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Highly Stereoselective and One-Pot Synthesis of Tetra-substituted Monofluoroalkenes with Aldehydes and Fluorobis(phenylsulfonyl)methane

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A highly stereoselective synthesis of tetrasubstituted monofluoroalkenes with aldehydes and fluorobis(phenylsulfonyl)methane (FBSM) in one pot has been developed. The reaction was amenable to *para*- and *meta*-substituted aryl aldehydes, 2-naphthaldehyde, and cinnamaldehyde, giving phenylsulfonyl-substituted monofluoroalkenes in 40%—86% yields with 98/2—99/1 *Z*/*E* ratios. The presence of the sulfonyl group enables the further transformation of the products into more useful monofluoroalkenes.

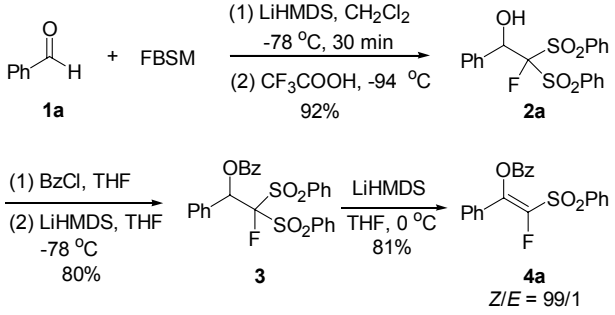
Keywords olefination, aldehydes, nucleophilic addition, sulfones, fluorine

Introduction

The selective incorporation of fluorine atoms or fluorinated moieties into organic molecules can often lead to great changes in their solubility, lipophilicity, metabolic stability, and chemical reactivity.[1] Therefore, fluorinated compounds have been widely used in pharmaceutical, agrochemical, and material sciences.[1,2] Among various fluorinated motifs contained in these fluorinated compounds, the monofluoroalkene is of particular interest. The monofluoroalkene moiety has been widely used as the peptide bond isostere in the design of protease inhibitors[1a,3] because of its similar charge distribution and dipole moment to that of amide bond. In addition, monofluoroalkenes can be used as fluorinated building blocks for further functionalization.[4]

Many methods have been developed towards the synthesis of monofluoroalkenes,[5] including the elimination reactions of vicinal halofluorides, fluorohydrins, fluorosulfoxides and fluorocarboxylates, the addition-elimination processes from *gem*-difluoroalkenes, and the fluoroolefination between fluorinated sulfoximines and nitrones.[6] The carbonyl compound-based methods, such as Witting reaction,[7] Horner-Wadsworth-Emmons reaction,[8] Peterson olefination,[9] and Julia-Kocienski olefination,[10] have also been used to synthesize monofluoroalkenes; however, the control of the *Z*/*E* selectivity in these one-pot reactions still remains a challenging task, especially for the synthesis of tetra-substituted monofluoroalkene. Herein, we report a highly stereoselective synthesis of tetra-substituted monofluoroalkenes by olefination of aldehydes with fluorobis(phenylsulfonyl)methane (FBSM) in one pot.

Scheme 1 Highly stereoselective preparation of tera-substituted monofluoroalkene in three steps[11f]



FBSM was independently developed by Shibata's[11b] and our group[11a] in 2006, and it has been successfully used as a monofluoromethylating agent in many nucleophilic fluoroalkylation reactions by tackling the "negative fluorine effect".[11,12] The addition reaction of aldehydes and FBSM, which was asserted to be inaccessible due to the high preference for retro-aldol type reaction,[13] was successfully tackled by us in 2011 using a lithium-oxygen coordination strategy (Scheme 1).[11f] When the addition product (**2**) was reacted with benzoyl chloride (BzCl), compound **3** was afforded (Scheme 1). Upon treatment of compound **3** with lithium hexamethyldisilazide (LiHMDS), monofluoroalkene **4a** was obtained with very high *Z*/*E* selectivity (99/1) (Scheme 1). Encouraged by the preliminary result,

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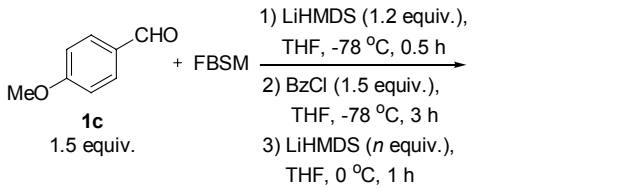
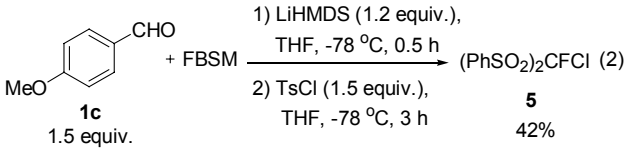
CHINESE JOURNAL OF CHEMISTRY

we made a further investigation on the scope and limitation of this stereoselective monofluoroolefination reaction. In addition, for the convenience of synthesis, we developed a one-pot procedure, which could furnish monofluoroolefins **4** without the isolation of the intermediates **2** and **3**.

Results and Discussion

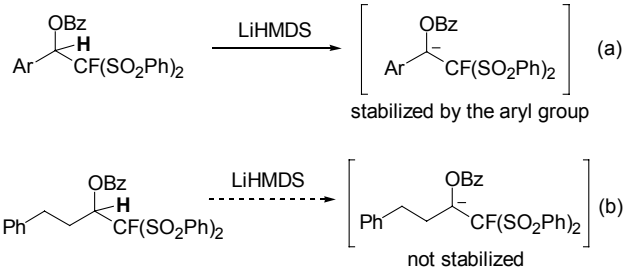
FBSM could be easily prepared according to the reported procedures.[14] At the outset, we chose 4-methoxybenzaldehyde (**1c**) as the model substrate to test the possibility of synthesizing monofluoroalkene **4c** in one pot (Eq. 1). The mixture of aldehyde **1c** (1.5 equiv.) and FBSM (1.0 equiv.) in THF was treated with LiHMDS (1.2 equiv.) for 0.5 h, followed by adding BzCl (1.5 equiv.). After 3 h, the solution was allowed to warm to 0 ℃, and another portion of LiHMDS (1.2 equiv.) was added to achieve the *β*-elimination. When the reaction was completed, the monofluoroalkene **4c** was given in a yield of 58% with the *Z*/*E* ratio of 99/1. Increasing the amount of LiHMDS used in the third step to 1.5 equiv., the yield of **4c** was improved to 70% without the loss of the *Z*/*E* selectivity. It is interesting to find that, when tosyl chloride (TsCl) was used instead of BzCl to protect the addition product, no tosylate could be obtained. The chlorination of FBSM occurred to afford product **5** in 42% yield (Eq. 2).





With the optimized reaction conditions in hand, we examined the substrate scope of the monofluoroolefination reaction with FBSM. The results are shown in Table 1. It was found that a wide range of aromatic aldehydes were transformed to monofluoroalkenes in moderate to good yields (40%—83%) with 99/1 *Z*/*E* selectivity (Table 1, Entries 1—6). 2-Naphthaldehyde (**1g**) can also undergo the monofluoroolefination reaction, affording compound **4g** in 86% yield with 99/1 *Z*/*E* selectivity (Table 1, Entry 7). To our delight, the current reaction conditions were also amenable to cinnamaldehyde (**1h**), giving the corresponding alkene **4h** in 86% yield and 98/2 *Z*/*E* selectivity (Table 1, Entry 8). However, the reaction was largely affected by the position of substituent on the aromatic ring. The yield of monofluoroalkenes decreased when the bromo substituent was changed from *para*- to *meta*-position (Table 1, Entries 4 and 5). When 2-bromobenzaldehyde (**1i**) was used as the substrate, the intermediate **6** was obtained in 65% yield without the formation of the desired monofluoroolefin (Table 1, Entry 9). We proposed that the strong steric interaction between compound **6** and LiHMDS probably hinders the approach of the base to the benzylic hydrogen, thus no deprotonation takes place. Aliphatic aldehyde **1j** was also not a suitable substrate for the monofluoroolefination reaction, and the intermediate **7** was afforded in 55% yield (Table 1, Entry 10). The failure of this reaction presumably arises from the relatively weak stabilization effect of the alkyl substituent on the carbanion, which renders the deprotonation of **7** to be much more difficult than that of the aryl-substituted ones (Scheme 2). The (*Z*)-configuration of compound **4g** was confirmed by its X-ray crystal structure analysis (Figure 1),[15] and those of the other monofluoroalkenes were assigned by analogy. The highly stereoselective formation of the (*Z*)-isomer probably results from the steric repulsion between the aryl group and the phenylsulfonyl group, which renders the *anti*-elimination of hydrogen and one sulfonyl group from the staggered conformer **A** to be much more favored than from the similar conformer **B** (Scheme 3).

Scheme 2 Stabilization effect of the substituents on the carbanions



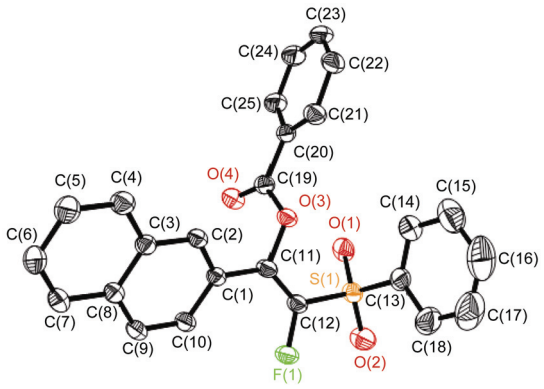
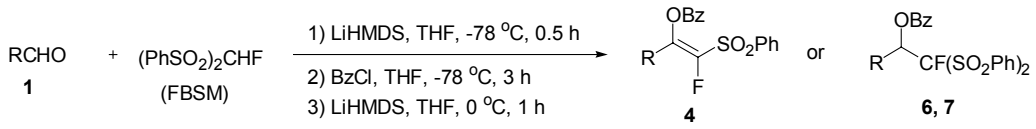
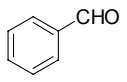
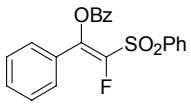
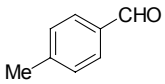
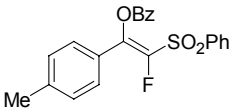
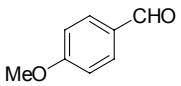
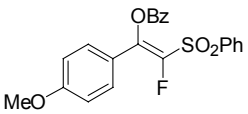
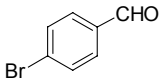
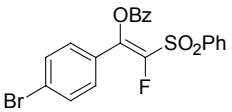
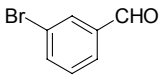
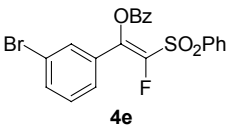
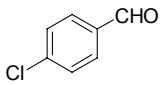
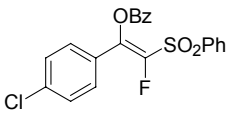
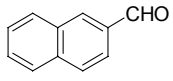
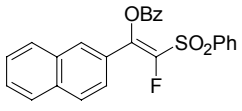
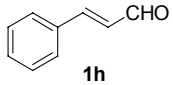
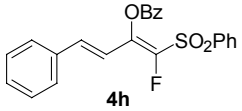
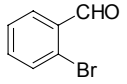
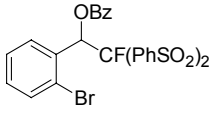
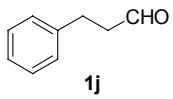
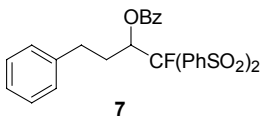


Figure 1 ORTEP drawing for compound **4g**.[15]

Table 1 Monofluoroolefination of aldehydes with FBSM



Entry	RCHO (**1**)	Products (**4**—**7**)	Yield[a]/%	Z/*E*[b]
1	 **1a**	 **4a**	72	99/1
2	 **1b**	 **4b**	55	99/1
3	 **1c**	 **4c**	70	99/1
4	 **1d**	 **4d**	83	99/1
5	 **1e**	 **4e**	40	99/1
6	 **1f**	 **4f**	60	99/1
7	 **1g**	 **4g**	86	99/1
8	 **1h**	 **4h**	73	98/2
9	 **1i**	 **6**	65	—
10	 **1j**	 **7**	55	—

[a] Isolated yield. [b] Determined by ^{19}F NMR.

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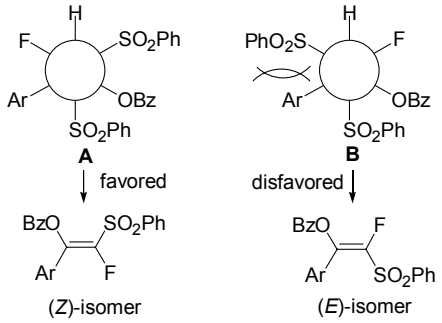
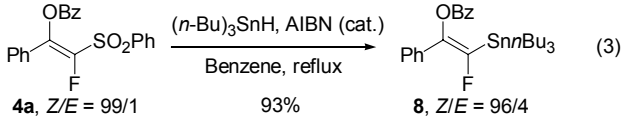
Scheme 3 Rationalization of the preference of (*Z*)-isomers

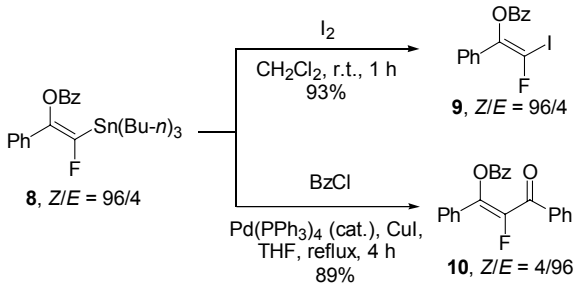


To demonstrate the synthetic utility of the aforementioned highly stereoselective monofluoroolefination protocol, product **4a** was transformed to organotin compound **8** in 93% yield and 96/4 *Z*/*E* selectivity by using the reported procedure (Eq. 3).[11f] When compound **8** was treated with I_2 in CH_2Cl_2 at room temperature for 1 h, the iodinated product **9** was obtained in 93% yield. Furthermore, the stereospecific Stille coupling reaction with benzoyl chloride efficiently converted **8** into fluorinated α,β-unsaturated ketone derivative **10** in 89% yield (Scheme 4).



(3)

Scheme 4 Synthetic application of compound **8**



Conclusions

In conclusion, we have successfully developed a highly stereoselective reaction for the synthesis of tetra-substituted monofluoroalkenes with aldehydes and FBSM in one pot. The reaction was amenable to *para*- and *meta*-substituted aryl aldehydes, 2-naphthaldehyde, and cinnamaldehyde, giving monofluoroalkenes in moderate to good yields (40%－86%) with excellent stereoselectivities (*Z*/*E*＝98/2－99/1). The presence of the sulfonyl group in the product afforded the convenience to prepare more useful monofluoroalkene compounds.

Experimental

^{1}H NMR spectra were recorded in $CDCl_3$ on a BRUKER AM-300 spectrometer (300 MHz) or Varian 400-MR spectrometer (400 MHz) with TMS as internal standard. ^{19}F NMR spectra were taken on a BRUKER AM-300 spectrometer (282 MHz) or Varian 400-MR spectrometer (376 MHz) using $CFCl_3$ as external standard. ^{13}C NMR spectra were recorded in $CDCl_3$ on a BRUKER AM-300 spectrometer (101 MHz) with TMS as internal standard. IR spectra were obtained with a Nicolet iN 10MX spectrometer. MS (ESI) were obtained on Shimadzu LCMS-2010EV mass spectrometer. MS (EI) were obtained on Waters Micromass GCT Premier mass spectrometer. HRMS (ESI) were obtained on FTMS-7 mass spectrometer. HRMS (MAILDI) were obtained on IonSpec 4.7 mass spectrometer. All the solvents were redistilled before use.

General procedure for monofluoroolefination of aryl aldehydes with FBSM

Under N_2, to a mixture of FBSM (94 mg, 0.3 mmol) and benzaldehyde **1a** (48 mg, 0.45 mmol) in dry THF (1 mL) was added LiHMDS (1 mol•L^{-1} in THF, 0.36 mL, 0.36 mmol) at 78 ℃. The solution was stirred at 78 ℃ for 0.5 h, followed by adding a solution of BzCl (64 mg, 0.45 mmol) in dry THF (1 mL). After 3 h, the solution was allowed to warm to r.t. and LiHMDS (1 mol•L^{-1} in THF, 0.45 mL, 0.45 mmol) was added. The mixture was reacted at r.t. for another 1 h, then was quenched with an excess of saturated NH_4Cl aqueous solution, followed by extraction with ethyl ether. The organic phase was washed with brine and then dried over anhydrous $MgSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using petroleum ether/ethyl acetate (*V*/*V*, 10/1) as eluent to give product **4a** (82 mg, 72%).

(*Z*)-2-Fluoro-1-phenyl-2-(phenylsulfonyl)vinyl benzoate (4a) White solid. m.p. 117－119 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.47 (d, J＝7.2 Hz, 2H), 8.27 (d, J＝7.3 Hz, 2H), 7.98－7.74 (m, 8H), 7.65 (br, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 138.4 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.15 (d, J＝2.4 Hz), 149.28 (d, J＝292.1 Hz), 140.80 (d, J＝28.4 Hz), 138.45, 134.70, 134.38, 131.15, 130.60, 129.78 (d, J＝5.4 Hz), 129.44, 128.88, 128.90, 128.68, 128.33, 127.53 (d, J＝7.7 Hz). MS (ESI) *m*/*z*: 400 (M＋NH_4^+). The characterization data were consistent with reference.[11f]

(*Z*)-2-Fluoro-2-(phenylsulfonyl)-1-*p*-tolylvinyl benzoate (4b) White solid. m.p. 84－85 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.20 (d, J＝7.4 Hz, 2H), 8.00 (d, J＝7.6 Hz, 2H), 7.67 (t, J＝7.1 Hz, 2H), 7.60－7.46 (m, 6H), 7.18 (d, J＝8.1 Hz, 2H), 2.33 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 139.38 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.16 (d, J＝2.5 Hz), 148.78 (d, J＝290.6 Hz), 141.70, 141.02 (d, J＝28.3 Hz), 138.60, 134.54, 134.26, 130.59, 129.58, 129.37, 128.83, 128.64, 128.44, 127.45 (d, J＝8.1 Hz), 126.91 (d, J＝5.5 Hz), 21.50; IR (film) *v*: 3479, 2922, 1751, 1609, 1449, 1347, 1244, 1148, 1019, 817, 705, 592, 567, 487 cm^{-1}. MS (ESI) *m*/*z*: 414 (M＋NH_4^+). HRMS (ESI) calcd for $C_{22}H_{17}FNaO_4S$ (M＋Na^+) 419.0724, found 419.0726.

(*Z*)-2-Fluoro-1-(4-methoxyphenyl)-2-(phenylsulfonyl)vinyl benzoate (4c) White solid. m.p. 80－81 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21 (d, J=7.3 Hz, 2H), 7.99 (d, J=7.5 Hz, 2H), 7.68 (s, 2H), 7.60 (t, J=7.3 Hz, 6H), 6.89 (d, J=8.8 Hz, 2H), 3.81 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −141.0 (s, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.11 (d, J=2.6 Hz), 161.62 (d, J=2.2 Hz), 148.09 (d, J=288.9 Hz), 140.81 (d, J=28.2 Hz), 138.65, 134.40, 134.20, 130.52, 129.28, 129.22 (d, J=8.4 Hz), 128.77, 128.53, 128.38, 121.87 (d, J=5.6 Hz), 114.29, 55.37; IR (film) v: 3067, 2840, 1749, 1604, 1512, 1449, 1347, 1248, 1184, 1148, 1020, 834, 706, 591, 512, 437 cm^{-1}. MS (ESI) m/z: 430.2 (M＋NH_4^+). HRMS (MALDI) calcd for $C_{22}H_{17}FNaO_5S$ (M＋Na^+) 435.0673, found 435.0688.

(*Z*)-1-(4-Bromophenyl)-2-fluoro-2-(phenylsulfonyl)vinyl benzoate (4d) White solid. m.p. 113－114 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.19 (d, J=7.4 Hz, 2H), 7.99 (d, J=7.6 Hz, 2H), 7.69 (t, J=7.1 Hz, 2H), 7.64－7.39 (m, 8H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 137.28 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.1 (d, J=2.5 Hz), 149.50 (d, J=293.4 Hz), 139.82 (d, J=28.5 Hz), 138.21, 134.74, 134.44, 132.15, 130.61, 129.44, 129.01, 128.93, 128.88, 128.75, 128.11, 125.4 (d, J=2.5 Hz); IR (film) v: 3468, 2924, 1746, 1643, 1486, 1348, 1247, 1151, 1143, 1006, 842, 756, 711, 681, 591, 561 cm^{-1}; MS (ESI) m/z: 478 (M＋NH_4^+). HRMS (MAIDI) calcd for $C_{21}H_{14}BrFNaO_4S$ (M ＋ Na^+) 482.9672, found 482.9670.

(*Z*)-1-(3-Bromophenyl)-2-fluoro-2-(phenylsulfonyl)vinyl benzoate (4e) White solid. m.p. 108－109 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.20 (d, J=8.0 Hz, 2H), 7.99 (d, J=7.9 Hz, 2H), 7.78－7.63 (m, 3H), 7.70 －7.60 (m, 6H), 7.25 (t, J=7.9 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 136.51 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.07 (d, J=2.7 Hz), 149.85 (d, J=294.3 Hz), 139.23 (d, J=28.3 Hz), 138.08, 134.85, 134.50, 134.04, 131.82 (d, J=5.4 Hz), 130.65, 130.40, 130.34, 129.49, 128.91, 128.78, 128.06, 126.11 (d, J=7.5 Hz), 122.94. IR (film) v: 3472, 2923, 2852, 1760, 1746, 1562, 1447, 1347, 1152, 1020, 800, 707, 567 cm^{-1}; MS (ESI) m/z: 478 (M ＋ NH_4^+). HRMS (ESI) calcd for $C_{21}H_{14}BrFNaO_4S$ (M＋Na^+) 482.9672, found 482.9690.

(*Z*)-1-(4-Chlorophenyl)-2-fluoro-2-(phenylsulfonyl)vinyl benzoate (4f) White solid. m.p. 107－109 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (d, J=7.6 Hz, 2H), 8.00 (d, J=7.7 Hz, 2H), 7.69 (t, J=7.2 Hz, 2H), 7.63－7.42 (m, 6H), 7.36 (d, J=8.6 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −137.63 (s); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.8 (d, J=2.5 Hz), 149.5 (d, J=294.8 Hz), 139.8 (d, J=28.3 Hz), 138.2, 137.2, 134.8, 134.5, 130.6, 129.5, 129.2, 128.9, 128.9 (d, J=8.1 Hz), 128.8, 128.3 (d, J=5.2 Hz), 128.1; IR (film) v: 3474, 3068, 2922, 1751, 1640, 1588, 1489, 1447, 1350, 1249, 1150, 1113, 1044, 1019, 840 741, 725, 630, 614, 589, 475 cm^{-1}; MS (ESI) m/z: 434 (M＋NH_4^+), 439 (M＋Na^+). HRMS (ESI) calcd for $C_{21}H_{14}ClFNaO_4S$ (M＋Na^+) 439.0178, found 439.0173.

(*Z*)-2-Fluoro-1-(naphthalen-2-yl)-2-(phenylsulfonyl)vinyl benzoate (4g) White solid. m.p. 116－117 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.13 (d, J=7.5 Hz, 2H), 7. 98 (s, 1H), 7.92 (d, J=7.6 Hz, 2H), 7.66 (t, J= 9.4 Hz, 3H), 7.55－7.52 (m, 3H), 7.42 (t, J=7.7 Hz, 4H), 7.35 (t, J=7.3 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 138.63 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.31 (d, J=2.5 Hz), 149.50 (d, J=291.9 Hz), 141.07 (d, J=28.2 Hz), 138.53, 134.70, 134.38, 134.23, 132.72, 130.69, 129.52, 128.97, 128.78, 128.74, 128.46, 128.39 (d, J=3.3 Hz), 128.12, 127.78, 127.16 (d, J= 5.6 Hz), 127.01, 123.62, 123.54; IR (film) v: 3445, 3063, 2918, 2842, 1749, 1635, 1448, 1346, 1230, 1146, 1039, 817, 703, 587, 473 cm^{-1}; MS (ESI) m/z: 450 (M＋NH_4^+). HRMS (ESI) calcd for $C_{25}H_{17}FNaO_4S$ (M＋Na^+): 455.0724, found 455.0717.

(1*Z*,3*E*)-1-Fluoro-4-phenyl-1-(phenylsulfonyl)-buta-1,3-dien-2-yl benzoate (4h) White solid. m.p. 146－147 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.27 (d, J=7.3 Hz, 2H), 7.98 (d, J=7.6 Hz, 2H), 7.70 (dd, J= 14.5, 7.3 Hz, 2H), 7.58 (t, J=7.0 Hz, 4H), 7.46－7.38 (m, 2H), 7.36－7.28 (m, 3H), 7.06－6.81 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 139.72 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.02 (d, J=2.5 Hz), 147.83 (d, J=291.6 Hz), 140.78 (d, J=29.9 Hz), 138.30, 136.54, 136.48, 134.87, 134.67, 134.35, 130.69, 129.91, 129.41, 128.92, 128.73, 128.32, 127.78, 115.15; IR (film) v: 3851, 3064, 2922, 1741, 1268, 1447, 1348, 1244, 1147, 1062, 969, 859, 745, 683, 587, 447 cm^{-1}; MS (ESI) m/z: 426 (M＋NH_4^+). HRMS (ESI) calcd for $C_{23}H_{17}FNaO_4S$ (M＋Na^+): 431.0724, found 419.0737.

1-(2-Bromophenyl)-2-fluoro-2,2-bis(phenylsulfonyl)ethyl benzoate (6) White solid. m.p. 222－223 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.31 (d, J=7.5 Hz, 2H), 7.95 (d, J=7.5 Hz, 5H), 7.66 (d, J=7.2 Hz, 3H), 7.53 (t, J=7.9 Hz, 6H), 7.43 (d, J=7.9 Hz, 1H), 7.36－7.21 (m, 1H), 7.20－7.07 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −137.08 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.10, 137.05, 135.48, 131.41 (d, J = 1.8 Hz), 133.90, 132.67, 131.95, 131.82, 131.71, 131.42, 131.40, 130.81, 130.64, 129.42, 128.69, 128.56, 128.52, 127.06, 124.07, 112.44 (d, J=272.1 Hz), 72.43 (d, J=26. 4 Hz). IR (film) v: 3071, 1934, 1731, 1583, 1468, 1355, 1257, 1093, 775, 686, 551, 525 cm^{-1}. MS (ESI) m/z: 620 (M＋NH_4^+). HRMS (ESI) calcd for $C_{27}H_{20}BrFNaO_6S_2$ (M＋Na^+): 624.9761, found 624.9775.

1-Fluoro-4-phenyl-1,1-bis(phenylsulfonyl)butan-2-yl benzoate (7) White solid, m.p. 204－205 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.01 (d, J=7.3 Hz, 2H), 7.91 (d, J=7.9 Hz, 2H), 7.76－7.54 (m, 5H), 7.54－7.39 (m, 6H), 7.34－7.11 (m, 5H), 5.85 (d, J=9.8 Hz, 1H), 3.30－2.37 (m, 4H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 138.37 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.42, 139.95, 135.82, 135.31, 135.17, 133.58, 131.16, 130.29, 128.95, 128.91, 128.78, 128.53, 128.45, 126.27, 112.29 (d, J=278.2 Hz), 70.86 (d, J=19.2 Hz), 31.99, 31.23; IR (film) v: 3448, 3068, 1973, 1736, 1583, 1449, 1351, 1264, 1172, 1096, 1030, 965, 735, 716, 586, 565,

518, 452 cm^{-1}; MS (ESI) *m*/*z*: 570 ($M+NH_4^+$). HRMS (ESI) calcd for $C_{29}H_{25}FNaO_6S_2$ ($M+Na^+$): 575.0969, found 575.0956.

Procedure for chlorination of FBSM in the presence of aldehyde 1c

Under N_2, to a mixture of FBSM (157 mg, 0.5 mmol) and 4-methoxybenzaldehyde **1c** (107 mg, 0.75 mmol) in dry THF (2 mL) was added LiHMDS (1 mol•L^{-1} in THF, 0.6 mL, 0.6 mmol) at 78 ℃. The solution was stirred at 78 ℃ for 0.5 h, followed by adding a solution of TsCl (147 mg, 0.75 mmol) in dry THF (1 mL). After 3 h, the reaction was quenched with an excess of saturated NH_4Cl aqueous solution, followed by extraction with CH_2Cl_2. The organic phase was washed with brine and then dried over anhydrous $MgSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using petroleum ether/ethyl acetate (*V*/*V*, 4/1) as eluent to give product **5** (73 mg, 42%).

Chlorofluorobis(phenylsulfonyl)methane (5) White solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.07 (d, J=7.7 Hz, 4H), 7.81 (t, J=7.5 Hz, 2H), 7.64 (t, J=7.7 Hz, 4H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 107.58 (s); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 136.26, 133.19, 131.58, 129.36, 118.60 (d, J=329.7 Hz); IR (film) *v*: 3061, 1580, 1449, 1367, 1190, 1078, 846, 684, 558 cm^{-1}; MS (ESI) *m*/*z*: 348.7 ($M+H^+$). HRMS (ESI) calcd for $C_{13}H_{10}ClFNaO_4S_2$ ($M+Na^+$): 370.9585, found 370.9597.

Procedure for preparation of organotin reagent 8

Under N_2, a mixture of compound **4a** (356 mg, 0.93 mmol), nBu$_3$SnH (0.45 mL, 1.71 mmol), and AIBN (14 mg, 0.08 mmol) in dry benzene (10 mL) was refluxed for 5 h. The solution was cooled to r.t., and saturated KF aqueuous solution (10 mL) was added. After 0.5 h, the mixture was extracted with ethyl ether. The organic phase was washed with brine and then dried over anhydrous $MgSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using petroleum ether as eluent to give product **8** (250 mg, 93%).

2-Fluoro-1-phenyl-2-(tributylstannyl)vinyl benzoate (8) Colorless oil. *Z*/*E* =96/4. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.16 (d, J=8.4 Hz, 2H), 7.65 (t, J=7.4 Hz, 1H), 7.59 (d, J=7.9 Hz, 2H), 7.51 (t, J=7.8 Hz, 2H), 7.34 (t, J=7.6 Hz, 2H), 7.26 (t, J=7.1 Hz, 1H), 1.55−1.42 (m, 6H), 1.31−1.17 (m, 6H), 1.06−0.98 (m, 6H), 0.83 (t, J=7.3 Hz, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 117.26 (s, 0.04F), 128.94 (s, 0.96F); MS (EI) *m*/*z*: 355 (100, M–*n*Bu–OBz), 475 (M–*n*Bu). The characterization data were consistent with reference.[11f]

Procedure for preparation of compound 9

Under N_2, to a solution of compound **8** (79 mg, 0.15 mmol) in dry CH_2Cl_2 (1 mL) was added a solution of I_2 (46 mg, 0.18 mmol) in CH_2Cl_2 (2 mL) at r.t. After 1 h, the reaction was quenched by adding saturated Na_2SO_3 aqueous solution (2 mL), followed by extraction with ethyl ether. The organic phase was washed with brine and then dried over anhydrous $MgSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using petroleum ether as eluent to give yellow oil (51 mg, 73%).

(*Z*)-2-Fluoro-2-iodo-1-phenylvinyl benzoate (9) ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.21 (d, J=7.3 Hz, 2H), 7.68 (t, J=7.4 Hz, 1H), 7.61−7.47 (m, 4H), 7.44−7.32 (m, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 96.93 (s, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.87, 141.32 (d, J=29.9 Hz), 134.12, 130.49, 130.42, 129.26, 128.79, 128.63, 126.45, 126.37, 107.74 (d, J=329.4 Hz); IR (film) *v*: 1748, 1600, 1495, 1451, 1243, 1138, 1104, 1043, 1020, 764,705, 646, 597 cm^{-1}; MS (EI) *m*/*z*: 105 (100, $[Bz]^+$), 241 (16.66, $[M–I]^+$). HRMS (EI) calcd for $C_{15}H_{10}FO_2$ ($[M–I]^+$): 241.0665, found 241.0666.

Procedure for preparation of compound 10

Under N_2, the solution of compound **8** (79 mg, 0.15 mmol), BzCl (26 mg, 0.18 mmol), $Pd(PPh_3)_4$ (16 mg, 0.015 mmol), and CuI (29 mg, 0.15 mmol) in dry THF (3 mL) was refluxed for 4 h. The mixture was directly subjected to silica gel column chromatography using petroleum ether/ethyl acetate (*V*/*V*, 10/1) as eluent to give compound **10** (46 mg, 89%).

2-Fluoro-3-oxo-1,3-diphenylprop-1-en-1-yl benzoate (10) Yellow solid. *Z*/*E*=4/96, m.p. 93−95 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.03 (d, J=8.4 Hz, 2H), 7.85 (d, J=7.0 Hz, 2H), 7.77 (dd, J=6.6, 3.0 Hz, 2H), 7.60 (t, J=7.5 Hz, 1H), 7.54−7.35 (m, 8H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: 119.06 (s, 0.04F), 132.96 (s, 0.96F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 186.96, 186.67, 164.27, 148.94 (d, J=262.6 Hz), 141.77 (d, J=33.1 Hz), 136.57, 136.55, 133.90, 133.11, 130.97, 130.92, 130.58, 130.49, 130.31, 129.10 (d, J=4.4 Hz), 128.88, 128.76, 128.58, 128.51, 128.46, 127.73 (d, J=8.3 Hz); IR (film) *v*: 3473, 3066, 2020, 1749, 1675, 1616, 1596, 1492, 1447, 1332, 1274, 1241, 1174, 1128, 983, 774, 706, 641, 553, 447 cm^{-1}; MS (EI) *m*/*z*: 105 (100, $[Bz]^+$), 346 (3.28, M^+). HRMS (EI) calcd for $C_{22}H_{15}FO_3$ (M^+): 346.1005, found 346.1007.

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[15] CCDC 936444 (**4g**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www. ccdc.cam.ac.uk/data_request/cif.

(Cheng, F.)

