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Nucleophilic Difluoro(phenylsulfonimidoyl)methylation of Unactivated Alkyl Bromides with PhSO(NTBS)CF_2H: Facile Entry into *gem*-Difluoroalkenes†

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An efficient nucleophilic difluoro(phenylsulfonimidoyl)methylation of unactivated primary alkyl bromides with PhSO(NTBS)CF_2H has been developed. It is particularly remarkable that, when 1.5 equiv. of alkyl bromides are used, the substitution products are obtained in moderate to excellent yields. The prepared difluoro(phenylsulfonimidoyl)methylated alkanes can be readily transformed to *gem*-difluoroalkenes via base-mediated *β*-elimination reaction.

Keywords nucleophilic fluoroalkylation, *β*-elimination, difluoroalkene, sulfoximine

Introduction

Selective introduction of fluorine atom(s) or fluorinated moieties can often result in changes of the physical, chemical and/or biological properties of the organic molecules.[1] Therefore, the synthesis of fluorinated compounds has attracted increasing attention in recent years.[1,2] Among various fluorinated motifs that have been used to modify organic molecules, the *gem*-difluorovinyl group is of particular interest in both organic synthesis and biological chemistry owing to the electrophilic character of the difluorovinyl carbon endowed by the highly electronegative fluorine atoms.[3-8] On the one hand, difluoroalkenes have been often used as valuable precursors for the preparation of di- and trifluoromethyl compounds,[3,4] monofluoroalkenes,[5] monofluorinated heterocycles,[6] carboxylic acids and esters.[7] The difluoroalkene moiety has also been used as the isostere of carbonyl group in the design of protease inhibitors.[8]

In the past decades, many methods based on the deoxygenative *gem*-difluoroolefination of carbonyl compounds have been developed towards the synthesis of difluoroalkenes,[9] including Wittig-type reaction,[10a-10g] Horner-Wadsworth-Emmons reaction,[10h] Horner-Wittig reaction,[10i] Julia reaction[10j,10k] and Julia-Kocienski reaction.[10l-10n] Several protocols involving the *β*-fluorine elimination of trifluoromethylated intermediates have also been developed.[9,11] However, methods for the preparation of *gem*-difluoroalkenes using alkyl halides as substrates are less studied.[4b,12] In recent years, the phenylsulfonyl group-assisted nucleophilic fluoroalkylation chemistry has been developed, which provides efficient methods for the synthesis of organofluorine compounds.[13] In 2004, Prakash and coworkers reported a nucleophilic difluoroalkylation of primary alkyl iodides **2** and alkyl bromides with *in-situ* generated $PhSO_2CF_2^-$ from $PhSO_2CF_2H$ (**1**) in the presence of *t*-BuOK, giving the substitution products **3** in 37%—80% yields (Scheme 1A).[12a] Upon treatment with a base, the substitution products could be further transformed to difluoroalkenes **4** in moderate to good yields. However, 4 equiv. of alkyl halides were needed for the substitution step, and the alkyl bromides gave much lower yields than the alkyl iodides. In 2010, our group improved this substitution reaction by using primary alkyl halides as the limiting reactants and $PhSO_2CF_2TMS$ as the fluoroalkylation reagent in the presence of CsF and 15-crown-5, giving the substitution products **3** in 62%—79% yields.[4b] Although allyl bromide and benzyl bromides could smoothly undergo the reaction, the unactivated alkyl bromides were not good substrates. Under these conditions, the low thermal stability (life time) of $PhSO_2CF_2^-$ might be one of the reasons for the inefficiency of its reaction with unactivated alkyl bromides. In recent years, our group has found that sulfoximine functionality can serve as a good modulating group to achieve efficient nucleophilic fluoroalkylation reactions.[14-16] Our previous study on the ring-opening

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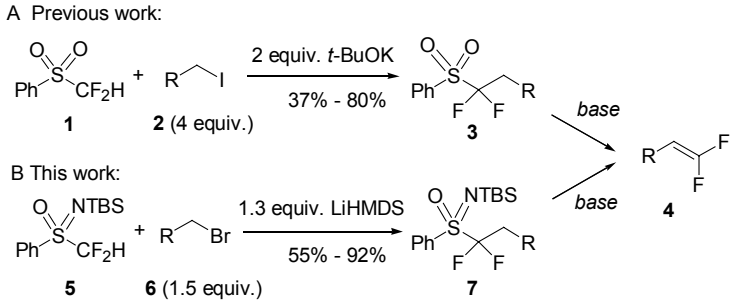
† Dedicated to Professor Chengye Yuan and Professor Li-Xin Dai on the occasion of their 90th birthdays.

Scheme 1 Nucleophilic difluoromethylation of alkyl halides and the application in the synthesis of *gem*-difluoroalkenes

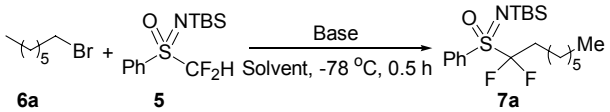


difluoromethylation of epoxides revealed that $PhSO(NTBS)CF_2^-$ possessed higher stability and/or nucleophilicity towards the epoxides than the corresponding $PhSO_2CF_2^-$.[15c] Herein, we disclose an efficient nucleophilic fluoroalkylation of unactivated alkyl bromides **6** with difluoromethyl sulfoximine $PhSO(NTBS)CF_2H$ (**5**) and its application in the synthesis of *gem*-difluoroalkenes (Scheme 1B).

Results and Discussion

The sulfoximine reagent $PhSO(NTBS)CF_2H$ (**5**) was prepared according to the reported procedure.[15c] At the outset, we chose 1-bromoheptane (**6a**) as the model substrate to test the possibility of its substitution reaction with sulfoximine **5**, and the results are summarized in Table 1. Normally, a base was added to the mixture of **5** and **6a** in a solvent at −78 ℃; after 0.5 h, the reaction was quenched with saturated aqueous NH_4Cl. When potassium hexamethyldisilazide (KHMDS) was used as the base, THF as the solvent, and the ratio of **6a**/**5**/KHMDS was 1.3/1/1.3, less than 10% yield of **7a** was given, and most of **5** decomposed (Table 1, Entry 1). When the base was changed to sodium hexamethyldisilazide (NaHMDS), only trace amount of **7a** was afforded (Table 1, Entry 2). To our delight, the addition of hexamethylphosphoramide (HMPA) as the co-solvent

Table 1 Optimization of the reaction conditions



Entry	**6a**/**5**/Base	Base	Solvent	Yield[a]/%
1	1.3/1/1.3	KHMDS	THF	＜10
2	1.3/1/1.3	NaHMDS	THF	trace
3	1.3/1/1.3	LiHMDS	THF	0
4	1.3/1/1.3	LiHMDS	THF/HMPA (*V*/*V*＝5/1)	98 (87)[b]
5	1.3/1/1.2	LiHMDS	THF/HMPA (*V*/*V*＝5/1)	93
6	1.5/1/1.3	LiHMDS	THF/HMPA (*V*/*V*＝5/1)	100 (90)[b]

[a] Yield was determined by ^{19}F NMR. [b] Yield in the parentheses refers to the isolated yield.

can promote the reaction, which led to the desired product **7a** in 87% isolated yield when lithium hexamethyldisilazide (LiHMDS) was used as the base. Further investigation of the ratio of the reactants showed that, when the ratio of **6a**/**5**/LiHMDS was 1.5/1/1.3, an isolated yield of 90% was achieved (Table 1, Entries 4—6).

With the optimized reaction conditions in hand, we examined the substrate scope of the nucleophilic fluoroalkylation of alkyl halides with $PhSO(NTBS)CF_2H$ (**5**), with the results being shown in Table 2. It was found that the reaction proceeded well with sterically less-hindered primary alkyl bromides, giving corresponding substitution products in 87%—92% yields (Table 2, Entries 1—7). Primary alkyl iodides were also amenable to this reaction. For example, when (3-iodopropyl)benzene (**2a**) was used as the substrate, product **7h** was given in 94% yield (Table 2, Entry 8). It is worth noting that the reaction was sensitive to the steric hindrance of the alkyl halides. When 1-bromo-2-methylpropane (**6i**) was subjected to the reaction conditions, product **4i** was obtained in only 54% yield (Table 2, Entry 9). When a secondary alkyl halide, such as 2-iodopropane (**2b**), was used as the substrate, the nucleophilic difluoromethylation product was given in less than 2% yield (Table 2, Entry 10).

β-Elimination of the sulfonyl group of alkyl substituted difluoromethyl sulfones has been demonstrated to be an efficient method for the synthesis of *gem*-difluoroalkenes.[4b,12a] Although the electron-withdrawing ability of PhSO(NTBS) group is weaker than $PhSO_2$ group, the *β*-elimination of the sulfonimidoyl group strategy is found to be feasible for the synthesis of *gem*-difluoroalkenes. When compound **7h** was treated with LiHMDS in DMF at 0 ℃ for 0.5 h, *gem*-difluoroalkene **4h** was obtained in 73% yield (Scheme 2).

In light of the fact that the *gem*-difluoroalkenes can be synthesized from the current reactions of unactivated alkyl bromides with $PhSO(NTBS)CF_2H$ (**5**), it is not difficult to realize that benzylic bromides can also be used to synthesize *gem*-difluoroalkenes. It was found that the synthesis of *gem*-difluoroalkenes with benzylic bromides and **5** could be carried out at −78 ℃ in one pot. After treating 2-(bromomethyl)naphthalene (**8**) and the sulfoximine reagent **5** with 2.1 equiv. of LiHMDS as

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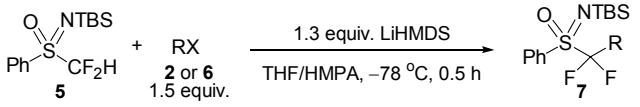
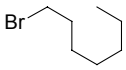
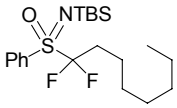
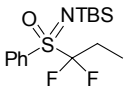
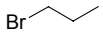
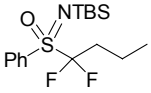
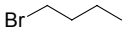
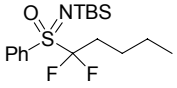
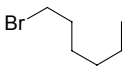
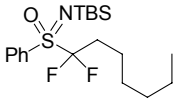
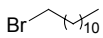
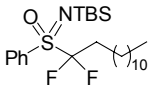
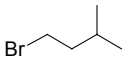
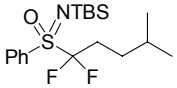
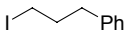
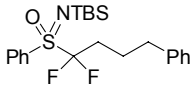
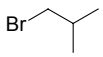
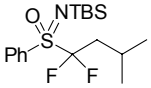
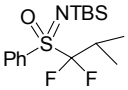
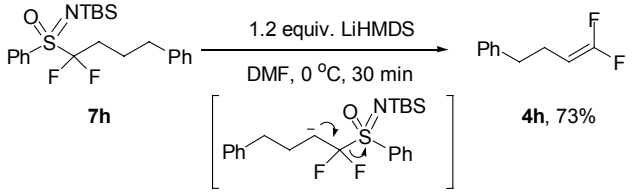
Table 2 Nucleophilic difluoromethylation of alkyl halides with $PhSO(NTBS)CF_2H$ (**5**)



Entry	RX		Product		Yield[a]/%
1		**6a**		**7a**	90
2		**6b**		**7b**	92
3		**6c**		**7c**	89
4		**6d**		**7d**	90
5		**6e**		**7e**	91
6		**6e**		**7f**	88
7		**6g**		**7g**	87
8		**2a**		**7h**	94
9		**6i**		**7i**	54
10		**2b**		**7j**	$<2^b$

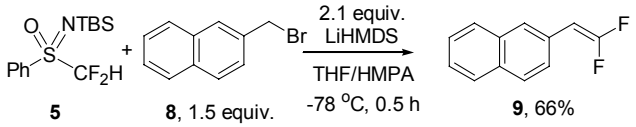
[a] Isolated yield. [b] Yield was determined by ^{19}F NMR with $PhCF_3$ as the internal standard.

Scheme 2 Preparation of *gem*-difluoroalkene **4h** from compound **7h** via *β*-elimination of sulfonimidoyl group



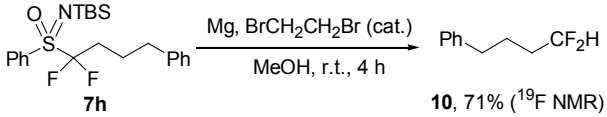
base in THF/HMPA at −78 ℃ for 0.5 h, difluoroalkene **9** was isolated in 66% yield (Scheme 3).

Scheme 3 Preparation of *gem*-difluoroalkene **9** from difluoromethyl sulfoximine **5** and 2-(bromomethyl)naphthalene (**8**) in one-pot



It is worth noting that the sulfonimidoyl group of compound **4h** could also be reductively removed under the $Mg/BrCH_2CH_2Br$ (cat.)/MeOH conditions, giving the difluoromethyl alkane **10** in 71% yield, according to the ^{19}F NMR determination (Scheme 4).

Scheme 4 Synthesis of difluoromethyl alkane **10** via reductive desulfonimidoylation of compound **7h**



Conclusions

In conclusion, we have successfully developed an efficient nucleophilic fluoroalkylation of unactivated primary alkyl bromides with $PhSO(NTBS)CF_2H$ (**5**), giving the substitution products in moderate to good yields. Compared to the previously reported difluoro(phenylsulfonyl)methylation of alkyl iodides,[4b,12a] this reaction possesses two advantages: (1) unactivated alkyl bromides served as the substrates; (2) only slightly excess of alkyl bromides were needed to achieve good yields. Moreover, the so-obtained substitution products could be easily transformed to *gem*-difluoroalkenes and difluoromethyl alkanes via *β*-elimination of sulfonimidoyl group and reductive desulfonimidoylation, respectively, demonstrating the synthetic potential of this difluoro(phenylsulfonimidoyl)methylation protocol.

Experimental

^1H NMR spectra were recorded in $CDCl_3$ on a BRUKER AM-300 spectrometer (300 MHz) or Varian 400-MR spectrometer (400 MHz) with TMS as internal standard. ^{19}F NMR spectra were taken on a BRUKER AM-300 spectrometer (282 MHz) or Varian 400-MR spectrometer (376 MHz) using $CFCl_3$ as external standard. ^{13}C NMR spectra were recorded in $CDCl_3$ on a BRUKER AM-300 spectrometer (75 MHz) or Varian 400-MR spectrometer (100 MHz) with TMS as internal standard. IR spectra were obtained with a Nicolet iN 10MX spectrometer. Mass spectra were obtained on a mass spectrometer. All the solvents were redistilled before use.

General procedure for nucleophilic difluoromethylation of alkyl halides with PhSO(NTBS)CF_2H (5)

Under N_2, to a solution of difluoromethyl sulfoximine (**5**, 122 mg) and 1-bromoheptane (**6a**, 94 μL, 0.6 mmol) in dried THF (4 mL) and dried HMPA (0.8 mL), was added LiHMDS (1 mol/L in THF, 0.52 mL, 0.52 mmol) at −78 ℃. After 30 min, the reaction was quenched by adding an excess of saturated NH_4Cl (aq.), followed by extraction with ethyl acetate. The organic phase was washed with brine and then dried over anhydrous $MgSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using petroleum ether as eluent to give product **7a** (145 mg, 90%).

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluorooctyl-*S*-phenylsulfoximine (7a)** Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.97 (d, J=7.7 Hz, 2H), 7.64 (t, J=7.3 Hz, 1H), 7.52 (dd, J=7.4 Hz, 2H), 2.19 (ddd, J=22.4, 15.6, 7.9 Hz, 2H), 1.73−1.47 (m, 2H), 1.45−1.17 (m, 8H), 0.99−0.80 (m, 12H), 0.12 (s, 6H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −104.78 (ddd, J=219.4, 23.4, 14.8 Hz, 1F), −106.79 (ddd, J=219.5, 24.7, 13.5 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.64, 133.41, 130.14, 128.65, 125.00 (t, J=287.0 Hz), 31.53, 29.17, 28.98 (t, J=21.0 Hz), 28.87, 25.82, 22.54, 21.01 (t, J=3.1 Hz), 18.02, 14.01, −2.49, −2.58; IR (film) v: 3069, 2955, 2929, 2857, 1584, 1471, 1347, 1252, 1171, 1089, 829, 777, 688, 593 cm^{-1}; MS (ESI) m/z: 404.1 (M+H$^+$); HRMS (ESI) m/z calcd for $C_{20}H_{35}F_2NNaOSSi$ (M+Na$^+$) 426.2069, found 426.2066.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluoropropyl-*S*-phenylsulfoximine (7b)** Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.96 (d, J=7.6 Hz, 2H), 7.64 (t, J=7.4 Hz, 1H), 7.54 (t, J=7.5 Hz, 2H), 2.46−1.90 (m, 2H), 1.10 (t, J=7.5 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 6H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −106.56 (ddd, J=219.3, 22.6, 13.5 Hz), −108.69 (ddd, J=219.4, 23.0, 13.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.69, 133.43, 130.12, 128.67, 125.01 (t, J=286.9 Hz), 25.81, 22.82 (t, J=21.7 Hz), 18.00, 5.35 (t, J=4.5 Hz), −2.50, −2.61; IR (film) v: 3069, 2954, 2929, 2857, 1584, 1464, 1347, 1253, 1172, 1080, 829, 778, 688, 564 cm^{-1}; MS (ESI) m/z: 334.0 (M+H$^+$); HRMS (ESI) m/z calcd for $C_{15}H_{25}F_2NNaOSSi$ (M+Na$^+$) 356.1286, found 356.1295.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluorobutyl-*S*-phenylsulfoximine (7c)** Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J=7.3 Hz, 2H), 7.63 (t, J=7.4 Hz, 1H), 7.53 (t, J=7.6 Hz, 2H), 2.28−2.00 (m, 2H), 1.68−1.49 (m, 2H), 0.99 (t, J=7.4 Hz, 3H), 0.93 (s, 9H), 0.11 (d, J=0.8 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −104.00−−104.85 (m), −106.33 (ddd, J=219.7, 23.2, 14.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.64, 133.41, 130.14, 128.66, 124.91 (t, J=287.1 Hz), 30.94 (t, J=20.9 Hz), 25.81, 18.01, 14.75 (t, J=3.6 Hz), 13.83, −2.49, −2.59; IR (film) v: 3070, 2956, 2930, 2857, 1645, 1471, 1347, 1252, 1171, 1087, 828, 777, 688, 592 cm^{-1}; MS (ESI) m/z: 348.1 (M+H$^+$); HRMS (ESI) m/z calcd for $C_{16}H_{27}F_2NNaOSSi$ (M+Na$^+$) 370.1443, found 370.1450.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluoropentyl-*S*-phenylsulfoximine (7d)** Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J=7.5 Hz, 2H), 7.63 (t, J=7.4 Hz, 1H), 7.54 (t, J=7.6 Hz, 2H), 2.40−1.99 (m, 2H), 1.69−1.48 (m, 2H), 1.47−1.28 (m, 2H), 0.99−0.88 (m, 12H), 0.11 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −104.45 (ddd, J=219.1, 23.3, 13.4 Hz), −106.39 (ddd, J=219.2, 23.9, 13.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.62, 133.42, 130.15, 128.66, 125.01 (t, J=286.9 Hz), 28.67 (t, J=20.9 Hz), 25.81, 23.05 (t, J=3.1 Hz), 22.37, 18.02, 13.68, −2.48, −2.58; IR (film) v: 3069, 2958, 2931, 2858, 1584, 1471, 1345, 1252, 1172, 1087, 829, 777, 688, 592 cm^{-1}; MS (ESI) m/z: 362.1 (M+H$^+$); HRMS (ESI) m/z calcd for $C_{17}H_{29}F_2NNaOSSi$ (M+Na$^+$) 384.1599, found 384.1608.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluoroheptyl-*S*-phenylsulfoximine (7e)** Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J=7.5 Hz, 2H), 7.63 (t, J=7.4 Hz, 1H), 7.53 (t, J=7.6 Hz, 2H), 2.30−2.07 (m, 2H), 1.66−1.51 (m, 2H), 1.41−1.20 (m, 6H), 0.93 (s, 9H), 0.88 (t, J=6.8 Hz, 3H), 0.12 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −104.42 (ddd, J=219.1, 23.2, 13.4 Hz), −106.35 (ddd, J=219.2, 23.9, 13.9 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.65, 133.42, 130.15, 128.69, 125.01 (t, J=287.0 Hz), 31.39, 29.00 (t, J=21.0 Hz), 28.89, 25.83, 22.38, 20.99 (t, J=3.1 Hz), 18.03, 13.97, −2.47, −2.57; IR (film) v: 3069, 2956, 2857, 1584, 1471, 1346, 1252, 1171, 829, 777, 688, 593 cm^{-1}; MS (ESI) m/z: 348.1 (M+H$^+$); HRMS (ESI) m/z calcd for $C_{19}H_{33}F_2NNaOSSi$ (M+Na$^+$) 412.1912, found 412.1917.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluorotridecyl-*S*-phenylsulfoximine (7f)** Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.96 (d, J=7.5 Hz, 2H), 7.63 (t, J=7.3 Hz, 1H), 7.53 (t, J=7.5 Hz, 2H), 2.37−1.95 (m, 2H), 1.72−1.47 (m, 2H), 1.43−1.19 (m, 18H), 0.93 (s, 9H), 0.88 (t, J=6.6 Hz, 3H), 0.11 (s, 6H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: −104.37 (ddd, J=219.2, 23.1, 13.6 Hz), −106.38 (ddd, J=219.0, 23.7, 14.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.65, 133.40, 130.14, 128.65, 125.00 (t, J=287.1 Hz), 31.89, 29.59, 29.53, 29.35, 29.32, 29.22, 29.20, 28.99 (t, J=20.9 Hz), 28.78, 25.82, 22.66, 21.02 (t, J=3.0 Hz), 18.01, 14.10, −2.48, −2.58; IR (film) v: 3069, 2927, 2855, 1470, 1447, 1346, 1170, 1024, 828, 688, 592 cm^{-1}; MS (ESI) m/z: 474.2 (M+H$^+$); HRMS (ESI) m/z calcd for $C_{25}H_{45}F_2NnaOSSi$ (M+Na$^+$) 496.2857, found 496.2869.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluoro-4-methylpentyl-*S*-phenylsulfoximine (7g)** Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J=7.5 Hz, 2H), 7.63 (t, J=7.4 Hz, 1H), 7.53 (t, J=7.6 Hz, 2H), 2.30−2.06 (m, 2H), 1.70−1.54 (m, 1H), 1.53−1.36 (m, 2H), 0.94 (s, 9H), 0.91 (d, J=6.6 Hz, 6H), 0.12 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ: −104.45 (ddd, J=218.6, 23.0, 13.2 Hz), −106.50 (ddd, J=218.6, 23.7, 13.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 137.63, 133.41, 130.14,

128.66, 125.01 (t, J=287.1 Hz), 28.68 (t, J=21.0 Hz), 25.81, 23.06 (t, J=3.0 Hz), 22.37, 18.02, 13.67, –2.49, –2.58; IR (film) ν: 3069, 2957, 2930, 2857, 1471, 1347, 1252, 1172, 1089, 828, 777, 688, 591 cm^{-1}; MS (ESI) *m/z*: 376.1 ($M+H^+$); HRMS (ESI) *m/z* calcd for $C_{18}H_{31}F_2NNaOSSi$ ($M+Na^+$) 398.1756, found 398.1757.

***N-tert*-Butyldimethylsilyl-*S*-1,1-difluoro-4-phenylbutyl-*S*-phenylsulfoximine (7h)** Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.93 (d, J=7.7 Hz, 2H), 7.63 (t, J=7.3 Hz, 1H), 7.53 (t, J=7.5 Hz, 2H), 7.34–7.09 (m, 5H), 2.76–2.52 (m, 2H), 2.35–2.05 (m, 2H), 2.05–1.72 (m, 2H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: –104.53 (ddd, J= 219.4, 25.7, 11.9 Hz, 1F); –106.59 (ddd, J=219.9, 25.3, 12.2 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 140.85, 137.51, 133.47, 130.16, 128.69, 128.47, 128.38, 126.12, 124.91 (t, J=287.3 Hz), 35.19, 28.43 (t, J=21.0 Hz), 25.82, 22.83 (t, J=2.9 Hz), 18.00, –2.49, –2.61; IR (film) ν: 3065, 2954, 2928, 2856, 1471, 1346, 1252, 1169, 1093, 828, 777, 688, 562 cm^{-1}; MS (ESI) *m/z*: 424.0 ($M+H^+$); HRMS (ESI) *m/z* calcd for $C_{22}H_{32}F_2NOSSi$ ($M+Na^+$) 424.1936, found 424.1920.

Procedure for preparation of *gem*-difluoroalkene 4h

Under N_2, to a solution of compound **4h** (212 mg, 0.5 mmol) in dried DMF (5 mL), was added LiHMDS (1 mol/L in THF, 0.6 mL, 0.6 mmol) at 0 ℃. After 30 min the reaction was quenched by adding an excess of saturated NH_4Cl (aq.), followed by extraction with ethyl acetate. The organic phase was washed with brine and then dried over anhydrous $NaSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using hexane as eluent to give colorless oil **4h** (61 mg, 73% yield).

(4,4-Difluorobut-3-en-1-yl)benzene (4h)[10l] Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.30 (t, J=7.4 Hz, 2H), 7.23–7.17 (m, 3H), 4.16 (dtd, J=25.4, 7.8, 2.3 Hz, 1H), 2.69 (t, J=7.6 Hz, 2H), 2.30 (q, J=7.7 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: –91.04 (ddt, J= 47.4, 25.6, 1.7 Hz); MS (EI) *m/z* (%): 168 (M^+, 17.8), 91 ($M^+-C_6H_5$, 100).

Procedure for preparation of *gem*-difluoroalkene 9 from difluoromethyl sulfoximine 5 and 2-(bromomethyl)naphthalene (8) in one-pot

Under N_2, to a solution of difluoromethyl sulfoximine **5** (122 mg, 0.4 mmol) and 2-(bromomethyl)naphthalene **8** (133 mg, 0.6 mmol, 1.5 equiv.) in dried THF (4 mL) and dried HMPA (0.8 mL), was added LiHMDS (1 mol/L in THF, 0.84 mL, 0.84 mmol, 2.1 equiv.) at –78 ℃. After 30 min, the reaction was quenched by adding an excess of saturated NH_4Cl (aq), followed by extraction with ethyl ether. The organic phase was washed with brine and then dried over anhydrous $NaSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the residue was subjected to silica gel column chromatography using hexane as eluent to give colorless oil **9** (50 mg, 66%).

2-(2,2-Difluorovinyl)naphthalene (9)[10l] White solid. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.85–7.68 (m, 4H), 7.52–7.43 (m, 3H), 5.42 (dd, J=26.2, 3.9 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: –81.86 (dd, J= 30.8, 26.2 Hz), –83.60 (dd, J=30.8, 3.9 Hz).

Procedure for reductive desulfoximination of compound 7h

To the mixture of Mg chips (360 mg, 15 mmol) in dry MeOH (2 mL), was added $BrCH_2CH_2Br$ (5 μL) at r.t. When the reaction gave off gas (about 3 min later), compound **7h** (423 mg, 1 mmol) and dry MeOH (6 mL) was added. The reaction was monitored by TLC. After compound **7h** was consumed, the yield of **10** was determined by ^{19}F NMR with $PhCF_3$ as the internal standard.

(4,4-Difluorobutyl)benzene (10)[17] ^{19}F NMR (282 MHz) δ: –116.18 (dt, J=57.0, 17.1 Hz).

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References

[1] (a) Kirsch, P. *Modern Fluoroorganic Chemistry*: *Synthesis*, *Reactivity*, *Applications*, 2nd Ed., Wiley-VCH, Weinheim, **2013**; (b) Uneyama, K. *Organofluorine Chemistry*, Blackwell, Oxford, **2006**; (c) Wang, J.; Liu, H. *Chin. J. Org. Chem.* **2011**, *31*, 1785 (in Chinese).

[2] For selected reviews, see: (a) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214; (b) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475; (c) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1; (d) Zhang, W.; Ni, C.; Hu, J. *Top. Curr. Chem.* **2012**, *308*, 25; (e) Ni, C.; Hu, J. *Synlett* **2011**, 770; (f) Hu, J.; Zhang, W.; Wang, F. *Chem. Commun.* **2009**, 7465; (g) Hu, J. *J. Fluorine Chem.* **2009**, *130*, 1130; (h) Prakash, G. K. S.; Hu, J. *Acc. Chem. Res.* **2007**, *40*, 921.

[3] Motherwell, W. B.; Tozer, M. J.; Ross, B. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1437.

[4] (a) Nguyen, B. V.; Burton, D. J. *J. Org. Chem.* **1997**, *62*, 7758; (b) Zhu, L.; Li, Y.; Zhao, Y.; Hu, J. *Tetrahedron Lett.* **2010**, *51*, 6150; (c) Gao, B.; Zhao, Y.; Ni, C.; Hu, J. *Org. Lett.* **2014**, *16*, 102.

[5] (a) Hayashi, S.-I.; Nakai, T.; Ichikawa, N.; Burton, D. J.; Naae, D. G.; Kesling, H. S. *Chem. Lett.* **1979**, *8*, 983; (b) For a recent review, see: Landelle, G.; Bergeron, M.; Turcotte-Savard, M.-O.; Paquin, J.-F. *Chem. Soc. Rev.* **2011**, *40*, 2867.

[6] (a) Ichikawa, J.; Wada, Y.; Okauchi, T.; Minami, T. *Chem. Commun.* **1997**, 1537; (b) Yokota, M.; Fujita, D.; Ichikawa, J. *Org. Lett.* **2007**, *9*, 4639.

[7] (a) Hayashi, S.-i.; Nakai, T.; Ishikawa, N. *Chem. Lett.* **1980**, *9*, 651; (b) Ichikawa, J.; Yokota, M.; Kudo, T.; Umezaki, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 4870.

[8] (a) Altenburger, J.-M.; Lassalle, G. Y.; Matrougui, M.; Galtier, D.; Jetha, J.-C.; Bocskei, Z.; Berry, C. N.; Lunven, C.; Lorrain, J.; Herault, J.-P.; Schaeffer, P.; O'Connor, S. E.; Herbert, J.-M. *Bioorg.*

Med. *Chem*. **2004**, *12*, 1713; (b) Weintraub, P. M.; Holland, A. K.; Gates, C. A.; Moore, W. R.; Resvick, R. J.; Bey, P.; Peet, N. P. *Bioorg*. *Med*. *Chem*. **2003**, *11*, 427.

[9] For reviews, see: (a) Chelucci, G. *Chem*. *Rev*. **2012**, *112*, 1344; (b) Liu, Y.; Deng, M.; Zhang, Z.; Ding, X.; Dai, Z.; Guan, J. *Chin*. *J*. *Org*. *Chem*. **2012**, *32*, 661 (in Chinese).

[10] For examples, see: (a) Fuqua, S. A.; Duncan, W. G.; Silverstein, R. M. *Tetrahedron Lett*. **1964**, 1461; (b) Burton, D. J.; Yang, Z. Y.; Qiu, W. M. *Chem*. *Rev*. **1996**, *96*, 1641; (c) Nowak, I.; Robins, M. J. *Org*. *Lett*. **2005**, *7*, 721; (d) Wang, F.; Li, L.; Ni, C.; Hu, J. *Beilstein J*. *Org*. *Chem*. **2014**, *10*, 344; (e) Zheng, J.; Cai, J.; Lin, J.-H.; Guo, Y.; Xiao, J.-C. *Chem*. *Commun*. **2013**, *49*, 7513; (f) Zheng, J.; Lin, J.-H.; Cai, J.; Xiao, J.-C. *Chem*.-*Eur*. *J*. **2013**, *19*, 15261; (g) Li, Q.; Lin, J.-H.; Deng, Z.-Y.; Zheng, J.; Cai, J.; Xiao, J.-C. *J*. *Fluorine Chem*. **2014**, *163*, 38; (h) Obayashi, M.; Ito, E.; Matsui, K.; Kondo, K. *Tetrahedron Lett*. **1982**, *23*, 2323; (i) Piettre, S. R.; Cabanas, L. *Tetrahedron Lett*. **1996**, *37*, 5881; (j) Edwards, M. L.; Stemerick, D. M.; Jarvi, E. T.; Matthews, D. P.; McCarthy, J. R. *Tetrahedron Lett*. **1990**, *31*, 5571; (k) Prakash, G. K. S.; Wang, Y.; Hu, J.; Olah, G. A. *J*. *Fluorine Chem*. **2005**, *126*, 1361; (l) Zhao, Y.; Huang, W.; Zhu, L.; Hu, J. *Org*. *Lett*. **2010**, *12*, 1444; (m) Wang, X.-P.; Lin, J.-H.; Xiao, J.-F.; Zheng, X. *Eur*. *J*. *Org*. *Chem*. **2014**, 928; (n) Gao, B.; Zhao, Y.; Hu, M.; Ni, C.; Hu, J. *Chem*. *Eur*. *J*. **2014**, *20*, 7803.

[11] (a) Cox, L. R.; DeBoos, G. A.; Fullbrook, J. J.; Percy, J. M.; Spencer, N. S.; Tolley, M. *Org*. *Lett*. **2003**, *5*, 337; (b) Ichikawa, J.; Fukui, H.; Ishibashi, Y. *J*. *Org*. *Chem*. **2003**, *68*, 7800; (c) Ichikawa, J.; Ishibashi, Y.; Fukui, H. *Tetrahedron Lett*. **2003**, *44*, 707; (d) Raghavanpillai, A.; Burton, D. J. *J*. *Org*. *Chem*. **2005**, *71*, 194; (e) Hu, M.; He, Z.; Gao, B.; Li, L.; Ni, C.; Hu, J. *J*. *Am*. *Chem*. *Soc*. **2013**, *135*, 17302.

[12] (a) Prakash, G. K. S.; Hu, J.; Wang, Y.; Olah, G. A. *Angew*. *Chem*., *Int*. *Ed*. **2004**, *43*, 5203; (b) Zibinsky, M.; Beier, P.; Prakash, G. K. S. *Chem*. *Sust*. *Dev*. **2008**, *16*, 69.

[13] For reviews, see: References 2d—2h; for selected examples, see: (a) Li, Y.; Hu, J. *Angew*. *Chem*., *Int*. *Ed*. **2005**, *44*, 5882; (b) Fukuzumi, T.; Shibata, N.; Sugiura, M.; Yasui, H.; Nakamura, S.; Toru, T. *Angew*. *Chem*., *Int*. *Ed*. **2006**, *45*, 4973; (c) Prakash, G. K. S.; Chacko, S.; Alconcel, S.; Stewart, T.; Mathew, T.; Olah, G. A. *Angew*. *Chem*., *Int*. *Ed*. **2007**, *46*, 4933; (d) Shen, X.; Zhang, L.; Zhao, Y.; Zhu, L.; Li, G.; Hu, J. *Angew*. *Chem*., *Int*. *Ed*. **2011**, *50*, 2588; (e) Shen, X.; Ni, C.; Hu, J. *Helv*. *Chim*. *Acta* **2012**, *95*, 2043; (f) Shen, X.; Ni, C.; Hu, J. *Chin*. *J*. *Chem*. **2013**, *31*, 878.

[14] For reviews on fluorinated sulfoximines as fluoroalkylation reagents, see: (a) Shen, X.; Hu, J. *Eur*. *J*. *Org*. *Chem*. **2014**, *2014*, 4437; (b) Bizet, V.; Kowalczyk, R.; Bolm, C. *Chem*. *Soc*. *Rev*. **2014**, *43*, 2426.

[15] For nucleophilic fluoroalkylation reactions using sulfoximine reagents, see: (a) Shen, X.; Zhang, W.; Zhang, L.; Luo, T.; Wan, X.; Gu, Y.; Hu, J. *Angew*. *Chem*., *Int*. *Ed*. **2012**, *51*, 6966; (b) Shen, X.; Zhang, W.; Ni, C.; Gu, Y.; Hu, J. *J*. *Am*. *Chem*. *Soc*. **2012**, *134*, 16999; (c) Shen, X.; Liu, Q.; Luo, T.; Hu, J. *Chem*. *Eur*. *J*. **2014**, *20*, 6795; (d) Shen, X.; Miao, W.; Ni, C.; Hu, J. *Angew*. *Chem*., *Int*. *Ed*. **2014**, *53*, 775; (e) Shen, X.; Zhou, M.; Ni, C.; Zhang, W.; Hu, J. *Chem*. *Sci*. **2014**, *5*, 117; (f) Zhang, W.; Hu, J. *Adv*. *Synth*. *Catal*. **2010**, *352*, 2799; (g) Zhang, W.; Huang, W.; Hu, J. *Angew*. *Chem*., *Int*. *Ed*. **2009**, *48*, 9858; (h) Boys, M. L.; Collington, E. W.; Finch, H.; Swanson, S.; Whitehead, J. F. *Tetrahedron Lett*. **1988**, *29*, 3365.

[16] For electrophilic fluoroalkylation reactions with sulfoximine reagents, see: (a) Zhang, W.; Wang, F.; Hu, J. *Org*. *Lett*. **2009**, *11*, 2109; (b) Noritake, S.; Shibata, N.; Nakamura, S.; Toru, T.; Shiro, M. *Eur*. *J*. *Org*. *Chem*. **2008**, 3465; (c) Urban, C.; Cadoret, F.; Blazejewski, J.-C.; Magnier, E. *Eur*. *J*. *Org*. *Chem*. **2011**, 4862; (d) Yang, Y.-D.; Lu, X.; Liu, G.; Tokunaga, E.; Tsuzuki, S.; Shibata, N. *ChemistryOpen* **2012**, *1*, 221.

[17] Gonzalez, J.; Foti, C. J.; Elsheimer, S. *J*. *Org*. *Chem*. **1991**, *56*, 4322.

(Zhao, X.)

