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Acid-promoted direct electrophilic trifluoromethylthiolation of phenols†

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The electrophilic aromatic ring trifluoromethylthiolation of various substituted phenols was accomplished using $PhNHSCF_3$ (*N*-trifluoromethylsulfanyl)aniline, (**1**) in the presence of $BF_3{\cdot}Et_2O$ (**2**) or triflic acid as the promoter. The functionalization was exclusively *para*-selective; phenols unsubstituted in both the *ortho*- and *para* positions solely gave the *para*-substituted SCF_3-products in all cases, while *para*-substituted phenols gave the *ortho*-substituted SCF_3-products. 3,4-Dialkyl substituted phenols yielded the corresponding products according to the Mills-Nixon effect, and estrone and estradiol furnished biologically interesting SCF_3-analogues. The highly reactive catechol and pyrogallol substrates gave the expected products smoothly in the presence of $BF_3{\cdot}Et_2O$, whereas less reactive phenols required triflic acid. 2-Allylphenol gave the expected *p*-SCF_3 analogue, which underwent an addition/cyclization sequence and furnished a new di-trifluoromethylthio substituted 2,3-dihydrobenzofuran derivative. Some additional transformations of 4-(trifluoromethylthio)phenol with NBS, NIS, HNO_3, HNO_3/H_2SO_4 and 4-bromobenzyl bromide were performed giving bromo-, iodo-, nitro- and benzyl substituted products. The latter derivative underwent Suzuki–Miyaura coupling with phenylboronic acid.

Introduction

The introduction of a fluorine atom or a fluorine-containing substituent into an organic molecule often favorably modulates the compounds' properties, thus making new functional and advanced materials.[1–6] Fluorinated organic molecules frequently possess enhanced stability, binding affinity and biological activity in comparison with their non-fluorinated precursors.[7,8] The trifluoromethyl group shares an exceedingly important part in biologically relevant molecules, and the number of newly introduced trifluoromethylated substances in the pharmaceutical and medicinal chemistry industries has been growing considerably.[9–11] Consequently, there has been a strong interest in the direct introduction of CF_3 groups into organic molecules regardless of the approach, *via* radical, nucleophilic or electrophilic modes, thus making trifluoromethylation a current topic of great interest.[12–19]

An interesting variety of the CF_3 group is the trifluoromethylthiol group SCF_3, which considerably contributes to enhanced lipophilicity, and is an indispensable moiety in the agrochemistry and medicinal chemistry industries;[20] however its introduction has received considerably less attention than the CF_3 group. A 2′-SCF_3 substituted uridine derivative was found to be a powerful label for probing the structure and function of RNA using ^{19}F NMR spectroscopy.[21]

Recently, significant progress in the introduction of a SCF_3 moiety has been achieved.[22] The introduction of the SCF_3 group could occur directly with CF_3SCl[23] or $(CF_3)_2S$,[24] (extremely noxious and hazardous gases that are not suitable for non-specialized laboratories) or indirectly *i.e.* by interconversion of functional groups.[25] Nucleophilic and radical sources of the SCF_3 group are often copper-[26] or silver-based[27] metallic reagents, or $[NH_4][SCF_3]$;[28] furthermore, trifluoromethylthiolation can also be realized with a combination of two different sources for the sulfur functionality and CF_3 group.[29] In particular, the popularity of electrophilic trifluoromethylthiolation has grown remarkably in recent years; the new period of interest began with the work of Billard, Langlois and coworkers.[30] They prepared $PhNHSCF_3$ and its derivatives: easy-to-handle electrophilic SCF_3-transfer reagents for use with alkenes and alkynes,[31] indoles,[32] tryptamines,[33] organometallic species,[34] amines,[35] and allyl silanes.[36] In addition, terminal alkynes were trifluoromethylthiolated in the presence of a catalytic amount of base.[37] Internal alkynes reacted with $PhNHSCF_3$, yielding the corresponding 3-(trifluoromethyl)thio derivatives of indoles,[38] benzofurans, benzothiophenes[39] and 1*H*-isochromen-1-ones.[40] Similarly, 4-((trifluoromethyl)thio)-2*H*-benzo[*e*][1,2]thiazine 1,1-dioxides were efficiently prepared in the presence of $BiCl_3$ in dichloroethane.[41] An interesting trifluoromethanesulfonyl hypervalent iodonium ylide able to

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† Electronic supplementary information (ESI) available: Copies of the ^1H, ^{13}C and ^{19}F NMR spectra for all products. See DOI: 10.1039/c4ob02633k

deliver the trifluoromethylthiol group was developed recently.[42] *N*-(Trifluoromethylthio)succinimide was utilized in the Pd-catalyzed trifluoromethylthiolation of arenes,[43] while an *in situ* formed reagent from $AgSCF_3$ and NCS was employed in the functionalization of alkynes.[44] A new thioperoxide[45,46] type of electrophilic trifluoromethylthiolating reagent was able to react with β-ketoesters, boronic acids,[47] alkynes and aliphatic carboxylic acids,[48] giving the corresponding SCF_3-substituted products. This thioperoxide reagent in combination with TMSOTf was also found to be a powerful activating agent of different thioglycosides.[49] Additionally, the thioperoxide reagent was used in enantioselective catalytic trifluoromethylthiolations,[50] as well as *N*-trifluoromethylthiophthalimide[51] and an $AgSCF_3$/trichloroisocyanuric acid system.[52] The latter system was also utilized in the synthesis of 3-((trifluoromethyl)thio)-4*H*-chromen-4-ones.[53] Electrophilic trifluoromethylthiolation of various carbonyl compounds[54] and aromatics[55] was accomplished using a new *N*-((trifluoromethyl)thio)benzenesulfonamide type of reagent. *N*-Trifluoromethylthiosaccharin was developed recently and utilized in the trifluoromethylation of alcohols, amines, thiols, electron-rich aromatics, aldehydes, ketones, acyclic β-ketoesters and alkynes.[56]

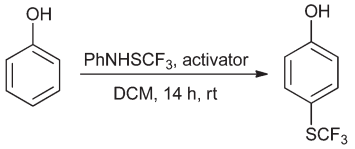
$PhNHSCF_3$ (*N*-trifluoromethylsulfanyl)aniline, (**1**) is a simple and easy-to-handle electrophilic reagent for the direct introduction of a SCF_3 group into organic molecules. Its electrophilic power usually requires activation with an appropriate promoter of the Lewis or Brønsted type. Its reactivity is mostly unexplored, and we decided to test it on phenols, since there are many biologically relevant phenols *i.e.* steroids of estrone type, epinephrine, thymol, and others. We report on a direct and remarkably highly regioselective trifluoromethylthiolation of phenols using $PhNHSCF_3$ in combination with a boron trifluoride etherate complex or triflic acid.

Results and discussion

Initially, the reaction conditions were examined using phenol (**3a**) as a model substrate; the results are summarized in Table 1. Initially **3a** was subjected to **1** without an activator, and remained unreacted (Table 1, entry 1). $BF_3{\cdot}Et_2O$ and *p*-$TsOH{\cdot}H_2O$ were found to be rather unpromising promoters for this reaction (entries 2–5).

We decided to examine the effect of considerably stronger activators, *i.e.* CH_3SO_3H (MSA) and triflic acid (TfOH). MSA was found to be a somewhat better activator (entries 6 and 7), while TfOH was the promoter of choice (entries 8 and 9). In all cases, 4-trifluoromethylthiophenol (**4a**) was obtained, and no *ortho* substitution was noted. Results from the functionalization of different phenols are presented in Table 2. 2-Methylphenol (**3b**) and 3-methylphenol (**3c**) both yielded the 4-SCF_3-substituted products **4b** and **4c** exclusively (Table 2, entries 1 and 2). 4-Methylphenol (**3d**) and 4-*i*-propylphenol (**3e**) yielded the corresponding 2-SCF_3-substituted products **4d** and **4e** as the sole products. In the cases of 2-*t*-butylphenol (**3f**) and 4-*t*-butylphenol (**3g**), *ipso* substitution could have been observed; however, the 4-SCF_3-substituted **4f** and 2-SCF_3-substituted product **4g** were formed as the sole products (entries 5 and 6). Similarly, 2-benzylphenol (**3h**) yielded the 4-SCF_3-substituted product **4h**, while no *ipso* substitution was observed. 4-Phenylphenol (**3i**) was regioselectively transformed into its 2-SCF_3-substituted product **4i**. The reactions of 2,5-dimethylphenol (**3j**) and 2,6-dimethylphenol (**3k**) cleanly furnished their 4-SCF_3-substituted derivatives **4j** and **4k** (entries 9 and 10). 2,3,5-Trimethylphenol (**3l**) and 2,3,6-trimethylphenol (**3m**) gave their 4-SCF_3-substituted derivatives **4l** and **4m** as the sole products (entries 11 and 12).

Table 1 Optimization of the reaction conditions[a]



3a **4a**

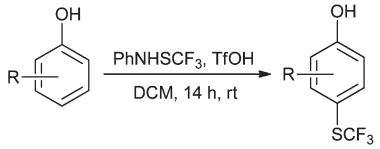
Entry	Activator	Amount (equiv.)	Conversion[b] (%)
1	—	—	0
2	$BF_3{\cdot}Et_2O$	2.5	0
3		5	0
4	*p*-$TsOH{\cdot}H_2O$	2.5	0
5		5	0
6	CH_3SO_3H	1.5	0
7		2	30
8	TfOH	1.2	91
9		1.3	100 (77)[c]

[a] Conditions: **3a** (1 mmol), $PhNHSCF_3$ (**1**, 1.2–1.3 mmol), activator, DCM (10 mL), 14 h, rt. [b] Conversion determined by ^1H NMR. [c] Isolated yield.

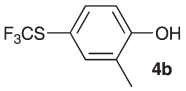
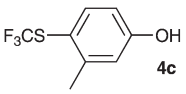
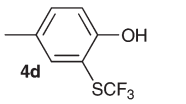
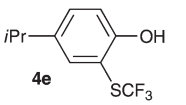
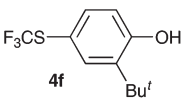
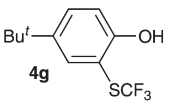
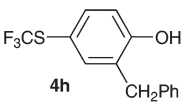
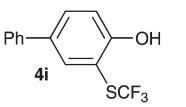
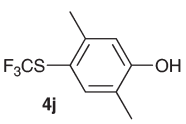
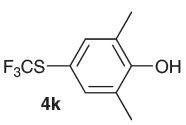
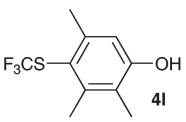
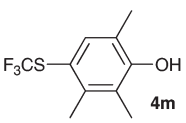
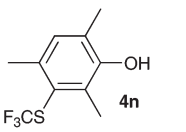
2,4,6-Trimethylphenol (**3n**) was an interesting substrate, because all potentially reactive positions were substituted. None of the possible *ipso* adducts were observed, but 2,4,6-trimethyl-3-trifluoromethylthiophenol (**4n**) was isolated as the sole product (entry 13).

Next, we examined the reactivity of 3,4-dimethylphenol (**5a**), 5-indanol (**5b**) and 5,6,7,8-tetrahydro-2-naphthol (**5c**) (Scheme 1). Such compounds possess unequally reactive *ortho* positions; this phenomenon is known as the Mills–Nixon effect.[57] **5a** furnished the expected **6a** as the major product, while no **6aa** was detected. Instead, double functionalization took place, yielding **6a′** as a minor product. The relative distribution ratio of **6a**/**6a′** was 94 : 6. **5b** yielded only one expected product **6b**; whereas no **6bb** was detected. **5c** reacted in accordance with the anticipated reactivity giving **6c** and **6cc** in a relative ratio of 56 : 44. The regioselectivity of trifluoromethylthiolation for 3,4-dimethylphenol and 5-indanol is similar to that of their bromination reactions,[58] while bromination of 5,6,7,8-tetrahydro-2-naphthol was more selective (78 : 22) than its trifluoromethylthiolation. Nitration of 3,4-dimethylphenol (57 : 43) and 5-indanol (58 : 42) with $NaNO_2$/H_2O_2/H_2SO_4 was less regioselective than trifluoromethylthiola-

Table 2 Acid-promoted trifluoromethylthiolation of phenols[a]



3 4

Entry	Reactant	Product	Yield[b] (%)
1	*o*-Cresol **3b**	 **4b**	81
2	*m*-Cresol **3c**	 **4c**	79
3	*p*-Cresol **3d**	 **4d**	80
4	4-*i*-Propylphenol **3e**	 **4e**	82
5	2-*t*-Butylphenol **3f**	 **4f**	64
6	4-*t*-Butylphenol **3g**	 **4g**	87
7	2-Benzylphenol **3h**	 **4h**	86
8	4-Phenylphenol **3i**	 **4i**	48
9	2,5-Dimethylphenol **3j**	 **4j**	90
10	2,6-Dimethylphenol **3k**	 **4k**	91
11	2,3,5-Trimethylphenol **3l**	 **4l**	84
12	2,3,6-Trimethylphenol **3m**	 **4m**	93
13	2,4,6-Trimethylphenol **3n**	 **4n**	83

[a] Conditions: **3** (1 mmol), $PhNHSCF_3$ (**1**, 1.2–1.3 mmol), TfOH (1.2–5 mmol), DCM (10 mL), 14 h, rt. [b] Isolated yield.

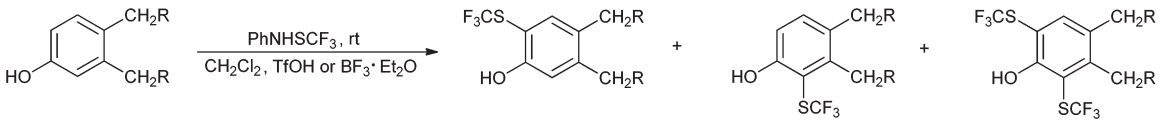
tion, while nitration was more selective in the case of 5,6,7,8-tetrahydro-2-naphthol (63 : 37).[59]

It is known that $PhNHSCF_3$ reacts with alkenes,[31] and so we examined the reactivity of 2-allylphenol (**7**) due to the two diverse potential reaction sites (Scheme 2). We established that **7** reacted with **1** in the presence of TfOH as both phenol and alkene, thus proposed a secondary carbocation intermediate **8**. The reaction proceeded in dichloromethane in the absence of a good nucleophile, and the phenolic oxygen atom took part in an intramolecular cyclization thus producing five-membered product **9** as a novel type of trifluoromethylthiolated product. It appears that the stability of **8** was of crucial importance for the reaction selectivity. The other possible product, a six-membered isomeric product originating from a reversed addition of $PhNHSCF_3$ to the double bond that would have generated a primary carbocation, was not observed. The structure of **9** was confirmed using NMR spectroscopy, and the key experiment was DEPT 135. The carbon atom attached to the SCF_3 group appeared as a quartet in the same phase with the second aliphatic signal, whereas the third aliphatic signal was in the opposite phase. This was a clear indication that the SCF_3 group was attached to the CH_2, and not to a CH group.

The reactivity of highly reactive bicyclic-, alkoxy- and hydroxyphenols with $PhNHSCF_3$ is summarized in Table 3.

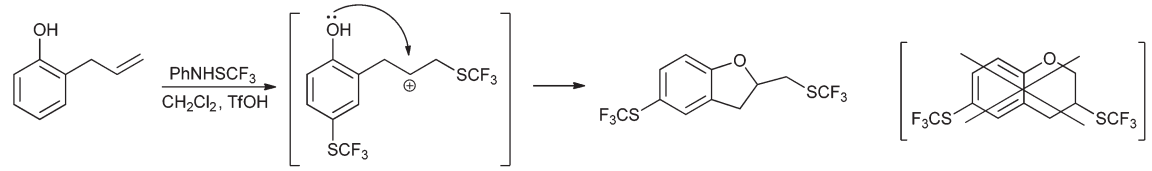
2-Methoxy-4-methylphenol (**10a**) produced 6-SCF_3 analogue **11a** as the sole product, while 2,6-dimethoxyphenol (**10b**) selectively yielded its 3-SCF_3 derivative **11b** (Table 3, entries 1 and 2). 5,6,7,8-Tetrahydro-1-naphthol (**10c**) was regioselectively transformed into its 4-SCF_3 analogue **11c** in good yield. The transformations of 1-naphthol (**10d**) and 2-naphthol (**10e**) were completely selective in both cases. The former led to its 4-SCF_3 derivative **11d**, whereas the latter led to its 1-SCF_3 analogue **11e** (entries 4 and 5). Additionally, 2,7-dihydroxynaphthalene (**10f**) was tested due to the possibility of double functionalization. Indeed, 1,8-diSCF_3 derivative **11f** was isolated as a single product in good yield. 2′,6′-dihydroxyacetophenone (**10g**) was smoothly converted into its 3-SCF_3 derivative **11g** (entry 7). In continuation, some naturally occurring phenols were successfully transformed into their trifluoromethylthio analogues. Catechol (**10h**) selectively produced its 4-SCF_3 derivative **11h**, and 4-methylcatechol (**10i**) yielded its 5-SCF_3 derivative **11i** exclusively (entries 8 and 9). Functionalization of resorcinol (**10j**) smoothly afforded its 4-SCF_3 analogue **11j** in a good yield. The highly oxidation-prone pyrogallol (**10k**) was also efficiently transformed into its 3-SCF_3 derivative **11k** (entry 11). It could be concluded that the reaction system of $PhNHSCF_3$/activator is compatible with highly electron-rich phenols and that introduction of the SCF_3 group took place efficiently without a noticeable amount of oxidation.

In addition, we tested some biologically relevant molecules possessing a phenolic functionality (Scheme 3). 3,4-(Methylenedioxy)phenol (**12a**) as a highly reactive substance afforded the corresponding 6-SCF_3 derivative **13a** as the sole product. The reaction was complete within 20 minutes, and the product, **13a**, was obtained in good yield. 6-Hydroxy-1,3-benzoxathiol-2-one (**12b**) was successfully converted into its 5-



5a R = H **6a/6a'** (94/6) **6a** R = H (88%) **6aa** R = H (0%) **6a'** R = H (6%)
5b R + R = CH_2 **6b/6bb** (100/0) **6b** R + R = CH_2 (95%) **6bb** R + R = CH_2 (0%)
5c R + R = $(CH_2)_2$ **6c/6cc** (56/44) **6c** R + R = $(CH_2)_2$ (39%) **6cc** R + R = $(CH_2)_2$ (31%)

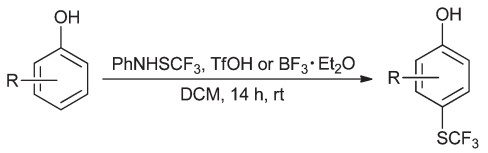
Scheme 1 The effect of the structure of 3,4-dialkyl substituted phenols on trifluoromethylthiolation.



7 **8** **9**

Scheme 2 The double functionalization of 2-allylphenol with $PhNHSCF_3$.

Table 3 Reactivity of highly electron-rich phenols with $PhNHSCF_3$ [a,b]



10 **11**

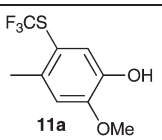
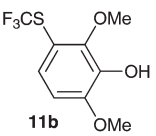
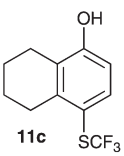
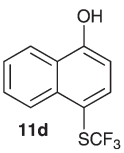
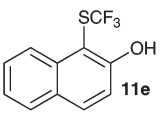
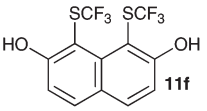
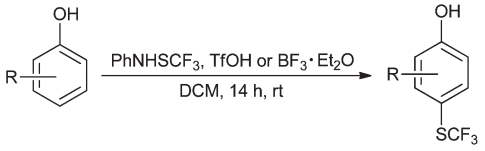
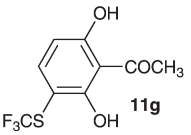
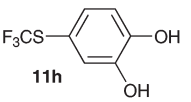
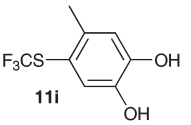
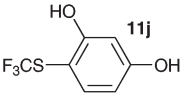
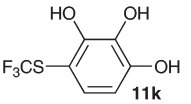
Entry	Reactant	Product	Yield[c] (%)
1	2-Methoxy-4-methylphenol **10a**	 **11a**	97
2	2,6-Dimethoxyphenol **10b**	 **11b**	84
3	5,6,7,8-Tetrahydronaphth-1-ol **10c**	 **11c**	93
4	1-Naphthol **10d**	 **11d**	95
5	2-Naphthol **10e**	 **11e**	82
6	2,7-Dihidroxynaphthalene **10f**	 **11f**	86

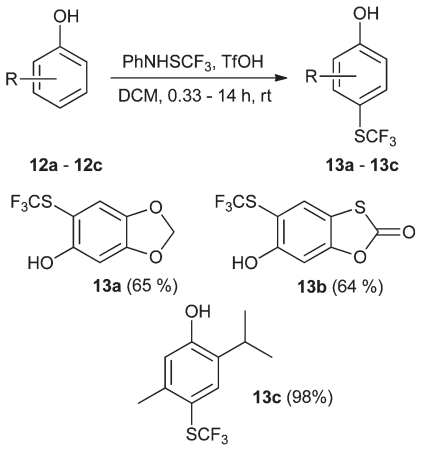
Table 3 *(Contd.)*



10 **11**

Entry	Reactant	Product	Yield[c] (%)
7	2′,6′-Dihydroxyacetophenone **10g**	 **11g**	79
8	Catechol **10h**	 **11h**	70
9	4-Methylcatechol **10i**	 **11i**	88
10	Resorcinol **10j**	 **11j**	80
11	Pyrogallol **10k**	 **11k**	60

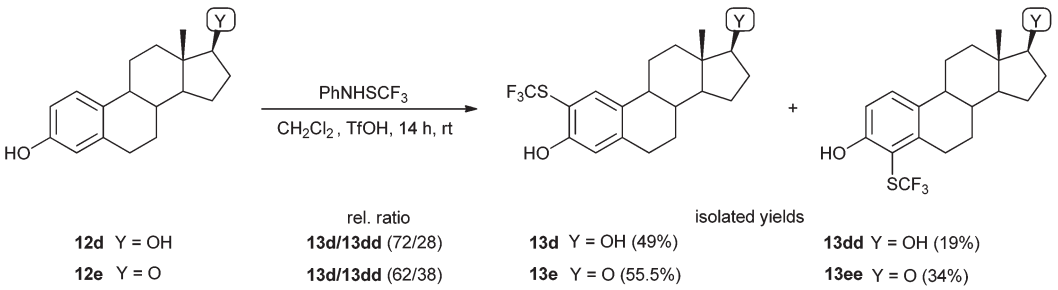
[a] Conditions: **10** (1 mmol), $PhNHSCF_3$ (**1**, 1.2–1.3 mmol), TfOH (1.3–4 mmol) or $BF_3{\cdot}Et_2O$ (**2**, 2–3 mmol), DCM (10 mL), 14 h, rt. [b] TfOH was used in entries 1, 2, 5, 6 and 7. $BF_3{\cdot}Et_2O$ was used in rest of the entries. [c] Isolated yield.



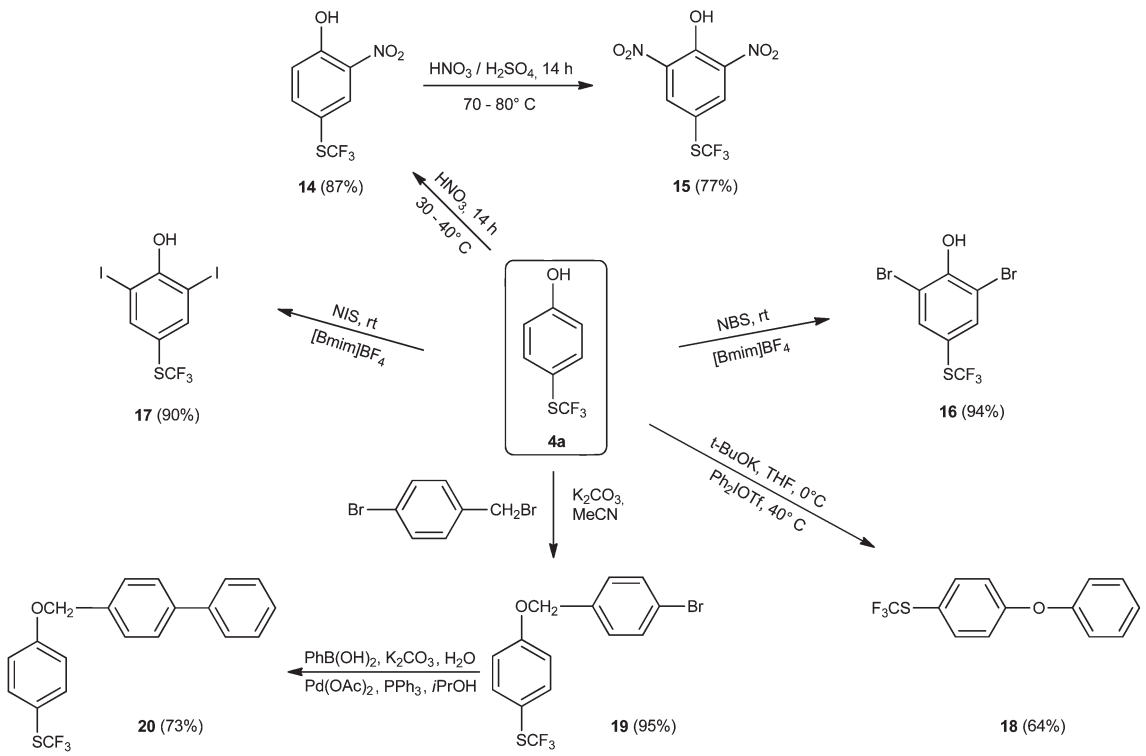
Scheme 3 The reactivity of some biologically active phenols with $PhNHSCF_3$.

SCF_3 derivative **13b** in spite of the acid-sensitive oxathiolone functional group. This is a good demonstration that the acidic reaction system is also compatible with sensitive functionalities. Thymol (**12c**) was effectively transformed into its 4-SCF_3 derivative **13c** in high yield. Estrone (**12d**) and estradiol (**12e**) are important steroid hormones bearing a phenolic functionality. Both were regioselectively transformed into the corresponding *o*-SCF_3 analogues (**13d**, **13dd**, and **13e**, **13ee**; Scheme 4). The regioselectivity of functionalization of estrone was similar to that of the nitration reaction;[59] however, the selectivity of trifluoromethylthiolation was higher in the case of estradiol.

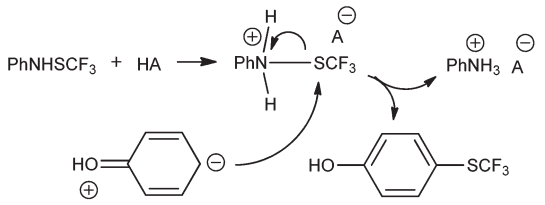
In addition, some further functionalizations of 4-(trifluoromethylthio)phenol (**4a**) were studied (Scheme 5). The strong electron-withdrawing nature of the trifluoromethylthio group significantly influences the reactivity of such compounds. **4a** was nitrated with 65% HNO_3 under solvent-free reaction conditions for 14 hours at 30–40 °C, selectively yielding mono-



Scheme 4 Electrophilic trifluoromethylthiolation of estrogenic hormones with $PhNHSCF_3$.



Scheme 5 The reactivity of 4-(trifluoromethylthio)phenol (**4a**) with different reagents.



Scheme 6 A plausible reaction mechanism.

nitrated product **14**, and no over-nitration took place. The reason for the perfect selectivity is that dinitration required considerably more rigorous reaction conditions to occur: 70–80° C and the presence of concentrated sulfuric acid. The dinitrophenol derivative **15** was isolated in a 78% yield. The introduction of halogens is highly significant because of the possibility for additional reactions, particularly various cross-couplings. Bromination of **4a** with NBS in 1-methyl-3-butylimidazolium tetrafluoroborate ([Bmim]BF_4) and in the presence of a small amount of water[60] afforded dibromo analogue **16** in 94% yield. Iodination was performed using the same reaction medium, producing diiodo derivative **17**. Preparation of diphenyl ether derivative **18** was accomplished using *t*-BuOK and diphenyliodonium triflate[61] in THF. Finally, **4a** was converted into its 4-bromobenzyl ether **19**, which reacted with phenyl boronic acid in the presence of $Pd(OAc)_2$ and PPh_3 to yield a cross-coupled derivative **20** in good yield.

The detailed reaction mechanism is not known; however, the most likely reaction pathway is an electrophilic one. The reaction selectivity for *para*- and *ortho*- positions is one of the strong arguments in favor of an electrophilic pathway. The reagent $PhNHSCF_3$ (**1**) is principally an amine and a relatively weak electrophilic reagent. The strong Brønsted acid TfOH seemingly protonates **1**, thus forming a corresponding salt with considerably more pronounced polarization between the nitrogen and sulfur atoms. The strong electron deficiency of the nitrogen atom presumably tends to attract electron density; thus resulting in a weaker C–S bond and a stronger sulfur electrophile able to react with phenols (Scheme 6).

Trifluoromethylthiolation of *m*-cresol in the presence of the free radical TEMPO[62,63] took place in the same manner as without TEMPO. This is another indication that a radical pathway is not very likely to be the chief reaction course.

Conclusions

In summary, we have developed a new highly regioselelective and efficient method for the trifluoromethylthiolation of phenols. The reaction pathway is most likely to be an electrophilic substitution pathway. The method is suitable for non-specialized laboratories because the transformation was accomplished with $PhNHSCF_3$ and without the extremely noxious CF_3SCl or $(CF_3)_2S$. An additional advantage was operational simplicity; specifically, the reactions were performed with non-dried dichloromethane in an air atmosphere at room temperature. The reaction selectivity was remarkably high; when both the *para*- and *ortho*- sites were unsubstituted, only *para*- functionalization took place. When the *para*- position was already substituted, functionalization of the *ortho*- site took place, and no *ipso*-substitution was noted. The reaction conditions were also demonstrated to be compatible with acid sensitive groups *i.e.* the thioxolone moiety.

Experimental section

General information

All transformations were carried out in untreated dichloromethane under an air atmosphere with stirring at room temperature. The starting phenols and other chemicals were obtained from commercial sources; $PhNHSCF_3$ **1** was prepared using the literature procedure.[30] The crude products were purified by column chromatography on silica gel (63–200 μm, 70–230 mesh ASTM; Fluka). TLC was performed on Merck-60-F_{254} plates using mixtures of hexane and diethyl ether. The melting points were determined in open-capillaries on Büchi 535 apparatus and are uncorrected. All products were characterized using ^1H, ^{13}C and ^{19}F NMR spectra, IR, HRMS and/or elemental analysis, and also using the melting points when solid. The ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300 DPX and Bruker Avance III 500 instruments, while the ^{19}F NMR spectra were only recorded on the latter instrument. Chemical shifts are reported in δ (ppm), values are relative to δ = 7.26 ppm in $CDCl_3$ or δ = 2.05 ppm in acetone-d_6 for ^1H NMR, and to the central peak of $CDCl_3$ (δ = 77.00 ppm) or the central peak of acetone-d_6 (δ = 30.83 ppm) for ^{13}C NMR. ^{19}F NMR spectra are referenced to $CFCl_3$ (δ = 0.00 ppm).

Representative procedure for the acid-promoted trifluoromethylthiolaton of phenols

To a solution of phenol (1 mmol, or 0.5 mmol in the case of the steroids) in dichloromethane (10 mL), $PhNHSCF_3$ (1.2–1.3 equiv.) was added along with a corresponding amount of triflic acid (1.2–5 equiv.) or $BF_3{\cdot}Et_2O$ (2–3 equiv.). The resulting mixture was stirred at room temperature for up to 16 h. In most cases, the starting phenol was fully consumed, as determined by TLC. The reaction mixture was diluted with 10 ml of dichloromethane, washed with a 10% solution of $NaHCO_3$, then water and then dried over anhydrous Na_2SO_4. The crude reaction mixture was subjected to column chromatography after removal of the solvent. In numerous cases, this was only a 'filtration' over silica gel, because of the excellent reaction selectivity.

Reactivity of 4a with different reagents

Reaction with HNO_3. To 4-(trifluoromethylthio)phenol (**4a**) (0.4 mmol, 77 mg), HNO_3 (65%, 1.6 mmol, 156 mg) was added and the resulting reaction mixture was stirred at 30–40 °C overnight. TLC revealed the full consumption of **4a**. The reaction mixture was cooled to room temperature, and the product was extracted three times using 5 mL of dichloromethane, washed

two times with water, and then dried over anhydrous Na_2SO_4. Pure product **14** (84 mg, 87%) was obtained as a yellow solid after column chromatography (hexane–diethyl ether).

Reaction with HNO_3/H_2SO_4. HNO_3 (65%, 1.6 mmol, 156 mg) was added to **4a** (0.4 mmol, 77 mg) and the resulting reaction mixture was stirred at 30–40 °C overnight. TLC revealed the full consumption of **4a**. HNO_3 (65%, 1.6 mmol, 156 mg) and concentrated H_2SO_4 (98%, 0.8 mmol, 80 mg) were then added and reaction mixture was stirred at 70–80 °C overnight. TLC showed the disappearance of the mononitro product. The reaction mixture was cooled to room temperature, and the product was extracted three times using 5 mL of dichloromethane and brine. The organic phase was dried over anhydrous Na_2SO_4, and the solvent evaporated. After column chromatography (hexane–diethyl ether), pure product **15** (88 mg, 77%) was obtained as a yellow solid.

Reaction with NBS in [Bmim]BF_4. The reaction was performed according to the reported procedure.[60] **4a** (0.3 mmol, 58 mg) reacted with *N*-bromosuccinimide (0.72 mmol, 128 mg) in 20 minutes. The crude reaction mixture was purified by chromatography (hexane–diethyl ether), and a yellowish solid product, **16** (98 mg, 94%), was obtained.

Reaction[60] with NIS in [Bmim]BF_4. The same reaction procedure and reagent amounts were used as in the case of NBS. From **4a** (0.3 mmol, 58 mg), after column chromatography **17** (120 mg, 90%) was obtained as a grey solid.

Reaction with Ph_2IOTf/*t*-BuOK. The transformation was performed according to the literature.[61] A solution of **4a** (0.4 mmol, 77 mg) in dry THF (1 mL) under an argon atmosphere was cooled to 0 °C and *t*-BuOK (0.5 mmol, 56 mg) was added, and then the mixture was stirred for 15 minutes at 0 °C. The reaction mixture was warmed to 40 °C, diphenyliodonium triflate (0.6 mmol, 258 mg) was added, and the mixture was stirred for three hours at 40 °C. The crude product was purified by chromatography (hexane–diethyl ether) and a colorless oily product, **18** (69 mg, 64%), was obtained.

Reaction with 4-bromobenzyl bromide/K_2CO_3. A mixture of **4a** (0.4 mmol, 77 mg), 4-bromobenzyl bromide (0.4 mmol, 100 mg) and K_2CO_3 (0.48 mmol, 66 mg) was stirred for one hour at 80 °C in acetonitrile. TLC showed consumption of the starting phenol **4a**. The reaction mixture was cooled to room temperature, and the solvent was removed under vacuum. The product was extracted three times using 5 mL of dichloromethane and water, and then dried over anhydrous Na_2SO_4. The solvent was removed and the product purified by chromatography (hexane–diethyl ether), thus giving a bright yellow product, **19** (137 mg, 95%).

Suzuki–Miyaura coupling. Phenylboronic acid (0.275 mmol, 33 mg) was added to a solution of **18** (0.25 mmol, 90 mg) in isopropanol (5 mL) and the mixture was purged with argon for 10 minutes. $Pd(OAc)_2$ (0.022 mmol, 5 mg), triphenylphosphine (0.095 mmol, 25 mg), a degassed solution of K_2CO_3 (1.5 mL, 2 M) and deionized water (1 mL) were added consecutively. The resulting mixture was stirred for 1 hour at reflux temperature, and TLC showed consumption of **18**. The mixture was cooled, concentrated under vacuum, and diluted with dichloromethane (10 mL) and water (10 mL). After separation of the phases, the aqueous phase was additionally extracted three times with 5 mL of dichloromethane. The combined organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent removed. The crude product was purified by chromatography (hexane–diethyl ether), thus yielding a white solid, **20** (66 mg, 73%).

Spectroscopic and analytical data

4-(Trifluoromethylthio)phenol 4a.[56] Colorless solid; mp 52.9–53.5 °C; (1 mmol **3a**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.23 (br s, 1H), 6.84–6.90 (m, 2H), 7.51–7.57 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 115.2 (q, J = 2.0 Hz), 116.5, 129.5 (q, J = 308.1 Hz), 138.6, 158.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.4 (s, SCF_3); IR: 3221, 1670, 1584, 1493, 1436, 1364, 1346, 1226, 1083, 826, 754, 650 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_7H_4F_3OS$ $(M - H)^-$ 192.9935, found 192.9945.

2-Methyl-4-(trifluoromethylthio)phenol 4b. Yellow, viscous liquid; (1 mmol **3b**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.26 (s, 3H), 5.07 (br s, 1H), 6.79 (d, J = 8.3 Hz, 1H), 7.38 (dd, J = 8.3, 1.8 Hz, 1H), 7.42 (d, J = 1.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.6, 114.7 (q, J = 1.7 Hz), 115.9, 125.3, 129.6 (q, J = 308.1 Hz), 136.0, 139.4, 156.3; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.4 (s, SCF_3); IR: 3409, 1588, 1495, 1401, 1261, 1087, 891, 814, 755 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_8H_6F_3OS$ $(M - H)^-$ 207.0097, found 207.0095.

3-Methyl-4-(trifluoromethylthio)phenol 4c. Orange, viscous liquid; (1 mmol **3c**, 1.3 mmol $PhNHSCF_3$, 1.2 mmol TfOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.49 (s, 3H), 5.13 (br s, 1H), 6.70 (dd, J = 8.4, 2.7 Hz, 1H), 6.80 (d, J = 2.7 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.3, 114.1, 114.8 (q, J = 1.5 Hz), 117.8, 129.8 (q, J = 308.6 Hz), 140.3, 146.4, 158.1; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.0 (s, SCF_3); IR: 3348, 1594, 1575, 1480, 1453, 1294, 1240, 1098, 1046, 947, 857, 812, 754, 731 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_8H_6F_3OS$ $(M - H)^-$ 207.0097, found 207.0095.

4-Methyl-2-(trifluoromethylthio)phenol 4d. Light yellow solid; mp 42.5–43.1 °C; (1 mmol **3d**, 1.3 mmol $PhNHSCF_3$, 2 mmol TfOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.30 (s, 3H), 6.14 (s, 1H), 6.97 (d, J = 8.4 Hz, 1H), 7.24 (dd, J = 8.4, 1.7 Hz, 1H), 7.36 (d, J = 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.2, 107.7 (q, J = 1.2 Hz), 115.9, 128.7 (q, J = 310.5 Hz), 130.9, 135.1, 138.0, 155.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.4 (s, SCF_3); IR: 3417, 1489, 1136, 1097, 1055, 825 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_8H_6F_3OS$ $(M - H)^-$ 207.0097, found 207.0094.

4-Isopropyl-2-(trifluoromethylthio)phenol 4e. White solid; mp 36.8–37.4 °C; (1 mmol **3e**, 1.3 mmol $PhNHSCF_3$, 2.0 mmol TfOH); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.23 (d, J = 6.9 Hz, 6H), 2.87 (septet, J = 6.9 Hz, 1H), 6.15 (br s, 1H), 7.00 (d, J = 8.5 Hz, 1H), 7.30 (dd, J = 8.5, 2.1 Hz, 1H), 7.40 (d, J = 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.0, 33.1, 107.7 (q, J = 1.2 Hz), 115.9, 128.8 (q, J = 310.5 Hz), 132.5, 135.6, 142.0, 156.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.4 (s, SCF_3); IR: 3429, 3410, 1487, 1467, 1456, 1283, 1183, 1103, 832, 728 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{10}H_{10}F_3OS$ $(M - H)^-$ 235.0410, found 235.0409.

2-*tert*-Butyl-4-(trifluoromethylthio)phenol 4f. Yellow, viscous liquid; (1 mmol **3f**, 1.3 mmol $PhNHSCF_3$, 1.2 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 1.41 (s, 9H), 5.15 (br s, 1H), 6.69 (d, J = 8.2 Hz, 1H), 7.37 (dd, J = 8.2, 2.2 Hz, 1H), 7.53 (d, J = 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 29.3, 34.7, 114.8 (d, J = 1.8 Hz), 117.5, 129.7 (q, J = 308.1 Hz), 135.7, 136.0, 137.6, 156.7; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.4 (s, SCF_3); IR: 3408, 2962, 1587, 1494, 1260, 1113, 1097, 1080, 815, 755 cm^{-1}; ESI-HRMS: m/z calcd for $C_{11}H_{12}F_3OS$ $(M - H)^-$ 249.0566, found 249.0566.

4-*tert*-Butyl-2-(trifluoromethylthio)phenol 4g. Yellow, viscous liquid; (1 mmol **3g**, 1.3 mmol $PhNHSCF_3$, 2 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 9H), 6.14 (br s, 1H), 7.00 (d, J = 8.6 Hz, 1H), 7.47 (dd, J = 8.6, 2.4, Hz, 1H), 7.54 (d, J = 2.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 31.3, 34.2, 107.5 (q, J = 1.1 Hz), 115.6, 128.8 (q, J = 310.5 Hz), 131.6, 134.7, 144.5, 155.8; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.4 (s, SCF_3); IR: 3507, 1490, 1365, 1103, 822, 755 cm^{-1}; ESI-HRMS: m/z calcd for $C_{11}H_{12}F_3OS$ $(M - H)^-$ 249.0561, found 249.0566.

2-Benzyl-4-(trifluoromethylthio)phenol 4h. Yellow, viscous liquid; (1 mmol **3h**, 1.3 mmol $PhNHSCF_3$, 1.5 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 3.98 (s, 2H), 5.12 (br s, 1H), 6.77–6.81 (m, 1H), 7.18–7.26 (m, 3H), 7.28–7.33 (m, 2H), 7.39–7.44 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 36.2, 115.1 (q, J = 1.9 Hz), 116.8, 126.7, 128.5, 128.6, 128.8, 129.6 (q, J = 308.1 Hz), 136.6, 138.8, 139.4, 156.3; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.4 (s, SCF_3); IR: 3523, 1587, 1494, 1453, 1411, 1091, 823, 729, 697 cm^{-1}; ESI-HRMS: m/z calcd for $C_{14}H_{10}F_3OS$ $(M - H)^-$ 283.0410, found 283.0410.

3-(Trifluoromethylthio)biphenyl-4-ol 4i. White solid; mp 101.6–101.9 °C; (1 mmol **3i**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 6.32 (br s, 1H), 7.16 (d, J = 8.5 Hz, 1H), 7.32–7.40 (m, 1H), 7.40–7.49 (m, 2H), 7.50–7.58 (m, 2H), 7.68 (dd, J = 8.5, 2.2 Hz, 1H), 7.81 (d, J = 2.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 108.7 (q, J = 1.2 Hz), 116.6, 126.7, 127.4, 128.7 (q, J = 310.7 Hz), 128.9, 133.0, 134.9, 136.5, 139.2, 157.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.2 (s, SCF_3); IR: 3408, 1602, 1473, 1334, 1194, 1155, 1132, 1100, 1055, 895, 860, 763, 738, 700 cm^{-1}; ESI-HRMS: m/z calcd for $C_{13}H_8F_3OS$ $(M - H)^-$ 269.0253, found 269.0253.

2,5-Dimethyl-4-(trifluoromethylthio)phenol 4j. Yellow, viscous liquid; (1 mmol **3j**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H), 2.45 (s, 3H), 4.91 (br s, 1H), 6.73 (s, 1H), 7.41 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 20.8, 114.3 (q, J = 1.6 Hz), 117.3, 122.6, 129.9 (q, J = 308.7 Hz), 141.1, 143.6, 156.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.0 (s, SCF_3); IR: 3602, 3412, 2866, 1395, 1377, 1256, 1222, 1094, 1017, 892, 852, 754, 625 cm^{-1}; ESI-HRMS: m/z calcd for $C_9H_8F_3OS$ $(M - H)^-$ 221.0253, found 221.0255.

2,6-Dimethyl-4-(trifluoromethylthio)phenol 4k. Yellow solid; mp 40.4–42.7 °C; (1 mmol **3k**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 2.26 (s, 6H), 4.91 (br s, 1H), 7.28 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.7, 113.9 (q, J = 1.8 Hz), 124.3, 129.7 (q, J = 308.0 Hz), 137.0, 154.7; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.4 (s, SCF_3); IR: 3613, 3449, 1586, 1473, 1330, 1153, 1093, 876, 754, 730 cm^{-1}; ESI-HRMS: m/z calcd for $C_9H_8F_3OS$ $(M - H)^-$ 221.0253, found 221.0253.

2,3,5-Trimethyl-4-(trifluoromethylthio)phenol 4l. White solid; mp 82.1–82.4 °C; (1 mmol **3l**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 2.19 (s, 3H), 2.50 (s, 3H), 2.55 (s, 3H), 5.02 (br s, 1H), 6.64 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.5, 19.1, 22.3, 115.0 (q, J = 1.2 Hz), 115.1, 121.7, 130.1 (q, J = 309.5 Hz), 144.0, 145.8, 155.5; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.5 (s, SCF_3); IR: 3321, 1690, 1575, 1446, 1298, 1097, 1076, 858, 846, 753 cm^{-1}; ESI-HRMS: m/z calcd for $C_{10}H_{10}F_3OS$ $(M - H)^-$ 235.0410, found 235.0411.

2,3,6-Trimethyl-4-(trifluoromethylthio)phenol 4m. Yellow solid; mp 51.6–54.2 °C (1 mmol **3m**, 1.3 mmol $PhNHSCF_3$, 1.2 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H), 2.23 (s, 3H), 2.48 (s, 3H), 4.89 (br s, 1H), 7.35 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.7, 15.5, 18.2, 114.2 (q, J = 1.5 Hz), 121.1, 123.4, 129.9 (q, J = 308.6 Hz), 138.0, 142.0, 154.6; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.3 (s, SCF_3); IR: 3477, 1465, 1400, 1213, 1184, 1144, 1100, 1020, 909, 754 cm^{-1}; ESI-HRMS: m/z calcd for $C_{10}H_{10}F_3OS$ $(M - H)^-$ 235.0410, found 235.0412.

2,4,6-Trimethyl-3-(trifluoromethylthio)phenol 4n. Light yellow solid; mp 75.5–76.4 °C; (1 mmol **3n**, 1.3 mmol $PhNHSCF_3$, 5 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 2.48 (s, 3H), 2.51 (s, 3H), 4.62 (br s, 1H), 6.99 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.9, 16.1, 21.6, 121.3 (q, J = 1.4 Hz), 126.9, 130.1, 130.1 (q, J = 309.4 Hz), 130.2, 137.0, 150.8; ^{19}F NMR (470 MHz, $CDCl_3$): δ −42.8 (s, SCF_3); IR: 3365, 1470, 1378, 1299, 1151, 1096, 998, 871, 801, 753 cm^{-1}; ESI-HRMS: m/z calcd for $C_{10}H_{10}F_3OS$ $(M - H)^-$ 235.0410, found 235.0408.

4,5-Dimethyl-2-(trifluoromethylthio)phenol 6a. White solid; mp 65.6–65.8 °C; (1 mmol **5a**, 1.3 mmol $PhNHSCF_3$, 1.2 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 2.20 (s, 3H), 2.26 (s, 3H), 6.06 (s, 1H), 6.88 (s, 1H), 7.30 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.6, 20.1, 104.5 (q, J = 1.2 Hz), 117.0, 128.8 (q, J = 310.6 Hz), 129.9, 138.2, 144.0, 156.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.8 (s, SCF_3); IR: 3398, 3372, 1480, 1313, 1210, 1145, 1101, 1022, 871 cm^{-1}; ESI-HRMS: m/z calcd for $C_9H_8F_3OS$ $(M - H)^-$ 221.0253, found 221.0250.

3,4-Dimethyl-2,6-bis(trifluoromethylthio)phenol 6a′. White solid; mp 48.5–48.9 °C; (1 mmol **5a**, 1.3 mmol $PhNHSCF_3$, 1.2 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 2.28 (s, 3H), 2.53 (s, 3H), 6.86 (s, 1H), 7.53 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.0, 20.1, 107.0 (q, J = 1.7 Hz), 110.9 (q, J = 1.3 Hz), 128.9 (q, J = 311.3 Hz), 129.1 (q, J = 310.1 Hz), 130.6, 142.7, 149.1, 158.7; ^{19}F NMR (470 MHz, $CDCl_3$): δ −42.6 (s, SCF_3), −43.2 (s, SCF_3); IR: 3455, 1440, 1391, 1271, 1092, 904, 755, 671 cm^{-1}; Anal Calcd for $C_{10}H_8F_6OS_2$: C, 37.27; H, 2.50. Found: C, 37.41; H, 2.48.

6-(Trifluoromethylthio)-2,3-dihydro-1*H*-inden-5-ol 6b. White solid; mp 73.7–74.5 °C; (1 mmol **5b**, 1.3 mmol $PhNHSCF_3$, 3 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.09 (quintet, J = 7.4 Hz, 2H), 2.85 (t, J = 7.4 Hz, 2H), 2.90 (t, J = 7.4 Hz, 2H), 6.19 (br s, 1H), 6.94 (s, 1H), 7.37 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.7, 31.7, 33.3, 105.1 (q, J = 1.2 Hz), 111.8, 128.8 (q, J = 310.7 Hz), 133.0, 137.3, 152.0, 156.6; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.9 (s, SCF_3); IR: 3418, 3401, 1471, 1440, 1430,

1330, 1129, 1103, 897, 879 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{10}H_8F_3OS$ $(M - H)^-$ 233.0248, found 233.0253.

3-(Trifluoromethylthio)-5,6,7,8-tetrahydronaphthalen-2-ol 6c. White solid; mp 52.8–53.0 °C; (1 mmol **5c**, 1.3 mmol $PhNHSCF_3$, 3 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.74–1.81 (m, 4H), 2.67–2.73 (m, 2H), 2.73–2.79 (m, 2H), 6.03 (br s, 1H), 6.78 (s, 1H), 7.25 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 22.6, 22.9, 28.3, 29.6, 105.0 (q, J = 1.1 Hz), 115.8, 128.8 (q, J = 310.5 Hz), 130.6, 138.2, 144.4, 155.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.7 (s, SCF_3); IR: 3411, 2941, 2857, 1612, 1564, 1476, 1210, 1129, 1099, 1031, 863, 754 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{11}H_{10}F_3OS$ $(M - H)^-$ 247.0410, found 247.0411.

1-(Trifluoromethylthio)-5,6,7,8-tetrahydronaphthalen-2-ol 6cc. White solid; mp 49.3–49.5 °C; (1 mmol **5c**, 1.3 mmol $PhNHSCF_3$, 3 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.72–1.85 (m, 4H), 2.69–2.74 (m, 2H), 2.92–2.97 (m, 2H), 6.39 (s, 1H), 6.87 (d, J = 8.4 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 22.5, 22.9, 28.8, 29.1, 107.8, 113.1, 128.9 (q, J = 311.7 Hz), 130.6, 134.9, 143.2, 156.6; ^{19}F NMR (470 MHz, $CDCl_3$): δ −42.2 (s, SCF_3); IR: 3422, 2938, 1592, 1579, 1471, 1430, 1303, 1204, 1146, 1128, 1094, 832, 818, 752, 734 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{11}H_{10}F_3OS$ $(M - H)^-$ 247.0410, found 247.0410.

5-(Trifluoromethylthio)-2-((trifluoromethylthio)methyl)-2,3-dihydrobenzofuran 9. Yellow, viscous liquid; (1 mmol **7**, 2.5 mmol $PhNHSCF_3$, 4 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 3.08 (dd, J = 16.1, 6.6 Hz, 1H), 3.16 (dd, J = 14.0, 6.3 Hz, 1H), 3.28 (dd, J = 14.0, 6.3 Hz, 1H), 3.46 (dd, J = 16.1, 9.2 Hz, 1H), 5.05–5.13 (m, 1H), 6.82 (d, J = 8.1 Hz, 1H), 7.42–7.47 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 34.2, 81.6, 110.7, 115.2 (d, J = 1.9 Hz), 127.4, 129.6 (q, J = 308.2 Hz), 130.7 (q, J = 306.4 Hz), 133.6, 137.9, 161.3; ^{19}F NMR (470 MHz, $CDCl_3$): δ −41.4 (s, SCF_3), −44.5 (s, SCF_3); IR: 1604, 1589, 1474, 1237, 1092, 974, 819, 755 cm^{-1}; Anal Calcd for $C_{11}H_8F_6OS_2$: C, 39.52; H: 2.41. Found: C, 39.30; H, 2.34.

2-Methoxy-4-methyl-5-(trifluoromethylthio)phenol 11a. Light yellow solid; mp 51.9–52.1 °C; (1 mmol **10a**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 2.47 (s, 3H), 3.91 (s, 3H), 5.49 (br s, 1H), 6.79 (s, 1H), 7.21 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.8, 55.9, 112.6, 114.4 (q, J = 1.5 Hz), 123.6, 129.8 (q, J = 308.8 Hz), 136.7, 143.8, 148.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.7 (s, SCF_3); IR: 3343, 1580, 1266, 1135, 1100, 1043, 872, 850, 817, 753 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_9H_8F_3O_2S$ $(M - H)^-$ 237.0203, found 237.0200.

2,6-Dimethoxy-3-(trifluoromethylthio)phenol 11b. Brown solid; mp 44.7–46.5 °C; (1 mmol **10b**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 3H), 3.97 (s, 3H), 5.66 (br s, 1H), 6.69 (d, J = 8.7 Hz, 1H), 7.16 (d, J = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 56.3, 61.2, 106.7, 109.5 (d, J = 1.8 Hz), 129.0, 129.4 (q, J = 308.7 Hz), 139.2, 148.9, 150.5; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.6 (s, SCF_3); IR: 3523, 3371, 1594, 1489, 1469, 1439, 1294, 1219, 1083, 892, 796 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_9H_8F_3O_3S$ $(M - H)^-$ 253.0152, found 253.0151.

4-(Trifluoromethylthio)-5,6,7,8-tetrahydronaphthalen-1-ol 11c. Grey solid; mp 65.2–67.5 °C; (1 mmol **10c**, 1.3 mmol $PhNHSCF_3$, 3 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (500 MHz, $CDCl_3$): δ 1.76–1.86 (m, 4H), 2.61–2.67 (m, 2H), 2.93–2.99 (m, 2H), 5.04 (br s, 1H), 6.66 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 22.0, 22.5, 23.2, 28.9, 112.8, 114.7 (q, J = 1.5 Hz), 125.3, 129.8 (q, J = 308.7 Hz), 137.1, 144.7, 156.1; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.8 (s, SCF_3); IR: 3590, 3461, 1573, 1456, 1440, 1416, 1073, 1029, 819, 805, 750 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{11}H_{10}F_3OS$ $(M - H)^-$ 247.0410, found 247.0411.

4-(Trifluoromethylthio)naphthalen-1-ol 11d. Gray solid; mp 64.8–67.2 °C; (1 mmol **10d**, 1.3 mmol $PhNHSCF_3$, 3 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (300 MHz, $CDCl_3$): δ 6.84 (d, J = 7.9 Hz, 1H), 7.54–7.61 (m, 1H), 7.64–7.71 (m, 1H), 7.82 (d, J = 7.9 Hz, 1H), 8.23–8.29 (dd, J = 8.3, 0.5 Hz, 1H), 8.47–8.53 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 108.6, 112.5 (q, J = 1.5 Hz), 122.3, 125.1, 125.9, 126.0, 128.2, 129.6 (q, J = 309.5 Hz), 136.7, 138.7, 155.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.8 (s, SCF_3); IR: 3346, 1591, 1569, 1510, 1348, 1158, 1092, 1047, 830, 763, 753 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{11}H_6F_3OS$ $(M - H)^-$ 243.0097, found 243.0096.

1-(Trifluoromethylthio)naphthalen-2-ol 11e. Light yellow solid; mp 91.8–92.2 °C (lit.[56] 88.8–90.7 °C); (1 mmol **10e**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 6.92 (br s, 1H), 7.30 (d, J = 9.0 Hz, 1H), 7.39–7.47 (m, 1H), 7.58–7.67 (m, 1H), 7.77–7.85 (m, 1H), 7.95 (d, J = 9.0 Hz, 1H), 8.30–8.36 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 100.8 (q, J = 0.6 Hz), 117.1, 124.3, 124.4, 128.4, 128.5, 128.8 (q, J = 312.8 Hz), 129.4, 134.9, 135.8, 158.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −42.3 (s, SCF_3); IR: 3415, 1618, 1591, 1569, 1462, 1384, 1196, 1146, 1125, 1101, 1029, 867, 772, 655 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{11}H_6F_3OS$ $(M - H)^-$ 243.0097, found 243.0097.

1,8-Bis(trifluoromethylthio)naphthalene-2,7-diol 11f. Light orange solid; mp 90.3–91.4 °C; (1 mmol **10f**, 2.4 $PhNHSCF_3$, 4.0 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, J = 8.8 Hz, 2H), 7.71 (s, 2H), 7.87 (d, J = 8.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 99.9, 115.0, 125.9, 128.5 (q, J = 312.8 Hz), 136.5, 137.2, 161.7; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.5 (s, SCF_3); IR: 3411, 1607, 1514, 1430, 1355, 1155, 1084, 841, 752 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_{12}H_5F_6O_2S_2$ $(M - H)^-$ 358.9641, found 358.9650.

1-(2,6-Dihydroxy-3-(trifluoromethylthio)phenyl)ethanone 11g. Yellow solid; mp 114.7–117.5 °C; (1 mmol **10g**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 2.77 (s, 3H), 6.60 (d, J = 8.8 Hz, 1H), 7.58 (br s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 13.40 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.5, 98.2 (q, J = 1.5 Hz), 110.0, 111.9, 128.4 (q, J = 311.7 Hz), 144.1, 160.7, 168.1, 204.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.4 (s, SCF_3); IR: 3343, 1622, 1581, 1472, 1440, 1373, 1245, 1235, 1158, 1120, 1097, 1042, 963, 903, 819, 656 cm^{-1}; ESI-HRMS: *m*/*z* calcd for $C_9H_6F_3O_3S$ $(M - H)^-$ 250.9995, found 250.9994.

4-(Trifluoromethylthio)benzene-1,2-diol 11h. White solid; mp 67.8–69.0 °C; (1 mmol **10h**, 1.3 mmol $PhNHSCF_3$,

2.0 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (500 MHz, $CDCl_3$): δ 5.60 (br s, 1H), 5.78 (br s, 1H), 6.90 (d, J = 8.2 Hz, 1H), 7.14 (dd, J = 8.2, 1.8 Hz, 1H), 7.18 (d, J = 1.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 115.1 (q, J = 2.0 Hz), 116.0, 123.3, 129.5 (q, J = 308.2 Hz), 130.5, 143.6, 146.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.3 (s, SCF_3); IR: 3533, 3486, 3349, 1593, 1507, 1276, 1245, 1124, 1100, 811, 782 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_4F_3O_2S$ $(M - H)^-$ 208.9890, found 208.9889.

4-Methyl-5-(trifluoromethylthio)benzene-1,2-diol 11i. White solid; mp 71.1–71.5 °C; (1 mmol **10i**, 1.3 mmol $PhNHSCF_3$, 2.0 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (500 MHz, $CDCl_3$): δ 2.42 (s, 1H), 5.25 (br s, 1H), 5.61 (br s, 1H), 6.84 (s, 1H), 7.17 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.4, 113.9 (q, J = 1.6 Hz), 117.5, 124.8, 129.8 (q, J = 308.8 Hz), 138.1, 141.3, 146.6; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.9 (s, SCF_3); IR: 3284, 1593, 1508, 1447, 1272, 1094, 875, 866, 816 cm^{-1}; ESI-HRMS: m/z calcd for $C_8H_6F_3O_2S$ $(M - H)^-$ 223.0046, found 223.0045.

4-(Trifluoromethylthio)benzene-1,3-diol 11j. White solid; mp 48.5–49.7 °C; (1 mmol **10j**, 1.3 mmol $PhNHSCF_3$, 3.0 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.16 (br s, 1H), 6.30 (br s, 1H), 6.47 (dd, J = 8.5, 2.7 Hz, 1H), 6.54 (d, J = 2.7 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 99.6 (q, J = 1.1 Hz), 102.9, 109.6, 128.6 (q, J = 310.9 Hz), 139.4, 159.4, 160.8; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.5 (s, SCF_3); IR: 3645, 3492, 3338, 1592, 1473, 1324, 1134, 1094, 1057, 968, 843, 809 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_4F_3O_2S$ $(M - H)^-$ 208.9890, found 208.9889.

4-(Trifluoromethylthio)benzene-1,2,3-triol 11k. Brown solid; mp 82.0–84.9 °C; (1 mmol **10k**, 1.3 mmol $PhNHSCF_3$, 2.0 mmol $BF_3{\cdot}Et_2O$); ^1H NMR (300 MHz, $CDCl_3$/acetone-d_6): δ 6.47 (d, J = 8.6 Hz, 1H), 6.92 (d, J = 8.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$/acetone-d_6): δ 99.2 (q, J = 1.7 Hz), 108.4, 128.9 (q, J = 310.2 Hz), 129.4, 131.9, 147.0, 148.5; ^{19}F NMR (470 MHz, $CDCl_3$/acetone-d_6): δ −44.3 (s, SCF_3); IR: 3507, 3484, 3397, 3218, 1601, 1503, 1460, 1291, 1267, 1090, 1007, 888, 800, 754, 657 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_4F_3O_3S$ $(M - H)^-$ 224.9839, found 224.9838.

6-(Trifluoromethylthio)benzo[*d*][1,3]dioxol-5-ol 13a. Light yellow solid; mp 82.2–82.7 °C; (1 mmol **12a**, 1.3 mmol $PhNHSCF_3$, 1.3 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 5.99 (s, 2H), 6.18 (br s, 1H), 6.59 (s, 1H), 6.94 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 97.7, 102.0, 115.0, 128.6 (q, J = 311.5 Hz), 142.0, 152.7, 154.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.5 (s, SCF_3); IR: 3433, 1614, 1496, 1470, 1160, 1099, 1030, 930, 871, 830, 754, 713 cm^{-1}; ESI-HRMS: m/z calcd for $C_8H_4F_3O_3S$ $(M - H)^-$ 236.9839, found 236.9840.

6-Hydroxy-5-(trifluoromethylthio)benzo[*d*][1,3]oxathiol-2-one 13b. Light yellow solid; mp 128.9–131.7 °C; (1 mmol **12b**, 1.3 mmol $PhNHSCF_3$, 4.0 mmol TfOH); ^1H NMR (500 MHz, acetone-d_6): δ 7.12 (s, 1H), 7.96 (s, 1H), 9.93 (br s, 1H); ^{13}C NMR (125 MHz, acetone-d_6): δ 102.4, 108.6 (q, J = 1.5 Hz), 115.7, 131.5 (q, J = 308.4 Hz), 134.3, 153.7, 161.7, 170.6; ^{19}F NMR (470 MHz, acetone-d_6): δ −43.0 (s, SCF_3); IR: 3416, 1732, 1603, 1454, 1428, 1327, 1145, 1090, 1032, 1013, 881, 865 cm^{-1}; ESI-HRMS: m/z calcd for $C_8H_2F_3O_3S_2$ $(M - H)^-$ 266.9403, found 266.9404.

2-Isopropyl-5-methyl-4-(trifluoromethylthio)phenol 13c. Colorless, viscous liquid; (1.0 mmol **12c**, 1.3 mmol $PhNHSCF_3$, 2.0 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 1.25 (d, J = 6.9 Hz, 6H), 2.44 (s, 3H), 3.14 (septet, J = 6.9 Hz, 1H), 4.95 (br s, 1H), 6.70 (s, 1H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.7, 22.4, 26.8, 114.7 (q, J = 1.7 Hz), 117.7, 129.9 (q, J = 308.7 Hz), 133.4, 137.1, 143.1, 155.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.0 (s, SCF_3); IR: 3422, 1397, 1256, 1152, 1095, 1070, 736 cm^{-1}; ESI-HRMS: m/z calcd for $C_{11}H_{12}F_3OS$ $(M - H)^-$ 249.0566, found 249.0567.

(13*S*)-13-Methyl-2-(trifluoromethylthio)-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol 13d. White solid; mp 96.1–98.9 °C; (0.5 mmol **12d**; 0.65 mmol $PhNHSCF_3$, 0.65 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.79 (s, 3H), 1.10–1.60 (m, 8H), 1.63–1.77 (m, 1H), 1.83–2.02 (m, 2H), 2.06–2.22 (m, 2H), 2.24–2.35 (m, 1H), 2.81–2.91 (m, 2H), 3.74 (t, J = 8.4 Hz, 1H), 6.04 (br s, 1H), 6.79 (s, 1H), 7.44 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.0, 23.1, 26.2, 26.8, 29.6, 30.5, 36.5, 38.4, 43.2, 43.6, 49.9, 81.8, 105.1 (q, J = 0.9 Hz), 115.8, 128.8 (q, J = 310.6 Hz), 134.1, 135.0, 144.2, 155.6; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.7 (s, SCF_3); IR: 3318, 2921, 2867, 1560, 1447, 1102, 1055, 1011, 797 cm^{-1}; ESI-HRMS: m/z calcd for $C_{19}H_{22}F_3O_2S$ $(M - H)^-$ 371.1298, found 371.1303.

(13*S*)-13-Methyl-4-(trifluoromethylthio)-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthrene-3,17-diol 13dd. White solid; mp 84.8–87.5 °C; (0.5 mmol **12d**; 0.65 mmol $PhNHSCF_3$, 0.65 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 0.78 (s, 3H), 1.14–1.22 (m, 1H), 1.23–1.43 (m, 5H), 1.43–1.55 (m, 2H), 1.67–1.76 (m, 1H), 1.92–2.00 (m, 2H), 2.08–2.22 (m, 2H), 2.25–2.33 (m, 1H), 2.84–2.95 (m, 1H), 3.14–3.22 (m, 1H), 3.74 (t, J = 8.5 Hz, 1H), 6.43 (br s, 1H), 6.91 (d, J = 8.6 Hz, 1H), 7.40 (d, J = 8.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.0, 23.0, 26.4, 27.0, 29.2, 30.6, 36.6, 38.0, 43.2, 44.1, 49.9, 81.8, 108.0, 113.0, 128.9 (q, J = 311.8 Hz), 131.1, 134.0, 143.2, 156.5; ^{19}F NMR (470 MHz, $CDCl_3$): δ −42.0 (s, SCF_3); IR: 3645, 3455, 2938, 2857, 1572, 1352, 1156, 1114, 1098, 1009, 821, 802, 755 cm^{-1}; ESI-HRMS: m/z calcd for $C_{19}H_{22}F_3O_2S$ $(M - H)^-$ 371.1298, found 371.1307.

(13*S*)-3-Hydroxy-13-methyl-2-(trifluoromethylthio)-7,8,9,11,12,13,15,16-octahydro-6*H*-cyclopenta[*a*]phenanthren-17(14*H*)-one 13e. White solid; mp 160.4–160.9 °C; (0.5 mmol **12e**, 0.65 mmol $PhNHSCF_3$, 0.65 mmol TfOH); ^1H NMR (300 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.34–1.74 (m, 6H), 1.90–2.30 (m, 5H), 2.34–2.43 (m, 1H), 2.45–2.58 (m, 1H), 2.85–2.97 (m, 2H), 6.09 (br s, 1H), 6.81 (s, 1H), 7.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 21.5, 25.8, 26.2, 29.5, 31.4, 35.8, 37.9, 43.6, 47.9, 50.4, 105.4 (q, J = 1.2 Hz), 115.9, 128.8 (q, J = 310.6 Hz), 133.5, 135.0, 143.9, 155.8, 220.5; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.7 (s, SCF_3); IR: 3323, 1723, 1601, 1502, 1410, 1103, 895, 877, 674 cm^{-1}; ESI-HRMS: m/z calcd for $C_{19}H_{20}F_3O_2S$ $(M - H)^-$ 369.1142, found 369.1141.

(13*S*)-3-Hydroxy-13-methyl-4-(trifluoromethylthio)-7,8,9,11,12,13,15,16-octahydro-6*H*-cyclopenta[*a*]phenanthren-17(14*H*)-one 13ee. White solid; mp 171.7–172.7 °C; (0.5 mmol **12e**, 0.65 mmol $PhNHSCF_3$, 0.65 mmol TfOH); ^1H NMR (500 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.37–1.58 (m, 5H), 1.59–1.70 (m, 1H),

1.93–2.00 (m, 1H), 2.02–2.11 (m, 2H), 2.11–2.20 (m, 1H), 2.21–2.29 (m, 1H), 2.34–2.42 (m, 1H), 2.48–2.66 (m, 1H), 2.89–3.00 (m, 1H), 3.21–3.28 (m, 1H), 6.44 (br s, 1H), 6.92 (d, J = 8.7 Hz, 1H), 7.40 (d, J = 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.8, 21.5, 26.0, 26.3, 29.0, 31.5, 35.8, 37.5, 44.1, 47.9, 50.3, 108.0, 113.2, 128.9 (q, J = 311.8 Hz), 131.1, 133.4, 143.0, 156.7, 220.7; ^{19}F NMR (470 MHz, $CDCl_3$): δ −41.9 (s, SCF_3); IR: 3396, 1732, 1471, 1154, 1118, 1092, 824, 754 cm^{-1}; ESI-HRMS: m/z calcd for $C_{19}H_{20}F_3O_2S$ $(M - H)^-$ 369.1142, found 369.1143.

2-Nitro-4-(trifluoromethylthio)phenol 14. Yellow solid; mp 51.6–52.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 (d, J = 8.8 Hz, 1H), 7.84 (dd, J = 8.8, 2.2 Hz, 1H), 8.45 (d, J = 2.2 Hz, 1H), 10.77 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 115.7 (q, J = 2.3 Hz), 121.5, 129.1 (q, J = 308.8 Hz), 133.6, 133.7, 144.8, 156.9; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.7 (s, SCF_3); IR: 3256, 1614, 1519, 1474, 1413, 1316, 1243, 1150, 1108, 1088, 1072, 848, 672 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_3F_3NO_3S$ $(M - H)^-$ 237.9791, found 237.9792.

2,6-Dinitro-4-(trifluoromethylthio)phenol 15. Yellow solid; decomp., 170 °C; ^{1}H NMR (500 MHz, acetone-d_6): δ 8.38 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6): δ 106.8, 131.3 (q, J = 308.0 Hz), 140.1, 143.5, 158.4; ^{19}F NMR (470 MHz, acetone-d_6): δ −44.0 (s, SCF_3); IR: 3438, 3091, 1624, 1527, 1338, 1252, 1136, 1090, 913, 776, 724, 683 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_2F_3N_2O_5S$ $(M - H)^-$ 282.9642, found 282.9643.

2,6-Dibromo-4-(trifluoromethylthio)phenol 16. Yellow solid; mp 51.3–53.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.23 (br s, 1H), 7.77 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 110.2, 117.2 (q, J = 2.2 Hz), 129.1 (q, J = 308.9 Hz), 139.7, 152.1; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.8 (s, SCF_3); IR: 3459, 1452, 1383, 1325, 1159, 1094, 877, 735, 709 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_2Br_2F_3OS$ $(M - H)^-$ 348.8151, found 348.8152.

2,6-Diiodo-4-(trifluoromethylthio)phenol 17. Gray solid; mp 86.0–87.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.05 (br s, 1H), 7.97 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 82.2, 118.3 (q, J = 2.0 Hz), 129.1 (q, J = 308.9 Hz), 146.7, 156.1; ^{19}F NMR (470 MHz, $CDCl_3$): δ −43.8 (s, SCF_3); IR: 3439, 1440, 1375, 1302, 1105, 895, 753, 699 cm^{-1}; ESI-HRMS: m/z calcd for $C_7H_2F_3I_2OS$ $(M - H)^-$ 444.7873, found 444.7883.

(4-Phenoxyphenyl)(trifluoromethyl)sulfane 18. Colorless, viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.96–7.03 (m, 2H), 7.04–7.10 (m, 2H), 7.16–7.23 (m, 1H), 7.35–7.44 (m, 2H), 7.56–7.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 117.2 (q, J = 1.9 Hz), 118.6, 120.1, 124.6, 129.5 (q, J = 308.2 Hz), 130.0, 138.3, 155.5, 160.4; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.1 (s, SCF_3); IR: 1581, 1485, 1240, 1110, 1081, 869, 834, 754, 692 cm^{-1}; Anal Calcd for $C_{13}H_9F_3OS$: C, 57.77; H, 3.36. Found: C, 57.73; H, 3.09.

(4-(4-Bromobenzyloxy)phenyl)(trifluoromethyl)sulfane 19. Light yellow solid; mp 54.8–55.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.04 (s, 2H), 6.96–7.00 (m, 2H), 7.30 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.56–7.60 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 69.4, 115.4 (q, J = 1.9 Hz), 115.8, 122.2, 129.1, 129.6 (q, J = 308.2 Hz), 131.8, 135.2, 138.3, 160.7; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.3 (s, SCF_3); IR: 1590, 1494, 1453, 1411, 1377, 1251, 1107, 1088, 1042, 1012, 831, 809, 799, cm^{-1}; ESI-HRMS: m/z calcd for $C_{14}H_9BrF_3OS$ $(M - H)^-$ 360.9515, found 360.9522.

(4-(Biphenyl-4-ylmethoxy)phenyl)(trifluoromethyl)sulfane 20. White solid; mp 107.0–108.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.14 (s, 2H), 7.01–7.07 (m, 2H), 7.33–7.41 (m, 1H), 7.42–7.54 (m, 4H), 7.57–7. 67 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 69.9, 115.2 (q, J = 1.9 Hz), 115.8, 127.1, 127.5, 128.0, 128.8, 129.6 (q, J = 308.2 Hz), 135.1, 138.3, 140.6, 141.3, 161.0; ^{19}F NMR (470 MHz, $CDCl_3$): δ −44.3 (s, SCF_3); IR: 1589, 1491, 1380, 1247, 1106, 1083, 1028, 1005, 826, 763, 700 cm^{-1}; ESI-HRMS: m/z calcd for $C_{20}H_{14}F_3OS$ $(M - H)^-$ 359.0723, found 359.0720.

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References

1 W. K. Hagmann, *J. Med. Chem.*, 2008, **51**, 4359–4369.
2 K. Müller, C. Faeh and F. Diederich, *Science*, 2007, **317**, 1881–1886.
3 P. Kirsch, *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*, Wiley-VCH, Weinheim, 2006.
4 *Modern Fluoropolymers: High Performance Polymers for Diverse Applications*, ed. J. Scheirs, John Wiley & Sons, Chichester, 2000.
5 W. Grot, *Fluorinated Ionomers*, Elsevier, Oxford, 2011.
6 J. A. Gladysz, D. P. Curran and I. T. Horváth, *Handbook of Fluorous Chemistry*, Wiley-VCH, Weinheim, 2004.
7 A. M. Thayer, *Chem. Eng. News*, 2006, **84**, 15–25.
8 K. L. Kirk, *J. Fluorine Chem.*, 2006, **127**, 1013–1029.
9 D. O'Hagan, *J. Fluorine Chem.*, 2010, **131**, 1071–1081.
10 J.-P. Bégué and D. Bonnet-Delpon, *J. Fluorine Chem.*, 2006, **127**, 992–1012.
11 S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320–330.
12 (*a*) Z. Jin, G. B. Hammond and B. Xu, *Aldrichimica Acta*, 2012, **45**, 67–83; (*b*) H. Egami and M. Sodeoka, *Angew. Chem., Int. Ed.*, 2014, **53**, 8294–8308.
13 J.-A. Ma and D. Cahard, *Chem. Rev.*, 2008, **108**, PR1–PR43.
14 N. Shibata, A. Matsnev and D. Cahard, *Beilstein J. Org. Chem.*, 2010, **6**, 65.
15 O. A. Tomashenko and V. V. Grushin, *Chem. Rev.*, 2011, **111**, 4475–4521.
16 A. Studer, *Angew. Chem., Int. Ed.*, 2012, **51**, 8950–8958.
17 (*a*) P. Chen and G. Liu, *Synthesis*, 2013, 2919–2939; (*b*) G. Landelle, A. Panossian, S. Pazenok, J.-P. Vors and F. R. Leroux, *Beilstein J. Org. Chem.*, 2013, **9**, 2476–2536.

18 X.-F. Wu, H. Neumann and M. Beller, *Chem. – Asian J.*, 2012, **7**, 1744–1754.
19 L. Chu and F.-L. Qing, *Acc. Chem. Res.*, 2014, **47**, 1513–1522.
20 G. Landelle, A. Panossian and F. R. Leroux, *Curr. Top. Med. Chem.*, 2014, **14**, 941–951.
21 K. Fauster, C. Kreutz and R. Micura, *Angew. Chem., Int. Ed.*, 2012, **51**, 13080–13084.
22 (*a*) F. Toulgoat, S. Alazet and T. Billard, *Eur. J. Org. Chem.*, 2014, 2415–2428; (*b*) A. Tlili and T. Billard, *Angew. Chem., Int. Ed.*, 2013, **52**, 6818–6819.
23 S. Munavalli, D. K. Rohrbaugh, D. I. Rossman and H. D. Durst, *J. Fluorine Chem.*, 1999, **98**, 3–9.
24 L. Dieu, I. Popov and O. Daugulis, *J. Am. Chem. Soc.*, 2012, **134**, 18237–18240.
25 V. N. Boiko, *Beilstein J. Org. Chem.*, 2010, **6**, 880–921.
26 (*a*) D. J. Adams, A. Goddard, J. H. Clark and D. J. Macquarrie, *Chem. Commun.*, 2000, 987–988; (*b*) M. Hu, J. Rong, W. Miao, C. Ni, Y. Han and J. Hu, *Org. Lett.*, 2014, **16**, 2030–2033; (*c*) M. Rueping, N. Tolstoluzhsky and P. Nikolaienko, *Chem. – Eur. J.*, 2013, **19**, 14043–14046; (*d*) G. Danoun, B. Bayarmagnai, M. F. Gruenberg and L. J. Goossen, *Chem. Sci.*, 2014, **5**, 1312–1316; (*e*) Q. Lefebvre, E. Fava, P. Nikolaienko and M. Rueping, *Chem. Commun.*, 2014, **50**, 6617–6619; (*f*) D. Kong, Z. Jiang, S. Xin, Z. Bai, Y. Yuan and Z. Weng, *Tetrahedron*, 2013, **69**, 6046–6050; (*g*) P. Zhu, X. He, X. Chen, Y. You, Y. Yuan and Z. Weng, *Tetrahedron*, 2014, **70**, 672–677; (*h*) Z. Weng, W. He, C. Chen, R. Lee, D. Tan, Z. Lai, D. Kong, Y. Yuan and K.-W. Huang, *Angew. Chem., Int. Ed.*, 2013, **52**, 1548–1552; (*i*) Z. Wang, Q. Tu and Z. Weng, *J. Organomet. Chem.*, 2014, **751**, 830–834; (*j*) B. Bayarmagnai, C. Matheis, E. Risto and L. J. Goossen, *Adv. Synth. Catal.*, 2014, **356**, 2343–2348.
27 (*a*) Q. Xiao, J. Sheng, Q. Ding and J. Wu, *Eur. J. Org. Chem.*, 2014, 217–221; (*b*) F. Yin and X.-S. Wang, *Org. Lett.*, 2014, **16**, 1128–1131; (*c*) X. Wang, Y. Zhou, G. Ji, G. Wu, M. Li, Y. Zhang and J. Wang, *Eur. J. Org. Chem.*, 2014, 3093–3096; (*d*) G. Teverovskiy, D. S. Surry and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2011, **50**, 7312–7314; (*e*) D. J. Adams and J. H. Clark, *J. Org. Chem.*, 2000, **65**, 1456–1460; (*f*) C. Chen, X.-H. Xu, B. Yang and F.-L. Qing, *Org. Lett.*, 2014, **16**, 3372–3375.
28 (*a*) C.-P. Zhang and D. A. Vicic, *J. Am. Chem. Soc.*, 2012, **134**, 183–185; (*b*) C.-P. Zhang and D. A. Vicic, *Chem. – Asian J.*, 2012, **7**, 1756–1758.
29 See, for example: (*a*) C. Pooput, M. Medebielle and W. R. Dolbier Jr., *Org. Lett.*, 2004, **6**, 301–303; (*b*) I. Kieltsch, P. Eisenberger and A. Togni, *Angew. Chem., Int. Ed.*, 2007, **46**, 754–757; (*c*) N. Santschi and A. Togni, *J. Org. Chem.*, 2011, **76**, 4189–4193; (*d*) S. Capone, I. Kieltsch, O. Flögel, G. Lelais, A. Togni and D. Seebach, *Helv. Chim. Acta*, 2008, **91**, 2035–2056; (*e*) C. Chen, Y. Xie, L. Chu, R.-W. Wang, X. Zhang and F.-L. Qing, *Angew. Chem., Int. Ed.*, 2012, **51**, 2492–2495; (*f*) C. Chen, L. Chu and F.-L. Qing, *J. Am. Chem. Soc.*, 2012, **134**, 12454–12457; (*g*) L. Zhai, Y. Li, J. Yin, K. Jin, R. Zhang, X. Fu and C. Duan, *Tetrahedron*, 2013, **69**, 10262–10266; (*h*) V. N. Movchun, A. A. Kolomeitsev and Y. L. Yagupolskii, *J. Fluorine Chem.*, 1995, **70**, 255–257; (*i*) T. Billard, S. Large and B. R. Langlois, *Tetrahedron Lett.*, 1997, **38**, 65–68; (*j*) Y. Huang, X. He, X. Lin, M. Rong and Z. Weng, *Org. Lett.*, 2014, **16**, 3284–3287.
30 A. Ferry, T. Billard, B. R. Langlois and E. Bacqué, *J. Org. Chem.*, 2008, **73**, 9362–9365.
31 A. Ferry, T. Billard, B. R. Langlois and E. Bacqué, *Angew. Chem., Int. Ed.*, 2009, **48**, 8551–8555.
32 A. Ferry, T. Billard, E. Bacqué and B. R. Langlois, *J. Fluorine Chem.*, 2012, **134**, 160–163.
33 Y. Yang, X. Jiang and F.-L. Qing, *J. Org. Chem.*, 2012, **77**, 7538–7547.
34 F. Baert, J. Colomb and T. Billard, *Angew. Chem., Int. Ed.*, 2012, **51**, 10382–10385.
35 S. Alazet, K. Ollivier and T. Billard, *Beilstein J. Org. Chem.*, 2013, **9**, 2354–2357.
36 J. Liu, L. Chu and F.-L. Qing, *Org. Lett.*, 2013, **15**, 894–897.
37 S. Alazet, L. Zimmer and T. Billard, *Angew. Chem., Int. Ed.*, 2013, **52**, 10814–10817.
38 J. Sheng, S. Li and J. Wu, *Chem. Commun.*, 2014, **50**, 578–580.
39 J. Sheng, C. Fan and J. Wu, *Chem. Commun.*, 2014, **50**, 5494–5496.
40 Y. Li, G. Li and Q. Ding, *Eur. J. Org. Chem.*, 2014, 5017–5022.
41 Q. Xiao, J. Sheng, Z. Chen and J. Wu, *Chem. Commun.*, 2013, **49**, 8647–8649.
42 Y.-D. Yang, A. Azuma, E. Tokunaga, M. Yamasaki, M. Shiro and N. Shibata, *J. Am. Chem. Soc.*, 2013, **135**, 8782–8785.
43 C. Xu and Q. Shen, *Org. Lett.*, 2014, **16**, 2046–2049.
44 S.-Q. Zhu, X.-H. Xu and F.-L. Qing, *Eur. J. Org. Chem.*, 2014, 4453–4456.
45 X. Shao, X. Wang, T. Yang, L. Lu and Q. Shen, *Angew. Chem., Int. Ed.*, 2013, **52**, 3457–3460.
46 E. V. Vinogradova, P. Müller and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2014, **53**, 3125–3128.
47 X. Shao, T. Liu, L. Lu and Q. Shen, *Org. Lett.*, 2014, **16**, 4738–4741.
48 F. Hu, X. Shao, D. Zhu, L. Lu and Q. Shen, *Angew. Chem., Int. Ed.*, 2014, **53**, 6105–6109.
49 H. He and X. Zhu, *Org. Lett.*, 2014, **16**, 3102–3105.
50 (*a*) X. Wang, T. Yang, X. Cheng and Q. Shen, *Angew. Chem., Int. Ed.*, 2013, **52**, 12860–12864; (*b*) Q.-H. Deng, C. Rettenmeier, H. Wadepohl and L. H. Gade, *Chem. – Eur. J.*, 2014, **20**, 93–97.
51 (*a*) T. Bootwicha, X. Liu, R. Pluta, I. Atodiresei and M. Rueping, *Angew. Chem., Int. Ed.*, 2013, **52**, 12856–12859; (*b*) M. Rueping, X. Liu, T. Bootwicha, R. Pluta and C. Merkens, *Chem. Commun.*, 2014, **50**, 2508–2511.
52 X.-L. Zhu, J.-H. Xu, D.-J. Cheng, L.-J. Zhao, X.-Y. Liu and B. Tan, *Org. Lett.*, 2014, **16**, 2192–2195.
53 H. Xiang and C. Yang, *Org. Lett.*, 2014, **16**, 5686–5689.
54 S. Alazet, L. Zimmer and T. Billard, *Chem. – Eur. J.*, 2014, **20**, 8589–8593.

55 S. Alazet and T. Billard, *Synlett*, 2015, 76–78.
56 C. Xu, B. Ma and Q. Shen, *Angew. Chem., Int. Ed.*, 2014, **53**, 9316–9320.
57 W. H. Mills and I. G. Nixon, *J. Chem. Soc.*, 1930, 2510–2524.
58 J. L. G. Nilsson, H. Selander, H. Sievertsson, I. Skånberg and K.-G. Svensson, *Acta Chem. Scand.*, 1971, **25**, 94–100.
59 M. Jereb, *Curr. Org. Chem.*, 2013, **17**, 1694–1700.
60 R.-Y. Tang, P. Zhong and Q.-L. Lin, *J. Fluorine Chem.*, 2007, **128**, 636–640.
61 N. Jalalian, T. B. Petersen and B. Olofsson, *Chem. – Eur. J.*, 2012, **18**, 14140–14149.
62 W. Kong, M. Casimiro, N. Fuentes, E. Merino and C. Nevado, *Angew. Chem., Int. Ed.*, 2013, **52**, 13086–13090.
63 E. Pair, N. Monteiro, D. Bouyssi and O. Baudoin, *Angew. Chem., Int. Ed.*, 2013, **52**, 5346–5349.