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Nucleophilic (phenylsulfinyl)difluoromethylation of carbonyl compounds with difluoromethyl phenyl sulfoxide

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Dedicated to Professor Kenji Uneyama with friendship and admiration on the occasion of his receipt of 2007 ACS Award for Creative Work in Fluorine Chemistry.

Abstract

We have successfully achieved nucleophilic (phenylsulfinyl)difluoromethylation of both enolizable and non-enolizable aldehydes and ketones by using difluoromethyl phenyl sulfone (**1**) as the fluoroalkylating agent. Although the chemical yields of the reactions are good to excellent, the observed diastereoselectivity is poor (dr = 1:1.04–2.03). The present synthetic methodology provides a convenient alternative for the preparation of α-(phenylsulfinyl)difluoromethylated carbinols that were previously synthesized via a two-step procedure.

Keywords: (Phenylsulfinyl)difluoromethylation; Difluoromethyl sulfoxide; Nucleophilic addition

1. Introduction

Nucleophilic fluoroalkylation with fluorinated carbanions (R_F^-, the fluorine substitution is commonly on the carbanion center) is one of the most important methods to introduce fluorinated moieties into organic molecules [1–8]. Although there is a recent argument that ''fluorine is more effective than the heavier halogens'' in α-stabilization of carbanions [9], most primary and secondary fluorinated carbanions are well recognized as kinetically unstable species [1]. The lifetimes, reactivity and synthetic utility of fluorinated carbanions are effected by many factors, and as a result, the chemistry of fluorinated carbanions is much different from their non-fluorinated counterparts [1,2]. α-Functionalization of the fluorinated carbanions with softening group(s) (such as phenylsulfonyl group) is a useful approach to alleviate the ''negative fluorine effect'' and enhance the nucleophilicity of the R_F^- species [10a]. In this context, we have been interested in the chemistry of phenylsulfonyl-substituted fluorinated carbanions that are generated from fluorinated sulfones [10–11]. However, the chemistry on the phenylsulfinyl-substituted fluorinated carbanions has been rarely explored [12].

Recently, Pohmakotr et al. [13] reported a two-step preparation of (phenylsulfinyl)difluoromethylated carbinols **5**, which can be converted to the corresponding *gem*-difluoroalkenes **6** by pyrolysis (see Scheme 1, eq (1)). We envisioned that it would be more convenient if compounds **5** can be prepared from one-step (phenylsulfinyl)difluoromethylation with $PhSOCF_2^-$ anion (generated from $PhSOCF_2H$ (**1**) and a base; see Scheme 1, eq. (2)). Furthermore, during a recent symposium [14] a question was raised regarding the diastereoselectivity issue of the reaction between carbonyl compounds **3** and **1** (as shown in Scheme 1, eq. (2)). Intrigued by these factors, we studied the nucleophilic (phenylsulfinyl)difluoromethylation of carbonyl compounds with difluoromethyl phenyl sulfoxide ($PhSOCF_2H$, **1**).

2. Results and discussion

Difluoromethyl phenyl sulfoxide (**1**) (in a racemic form) was prepared in 88% isolated yield by simple oxidation of

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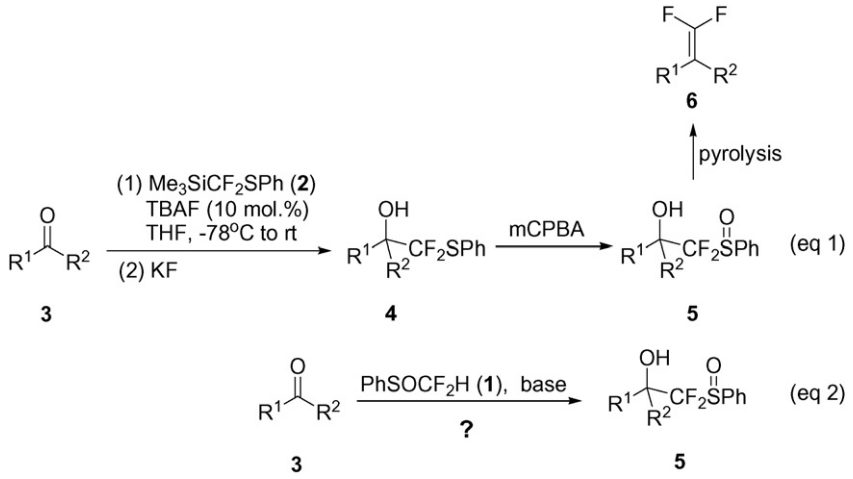
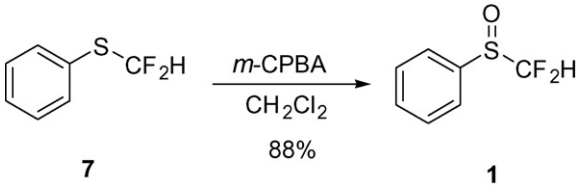


Scheme 1.



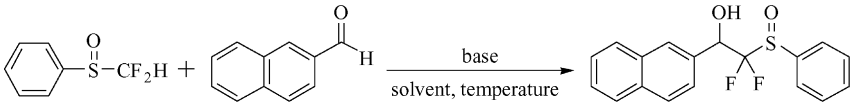
Scheme 2.

difluoromethyl phenyl sulfide **7** [15] with *m*-chloroperbenzoic acid (Scheme 2). With compound **1** in hand, we quickly scanned the reaction conditions between **1** and 2-naphthaldehyde. As shown in Table 1, when lithium hexamethyldisilazide (LiHMDS) was applied as a base, the product yields were only 19–76% (entries 1–3). The best yield (93%) of **5a** was obtained when potassium *tert*-butoxide was used as a base and DMF was used as a solvent (entry 4).

Encouraged by the above result, we examined the scope of the nucleophilic (phenylsulfinyl)difluoromethylation. The typical reaction procedure is as follows: into the mixture of difluoromethyl phenyl sulfoxide **2** (1 mmol), carbonyl compounds **3** (2 mmol) and DMF (5 mL) at −30 °C, was added dropwise *t*-BuOK (2 mmol, dissolved in 1 mL of DMF). The reaction mixture was usually stirred at −30 °C for 30 min after the addition was complete. The products **5** were obtained after simple work-up and purification with silica gel column chromatography. The results are summarized in Table 2. Both enolizable and non-enolizable aldehydes and ketones **3** can be readily (phenylsulfinyl)difluoromethylated to give corresponding carbinol products **5** in 77–99% yields. The reaction yield for enolizable aldehyde (Table 2, entry 6) was somewhat lower than those for enolizable ketones (entries 7 and 12), which is similar to our previous report of (phenylsulfonyl)difluoromethylation with $PhSO_2CF_2H$ [11c]. All these results indicate that the (phenylsulfinyl)difluoromethyl anion ($PhSOCF_2^-$, generated in situ from **1** and *t*-BuOK) has good nucleophilicity towards carbonyl compounds. However, as shown in Table 2, the diastereoselectivities of the reactions were generally poor (dr = 1:1.04–2.03), which were determined by ^{19}F NMR on the product mixtures (for an example, see Fig. 1). This low diastereoselectivity is similar to the known reactions of non-fluorinated α-sulfinyl carbanions with carbonyl compounds, which also resulted in low diastereoselectivity [16].

To demonstrate other synthetic application of difluoromethyl phenyl sulfoxide **1**, we also subjected **1** in the one-pot synthesis of anti-2,2-difluoro-1,3-diol (**8**) (Scheme 3). Compounds **1** (1

Table 1
Survey of reaction conditions

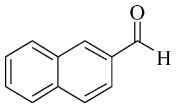
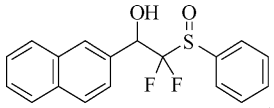
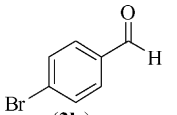
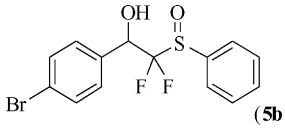
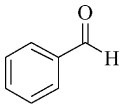
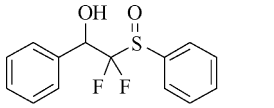
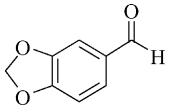
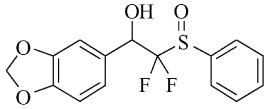
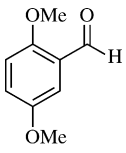
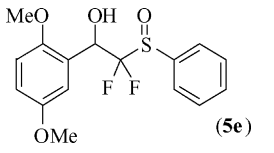
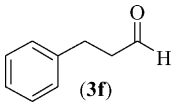
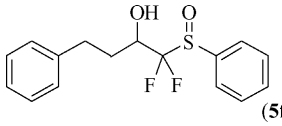
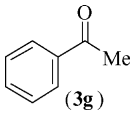
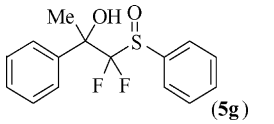
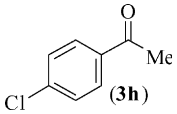
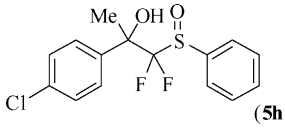
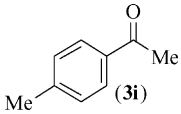
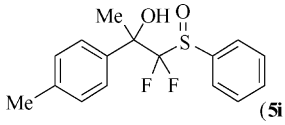
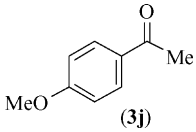
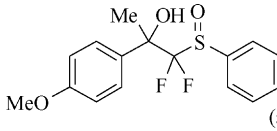
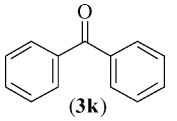
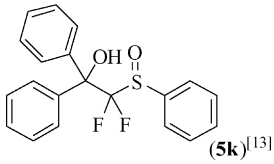
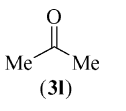
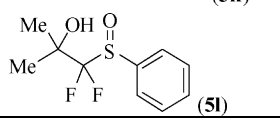


1 (1.0 equiv) **3a** **5a**

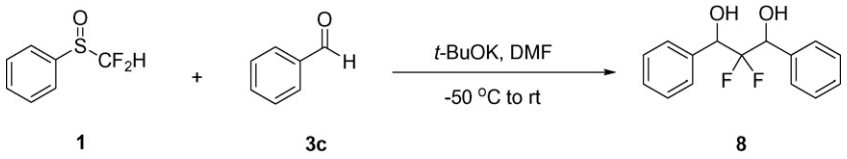
Entry[a]	**3a** (equiv)	Base	Solvent	Temperature	Time (h)	Yield of **5a** (%)[b]	Recovery of **1** (%)[c]
1	1.05	LiHMDS (1.1 equiv)	THF	−78 °C to rt	12	19	53
2	2.0	LiHMDS (2.2 equiv)	THF/HMPA[c]	−78 °C to rt	12	36	43
3	2.0	LiHMDS (2.0 equiv)	DMF/HMPA[c]	−30 °C to rt	12	76	20
4	2.0	*t*-BuOK (2.0 equiv)	DMF	−30 °C	0.5	93	0

[a] Typical procedure: into a mixture of **1**, **3a** and solvent, base (dissolved in THF or DMF) was added at −30 °C or −78 °C.
[b] Isolated yield based on compound **1** used.
[c] Solvent ratio = 10:1 (v/v).

Table 2
Nucleophilic (phenylsulfinyl)difluoromethylation of carbonyl compounds with $PhSOCF_2H$ (**1**)

Entry[a]	Carbonyl compounds **3**	Product **5**	Yield (%)[b]	dr[c]
1	 (**3a**)	 (**5a**)	93	48:52
2	 (**3b**)	 (**5b**)	82	43:57
3	 (**3c**)	 (**5c**)	80	33:67
4	 (**3d**)	 (**5d**)	82	47:53
5	 (**3e**)	 (**5e**)	82	42:58
6	 (**3f**)	 (**5f**)	77	49:51
7	 (**3g**)	 (**5g**)	94	33:67
8	 (**3h**)	 (**5h**)	99	44:56
9	 (**3i**)	 (**5i**)	92	46:54
10	 (**3j**)	 (**5j**)	95	48:52
11	 (**3k**)	 (**5k**)[13]	94	–
12	 (**3l**)	 (**5l**)	96	–

[a] Typical procedure: A mixture of **1** (1 mmol), **3** (2 mmol), *t*-BuOK (2 mmol) and DMF (6 mL) was stirred at −30 °C for 30 min, followed by usual work-up and purification.
[b] Isolated yields of **5** based on reagent **1** used.
[c] Diasteromeric ratios were determined by ^{19}F NMR spectroscopy.



Scheme 3.

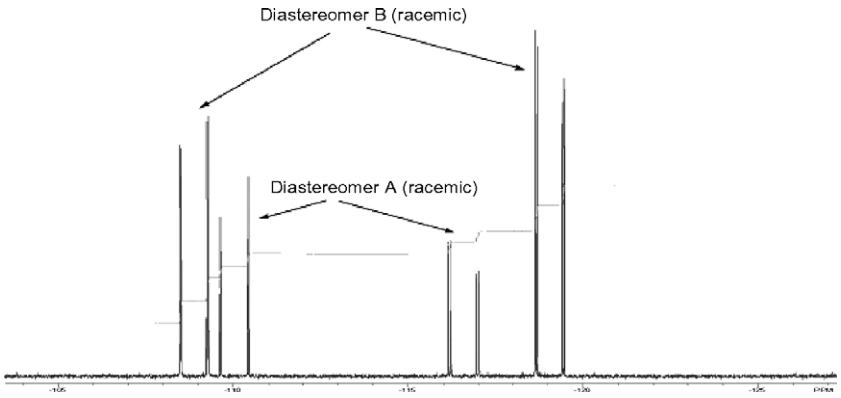


Fig. 1. ^{19}F NMR of the product **5c** (as a diastereomeric mixture with dr (*A*/*B*) = 33:67).

equiv), **3c** (3 equiv) and *t*-BuOK (4 equiv) were mixed under N_2 atmosphere at −50 °C, and the mixture was stirred at −50 °C to rt overnight to give product **8** in 68% yield (not optimized) with 94:6 dr (anti/syn). The mechanism of this transformation is expected to be similar to those proposed by us [11f] and Liu et al. [17] (but with different difluoromethylene dianion synthons).

3. Conclusions

In conclusion, we have successfully achieved nucleophilic (phenylsulfinyl)- difluoromethylation of both enolizable and non-enolizable aldehydes and ketones by the use of difluoromethyl phenyl sulfone (**1**) as the fluoroalkylating agent. Although the chemical yields of the reactions are good to excellent, the observed diastereoselectivity is poor (dr = 1:1.04–2.03). The present synthetic methodology provides a convenient alternative for the preparation of α-(phenylsulfinyl)difluoromethylated carbinols that were previously synthesized via a two-step procedure [13].

4. Experimental

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. DMF was freshly distilled over calcium hydride and stored under nitrogen atmosphere. Difluoromethyl phenyl sulfide was prepared from PhSH and $CHClF_2$ using a modified procedure as described in [15]. ^1H NMR spectra were recorded on Bruker 300 or Mercury 300 spectrometers with Me_4Si as internal standard. ^{19}F NMR spectra were recorded on Bruker 300 or Mercury 300 spectrometers with $CFCl_3$ as external standard. ^{13}C NMR spectra were recorded on Avance 500 or DPX-400 spectrometers. Mass spectra were obtained on a HP5989A spectrometer. High-resolution mass data were recorded on a high-resolution mass spectrometer in the EI or MALDI mode.

4.1. Preparation of difluoromethyl phenyl sulfoxide *1*

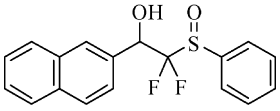
To a solution of $PhSCHF_2$ (6.367 g, 39.7 mmol) in CH_2Cl_2 (80 mL) was added *m*-CPBA (85%, 8.473 g, 41.734 mmol) at 0 °C and then the reaction mixture was stirred overnight at room temperature. After filtration, the filtrate was washed with cold 1 M sodium hydroxide solution, dried over Na_2SO_4. The solvent was removed under vacuum and the crude product was purified by flash column chromatography (petroleum ether/ethyl acetate = 12:1) to give the sulfoxide **1** [11e,18] as a colorless oily liquid (6.132 g, 88% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.76–7.58 (m, 5H), 6.05 (*t*, J_{H-F} = 55.4 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −119.7 (dd, J_{F-F} = 8.6 Hz, J_{H-F} = 55.5 Hz, 2F).

4.2. Typical experimental procedure for nucleophilic (phenylsulfinyl)difluoromethylation of carbonyl compounds with *1*

The reaction was carried out in a Schlenk flask under a nitrogen atmosphere. To a solution of difluoromethyl phenyl sulfoxide **1** (176 mg, 1 mmol) and 2-naphthal- dehyde **3a** (312 mg, 2 mmol) in DMF (5 mL) at −30 °C, was added a solution of *t*-BuOK (224 mg, 2 mmol) in anhydrous DMF (1 mL). The reaction mixture was kept at −30 °C for 30 min. The reaction mixture was poured into water (10 mL) and extracted with Et_2O (4 × 15 mL). The combined ether phase was washed with a saturated aqueous solution of NH_4Cl. After drying over Na_2SO_4, the ether solvent was removed under vacuum. The crude product was further purified by flash column chromatography (petroleum ether/ethyl acetate

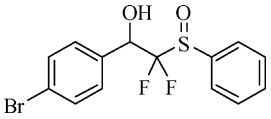
6/1, then 3/1) to afford product **5a** (pale yellow solid) as a mixture of two diastereomers (dr = 48:52), yield: 308 mg, 93% yield.

*4.2.1. 2,2-Difluoro-1-(naphthalen-2-yl)-2-(phenylsulfinyl)ethanol (**5a**)*



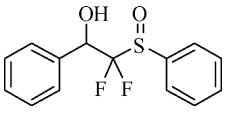
Pale yellow solid; m.p.: 109–111 °C; 93% yield. A mixture of two diastereomers (48:52). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00–7.48 (m, 12H), 5.66–5.52 (m, 1H), 4.73(d, J_{H-H} = 5.4 Hz, 0.48H), 3.89 (d, J_{H-H} = 3.6 Hz, 0.52H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.1 (dd, J = 10.4, 218.6 Hz, 0.48 F) and −116.4 (dd, J = 22.9, 224.4 Hz, 0.48F); −110.0 (d, J = 226.2 Hz, 0.52F) and −118.9 (dd, J = 15.1, 218.4 Hz, 0.52F). IR (KBr): 3294, 1602, 1510, 1445, 1271, 1194, 1111, 1085, 1040, 987, 973, 794, 747, 687 cm^{-1}. MS (EI, *m/z*, %): 332(M^+, 2), 126(100). HRMS (EI, *m/z*) calculated for $C_{18}H_{14}O_2F_2S(M^+)$: 332.0683; found: 332.0676.

*4.2.2. 1-(4-Bromophenyl)-2,2-difluoro-2-(phenylsulfinyl)ethanol (**5b**)*



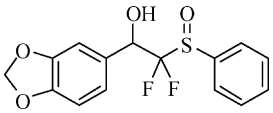
White solid; m.p.: 130–132 °C; 82% yield. A mixture of two diastereomers (43:57). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71–7.33 (m, 9H), 5.45–5.33 (m, 1H), 5.13 (d, J = 4.2 Hz, 0.43H), 4.11 (d, J = 3.3 Hz, 0.57H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.3 (dd, J = 8.8 Hz, 219.9 Hz, 0.57F) and −120.0(dd, J = 15.1, 219.5 Hz, 0.57F); −111.0 (d, J = 222.5 Hz, 0.43F) and −117.6 (dd, J = 22.9, 225.3 Hz, 0.43F). IR (KBr): 3287, 1591, 1489, 1475, 1446, 1399, 1203, 1194, 1122, 1108, 1083, 1041, 975, 773,767, 749, 689 cm^{-1}. MS (EI, *m/z*, %): 362([M + 1]$^+$, 1), 126(100). HRMS (EI, *m/z*): calculated for $C_{14}H_{11}O_2F_2SBr(M^+)$: 359.9624; found: 359.9631.

*4.2.3. 2,2-Difluoro-1-phenyl-2-(phenylsulfinyl)ethanol (**5c**)*



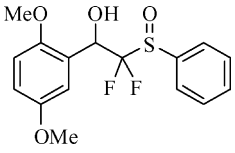
White solid; m.p.: 103–107 °C; 80% yield. A mixture of two diastereomers (33:67). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74–7.36 (m, 10H), 5.47–5.32 (m, 1H), 4.48 (d, J = 5.4 Hz, 0.43H), 4.11 (d, J = 3.3 Hz, 0.57H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −108.9 (dd, J = 9.2, 219.3 Hz, 0.33F) and −116.6 (dd, J = 21.7, 224.8 Hz, 0.33F); −110.0 (d, J = 224.8 Hz, 0.67F) and −119.1(dd, J = 14.8, 219.3 Hz, 0.67F). MS (EI, *m/z*, %) 282 (M^+, 1), 126 (100). IR (KBr): 3296, 1494, 1446, 1203, 1109, 1083, 1036, 976, 751, 727, 698, 689 cm^{-1}. HRMS (EI, *m/z*) calculated for $C_{14}H_{12}O_2F_2S(M^+)$: 282.0526; found: 282.0530.

*4.2.4. 1-(Benzo[1,3]dioxol-5-yl)-2,2-difluoro-2-(phenylsulfinyl)ethanol (**5d**)*



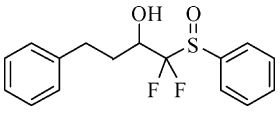
Pale yellow solid; m.p.: 105–108 °C; 82% yield. A mixture of two diastereomers (47:53). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75–7.54 (m, 5H), 7.02–6.77 (m, 3H), 5.98 (s, 0.53 × 2H), 5.96 (s, 0.47 × 2H), 5.35–5.26 (m, 1H), 4.22 (d, J = 4.5 Hz, 0.47H), 3.57 (d, J = 4.5 Hz, 0.53H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.4 (dd, J = 9.9, 218.8 Hz, 0.53F) and −119.6 (dd, J = 14.7, 218.3 Hz, 0.53F); −109.9 (d, J = 224.5 Hz, 0.47F) and −117.2 (dd, J = 21.9, 225.2 Hz, 0.47F). IR (KBr): 3262, 1504, 1490, 1446, 1250, 1110, 1036, 982, 921, 788, 762, 749, 686 cm^{-1}. MS (EI, *m/z*, %): 326 (M^+, 2), 126 (100). HRMS (EI, *m/z*): calculated for $C_{15}H_{12}O_2F_2S(M^+)$: 326.0424; found: 326.0424.

*4.2.5. 1-(2,5-Dimethoxyphenyl)-2,2-difluoro-2-(phenylsulfinyl)ethanol (**5e**)*



Pale yellow solid; m.p.: 123–127 °C; 82% yield. A mixture of two diastereomers (42:58). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81–7.55 (m, 5H), 7.00 (m, 3H), 5.73–5.40 (m, 1H), 4.46(s, 0.42H), 4.45 (d, J = 6.3 Hz, 0.58H) 3.84 (s, 3 × 0.58H), 3.76 (s, 3H), 3.74 (s, 3 × 0.42H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.6 (dd, J = 8.2, 219.1 Hz, 0.58F) and −119.8 (dd, J = 17.8, 216.2 Hz, 0.58F); −111.8 (d, J = 221.0 Hz, 0.42F) and −117.7 (dd, J = 24.3, 223.3 Hz, 0.42F). IR (KBr): 3287, 1504, 1467, 1446, 1430, 1280, 1220, 1160, 1116, 1085, 1068, 1045, 1022, 983, 815, 755, 703, 693 cm^{-1}. MS (EI, *m/z*, %): 342 (M^+, 15), 216 (100). HRMS (EI, *m/z*): 342.0743, calculated for $C_{16}H_{16}O_4F_2S$: 342.0737.

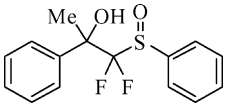
*4.2.6. 1,1-Difluoro-4-phenyl-1-(phenylsulfinyl)butan-2-ol (**5f**)*



Yellow solid; m.p.: 95–99 °C; 77% yield. A mixture of two diastereomers (49:51). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74–7.53 (m, 5H), 7.32–7.16 (m, 5H), 4.75 (d, J = 6.6 Hz, 0.49H), 4.38–4.10 (m, 1H), 3.65 (d, J = 6.3 Hz, 0.51H), 3.00–2.67 (m, 2H), 2.13–1.89 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.1 (dd, J = 5.9, 219.6 Hz, 0.51F) and −119.7 (dd, J = 14.0, 220.9 Hz, 0.51F); −114.0 (d, J = 221.9 Hz, 0.49F) and −118.9 (dd, J = 22.9, 221.9 Hz, 0.49F). IR (KBr): 3326,

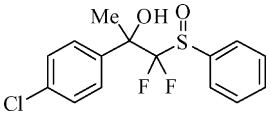
2952, 1603, 1497, 1455, 1446, 1205, 1100, 1085, 1031, 1021, 1007, 996, 945, 931, 751, 700, 689 cm^{-1}. MS (EI, *m/z*, %): 311 (M^+, 1), 126 (100). HRMS (EI, *m/z*): calculated for $C_{16}H_{16}O_4F_2S$: 310.0839(M^+); found: 310.0830.

4.2.7. 1,1-Difluoro-2-phenyl-1-(phenylsulfinyl)propan-2-ol (**5g**)



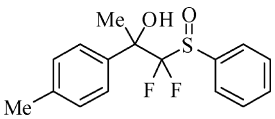
Pale yellow solid; m.p.: 114–117 °C; 94% yield. A mixture of two diastereomers (33:67). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71–7.32 (m, 10H), 4.80 (s, 0.67H), 4.38 (s, 0.33H), 2.08 (s, 0.33 × 3H), 1.75 (s, 0.67 × 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −104.7 (d, J = 220.8 Hz, 0.33F) and −116.5 (d, J = 221.3 Hz, 0.33F); −106.1 (d, J = 221.3 Hz, 0.67F) and −119.0 (d, J = 219.9 Hz, 0.67F). IR (KBr): 3294, 3063, 1494, 1477, 1447, 1397, 1371, 1236, 1121, 1085, 1074, 1046, 968, 937, 747, 699, 687, 670 cm^{-1}. MS (EI, *m/z*, %): 297 ([M + 1]$^+$, 1), 126 (100). HRMS (EI, *m/z*): calculated for $C_{15}H_{14}O_2F_2S$(M^+): 296.0683; found: 296.0674.

4.2.8. 2-(4-Chlorophenyl)-1,1-difluoro-1-(phenylsulfinyl)propan-2-ol (**5h**)



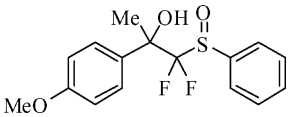
White solid; m.p.: 122–124 °C; 99% yield. A mixture of two diastereomers (44:56). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69–7.29 (m, 9H), 4.89 (s, 0.56H), 4.54 (s, 0.44H), 2.04 (s, 0.44 × 3H), 1.73 (s, 0.56 × 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −104.7 (d, J = 223.3 Hz, 0.44F) and −116.4 (d, J = 221.0 Hz, 0.44F); −105.8 (d, J = 220.2 Hz, 0.56F) and −118.9 (d, J = 220.2 Hz, 0.56F). IR (KBr): 3422, 3325, 1595, 1492, 1446, 1405, 1375, 1217, 1194, 1165, 1133, 1122, 1106, 1092, 1083, 1045, 1012, 779, 746, 726, 686 cm^{-1}. MS (EI, *m/z*, %): 330 (M^+, 0.2), 126 (100). HRMS (EI, *m/z*): calculated for $C_{15}H_{13}O_2F_2SCl$(M^+): 330.0293; found: 330.0281.

4.2.9. 1,1-Difluoro-1-(phenylsulfinyl)-2-p-tolylpropan-2-ol (**5i**)



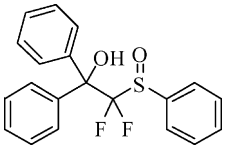
White solid; m.p.: 108–110 °C; 92% yield. A mixture of two diastereomers (46:54). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70–7.15 (m, 9H), 4.76 (s, 0.54H), 4.26 (s, 0.44H), 2.41 (s, 0.54 × 3), 2.33 (s, 0.46 × 3), 2.05 (s, 0.46 × 3), 1.72 (s, 0.54 × 3). ^{19}F NMR (282 MHz, $CDCl_3$): δ −104.0 (d, J = 219.2 Hz, 0.46F) and −116.7 (d, J = 218.9 Hz, 0.46F); −106.2 (d, J = 219.4 Hz, 0.54F) and −119.1 (d, J = 218.7 Hz, 0.54F). IR(KBr): 3308, 2920, 1610, 1511, 1475, 1446, 1409, 1396, 1372, 1232, 1220, 1185, 1161, 1118, 1046, 1021, 966, 820, 806, 763, 745, 698, 687 cm^{-1}. MS (EI, *m/z*, %): 310 (M^+, 1), 126 (100). HRMS (EI, *m/z*): calculated for $C_{16}H_{16}O_2F_2S$(M^+): 310.0839; found: 310.0838.

4.2.10. 1,1-Difluoro-2-(4-methoxyphenyl)-1-(phenylsulfinyl)propan-2-ol (**5j**)



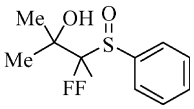
Sticky oil; 95% yield. A mixture of two diastereomers (48:52). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70–7.49 (m, 7H), 6.99 (d, J = 9.0 Hz, 1H), 6.87 (d, J = 8.7Hz, 1H), 4.80 (s, 0.52H), 4.33 (s, 0.48H), 3.85 (s, 0.52 × 3H), 3.79 (s, 0.48 × 3H), 2.04 (s, 0.48 × 3H), 1.72 (s, 0.52 × 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −104.9 (d, J = 218.8 Hz, 0.48F) and −116.9 (d, J = 221.0 Hz, 0.48F); −106.0 (d, J = 218.5 Hz, 0.52F) and −118.9 (d, J = 217.1 Hz, 0.52F). IR (KBr): 3371, 3002, 2839, 1611, 1584, 1513, 1446, 1377, 1303, 1253, 1181, 1034, 967, 922, 836, 810, 750, 689 cm^{-1}. MS (EI, *m/z*, %) 326 (M^+, 0.1), 126 (100). HRMS (EI, *m/z*): calculated for $C_{16}H_{16}O_3F_2S$(M^+): 326.0788; found: 326.0779.

4.2.11. 2,2-difluoro-1,1-diphenyl-2-(phenylsulfinyl)ethanol (**5k**)[13]



White solid; 94% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84–7.26 (m, 15H), 5.20 (s, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −98.6 (d, $J_{F–F}$ = 219.4 Hz, 1F), −112.5 (d, $J_{F–F}$ = 219.4 Hz, 1F). The data are consistent with the previous report [13].

4.2.12. 1,1-Difluoro-2-methyl-1-(phenylsulfinyl)propan-2-ol (**5l**)



White solid; m.p.:75–77 °C; 96% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76–7.55 (m, 5H), 3.66 (s, 1H), 1.63 (s, 3H), 1.46 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −107.7 (d, J_{F-F} = 218.8 Hz, 1F), −120.1 (d, J_{F-F} = 219.9 Hz, 1F). IR (KBr): 3370, 2995, 2949, 1583, 1471, 1448, 1368, 1310, 1257, 1210, 1122,,1095, 1084, 1055, 1011, 987, 952, 827, 748, 690 cm^{-1}. MS (EI, *m/z*, %): 235 (M^+, 11), 126 (100). HRMS (EI, *m/z*): calculated for $C_{10}H_{12}O_2F_2S$(M^+): 234.0526; found: 234.0532.

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References

[1] W.B. Farnham, Chem. Rev. 96 (1996) 1633–1640, and the references cited therein.
[2] R.D. Chambers, Fluorine in Organic Chemistry, Blackwell, Oxford, 2004.
[3] K. Uneyama, Organofluorine Chemistry, Blackwell, New Delhi, 2006.
[4] P. Kirsch, Modern Fluoroorganic Chemistry, Wiley-VCH, Weinheim, 2004.
[5] T. Hiyama, Organofluorine Compounds: Chemistry and Applications, Springer, New York, 2000.
[6] G.K.S. Prakash, A. Yudin, Chem. Rev. 97 (1997) 757–786.
[7] G.K.S. Prakash, M. Mandal, J. Fluorine Chem. 112 (2001) 123–131.
[8] G.K.S. Prakash, J. Hu, New Nucleophilic Fluoroalkylation Chemistry, in Fluorine-Containing Synthons (V.A. Soloshonok, Ed.), ACS Symposium Series 911, American Chemical Society, 2005.
[9] F.M. Bickelhaupt, H.L. Hermann, G. Boche, Angew. Chem. Int. Ed. 45 (2006) 823–826.
[10] (a) C. Ni, Y. Li, J. Hu, J. Org. Chem. 71 (2006) 6829–6833;
(b) C. Ni, J. Liu, L. Zhang, J. Hu, Angew. Chem. Int. Ed. 46 (2007) 786–789;
(c) Y. Li, C. Ni, J. Liu, L. Zhang, J. Zheng, L. Zhu, J. Hu, Org. Lett. 8 (2006) 1693–1696;
(d) J. Liu, C. Ni, Y. Li, L. Zhang, G. Wang, J. Hu, Tetrahedron Lett. 47 (2006) 6753–6756;
(e) Y. Li, J. Hu, Angew. Chem. Int. Ed. 44 (2005) 5882–5886;
(f) C. Ni, J. Hu, Tetrahedron Lett. 46 (2005) 8273–8277.
[11] (a) G.K.S. Prakash, J. Hu, Y. Wang, G.A. Olah, J. Fluorine Chem. 126 (2005) 529–534;
(b) G.K.S. Prakash, Y. Wang, J. Hu, G.A. Olah, J. Fluorine Chem. 126 (2005) 1361–1367;
(c) G.K.S. Prakash, J. Hu, Y. Wang, G.A. Olah, Eur. J. Org. Chem. (2005) 2218–2223;
(d) G.K.S. Prakash, J. Hu, Y. Wang, G.A. Olah, Angew. Chem. Int. Ed. 43 (2004) 5203–5206;
(e) G.K.S. Prakash, J. Hu, Y. Wang, G.A. Olah, Org. Lett. 6 (2004) 4315–4317;
(f) G.K.S. Prakash, J. Hu, T. Mathew, G.A. Olah, Angew. Chem. Int. Ed. 42 (2003) 5216–5219;
(g) G.K.S. Prakash, J. Hu, G.A. Olah, Org. Lett. 5 (2003) 3253–3256;
(h) G.K.S. Prakash, J. Hu, G.A. Olah, J. Org. Chem. 68 (2003) 4457–4463.
[12] (a) V. Reutrakul, V. Rukachaisirikul, Tetrahedron Lett. 24 (1983) 725–728;
(b) V. Reutrakul, T. Kruahong, M. Pohmaktor, Tetrahedron Lett. 35 (1994) 4851–4852.
[13] M. Pohmakotr, K. Boonkitpattarakul, W. Ieawsuwan, S. Jarussophon, N. Duangdee, P. Tuchinda, V. Reutrakul, Tetrahedron 62 (2006) 5973–5985.
[14] The Japan–Korea–China Joint Seminar on Fluorine Chemistry, Kyoto, Japan, January 25–26, 2007.
[15] K.I. Petko, L.M. Yagupol'skii, Russ. J. Org. Chem. 40 (2004) 601–602.
[16] See reviews on α-sulfinyl carbanion chemistry:
(a) G. Hanquet, F. Colobert, S. Lanners, G. Solladie, ARKIVOC Vii (2003) 328–401;
(b) M.C. Carrenno, Chem. Rev. 95 (1995) 1717–1760;
(c) A.J. Walker, Tetrahedron Asymm. 3 (1992) 961–998;
(d) S. Patai, Z. Rappoport, C.J.M. Stirling (Eds.), The Chemistry of Sulfones and Sulfoxides, Wiley, Chichester, UK, 1988.
[17] J.-L. Li, J.-T. Liu, Tetrahedron 63 (2007) 898–903.
[18] (a) J. Chiba, T. Sugihara, C. Kaneko, Chem. Lett. 24 (1995) 581–582;
(b) A. Toyota, Y. Ono, J. Chiba, T. Sugihara, C. Kaneko, Chem. Pharm. Bull. 44 (1996) 703–708.