 (t, J=7.2 Hz), 111.6 (t, J=246.1 Hz), 40.9, 32.0, 21.6, 13.8.

Z-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.14–8.10 (2H, m), 7.57–7.48 (3H, m), 6.68 (1H, t, J_{H-F}=10.9 Hz), 2.66 (2H, t, J=7.2 Hz), 1.60–1.53 (2H, m), 1.40–1.30 (2H, m), 0.95 (3H, t, J=7.4 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −90.6 (2F, d, J_{H-F}=10.3 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.0 (t, J=35.9 Hz), 168.9, 131.8, 129.0, 127.7, 127.6 (t, J=29.9 Hz), 125.8, 118.0 (t, J=9.7 Hz), 112.2 (t, J=241.7 Hz), 46.7, 31.1, 21.2, 13.7.

EIMS (m/z) 404 (M^+, 2), 322 (30), 277 (11), 195 (100), 145 (37), 77 (16); IR (cm^{-1}, KBr) 3066, 2960, 1632, 1446, 755, 692; HRMS calcd for $C_{15}H_{15}F_2IN_2O$: 404.0197, found: 404.0197.

4.2.10. 4,4-Difluoro-2-iodo-4-(3-phenyl-[1,2,4]oxadiazol-5-yl)-but-2-en-1-ol (6g). Colorless liquid; E/Z=1:2.1. E-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.01–7.98 (2H, m), 7.51–7.42 (3H, m), 6.76 (1H, t, J_{H-F}=12.9 Hz), 4.39 (2H, d, J=5.5 Hz), 2.49 (1H, t, J=6.8 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −88.63 (2F, d, J_{H-F}=13.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 170.0 (t, J=36.1 Hz), 167.8, 131.0, 130.8 (t, J=28.2 Hz), 128.1, 126.6, 124.3, 118.6 (t, J=7.5 Hz), 110.4 (t, J=245.8 Hz), 65.2.

Z-Isomer: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.04–8.00 (2H, m), 7.48–7.40 (3H, m), 7.10 (1H, t, J_{H-F}=11.2 Hz), 4.30 (2H, s), 2.74 (1H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −91.14 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 169.9 (t, J=35.9 Hz), 167.9, 130.9, 128.1, 126.6, 124.7 (t, J=29.6 Hz), 124.5, 114.2 (t, J=8.6 Hz), 111.3 (t, J=242.6 Hz), 70.7.

EIMS (m/z) 378 (M^+, 3), 251 (54), 145 (100), 77 (57); IR (cm^{-1}, KBr) 3439, 3037, 1650, 1066, 755, 691; HRMS calcd for $C_{12}H_9F_2IN_2O_2$: 377.9677, found: 377.9676.

4.3. General procedure for the reduction of difluoromethylene vinylic iodides

A mixture of **5a** (1.0 mmol), AcOH (0.5 mL), water (0.5 mL), and freshly activated zinc powder (75 mg, 1.2 mmol) was stirred at room temperature. After completion of the reaction, the mixture was diluted with water (5 mL), extracted with $CHCl_3$ (5 mL×2), and dried with $MgSO_4$. Column chromatography gave **7a** in 80% yield.

4.3.1. 5-(1,1-Difluoro-3-phenyl-allyl)-3-phenyl-[1,2,4]oxadiazole (7b). Colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.98–7.96 (2H, m), 7.51–7.42 (3H, m), 7.29–7.17 (5H, m), 7.11 (1H, d, J_{H-H}=12.5 Hz), 6.17 (1H, q, J=12.5 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −87.3 (2F, d, J_{H-F}=12.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 172.2 (t, J=35.6 Hz), 169.2, 141.1 (t, J=8.2 Hz), 134.5, 132.3, 129.5, 129.4, 129.3, 128.8, 128.2, 126.3, 122.4 (t, J=27.5 Hz), 112.9 (t, J=244.4 Hz); EIMS (m/z) 298 (M^+, 79), 195 (35), 133 (100), 103 (58), 77 (25); IR (cm^{-1}, KBr) 3062, 1648, 1446, 759, 695; HRMS calcd for $C_{17}H_{12}F_2N_2O$: 298.0918, found: 298.0919.

4.4. General procedure for the preparation of 3

The mixture of bromodifluoromethyl phenyl thioether (0.126 mol), NaI (57 g, 0.38 mol), acetone (88 mL), and DMF (20 mL) was stirred at reflux for a week. After evaporation of acetone, water (60 mL) was added. The mixture was extracted with ethyl ether (3×50 mL). The organic layer was combined and washed with saturated Na_2SO_3 and brine. After removal of the solvent, the residue underwent fractional distillation to give a pale yellow oil **3a** in 56% yield (bp 70–72 °C/1 mmHg) and **3b** in 50% yield (bp 80–84 °C/1 mmHg).

4.5. General procedure for the addition of iododifluoromethyl phenyl thioether and derivative 3 to terminal alkynes

Under nitrogen atmosphere, a mixture of iododifluoromethyl phenyl thioether and derivative **3** (5.0 mmol), alkyne **4** (6.0 mmol) and AIBN (100 mg) were stirred at 65 °C for 24 h. The reaction mixture was dissolved in CH_2Cl_2 (20 mL), and then silica gel (200–300 mesh) was added. The solvent was evaporated to dryness and the powder was exposed to air overnight, and then purified by flash column chromatography (silica gel, eluting with petroleum ether/ethyl acetate=100:1).

4.5.1. 3-Iodo-3-phenyl-thioacrylic acid *S*-phenyl ester (9aa). Yellow solid; mp 130–131 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37–7.27 (10H, m), 7.15 (1H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 185.8, 142.6, 137.9, 135.1, 130.3,

130.2, 129.9, 128.7, 128.6, 127.8, 117.3; EIMS (*m/z*) 366 (M^+, 0.2), 257 (100), 129 (12), 102 (36); IR (cm^{-1}, KBr) 3051, 1689, 1577. Anal. Calcd for $C_{15}H_{11}IOS$: C, 49.20; H, 3.03. Found: C, 49.36; H, 2.96.

4.5.2. 3-Iodo-3-phenyl-thioacrylic acid *S*-(4-chloro-phenyl) ester (9ab). Yellow solid; mp 103–104 °C; *E*/*Z*=7.6:1. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42–7.22 (9H, m), 7.08 (1H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 186.0, 143.9, 136.8, 136.4, 131.5, 131.2, 130.2, 129.7, 129.2, 126.1, 114.0.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42–7.22 (9H, m), 7.14 (1H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 185.1, 142.5, 137.5, 136.7, 136.3, 130.4, 130.1, 128.7, 128.5, 126.2, 118.1.

EIMS (*m/z*) 400 (M^+, 0.1), 257 (100), 102 (41); IR (cm^{-1}, KBr) 3050, 1691, 1570, 1092. Anal. Calcd for $C_{15}H_{10}ClIOS$: C, 44.97; H, 2.52. Found: C, 45.39; H, 2.36.

4.5.3. 4,4-Difluoro-2-iodo-4-phenylsulfanyl-but-2-enoic acid methyl ester (8ba). Light yellow liquid; *E*/*Z*=2.7:1. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.67–7.44 (5H, m), 7.56 (1H, t, J_{H-F}=10.4 Hz), 3.85 (3H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −71.84 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.6, 143.5 (t, *J*=30.1 Hz), 137.5, 131.1, 129.9, 128.2, 125.4 (t, *J*=279.5 Hz), 97.5, 55.0.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.61–7.37 (5H, m), 6.49 (1H, t, J_{H-F}=10.7 Hz), 3.78 (3H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −71.79 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 165.8, 137.5 (t, *J*=27.9 Hz), 137.4, 131.0, 129.9, 126.2, 125.6 (t, *J*=279.5 Hz), 91.5 (t, *J*=6.1 Hz), 53.9.

EIMS (*m/z*) 370 (M^+, 8), 261 (100), 243 (32), 223 (28), 134 (6), 109 (18); IR (cm^{-1}, KBr) 2952, 1737, 751; HRMS calcd for $C_{11}H_9F_2IO_2S$: 369.9336, found: 369.9336.

4.5.4. 4-(4-Chloro-phenylsulfanyl)-4,4-difluoro-2-iodo-but-2-enoic acid methyl ester (8bb). Light yellow liquid; *E*/*Z*=1.4:1. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.58 (2H, d, *J*=8.3 Hz), 7.38 (2H, d, *J*=8.3 Hz), 7.56 (1H, t, J_{H-F}=10.5 Hz), 3.87 (3H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −71.7 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.5, 143.1 (t, *J*=29.9 Hz), 138.7, 137.9, 130.2, 130.0, 125.2 (t, *J*=280.1 Hz), 98.0, 55.0.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.52 (2H, d, *J*=8.4 Hz), 7.38 (2H, d, *J*=8.3 Hz), 6.50 (1H, t, J_{H-F}= 10.7 Hz), 3.79 (3H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −71.7 (2F, d, J_{H-F}=10.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 165.7, 138.6, 137.8, 137.2 (t, *J*=27.9 Hz), 130.2, 130.0, 125.4 (t, *J*=280.1 Hz), 92.0 (t, *J*=6.1 Hz), 54.0.

EIMS (*m/z*) 406 (M+2$^+$, 7), 404 (M^+, 18), 279 (12), 277 (32), 261 (100); IR (cm^{-1}, KBr) 2953, 1736, 1093, 745; HRMS calcd for $C_{11}H_8ClF_2IO_2S$: 403.8946, found: 403.8946.

4.5.5. 3-Iodo-hept-2-enethioic acid *S*-phenyl ester (9ca). Light yellow liquid; *E*/*Z*=1:3.4. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42 (5H, s), 6.97 (1H, s), 3.05 (2H, t, *J*=7.5 Hz), 1.56–1.49 (2H, m), 1.37–1.29 (2H, m), 0.89 (3H, t, *J*=7.3 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 186.0, 136.8, 135.2, 130.3, 129.9, 129.9, 118.9, 42.9, 32.6, 22.3, 14.5.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.42 (5H, s), 6.78 (1H, s), 2.69 (2H, t, *J*=7.4 Hz), 1.62–1.56 (2H, m), 1.37–1.29 (2H, m), 0.94 (3H, t, *J*=7.4 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 186.0, 136.8, 135.2, 130.2, 130.0, 128.0, 118.8, 48.4, 32.1, 22.1, 14.5.

EIMS (*m/z*) 346 (M^+, 1), 237 (100), 219 (3), 109 (11); IR (cm^{-1}, KBr) 2957, 1689, 1584, 745; HRMS calcd for $C_{13}H_{15}IOS$: 345.9888, found: 345.9887.

4.5.6. 3-Iodo-hept-2-enethioic acid *S*-(4-chloro-phenyl) ester (9cb). Light yellow liquid; *E*/*Z*=1:1.8. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.40–7.36 (4H, m), 6.95 (1H, s), 3.05 (2H, t, *J*=7.5 Hz), 1.55–1.47 (2H, m), 1.37–1.29 (2H, m), 0.89 (3H, t, *J*=7.4 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 185.3, 136.7, 136.3, 130.1, 129.8, 126.4, 119.8, 42.9, 32.5, 22.3, 14.5.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35–7.32 (4H, m), 6.78 (1H, s), 2.70 (2H, t, *J*=7.4 Hz), 1.61–1.55 (2H, m), 1.37–1.29 (2H, m), 0.94 (3H, t, *J*=7.4 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 185.2, 136.6, 136.4, 130.9, 130.1, 126.3, 119.8, 48.5, 32.1, 21.9, 14.4.

EIMS (*m/z*) 382 (M+2$^+$, 1), 380 (M^+, 2), 237 (100), 145 (5), 143 (16); IR (cm^{-1}, KBr) 2958, 1691, 1584, 746; HRMS calcd for $C_{13}H_{14}ClIOS$: 379.9499, found: 379.9480.

4.5.7. 3-Iodo-3-trimethylsilanyl-thioacrylic acid *S*-phenyl ester (9da). Light yellow liquid; *E*/*Z*=1:2. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.66 (1H, s), 7.22 (5H, s), 0.08 (9H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 187.4, 150.2, 134.9, 130.3, 130.0, 130.0, 127.8, 1.4.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.26 (5H, s), 7.10 (1H, s), 0.06 (9H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 186.2, 139.4, 135.1, 133.2, 130.3, 127.8, 123.3, −0.9.

EIMS (*m/z*) 362 (M^+, 4), 347 (13), 253 (100), 235 (15), 109 (20); IR (cm^{-1}, KBr) 2954, 1682, 1539, 843, 746; HRMS calcd for $C_{12}H_{15}IOSSi$: 361.9658, found: 361.9654.

4.5.8. 3-Iodo-3-trimethylsilanyl-thioacrylic acid *S*-(4-chloro-phenyl) ester (9db). Light yellow liquid; *E*/*Z*= 1:2.2. *Z*-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.85 (1H, s), 7.41–7.38 (4H, m), 0.27 (9H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 187.3, 149.9, 136.3, 136.2, 130.3, 130.2, 126.3, 1.3.

E-Isomer: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.35–7.33 (4H, m), 7.29 (1H, s), 0.26 (9H, s); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 185.8, 139.1, 136.8, 136.2, 134.2, 126.3, 124.3, 1.3.

EIMS (*m/z*) 398 (M+2$^+$, 1), 396 (M^+, 2), 383 (5), 381 (11), 253 (100) 145 (7), 143 (18); IR (cm^{-1}, KBr) 2955, 1685, 1539, 844, 759; HRMS calcd for $C_{12}H_{14}ClIOSSi$: 395.9268, found: 395.9265.

4.6. General procedure for the cross-coupling of 5a and 6a with terminal alkyne 4

Under nitrogen atmosphere, a mixture of **5a** (0.5 mmol), alkyne **4** (0.8 mmol), $PdCl_2(PPh_3)_2$ (2 mol %), CuI (5 mol %), and DABCO (0.75 mmol) was stirred in THF at room temperature overnight. The reaction mixture was extracted with ethyl ether (2×20 mL), which was washed with water (2×10 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by flash column chromatography (silica gel, eluting with petroleum ether/ethyl acetate=50:1) to give **10**.

4.6.1. 2,2-Difluoro-4,6-diphenyl-hex-3-en-5-ynoic acid ethyl ester (10a). Red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48–7.30 (10H, m), 6.35 (1H, t, J_{H-F}=12.3 Hz), 3.92 (2H, q, J=7.2 Hz), 1.14 (3H, t, J=7.2 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −92.9 (2F, d, J_{H-F}=12.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.5 (t, J=33.6 Hz), 136.2, 134.4 (t, J=10.0 Hz), 132.5, 129.8, 129.7, 129.4, 129.1, 128.9, 127.5 (t, J=28.0 Hz), 122.8, 112.6 (t, J=245.6 Hz), 94.3, 89.8, 63.6, 14.3; EIMS (*m*/*z*) 326 (M^+, 20), 253 (100), 127 (27); IR (cm^{-1}, KBr) 3059, 2985, 2205, 1772, 1617, 757, 693; HRMS calcd for $C_{20}H_{16}F_2O_2$: 326.1118, found: 326.1109.

4.6.2. 2,2-Difluoro-4-phenyl-dec-3-en-5-ynoic acid ethyl ester (10b). Red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38–7.32 (5H, m), 6.17 (1H, t, J_{H-F}=12.3 Hz), 3.88 (2H, q, J=7.2 Hz), 2.35 (2H, t, J=7.1 Hz), 1.56–1.49 (2H, m), 1.45–1.38 (2H, m), 1.11 (3H, t, J=7.2 Hz), 0.91 (3H, t, J=7.3 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −92.4 (2F, d, J_{H-F}=12.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 164.7 (t, J=33.6 Hz), 137.8, 136.0 (t, J=10.1 Hz), 130.6, 130.2, 129.7, 127.6 (t, J=28.2 Hz), 113.7 (t, J=245.0 Hz), 97.4, 82.6, 64.5, 32.1, 23.7, 20.8, 15.3, 15.2; EIMS (*m*/*z*) 306 (M^+, 10), 233 (100), 127 (10), 91 (3); IR (cm^{-1}, KBr) 3059, 2960, 2872, 2219, 1772, 1619, 776, 699; HRMS calcd for $C_{18}H_{20}F_2O_2$: 306.1431, found: 306.1428.

4.6.3. 2,2-Difluoro-4-phenyl-6-trimethylsilanyl-hex-3-en-5-ynoic acid ethyl ester (10c). Red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.40–7.33 (5H, m), 6.29 (1H, t, J_{H-F}=12.2 Hz), 3.89 (2H, q, J=7.2 Hz), 1.11 (3H, t, J=7.2 Hz), 0.20 (9H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −92.9 (2F, d, J_{H-F}=12.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.4 (t, J=33.5 Hz), 135.9, 134.2 (t, J=9.9 Hz), 129.8, 129.3, 128.8, 128.4 (t, J=28.2 Hz), 112.4 (t, J=245.4 Hz), 104.8, 100.0, 63.6, 14.3, 0.3; EIMS (*m*/*z*) 322 (M^+, 13), 307 (9), 249 (100), 152 (22), 77 (6); IR (cm^{-1}, KBr) 3060, 2962, 2151, 1774, 1615, 761, 699; HRMS calcd for $C_{17}H_{20}F_2O_2Si$: 322.1201, found: 322.1200.

4.6.4. Benzoic acid 6-ethoxycarbonyl-6,6-difluoro-4-phenyl-hex-4-en-2-ynyl ester (10d). Light yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.07 (2H, d, J=8.3 Hz), 7.60–7.34 (8H, m), 6.31 (1H, t, J_{H-F}=12.1 Hz), 5.08 (2H, s), 3.90 (2H, q, J=7.2 Hz), 1.12 (3H, t, J=7.2 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −93.4 (2F, d, J_{H-F}=11.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 166.4, 163.3 (t, J=33.6 Hz), 135.5, 134.1 (t, J=6.6 Hz), 133.3 (t, J=9.9 Hz), 130.5, 130.0, 129.2, 129.1, 128.9, 112.3 (t, J=245.7 Hz), 88.0, 86.7, 63.7, 53.5, 14.2; EIMS (*m*/*z*) 384 (M^+, 16), 311 (7), 253 (13), 105 (100), 77 (10); IR (cm^{-1}, KBr) 3300, 3063, 2928, 2855, 1772, 1727, 1621, 777, 713; HRMS calcd for $C_{22}H_{18}F_2O_4$: 384.1173, found: 384.1174.

4.6.5. 2,2-Difluoro-4-phenyl-dodec-3-en-5-ynoic acid ethyl ester (10e). Red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38–7.32 (5H, m), 6.17 (1H, t, J_{H-F}=12.3 Hz), 3.88 (2H, q, J=7.2 Hz), 2.34 (2H, t, J=7.2 Hz), 1.57–1.51 (2H, m), 1.42–1.25 (6H, m), 1.12 (3H, t, J=7.2 Hz), 0.88 (3H, t, J=7.0 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −92.5 (2F, d, J_{H-F}=12.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.7 (t, J=33.5 Hz), 136.9, 135.0 (t, J=10.1 Hz), 129.6, 129.2, 128.7, 126.5 (t, J=28.2 Hz), 112.7 (t, J=245.1 Hz), 96.5, 81.6, 63.5, 31.9, 29.2, 29.0, 23.2, 20.2, 14.7, 14.3; EIMS (*m*/*z*) 334 (M^+, 11), 261 (100), 127 (16), 91(9); IR (cm^{-1}, KBr) 2930, 2858, 2219, 1773, 1618, 699; HRMS calcd for $C_{20}H_{24}F_2O_2$: 334.1744, found: 334.1744.

4.6.6. 2,2-Difluoro-7,7-dimethyl-4-phenyl-oct-3-en-5-ynoic acid ethyl ester (10f). Red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.39–7.31 (5H, m), 6.16 (1H, t, J_{H-F}=12.3 Hz), 3.87 (2H, q, J=7.2 Hz), 1.25 (9H, s), 1.10 (3H, t, J=7.2 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −92.1 (2F, d, J_{H-F}=12.2 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 163.6 (t, J=33.6 Hz), 136.9, 135.0 (t, J=10.3 Hz), 129.6, 129.2, 128.7, 126.4 (t, J=28.4 Hz), 112.7 (t, J=244.9 Hz), 104.0, 80.2, 63.5, 31.3, 28.7, 14.3; EIMS (*m*/*z*) 306 (M^+, 19), 233 (100), 218 (21), 203 (10), 127 (13), 91 (6); IR (cm^{-1}, KBr) 2970, 2869, 2217, 1774, 1618, 761, 700; HRMS calcd for $C_{18}H_{20}F_2O_2$: 306.1431, found: 306.1431.

4.6.7. 5-(1,1-Difluoro-3,5-diphenyl-pent-2-en-4-ynyl)-3-phenyl-[1,2,4]oxadiazole (11a). Light red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.97–7.93 (2H, m), 7.52–7.44 (5H, m), 7.37–7.32 (5H, m), 7.25–7.18 (3H, m), 6.63 (1H, t, J_{H-F}=11.5 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −85.4 (2F, d, J_{H-F}=11.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.8 (t, J=35.5 Hz), 169.2, 136.3 (t, J=9.6 Hz), 135.8, 132.5, 132.3, 129.9, 129.8, 129.5, 129.1, 128.9, 128.8, 128.2, 127.1 (t, J=28.1 Hz), 126.3, 122.6, 112.7 (t, J=240.5 Hz), 95.7, 89.4; EIMS (*m*/*z*) 398 (M^+, 5), 298 (10), 269 (100), 167 (51), 77 (16); IR (cm^{-1}, KBr) 3060, 2205, 1600, 1445, 757, 692; HRMS calcd for $C_{25}H_{16}F_2N_2O$: 398.1231, found: 398.1230.

4.6.8. 5-(1,1-Difluoro-3-phenyl-non-2-en-4-ynyl)-3-phenyl-[1,2,4]oxadiazole (11b). Light red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.94–7.91 (2H, m), 7.53–7.42 (3H, m), 7.28–7.10 (5H, m), 6.46 (1H, t, J_{H-F}=11.5 Hz), 2.36 (2H, t, J=7.1 Hz), 1.56–1.48 (2H, m), 1.45–1.38 (2H, m), 0.91 (3H, t, J=7.4 Hz); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −85.2 (2F, d, J_{H-F}=11.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.9 (t, J=35.2 Hz), 169.1, 136.9 (t, J=9.6 Hz), 136.4, 132.2, 130.1, 129.5, 128.7, 127.9, 126.3 (t, J=28.1 Hz), 112.8 (t, J=240.0 Hz), 98.0, 81.3, 31.0, 22.6, 19.9, 14.2; EIMS (*m*/*z*) 378 (M^+, 8), 269 (100), 167 (45), 77 (25); IR (cm^{-1}, KBr) 3061, 2219, 1600, 1446, 757, 696.

4.6.9. 5-(1,1-Difluoro-3-phenyl-5-trimethylsilanyl-pent-2-en-4-ynyl)-3-phenyl-[1,2,4]oxadiazole (11c). Light red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.93–7.90 (2H, m), 7.50–7.41 (3H, m), 7.28–7.11 (5H, m), 6.56 (1H, t,

J_{H-F}=11.5 Hz), 0.19 (9H, s); ^{19}F NMR ($CDCl_3$, 470 MHz) δ −85.7 (2F, d, J_{H-F}=11.8 Hz); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.6 (t, J=35.4 Hz), 169.2, 136.1 (t, J=9.6 Hz), 135.5, 132.3, 129.7, 129.5, 128.8, 128.2, 126.2, 112.6 (t, J=240.5 Hz), 104.3, 101.6, 0.3; EIMS (*m*/*z*) 394 (M^+, 1), 269 (100), 167 (37), 77 (17); IR (cm^{-1}, KBr) 3062, 1601, 1446, 757, 697.

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