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Stereospecific Preparation of (*Z*)- and (*E*)-2,3-Difluoro-3-stannylacrylic Ester Synthons and a New, Efficient Stereospecific Route to (*Z*)- and (*E*)-2,3-Difluoroacrylic Esters[1]

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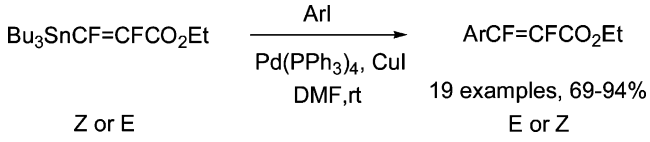

The (*Z*)-2,3-difluoro-3-stannylacrylic ester is readily prepared from (*Z*)-1,2-difluorovinyltriethylsilane via stereospecific stannyl/silyl exchange with KF/$(Bu_3Sn)_2O$ or Bu_3SnCl in DMF at 70 °C. The corresponding (*E*)-2,3-difluoro-3-stannylacrylate is prepared by stereospecific carbonylation of (*E*)-1,2-difluorovinyl iodide followed by low temperature/in situ stannylation of the resultant (*Z*)-2,3-difluoroacrylic ester. With Cu(I) iodide and $Pd(PPh_3)_4$ catalysis, the (*Z*)- and (*E*)-stannylacrylate esters readily couple with aryl iodides and vinyl bromides, as well as 2-iodothiophene, at room temperature to stereospecifically produce the respective (*E*)- and (*Z*)-2,3-difluoro-3-aryl substituted acrylic esters or conjugated dienes in high yields.

Introduction

The unique properties of organic compounds that contain one or more fluorine atoms at strategic positions in the molecule continue to attract the interest of polymer chemists, pharmaceutical chemists, and agrochemists.[2] 2,3-Difluoroacrylic esters are especially interesting intermediates in organic chemistry due to their prolific chemistry[3] and potential for further elaboration into fluorinated analogues of natural products,[4] application in polymers,[5] and in liquid crystal composition for liquid crystal display (LCD).[6] Although methodology for the introduction of the *trans*-1,2-difluoroethenyl unit has been investigated by Normant and us,[7] the preparation of *cis*-1,2-functionalized difluoroethenyl units still remains a challenging problem.[8] One functional derivative of high interest to synthetic chemists is the preparation of isomerically pure (*Z*)- and (*E*)-2,3-difluoroacrylic esters, and we address this unsolved problem in this article.

A few methods have been reported for the stereoselective synthesis of (*E*)-2,3-difluoroacrylic esters. Normant and co-workers reported the palladium catalyzed cross-coupling reaction of (*Z*)-RCF=CFZnCl with ethyl chloroformate;[9] however, in our hands this approach has been problematic.[10,11] Lu and Zhang[3a] partially circumvented

(1) Presented in part at the 227th ACS National Meeting, Anaheim, CA, March 28−April 1, 2004; FLUO-004.

(2) (a) *Biochemical Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Eds.; Elsevier Biomedical Press and Kodansha Ltd: Amsterdam, Tokyo, Japan, 1982. (b) *Fluorine in Bioorganic Chemistry*; Welch, J. T., Eswarakrishnan, S., Eds.; Wiley & Sons: New York, 1991. (c) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123. (d) *Organofluorine Compounds: Chemistry and Application*; Hiyama, T., Ed.; Springer: New York, 2000. (e) *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum: New York, 1994.

(3) (a) Zhang, Q.; Lu, L. *Tetrahedron Lett.* **2000**, *41*, 8545−8548. (b) Hudlicky, M. *J. Fluorine Chem.* **1988**, *40*, 99−108. (c) Knunyants I. L.; Postovoi, S. A.; Delyagina, N. I.; Zeifman, Yu. V. *Izv. Akad. Nauk, Ser. Khim.* **1987**, *10*, 2256−2261. (d) Linhart, I.; Trska, P.; Dedek, V. *Collect. Czech. Chem. Commun.* **1985**, *50*, 1727−1736.

(4) (a) Asato, A. E.; Liu, R. S. H. *Tetrahedron Lett.* **1986**, *27*, 3337−3340. (b) Colmenares, L. U.; Zou, X.; Liu, J.; Asato, A. E.; Liu, R. S. H. *J. Am. Chem. Soc.* **1999**, *121*, 5803−5804.

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(6) Selected references: (a) Heckmeier, M.; Goetz, A.; Czanta, M. Ger. Offen. DE 200410241301, 2004; *Chem. Abstr.* **2004**, *140*, 278503. (b) Heckmeier, M.; Goetz, A. PCT Int. Appl. WO 2002093244, 2002; *Chem. Abstr.* **2002**, *137*, 391146. (c) Kirsch, P.; Krause, J.; Heckmeier, M. Ger. Offen. DE10151492, 2002; *Chem. Abstr.* **2002**, *136*, 361922.

(7) (a) Normant, J. F. *J. Organomet. Chem.* **1990**, *400*, 19−34. (b) Liu, Q.; Burton, D. J. *Tetrahedron Lett.* **2000**, *41*, 8045−8048. (c) Liu, Q.; Burton, D. J. *Org. Lett.* **2002**, *4*, 1483−1485.

(8) (a) Leroy, J. *J. Org. Chem.* **1981**, *46*, 206−209. (b) Dubuffet, T.; Bidon, C.; Martinet, P.; Sauvetre, R.; Normant, J. F. *J. Organomet. Chem.* **1990**, *393*, 161−172. (c) Spawn, T.; Heinze, P.; Bailey, A.; Shin-Ya, S.; Burton, D. J. *J. Fluorine Chem.* **1988**, *38*, 131−134. (d) Davis, C. R.; Burton, D. J. *J. Org. Chem.* **1997**, *62*, 9217−9222. (e) Fontana, S. A.; Davis, C. R.; He, Y.; Burton, D. J. *Tetrahedron* **1996**, *52*, 37−44.

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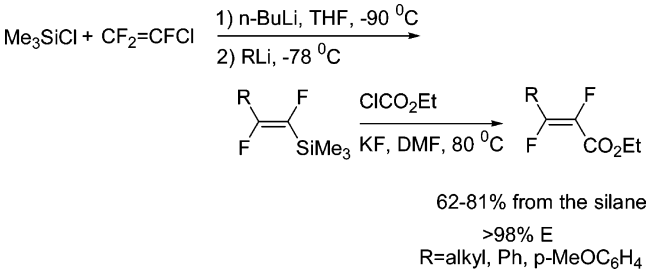
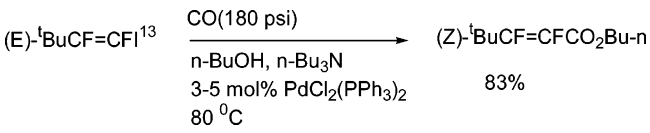
SCHEME 1. Lu and Zhang's Preparation of (*E*)-2,3-Difluoropropenoates



SCHEME 2. Wesolowski and Burton's Stereospecific Carboalkoxylation of Vinyl Iodides

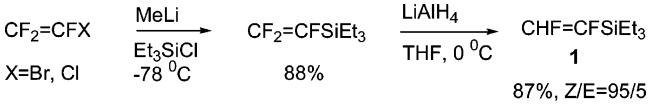


this difficulty via a modified Normant/Hiyama route outlined in Scheme 1.

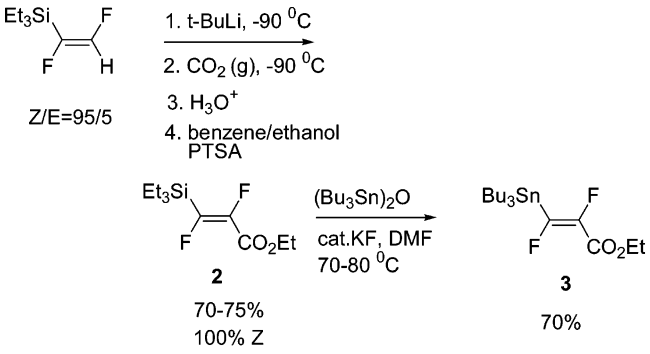
However, this route is applicable only to simple alkyl groups and aryl groups that contain functionality compatible with RLi reagents and thus of limited use with functionalized derivatives. Czech workers utilized an addition−elimination reaction between potassium cyanide and methyl trifluoropropenoate to prepare a precursor to the acrylic ester.[12] However, this approach yielded a mixture of (*E*)- and (*Z*)-$MeO_2CCF{=}CFCN$. Liu and coworkers reported the Wohl−Ziegler bromination of an isomeric mixture of ethyl 2,3-difluoro-2-butenoate to stereospecifically afford (*Z*)-4-bromo-2,3-difluoro-2-butenoate, which was subsequently utilized in the preparation of difluororetinal analogues.[4b] Although this report provided an interesting example of a *cis*-1,2-difluoroethenyl unit, this work is not a general entry to (*Z*)- and (*E*)-2,3-difluoroacrylic esters. The only stereospecific preparation of (*Z*)- and (*E*)-2,3-difluoroacrylic esters reported in the literature is that of Wesolowski and Burton,[10,11] who synthesized this class of esters via the palladium-catalyzed stereospecific carboalkoxylation of 1,2-difluoro-1-iodoalkenes and α,β-difluoro-β-iodostyrenes (Scheme 2).

Although this route stereospecifically provides the (*E*)- and (*Z*)-acrylic esters, it has two major limitations. For the aryl derivatives the requisite number of steps for the preparation of the vinyl iodide is high, and second and more importantly, each vinyl iodide must be prepared independently.[8d] A common synthon for the introduction of the aryl group in the final step of the synthetic sequence would be more advantageous and efficient. Thus, our goal in this work has been to design the (*E*)- and (*Z*)-synthons that allow introduction of the aryl group in the last step and would not be limited by the types of substituent on a functionalized aryl ring.[14]

SCHEME 3. Preparation of (*Z*)-1,2-Difluoro-2-triethylsilylethene



SCHEME 4. Stereospecific Preparation of 3



Results and Discussion

Our initial target molecule for the preparation of a general *trans* synthon to acrylic esters was (*Z*)-1,2-difluoro-2-triethylsilylethene, **1**, which can be readily prepared on a molar scale from commercial precursors, such as $CF_2{=}CFCl$ or $CF_2{=}CFBr$[8e] (Scheme 3).

Treatment of **1** with *n*-BuLi at −90 °C, followed by addition of ethyl chloroformate, however, gave the desired ester, ethyl (*Z*)-2,3-difluoro-3-(triethylsilyl)acrylate, **2**, only as minor product. Similarly, treatment of **1** with *n*-BuLi, followed by ZnI_2, followed by ethyl chloroformate, gave only a complicated mixture of products. Since **1** gave a stable lithium reagent at low temperatures, (*Z*)-$Et_3SiCF{=}CFLi$ was generated at −90 °C via reaction of **1** with *t*-BuLi, followed by treatment of the resultant lithium reagent with CO_2 (g), maintaining the internal temperature of the reaction mixture below −85 °C (ca. 0.5 h), to give a stable lithium carboxylate, which on acidification with an aqueous HCl solution afforded the corresponding acid. Without further purification, esterification of the crude acid in the presence of PTSA, using a Dean−Stark trap, gave **2** in 70−75% isolated yield (Scheme 4).

Under these conditions, the unstable (*E*)-$Et_3SiCF{=}CFLi$ decomposes, and **2** is isolated isomerically pure as exclusively the (*Z*)-isomer. Treatment of **2** with bis(tri-*n*-butyltin) oxide and a catalytic amount of KF in DMF at 70−80 °C stereospecifically gives ethyl (*Z*)-2,3-difluoro-3-(tributylstannyl)acrylate, **3**, in 70% isolated yield[15] (Scheme 4). Thus, **3** is readily prepared in four steps from $CF_2{=}CFCl$ in about 40% overall yield via readily scalable processes. **3** is colorless oil and can be stored in a refrigerator for an extended period without detectable decomposition or isomerization.

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(11) Wesolowski, C. A.; Burton, D. J. *Tetrahedron Lett.* **1999**, *40*, 2243−2246.

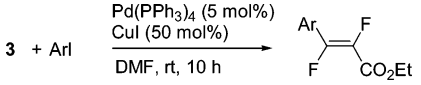
(12) Svoboda, J.; Paleta, O.; Dedek, V. *Collect. Czech. Chem. Commun.* **1981**, *46*, 1495−1503.

(13) (*Z*)-^{t}BuCF=CFI was prepared in three steps from $CF_2{=}CFCl$. (*E*)-^{t}BuCF=CFI can be prepared in five steps from $CF_2{=}CFCl$ or $CF_2{=}CFBr$.

(14) The alkyl derivatives in Wesolowski's report are based on a cheap, commercial precursor ($CF_2{=}CFCl$) and commercially available RLi reagents. Thus, the number of steps in the overall reaction sequence is of less importance than with the aryl analogues.

(15) (a) Xue, L.; Lu, L.; Pederson, S.; Liu, Q.; Narske, R.; Burton, D. J. *Tetrahedron Lett.* **1996**, *37*, 1921−1924. (b) Xue, L.; Lu, L.; Pederson, S.; Liu, Q.; Narske, R.; Burton, D. J. *J. Org. Chem.* **1997**, *62*, 1064−1071.

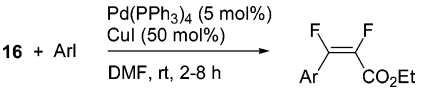
TABLE 1. Reactions of 3 with Organic Halides



entry	ArI	product	isolated yield (%)[a,b]
1	4-iodotoluene	(*E*)-4-$CH_3C_6H_4CF{=}CFCO_2Et$ (**4**)	84
2	iodobenzene	(*E*)-$C_6H_5CF{=}CFCO_2Et$ (**5**)	87
3	4-iodobenzonitrile	(*E*)-4-$NCC_6H_4CF{=}CFCO_2Et$ (**6**)	90
4	3-iodobenzotrifluoride	(*E*)-3-$F_3CC_6H_4CF{=}CFCO_2Et$ (**7**)	83
5	1-iodonaphthalene	(*E*)-$C_{10}H_7CF{=}CFCO_2Et$ (**8**)	74
6	2-iodothiophene	(*E*)-$C_4H_3SCF{=}CFCO_2Et$ (**9**)	83
7	1-bromo-4-iodobenzene	(*E*)-4-$BrC_6H_4CF{=}CFCO_2Et$ (**10**)	94
8	1-iodo-4-nitrobenzene	(*E*)-4-$O_2NC_6H_4CF{=}CFCO_2Et$ (**11**)	89
9	1-fluoro-4-iodobenzene	(*E*)-4-$FC_6H_4CF{=}CFCO_2Et$ (**12**)	88
10	(*E*)-CHBr=$CHCO_2Et$	(2*E*,4*E*)-$EtO_2CCH{=}CHCF{=}CFCO_2Et$ (**13**)	81

[a] Isolated yields based on **3**. [b] Configuration assigned on the basis of $J_{F,F\ trans}$ = 100−140 Hz.[18,19]

TABLE 2. Reactions of 16 with Organic Halides



entry	ArI	product	isolated yield (%)[a,b]
1	iodobenzene	(*Z*)-$C_6H_5CF{=}CFCO_2Et$ (**17**)	75
2	4-iodoanisole	(*Z*)-4-$CH_3OC_6H_4CF{=}CFCO_2Et$ (**18**)	83
3	1-iodo-4-nitrobenzene	(*Z*)-4-$O_2NC_6H_4CF{=}CFCO_2Et$ (**19**)	78
4	1-iodo-3-nitrobenzene	(*Z*)-3-$O_2NC_6H_4CF{=}CFCO_2Et$ (**20**)	86
5	2-iodothiophene	(*Z*)-$C_4H_3SCF{=}CFCO_2Et$ (**21**)	73
6	3-iodoanisole	(*Z*)-3-$CH_3OC_6H_4CF{=}CFCO_2Et$ (**22**)	74
7	1-bromo-4-iodobenzene	(*Z*)-4-$BrC_6H_4CF{=}CFCO_2Et$ (**23**)	69
8	(*E*)-CHBr=$CHCO_2Et$	(2*Z*,4*E*)-$EtO_2CCH{=}CHCF{=}CFCO_2Et$ (**24**)	94
9	(*Z*)-CHBr=$CHCO_2Et$	(2*Z*,4*Z*)-$EtO_2CCH{=}CHCF{=}CFCO_2Et$ (**25**)	86

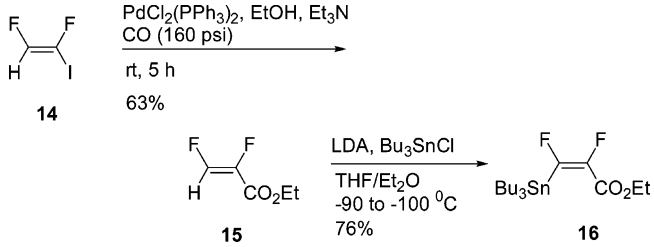
[a] Isolated yields based on **16**. [b] Configuration assigned on the basis of $J_{F,F\ cis}$ = 0−22 Hz.[18,19]

Although Stille reported that $Pd(PPh_3)_4$ catalyzed the coupling reaction of vinylstannanes with organic halides,[16] the use of $Pd(PPh_3)_4$ alone was ineffective for the coupling of **3** with iodobenzene (24 h/rt). Cu(I) iodide did not catalyze the coupling reaction with **3** either. However, the combination of $Pd(PPh_3)_4$ (5 mol %)/CuI (50 mol %) (Liebeskind conditions[17]) effectively catalyzed the cross-coupling reactions of **3** with aryl iodides and vinyl bromides, as well as 2-iodothiophene. These results are summarized in Table 1.

Both electron-withdrawing and electron-releasing substituents worked well (entries 1−5, 7−9); the heterocyclic iodide also worked well (entry 6), and the use of a vinyl halide (entry 10) demonstrated that the methodology could also be utilized as a stereospecific route to conjugated dienes.[19] Moreover, a common synthon precursor was employed to prepare the various derivatives.

The procedure outlined above for the preparation of **2**, however, could not be utilized for the synthesis of the analogous synthon, (*E*)-$Et_3SiCF{=}CFCO_2Et$, due to the instability of the precursor, (*E*)-$Et_3SiCCF{=}CFLi$. We attempted to react (*E*)-$CHF{=}CFSiMe_3$ and ethyl chloroformate in the presence of KF to prepare (*Z*)-$CHF{=}CFCO_2Et$ (Lu and Zhang's approach[3a]) without success. We were able, however, to modify the chemistry of Wesolowski and Burton[11] to ultimately prepare the appropriate precursor (*Z*)-$CHF{=}CFCO_2Et$. Thus, isomerically pure (*E*)-CHF=CFI, **14**, was prepared by the methodology reported by Wesolowski.[20] Carboalkoxylation of (*E*)-CHF=CFI stereospecifically gave (*Z*)-$CHF{=}CFCO_2Et$ (**15**), which reacted in situ with Bu_3SnCl and LDA at −90 to −100 °C and provided the ethyl (*E*)-2,3-difluoroacrylic ester[21] (Scheme 5).

SCHEME 5. Stereospecific Preparation of 16



Under Liebeskind conditions, **16** readily couples with aryl iodides (entries 1, 4, 6, and 7), 2-iodothiophene (entry 5), and vinyl bromides (entries 8 and 9) to stereospecifi-

(16) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508−524. (b) Stille, J. K. *Pure Appl. Chem.* **1985**, *57*, 1771−1780. (c) Espinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4704−4734.

(17) (a) Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905−5911 and references therein. (b) Farina, V. *Pure Appl. Chem.* **1996**, *68*, 73−78. (c) Casado, A. L.; Espinet, P. *Organometallics* **2003**, *22*, 1305−1309. (d) Lu, L.; Burton, D. J. *Tetrahedron Lett.* **1997**, *38*, 7673−7676.

(18) (a) Martin, S.; Sauvetre, R.; Normant, J. F. *Tetrahedron Lett.* **1982**, *23*, 4329−4332. (b) Martin, S.; Sauvetre, R.; Normant, J. F. *Tetrahedron Lett.* **1983**, *24*, 5615−5618.

(19) Zhang, X.; Lu, L.; Burton, D. J. *Collect. Czech. Chem. Commun.* **2002**, *67*, 1247−1261.

(20) Wesolowski, C. A. Ph.D. Thesis, University of Iowa, Iowa City, IA, 2000; pp 104−119.

(21) See ref 8e for similar in situ capture of an unstable vinyllithium.

cally give the isomerically pure (*Z*)-acrylic esters or conjugated dienes. These results are summarized in Table 2.

Aryl iodides substituted with either electron-donating or electron-withdrawing groups reacted smoothly with **16** under the coupling conditions to give the (*Z*)-acrylic esters in good to excellent yields. With 1-bromo-4-iodobenzene (entry 7) only the iodide site coupled. The (*E*)- and (*Z*)-vinyl bromides readily coupled to stereospecifically give the conjugated dienes.

The configuration of both the (*Z*)- and (*E*)-2,3-difluoro-3-stannylacrylic esters, as well as the configuration of the aryl acrylic esters and dienes, was unambiguously assigned on the basis of ^{19}F and ^{1}H coupling constants. All products exhibited vicinal couplings ($^{3}J_{F,F} = 0-22$ Hz) consistent with the *cis*-CF=CF− configuration versus the vicinal coupling ($^{3}J_{F,F} = 100-140$ Hz) for the *trans*-CF=CF− configuration.[18] Vicinal coupling of $^{3}J_{H,H} = 6-12$ Hz for *cis* and $^{3}J_{H,H} = 12-18$ Hz for *trans* was used to assign the configuration of the −CH=CH− unit in the dienes.[22]

Conclusions

We have developed a useful methodology for the preparation of both (*Z*)- and (*E*)-2,3-difluoro-3-stannylacrylic esters. These new synthons readily undergo cross-coupling reactions under Liebeskind conditions [(Pd(PPh$_3$)$_4$/CuI)] with aryl iodides and vinyl bromides, as well as 2-iodothiophene, to stereospecifically provide the corresponding 2,3-difluoro-3-arylacrylate esters and conjugated dienes from a common synthon precursor, thus providing a new, efficient entry to this important class of compounds.

Experimental Section

The preparation of (*Z*)-2,3-difluoro-3-(tri-*n*-butyl)stannylacrylate **3** has been described in a previous report.[19] Compound **14** was prepared according to the reported procedure.[8d]

General Procedure for the Stille−Liebeskind Cross-Coupling Reactions of Ethyl (*Z*)- or (*E*)-2,3-Difluoro-3-(tri-*n*-butyl)stannylpropenoate with Aromatic Iodides and Vinyl Bromides. A round-bottomed flask was charged with a stirring bar and nitrogen tee, CuI (0.05 g, 0.26 mmol), Pd(PPh$_3$)$_4$ (0.03 g, 0.026 mmol), and 3 mL of dry DMF. Ethyl (*Z*)- or (*E*)-2,3-difluoro-3-(tri-*n*-butyl)stannylpropenoate (0.21 g, 0.5 mmol) and 0.55 mmol of aromatic iodide or vinyl bromide were added sequentially. After the reaction was completed (the reaction progress was monitored by TLC), the reaction mixture was diluted with ether (100 mL) and washed with aqueous KF solution (15%, 50 mL). The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography. An alternative procedure of workup is to use Co(OAc)$_2$·4H$_2$O[23] instead of aqueous KF solution. Therefore, after the reaction was completed, Co(OAc)$_2$·4H$_2$O (0.25 g, 1 mmol) was added to the reaction mixture, and the mixture was stirred for 10 min at room temperature. Then the mixture was poured directly onto silica gel and purified by column chromatography.

Ethyl (*E*)-2,3-Difluoro-3-(4-methylphenyl)-2-propenoate (4). The reaction mixture of (*Z*)-2,3-difluoro-3-(tri-*n*-butyl)-stannylpropenoate (0.50 g, 1.17 mmol) with 4-iodotoluene (0.22 g, 1.01 mmol) in the presence of Pd(PPh$_3$)$_4$ (0.05 g, 0.043 mmol), CuI (0.10 g, 0.52 mmol) in DMF (5 mL) was stirred at room temperature for 10 h. Column chromatography with a mixture of hexane and ethyl acetate (30:1) afforded 0.19 g of the cross coupling product as an oil. ^{19}F NMR ($CDCl_3$) δ −134.8 (d, J = 127.8 Hz, 1 F), −162.8 (d, J = 127.8 Hz, 1 F) ppm; ^{1}H NMR ($CDCl_3$) δ 7.53 (d, J = 8.1 Hz, 2 H), 7.14 (d, J = 8.1 Hz, 2 H), 4.27 (qd, J = 7.1, 0.6 Hz, 2 H), 1.27 (td, J = 7.1, 0.9 Hz, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.1 (dd, J = 29.9, 6.1 Hz), 155.8 (dd, J = 58.7, 19.1 Hz), 141.7 (d, J = 2.4 Hz), 139.2 (dd, J = 243.0, 44.0 Hz), 129.3 (d, J = 2.5 Hz), 126.9 (dd, J = 9.8, 8.6 Hz), 125.4 (dd, J = 23.2, 6.1 Hz), 61.5, 12.3, 14.0 ppm; GC−MS *m/z* (relative intensity): 226 (M$^+$, 87), 197 (26), 181 (28), 154 (100); HRMS calcd 226.0805 for $C_{12}H_{12}F_2O_2$, found 226.0813.

Ethyl (*Z*)-2,3-Difluoro-2-propenoate (15). (*E*)-1,2-Difluoro-1-iodoethylene (16.20 g, 85 mmol), triethylamine (12.0 mL, 86 mmol), $PdCl_2(PPh_3)_2$ (0.72 g, 1 mmol), and EtOH (30 mL) were added to a 120-mL Hastelloy Parr pressure reactor with a stirring bar (*caution: the reaction should be carried out behind a safety shield in a well-ventilated hood*).The pressure reactor was pressurized to 160 psi of CO, and the pressure was released. This process was repeated 4 times to rid the system of air. Finally, the reactor was pressurized to 160 psi of CO and was stirred vigorously at room temperature. After 5 h, when the reaction was completed, the pressure was carefully released. The mixture was transferred to a separatory funnel containing 100 mL of ether. The organic layer was washed with water (20 mL), 10% aqueous HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated by rotary evaporation. The crude product was purified by fractional distillation (7.28 g colorless oil, yield: 63%, bp: 88−90 °C/760 mm). ^{19}F NMR ($CDCl_3$) δ −145.2 (dd, J = 70.5, 6.8 Hz, 1 F), −151.6 (dd, J = 14.1, 6.8 Hz, 1 F) ppm; ^{1}H NMR ($CDCl_3$) δ 7.34 (dd, J = 70.6, 14.1 Hz, 1 H), 4.32 (q, J = 7.1 Hz, 2 H), 1.34 (t, J = 7.1 Hz, 3 H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.2 (dd, J = 28.6, 8.5 Hz), 144.0 (dd, J = 274.5, 10.4 Hz), 139.5 (dd, J = 255.5, 9.1 Hz), 61.9, 14.1 ppm; HRMS for $C_5H_6F_2O_2$ calcd 136.0336, found 136.0333.

Ethyl (*E*)-2,3-Difluoro-3-(tri-*n*-butyl)stannyl-2-propenoate (16). To a two-necked round-bottomed flask with a stirring bar was added ethyl (*Z*)-2,3-difluoropropenoate (0.68 g, 5 mmol) and 1.68 mL of Bu_3SnCl (6.2 mmol) in a mixture of 5 mL of dry THF and 5 mL of dry ether. The solution was cooled to −100 °C in a hexane/liquid nitrogen bath. A solution of LDA (6.2 mmol) (prepared by reaction of $^{i}Pr_2NH$ and *n*-BuLi) was added dropwise, carefully maintaining the internal temperature at −90 to −100 °C throughout the addition. After the addition was completed, the reaction mixture was stirred at −100 °C for 1 h and slowly warmed to room temperature. Water (2 mL) was added to quench any unreacted base. The mixture was transferred to a 125-mL separatory funnel containing 50 mL of ether. The organic layer was washed with 20 mL of water and 5 mL of brine, dried over anhydrous Na_2SO_4, and concentrated by rotary evaporation. The crude stannane was purified by silica gel chromatography (hexane/ethyl acetate = 30:1) to yield 1.61 g of colorless oil. ^{19}F NMR ($CDCl_3$) δ −116.6 (s, 1 F), −138.6 (s, 1 F) ppm; ^{1}H NMR ($CDCl_3$) δ 4.29 (q, J = 7.1 Hz, 2 H), 1.62−1.44 (m, 6 H), 1.37−1.27 (m, 6 H), 1.10 (t, J = 8.1 Hz, 3 H), 0.90 (t, J = 7.3 Hz, 9 H) ppm; ^{13}C NMR ($CDCl_3$) δ 171.3 (dd, J = 333.5, 7.7 Hz), 162.5 (dd, J = 29.0, 12.3 Hz), 145.7 (dd, J = 279.2, 10.7 Hz), 61.6, 28.7, 27.1, 14.2, 13.6, 11.2 ppm; HRMS calcd for $C_{17}H_{31}F_2O_2{}^{120}Sn-C_4H_9$ 369.0688, found 369.0680.

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Supporting Information Available: Experimental procedure for the synthesis of **5**−**13** and **17**−**25** and their characterization by ^{1}H, ^{19}F, ^{13}C NMR, GC−MS, and HRMS. Copies of ^{1}H, ^{19}F, and ^{13}C NMR of compounds **4**−**13** and **15**−**25**. This material is available free of charge via the Internet at http://pubs.acs.org.

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