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Nucleophilic tetrafluoroethylation of carbonyl compounds with fluorinated sulfones

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ABSTRACT

Global interest in the "CF_2CF_2" building blocks (tetrafluoroethylene, tetrafluoroethyl) is still rather marginal. One of the main reasons is the lack of efficient and selective tetrafluoroethylation reagents. In this context, we present here three new reagents ($PhSO_2CF_2CF_2R$, R = $SiMe_3$, $SiEt_3$ and H) capable of nucleophilic addition to carbonyl compounds, thus affording rare alcohols containing the CF_2CF_2 motif. The experimental observations are complemented with a brief computational study which confirmed that the reactivity of the nucleophilic reagents is strongly dependent on electronic properties of substituents on both ends of the CF_2CF_2 group.

1. Introduction

Selective and efficient methods for the synthesis of organofluorine compounds are nowadays subject of intensive research due to the increasing popularity of fluorine especially in the pharmaceutical [1] and agrochemical [2] sectors.

The trifluoromethyl group is one of the most frequently used fluoroalkyl substituents. Its attractiveness is based on structural simplicity and the unique combination of physicochemical properties together with availability of reagents, which can be formally nucleophilic [3], radical [4] or electrophilic [5]. Similarly, there are a number of selective and efficient routes for the introduction of fluoromethyl, fluoromethylene, difluoromethyl, difluoromethylene and $(CF_2)_n$ ($n > 2$) groups [6]. This is in a distinct contrast with the tetrafluoroethyl (CF_2CF_2H) and tetrafluoroethylene (CF_2CF_2) building blocks. Until recently, the only CF_2CF_2 fluoroalkylation reagents have been the 1,2-dibromo-1,1,2,2-tetrafluoroethane ($BrCF_2CF_2Br$) and other 1,2-dihalotetrafluoroethanes, which can add to alkenes and alkynes under radical conditions [7]. However, organometallic compounds derived from these halides undergo facile β-halogen elimination and their application is thus limited [8].

In 2011, we reported the use of trimethyl(1,1,2,2-tetrafluoro-2-phenylsulfanylethyl)silane ($PhSCF_2CF_2SiMe_3$, **1**) as a tandem radical and anion CF_2CF_2 synthon [9]. In the presence of catalytic amounts of fluoride initiator, the silicon-capped end of the reagent underwent activation and nucleophilic addition to carbonyl compounds, furnishing alcohols containing the $PhSCF_2CF_2$ group. Upon transforming the alcohol group to an allyl ether, the corresponding tetrafluoro-tetrahydropyran derivatives were prepared by the ring closure *via* radical additions of the fluoroalkyl groups to the allyl substituents. The sulfanyl moiety could also be removed, giving the terminal tetrafluoroethyl group. We followed up by showing the nucleophilic addition of **1** to cyclic imides employing the same concept as described above with carbonyl compounds [10]. In 2013, we used $PhSCF_2CF_2Br$ as a radical synthon with the advantage of controlled reactivity of both ends of the reagent [11].

We present here the trimethyl(1,1,2,2-tetrafluoro-2-phenylsulfonylethyl)silane ($PhSO_2CF_2CF_2SiMe_3$, **2**), a reagent that complements the ones described above potentially being a dinucleophilic synthon. Very recently, we have reported this reagent's capability of adding to enamines, thus providing CF_2CF_2-containing amines [12]. This work represents an extension of substrate scope toward carbonyl compounds.

2. Results and discussion

Compound **2** was synthesized directly from **1** (Scheme 1) by the oxidation with 3-chloroperoxybenzoic acid (mCPBA).

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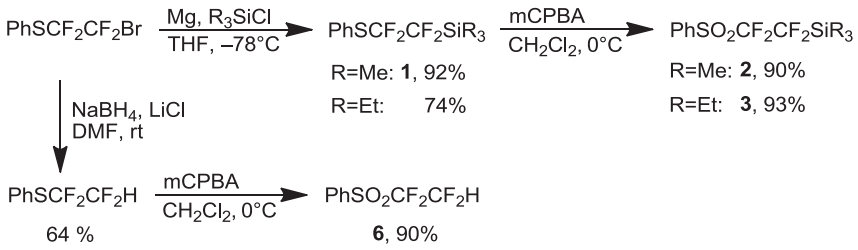


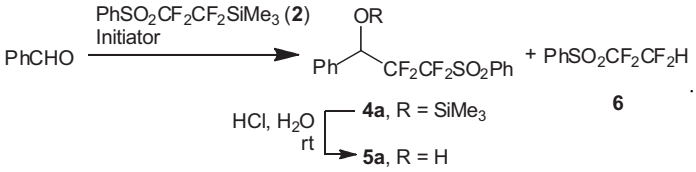
Scheme 1. Synthesis of reagents **1**, **2**, **3** and **6**.

Inspired by the reactions of **1** with aldehydes and ketones [9], we chose benzaldehyde as a model electrophilic substrate and tested different initiators, mostly containing the fluoride ion (Table 1). However, while the catalytic amount of tetrabutylammonium difluorotriphenylsilicate (TBAT) could activate **1** [9], no reaction was observed with reagent **2** under such conditions (Table 1, Entry 1).

Similarly, tetramethylammonium fluoride (TMAF) and cesium carbonate could not promote the desired reaction. Only potassium fluoride and cesium fluoride at substoichiometric amounts acted as competent initiators furnishing the trimethylsilyl ether **4a** (Entry 10), which was *in situ* transformed to alcohol **5a** upon treatment with acid.

Various aromatic and aliphatic aldehydes were tested under these conditions (Table 2), all giving moderate yields of alcohols **5**. The inferior reactivity of 1-naphthaldehyde compared to 2-naphthaldehyde (Entries 4 and 5) was probably caused by the proximity of the carbonyl group and the aromatic hydrogen in the *peri*-position, which has been reported to deteriorate the reactivity of functional groups in position 1 [13]. Simple aromatic and

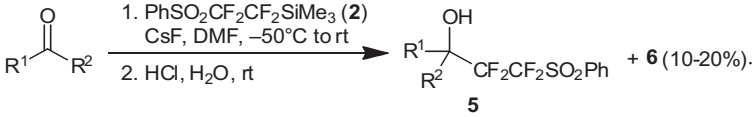
Table 1
Screening reaction conditions for nucleophilic addition of **2** to benzaldehyde.[a]



Entry	Initiator (eq.)	Solvent	Temp. (°C)	Time (h)	(4a + 5a):6[b]
1	TBAT (0.2)	THF	rt	15	0:100
2	TMAF (1)	DMF	rt	1.5	6:94
3	Cs_2CO_3 (1)	DMF	rt	2.5	0:100
4	KF (1)	THF	rt	15	16:84
5	KF (0.5)	DMF	–78 to rt	20	38:62
6	CsF (2)	THF	rt	15	65:35
7	CsF (1)	THF	rt	1	20:80
8	CsF (0.5)	THF	rt	2	32:68
9	CsF (0.5)	DMF	rt	2	35:65
10	CsF (0.5)	DMF	–78 to–50	2.5	88:12
11	CsF (0.1)	DMF	–78 to–50	15	66:34

[a] Reactions were performed with **2** (0.4 mmol), PhCHO (0.8 mmol, 2 eq.) in 5 mL of solvent.
[b] Determined by GCMS.

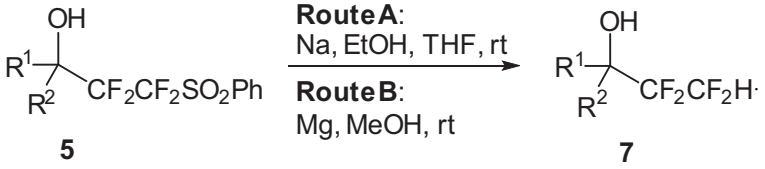
Table 2
Synthesis of alcohols **5** by fluoride-initiated nucleophilic addition of **2** to carbonyl compounds.[a]



Entry	R^1	R^2	**5**, Yield (%)[b]
1	Ph	H	**5a**, 72
2	4-ClC_6H_4	H	**5b**, 56
3	4-BrC_6H_4	H	**5c**, 71
4	4-$MeOC_6H_4$	H	**5d**, 51
5	1-Naphthyl	H	**5e**, 40
6	2-Naphthyl	H	**5f**, 56
7	*n*-C_6H_{13}	H	**5g**, 51
8	$PhCH_2CH_2$	H	**5h**, 51
9	Ph	CF_3	**5i**, 48

[a] Reactions were performed with **2** (2.5 mmol), carbonyl compound (5 mmol, 2 eq.) and CsF (1.25 mmol, 0.5 eq.) in DMF (20 mL), –50 °C to rt, 1–4 h, followed by addition of 1 M HCl (10 mL), rt, 0.5 h.
[b] Isolated yield.

Table 3
Synthesis of alcohols **7** by reductive desulfonylation of compounds **5** *via* Routes A[a] or B.[b]



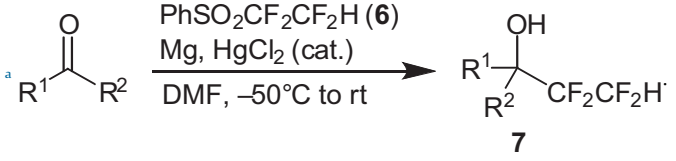
Entry	5	R^1	R^2	Route	7, Yield (%)[c]
1	**5a**	Ph	H	B	**7a**, 69
2	**5b**	4-ClC_6H_4	H	A	**7b**, 12[d]
3	**5b**	4-ClC_6H_4	H	B	**7b**, 87
4	**5c**	4-BrC_6H_4	H	B	**7c**, 57[e]
5	**5d**	4-$MeOC_6H_4$	H	A	**7d**, 73[d]
6	**5e**	1-Naphthyl	H	A	**7e**, 33
7	**5f**	2-Naphthyl	H	B	**7f**, 88
8	**5g**	*n*-C_6H_{13}	H	A	**7g**, 70[d]
9	**5g**	*n*-C_6H_{13}	H	B	**7g**, 83[d], 74
10	**5h**	$PhCH_2CH_2$	H	B	**7h**, 86
11	**5i**	Ph	CF_3	A	**7i**, 58[d]

[a] Reactions were performed with **5** (0.5 mmol), Na (2.5 mmol, 5 eq.) and EtOH (2.5 mmol, 5 eq.) in THF (5 mL), rt, 2–16 h.
[b] Reactions were performed with **5** (0.75 mmol), Mg (16.5 mmol, 22 eq.) in MeOH (20 mL), rt, 2 h.
[c] Isolated yield unless stated otherwise.
[d] Determined by ^{19}F NMR using $PhCF_3$ as internal standard.
[e] In addition to **7c**, **7a** was formed in 26% yield.

aliphatic ketones (acetophenone and cyclohexanone) were unreactive, however, more electrophilic trifluoroacetophenone afforded product **5i** in moderate yield (Entry 9). $PhSO_2CF_2CF_2H$ (**6**) was formed *via* protodesilylation of **2** as a common side-product in these reactions in *ca* 10–20% yields. The desilylation of silyl ethers **4** to alcohols **5** (fully or partially) occurred prior to the addition of HCl, which is thought to be due to the high content of CsF.

Next, desulfonylation of adduct **5** to afford alcohols **7** containing the terminal CF_2CF_2H group was investigated (Table 3). Sodium metal in ethanol (Route A) gave only moderate yields and was incompatible with the chlorinated substrate **5b** (Entry 2). In contrast, magnesium metal in methanol (Route B) afforded desulfonylation products **7** in high yields even with **5b** (Entry 3). Only in the case of bromine-containing alcohol **5c**, **7a** was formed in 26% yield together with major product **7c** (Entry 4).

Table 4
Synthesis of alcohols **7** *via* reductive nucleophilic addition of **6** to carbonyl compounds.



Entry	R^1	R^2	7, Yield (%)[b]
1	Ph	H	**7a**, 57
2	4-ClC_6H_4	H	**7b**, 27
3	4-BrC_6H_4	H	**7c**, 20
4	4-$MeOC_6H_4$	H	**7d**, 77
5	1-Naphthyl	H	**7e**, 24
6	2-Naphthyl	H	**7f**, 80
7	*n*-C_6H_{13}	H	**7g**, 91
8	$PhCH_2CH_2$	H	**7h**, 74
9	Ph	CF_3	**7i**,–[c]

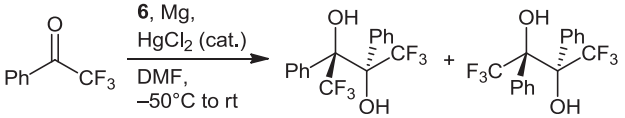
[a] Reactions were performed with **6** (1 mmol), carbonyl compound (2 mmol), Mg (3 mmol) and $HgCl_2$ (0.06 mmol) in DMF (5 mL), −50 °C to rt, 4–8 h.
[b] Isolated yield.
[c] Pinacol coupling proceeded instead of expected formation of **7i**.

Considering the potentially high attractiveness of tetrafluoroethyl-containing secondary alcohols **7** as analogs of α-trifluoromethylated alcohols, we aimed at developing a direct way of their preparation from aldehydes. Inspired by the work of Hu et al. [14], who described the addition of $PhSO_2CF_3$ to aldehydes in the Mg/$HgCl_2$/DMF system, we synthesized analogous reagent $PhSO_2CF_2CF_2H$ (**6**) from $PhSCF_2CF_2Br$ *via* a mild debromination with $NaBH_4$/LiCl [15] and subsequent oxidation with mCPBA (Scheme 1).

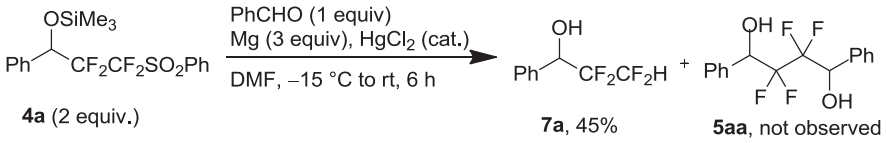
For the reaction of **6** with aldehydes, we adapted and optimized the conditions reported by Hu and then tested the method on a series of aldehydes (Table 4). Good yields of alcohols **7** were obtained except for alcohols **7b** and **7c** pointing to the limitation of the method with halogenated substrates (Entries 2 and 3). The marked difference between the two naphthyl isomers (Entries 5 and 6) can also be explained by the presence of sterically unfavorable *peri*-hydrogen [13]. Interestingly, trifluoroacetophenone (Entry 9) was unreactive; instead, the mixture of diastereomeric products of pinacol coupling [16] was identified by GCMS (Scheme 2). The reaction with acetophenone afforded only traces of the desired product.

Reductive nucleophilic addition of **4a** to benzaldehyde was attempted in order to obtain the diol **5aa**. However, the treatment of **4a** with magnesium metal and catalytic $HgCl_2$ resulted in the formation of alcohol **7a** in moderate yield and the desired diol **5aa** was not observed (Scheme 3).

The triethylsilyl-containing sulfone **3** was prepared for comparison with **2** in nucleophilic additions to carbonyl compounds (Scheme 1). The addition of **3** to 2-naphthaldehyde and trifluoroacetophenone afforded products **5e** and **5i** in 22% and 19%



Scheme 2. The formation of the pinacol coupling products observed when attempting tetrafluoroethylation of trifluoroacetophenone with **6**.



Scheme 3. Attempted nucleophilic addition of **4a** to benzaldehyde.

Table 5
Charge analysis of reagents **1**–**3**.[a]

		NPA		Hirshfeld		CM5	
	Reagent	C–S	C–Si	C–S	C–Si	C–S	C–Si
Gas phase	$PhSCF_2CF_2SiMe_3$ (**1**)	0.567	0.341	0.2035	0.1076	0.1518	0.0395
	$PhSO_2CF_2CF_2SiMe_3$ (**2**)	0.467	0.343	0.2076	0.1121	0.1586	0.0445
	$PhSO_2CF_2CF_2SiEt_3$ (**3**)	0.467	0.338	0.2079	0.1138	0.1587	0.0466
Solvated[b]	$PhSCF_2CF_2SiMe_3$ (**1**)	0.568	0.342	0.2035	0.1084	0.1519	0.0411
	$PhSO_2CF_2CF_2SiMe_3$ (**2**)	0.470	0.345	0.2079	0.1129	0.1587	0.0464
	$PhSO_2CF_2CF_2SiEt_3$ (**3**)	0.471	0.340	0.2082	0.1145	0.1589	0.0483

[a] The charges on fluorinated carbon atoms were calculated at the RMP2//RB3LYP/Def2-TZVP level in *Gaussian 09*.
[b] The IEFPCM model was used to simulate solvation in DMF.

yields, respectively, under the conditions described in Table 2 (except for higher starting temperature of −10 °C). Thus the reagent **3** proved to be even less reactive than **2**, judged from lower product yields and the necessity of increased reaction temperature. This may be a result of higher steric demand of the triethylsilyl group compared to the trimethylsilyl group. However, electronic factors are also important and to evaluate those, a brief computational study of reagents **1**–**3** was conducted. The geometries were optimized at a DFT level of theory and subsequently, atomic charges on the CF_2 carbons were calculated by several methods at the MP2 level (Table 5).

The NPA charges at the silylated carbon were shown to be quite indifferent to the structural changes on either end of the CF_2CF_2 block. In contrast, both Hirshfeld and CM5 charges correlated with reactivity of the reagents. The least reactive reagent **3** featured the highest charge values on the carbon next to the silicon atom, which corresponds to the lowest nucleophilicity in the series. Compound **1** on the other hand showed the lowest charge value. From the comparison of **1** (bearing the electron-donating phenylsulfanyl group) and **2** (containing the electron-withdrawing sulfonyl) it can be deduced that the nucleophilicity of the silane reagents strongly depends on the nature of substituents on both ends of the molecule.

3. Conclusion

In conclusion, two novel reagents **2** and **3** were developed for nucleophilic tetrafluoroethylation of carbonyl compounds to afford alcohols containing the $CF_2CF_2SO_2Ph$ group. Desulfonylation using magnesium metal in methanol provided tetrafluoroethyl-containing alcohols. These alcohols were also prepared directly from aldehydes using new reagent **6** in the presence of activated magnesium metal. The experimentally observed nucleophilicity of the reagents toward carbonyl compounds were in the following order: **1** > **2** > **3**, which corroborated with the theory. These newly reported reagents extend the synthetic toolkit for selective introduction of tetrafluoroethyl groups by nucleophilic additions.

4. Experimental

4.1. General information

Reactions with moisture-sensitive materials were carried out under argon atmosphere using standard Schlenk techniques. THF was dried by distillation using sodium/benzophenone. DMF and methanol were dried by activated molecular sieves (3 Å). Flash column chromatography was performed using silica gel 60 and TLC analyses were obtained using TLC silica gel 60 F254 aluminum sheets. The melting points are uncorrected. ^1H, ^{13}C and ^{19}F NMR spectra were measured at ambient temperature in $CDCl_3$ at 400.13, 100.62 and 376.46 MHz, respectively using 5 mm diameter NMR tubes. ^{13}C NMR spectra were proton decoupled. Chemical shift values (δ) are reported in ppm relative to internal Me_4Si (0 ppm for ^1H NMR), $CDCl_3$ (77.0 ppm for ^{13}C NMR) and $CFCl_3$ (0 ppm for ^{19}F NMR). Coupling constants (J) are reported in Hertz. For the determination of ^{19}F NMR yield, CF_3Ph was used as an internal standard and the D1 delay was set to 20 s to improve accuracy of integration. IR spectra were measured on Nicolet 6700 FTIR instrument. GCMS spectra were recorded on an Agilent 7890A GC (column HP-5MS, 30 m × 0.25 mm × 0.25 μm, 5% phenyl methylpolysiloxane) coupled with 5975C quadrupole mass selective electron impact (EI) detector (70 eV). High resolution MS spectra (HRMS) were recorded on an LTQ Orbitrap XL using electrospray ionization (ESI) or on an Agilent 7890A GC coupled with Waters GCT Premier orthogonal acceleration time-of-flight detector using electron impact (EI) ionization.

4.2. Synthesis and characterization of products

Compounds **2** [12] and $PhSCF_2CF_2Br$ [17] were synthesized following literature procedures. The characterization of compounds **7a**, **7b** and **7d**–**7h** can be found in the literature [9]. Other compounds not mentioned herein were of commercial origin.

4.2.1. Triethyl(1,1,2,2-tetrafluoro-2-phenylsulfanylethyl)silane ($PhSCF_2CF_2SiEt_3$)

Mg powder (0.30 g, 12.5 mmol), Et_3SiCl (4.30 mL, 24.9 mmol) and anhydrous THF (60 mL) were stirred in an oven-dried Schlenk flask under argon at −78 °C. $PhSCF_2CF_2Br$ (1.80 g, 6.23 mmol) was added dropwise and the reaction mixture was stirred for 5 h at −70 °C and then gradually warmed up to rt. THF was evaporated and hexane was added. The resulting suspension was filtered and the filtrate concentrated to give crude $PhSCF_2CF_2SiEt_3$, which was purified by flash column chromatography (hexane). The product (1.49 g, 74%, GCMS purity > 98%) was obtained as a colorless liquid: R_f 0.59 (hexane); ^1H NMR ($CDCl_3$): δ 0.81 (q, 6H, J = 7.8, CH_2), 1.02 (t, 9H, J = 7.9, CH_3), 7.38 (m, 2H, m-$C_{Ar}H$-SO_2), 7.44 (m, 1H, p-$C_{Ar}H$), 7.65 (m, 2H, o-$C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 1.4 (CH_2), 6.7 (CH_3), 123.8

(tt, $^1J_{CF}$ = 272.0, $^2J_{CF}$ = 47.0, CF_2), 124.6 (s, C_{Ar}), 127.0 (tt, $^1J_{CF}$ = 282.0, $^2J_{CF}$ = 35.0, CF_2), 129.0 (s, $C_{Ar}H$), 130.1 (s, $C_{Ar}H$), 137.1 (s, $C_{Ar}H$); $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ −117.9 (t, 2F, $^3J_{FF}$ = 5.3, CF_2), −83.2 (t, 2F, $^3J_{FF}$ = 5.3, CF_2); FTIR (CCl_4): ν_{max} 3081, 3066, 3040, 3027, 3009, 2960, 2942, 2916, 2882, 1584, 1577, 1475, 1467, 1460, 1442, 1416, 1383, 1328, 1243, 1199, 1158, 1125, 1091, 1082, 1065, 1025, 1009, 968, 953, 888, 728, 704, 690, 585, 560, 499, 418 cm^{-1}; MS (EI): *m*/*z* (%) 324 (7) $[M]^+$, 295 (66), 224 (11), 190 (42), 171 (22), 127 (100), 115 (33), 109 (31), 87 (58), 77 (50), 59 (22), 51 (7); HRMS (CI^+): calcd for $C_{14}H_{21}F_4SSi$ $[M+H]^+$ 325.1069, found 325.1064.

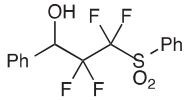
4.2.2. Triethyl(1,1,2,2-tetrafluoro-2-phenylsulfonylethyl)silane ($PhSO_2CF_2CF_2SiEt_3$, 3)

$PhSCF_2CF_2SiEt_3$ (0.97 g, 3.00 mmol) was dissolved in dichloromethane (30 mL) and the solution was cooled to 0 °C. 3-Chloroperoxybenzoic acid (70%; 2.2 g, 9.0 mmol) was added and the mixture was stirred at rt for 26 h. The residual acid was quenched with saturated solution of $Na_2S_2O_3$ (10 mL) and the suspension was filtered. The product was extracted to dichloromethane (3× 20 mL), washed with $NaHCO_3$ (5× 20 mL), dried over $MgSO_4$, then filtered and evaporated. The product (1.00 g, 93%, GCMS purity 96%) was obtained as a white amorphous substance: R_f 0.68 (EtOAc:hexane, 3:20); ^1H NMR ($CDCl_3$): δ 0.81 (q, 6H, *J* = 7.9, CH_2), 1.00 (t, 9H, *J* = 7.9, CH_3), 7.63 (m, 2H, *m*-$C_{Ar}H$-SO_2), 7.77 (m, 1H, *p*-$C_{Ar}H$), 8.03 (m, 2H, *o*-$C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 1.2 (s, CH_2), 6.5 (s, CH_3), 117.1 (tt, $^1J_{CF}$ = 291.7, $^2J_{CF}$ = 33.4, CF_2), 125.2 (tt, $^1J_{CF}$ = 275.0, $^2J_{CF}$ = 43.4, CF_2), 129.3 (s, $C_{Ar}H$), 130.7 (s, $C_{Ar}H$), 134.2 (s, C_{Ar}), 135.5 (s, $C_{Ar}H$); $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ −121.9 (m, 2F, CF_2), −108.9 (m, 2F, CF_2); FTIR (film): ν_{max} 3070, 2962, 2944, 1584, 1478, 1460, 1450, 1416, 1384, 1359, 1314, 1287, 1243, 1217, 1184, 1047, 1024, 1000, 729, 699, 686, 584, 566, 533, 509, 423 cm^{-1}; MS (EI): *m*/*z* (%) 327 (89), 227 (76), 163 (100), 135 (87), 115 (28), 87 (38), 77 (67), 59 (22), 51 (16); HRMS (CI^+): calcd for $C_{14}H_{21}F_4O_2SSi$ $[M+H]^+$ 357.0968, found 357.0960.

4.2.3. General procedure for the synthesis of compounds **5** by nucleophilic addition of **2** to carbonyl compounds

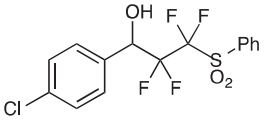
CsF (190 mg, 1.25 mmol) was suspended in dry DMF (15 mL) under Ar in an oven-dried Schlenk flask. The reaction mixture was cooled to −60 °C and the carbonyl compound (5 mmol) was added, followed by addition of **2** (786 mg, 2.5 mmol) in DMF (7 mL). The mixture was stirred at −50 °C and monitored by GCMS until **2** was fully consumed (1–4 h). In case the silylated adduct **4** was present, 1 M HCl (8 mL) was added. The mixture was warmed up to rt, quenched with aqueous NH_4Cl (10 mL), extracted to Et_2O (3 × 15 mL), dried over $MgSO_4$ and evaporated to dryness. Product **5** was purified by flash column chromatography (typically EtOAc:hexane, 3:20).

4.2.3.1. 2,2,3,3-Tetrafluoro-1-phenyl-3-(phenylsulfo-nyl)propan-1-ol (**5a**).



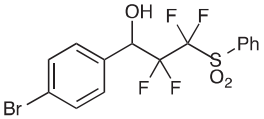
Yield: 318 mg (72%, GCMS purity > 98%), white solid; mp 82–84 °C; R_f 0.07 (EtOAc:hexane, 5:95); ^1H NMR ($CDCl_3$): δ 3.15–3.25 (br s, 1H, OH), 5.38 (dt, 1H, *J* = 19.8, 4.6, CH), 7.35–7.44 (m, 3H, $C_{Ar}H$), 7.45–7.53 (m, 2H, $C_{Ar}H$), 7.61–7.71 (m, 2H, $C_{Ar}H$), 7.78–7.86 (m, 1H, $C_{Ar}H$), 8.00–8.08 (m, 2H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 72.2 (dd, $^2J_{CF}$ = 28.6, 22.1, CH), 115.2 (ddt, $^1J_{CF}$ = 266.6, 257.9, $^2J_{CF}$ = 25.6, CF_2), 116.2 (tt, $^1J_{CF}$ = 300.9, $^2J_{CF}$ = 34.8, CF_2), 128.1 (s, $C_{Ar}H$), 128.4 (s, $C_{Ar}H$), 129.4 (s, $C_{Ar}H$), 129.5 (s, $C_{Ar}H$), 131.0 (s, $C_{Ar}H$), 132.4 (s, C_{Ar}), 133.8 (s, C_{Ar}), 136.2 (s, $C_{Ar}H$); $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ = −124.5 (dd, 1F, $^2J_{FF}$ = 280.3, $^3J_{FF}$ = 6.3, CF^aF^b), −113.1 (dd, 1F, $^2J_{FF}$ = 280.3, $^3J_{FF}$ = 10.0, CF^aF^b), −111.6 (dd, 1F, $^2J_{FF}$ = 254.3, $^3J_{FF}$ = 6.3, CF^aF^b), −110.6 (d, 1F, $^2J_{FF}$ = 254.3, CF^aF^b); FTIR (film): ν_{max} 3534, 3068, 1602, 1584, 1450, 1357, 1315, 1165, 1075, 1066, 1028, 999, 756, 597, 542 cm^{-1}; MS (EI): *m*/*z* (%) 348 (0.2) $[M]^+$, 248 (9), 187 (14), 107 (100), 77 (48), 51 (14); HRMS (ESI^+): calcd for $C_{15}H_{12}F_4O_3SNa$ $[M+Na]^+$ 371.03355, found 371.03354.

4.2.3.2. 2,2,3,3-Tetrafluoro-1-(4-chlorophenyl)-3-(phenylsulfonyl)-propan-1-ol (**5b**).



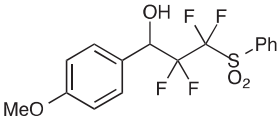
Yield: 213 mg (56%, GCMS purity 97%), white solid; mp 118–120 °C; R_f 0.10 (EtOAc:hexane, 3:20); ^1H NMR ($CDCl_3$): δ = 3.35 (br s, 1H), 5.38 (dd, 1H, *J* = 19.6, 4.8, CH), 7.31–7.47 (m, 4H, $C_{Ar}H$), 7.59–7.71 (m, 2H, $C_{Ar}H$), 7.74–7.85 (m, 1H, $C_{Ar}H$), 7.97–8.09 (m, 2H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ = 71.5 (dd, $^2J_{CF}$ = 28.4, 22.2, CH), 115.1 (tt, $^1J_{CF}$ = 268.4, $^2J_{CF}$ = 25.3, CF_2), 116.1 (tt, $^1J_{CF}$ = 301.1, $^2J_{CF}$ = 34.0, CF_2), 128.6 (s, $C_{Ar}H$), 129.5 (s, $C_{Ar}H$), 129.6 (s, $C_{Ar}H$), 131.0 (s, $C_{Ar}H$), 132.1 (s, C_{Ar}), 132.2 (s, C_{Ar}), 135.4 (s, C_{Ar}), 136.3 (s, $C_{Ar}H$); $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ −124.7 (dd, 1F, $^2J_{FF}$ = 280.4, $^3J_{FF}$ = 5.5, CF^aF^b), −112.8 (d, 1F, $^2J_{FF}$ = 280.4, CF^{ab}), −119.6 (dd, 1F, $^2J_{FF}$ = 254.3, $^3J_{FF}$ = 4.9, CF^aF^b), −110.6 (d, 1F, $^2J_{FF}$ = 254.3, CF^aF^b); FTIR (film): ν_{max} 3569, 3523, 3034, 1598, 1582, 1493, 1450, 1416, 1357, 1315, 1288, 1160, 1112, 1091, 1075, 999, 847, 756, 598, 534 cm^{-1}; MS (EI): *m*/*z* (%) 382 (0.2) $[M]^+$, 282 (6), 221 (10), 141 (100), 77 (62), 51 (14); HRMS (CI^+): calcd for $C_{15}H_{12}ClF_4O_3S$ $[M-OH]^+$ 365.0026, found 365.0038.

4.2.3.3. 2,2,3,3-Tetrafluoro-1-(4-bromophenyl)-3-(phenylsulfonyl)-propan-1-ol (**5c**).



Yield: 757 mg (71%, GCMS purity 97%), white solid; mp 112–114 °C; R_f 0.21 (EtOAc:hexane, 1:5); ^1H NMR ($CDCl_3$): δ 5.29 (s, 1H, OH), 5.37 (dd, 1H, *J* = 19.5, 4.9, CH), 7.35–7.40 (m, 2H, $C_{Ar}H$), 7.45–7.57 (m, 2H, $C_{Ar}H$), 7.61–7.67 (m, 2H, $C_{Ar}H$), 7.78–7.86 (m, 1H, $C_{Ar}H$), 7.98–8.06 (m, 2H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 71.5 (dd, $^2J_{CF}$ = 28.5, 22.3, CH), 115.0 (ddt, $^1J_{CF}$ = 267.3, 258.4, $^2J_{FF}$ = 25.0, CF_2), 116.0 (tt, $^1J_{FF}$ = 301.0, $^2J_{FF}$ = 32.8, CF_2), 123.5 (s, C_{Ar}), 129.6 (s, $C_{Ar}H$), 129.7 (s, $C_{Ar}H$), 131.0 (s, $C_{Ar}H$), 131.5 (s, $C_{Ar}H$), 132.1 (s, C_{Ar}), 132.8 (s, C_{Ar}), 136.3 (s, $C_{Ar}H$); $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ −124.7 (dd, 1F, $^2J_{FF}$ = 280.4, $^3J_{FF}$ = 6.3, CF^aF^b), −112.8 (d, 1F, $^2J_{FF}$ = 280.4 Hz), −111.9 (dd, 1F, $^2J_{FF}$ = 254.2, $^3J_{FF}$ = 6.3, CF^aF^b), −110.6 (d, 1F, $^2J_{FF}$ = 254.2, CF^aF^b); FTIR (film): ν_{max} 3530, 1595, 1584, 1489, 1450, 1357, 1315, 1165, 1075, 1024, 1013, 999, 958, 684, 597, 542 cm^{-1}; MS (EI): *m*/*z* (%) 427 (1) $[M]^+$, 326 (7), 265 (8), 185 (100), 77 (77), 51 (20); HRMS (CI^+): calcd for $C_{15}H_{10}F_4O_2SBr$ $[M-OH]^+$ 408.9521, found 408.9557.

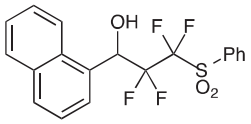
4.2.3.4. 2,2,3,3-Tetrafluoro-1-(4-methoxyphenyl)-3-(phenylsulfo-nyl)propan-1-ol (**5d**).



Yield: 150 mg (51%, GCMS purity 95%), white solid; mp 154–156 °C; R_f 0.04 (EtOAc:hexane, 10:90); ^1H NMR ($CDCl_3$): δ 3.50 (br s, 1H, OH), 3.82 (s, 3H, OCH_3), 5.32 (dd, 1H, *J* = 19.2, 5.2, CH), 6.85–6.98 (m, 2H, $C_{Ar}H$), 7.35–7.47 (m, 2H, $C_{Ar}H$), 7.59–7.71 (m, 2H, $C_{Ar}H$), 7.76–7.86 (m, 1H), 7.96–8.10 (m, 2H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 55.2 (s, OCH_3), 71.8 (dd, $^2J_{CF}$ = 28.5, 22.0, CH), 113.7

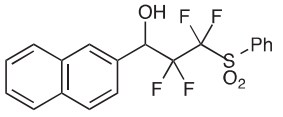
(s, $C_{Ar}H$), 126.3 (s, C_{Ar}), 129.4 (s, $C_{Ar}H$), 130.9 (s, $C_{Ar}H$), 136.0 (s, $C_{Ar}H$), 160.3 (s, C_{Ar}); ^{19}F {^1H} NMR ($CDCl_3$): δ −124.6 (d, 1F, $^2J_{FF}$ = 280.0, CF^aF^b), −113.4 (d, 1F, $^2J_{FF}$ = 280.0, CF^aF^b), −111.5 (d, 1F, $^2J_{FF}$ = 255.5, CF^aF^b), −110.7 (d, 1F, $^2J_{FF}$ = 255.5, CF^aF^b); FTIR (film): ν_{max} 3527, 3451, 2841, 1613, 1584, 1515, 1450, 1358, 1315, 1255, 1169, 1076, 1068, 1031, 999, 846, 758, 685, 634, 597, 534 cm^{-1}; MS (EI): *m/z* (%) = 378 (2) $[M]^+$, 207 (11), 149 (23), 137 (100), 77 (29); HRMS (ESI^-): calcd for $C_{16}H_{13}F_4O_3S$ $[M-OH]^-$ 361.0522, found 361.0532.

*4.2.3.5. 2,2,3,3-Tetrafluoro-1-(naphthalen-1-yl)-3-(phenylsulfonyl)-propan-1-ol (**5e**).*



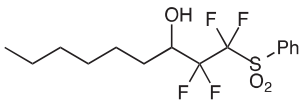
Yield: 150 mg (40%, GCMS purity 95%), yellow oil; R_f 0.10 (EtOAc:hexane, 10:90); ^1H NMR ($CDCl_3$): δ 3.46 (br s, 1H, OH), 6.32 (d, 1H, *J* = 20.8, CH), 7.42–7.65 (m, 5H, $C_{Ar}H$), 7.69–7.77 (m, 1H, $C_{Ar}H$), 7.82–7.91 (m, 3H, $C_{Ar}H$), 7.98–8.10 (m, 3H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 67.7 (dd, $^2J_{CF}$ = 30.0, 21.7, CH), 115.8 (ddt, $^1J_{CF}$ = 259.0, $^2J_{FF}$ = 26.5, $^2J_{FF}$ = 25.4, CF_2), 116.7 (ddt, $^1J_{CF}$ = 301.5, $^2J_{FF}$ = 32.2, $^2J_{FF}$ = 35.0, CF_2), 123.1 (s, $C_{Ar}H$), 125.1 (s, $C_{Ar}H$), 125.7 (s, $C_{Ar}H$), 126.7 (s, $C_{Ar}H$), 126.8 (s, $C_{Ar}H$), 129.5 (s, $C_{Ar}H$), 129.9 (s, $C_{Ar}H$), 129.9 (s, $C_{Ar}H$), 130.1 (s, C_{Ar}), 130.9 (s, $C_{Ar}H$), 131.4 (s, C_{Ar}), 132.2 (s, C_{Ar}), 133.5 (s, C_{Ar}), 136.2 (s, $C_{Ar}H$); ^{19}F {^1H} NMR ($CDCl_3$): δ −125.3 (dd, 1F, J_{FF} = 280.8, 5.86, CF^aF^b), −112.0 (ddd, 1F, $^2J_{FF}$ = 253.0, $^3J_{FF}$ = 7.6, 2.7, CF^aF^b), −110.8 (dd, 1F, $^2J_{FF}$ = 280.8, $^3J_{FF}$ = 2.7, CF^aF^b), −110.6 (dd, 1F, $^2J_{FF}$ = 253.0, $^3J_{FF}$ = 2.7, CF^aF^b); FTIR (film): ν_{max} 3536, 3066, 1624, 1598, 1583, 1514, 1450, 1356, 1315, 1163, 1122, 1075, 1061, 999, 816, 757, 596, 537 cm^{-1}; MS (EI): *m/z* (%) 398 (8) $[M]^+$, 281 (23), 207 (100), 157 (85), 129 (40), 77 (21); HRMS (CI^+): calcd for $C_{19}H_{15}O_3F_4S$ $[M+H]^+$ 399.0678, found 399.0670.

*4.2.3.6. 2,2,3,3-Tetrafluoro-1-(naphthalen-2-yl)-3-(phenylsulfonyl)-propan-1-ol (**5f**).*



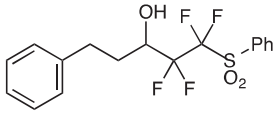
Yield: 559 mg (56%, GCMS purity 96%), off-white solid; mp 106–110 °C; R_f 0.12 (EtOAc:hexane, 1:5); ^1H NMR ($CDCl_3$): δ 3.18 (br s, 1H, OH), 5.58 (dd, 1H, $^3J_{HF}$ = 19.8, $^4J_{H-H}$ = 6.0, CH), 7.47–8.13 (m, 12H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 72.4 (dd, $^2J_{CF}$ = 28.5, 22.1, CH), 112.5–119.5 (m, CF_2CF_2), 125.1 (s, $C_{Ar}H$), 126.4 (s, $C_{Ar}H$), 126.7 (s, $C_{Ar}H$), 127.7 (s, $C_{Ar}H$), 128.0 (s, $C_{Ar}H$), 128.2 (s, $C_{Ar}H$), 128.3 (s, $C_{Ar}H$), 129.6 (s, *m*-$C_{Ar}H$-SO_2), 131.0 (s, *o*-$C_{Ar}H$-SO_2), 131.2 (s, C_{Ar}), 132.3 (s, C_{Ar}), 132.9 (s, C_{Ar}), 133.7 (s, C_{Ar}), 136.2 (s, *p*-$C_{Ar}H$-SO_2); ^{19}F {^1H} NMR ($CDCl_3$): δ −124.4 (ddd, 1F, $^2J_{FF}$ = 279.8, $^3J_{HF}$ = 19.8, $^3J_{FF}$ = 6.4, CF^aF^b), −112.4 (d, 1F, $^2J_{FF}$ = 279.6, CF^aF^b), −111.9 (ddd, 1F, $^2J_{FF}$ = 254.0, $^3J_{FF}$ = 6.6, 2.3, CF^aF^b), −110.5 (dd, 1F, $^2J_{FF}$ = 254.0, $^3J_{FF}$ = 1.7, CF^aF^b); FTIR (film): ν_{max} 3612, 3560, 3067, 1604, 1585, 1577, 1512, 1479, 1450, 1376, 1355, 1314, 1270, 1186, 1168, 1154, 1130, 1126, 1095, 1063, 1024, 999, 964, 952, 881, 861, 625, 596, 557, 520, 478 cm^{-1}; MS (EI): *m/z* (%) 398 (18) $[M]^+$, 157 (100), 129 (58), 77 (18); HRMS (CI^+): calcd for $C_{19}H_{14}O_3SF_4$ $[M]^+$ 398.0600, found 398.0596.

*4.2.3.7. 1,1,2,2-Tetrafluoro-1-(phenylsulfonyl)nonan-3-ol (**5g**).*



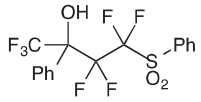
Yield: 135 mg (51%, GCMS purity > 98%), colorless oil; R_f 0.18 (EtOAc:hexane, 5:95); ^1H NMR ($CDCl_3$): δ 0.76–0.98 (m, 3H, CH_3), 1.22–1.43 (m, 7H, 3 × CH_2, CH^aH^b), 1.57–1.68 (m, 2H, CH_2), 1.71–1.83 (m, 1H, CH^aH^b), 2.17 (br s, 1H, OH), 4.19–4.34 (m, 1H, CH), 7.62–7.72 (m, 2H, $C_{Ar}H$), 7.79–7.89 (m, 1H, $C_{Ar}H$), 8.01–8.09 (m, 2H, $C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 14.0 (s, CH_3), 22.6 (s, CH_2), 25.1 (s, CH_2), 28.6 (s, CH_2), 31.6 (s, CH_2), 70.4 (dd, $^2J_{CF}$ = 27.5, 23.2, CH), 129.5 (s, $C_{Ar}H$), 131.0 (s, $C_{Ar}H$), 132.3 (s, $C_{Ar}H$), 136.2 (s, $C_{Ar}H$); ^{19}F {^1H} NMR ($CDCl_3$): δ −125.9 (dd, 1F, $^2J_{FF}$ = 278.5, $^3J_{FF}$ = 6.0, CF^aF^b), −115.9 (dd, 1F, $^2J_{FF}$ = 278.5, $^3J_{FF}$ = 2.8 Hz), −112.5 (dd, 1F, $^2J_{FF}$ = 254.2, $^3J_{FF}$ = 6.0, CF^aF^b), −110.6 (d, 1F, $^2J_{FF}$ = 254.2, $^3J_{FF}$ = 2.8 Hz, CF^aF^b); FTIR (film): ν_{max} 3536, 3070, 2958, 2931, 1860, 1584, 1468, 1359, 1315, 1176, 1095, 1076, 1024, 757, 685, 597, 538 cm^{-1}; MS (EI): *m/z* (%) 356 (1) $[M]^+$, 256 (19), 195 (18), 141 (100), 115 (37), 97 (41), 77 (96), 55 (37); HRMS (CI^+): calcd for $C_{15}H_{21}F_4O_3S$ $[M+H]^+$ 357.1148, found 357.1156.

*4.2.3.8. 1,1,2,2-Tetrafluoro-5-phenyl-1-(phenylsulfonyl)pentan-3-ol (**5h**).*



Yield: 479 mg (51%, GCMS purity 98%), yellow oil; R_f 0.24 (EtOAc:hexane, 1:5); ^1H NMR ($CDCl_3$): δ 1.93–2.13 (m, 2H, CH_2), 2.74 (m, 2H, CH_2), 2.98 (m, 1H, CH), 4.27 (m, 1H, OH), 7.20–7.34 (m, 5H, $C_{Ar}H$), 7.64 (2H, *m*-$C_{Ar}H$-SO_2), 7.81 (1H, *p*-$C_{Ar}H$-SO_2), 8.00 (d, 2H, $^3J_{HH}$ = 7.7, *o*-$C_{Ar}H$-SO_2); ^{13}C NMR ($CDCl_3$): δ 30.2 (CH_2), 31.1 (CH_2), 69.5 (dd, $^2J_{CF}$ = 27.6, 23.3, CH), 112.9–119.5 (m, CF_2CF_2), 126.2 (s, $C_{Ar}H$), 128.5 (s, $C_{Ar}H$), 128.6 (s, $C_{Ar}H$), 129.6 (s, *m*-$C_{Ar}H$-SO_2), 131.0 (s, *o*-$C_{Ar}H$-SO_2), 132.1 (s, C_{Ar}), 136.2 (s, *p*-$C_{Ar}H$-SO_2), 140.7 (s, C_{Ar}-SO_2); ^{19}F {^1H} NMR ($CDCl_3$): δ −125.6 (dddd, 1F, $^2J_{FF}$ = 278.9, $^3J_{HF}$ = 19.3, $^3J_{FF}$ = 6.6, 3.3, CF^aF^b), −115.8 (dm, 1F, $^2J_{FF}$ = 278.9, CF^aF^b), −112.6 (ddd, 1F, $^2J_{FF}$ = 254.5, $^3J_{FF}$ = 6.6, 2.8, CF^aF^b), −110.8 (dd, 1F, $^2J_{FF}$ = 254.6, $^3J_{FF}$ = 3.3, CF^aF^b); MS (EI): *m/z* (%) 376 (9) $[M]^+$, 215 (23), 197 (100), 91 (69), 77 (43); HRMS (CI^+): calcd for $C_{17}H_{17}O_3SF_4$ $[M+H]^+$ 377.0835, found 377.0838.

*4.2.3.9. 1,1,1,3,3,4,4-Heptafluoro-2-phenyl-4-(phenylsulfonyl)butan-2-ol (**5i**).*



Yield: 86 mg (48%, GCMS purity 95%), white solid; mp 107–109 °C; R_f 0.12 (EtOAc:hexane, 10:90); ^1H NMR ($CDCl_3$): δ 4.50 (br s, 1H, OH), 7.50–7.58 (m, 3H, $C_{Ar}H$), 7.67–7.76 (m, 2H, $C_{Ar}\delta$), 7.80–7.93 (m, 3H, $C_{Ar}\delta$), 8.02–8.12 (m, 2H, $C_{Ar}\delta$); ^{13}C NMR ($CDCl_3$): δ 115.5–116.0 (m, CF_2), 116.1 (tt, $^1J_{CF}$ = 300.0, $^2J_{CF}$ = 27.6, CF_2), 118.8 (m, CF_3), 121.6 (s, C_{Ar}), 126.8 (s, $C_{Ar}H$), 128.3 (s, $C_{Ar}H$), 129.5 (s, $C_{Ar}H$), 129.9 (s, $C_{Ar}H$), 131.0 (s, $C_{Ar}H$), 132.6 (s, C_{Ar}), 136.1 (s, $C_{Ar}H$); ^{19}F NMR ($CDCl_3$): δ −114.5 to −113.5 (m, 1F), −112.8 to −111.8 (m, 1F), −108.9 to −107.9 (m, 1F), −107.0 to −106.1 (m, 1F), −74.3 to −74.1 (m, 3F, CF_3); FTIR (film): ν_{max} 3471, 1584, 1501, 1451, 1361, 1350, 1315, 1188, 1156, 1078, 997, 757, 705, 683, 589, 529 cm^{-1}; MS (EI): *m/z* (%) 416 (1) $[M]^+$, 347 (16), 175 (100), 141 (44), 105 (62), 77 (96), 51 (23); HRMS (CI^+): calcd for $C_{16}H_{12}F_7O_3S$ $[M+H]^+$ 417.0395, found 417.0392.

4.2.4. Phenyl(1,1,2,2-tetrafluoroethyl)sulfide ($PhSCF_2CF_2H$)

$NaBH_4$ (1.13 g, 30.0 mmol) and LiCl (1.27 g, 30.0 mmol) were suspended in dry DMF (40 mL) in an oven-dried Schenk flask under Ar. $PhSCF_2CF_2Br$ (2.89 g, 10.0 mmol) was added dropwise at rt over a period of 30 min and the mixture was stirred for 30 min. Water (20 mL) was added slowly, the mixture was extracted with Et_2O (3 × 20 mL), washed with brine (3 × 15 mL) and water (2 × 20 mL). Solvent was removed under vacuum, affording product (1.34 g,

64%, GCMS purity > 98%) as colorless liquid: R_f 0.49 (hexane); ^{1}H NMR ($CDCl_3$): δ 5.76 (tt, 1H, J = 53.7, 3.4, CF_2H), 7.40 (dd, 2H, J = 7.5, 7.4, m-$C_{Ar}H$-SO_2), 7.47 (tt, 1H, J = 7.4, 1.2, p-$C_{Ar}H$), 7.65 (dd, 2H, J = 7.5, 1.2, o-$C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 109.4 (tt, $^1J_{CF}$ = 252.8, $^2J_{CF}$ = 37.5, CF_2H), 122.5 (tt, $^1J_{CF}$ = 284.1, $^2J_{CF}$ = 29.5, CF_2), 123.4 (t, $^3J_{CF}$ = 2.8, C_{Ar}), 129.4 (s, $C_{Ar}H$), 130.7 (s, $C_{Ar}H$), 137.0 (s, $C_{Ar}H$); ^{19}F NMR ($CDCl_3$): δ −132.6 (dt, 2F, $^2J_{HF}$ = 53.9, $^3J_{FF}$ = 9.2, CF_2H), −92.0 (dt, 2F, $^3J_{FF}$ = 9.2, $^3J_{HF}$ = 3.4, CF_2); MS (EI): m/z (%) 210 (100) $[M]^+$, 191 (3), 171 (6), 159 (89), 109 (69), 101 (10), 77 (28), 51 (21); HRMS (CI^+): calcd for $C_8H_7F_4S$ $[M+H]^+$ 211.0205, found 211.0201.

*4.2.5. Phenyl(1,1,2,2-tetrafluoroethyl)sulfone ($PhSO_2CF_2CF_2H$, **6**)*

$PhSCF_2CF_2H$ (2.45 g, 11.7 mmol) was dissolved in CH_2Cl_2 (80 mL) and the solution was cooled to 0 °C. 3-Chloroperoxybenzoic acid (70%; 8.6 g, 35 mmol) was added and the mixture was stirred at rt for 26 h. The residual acid was quenched with saturated solution of $Na_2S_2O_3$ (100 mL) and the suspension was filtered. The product was extracted to CH_2Cl_2 (3 × 40 mL), washed with $NaHCO_3$ (5 × 70 mL) and brine (100 mL), dried over $MgSO_4$, then filtered and evaporated. The product (2.55 g, 90%, GCMS purity > 98%) was obtained as a pale yellow liquid: R_f 0.42 (EtOAc:hexane, 3:20); ^{1}H NMR ($CDCl_3$): δ 6.31 (tt, 1H, J = 52.2, 5.7, CF_2H), 7.69 (dd, 2H, J = 7.5, 7.8, m-$C_{Ar}H$-SO_2), 7.85 (tt, 1H, J = 7.5, 1.2; p-$C_{Ar}H$), 8.04 (dd, 2H, J = 7.8, 1.2, o-$C_{Ar}H$); ^{13}C NMR ($CDCl_3$): δ 107.5 (tt, $^1J_{CF}$ = 255.8, $^2J_{CF}$ = 29.2, CF_2H), 114.4 (tt, $^1J_{CF}$ = 295.9, $^2J_{CF}$ = 26.8, CF_2), 129.6 (s, $C_{Ar}H$), 130.9 (s, $C_{Ar}H$), 132.0 (t, $^3J_{CF}$ = 2.8, C_{Ar}), 136.3 (s, $C_{Ar}H$); ^{19}F NMR ($CDCl_3$): δ −134.9 (dt, 2F, $^2J_{HF}$ = 52.2, $^3J_{FF}$ = 8.1, CF_2H), −119.7 (dt, 2F, $^3J_{FF}$ = 8.1, $^3J_{HF}$ = 5.9, CF_2); FTIR (film): ν_{max} 3073, 3011, 1584, 1479, 1451, 1359, 1316, 1243, 1174, 1125, 1072, 999, 758, 721, 684, 601, 590, 528 cm^{-1}; MS (EI): m/z (%) 242 (2) $[M]^+$, 159 (1); 141 (54), 125 (8), 101 (12), 77 (100), 51 (42); HRMS (CI^+): calcd for $C_8H_7O_2F_4S$ $[M+H]^+$ 243.0103, found 243.0097.

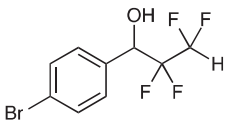
*4.2.6. General procedure for the synthesis of compounds **7** by desulfonylation of **5** with sodium (Route A)*

Sodium metal (58 mg, 2.5 mmol), **5** (0.5 mmol) and dry THF (4 mL) were stirred in an oven-dried Schlenk flask. Dry EtOH (150 μL, 2.5 mmol) was added *via* syringe. The mixture was stirred at rt until full conversion to **7** was reached. On addition of MeOH (10 mL), water (20 mL) and 1 M HCl (20 mL), the product was extracted to Et_2O (5 × 20 mL), washed with brine (1 × 20 mL), dried over $MgSO_4$, filtered, and the solvent was evaporated. The yield of **7** was either determined by ^{19}F NMR or the product was isolated by flash column chromatography (EtOAc:hexane, 3:20).

*4.2.7. General procedure for the synthesis of compounds **7** by desulfonylation of **5** with magnesium (Route B)*

Magnesium metal (396 mg, 16.5 mmol) and I_2 (cat.) were stirred in an oven-dried Schlenk tube under Ar for 10 min. Compound **5** (0.75 mmol) was added and the mixture was slightly heated with a heat gun. MeOH (20 mL) was added and the solution quickly turned yellow and then gray during 5 min. After stirring for 2 h, NH_4Cl (10 mL) and 1 M HCl (30 mL) were added. The product was extracted to Et_2O (5 × 20 mL), washed with brine (1 × 20 mL), dried over $MgSO_4$, filtered, and solvent was evaporated yielding crude **7**, which was purified by flash column chromatography (typically EtOAc:hexane, 3:20).

*4.2.7.1. 1-(4-Bromophenyl)-2,2,3,3-tetrafluoropropan-1-ol (**7c**).*



Yield: 123 mg (57%, GCMS purity 95%), yellow oil; R_f 0.40 (EtOAc:hexane, 1:5); ^{1}H NMR ($CDCl_3$): δ 3.12 (d, 1H, J = 4.8), 4.98–5.07 (m, 1H), 5.99 (m 1H), 7.30–7.55 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 71.5 (dd, $^2J_{CF}$ = 29.2, 23.1, CH), 109.3 (dddd, J = 252.3, 248.8, 37.9, 30.1, CF_2H), 114.6 (dddd, J = 254.1, 252.9, 27.4, 23.3, CF_2), 123.7 (s, $C_{Ar}Br$), 129.4 (s, $C_{Ar}H$), 131.8 (s, $C_{Ar}H$), 133.4 (s, C_{Ar}); ^{19}F NMR ($CDCl_3$): δ −141.7 (ddd, 1F, J = 300.7, 9.9, 6.8), −137.3 (ddd, 1F, J = 300.8, 52.6, 10.7), −131.4 (ddd, 1F, J = 271.0, 17.5, 10.0), −128.5 (ddd, 1F, J = 271.1, 18.3, 6.9); FTIR (film): ν_{max} 3595, 3452, 3094, 3069, 3037, 1595, 1577, 1490, 1406, 1239, 1181, 1120, 1107, 1076, 1059, 1012, 789, 701, 628, 593 cm^{-1}; MS (EI): m/z (%) 286 (10) $[M]^+$, 185 (100), 156 (21), 101 (10), 77 (76), 51 (25); HRMS (CI^+): calcd for $C_9H_8OF_4Br$ $[M+H]^+$ 286.9695, found 286.9705.

*4.2.8. General procedure for the synthesis of compounds **7** by addition of **6** to carbonyl compounds*

Magnesium metal (72 mg, 3 mmol), $HgCl_2$ (16 mg, 0.06 mmol) and I_2 (cat.) were suspended in dry DMF at −60 °C in an oven-dried Schlenk flask under Ar. Compound **6** (242 mg, 1 mmol) was added, followed by the carbonyl compound (2 mmol). The temperature was slowly increased while the reaction was monitored by GCMS. On full consumption of **6**, 1 M HCl (10 mL) was added. The product was extracted to Et_2O (5 × 20 mL), washed with brine (1 × 20 mL), dried over $MgSO_4$, filtered, and solvent was evaporated yielding crude **7**, which was purified by flash column chromatography (typically EtOAc:hexane, 3:20).

4.3. Computational methods

All computations were performed in *Gaussian 09*, Revision D.01 [18]. The geometry optimizations were done at the density functional theory (DFT) level employing the B3LYP functional and Def2-TZVP basis set for all atoms. The basis sets were downloaded from Basis Set Exchange (https://bse.pnl.gov/) [19]. The charge analyses (NPA, Hirshfeld and CM5) were calculated using the Møller-Plesset perturbation theory of the second order (MP2) with the Def2-TZVP [20] basis set. In the cases where solvation effects were considered, both optimization and charge analysis were calculated using the integral equation formalism (IEFPCM) model with the universal force field (UFF) topology (DMF: ε = 37.219) [21].

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