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Facile synthesis of α-monofluoromethyl alcohols: Nucleophilic monofluoromethylation of aldehydes using $TMSCF(SO_2Ph)_2$ ☆

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ABSTRACT

α-Fluoromethyl phenyl sulfone derivatives have been extensively employed in various reactions as versatile fluoromethylating reagents. While nucleophilic monofluoromethylations of aldehydes have been achieved using fluoromethyl phenyl sulfone or fluorobis(sulfonyl)methanes, a facile protocol under mild reaction conditions remains an ardently sought goal. We now report a feasible synthetic approach toward β-monofluorinated alcohols using α-trimethylsilyl-α-fluorobis(phenylsulfonyl)methane [$TMSCF(SO_2Ph)_2$, TFBSM] as a novel monofluoromethylating reagent. Initiated by a catalytic amount of fluoride, the reagent can be readily added to a variety of aldehydes providing the desired products in high yields. Computational and kinetic studies have revealed the exceptional lability of the Si–C bond in TFBSM compared with other fluoromethylsilane counterparts.

1. Introduction

Selective incorporation of fluoromethyl moieties into organic molecules has received increasing attention because of the immense potential of fluoroorganics in life and materials sciences [1]. To address this synthetic demand, α-fluoromethyl phenyl sulfone derivatives were recently developed as viable fluoromethylating reagents [2]. Of particular interest, fluorobis(phenylsulfonyl)methane (FBSM) and its analogues have facilitated many transformations, which are otherwise difficult to achieve [3]. In spite of these successful documentations, the nucleophilic addition of FBSM to aldehydes was previously claimed to be unattainable because of its reversibility, thereby necessitating the utilization of 2-fluoro-1,3-benzodithiole-1,1,3,3-tetraoxide as the pronucleophile [4]. Hu et al., however, showed that FBSM anion can be added to aldehydes using LiHMDS as the base [5]. The obtained lithium carbinolates, stabilized through strong Li–O interactions, were then *in situ* quenched with Bronsted acids (for example, trifluoroacetic acid) to afford the corresponding alcohols (Scheme 1). We therefore surmised that FBSM anion-aldehyde adducts (carbinolates) can also be captured through a reaction with Lewis acids. Moreover, a one-pot addition reaction between the FBSM anion and aldehydes can be achieved under a *self*-quenching mechanism by utilizing α-trimethylsilyl-α-fluorobis(phenylsulfonyl)methane [$TMSCF(SO_2Ph)_2$, TFBSM], which serves as both a pronucleophile and a Lewis acid [6,7].

2. Results and discussion

To examine our proposal, we initially focused on the preparation of TFBSM using FBSM, which was readily obtained on large scale according to a method developed in our laboratory [8]. After an extensive reaction condition screening, the desired reagent was successfully prepared in 43% yield by treating FBSM sodium salt with TMSCl in THF (Scheme 2). The compound was found to be stable and can be stored in a glove box for several months. However, it underwent a swift decomposition (usually within a few days) to FBSM in the presence of moisture or in $CDCl_3$ solution, which contains some protic acid impurities. Surprisingly, unlike $TMSCF_3$ (the Ruppert-Prakash reagent) and [(phenylsulfonyl)difluoromethyl]trimethylsilane ($TMSCF_2SO_2Ph$), which are substantially inert toward aqueous HCl solution, instantly hydrolysis of TFBSM was observed in concentrated aq. HCl (12 M), indicating the exceptional lability of the $Si–C_F$ bond.

With the desired reagent in hand, we initially performed the reaction between TFBSM and benzaldehyde using tetra-*n*-butylammonium difluorotriphenylsilicate (TBAT) as an initiator in THF. As expected, the desired β-fluoro silyl ether was obtained, however, in only 22% yield (Table 1, entry 1). In an effort to enhance the efficacy of the protocol, we further investigated various reaction parameters, such as initiators, solvents, temperatures, and proportions of substrates. We found that the proportions of the substrates can significantly impact outcomes of the reaction

☆ Dedicated to Professor Wei-Yuan Huang on the occasion of his Ninetieth Birthday.

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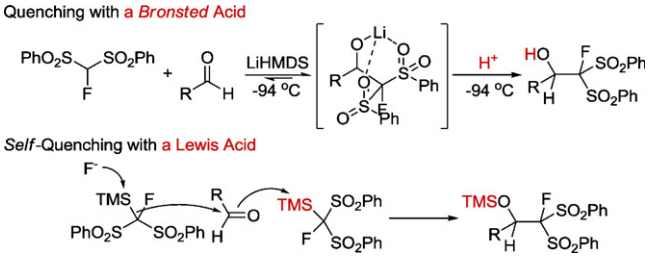
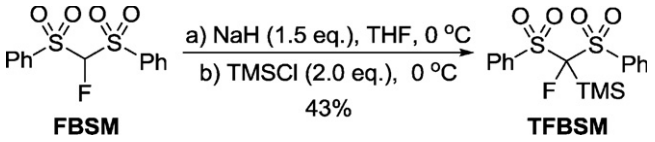


Scheme 1. Nucleophilic addition of FBSM and TFBSM to aldehydes.

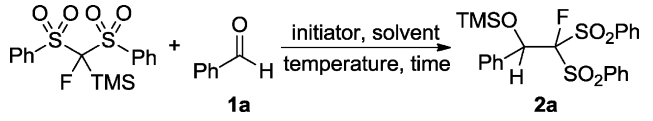


Scheme 2. Preparation of α-trimethylsilyl-α-fluorobis(phenylsulfonyl)methane (TFBSM).

(Table 1, entries 1–5 and 6–9). Low yields observed in entries 1–5 can be rationalized as the competitive protonation of FBSM anion due to the presence of moisture in the reaction system. Employing an excess amount of TFBSM can, therefore, compensate the consumption of the pronucleophile. In addition, CsF was found to be a superior initiator over several other Lewis bases (Table 1, entries 1–9). Solvent effects were also pronounced (Table 1, entries 9, 11–13), which showed THF as the optimal reaction medium. While addition sequences of reagents were critical (Table 1, entries 8 and 10), yields did not decrease, when the reaction time was shortened to 4 h (Table 1, entry 14). In particular, performing the reaction at room temperature resulted in a decrease in yield to 75%.

With optimized reaction conditions established, we explored the scope of this protocol (Table 2). The reaction was found to be applicable to aromatic aldehydes bearing both electron-withdrawing and electron-donating groups, and furnished products in high yields (entries 1–5, Table 2). While the 2,4,6-trimethoxybenzaldehyde **1d** underwent the reaction smoothly (entry 4, Table 2), the

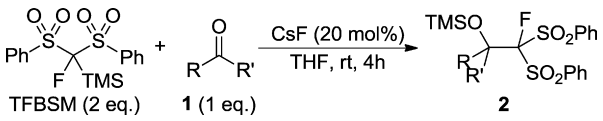
Table 1
Optimization of the addition reaction of TFBSM with benzaldehyde.

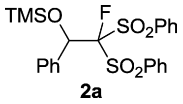
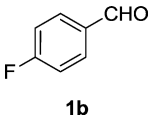
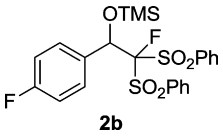
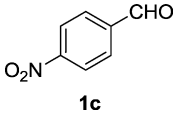
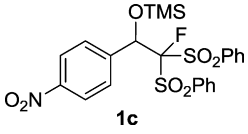
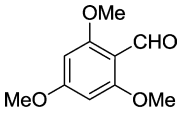
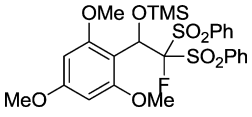
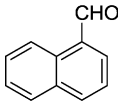
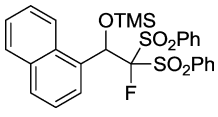
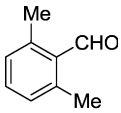
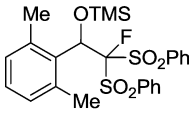
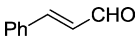
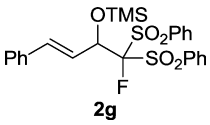
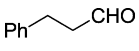
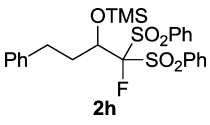
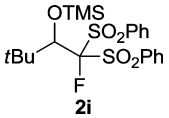
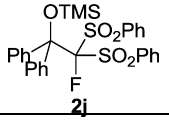


Entry	Initiator	Solvent	TFBSM/**1a**/Initiator	Temp. (°C)	Time (h)	Yield (%)[c]
1[a]	TBAT	THF	1/2/0.05	0–rt	12	22
2[a]	TBAF[d]	THF	1/2/0.05	0–rt	12	0
3[a]	$Me_3N^+–O^-$	THF	1/2/0.20	0–rt	12	34
4[a]	KF	THF	1/2/0.20	0–rt	12	38
5[a]	CsF	THF	1/2/0.20	0–rt	12	31
6[a]	TBAT	THF	2/1/0.05	0–rt	12	66
7[a]	$Me_3N^+–O^-$	THF	2/1/0.20	0–rt	12	71
8[a]	KF	THF	2/1/0.20	0–rt	12	78
9[a]	CsF	THF	2/1/0.20	0–rt	12	99
10[b]	KF	THF	2/1/0.20	0–rt	12	0
11[a]	CsF	Et_2O	2/1/0.20	0–rt	12	25
12[a]	CsF	DMF	2/1/0.20	0–rt	12	0
13[a]	CsF	Toluene	2/1/0.20	0–rt	12	54
14[a]	CsF	THF	2/1/0.30	0	4	99
15[a]	CsF	THF	2/1/0.20	rt	4	75

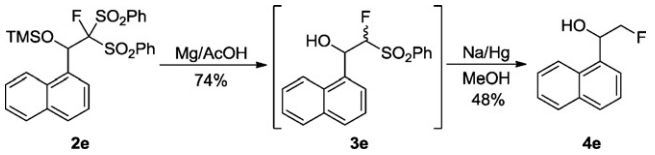
[a] Fluoride source in THF was added to a mixture of TFBSM and **1a** in THF.
[b] TFBSM in THF was added to a mixture of KF and 1**a** in THF.
[c] ^{19}FNMR yields.
[d] A TBAF solution in THF (1M) containing 5 wt% H_2O was used.

Table 2
Monofluoromethylation of aldehydes with TFBSM.



Entry	Carbonyl compounds	Product	Yield (%)[a]
1	PhCHO **1a**	 **2a**	99/81
2	 **1b**	 **2b**	93/90
3	 **1c**	 **1c**	99/86
4	 **1d**	 **2d**	97/87
5	 **1e**	 **1e**	96/83
6	 **1f**	 **2f**	0/0
7	 **1g**	 **2g**	88/80
8	 **1h**	 **2h**	64/54
9	*t*Bu–CHO **1i**	 **2i**	0/0
10	 **1j**	 **2j**	0/0

[a] ^{19}F NMR yields/isolated yields.



Scheme 3. Synthesis of 2-fluoro-1-(naphthalen-1-yl)ethanol via reductive desulfonation of **2e**.

addition reaction was completely impeded in the case of 2,4-dimethyl benzaldehyde (**1f**), probably due to more effective steric demand of the methyl groups (entry 6, Table 2). The protocol was also suitable to α,β-unsaturated aldehyde (cinnamaldehyde) **1g**, which exclusively gave 1,2-adduct (**2g**) in 80% yield (entry 7, Table 2). Aliphatic aldehyde **1h** was also compatible to the method, which, however, afforded the corresponding carbinol **2h** in a lower yield (entry 8, Table 2). Similar to the addition reaction to aromatic aldehydes, the steric encumbrance of aliphatic aldehydes can considerably affect the outcome of the reaction as well. As demonstrated, pivalaldehyde (**1i**) was unable to participate in the addition reaction (entry 9, Table 2). It is worth noting that the attempt to add TFBSM to benzophenone was unsuccessful under similar reaction conditions, indicating the limitation of the present protocol (entry 10, Table 2). Since the previous study demonstrated that fluoromethyl phenyl sulfone ($PhSO_2CH_2F$) readily underwent addition reaction with various ketones [9], the low reactivity of the FBSM anion toward ketones can be probably attributed to steric effects.

To demonstrate the synthetic utility of the present protocol, β-fluoro silyl ether **2e** was subjected to the reductive Mg/acetic acid desulfonation system. As depicted in Scheme 3, the corresponding monosulfones (**3e**) were generated in 74% yield as a mixture of two diastereomers under the reaction conditions. Further desulfonation of the monosulfones was achieved using Na/Hg/MeOH system to form β-monofluorinated alcohol **4e** in 48% yield. Importantly, we noticed that the rate of the desilylation of **2e** was slower than that of its desulfonation in Mg/acetic acid system, thereby permitting the desulfonation without significant decomposition of **2e**. In comparison, rapid degradation of **2e** was found to be inevitable under Mg/MeOH reductive conditions.

As aforementioned, the Si–C_F bond in TFBSM was found to be rather labile compared with those in $TMSCF_3$ and $PhSO_2CF_2TMS$. This observation intrigued us to explore the nature of Si–C_F bonds in these fluoromethylating reagents. The previously reported crystal structure of $TMSCF_3$ (**4**) has showed an elongated Si–C_F bond (1.944 Å) compared with other Si–C_H bond in the same

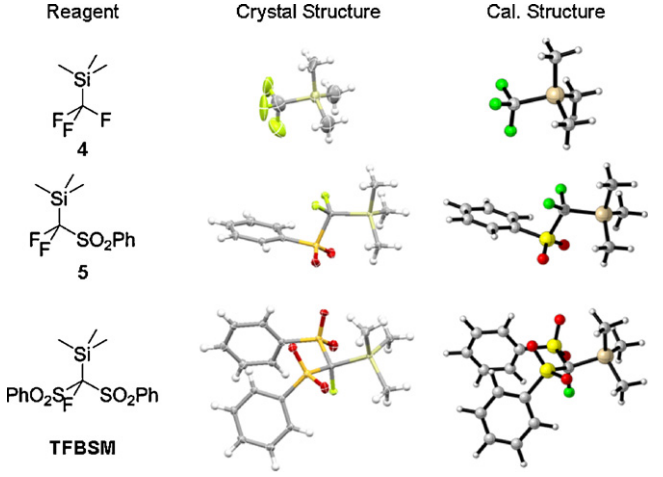
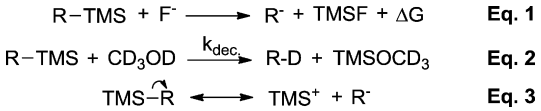


Fig. 1. Crystal structures of various fluoromethyl silane reagents and their computed structures at the B3LYP/6-311+G(d,p) level.

molecule (bond distances range from 1.848 to 1.862 Å) (Fig. 1 and Table 3) [10]. Crystal structures of [(phenylsulfonyl)difluoromethyl]trimethylsilane ($TMSCF_2SO_2Ph$, **5**) and TFBSM were obtained herein, which demonstrated even longer Si–C_F bonds of 1.957 Å and 1.994 Å, respectively (Fig. 1 and Table 3). This result presumably suggests a gradual decrease in the strengths of Si–C_F bonds from $TMSCF_3$ to TFBSM.

To achieve a quantitative assessment of Si–C_F bond strengths in these reagents, systematic theoretical calculations on **4**, **5**, and TFBSM were carried out at the B3LYP/6-311+G(d,p) level [11]. As depicted in Fig. 1, optimized geometries of these molecules highly resemble their structures in the solid state. Consistent with the tendency observed in crystal structures, the Si–C_F bond distance order of TFBSM > $TMSCF_2SO_2Ph$ > $TMSCF_3$ is followed (column 2, Table 3). Wiberg bond indices [12] of Si–C_F bonds were computed to reveal the weakness of the Si–C_F bond in TFBSM, which was shown to be only 77% of the value of the TMS–CH_3 bond [13]! A more accurate evaluation of bond strengths was achieved on the basis of free energy changes (ΔG) of hypothesized reactions between silane reagents and a fluoride anion (Table 3, Eq. (1)). For all three reagents, the Si–C_F bond cleavage was thermodynamically favorable both in the gas phase and in THF solution. Among these reagents, the Si–C_F bond in TFBSM was found to be particularly labile (57.1 kcal/mol and 37.8 kcal/mol weaker than **4** and **5** in the gas phase, respectively). Intriguingly, such a bond strength order

Table 3
Investigation of Si–C_F bond strength in various fluoromethyl silane reagents.



R-TMS	Exp./Cal. Si–CF_n bond distances (Å)	NBO charge on Si	Wiberg bond indices (Si–CF_n)[a,b]	ΔG_{gas}[a] (kcal/mol)	ΔG_{THF}[a,c] (kcal/mol)	$k_{dec.}$[d] ($L\,mol^{-1}\,s^{-1}$)
$TMSCF(SO_2Ph)_2$	1.994/2.010	+1.618	0.6457 (77%)	−89.4	−34.6	Ins. Dec.
$TMSCF_2SO_2Ph$	1.957/1.971	+1.545	0.7085 (85%)	−51.6	−17.3	2.6×10^{-5}
$TMSCF_3$	1.943/1.953	+1.493	0.7564 (91%)	−32.3	−8.0	1.1×10^{-5}
$TMSCF_2H$	–/1.936	+1.497	0.7895 (95%)	−13.0	+9.8	–
$TMSCFH_2$	–/1.913	+1.518	0.8120 (97%)	+0.5	+23.5	–
$TMSCH_3$	–/1.891	+1.563	0.8339 (100%)	+11.0	+35.2	–

[a] Computed at the B3LYP/6-311+G(d,p) level.
[b] Compared with the Wiberg bond index of 0.8339 in tetramethylsilane.
[c] The effect of THF solvent was treated implicitly using the standard PCM method of Gaussian03.
[d] Determined via ^{19}F NMR a 0.1 M solution of the corresponding reagent at 298 K.

can also be experimentally supported by methanolysis rates of these reagents as TFBSM > $TMSCF_2SO_2Ph$ > $TMSCF_3$ (Eq. (2) and column 7, Table 1).

To rationalize the remarkably elongated Si–C_F bonds in TFBSM, we further computed Si–C_F bond distances in $TMSCF_2H$, $TMSCH_2F$, and $TMSCH_3$ at the B3LYP/6-311+G(d,p) level. Clear trends were observed through a systematic structural variation from $TMSCH_3$ to TFBSM. As shown in Table 3, the increase in bond distances and the decrease in Wiberg bond indices can be seen from $TMSCH_3$ to TFBSM, indicating a gradual weakening of the Si–C_F bonds. In particular, by comparing the Si–C_F bond distances of $TMSCH_2F$ < $TMSCF_3$ < TFBSM, we can conclude that the exceptionally long Si–C_F bond distance in TFBSM is unlikely to result from the removal of the fluorine substituent. Simply, it can be understood as the prevailing stabilizing effect of the phenylsulfonyl group over fluorine on the carbanions, which leads to more contribution from ionic resonance structures (comparing the NBO charges on Si atoms in column 3 in Table 3, and Eq. (3)) [14].

3. Conclusion

In conclusion, we have successfully synthesized α-trimethylsilyl-α-fluorobis(phenylsulfonyl)methane (TFBSM) as a viable nucleophilic monofluoromethylating reagent for aldehydes. Functioning as both a pronucleophile and a Lewis acid, the reagent allowed the one-step addition of the FBSM anion toward various aldehydes via a self-quenching mechanism. Undergoing a reductive desulfonation reaction, the silyl ether adduct can be further converted to β-monofluorinated alcohol, which, however, was not feasible from the corresponding β-bis(phenylsulfonyl)-β-fluoroalcohol. Mechanistic studies revealed the remarkably weak nature of the Si–C_F bond in TFBSM, which facilitated the facile cleavage of the Si–C_F bond.

4. Experimental

Unless otherwise mentioned, all chemicals were purchased from commercial sources. THF was freshly distilled over Na before use. The NMR spectra were recorded on 400 MHz and 500 MHz superconducting NMR spectrometers, respectively. All the unknown compounds have been fully characterized by NMR spectroscopy and high resolution MS analysis, whereas structures of all known products were confirmed by comparison of their ^{1}H NMR and ^{19}F NMR spectra with reported data. ^{1}H NMR chemical shifts (δ) were determined relative to internal tetramethylsilane at δ 0.0 ppm or to the signal of a residual solvent in $CDCl_3$ (δ 7.26 ppm). ^{13}C NMR chemical shifts were determined relative to internal tetramethylsilane at δ 0.0 ppm or to the ^{13}C signal of $CDCl_3$ at δ 77.16 ppm. ^{19}F NMR chemical shifts were determined relative to internal $CFCl_3$ at δ 0.0 ppm.

4.1. Typical procedure for the preparation of α-trimethylsilyl-α-fluorobis(phenylsulfonyl)methane (TFBSM)

To a suspension of NaH (216 mg, 9 mmol) in THF (11 mL) was slowly added a solution of FBSM (1.88 g, 6 mmol) in THF (11 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 30 min, and TMSCl (1.52 mL, 12 mmol, freshly distilled) was added dropwise to the reaction mixture. The reaction mixture was further stirred for 1 h and transferred into a 25 mL syringe through a needle. The suspension was then passed through a 25 mm GD/X Whatman syringe filter (0.45 μm GMF, heated in an oven at 90 °C for 1 h before use) into a Schlenk tube under Ar. Anhydrous hexanes (20 mL) was carefully added onto the top of the solution. Agitation of the THF layer should be avoided, so that a two-layer system can be formed. The Schlenk tube was subsequently stored in a freezer (−20 °C) for 24–48 h until a large amount of colorless needles was formed (a small amount of cloudy precipitate may be formed as well). The solvents were then removed from the tube via a syringe under Ar. The crystals were rinsed with anhydrous hexanes (2× 10 mL), which were also removed via a syringe. The product was dried under vacuum at room temperature and then stored in a glove box (997 mg, 43%).

^{1}H NMR (C_6D_6): δ 0.70 (d, J = 0.7 Hz, 9H), 6.45–6.48 (m, 4H), 6.67–6.70 (m, 2H), 7.35–7.37 (m, 4H). ^{19}F NMR (C_6D_6): δ −157.0 (s, 1F). ^{13}C NMR (C_6D_6): δ −0.43 (d, J = 2.4 Hz) 121.0 (d, J = 268.3 Hz), 128.4, 128.5, 130.2 (d, J = 1.9 Hz), 133.6. HRMS data were not obtained due to the extreme lability of the compound. M.p. dec. 139–147 °C.

4.2. Typical procedure for the addition reaction of TFBSM to aldehydes and benzophenone

To a solution of benzaldehyde (**1a**, 20.2 mg, 0.19 mmol) and TFBSM (147 mg, 0.38 mmol, 2 equiv.) in anhydrous THF (0.5 mL) was quickly added a suspension of CsF (6 mg, 0.04 mmol, 20 mol%) in anhydrous THF (0.5 mL) under Ar at 0 °C. The progress of the reaction was monitored via ^{19}F NMR spectroscopy, which showed the completion of the reaction after stirring for 4 h. The solvent was evaporated under vacuum. The resulting crude product was purified via silica gel column chromatography using ethyl acetate and hexanes as eluent.

(2-Fluoro-1-phenyl-2,2-bis(phenylsulfonyl)ethoxy)trimethylsilane (**2a**). ^{1}H NMR ($CDCl_3$): δ 0.10 (s, 9H), 5.92 (d, J = 7.8 Hz, 1H), 7.14–7.27 (m, 5H), 7.35–7.39 (m, 2H), 7.53–7.56 (m, 2H), 7.56–7.60 (m, 1H), 7.64–7.66 (m, 2H), 7.68–7.71(m, 1H), 7.98–8.00 (m, 2H). ^{19}F NMR ($CDCl_3$): δ −132.3 (d, J = 7.8 Hz, 1F). ^{13}C NMR ($CDCl_3$): δ 0.2, 73.7 (d, J = 23.1 Hz), 114.4 (d, J = 270.7 Hz), 127.8, 128.3 (d, J = 2.4 Hz), 128.4, 128.7, 128.8, 131.0 (d, J = 1.6 Hz), 131.4 (d, J = 1.8 Hz), 134.4, 135.0, 135.6 (d, J = 1.4 Hz), 136.5, 138.2. HRMS: calcd for $C_{23}H_{24}F_2NaO_5S_2Si^+$ 535.0695 (M+Na^+), found: 535.0692. M.p. 113–115 °C.

(2-Fluoro-1-(4-fluorophenyl)-2,2-bis(phenylsulfonyl)ethoxy)-trimethylsilane (**2b**). ^{1}H NMR ($CDCl_3$): δ 0.08 (s, 9H), 5.89 (d, J = 8.2 Hz, 1H), 6.86–6.90 (m, 2H), 7.15–7.18 (m, 2H), 7.38–7.42 (m, 2H), 7.52–7.56 (m, 2H), 7.56–7.61 (m, 1H), 7.66–7.72 (m, 3H), 7.95–7.97 (m, 2H). ^{19}F NMR ($CDCl_3$): δ −113.3 (m, 1F), −132.52 (d, J = 8.1 Hz, 1F). ^{13}C NMR ($CDCl_3$): δ 0.1, 73.3 (d, J = 23.0 Hz), 114.3 (d, J = 270.4 Hz), 114.7, 114.9, 128.5, 128.8, 130.2 (dd, J = 8.4 Hz, J = 2.5 Hz), 131.0 (dd, J = 30.0 Hz, J = 1.8 Hz), 131.4 (dd, J = 3.2 Hz, J = 1.8 Hz), 134.6, 135.0, 136.6, 138.1, 163.0 (d, J = 247.8 Hz). HRMS: calcd for $C_{23}H_{24}F_2NaO_5S_2Si^+$ 535.0695 (M+Na^+), found: 535.0692. M.p. 130–132 °C.

(2-Fluoro-1-(4-nitrophenyl)-2,2-bis(phenylsulfonyl)ethoxy)trimethylsilane (**2c**). ^{1}H NMR ($CDCl_3$): δ 0.09 (s, 9H), 6.00 (d, J = 7.0 Hz, 1H), 7.40–7.44 (m, 4H), 7.54–7.58 (m, 2H), 7.63–7.67 (m, 1H), 7.70–7.74 (m, 3H), 7.94–7.96 (m, 2H), 8.07–8.10 (m, 2H). ^{19}F NMR ($CDCl_3$): δ −132.5 (d, J = 7.0 Hz, 1F). ^{13}C NMR ($CDCl_3$): δ 0.1, 73.2 (d, J = 22.7 Hz), 113.8 (d, J = 270.3 Hz), 122.8, 128.6, 129.0, 129.3 (d, J = 2.7 Hz), 131.1 (d, J = 1.6 Hz), 131.2 (d, J = 1.8 Hz), 135.0, 135.3, 136.1, 137.6, 143.1 (d, J = 2.1 Hz), 148.1. HRMS: calcd for $C_{23}H_{25}FNO_7S_2Si^+$ 538.0820 (M+H^+), found: 538.0827. M.p. 126–127 °C.

(2-Fluoro-2,2-bis(phenylsulfonyl)-1-(2,4,6-trimethoxyphenyl)ethoxy)trimethylsilane (**2d**). ^{1}H NMR ($CDCl_3$): δ 0.00 (s, 9H), 3.47 (br s, 3H), 3.89 (s, 3H), 4.04 (br s, 3H), 5.75 (br s, 1H), 6.17(br s, 1H), 6.77 (d, J = 27.5 Hz, 1H), 7.39–7.44 (m, 2H), 7.59–7.67 (m, 5H), 7.76–7.80 (m, 1H), 8.15–8.17 (m, 2H). ^{19}F NMR ($CDCl_3$): δ −143.8 (d, J = 27.5 Hz, 1F). ^{13}C NMR ($CDCl_3$): δ 0.1, 54.9, 55.3, 56.3, 64.4 (d, J = 16.8 Hz), 89.9, 91.0, 106.4, 118.2 (d, J = 291.3 Hz), 128.0, 128.5, 130.0 (d, J = 1.8 Hz), 130.9 (d, J = 1.4 Hz), 133.8, 134.2, 137.9, 139.1, 162.4. HRMS: calcd for $C_{23}H_{24}FNO_8S_2^+$ 511.0891 (M−TMS+H^+), found: 511.0886. M.p. (dec.) 142–143 °C.

(2-Fluoro-1-(naphthalen-1-yl)-2,2-bis(phenylsulfonyl)ethoxy)trimethylsilane (**2e**). ^{1}H NMR ($CDCl_3$): δ 0.11 (s, 9H), 6.80 (br s, 1H), 7.21–7.25 (m, 1H), 7.33–7.37 (m, 3H), 7.41–7.47 (m, 4H), 7.51–7.59 (m, 1H), 7.67–7.79 (m, 5H), 7.92–7.96 (m, 3H). ^{19}F NMR ($CDCl_3$): δ −132.0 (br s, 1F) (Two rotamers were observed in ^{19}F NMR spectrum. The major rotamer appeared as a broad singlet, whereas the minor one, partially overlapped with the major isomer, was shown to be a doublet at −132.1 ppm). ^{13}C NMR ($CDCl_3$): δ 0.2, 69.9 (br s), 115.7 (d, J = 274.1 Hz), 123.3, 124.8, 125.5, 126.4, 128.0, 128.5, 128.7, 128.8, 129.7, 131.0, 131.2, 131.5, 131.7, 133.3, 134.4, 135.0, 136.1, 138.6. HRMS: calcd for $C_{27}H_{27}FNaO_5S_2Si^+$ 565.0945 (M+Na$^+$), found: 565.0945. M.p. 154–155 °C.

(E)-((1-Fluoro-4-phenyl-1,1-bis(phenylsulfonyl)but-3-en-2-yl)oxy)trimethylsilane (**2g**). ^{1}H NMR ($CDCl_3$): δ 0.00 (s, 9H), 5.37 (dd, J = 7.9 Hz, J = 4.9 Hz, 1H), 6.58–6.67 (m, 2H), 7.30–7.38 (m, 1H), 7.38–7.45 (m, 2H), 7.48–7.50 (m, 2H), 7.52–7.58 (m, 2H), 7.59–7.67 (m, 2H), 7.68–7.74 (m, 1H), 7.74–7.82 (m, 1H), 7.93–7.96 (m, 1H), 8.13–8.16 (m, 2H). ^{19}F NMR ($CDCl_3$): δ −136.87 (d, J = 7.9 Hz, 1F). ^{13}C NMR ($CDCl_3$): δ 0.1, 73.7 (d, J = 21.0 Hz), 114.1 (d, J = 269.5 Hz), 123.7 (d, J = 4.4 Hz), 127.2, 128.4, 128.5, 128.6, 128.7, 131.3 (d, J = 1.5 Hz), 131.8 (d, J = 1.5 Hz), 134.8, 134.9 (d, J = 1.5 Hz), 135.1, 136.2, 137.0, 137.9. HRMS: calcd for $C_{25}H_{27}FNaO_5S_2Si^+$ 541.0945 (M+Na$^+$), found: 541.0955. M.p. 135–136 °C.

((1-Fluoro-4-phenyl-1,1-bis(phenylsulfonyl)butan-2-yl)oxy)-trimethylsilane (**2h**). ^{1}H NMR ($CDCl_3$): δ 0.00 (s, 9H), 2.57–2.72 (m, 1H), 2.75–2.83 (m, 1H), 2.86–2.97 (m, 1H), 3.00–3.12 (m, 1H), 2.71 (ddd, J = 10.2 Hz, J = 8.3 Hz, J = 1.9 Hz, 1H), 7.41–7.46 (m, 3H), 7.50–7.54 (m, 2H), 7.63–7.74 (m, 4H), 7.83–7.92 (m, 2H), 8.06–8.11 (m, 4H). ^{19}F NMR ($CDCl_3$): δ −135.34 (d, J = 8.3 Hz, 1F). ^{13}C NMR ($CDCl_3$): δ 0.1, 33.0 (d, J = 0.6 Hz), 33.5 (d, J = 3.2 Hz), 73.3 (d, J = 17.0 Hz), 114.7 (d, J = 266.3 Hz), 126.3, 128.6(1), 128.6(5), 128.7(9), 128.8(0), 131.4 (d, J = 1.4 Hz), 131.6 (d, J = 1.8 Hz), 134.8, 135.2, 136.3, 138.2, 140.8. HRMS: calcd for $C_{22}H_{21}FNaO_5S_2^+$ 471.0707 (M−TMS+Na$^+$), found: 471.0705. M.p. 137–140 °C.

4.3. Procedure for the reductive desulfonation of 2e

4.3.1. 2-Fluoro-1-(naphthalen-1-yl)-2-(phenylsulfonyl)ethanol (3e)

To a solution of **2e** (456 mg, 0.84 mmol) in acetic acid and DMF (1:1, v:v, 8 mL) was added Mg turnings (408 mg, 16.8 mmol, 20 equiv.) all at once. The reaction mixture was stirred at 0 °C for 4 h until the completion of the reaction (monitored by ^{19}F NMR spectroscopy). The resulting slurry was diluted with 20 mL water and washed with hexanes/ethyl acetate (1:1, 25 × 3 mL). The organic solution was then washed with water (20 × 2 mL) and dried over $MgSO_4$. The solvent was removed under vacuum. The crude product was purified via silica gel column chromatography using ethyl acetate and hexanes as eluent to obtain **3e** as white solid (two separated diastereomers, combined weight 207 mg, 74%).

^{1}H NMR ($CDCl_3$): δ 5.29 (dd, J = 46.5, 8.8 Hz, 1H), 6.07–6.09 (m, 1H), 7.47–7.52 (m, 3H), 7.62–7.66 (m, 2H), 7.74–7.78 (m, 2H), 7.84–7.87 (m, 2H), 7.91–7.94 (m, 1H), 8.02–8.05 (m, 2H). ^{19}F NMR ($CDCl_3$): δ −176.0 (d, J = 46.6 Hz, 1F). HRMS: calcd for $C_{18}H_{15}FNaO_3S^+$ 353.0618 (M+Na$^+$), found: 353.0617.

^{1}H NMR ($CDCl_3$): δ 5.28 (dd, J = 46.1, 0.8 Hz, 1H), 6.51–6.57 (m, 1H), 7.50–7.55 (m, 2H), 7.59–7.62 (m, 3H), 7.71–7.74 (m, 1H), 7.83–7.86 (m, 2H), 7.90–7.92 (m, 1H), 8.00–8.03 (m, 3H). ^{19}F NMR ($CDCl_3$): δ −196.3 (dd, J = 46.1, 23.4 Hz, 1F). HRMS: calcd for $C_{18}H_{15}FNaO_3S^+$ 353.0618 (M+Na$^+$), found: 353.0622.

4.3.2. 2-Fluoro-1-(naphthalen-1-yl)ethanol (4e)

Under N_2 atmosphere, into a Schlenk flask containing **3e** (207 mg, 0.62 mmol) and Na_2HPO_4 (528 mg, 3.72 mmol, 6 equiv.) in anhydrous methanol (8 mL) at −20 °C, was added Na/Hg amalgam (10 wt% Na in Hg, net sodium content 90 mg, 3.72 mmol). The reaction mixture was stirred at −20 to 0 °C for 7 h. The liquid phase was decanted, and the solid residue was washed with Et_2O. The solid was then treated with elemental sulfur powder. The solvents were removed under vacuum, and 25 mL brine was added before extraction with Et_2O (20 × 3 mL). The combined ether phase was dried over $MgSO_4$, and the ether was removed to afford the crude product. The crude product was further purified via silica gel column chromatography using ethyl acetate and hexanes as eluent. Compound **4e** was obtained as white solid (57 mg, 48%). ^{1}H NMR ($CDCl_3$): δ 2.84–2.98 (m, 1H), 4.54 (ddd, J = 48.7, 9.8, 8.4 Hz, 1H), 4.71 (ddd, J = 48.6, 9.8, 2.8 Hz, 1H), 5.82 (ddt, J = 14.3, 8.4, 2.8 Hz, 1H), 7.76–7.72 (m, 4H), 7.83 (d, J = 8.2 Hz, 1H), 7.92–7.87 (m, 1H), 8.04 (d, J = 8.2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 70.0 (d, J = 20.0 Hz), 87.0 (d, J = 174.8 Hz), 122.5, 124.3 (d, J = 1.3 Hz), 125.6, 125.9, 126.6, 129.0, 129.2, 130.5, 133.7 (d, J = 8.7 Hz), 133.8. ^{19}F NMR ($CDCl_3$): δ −221.3 (ddt, J = 48.6, 14.3, 4.9 Hz). HRMS: calcd for $C_{12}H_{11}OF^+$ 190.0794 (M$^+$), found: 190.0793. M.p. 96–99 °C.

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