Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

© Wiley-VCH 2005

69451 Weinheim, Germany

"Difluoroallenyl Bromide as a Wide-Ranging Difluoromethylene Cation Equivalent: *De Facto* S_N2 Substitution of Difluoropropargyl Bromide Through Sequential S_E2' and S_N2' Reactions"

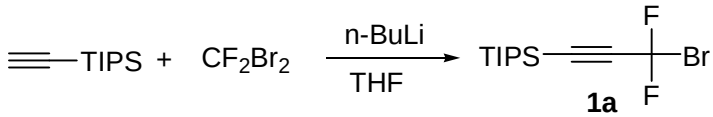
B. Xu and G. B. Hammond, Department of Chemistry, University of Louisville, Louisville, KY 40292.

General.

^1H, ^{13}C and ^{19}F NMR spectra were recorded on Varian Inova 500 instrument at 500, 126 and 470 MHz respectively, using $CDCl_3$ as a solvent. The chemical shifts are reported in d (ppm) values relative to $CHCl_3$ (d 7.26 ppm for ^1H NMR and d 77.0 ppm for ^{13}C NMR) and $CFCl_3$ (d 0 ppm for ^{19}F NMR). Coupling constants are reported in hertz (Hz). GC/MS analyses were performed on a Varian Saturn 2000 system. Infrared spectra were recorded using either a Mattson Infinity Series FTIR or Mattson Galaxy Series FTIR 5000 spectrometer. All air and/or moisture sensitive reactions were carried out under argon atmosphere. Dry solvents (tetrahydrofuran, ether, dichloromethane and DMF) was purchased from Aldrich were additionally purified on PureSolv PS-400-4 purification system (Innovative Technology, Inc.). All other reagents and solvents were employed without further purification. The products were purified using a Biotage flash+ system or Chromatotron apparatus. TLC was developed on Merck silica gel 60 F254 aluminum sheets. Elemental analysis was performed at Atlantic Microlabs Inc., Norcross, Georgia 30091. Accurate mass determinations were performed at the Nebraska Center for Mass Spectrometry, University of Nebraska-Lincoln, Nebraska 68588.

Gaussian 03, Revision C.02 at the HF/6-311++g level of theory. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford CT, **2004**.

1. Synthesis of compound (3-bromo-3,3-difluoroprop-1-ynyl)- triisopropylsilane (1a).[1]



A mixture of TIPS acetylene (10.98 g, 60 mmol) in dry THF (250 mL) was cooled to -78 °C under an argon atmosphere, and then 2.5 M solution of butyllithium in hexane (24 mL, 60 mmol) was added dropwise at -78 °C. After addition, the reaction mixture was stirred for 30 min. Then reaction mixture was cooled to -100 °C, dibromodifluoromethane (15.10g, 6.6 mL, 72 mmol) was added to the reaction mixture through a canula, (control the speed of addition to make sure the temperature not exceed -90 °C, the reaction produce a lot of heat, a internal thermometer is recommended). After addition, the reaction mixture was allowed to be warmed to -50°C, and then 100 mL sat. NH_4Cl solution was added to quench the reaction and then 100 mL hexane was added, the organic layer was washed by water and dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by distillation under reduced pressure (about 72 °C / 1 mmHg) to afford **1a** (16.6g , 90%) as a colorless oil. The spectrum data of the product is consistent with the literature report.[1]

2. Synthesis of the TIPS-indium complex 4.[1]

To a 0.15 M solution of (3-bromo-3,3-difluoroprop-1-ynyl)triisopropylsilane **1a** in a mixture of 2% NH_4Cl aqueous solution and THF (4:1) is added indium (1eq). This mixture was sonicated at 5-10 ^oC for 6-8h. The temperature in the ultrasound bath was adjusted by addition of ice periodically. An aliquot was analyzed in $CDCl_3$ by ^{19}F-NMR to monitor the completion of the reaction. After the starting material was consumed, the reaction mixture was extracted by ether and the organic layer was washed by brine and dried over $MgSO_4$. Then the most solvent was removed in reduced pressure to give the crude indium complex. (Not evaporation to complete dryness, because the indium complex is not stable when solvent was removed completely). The crude indium complex was used in next step directly without further purification. Although this indium complex can be kept in freezer for several days, using of the complex for next step immediately give better yield.

[1] The synthesis of compound **1a** and the indium complex was conducted by a slightly modified procedure of our previous published article. Arimitsu, Satoru; Xu, Bo; Kishbaugh, Tara L. S.; Griffin, Leanne; Hammond, Gerald B. *J. Fluorine Chem*. (2004), 125(4), 641-645.

3. Synthesis of (1-bromo-3,3-difluoropropa-1,2-dienyl)triisopropylsilane

.

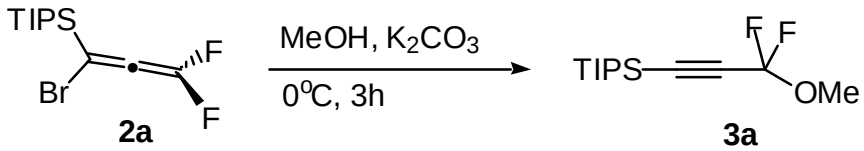
The freshly prepared indium complex **4** (prepared from compound **1a** (3.20g, 9.7 mmol)) was dissolved in 50 ml THF, then reaction mixture was cooled to -78 ^{o}C, then a solution of Br_2 (3.10g, 19.4 mmol) in 10 mL THF was added dropwise to the reaction mixture under stirring. The reaction mixture was warmed to -20 ^{o}C and was stirring for another 0.5h at -20 ^{o}C. Then 10 ml saturated $Na_2S_2O_3$ solution was added to quench the reaction. After stirring for 5 min at about 0 ^{o}C, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed by rotavapor, and the crude product was purified by flash silica gel chromatography (pure hexane) to give the bromoallene product 2.44 g (76%) as colorless oil. (The yield varied from 67-81% from compound **1a** (2 steps), the obtained fluoroallene **2a** is not very stable in solution, but neat **2a** can be stored in freezer for more than 1 month)

IR (neat): 2947, 2869, 1986, 1716, 1397, 1218, 1114, 882 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 1.08-1.13 (m, 18H), 1.29-1.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 11.39, 18.11, 111.80, 154.40 (t, *J* = 268 Hz), 179.14 (t, *J* = 36 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) d -97.9 (s); Anal. Calcd for $C_{12}H_{21}F_2Si$: C, 46.30; H, 6.80. Found: C, 48.88; H, 7.36. (Satisfactory EA and MS data couldn't be obtained because of the unstable nature of difluoroallene for long periods at room temperature).

4. Synthesis of RCF_2Nu (3).

<u>Note: The synthesis of 3a-j have not been fully optimized.</u>

(3,3-Difluoro-3-methoxyprop-1-ynyl)triisopropylsilane (3a).

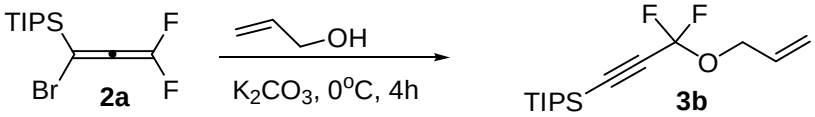


At 0°C, to a mixture of K_2CO_3 (212mg, 2 mmol) and MeOH 2 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL THF was introduced through a syringe, the reaction mixture was stirred for 3h at 0°C. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^{o}C, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (pure hexane to 10% ethyl acetate in hexane) to give the product 158 mg (61%) as a colorless oil.

IR (neat) 2846, 2868, 1463, 1265, 1172, 1026, 882, 679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 1.04-1.14 (m, 21H), 3.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) d 11.08, 18.53, 52.40, 88.63, 95.36 (t, *J* = 51 Hz), 114.14 (t, *J* = 241 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) d -

57.9 (s); GC/MS (EI) *m/z:* 243 (M^+-F), 219, 191, 163, 81; Anal. Calcd for $C_{13}H_{24}F_2OSi$: C, 59.50; H, 9.22. Found: C, 59.31; H, 9.21.

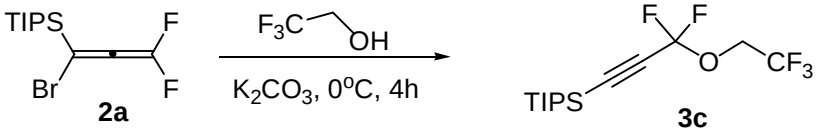
(3-(Allyloxy)-3,3-difluoroprop-1-ynyl)triisopropylsilane (3b)



At 0°C, to a mixture of K_2CO_3 (212mg, 2 mmol) and allylic alcohol 2 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL THF was introduced through a syringe, the reaction mixture was stirred for 4h at 0°C. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^oC, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (pure hexane to 10% ethyl acetate in hexane) to give the product **3b** 200 mg (70%) as a colorless oil.

IR (neat) 2946, 2868, 1463, 1256, 1162, 1025, 882 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): d 1.07-1.19 (m, 21H), 4.41-4.43 (m, 2H), 5.26 (d, *J* = 10 Hz, 1H), 5.38 (d, *J* = 17 Hz, 1H), 5.91-5.97 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 11.09, 18.58, 66.68, 88.61 (t, *J* = 5.3 Hz), 95.60 (t, *J* = 52 Hz), 113.84 (t, *J* = 242 Hz), 118.62, 132.15; ^{19}F NMR (470 MHz, $CDCl_3$) d -55.0 (s); GC/MS (EI) *m/z:* 269 (M^+-F), 227, 209, 185, 93; Anal. Calcd for $C_{15}H_{26}F_2OSi$: C, 62.46; H, 9.09. Found: C, 62.44; H, 9.20.

(3,3-Difluoro-3-(2,2,2-trifluoroethoxy)prop-1-ynyl)triisopropylsilane (3c)

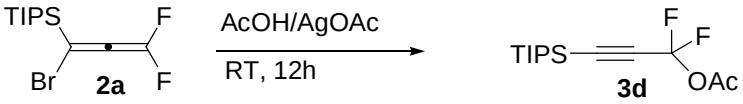


At 0°C, to a mixture of K_2CO_3 (212mg, 2 mmol) and trifluoroethanol 2 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL THF was introduced through a syringe, the reaction mixture was stirred for 4h at 0°C. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^oC, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (pure hexane) to give the product 224 mg (68%) as colorless oil.

IR (neat) 2948, 2871, 2200, 1463, 1294, 1257, 1172, 883 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): d 1.08-1.18 (m, 21H), 4.22 (q, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): d 11.02, 18.50, 62.24 (q, J = 37.0 Hz), 90.96 (t, *J* = 5.7 Hz), 93.77 (t, *J* = 49.6 Hz), 113.19

(t, *J* = 246 Hz), 122.60 (t, *J* = 276 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) d -56.69 (s, 2F), -74.75 (t, *J* = 8 Hz, 3F); GC/MS (EI) *m/z:* 330 (M^+), 204, 177, 131, 111, 91; Anal. Calcd for $C_{14}H_{23}F_5OSi$: C, 50.89; H, 7.02. Found: C, 51.38; H, 7.20.

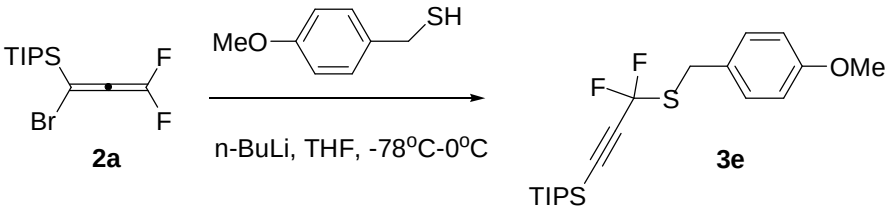
1,1-Difluoro-3-(triisopropylsilyl)prop-2-ynyl acetate (3d)



At room temperature, to a mixture of AgOAc (334 mg, 2 mmol) and acetic acid 2 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL acetic acid was introduced through a syringe, the reaction mixture was stirred for 12h at room temperature. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at RT, the reaction mixture was filtered and the solid collected was washed by ether. The resulting filtrate was extracted with ether (three times); the extract was washed by brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (pure hexane to 10% ethyl acetate in hexane) to give the product 188 mg (70%) as a colorless oil.

IR (neat) 2946, 2868, 2193, 1799, 1464, 1131, 882 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): d 1.09-1.12 (m, 21H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 11.04, 18.53, 21.18, 91.24, 93.98 (t, *J* = 46 Hz), 110.38 (t, *J* = 246 Hz), 165.02; ^{19}F NMR (470 MHz, $CDCl_3$) d -56.6 (s); GC/MS (EI) *m/z:* 247 (M^+-AcO), 209, 173, 149, 81; HRMS (EI): Calcd for $C_{15}H_{26}F_2OSi$ (M^+): 290.1514. Found: 290.1513

(3-(4-Methoxybenzylthio)-3,3-difluoroprop-1-ynyl)triisopropylsilane (3e)

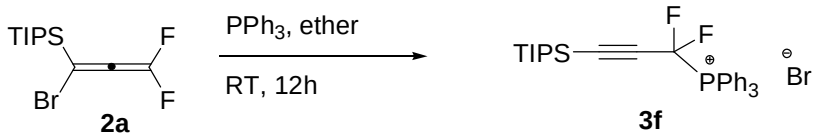


At -78 °C, to a solution of (4-methoxyphenyl)methanethiol (308mg, 278 μL, 2 mmol) in THF 2 mL, 2.5 M solution of butyllithium in hexane (0.64 mL, 1.6 mmol) was added under argon, the reaction mixture was stirred for about 0.5 h at -78 °C, and then the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL THF was introduced through a syringe, the reaction mixture was allow to be warmed to 0°C slowly. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 °C, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel

chromatography (hexane to 10% ethyl acetate in hexane) to give the product 202 mg (53%) as a colorless oil.

IR (neat) 2945, 2866, 1513, 1463, 1250, 1154 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): d 1.13-1.19 (m, 21H), 3.82 (s, 3H), 4.16 (s, 2H), 6.88 (d, *J* = 6.5 Hz, 2H), 7.29 (d, *J* = 6.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): d 11.16, 18.68, 34.31, 55.48, 94.01, 97.03 (t, *J* = 38 Hz), 114.42, 117.43 (t, *J* = 263 Hz), 127.62, 130.55, 159.40; ^{19}F NMR (470 MHz, $CDCl_3$) d -59.8 (s); GC/MS (EI) *m/z:* 383 (M^+-H), 341, 121; Anal. Calcd for $C_{20}H_{30}F_2OSSi$: C, 62.46; H, 7.86. Found: C, 62.52; H, 7.97.

(1,1-Difluoro-3-(triisopropylsilyl)prop-2-ynyl)triphenylphosphonium bromide (3f)

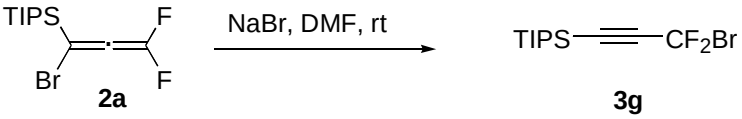


2a **3f**

At room temperature, to a mixture of PPh_3 (394mg, 1.5 mmol) in ether 4 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL ether was introduced through a syringe, the reaction mixture wa stirred for 12h at room temperature. Then reaction mixture was filtered and solid was washed by ether, and the white solid obtained was dried in vacuum (526 mg, 92%).

IR ($CHCl_3$ solution) 2946, 2866, 2166, 1584, 1438, 1158, 1108, 730, 686 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) d 0.83-0.95 (m, 21H), 7.71-7.74 (m, 2H), 7.79-7.83 (m, 2H), 7.87-8.01 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) d 10.81, 18.38, 92.52-92.68 (m), 107.68, 108.58-112.79 (m), 112.00 (d, *J* = 84 Hz), 131.60 (t, *J* = 13 Hz), 134.85 (t, *J* = 10 Hz), 137.87; ^{19}F NMR (470 MHz, $CDCl_3$) d -82.2 (d, *J* = 102 Hz); Anal. Calcd for $C_{30}H_{36}BrF_2PSi$: C, 62.82; H, 6.33. Found: C, 62.71; H, 6.63.

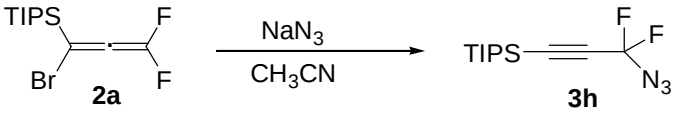
(3-Bromo-3,3-difluoroprop-1-ynyl)triisopropylsilane (3g)



2a **3g**

At 0°C, to a mixture of NaBr (212mg, 2 mmol) and DMF 2 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL DMF was introduced through a syringe, the reaction mixture was stirred for 12h at room temperaure. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^{o}C, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (pure hexane) to give the product 242 mg (78%) as colorless oil.
The spectrum data is same as **1a.**

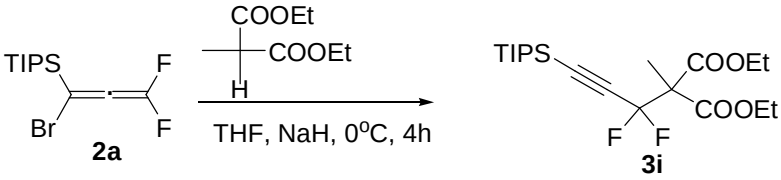
(3-Azido-3,3-difluoroprop-1-ynyl)triisopropylsilane (3h)



At 0 ^{o}C, to a mixture of NaN_3 (130 mg, 2 mmol) and CH_3CN 2 mL, the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL CH_3CN was introduced through a syringe, the reaction mixture was stirred for 12h at room temperature. Then 10 mL saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at RT, the reaction mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (pure hexane to 10% ethyl acetate in hexane) to give the product 212 mg (68%) as a colorless oil.

IR (neat) 2948, 2869, 2148, 1465, 1247, 1207, 1045, 883 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): d 1.11-1.13 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$): d 10.99, 18.50, 93.13 (t, J = 47 Hz), 93.79 (s), 111.93 (t, J = 239 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) d -58.18 (s); GC/MS (EI) *m/z:* 193, 178, 166, 151, 126, 97, 82, 67, 55;

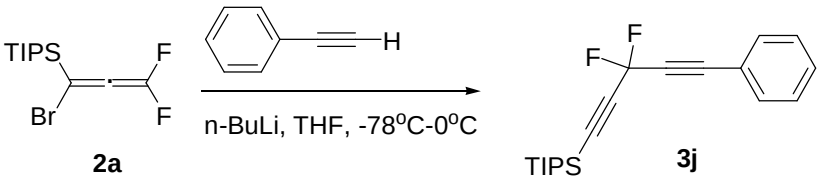
Diethyl 2-(1,1-difluoro-3-(triisopropylsilyl)prop-2-ynyl)-2-methylmalonate (3i)



At 0°C, to a solution of methyl diethyl malonate (348 mg, 2 mmol) in THF 2 mL, NaH (60% suspension in mineral oil) (72 mg, 1.8 mmol) was added under argon, the reaction mixture was stirred for about 0.5 h at 0°C, and then the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL THF was introduced through a syringe, the reaction mixture was stirred for 4h at 0°C. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^{o}C, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (10% ethyl acetate in hexane to 50% ethyl acetate in hexane) to give the product 282 mg (70%) as a colorless oil.
IR (neat) 2954, 2866, 1745, 1463, 1271, 1046, 883, 679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): d 1.08-1.10 (m, 21H), 1.27 (t, *J* = 7.1 Hz, 6H), 1.69 (s, 3H), 4.24 (q, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): d 11.10, 14.05, 17.50, 18.56, 61.97 (t, *J* = 25 Hz), 62.30, 92.31, 96.82 (t, *J* = 38 Hz), 111.64 (t, *J* = 240 Hz), 52.40, 88.63, 95.36 (t, *J* = 51 Hz), 114.14 (t, *J* = 241 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) d -87.6 (s); GC/MS (EI) *m/z:* 404

(M^+), 385, 361, 269, 241, 225; Anal. Calcd for $C_{20}H_{34}F_2O_4Si$: C, 59.38; H, 8.47. Found: C, 59.11; H, 8.48.

(3,3-difluoro-5-phenylpenta-1,4-diynyl)triisopropylsilane (3j)



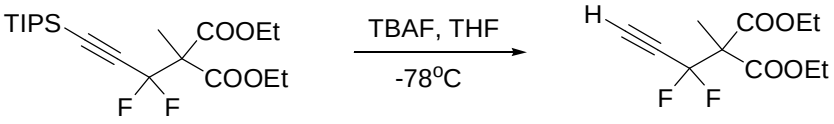
2a **3j**

At -78 °C, to a solution of 1-ethynylbenzene (204 mg, 2 mmol) in THF 2 mL, 2.5 M solution of butyllithium in hexane (0.64 mL, 1.6 mmol) was added under argon, the reaction mixture was stirred for about 0.5 h at -78 °C, and then the solution of bromoallene **2a** (311mg, 1 mmol) in 1 mL THF was introduced through a syringe, the reaction mixture was allow to be warmed to 0°C slowly. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^oC, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (hexane) to give the product 183 mg (55%) as colorless oil.

IR (neat) 2945, 2867, 2241, 1463, 1281, 1152, 1106, 1025, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): d 1.14-1.22 (m, 21H), 7.40-7.44(m, 3H), 7.55-7.56 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): d 11.21, 18.66, 81.56 (t, *J* = 43 Hz), 86.81, 91.58, 98.24 (t, *J* = 41 Hz), 100.85 (t, J = 222 Hz), 120.06, 128.77, 130.47, 132.50; ^{19}F NMR (470 MHz, $CDCl_3$) d -65.3 (s); GC/MS (EI) *m/z:* 312 (M^+-F), 289, 219, 165, 103; HRMS (EI): Calcd for $C_{20}H_{26}F_2Si$ (M^+): 332.1772. Found: 332.1777.

5. Deprotection of 3i.

Diethyl 2-(1,1-difluoroprop-2-ynyl)-2-methylmalonate (6a)



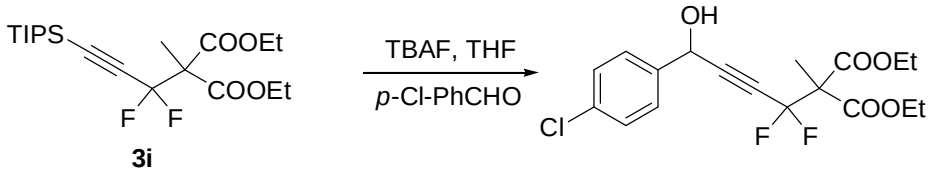
3i **6a**

At -78 °C, to a solution of diethyl 2-(1,1-difluoro-3-(triisopropylsilyl)prop-2-ynyl) -2-methylmalonate **3i** (104 mg, 0.257 mmol) in THF 2.5 mL, 1.0 M solution of TBAF in THF (0.3 mL, 0.3 mmol) was added under argon, the reaction mixture was stirred for about 0.5 h at -78 °C, the reaction mixture was allow to be warmed to -20 °C slowly. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^oC, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel

chromatography (10% AcOEt in hexane) to give the product 68 mg (92%) as colorless oil.

IR (neat) 3264, 2943, 2866, 2133, 1742, 1459, 1275, 1099, 645 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): d 1.26 (t, J = 5.5 Hz, 1H), 4.21-4.28 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): d 14.02, 16.96, 61.72 (t, *J* = 25 Hz), 62.53, 74.76 (t, *J* = 38 Hz), 111.89 (t, J = 241 Hz), 166.76; ^{19}F NMR (470 MHz, $CDCl_3$) d -89.4 (s); GC/MS (EI) *m/z:* 248 (M^+), 203, 111;

Diethyl-2-(4-(4-chlorophenyl)-1,1-difluoro-4-hydroxybut-2-ynyl)-2-methylmalon-ate (6b)



3i **6b**, 57%

At -78 °C, to a solution of diethyl 2-(1,1-difluoro-3-(triisopropylsilyl)prop-2-ynyl) -2-methylmalonate (104 mg, 0.257 mmol) and p-Cl-PhCHO (75.5 mg, 0.514 mmol) in 2.5 mL THF, 1.0 M solution of TBAF in THF (0.257 mL, 0.257 mmol) was added under argon, the reaction mixture was stirred for about 0.5 h at -78 °C, the reaction mixture was allow to be warmed to -20 °C slowly. Then 10 ml saturated NH_4Cl solution was added to quench the reaction. After stirring for 5 min at about 0 ^{o}C, the resulting aqueous mixture was extracted with ether (three times); the extract washed with brine (three times) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was purified by flash silica gel chromatography (10% to 30% AcOEt in hexane) to give the product 56 mg (57%) as colorless oil.

IR (neat) 3482, 2985, 2258, 1734, 1276, 1054 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): d 1.16 (t, *J* = 7.5 Hz, 3H), 1.17 (t, *J* = 7.5 Hz, 3H), 1.60 (s, 3H), 4.14 (q, *J* = 7.5 Hz, 2H), 4.15 (1, *J* = 7.5 Hz, 2H), 5.44 (s, 3H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): d 13.79, 16.62, 62.00 (t, *J* = 25.7 Hz), 62.36, 63.35, 77.75 (t, *J* = 39.1 Hz), 87.93 (t, *J* = 6.7 Hz), 111.00 (t, *J* = 240 Hz), 166.69,; ^{19}F NMR (470 MHz, $CDCl_3$) d -89.06 (s); GC/MS (EI) *m/z:* 388 (M^+), 370, 321, 295, 267, 249, 225, 176, 139, 111, 75. Anal. Calcd for $C_{18}H_{19}ClF_2O_5$: C, 55.61; H, 4.93. Found: C, 55.42; H, 5.04.