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Optically Pure Polyfluoroalkanesulfinamides: Synthesis and Application as Promising and Monitorable Chiral Auxiliaries

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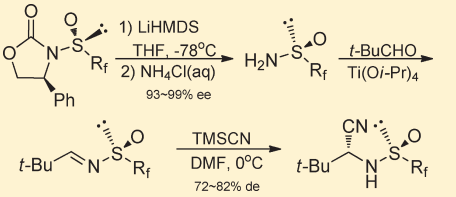
Supporting Information

ABSTRACT: Efficient synthesis of enantiopure polyfluoroalkanesulfinamides (PFSAs) has been achieved. Their application as novel chiral auxiliaries with an electron-withdrawing and ^{19}F NMR monitorable polyfluoroalkyl group was initially demonstrated in an asymmetric Strecker reaction under mild conditions.

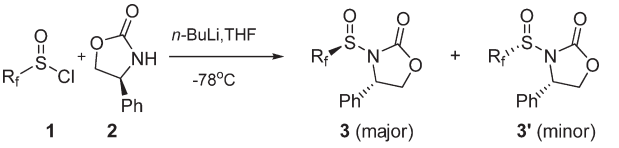


Because of the unique properties imparted by fluorine,[1] fluoroorganic compounds have seen diverse applications in synthetic, agricultural, and medicinal chemistry as well as in material science.[2] Recently, one emerging but still synthetically challenging area is their application in novel ligand,[3] catalyst,[4] and chiral auxiliary[5] design. Particularly with the few examples of fluorine-containing chiral auxiliaries, the possibility of monitoring the reaction process and diastereoselectivity by ^{19}F NMR spectroscopy has rarely been explored.

tert-Butanesulfinamide (TBSA) and *p*-toluenesulfinamide (*p*TSA)[6] are widely used as ideal auxiliaries with an electron-withdrawing sulfinyl group. The chiral alkanesulfinyl group enhances the nucleophilicity of the corresponding imine for nucleophilic addition. It also provides good diastereofacial selectivity and is easy to remove from adducts. Nevertheless, additives such as Lewis acid or base are usually needed to improve the reactivity of imines. To further enhance the nucleophilicity of the imines and therefore facilitate the reaction with nucleophiles and extend the reaction scope, we propose that polyfluoroalkanesulfinamides (PFSAs) might serve as a superior auxiliary because of the strong electron-withdrawing effect of polyfluoroalkyl group. In addition, our previous work has demonstrated the chiral induction potential of the polyfluoroalkanesulfinyl group due to the steric effect of the polyfluoroalkyl group in the Diels−Alder reaction of *N*-sulfinylpolyfluoroalkanesulfinamides with dienes.[7] As part of our ongoing program aimed at devising novel fluorine-containing chiral auxiliaries, we disclose herein the first synthesis of enantiopure polyfluoroalkanesulfinamides (PFSAs) and demonstrate their application as novel chiral auxiliaries with an electron-withdrawing and ^{19}F NMR monitorable polyfluoroalkyl group. The Strecker reaction was chosen as a demonstration example.

We envisaged that enantiopure PFSAs could be obtained from polyfluoroalkanesulfinyl chlorides **1**.[8] However, because of the high reactivity of **1**, it was difficult to prepare optically pure PFSAs from **1** directly. Recently, Qin et al. reported the successful synthesis of TBSA by ammonia hydrolysis of *N*-*tert*-butanesulfinyl-substituted Evans reagent with lithium ammonia.[9] Inspired by their work, we successfully prepared *N*-polyfluoroalkanesulfinyloxazolidinones in good yields and diastereoselectivities as shown in Scheme 1. The major product **3a**−**d** could be isolated from the reaction mixture simply by flash column chromatography or recrystallization.

Scheme 1. Preparation of *N*-Polyfluoroalkanesulfinyloxazolidinones



a: R_f = $ClCF_2CF_2$, 89% total yield, 81% de
b: R_f = CF_3CF_2, 81% total yield, 77% de
c: R_f = n-C_4F_9, 84% total yield, 75% de
d: R_f = CF_3, 75% total yield, 86% de

Ammonia hydrolysis of **3a** with LiHMDS was investigated next (Table 1). To our delight, the corresponding sulfinamide **4a** was obtained as expected when **3a** was added to a solution of LiHMDS at −78 °C. The result was quite different from the ring-opening reaction of (*S*)-(−)-1-trifluoromethanesulfinyl-(*R*)-4-phenyloxazolin-2-one with dimethylamine, which led to the corresponding 2-amino alcohol.[10] Solvent had a dramatic effect on both yield and enantioselectivity, and dichloromethane gave the best result among the solvents examined. Initially, an equal amount of LiHMDS was used, and **4a** was obtained in very low yield (entries 1 and 2). When the amount of LiHMDS was increased to 2.0 equiv, the yield of **4a** was raised to 53%, but lower ee was obtained (entry 3). To analyze the reason for low ee, the reaction was quenched at low conversion, and ^{19}F NMR analysis of the reaction mixture indicated that the diastereoisomer **3a′** was

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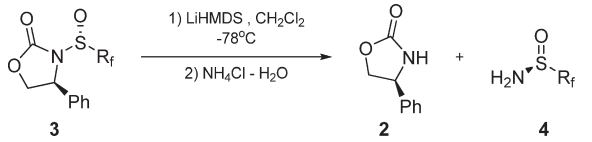
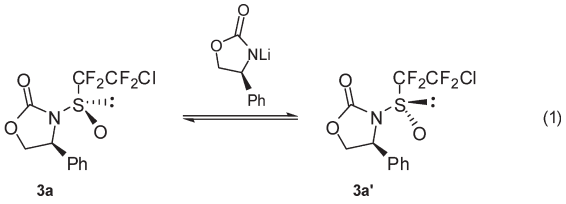
formed as a byproduct. In view of the S_N2 mechanism for the formation of **4a**, it is reasonable to believe that **3a**′ was formed from the reaction of **3a** with the lithium salt of **2**, which was produced in situ as illustrated in eq 1. It was the equilibrium between **3a** and **3a**′ in the reaction system that resulted in the racemization of (*S*)-**4a**. Therefore, reducing the concentration of the lithium salt of **2** should be helpful to suppress the formation of **3a**′ and thus improve the ee of the reaction, and an attempt was made by slowing the addition rate of **3a**. As expected, (*S*)-**4a** was obtained in 77% yield and 99% ee when the addition time of **3a** was prolonged to 3 h (entry 6, Table 1). Under the optimized reaction conditions, optically pure PFSAs **4b**−**d** were prepared in good yield and ee, respectively (entries 9−11).

Table 1. Synthesis of Optically Pure PFSAs



entry	3	ratio[a]	time[b] (h)	product	R_f	yield[c] (%)	ee[d] (%)
1	**3a**	1:1	0.5	(*S*)-**4a**	$ClCF_2CF_2$	10	99
2	**3a**	1:1	2.0	(*S*)-**4a**	$ClCF_2CF_2$	12	95
3	**3a**	2:1	0.5	(*S*)-**4a**	$ClCF_2CF_2$	53	87
4	**3a**	2:1	1.0	(*S*)-**4a**	$ClCF_2CF_2$	65	95
5	**3a**	2:1	2.0	(*S*)-**4a**	$ClCF_2CF_2$	68	96
6	**3a**	2:1	3.0	(*S*)-**4a**	$ClCF_2CF_2$	77	99
7	**3a**	2:1	4.0	(*S*)-**4a**	$ClCF_2CF_2$	67	96
8	**3a**′	2:1	3.0	(*R*)-**4a**	$ClCF_2CF_2$	63	93
9	**3b**	2:1	3.0	(*S*)-**4b**	CF_3CF_2	67	99
10	**3c**	2:1	3.0	(*S*)-**4c**	*n*-C_4F_9	75	93
11	**3d**	2:1	3.0	(*S*)-**4d**	CF_3	66	99

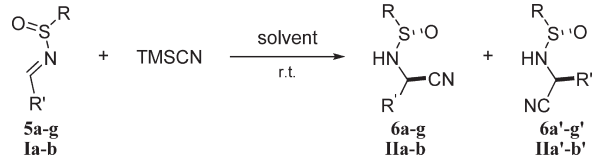
[a] Mole ratio of LiHMDS and **3**. [b] Addition time of **3**. [c] Isolated yield. [d] Determined by HPLC.



(1)

Taking the Strecker reaction as a demonstration example, we further explored the application of PFSAs in asymmetric synthesis as novel chiral auxiliaries. Strecker reaction[11] has been achieved with good yield and stereoselectivity with TBSA[12,13] and *p*TSA.[14−16] However, expensive Lewis acid, stoichiometric base, or toxic reagent must be used. Davis and co-workers, who pioneered the research on sulfinimines, reported that no desired α-amino nitrile was obtained when **Ib** derived from *p*TSA was treated with TMSCN and CsF in THF. Therefore, they used ethylaluminum cyanide and isopropyl alcohol as an alternative, and the corresponding adducts **IIb** and **IIb**′ were obtained in 98%

Table 2. Strecker Reaction of 5 with Different Chiral Auxiliaries



entry	imine	R	R′	solvent	*T* (°C)	time (h)	product	total yield (%)	de[a] (%)
1[15]	**Ib**	*p*-tolyl	*t*-Bu	THF/Et_2AlCN	−78		**IIb, IIb**′	91	80
2	**5a**	CF_2CF_2Cl	*t*-Bu	benzene	25	72	**6a, 6a**′	trace	
3	**5a**	CF_2CF_2Cl	*t*-Bu	CH_2Cl_2	25	72		N.R.	
4	**5a**	CF_2CF_2Cl	*t*-Bu	Et_2O	25	72		N.R.	
5	**5a**	CF_2CF_2Cl	*t*-Bu	THF	25	72		N.R.	
6	**5a**	CF_2CF_2Cl	*t*-Bu	CH_3NO_2	25	72		N.R.	
7	**5a**	CF_2CF_2Cl	*t*-Bu	MeCN	25	12	**6a, 6a**′	22[a]	56
8	**5a**	CF_2CF_2Cl	*t*-Bu	DMSO	25	12	**6a, 6a**′	90[a]	62
9	**5a**	CF_2CF_2Cl	*t*-Bu	TMU	25	46	**6a, 6a**′	93	76
10	**5a**	CF_2CF_2Cl	*t*-Bu	DMPU	25	9	**6a, 6a**′	90[a]	79
11	**5a**	CF_2CF_2Cl	*t*-Bu	DMF	25	12	**6a, 6a**′	88	78
12	**Ia**	*t*-Bu	*t*-Bu	DMF	25	72	**IIa, IIa**′	17	58
13	**Ib**	*p*-tolyl	*t*-Bu	DMF	25	72	**IIb, IIb**′	49	56
14	**5a**	CF_2CF_2Cl	*t*-Bu	DMF	0	45	**6a, 6a**′	80	82
15	**5b**	CF_2CF_3	*t*-Bu	DMF	0	20	**6b, 6b**′	79	80
16	**5c**	*n*-C_4F_9	*t*-Bu	DMF	0	36	**6c, 6c**′	90	81
17	**5d**	CF_3	*t*-Bu	DMF	0	77	**6d, 6d**′	85	72
18	**5e**	CF_2CF_2Cl	*i*-Pr	DMF	0	44	**6e, 6e**′	75	62
19	**5f**	CF_2CF_2Cl	*i*-Bu	DMF	0	70	**6f, 6f**′	86	72
20	**5g**	CF_2CF_2Cl	*n*-Pr	DMF	0	72	**6g, 6g**′	79	72

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

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yield with 80% de (Table 2, entry 1).[15] But extreme care should be taken since the reaction is very moisture sensitive. Hou's group further demonstrated that the presence of hydrogen at the α-position of the C═N bond was crucial for the reaction of imines derived from *p*TSA with TMSCN and CsF.[16] All these results might be attributed to the low reactivity of imines. Thus, we supposed that imines derived from PFSAs might be more reactive and could react with TMSCN under milder conditions.

Therefore, polyfluoroalkanesulfinimines **5a**−**d** derived from pivalaldehyde were prepared as typical substrates, and their Strecker reactions were investigated. Condition screening indicated that acceptable results could be obtained when the reaction was carried out in aprotic polar solvents without using any additives as shown in Table 2 (entries 8−11). It was reported that aprotic polar solvents such as DMF and DMSO could serve as a Lewis base and activate TMSCN because of the interaction between oxygen atom and silicon atom.[17] The efficiency of solvent correlates with the solvent hydrogen bond basicity.[18] It is noteworthy that the reaction of **5a** with TMSCN in DMF afforded **6a** and **6a**′ in 88% yield and 78% de at room temperature (entry 11), comparable to the best result reported with *p*TSA (entry 1).

To clarify the efficiency of these novel fluorine-containing auxiliaries, Strecker reactions of **Ia** and **Ib** derived from TBSA and *p*TSA, respectively, were carried out under similar conditions. Low conversion and poor de were obtained after 3 days as depicted in Table 2 (entries 12 and 13). Obviously, the presence of a strong electron-withdrawing polyfluoroalkanesulfinyl group significantly increased the reactivity of **5a** and made the Strecker reaction take place under very mild conditions. Furthermore, the reaction progress and stereoselectivity could be conveniently monitored by ^{19}F NMR spectroscopy during reaction without workup of the reaction mixture. This simplified our research greatly and provided a useful tool for the determination of stereoselectivity of the products. Figure 1 illustrated the consistency between the HPLC and ^{19}F NMR spectra of a mixture of **6a** and **6a**′ as a crude product. The diastereomeric ratio between **6a** and **6a**′ calculated from ^{19}F NMR spectra is 90.2:9.8, which is very close to the ratio of 90.6:9.4 determined by HPLC.

Further screening reaction conditions showed that up to 82% de was achieved at 0 °C. Different PFSAs (Table 2, entries 14−16) gave similar results with the exception that the reaction of **5d** went slower, and relatively lower de was obtained (entry 17). Under the same conditions, 2-chlorotetrafluoroethanesulfinyl-substituted imines **5e**−**g** derived from other aldehydes reacted with TMSCN smoothly to yield the corresponding α-amino nitriles with good disastereoslectivities (Table 2, entries 18−20).

To further demonstrate the application of these chiral PFSAs in asymmetric synthesis, optically pure α-amino nitrile (*R*)-**7a** was prepared from (*S*)-**4a** as shown in Scheme 2. No racemization was observed during the whole synthetic process as indicated by HPLC analysis of key intermediates. The absolute configuration of the major product (*Ss,Rc*)-**6a** was further proved by X-ray diffraction analysis (see the Supporting Information).

Compared with *tert*-butanesulfinyl and *p*-toluenesulfinyl, the polyfluoroalkanesulfinyl substituent in **6a** was much easier to remove. Treatment of **6a** with 5 N HCl at 50 °C or saturated HCl/Et_2O solution at room temperature for 2 h yielded the corresponding deprotected amine product **7a**. In HCl/Et_2O solution, the racemic polyfluoroalkanesulfinyl residue can be recycled in the form of sulfinyl chloride simply by filtration of the reaction mixture. To determine the ee of **7a**, a transformation[20] to **8a** was performed, and 98% ee was achieved.

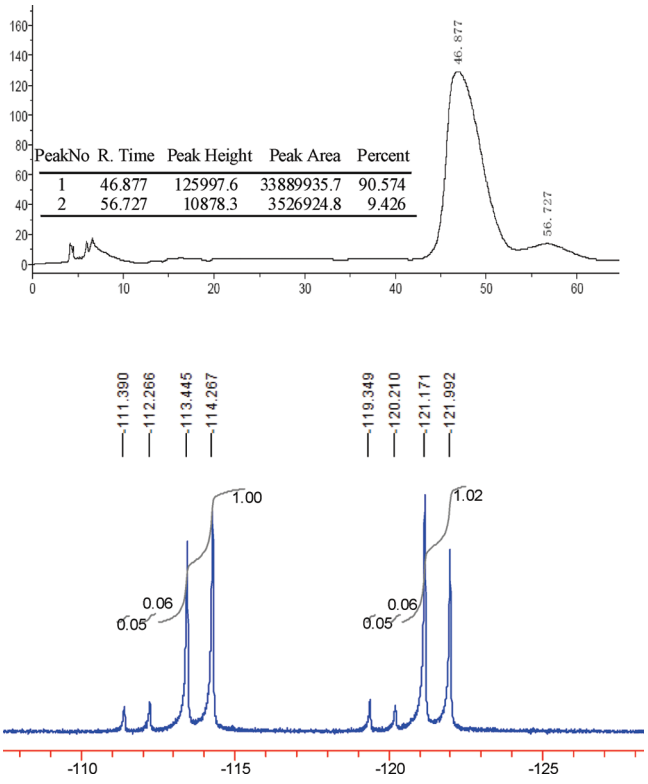
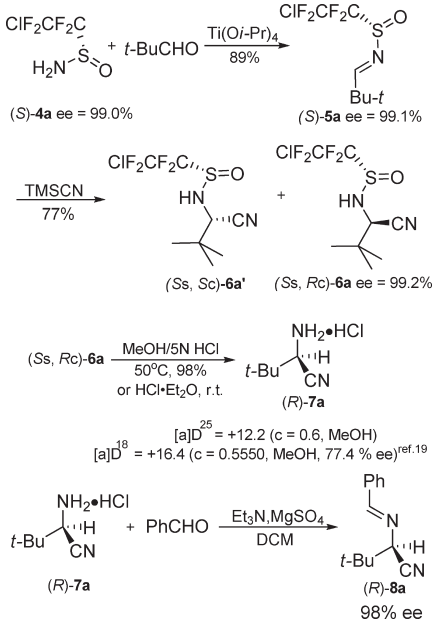


Figure 1. HPLC and ^{19}F NMR spectra of the mixture of **6a** and **6a**′.

Scheme 2. Synthesis of (*R*)-7a



In summary, optically pure PFSAs were synthesized for the first time, and their application as promising and ^{19}F NMR monitorable chiral auxiliaries in asymmetric synthesis was initially demonstrated. Taking advantage of the strong electron-withdrawing effect of polyfluoroalkyl group, Strecker reaction of a series of polyfluoroalkanesulfinimines derived from aldehydes with TMSCN was achieved under mild conditions with good diastereoselectivities

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without any additives. Furthermore, these fluorine-containing auxiliaries are easily removed, providing a practical and convenient method for the synthesis of chiral α-amino nitriles. Moreover, the presence of the polyfluoroalkyl group made it possible to monitor the process and stereoselectivities of the reaction conveniently by ^{19}F NMR and thus simplified the research greatly. Further studies on the application of these polyfluoroalkanesulfinamides in asymmetric synthesis are in progress in our laboratory.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of Polyfluoroalkanesulfinyloxazolindinones. *n*-BuLi (2.64 mL, 2.5 M in hexane) was added dropwise to the solution of **2** (0.978 g, 6 mmol) in THF (30 mL) at −78 °C under the protection of N_2. After addition, the mixture was stirred for another 0.5 h. Then polyfluoroalkanesulfinyl chloride (19.8 mmol) in 10 mL of THF was added dropwise. After being stirred for 3 h, the mixture was allowed to warm to room temperature. Solvent was removed, and the residue was purified by flash chromatography (EtOAc/petroleum ether 1/7).

*(R_S,S_C)-4-Phenyl-N-(2-chlorotetrafluoroethanesulfinyl)oxazolidin-2-one (**3a**):* white solid; mp 112−114 °C; FT-IR (KBr) 1786, 1761, 803, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.43−7.36 (m, 5H), 5.35 (dd, *J* = 9.1, 4.7 Hz, 1H), 4.87 (dd, *J* = 9.1, 9.1 Hz, 1H), 4.52 (dd, *J* = 9.1, 4.7 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.48 (s, 2F), −108.52 (d, J_{FF} = 223.9 Hz, 1F), −118.55 (d, J_{FF} = 223.9 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.9, 137.2, 129.8, 129.4, 127.7, 121.8 (tt, *J* = 298.3, 32.8 Hz), 116.5 (tt, *J* = 319.1, 36.3 Hz), 73.9, 53.9; EI-MS (*m*/*z*) 210 (72), 103 (100), 77 (66); $[\alpha]^{20}_D$ = +147.2 (*c* = 0.2, $CHCl_3$). Anal. Calcd for $C_{11}H_8ClF_4NO_3S$: C, 38.22; H, 2.33; N, 4.05. Found: C, 38.15; H, 2.44; N, 3.93.

*(S_S,R_C)-4-Phenyl-N-(2-chlorotetrafluoroethanesulfinyl)oxazolidin-2-one (**3a′**):* white solid; mp 110−112 °C; FT-IR (KBr) 1790, 1765, 803, 757 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.44−7.36 (m, 5H), 5.32 (dd, *J* = 8.9, 4.6 Hz, 1H), 4.87 (dd, *J* = 8.9, 8.9 Hz, 1H), 4.52 (dd, *J* = 8.9, 4.6 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.52 (s, 2F), −108.54 (d, J_{FF} = 217.1 Hz, 1F), −118.57 (d, J_{FF} = 217.1 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.9, 137.1, 129.9, 129.5, 127.7, 125.1−113.1 (m), 74.0, 53.9; EI-MS (*m*/*z*) 210 (47), 103 (100), 91 (77), 77 (67); $[\alpha]^{20}_D$ = −280.8 (*c* = 1.2 × 10^{-2}, $CHCl_3$). Anal. Calcd for $C_{11}H_8ClF_4NO_3S$: C, 38.22; H, 2.33; N, 4.05. Found: C, 38.23; H, 2.49; N, 4.00.

*(R_S,S_C)-4-Phenyl-N-(pentafluoroethanesulfinyl)oxazolidin-2-one (**3b**):* white solid; mp 99−100 °C; FT-IR (KBr) 1796, 1229, 770, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.44−7.36 (m, 5H), 5.35 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.88 (dd, *J* = 9.0, 9.0 Hz, 1H), 4.53 (dd, *J* = 9.0, 4.8 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −79.37 (s, 3F), −113.74 (d, J_{FF} = 233.2 Hz, 1F), −122.83 (d, J_{FF} = 233.2 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.9, 137.2, 129.9, 129.5, 127.6, 74.1, 53.8; EI-MS (*m*/*z*) 210 (70), 166 (57), 103 (100), 91 (75), 77 (70); $[\alpha]^{20}_D$ = +179.4 (*c* = 0.2, $CHCl_3$). Anal. Calcd for $C_{11}H_8F_5NO_3S$: C, 40.13; H, 2.45; N, 4.20. Found: C, 40.10; H, 2.61; N, 4.23.

*(R_S,S_C)-4-Phenyl-N-(nonafluorobutanesulfinyl)oxazolidin-2-one (**3c**):* mp 119−120 °C; FT-IR (KBr) 1786, 1764, 774, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.41−7.38 (m, 5H), 5.35 (dd, *J* = 8.9, 4.7 Hz, 1H), 4.88 (dd, *J* = 8.9, 8.9 Hz, 1H), 4.53 (dd, *J* = 8.9, 4.7 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −81.25 to −81.3 (m, 3F), −109.98 (d, J_{FF} = 234.8 Hz, 1F), −120.05 (d, J_{FF} = 234.8 Hz, 1F), −120.50 (d, J_{FF} = 306.9 Hz, 1F), 122.60 (d, J_{FF} = 306.9 Hz, 1F), −126.62 to −126.70 (m, 2F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.8, 137.1, 129.9, 129.5, 127.8, 121.0−107.9 (m), 74.0, 54.0; EI-MS (*m*/*z*) 210 (45), 103 (100), 91 (84), 77 (68); $[\alpha]^{20}_D$ = +117.2 (*c* = 0.1, $CHCl_3$). Anal. Calcd for $C_{13}H_8F_9NO_3S$: C, 36.37; H, 1.88; N, 3.26. Found: C, 36.25; H, 1.95; N, 3.21.

*(R_S,S_C)-4-Phenyl-N-(trifluoromethanesulfinyl)oxazolidin-2-one (**3d**):* mp 109−112 °C; FT-IR (KBr) 1759, 1197, 775, 706 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.44−7.34 (m, 5H), 5.38 (dd, *J* = 9.1, 4.7 Hz, 1H), 4.86 (dd, *J* = 9.1, 9.1 Hz, 1H), 4.47 (dd, *J* = 9.1, 4.7 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −73.18 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.2, 137.1, 129.9, 129.5, 127.3, 123.3 (q, *J* = 179.0 Hz), 74.0, 53.7; EI-MS (*m*/*z*) 210 (47), 117 (30), 103 (65), 91 (100), 77 (58); $[\alpha]^{20}_D$ = +203.0 (*c* = 0.4, $CHCl_3$). Anal. Calcd for $C_{10}H_8F_3NO_3S$: C, 43.01; H, 2.89; N, 5.02. Found: C, 43.05; H, 3.14; N, 5.03.

*(R_S,S_C)-4-Benzyl-N-(2-chlorotetrafluoroethanesulfinyl)oxazolindin-2-one (**3e**).* Since it is difficult to obtain the single crystal **3a**−**d**, **3e** was prepared using the same procedure for the determination of the absolute configuration of **3** by X-ray diffraction analysis: yield 54%; white solid; mp 80−83 °C; FT-IR (KBr) 1785, 1159, 1121 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.35−7.20 (m, 5H), 4.58−4.57 (m, 1H), 4.29 (d, *J* = 5.4 Hz, 2H), 3.40 (d, *J* = 12.3 Hz, 1H), 2.79 (dd, *J* = 12.3, 12.3 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −68.08 (m, 2F), −110.57 (d, J_{FF} = 221.9 Hz, 1F), −119.92 (d, J_{FF} = 221.9 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.3, 138.3, 133.1, 133.0, 131.6, 125.6 (tt, *J* = 298.9, 33.0 Hz), 120.4 (ddt, *J* = 315.2, 313.1, 36.5 Hz), 74.0, 55.4, 42.8 (dd, *J* = 5.7, 1.8 Hz); HRMS (EI) calcd for $C_{12}H_{10}Cl\,F_4NO_3S$ (M^+) 359.0006, found 359.0019.

Ammonia Hydrolysis of Polyfluoroalkanesulfinyloxazolidinones. A solution of **3** (0.5 mmol) in CH_2Cl_2 (7 mL) was added slowly to a solution of LiHMDS (1.0 mmol) in CH_2Cl_2 (3 mL) in 3 h at −78 °C under the protection of N_2. After addition, saturated NH_4Cl (aq) (5 mL) was added immediately. The resulting mixture was extracted with CH_2Cl_2 (5 mL × 3) and dried over Na_2SO_4. After concentration, the residue was purified by chromatography on silica gel (EtOAc/petroleum ether 1/5).

*(S)-2-Chlorotetrafluoroethanesulfinamide (S)-**4a**:* yield 72%; white solid; mp 42−43 °C; FT-IR (KBr) 3238, 3104, 1731, 1561, 1266, 1171 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.96 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.27 to −67.32 (m, 2F), −119.74 (d, J_{FF} = 243.6 Hz, 1F), −122.47 (d, J_{FF} = 243.6 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 122.4 (tt, *J* = 298.4, 33.4 Hz), 116.3 (ddt, *J* = 306.0, 302.0, 35.1 Hz); HRMS (EI) calcd for $C_2H_2ClF_4NOS$ (M^+) 198.9482, found 198.9480; $[\alpha]^{20}_D$ = −15.5 (*c* = 1.0, $CHCl_3$, 99% ee).

*(R)-2-Chlorotetrafluoroethanesulfinamide (R)-**4a**:* yield 63%; white solid; mp 41−43 °C; $[\alpha]^{20}_D$ = +11.4 (*c* = 0.8, $CHCl_3$, 93% ee).

*(S)-Pentafluoroethanesulfinamide (S)-**4b**:* yield 67%; white solid; mp 35−36 °C; FT-IR (KBr) 3244, 3115, 1735, 1342, 1216 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.16 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −79.62 (s, 3F), −125.14 (d, J_{FF} = 243.6 Hz, 1F), −126.34 (d, J_{FF} = 243.6 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 118.0 (ddq, *J* = 296.2, 32.5, 32.5 Hz), 114.3 (ddt, *J* = 303.3, 299.6, 38.8 Hz); HRMS (EI) calcd for $C_2H_2F_5NOS$ (M^+) 182.9777, found 182.9777; $[\alpha]^{20}_D$ = −18.0 (*c* = 0.6, $CHCl_3$, 99% ee).

*(S)-Nonafluorobutanesulfinamide (S)-**4c**:* yield 75%; white solid; mp 64−66 °C; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.86 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −81.18 to −81.26 (m, 3F), −121.85 to −122.00 (m, 2F), −121.84 (dt, *J* = 243.4, 4.5 Hz, 1F), −123.09 (dt, *J* = 243.4, 4.5 Hz, 1F), −126.48 to −126.55 (m, 2F); EI-MS (*m*/*z*) 69 (31), 64 (100); $[\alpha]^{20}_D$ = −6.0 (*c* = 0.8, $CHCl_3$, 93% ee).

*(S)-Trifluoromethanesulfinamide (S)-**4d**:* yield 66%; white solid; mp 30−32 °C; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.97 (s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −80.92 (s, 3F); EI-MS (*m*/*z*) 69 (34), 64 (100); $[\alpha]^{20}_D$ = −7.7 (*c* = 0.1, $CHCl_3$, 99% ee).

General Procedure for the Synthesis of Racemic 4a−c. To a flask containing neat HMDS (16 mL, 0.075 mol) was added **1** (0.075 mol) dropwise at 0 °C. After addition, stirring was continued for 2 h at room temperature. The TMS-substituted sulfinamide intermediate was obtained by distillation under reduced pressure (1.0 Torr), which was further treated with 50 mL of saturated NH_4Cl (aq) at room

temperature for 2 h. The resulting mixture was extracted with Et_2O (30 mL × 3) and dried over anhydrous Na_2SO_4. After concentration under reduced pressure, the residue was purified by column chromatography (EtOAc/petroleum ether 1/5).

General Procedure[21,22] for the Synthesis of Racemic 4d. A mixture of CH_3CN (600 mL), H_2O (600 mL), disodium phosphate (130.4 g, 0.92 mol), and sodium dithionite (193.2 g, 0.92 mol) was charged into a 2.0 L autoclave reactor. After the reactor as closed, a vacuum (20 Torr) was created. Trifluorobromomethane (180 g, 1.2 mol) was then introduced. The mixture was heated to 80 °C and stirred for 8 h. The resulting mixture was extracted with EtOAc (200 mL × 4) and dried over anhydrous Na_2SO_4. After removal of solvent, a white solid (40 g) was obtained, which was further treated with thionyl chloride and HMDS in sequence at −20 °C, and the resulting mixture was stirred at −10 °C for 3 h. Purification by flash column chromatography (EtOAc/petroleum ether 1/5) gave a colorless oil. Total yield: 25%.

General Procedure for the Synthesis of Sulfinimines. To a 10 mL reaction tube charged with PFSAs (3.0 mmol), titanium(IV) isopropoxide (4.5 mmol), and CH_2Cl_2 (3.0 mL) was added aldehyde (3.0 mmol). The mixture was stirred at room temperature and monitored by TLC. After completion, brine (5 mL) was added, and the resulting mixture was filtered through Celite. The filter cake was washed with CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 (5.0 mL × 3), and the combined organic phase was dried over anhydrous Na_2SO_4. After concentrated, the residue was purified by flash column chromatography (EtOAc/petroleum ether: 1/20).

*2-Chloro-N-(2,2-dimethylpropylidene)tetrafluoroethanesulfinamide (**5a**):* yield 85%; colorless oil; FT-IR (film) 1717 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.15 (s, 1H), 1.08 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.78 (s, 2F), −118.74 (d, J_{FF} = 234.6 Hz, 1F), −121.03 (d, J_{FF} = 234.6 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.3, 122.4 (tt, J = 298.5, 32.7 Hz), 116.8 (tt, J = 301.4, 36.5 Hz), 39.1, 26.3; HRMS (ESI) calcd for $C_7H_{11}ClF_4NOS$ $(M + H)^+$ 268.0186, found 268.0181.

*N-(2,2-Dimethylpropylidene)pentafluoroethanesulfinamide (**5b**):* yield 82%; colorless oil; FT-IR (film) 1707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.21 (s, 1H), 1.20 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −78.70 (s, 3F), −120.87 (d, J_{FF} = 242.0 Hz, 1F), −124.32 (d, J_{FF} = 242.0 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.7, 123.0−112.5 (m), 39.2, 26.2; HRMS (EI) calcd for $C_6H_{10}F_3NOS$ (M^+) 201.0435, found 201.0428.

*N-(2,2-Dimethylpropylidene)nonafluorobutanesulfinamide (**5c**):* colorless oil; FT-IR (film) 1619 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.23 (s, 1H), 1.20 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −81.15 to −81.22 (m, 3F), −114.48 (d, J_{FF} = 243.6, 1F), −121.69 (d, J_{FF} = 243.6, 1F), −121.71 to −121.79 (m, 2F), −116.89 (d, J_{FF} = 296.1 Hz, 1F), −123.31 (d, J_{FF} = 296.1 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.7, 122.2−105.7 (m), 39.2, 26.2; HRMS (EI) calcd for C_5HF_9NOS $(M - C_4H_9)^+$ 293.9635, found 293.9634.

*N-(2,2-Dimethylpropylidene)trifluoromethanesulfinamide (**5d**):* yield 71%; colorless oil; FT-IR (film) 1707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.21 (s, 1H), 1.20 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −77.15 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.5, 123.8 (q, J = 332.2 Hz), 39.1, 26.5; HRMS (EI) calcd for $C_6H_{10}F_3NOS$ $(M)^+$ 201.0435, found 201.0428.

*2-Chloro-N-(2-methylpropylidene)tetrafluoroethanesulfinamide (**5e**):* yield 76%; colorless oil; FT-IR (film) 1624 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.28 (d, J = 4.2 Hz, 1H), 2.85−2.74 (m, 1H), 1.19 (d, J = 3.9 Hz, 3H), 1.18 (d, J = 3.0 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −65.88 (s, 2F), −116.77 (d, J_{FF} = 230.4 Hz, 1F), −117.91 (d, J_{FF} = 230.4 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 179.2, 122.2 (tt, J = 299.2, 32.7 Hz), 116.6, (tt, J = 270.6, 36.5 Hz), 35.7, 18.4, 18.2; HRMS (ESI) calcd for $C_6H_9ClF_4NOS$ $(M + H)^+$ 254.0030, found 254.0024.

*2-Chloro-N-(3-methylbutylidene)tetrafluoroethanesulfinamide (**5f**):* yield 87%; colorless oil; FT-IR (film) 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.29 (t, J = 5.4 Hz), 2.53−2.38 (m, 2H), 2.13−1.99 (m, 1H), 0.95 (d, J = 3.0 Hz, 3H), 0.92 (d, J = 2.7 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −66.36 (s, 2F), −117.22 (d, J_{FF} = 230.7 Hz, 1F), −117.73 (d, J_{FF} = 230.7 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.4, 122.2 (tt, J = 299.2, 33.1 Hz), 116.5 (tt, J = 272.5, 36.5 Hz), 45.3, 26.0, 22.4, 22.3; HRMS (ESI) calcd for $C_7H_{11}ClF_4NOS$ $(M + H)^+$ 268.0186, found 268.0181.

*2-Chloro-N-(n-butylidene)tetrafluoroethanesulfinamide (**5g**):* yield 76%; colorless oil; FT-IR (film) 1622 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.36 (t, J = 4.5 Hz, 1H), 2.59 (dt, J = 7.4, 4.5 Hz, 2H), 1.76−1.63 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −66.39 (s, 2F), −117.62 (s, 2F); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 175.4, 122.0 (tt, J = 373.8, 45.6 Hz), 116.6(tt, J = 387.5, 45.6 Hz), 38.4, 18.3,13.4; HRMS (ESI) calcd for $C_6H_9ClF_4NOS$ $(M + H)^+$ 254.0030, found 254.0024.

General Procedure for the Strecker Reaction. To a solution of polyfluoroalkanesulfinimine (0.5 mmol) in anhydrous DMF (1.0 mL) was added TMSCN (1.0 mmol) dropwise via a syringe at 0 °C. The resulting mixture was stirred at 0 °C and monitored by ^{19}F NMR. After completion, the mixture was quenched with brine (5 mL) and extracted with Et_2O (5 mL × 3). The combined organic phase was washed with water (1 mL × 3) and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by column chromatography (EtOAc/petroleum ether: 1/20) to give the corresponding products.

*(±)-(R_CS_S)-1-(tert-Butylsulfinylamino)-2,2-dimethylbutyronitrile (**IIa**):* white solid; mp 89−90 °C; FT-IR (KBr) 3214, 2245 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.78 (d, J = 9.9 Hz, 1H), 3.70 (d, J = 9.9 Hz, 1H), 1.25 (s, 9H), 1.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 118.5, 57.4, 56.7, 35.8, 25.8, 22.7; EI-MS (m/z) 57 (100). Anal. Calcd for $C_{10}H_{20}N_2OS$: C, 55.52; H, 9.32; N, 12.95. Found: C, 55.68; H, 9.40; N, 12.98.

*(±)-(S_CS_S)-1-(tert-Butylsulfinylamino)-2,2-dimethylbutyronitrile (**IIa′**):* colorless oil; FT-IR (film) 3224, 2240 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.96 (dd, J = 6.6, 2.0 Hz, 1H), 3.52 (d, J = 6.6 Hz, 1H), 1.24 (d, J = 2.1 Hz, 9H), 1.10 (d, J = 2.1 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 117.9, 58.5, 57.0, 35.4, 25.9, 22.3; EI-MS (m/z) 57 (100). Anal. Calcd for $C_{10}H_{20}N_2OS$: C, 55.52; H, 9.32; N, 12.95. Found: C, 55.59; H, 9.45; N, 12.91.

*(±)-(R_CS_S)-1-(p-Toluenesulfinylamino)-2,2-dimethylbutyronitrile (**IIb**):* ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.59 (d, J = 7.5 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H), 4.84 (d, J = 10.2 Hz, 1H), 3.54 (d, J = 10.2 Hz, 1H), 2.42 (s, 3H), 1.09 (s, 9H); EI-MS (m/z) 250 (M^+, 4), 156 (100).

*(±)-(S_CS_S)-1-(p-Toluenesulfinylamino)-2,2-dimethylbutyronitrile (**IIb′**):* ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.59 (d, J = 7.5 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H), 4.68 (d, J = 9.0 Hz, 1H), 3.81 (d, J = 9.0 Hz, 1H), 2.42 (s, 3H), 1.09 (s, 9H); EI-MS (m/z) 250 (M^+, 4), 156 (100).

*(±)-(R_CS_S)-1-(2-Chlorotetrafluoroethanesulfinylamino)-2,2-dimethylbutyronitrile (**6a**):* white solid; mp 80−81 °C; FT-IR (KBr) 3207, 2245 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.15 (d, J = 9.6 Hz, 1H), 4.06 (d, J = 9.6 Hz, 1H), 1.14 (d, J = 2.7 Hz, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.73 (s, 2F), −115.17 (d, J_{FF} = 230.7, 1F), −122.55 (d, J_{FF} = 230.7, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 122.0 (tt, J = 281.1, 33.0 Hz), 116.4 (tt, J = 309.6, 39.6 Hz), 117.0, 55.9, 35.8, 25.6; MS (ESI) $(M + NH_4)^+$ 312. Anal. Calcd for $C_8H_{11}ClF_4N_2OS$: C, 32.60; H, 3.76; N, 9.51. Found: C, 32.89; H, 3.99; N, 9.51.

*(R_CS_S)-**6a**:* white solid; yield 77%; $[\alpha]^{28}_D$ = +35.0 (c = 0.1, $CHCl_3$, 99% ee).

*(±)-(R_CS_S)-1-(Pentafluoroethanesulfinylamino)-2,2-dimethylbutyronitrile (**6b**):* white solid; mp 91−92 °C; FT-IR (KBr) 3273, 2267 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.77 (d, J = 9.9 Hz,

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1H), 4.06 (d, J = 9.9 Hz, 1H), 1.16 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −78.88 (s, 3F), −119.99 (d, J_{FF} = 233.1 Hz, 1F), −125.69 (d, J_{FF} = 233.1 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 122.9−112.4 (m), 117.2, 56.2, 36.0, 25.8; EI-MS (m/z) 159 (50), 96 (74), 57 (100). Anal. Calcd for $C_8H_{11}F_5N_2OS$: C, 34.53; H, 3.98; N, 10.07. Found: C, 34.56; H, 3.99; N, 10.03.

*(±)-(S_C,S_S)-1-(Pentafluoroethanesulfinylamino)-2,2-dimethylbutyronitrile (**6b′**):* white solid; mp 71−73 °C; FT-IR (KBr) 3261, 2252 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.23 (s, 1H), 4.13 (s, 1H), 1.11 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −79.11 (s, 3F), −118.01 (d, J_{FF} = 243.4 Hz, 1F), −124.15 (d, J_{FF} = 243.4 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 117.1, 53.4, 35.9, 25.9; HRMS (EI) calcd for $C_6H_{11}N_2OS$ (M-C_2F_5)$^+$ 159.0592, found 159.0593.

*(±)-(R_C,S_S)-1-(Nonafluorobutanesulfinylamino)-2,2-dimethylbutyronitrile (**6c**):* white solid; mp 93−94 °C; FT-IR (KBr) 3308, 2244 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.91 (d, J = 9.3 Hz, 1H), 4.06 (d, J = 9.3 Hz, 1H), 1.16 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −81.09 to −81.15 (m, 3F), −116.89 (dt, J = 247.6, 12.0 Hz, 1F), −121.96 to −122.07 (m, 2F), −123.31 (dt, J = 247.6, 12.0 Hz, 1F), −125.41 to −127.68 (m, 2F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 117.2, 56.3, 36.1, 25.8; EI-MS (m/z) 159 (54), 96 (81), 57 (100). Anal. Calcd for $C_{10}H_{11}F_9N_2OS$: C, 31.75; H, 2.93; N, 7.41. Found: C, 31.69; H, 2.94; N, 7.32.

*(±)-(S_C,S_S)-1-(Nonafluorobutanesulfinylamino)-2,2-dimethylbutyronitrile (**6c′**):* white solid; mp 89−90 °C; FT-IR (KBr) 3298, 2244 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.09 (d, J = 9.6 Hz, 1H), 4.17 (d, J = 9.9 Hz, 1H), 1.11 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −81.16 (s, 3F), −114.48 (d, J_{FF} = 249.6 Hz, 1F), −121.69 (d, J_{FF} = 249.6 Hz, 1F), −122.08 (s, 2F), −126.59 (s, 2F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 117.0, 52.7, 35.9, 25.9; HRMS (EI) calcd for $C_6H_2F_9N_2OS$ (M − C_4H_9)$^+$ 320.9744, found 320.9746.

*(±)-(R_C,S_S)-1-(Trifluoromethanesulfinylamino)-2,2-dimethylbutyronitrile (**6d**):* white solid; mp 63−64 °C; FT-IR (KBr) 3297, 2237 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.86 (d, J = 9.6 Hz, 1H), 4.05 (d, J = 9.6 Hz, 1H), 1.15 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −77.85 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 123.8 (q, J = 332.7 Hz), 117.6, 54.9, 35.9, 25.9; HRMS (EI) calcd for $C_3H_2F_3N_2OS$ (M − C_4H_9)$^+$ 170.9840, found 170.9844.

*(±)-(S_C,S_S)-1-(Trifluoromethanesulfinylamino)-2,2-dimethylbutyronitrile (**6d′**):* colorless oil; FT-IR (film) 3262, 2259 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.23 (s, 1H), 4.13 (s, 1H), 1.11 (s, 9H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −76.33 (s, 3F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 123.8 (q, J = 337.8 Hz), 117.1, 54.4, 35.7, 25.9; HRMS (EI) calcd for $C_6H_{11}N_2OS$ (M-CF_3)$^+$ 159.0592, found 159.0591.

*(±)-(R_C,S_S)-1-(2-Chlorotetrafluorosulfinylamino)-2-methylbutyronitrile (**6e**):* white solid; mp 41−42 °C; FT-IR (KBr) 3208, 2243 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.39 (d, J = 8.7 Hz, 1H), 4.24 (dd, J = 8.7, 6.0 Hz, 1H), 2.21−2.10 (m, 1H), 1.15 (d, J = 5.1 Hz, 3H), 1.13 (d, J = 5.4 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.68 (m, 2F), −115.51 (d, J_{FF} = 231.0 Hz, 1F), −121.22 (d, J_{FF} = 231.0 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 121.8 (tt, J = 298.8, 33.4 Hz), 117.0, 116.5 (tt, J = 308.1, 35.5 Hz), 50.8, 32.6, 18.6, 17.5; EI-MS (m/z) 145 (59), 82 (100), 43 (24). Anal. Calcd for $C_7H_9ClF_4N_2OS$: C, 29.95; H, 3.23; N, 9.98. Found: C, 30.20; H, 3.34; N, 9.91.

*(±)-(R_C,S_S)-1-(2-Chlorotetrafluorosulfinylamino)-3-methylpentanenitrile (**6f**):* white solid; mp 97−99 °C; FT-IR (KBr) 3185, 2213 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.28 (d, J = 7.2 Hz, 1H), 4.40 (dd, J = 15.5, 8.3 Hz, 1H), 1.95−1.84 (m, 2H), 1.80−1.70 (m, 1H), 1.01 (d, J = 5.7 Hz, 3H), 0.99 (d, J = 4.8 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −66.99 (m, 2F), −114.82 (d, J_{FF} = 230.7 Hz, 1F), −120.25 (d, J_{FF} = 230.7 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 121.4 (tt, J = 298.8, 33.2 Hz), 118.4, 116.4 (tt, J = 271.1, 35.9 Hz), 43.2, 42.8, 24.6, 22.1, 21.3; MS (ESI) (M + NH_4)$^+$ 312. Anal. Calcd for $C_8H_{11}ClF_4N_2OS$: C, 32.60; H, 3.76; N, 9.51. Found: C, 32.67; H, 3.76; N, 9.33.

*(±)-(S_C,S_S)-1-(2-Chlorotetrafluorosulfinylamino)-3-methylpentanenitrile (**6f′**):* white solid; mp 54−55 °C; FT-IR (KBr) 3240, 2552 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.95 (d, J = 8.7 Hz, 1H), 4.48 (dd, J = 16.1, 7.8 Hz, 1H), 1.91−1.71 (m, 3H), 1.02 (d, J = 6.3 Hz, 3H), 0.98 (d, J = 6.6 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −66.71 (m, 2F), −113.31 (d, J_{FF} = 232.7 Hz, 1F), −119.41 (d, J_{FF} = 232.7 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 121.7 (tt, J = 214.4, 33.0 Hz), 118.7, 116.5 (tt, J = 307.0, 35.4 Hz), 43.8, 40.9, 24.5, 21.8, 21.6; HRMS (ESI) calcd for $C_8H_{11}ClF_4N_2NaOS$ (M + Na)$^+$ 317.0114, found 317.0109. Anal. Calcd for $C_8H_{11}ClF_4N_2OS$: C, 32.60; H, 3.76; N, 9.51. Found: C, 32.67; H, 3.89; N, 9.51.

*(±)-(R_C,S_S)-1-(2-Chlorotetrafluorosulfinylamino)pentanenitrile (**6g**):* white solid; mp 64−65 °C; FT-IR (KBr) 3192, 2245 cm^{-1} ; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.21 (d, J = 8.4 Hz, 1H), 4.39 (dd, J = 15.3, 8.1 Hz, 1H), 1.97−1.85 (m, 2H), 1.64−1.52 (m, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ (ppm) −67.59 (s, 2F), −115.54 (d, J_{FF} = 231.7 Hz, 1F), −120.59 (d, J_{FF} = 231.7 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 121.8 (tt, J = 298.8, 33.1 Hz), 118.1, 116.5 (tt, J = 307.5, 35.8 Hz), 44.4, 36.9, 18.6, 13.0; HRMS (ESI) calcd for $C_7H_9ClF_4N_2OS$ (M^+) 252.9951, found 252.9952. Anal. Calcd for $C_7H_9ClF_4N_2OS$: C, 29.95; H, 3.23; N, 9.98. Found: C, 29.98; H, 3.23; N, 9.82.

Removal of Chiral Auxiliary. *Method A.* To a 10 mL round-bottom flask equipped with a reflux condenser were added (S_S,R_C)-**6a** (50 mg, 0.17 mmol), 5 N HCl (0.34 mL), and MeOH (0.34 mL). The mixture was stirred at 50 °C and monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature, adjusted to pH = 10 with 2 M NaOH, and then extracted with EtOAc (1.0 mL × 5). Dry hydrogen chloride was bubbled through the combined organic solution for 5 min, and a white solid precipitated. Evaporation of the volatile solvent under reduced pressure afforded 24.7 mg (98% yield) of (*R*)-**7a**:[19] $[\alpha]^{25}_D$ = +12.2 (c = 0.6, MeOH); ^{1}H NMR (300 MHz, D_2O) δ (ppm) 0.22 (s, 9H), 3.42 (s, 1H).

Method B. To a 10 mL round-bottom flask were added (S_S,R_C)-**6a** (50 mg, 0.17 mmol) and saturated HCl/Et_2O (1.0 mL), and a white solid precipitated. After 2 h, the reaction mixture was filtrated and washed with diethyl ether (1.0 mL × 2) to give the corresponding product (*R*)-**7a** as a white solid.

Determination of ee of (*R*)-7a. To the solution of benzaldehyde (11.7 mg, 0.11 mmol) in CH_2Cl_2 (1 mL) were added $MgSO_4$ (43.2 mg, 0.36 mmol), (*R*)-**7a** (17.8 mg, 0.12 mmol), and Et_3N (10.1 mg, 0.1 mmol). After the mixture was stirred overnight at room temperature, $MgSO_4$ was removed by filtration, and the solvent was removed in vacuum. The residue was purified by flash column chromatography (EtOAc/petroleum ether, 1/20) to give (*R*)-**8a**: yield 73%; $[\alpha]^{26}_D$ = +19.2 (c = 1.0, $CHCl_3$, 98% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.47 (s, 1H), 7.82−7.80 (m, 2H), 7.46−7.45 (m, 3H), 4.32 (d, J = 1.2 Hz, 1H), 1.13 (d, J = 3.6 Hz, 9H).

■ ASSOCIATED CONTENT

Supporting Information. NMR spectra of all new compounds and X-ray ORTEP and crystallographic data for compounds **3e** and (*Ss*,*Rc*)-**6a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) (a) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308. (b) Krafftm, M. P.; Riess, J. G. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 1185. (c) Jäckel, C.; Koksch, B. *Eur. J. Org. Chem.* **2005**, *70*, 4483.

(2) (a) Zhang, W.; Cai, C. *Chem. Commun.* **2008**, 5686. (b) Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943. (c) *Fluoropolymers: Topics in Applied Chemistry*; Katritzky, A. R., Sabongi, G. J., Eds.; Kluwer Academic: Dordrecht, 2002.

(3) (a) Bonaccorsi, C.; Bachmann, S.; Mezzetti, A. *Tetrohedron: Asymmetry* **2003**, *14*, 845. (b) RajanBabu, T. V.; Casalnuovo, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 6325. (c) Sibi, M. P.; Tatamidani, H.; Patil, K. *Org. Lett.* **2005**, *7*, 2571.

(4) (a) Ishihara, K.; Yamamoto, H.; Konodo, S.; Kurihara, H. *J. Am. Chem. Soc.* **1996**, *118*, 3049. (b) Sohtome, Y.; Tanatani, A.; Hashimoto, Y.; Nagasawa, K. *Tetrahedron Lett.* **2004**, *45*, 5589. (c) Tillman, A. L.; Ye, J.; Dixon, D. J. *Chem. Commun.* **2006**, *11*, 1191. (d) Cao, C.-L.; Sun, X.-L.; Kang, Y.-B.; Tang, Y. *Org. Lett.* **2007**, *9*, 4151.

(5) For fluorous-supported Evans auxiliary, see: (a) Hein, J. E.; Hultin, P. G. *Synlett* **2003**, 635. (b) Hein, J. E.; Zimmerman, J.; Sibi, M. P.; Hultin, P. G. *Org. Lett.* **2005**, *7*, 2755. (c) Hein, J. E.; Hultin, P. G. *Tetrahedron: Asymmetry* **2005**, *16*, 2341. For 2-trifluoromethyloxoazolidines, see: (d) Lubin, H.; Tessier, A.; Chaume, G.; Pytkowicz, J.; Brigaud, T. *Org. Lett.* **2010**, *12*, 1496. (e) Tessier, A.; Pytkowicz, J.; Brigaud, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 3677. (f) Tessier, A.; Lahmar, N.; Pytkowicz, J.; Brigaud, T. *J. Org. Chem.* **2008**, *73*, 3970. (g) Ishii, A.; Higashiyama, K.; Mikami, K. *Synlett.* **1997**, 1381.

(6) For reviews, see: (a) Ferreira, F.; Botuha, C.; Chemla, F.; Pérez-Luna, A. *Chem. Soc. Rev.* **2009**, *38*, 1162. (b) Lin, G.-Q.; Xu, M.-H.; Zhong, Y.-W.; Sun, X.-W. *Acc. Chem. Rev.* **2008**, *41*, 831. (c) Davis, F. A. *J. Org. Chem.* **2006**, *71*, 8993. (d) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600.

(7) Wang, X.-J.; Liu, J.-T. *Tetrahedron* **2005**, *61*, 6982.

(8) Wakayama, M.; Ellman, J. A. *J. Org. Chem.* **2009**, *74*, 2646.

(9) Qin, Y.; Wang, C.-H.; Huang, Z.-Y.; Xiao, X.; Jiang, Y.-Z. *J. Org. Chem.* **2004**, *69*, 8533.

(10) Romanenko, V. D.; Thoumazet, C.; Lavallo, V.; Tham, F. S.; Bertrand, G. *Chem. Commun.* **2003**, 1680.

(11) (a) Strecker, A. *Ann. Chem. Pharm.* **1850**, *75*, 27. (b) Merino, P.; Marqués-López, E.; Tejero, T.; Herrera, R. P. *Tetrahedron* **2009**, *65*, 1219.

(12) Mabic, S.; Cordi, A. A. *Tetrahedron* **2001**, *57*, 8861.

(13) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600.

(14) Davis, F. A.; Sirajan, V. *J. Org. Chem.* **2000**, *65*, 3248.

(15) Davis, F. A.; Reddy, R. E.; Portonovo, P. S. *Tetrahedron Lett.* **1994**, *35*, 9351.

(16) Li, B.-F.; Yuan, K.; Zhang, M.-J.; Wu, H.; Dai, L.-X.; Wang, Q.-R.; Hou, X.-L. *J. Org. Chem.* **2003**, *68*, 6264.

(17) Wang, H.; Zhao, X.-M.; Li, Y.-H.; Lu, L. *Org. Lett.* **2006**, *8*, 1379.

(18) Wang, X.-L.; Salaski, E. J.; Berger, D. M.; Powell, D. *Org. Lett.* **2009**, *11*, 5662.

(19) Shibasaki, M.; Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M. *Chem. Pharm. Bull.* **2000**, *48* (10), 1586.

(20) Belinskaja, J. *Zh. Obshch. Khim.* **1958**, *28*, 772.

(21) Tordeux, M.; Langlois, B.; Wakselman, C. *J. Org. Chem.* **1989**, *54*, 2452.

(22) Shreeve, J. M.; Sauer, D. T. *Inorg. Chem.* **1971**, *10*, 358.