

Deoxygenative perfluoroalkylthiolation of carboxylic acids with benzothiazolium reagents

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ABSTRACT

Deoxygenative perfluoroalkylthiolation reactions of readily available carboxylic acid derivatives have been developed using a series of 2-(perfluoroalkylthio)benzothiazolium (BT-SR_F) reagents as convenient sources of perfluoroalkylthiolate anions. This method avoids pre-activation of the substrates and delivers rarely reported perfluoroalkyl thioesters featuring SR_F groups up to C₆F₁₃. A survey of carboxylic acid substrates with the pentafluoroethylthiolating reagent BT-SC₂F₅ also revealed the generality of the approach as a method for accessing underexplored fluorinated compounds.

1. Introduction

Fluorinated organic compounds play an important role in the pharmaceutical, agrochemical and materials science industries, due to their ability to modulate the physical and chemical properties of a molecule. In recent years, chemists have sought to expand the repertoire of fluorinated groups incorporated into drugs and other valuable structures [1–11]. The trifluoromethylthio (SCF₃) group, for example, can impart remarkable hydrophobic properties on a parent molecule while exerting a strong electron withdrawing influence on nearby functional groups.

While recent years have seen a resurgence in interest in the SCF₃ group [12–16], studies on longer chain perfluoroalkyl derivatives are surprisingly scarce. Nevertheless, a selection of SR_F-containing molecules (R_F = C_nF_{2n+1}, *n* > 1) have found applications in liquid crystals [17,18], while some intriguing studies on pharmaceutical and agrochemical structures suggest perfluoroalkylthio motifs such as SC₂F₅, S(*n*-C₃F₇) and S(*n*-C₄F₉) could also find roles in these fields [19,20]. Direct comparisons of drug molecules featuring CF₃ and C₂F₅ groups have been conducted and several examples have been identified, wherein the higher perfluoroalkyl homologue results in improved pharmacological properties [21–23]. While further studies would be required to determine whether such an effect is maintained in fluoroalkylthio moieties,

the potential for modulating a pharmaceutical's performance in this way is an intriguing prospect.

Perfluoroalkylthio groups are most commonly prepared through perfluoroalkylthiolation of the corresponding thiol, disulfide or thiocyanide (Scheme 1a) [19,24–29]. In many cases, however, direct installation of the entire SR_F motif in a perfluoroalkylthiolation process is more desirable as these reactions do not require pre-functionalisation of the substrate with a sulfur atom. Unfortunately, such methods are scarce in the literature and, while there have been some successful reports of direct electrophilic perfluoroalkylthiolation [30–37], nucleophilic approaches are very challenging due to the low nucleophilicity of perfluoroalkylthiolate anions and their relative instability towards β-fluoride elimination [38–41].

In 2019, our group introduced the benzothiazolium reagent BT-SCF₃ as an easily accessible and practical reagent for conducting nucleophilic trifluoromethylthiolation reactions [42,43]. Moreover, by employing longer chain perfluoroalkyl iodides in place of CF₃I in the reagent synthesis, we were able to prepare several BT-SR_F derivatives featuring a range of different perfluoroalkyl groups (Scheme 1b) [44]. These salts are easy to handle under standard organic laboratory conditions and a systematic study on their reactivity in nucleophilic deoxyperfluoroalkylthiolation reactions of activated alkyl alcohols revealed their

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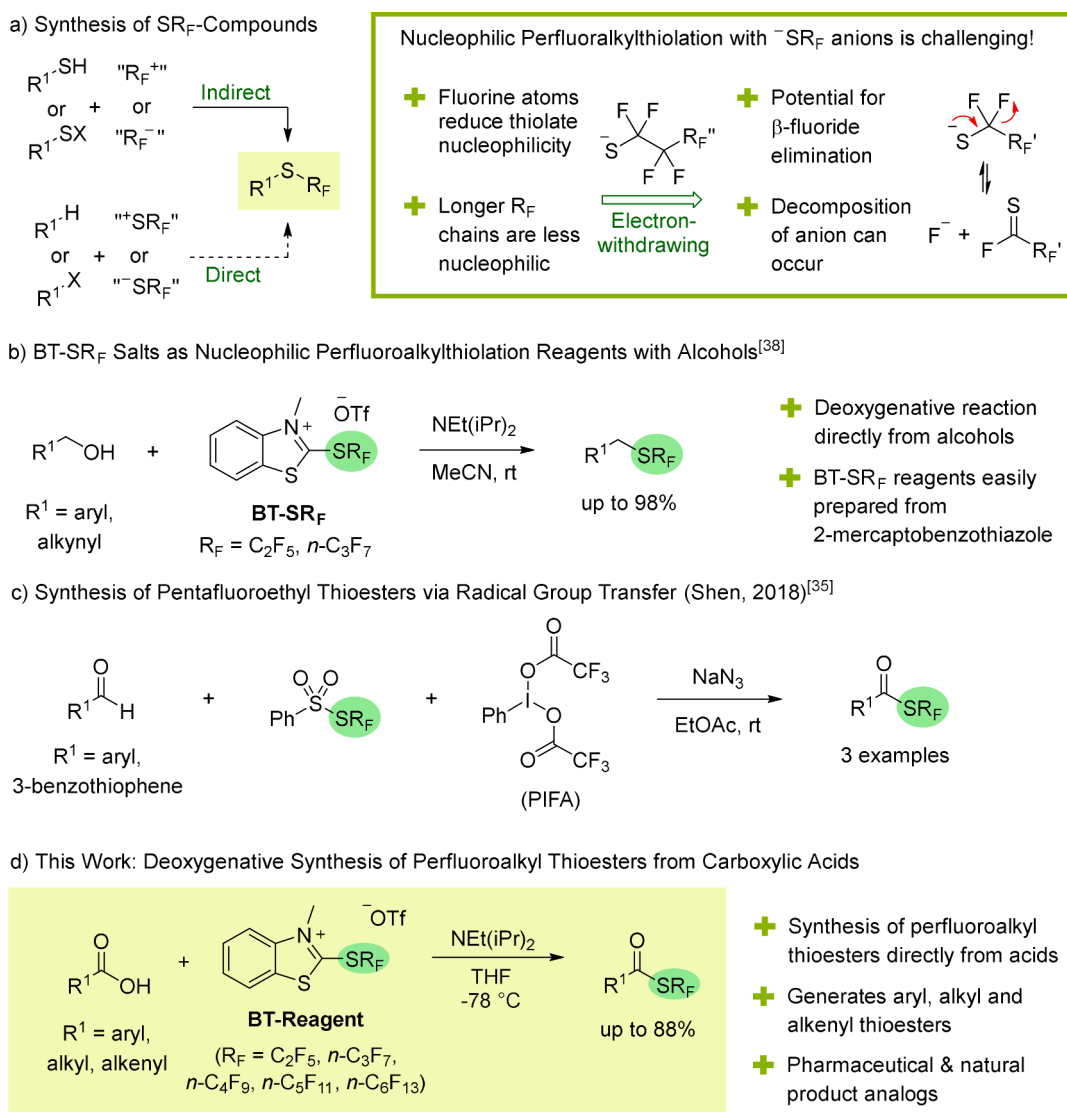
competence in nucleophilic substitution reactions [45,46].

Inspired by this success, we considered whether BT-SR_F reagents could provide easy access to other classes of perfluoroalkylthiolated molecules. In previous work, we have demonstrated that BT-SCF₃ can efficiently convert readily available carboxylic acids into the corresponding trifluoromethyl thioesters [47,48]. An analogous process with BT-SR_F reagents would deliver perfluoroalkyl thioesters in one step without requiring pre-activation of the acid. Despite their potential as useful fluorine-containing feedstocks for medicinal and agrochemistry and, conceivably, as highly electron deficient acyl electrophiles for organic synthesis, examples of longer chain perfluoroalkyl thioesters are scarce in the literature. As part of a larger study on fluorinated thioesters in 2018, the Shen group reported the synthesis of three pentafluoroethyl thioesters from the corresponding aldehydes employing PhSO₂SC₂F₅ as an SC₂F₅ radical transfer reagent (Scheme 1c) [41]. Studies exploring the synthesis and properties of a wider range of thioesters, including those featuring perfluoroalkyl groups other than SC₂F₅ are, however, lacking and, to the best of our knowledge, there are no known nucleophilic methods affording thioesters from formal perfluoroalkylthiolate anion sources. In this work we report the successful development of a deoxygenative perfluoroalkylthiolation reaction affording thioesters

directly from unactivated carboxylic acids (Scheme 1d).

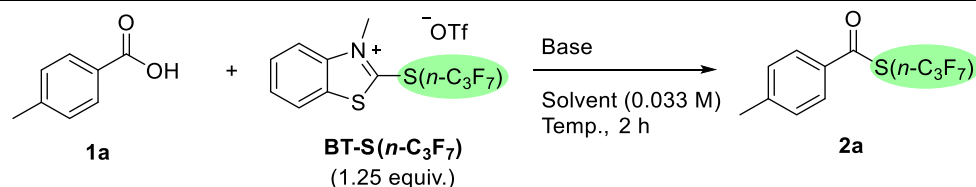
2. Results and discussion

At the start of the study, we sought to validate the proposed reactivity. 4-Methylbenzoic acid (**1a**) was selected as a representative carboxylic acid while BT-S(*n*-C₃F₇), which had been prepared previously, was employed as the benzothiazolium reagent. These compounds were duly reacted under the conditions optimised for the deoxygenative trifluoromethylthiolation process using BT-SCF₃ previously developed by our group (Table 1, Entry 1): **1a** (1.0 equiv.), BT-S(*n*-C₃F₇) (1.25 equiv.), NaH (3.0 equiv.), THF (0.03 M), -78 °C, 2 h). Disappointingly, ¹H and ¹⁹F NMR analysis of the crude mixture revealed a complex reaction mixture with no appreciable formation of the desired heptafluoropropyl thioester product **2a**. Increasing the reaction temperature to rt had no beneficial effect with **2a** being identified only in trace amounts (Entry 2). Upon switching the base additive from NaH to NEt(*i*-Pr)₂ (1.0 equiv.), however, new peaks consistent with a heptafluoropropyl thioester were observed indicating that **2a** had been formed in 22 % ¹⁹F NMR yield (internal standard: PhCF₃, Entry 3). Encouraged by this promising result, a short optimisation was carried out (Table 1).



Scheme 1. Synthesis of perfluoroalkyl thioesters. a) Traditional nucleophilic approaches to thioesters. b) BT-SR_F reagents as nucleophilic reagents for installing fluoroalkylthio groups^[44]. c) Synthesis of pentafluoroethyl thioesters from aldehydes by Shen and co-workers^[41]. d) This work: deoxygenative perfluoroalkylthiolation of carboxylic acids with BT-SR_F reagents.

Table 1
Optimisation of the deoxygenative heptafluoropropylthiolation process.



Entry ^a	Base	Solvent	Temp.	¹⁹ F NMR Yield of 2a ^b
1	NaH (3 equiv.)	THF	−78 °C	—
2	NaH (3 equiv.)	THF	rt	trace
3	NEt(<i>i</i> -Pr) ₂ (1 equiv.)	THF	rt	22 %
4	NEt(<i>i</i> -Pr) ₂ (1 equiv.)	THF	−78 °C	55 %
5 ^c	NEt(<i>i</i> -Pr) ₂ (1 equiv.)	THF	−78 °C	63 %
6 ^c	NEt(<i>i</i> -Pr) ₂ (1 equiv.)	1,4-Dioxane	−78 °C	15 %
7 ^c	NEt(<i>i</i> -Pr) ₂ (1 equiv.)	Et ₂ O	−78 °C	32 %
8 ^{c,d}	NEt(<i>i</i> -Pr) ₂ (1 equiv.)	THF	−78 °C	81 % (50 %)

^a Conditions: **1a** (0.1 mmol, 1.0 equiv.), BT-SR_F (0.125 mmol, 1.25 equiv.) and base (0.1–0.3 mmol, 1.0–3.0 equiv.) stirred in the designated solvent (3.0 mL) for 2 h at the stated temperature.

^b ¹⁹F NMR yields determined using PhCF₃ as an internal standard.

^c Solution of **1a** and NEt(*i*-Pr)₂ in THF (1.5 mL) added slowly to solution of BT-S(*n*-C₃F₇) in THF (1.5 mL) over 15 mins.

^d 2 equiv. of BT-S(*n*-C₃F₇).

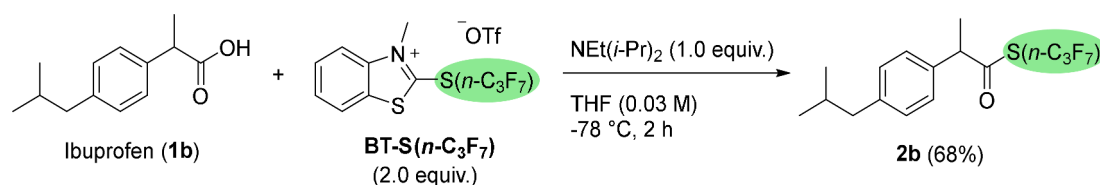
Reducing the temperature back down to −78 °C led to an increase in NMR yield of 55 % while slow addition of a solution of **1a** and the base to the BT-reagent over 15 min resulted in a further rise to 63 % (Entries 4,5). While a survey of alternative ether solvents did not lead to an improvement in yield (Entries 6,7), increasing the stoichiometry of BT-S(*n*-C₃F₇) to 2 equivalents delivered **2a** in an excellent NMR yield of 81 % (Entry 8). Upon purification by column chromatography, some decomposition was observed, however **2a** could be isolated in 50 % yield and unambiguously characterised. Hypothesising that aliphatic perfluoroalkylthioesters may be less prone to hydrolysis-induced decomposition than aryl derivatives, we selected the common painkiller ibuprofen **1b** and reacted it under the same optimised conditions. After 2 h at −78 °C, ¹⁹F NMR indicated the formation of a heptafluoropropyl thioester in 76 % yield with isolation via column chromatography proceeding smoothly to afford pure **2b** in 68 % yield (Scheme 2).

As the first nucleophilic and first deoxygenative route to perfluoroalkyl thioesters with R_F groups longer than CF₃, we next sought to investigate the generality of the approach for accessing novel thioesters with different perfluoroalkyl chains. As a result, six additional benzothiazolium reagents alongside BT-S(*n*-C₃F₇) were selected; five linear BT-SR_F derivatives (BT-SC₂F₅, BT-S(*n*-C₄F₉), BT-S(*n*-C₅F₁₁), BT-S(*n*-C₆F₁₃) and BT-(*n*-SC₈F₁₇)) and the heptafluoroisopropyl species BT-S(*i*-C₃F₇), which would allow for an evaluation of sterically more demanding groups. While most of the reagents were reported in our prior study, BT-S(*n*-C₄F₉) and BT-(*n*-C₆F₁₃) had not been prepared before and these compounds were synthesised according to the general two step method developed in our group (Scheme 3)[42–44]. Firstly, the BT-SR_F precursors **3** and **4** were synthesised via UVA-light induced radical trifluoromethylation of inexpensive 2-mercaptobenzothiazole (MBT) with the corresponding perfluoroalkyl iodide (I-R_F) in the presence of sodium hydride. *N*-Methylation with methyl trifluoromethanesulfonate then delivered the BT-SR_F reagents, which after trituration with diethyl ether, were obtained as off-white solids in 41 and 72 % yield, respectively over two steps.

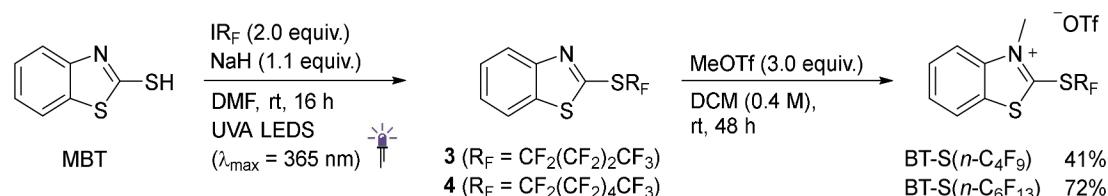
The synthesised BT-SR_F reagents were then tested in the deoxygenative perfluoroalkylthiolation reaction with ibuprofen (**1b**, Table 2). Among the seven BT-reagents employed, five reacted successfully to afford the corresponding perfluoroalkyl thioester in at least moderate ¹⁹F NMR yields (>50 %, Entries 1–5). The success of these reactions

demonstrates the ability of BT-SR_F to facilitate access to hitherto scarcely reported and underexplored fluorinated thioester compounds. A noticeable, if somewhat irregular, trend in the reaction efficiency was observed, however, with the ¹⁹F NMR yield of thioesters generally decreasing with longer perfluoroalkyl chains. For example, while the SC₂F₅ compound **5b** was formed in 79 % ¹⁹F NMR yield, the S(*n*-C₆F₁₃)-containing thioester **8b** was obtained in only 58 % ¹⁹F NMR yield. The reaction with BT-S(*n*-C₈F₁₇) was altogether unsuccessful, delivering a complex mixture of products with only traces of the corresponding thioester (Entry 6). A similar trend was observed previously in reactions of BT-SR_F salts with benzylic alcohols where decreasing yields of perfluoroalkyl thioethers were obtained in correlation with increasing chain length. These observations likely result from the lower nucleophilicity of perfluoroalkylthiolate species containing higher numbers of electron withdrawing fluorine atoms. Longer chain perfluoroalkyl-containing thioesters were also found to be less stable to attempted isolation via column chromatography with likely hydrolysis or other nucleophilic decomposition pathways occurring on silica. While thioesters **5b** and **2b** could be isolated successfully, from S(*n*-C₄F₉) onwards, increasing amounts of inseparable impurities with NMR signals consistent with the corresponding acid fluorides were obtained. The lack of reactivity observed with the perfluoroisopropyl benzothiazolium reagent BT-(*i*-C₃F₇) is consistent with the expected lower nucleophilicity of this comparatively sterically encumbered fluoroalkylthio group (Entry 7).

Informed by DFT calculations conducted as part of our previous work on related tri- and difluoromethylthiolation reactions of carboxylic acids, we tentatively propose that the perfluoroalkylthiolation reactions proceed via a concerted mechanism of the kind shown in Scheme 4. Initial attack of the carboxylate anion to the 2-position of the BT-reagent affords intermediate **A**, which then collapses into the product and the thiocarbamate by-product **B** via a 4-membered transition state. This mechanism avoids the formation of discrete perfluoroalkylthiolate anions, which could otherwise decompose into the corresponding thiocarbamyl fluorides via β-fluoride elimination. Indeed, side-products potentially resulting from such pathways were increasingly observed in the crude reaction mixtures of reactions with longer chain BT-SR_F reagents. For example, acid fluorides, which have been shown to result from β-fluoride elimination of Me₄NSCF₃ by Schoenebeck and co-



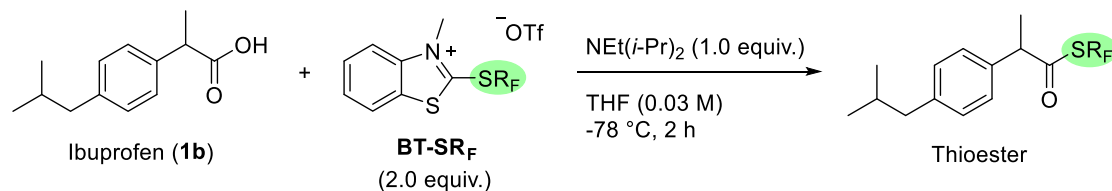
Scheme 2. Synthesis of heptafluoropropyl thioester **2b** from ibuprofen **1b**. (Conditions from Table 1, Entry 8).



Scheme 3. Two-step synthesis of BT-SR_F reagents from MBT.

Table 2

Deoxygenative perfluoroalkylthiolation of ibuprofen **1b** with different BT-SR_F reagents.



Entry ^a	R _F	Thioester ^b
1	CF ₂ CF ₃	5b : 79 %
2	CF ₂ CF ₂ CF ₃	2b : 76 %
3	CF ₂ (CF ₂) ₂ CF ₃	6b : 61 %
4	CF ₂ (CF ₂) ₃ CF ₃	7b : 51 %
5	CF ₂ (CF ₂) ₄ CF ₃	8b : 58 %
6	CF ₂ (CF ₂) ₆ CF ₃	Traces
7	CF(CF ₃) ₂	Traces

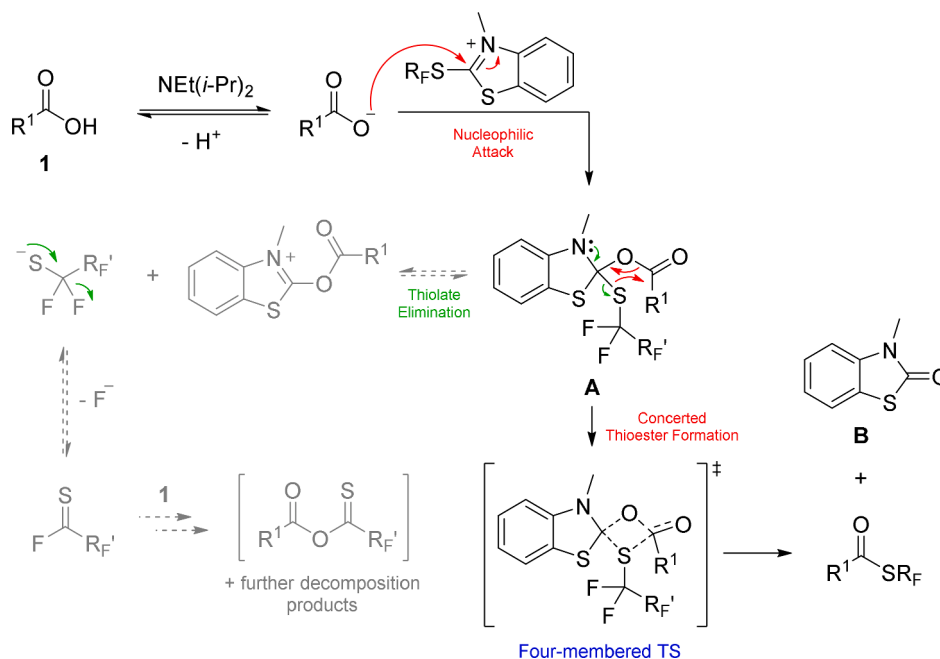
^a Conditions: **1b** (0.1 mmol, 1.0 equiv.) and NEt(*i*-Pr)₂ (0.1 mmol, 1.0 equiv.) in THF (1.5 mL) added slowly over 15 mins to solution of BT-SR_F (0.2 mmol, 2.0 equiv.) in THF (1.5 mL) at -78 °C. Mixture stirred for 2 h.

^b ¹⁹F NMR yields determined using PhCF₃ as an internal standard.

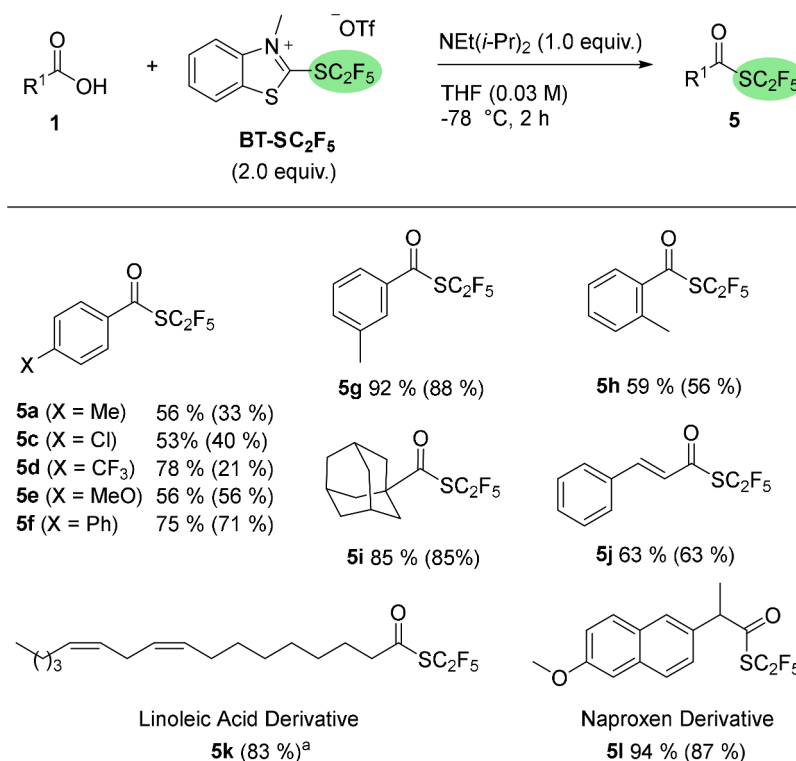
workers were often observed as minor by-products while ¹⁹F NMR signals consistent with thioic acid anhydride species were also observed. Notably, the reaction between ibuprofen **1b** and BT-(*n*-SC₈F₁₇) did not provide the corresponding perfluoroalkyl thioester but instead led to a complex mixture of decomposition products including the acid fluoride (Entry 6). A further possible reason for the decreasing yields of thioester obtained with longer chain perfluoroalkylthio groups is their likely lower stability towards hydrolysis. With increasing fluorine content, the thioesters would be expected to be increasingly susceptible to nucleophilic attack by water at the carbonyl carbon, which could in turn regenerate the carboxylic acid starting material and subsequently form acid fluorides, thioic acid anhydrides and other side-products. Decomposition in this way was indeed observed to varying extents during isolation and attempted characterisation of the thioester products including for example with **2a** as described above.

Having established the feasibility of the deoxygenative perfluoroalkylthiolation reaction with ibuprofen, we next explored the scope of the process with a range of different carboxylic acid substrates. As SC₂F₅ groups arguably hold most promise as substituents in biologically relevant compounds and also proved most efficient among the different perfluoroalkylthio moieties tested above, we focused our attention on the pentafluoroethylthiolation process. A selection of

different carboxylic acids **1** were reacted under the optimised conditions with BT-SC₂F₅ (2.0 equiv.) and NEt(*i*-Pr)₂ (1.0 equiv.) in THF at -78 °C for 2 h (Scheme 5). In analogy to the results obtained using BT-S(*n*-C₃F₇), deoxypentafluoroethylthiolation of 4-methylbenzoic acid **1a** proceeded smoothly in 56 % ¹⁹F NMR yield, however purification via column chromatography proved challenging with significant decomposition being observed. Further decomposition was observed upon standing in solution with the long residence times required for ¹³C NMR acquisition resulting in not insignificant amounts of impurities being observed in the resulting spectrum. Similar results were obtained with other benzoic acid derivatives bearing electron-neutral or electron-withdrawing *para*-substituents. The high electrophilicity of the carbonyl carbon in these compounds likely leads to instability towards hydrolysis or other nucleophilic attack-induced decomposition. Nevertheless, ¹³C peaks consistent with the thioester products **5** were always observed, with ¹H and ¹⁹F NMR, which have much shorter acquisition times, further supporting the assignment of the products obtained after



Scheme 4. Proposed mechanism for the deoxygenative perfluoroalkylthiolation of carboxylic acids using BT-SR_F reagents.



Scheme 5. Scope of the deoxygenative perfluoroalkylthiolation of carboxylic acids using BT-SC₂F₅. Conditions: **1** (0.3 mmol, 1.0 equiv.) and NEt(*i*-Pr)₂ (0.3 mmol, 1.0 equiv.) in THF (1.5 mL) added slowly over 15 mins to solution of BT-SR_F (0.6 mmol, 2.0 equiv.) in THF (1.5 mL) at $-78\text{ }^{\circ}\text{C}$. Mixture stirred for 2 h. ¹⁹F NMR yield (internal standard: PhCF₃), isolated yields after column chromatography in parentheses. ^a ¹⁹F NMR yield not measured.

chromatography¹. Benzoic acid derivatives featuring the more electron-donating groups -OMe and -pH at the *para*-position were seemingly

¹ In some cases, however, the thioester products could not be separated from trace amounts of 2,6-di-*tert*-butyl-4-methylphenol (BHT, < 10%), which is present as a stabilizer in the THF reaction solvent.

more stable with **5e** and **5f** being isolated in 56 and 71 % yield, respectively without significant composition upon purification or characterisation. Good isolated yields were obtained with thioesters **5g** (88 %) and **5h** (56 %), which feature methyl substituents at the *meta*- and *ortho*-positions.

As indicated from the experiments with ibuprofen discussed above, aliphatic carboxylic acids reacted efficiently with the adamantyl

thioester **5i** being isolated in 83 % yield after column chromatography. Cinnamic acid **1j** was also smoothly converted into the corresponding thioester **5j** in 63 % isolated yield implying that alkenyl carboxylic acid derivatives are also suitable substrates for deoxygenative pentafluoroethylthiolation with BT-SC₂F₅. Finally, in addition to ibuprofen, two more biologically active carboxylic acids were tested. The successful isolation of the pentafluoroethyl thioester derivatives of the omega-6 fatty acid linoleic acid (**5k**) and the painkiller Naproxen (**5l**) in 83 and 87 % yields, respectively, demonstrates the potential of this approach to deliver novel fluorinated analogues of important biologically relevant compounds.

3. Conclusions

In conclusion, we have investigated benzothiazolium salts bearing long chain SR_F groups (R_F = C_nF_{2n+1}, *n* > 1) at the 2-position as nucleophilic reagents for the synthesis of perfluoroalkyl thioesters. This has led to the development of a new methodology involving direct deoxygenative substitution of readily available carboxylic acids without requiring pre-activation of the starting materials or the use of expensive additives. A survey of perfluoroalkylthio groups with ibuprofen as a representative substrate revealed the suitability of this approach to prepare thioesters featuring long chain perfluoroalkyl groups up to C₆F₁₃ while a scope and limitations study with BT-SC₂F₅ demonstrated the generality of the pentafluoroethylthiolation method, particularly with aliphatic, alkenyl and relatively electron-rich aromatic carboxylic acids. While some products were found to be relatively unstable, given the lack of studies on perfluoroalkyl thioesters in the literature and their potential as fluorine-containing feedstocks and synthetic intermediates, we believe this work will be of significant interest and inspire more investigations into these compounds.

4. Experimental section

4.1. General information

All compounds and solvents utilised were purchased from commercial suppliers and used without further treatment, unless specified otherwise. Benzothiazolium reagents were synthesized according to literature known procedures [44].

Thin-layer chromatography was performed on silica gel coated aluminium plates from TLC Silica gel 60 F₂₅₄ and aluminium oxide 60 F₂₅₄ neutral. The product spots were detected by UV light (254 nm) or as permanganate stains. Flash column chromatography was performed with silica gel 60 M (0.040–0.063 mm, 230–400 mesh).

¹H, ¹⁹F and ¹³C NMR spectra were acquired on a Bruker Avance III 300 (300 MHz), Bruker Avance II 400 (400 MHz), Bruker Avance Neo 400 (400 MHz), Bruker Avance III HD 500 (500 MHz), or a Bruker Avance III HD 700 (700 MHz) and analysed on MestReNova 14.1.1. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethyl silane (TMS) and coupling constants (*J*) are presented in hertz (Hz). CD₃CN or CDCl₃ were used as deuterated solvents and the residual solvent signals were used as references in the ¹H and ¹³C NMR spectra. ¹⁹F NMR spectra were not calibrated by an internal reference. ¹⁹F NMR yields were measured using α,α,α-trifluorotoluene as an internal standard. The multiplicities are described using the following abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *p* = pentet, and *m* = multiplet.

High-resolution mass spectra were measured with an Agilent (6210) ESI-TOF; 4 μL/min, 1.0 bar, 4 kV) and HR-APCI-MS: Waters Xevo G2-XS QToF with Acquity UPLC iClass instruments. In instances where molecular ion peaks could not be observed due to instability, the constituent fragments are reported.

Infrared spectra were measured with a PerkinElmer UATR Two FT-IR Spectrometer. Characteristic absorption bands are displayed in wavenumbers $\tilde{\nu}$ in cm⁻¹.

4.2. Synthesis of 2-((Perfluoroalkyl)thio)benzothiazoles **3** and **4**

General Procedure 1: Sodium hydride (60% wt, 1.1 equiv., 6.6 mmol, 0.26 g) was added to 2-mercaptobenzothiazole (1.0 equiv., 6.0 mmol, 1 g) in DMF (0.2 M, 30 mL) and the suspension was stirred at rt for 30 min. Perfluoroalkyl iodide was added (2 equiv., 12 mmol) and the mixture was stirred at rt for 16 h under UVA light irradiation. The orange solution was quenched with water, extracted with EtOAc and dried over MgSO₄. After filtration, the solvent was removed under reduced pressure and the product was obtained as a mixed fraction after flushing through a silica plug. The product was directly used without further purification.

4.2.1. 2-((Perfluorobutyl)thio)benzo[d]thiazole **3**

Prepared according to General Procedure 1 with I(*n*-C₄F₉) (2.0 mL). Product **3** was purified via column chromatography (Petroleum ether (40:60):ethyl acetate, 10:1) and isolated in 61% yield (1.41 g, 3.7 mmol).

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 8.16 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.55 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.50 (dd, *J* = 8.0, 7.2 Hz, 1H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -80.9 (t, *J* = 10 Hz), -86.2 (t, *J* = 13 Hz), -119.8 (m), -125.5 (m).

The data agrees with the literature values [49].

4.2.2. 2-((Perfluorohexyl)thio)benzo[d]thiazole **4**

Prepared according to the General Procedure 1 with I(*n*-C₆F₁₃) (2.0 mL). Product **4** was purified via column chromatography (Petroleum ether (40:60):ethyl acetate, 10:1) and isolated in 83% yield (2.53 g, 5.2 mmol).

¹H NMR (700 MHz, CDCl₃): δ [ppm] = 8.17 (dm, *J* = 8.2 Hz, 1H), 7.91 (dm, *J* = 8.0 Hz, 1H), 7.57 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.52 (td, *J* = 7.7, 1.2 Hz, 1H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -80.8 (t, *J* = 10 Hz), -84.9 (t, *J* = 14 Hz), -118.9 (td, *J* = 16, 7 Hz), -121.4 (m), -122.7 (m), -126.1 (m). ¹³C NMR (176 MHz, CDCl₃): δ [ppm] = 153.4, 150.1, 138.7, 127.2, 127.1, 124.6, 122.8 (tt, *J* = 298, 36 Hz), 121.5, 118.9 (qt, *J* = 288, 33 Hz), 106.5 – 113.2 (m). Note: Four CF₂ peaks are overlapping. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3066, 1553, 1456, 1410, 1361, 1314, 1289, 1230, 1196, 1139, 1123, 1098, 1040, 1017, 997, 881, 854, 799, 767, 760, 731, 724, 695, 656, 635, 601, 591, 562, 530, 505, 450, 427. HRMS (APCI) calculated for [C₁₃H₄F₁₃NS₂]⁺ ([M]⁺): 485.9650, measured: 485.9650.

4.3. Synthesis of benzothiazolium reagents

General Procedure 2: 2-Substituted benzothiazoles (1.0 equiv) were dissolved in dry DCM (0.10 M) and methyl trifluoromethanesulfonate (3.0 equiv) was added. The reaction mixture was stirred at rt for 48 h and the product was precipitated with diethyl ether. The suspension was filtered, and the residue washed with diethyl ether (3 ×). After drying *in vacuo*, BT-SR_F salts were obtained as off-white solids.

4.3.1. 3-Methyl-2-((perfluorobutyl)thio)benzo[d]thiazol-3-ium trifluoromethanesulfonate (BT-S(*n*-C₄F₉))

BT-(*n*-SC₄F₉) was prepared according to General Procedure 2. BT-(*n*-SC₄F₉) (2.21 g, 4.0 mmol, 67%) was dried under reduced pressure and obtained as a white powder.

¹H NMR (700 MHz, CD₃CN) δ [ppm] = 8.43 (d, *J* = 8.4 Hz, 1H), 8.32 (d, *J* = 8.7 Hz, 1H), 8.10 (t, *J* = 7.6 Hz, 1H), 8.02 (t, *J* = 7.8 Hz, 1H), 4.50 (s, 3H). ¹⁹F NMR (376 MHz, CD₃CN) δ [ppm] = -79.4, -81.6 (t, *J* = 10 Hz), -83.0 (t, *J* = 14 Hz), -119.7, -126.0. ¹³C NMR (176 MHz, CD₃CN): δ [ppm] = 158.4, 143.9, 134.7, 132.6, 131.8, 125.3, 123.0 (tt, *J* = 301, 35 Hz), 122.1 (q, *J* = 321 Hz), 119.6, 118.0 (qt, *J* = 286, 35 Hz), 113.0 – 107.5 (m), 40.2. Note: Two CF₂ peaks are overlapping. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3100, 1577, 1490, 1463, 1432, 1382, 1348, 1275, 1242, 1224, 1200, 1160, 1136, 1098, 1052, 1029, 1016, 962, 814, 790, 747, 730, 728, 701, 638, 606, 573, 540, 516. HRMS (ESI) calculated for [C₁₂H₇F₉NS]⁺ ([M-OTf]⁺): 399.9871, measured: 399.9876.

4.3.2. 3-Methyl-2-((perfluorohexyl)thio)benzo[d]thiazol-3-ium trifluoromethanesulfonate (BT-S(*n*-C₆F₁₃))

BT-S(*n*-C₆F₁₃) was prepared according to General Procedure 2. BT-S(*n*-C₆F₁₃) (2.81 g, 4.32 mmol, 87%) was dried under reduced pressure and obtained as a white powder.

¹H NMR (300 MHz, CD₃CN) δ [ppm] = 8.40 (dm, *J* = 8.2 Hz, 1H), 8.30 (dm, *J* = 8.4 Hz, 1H), 8.03 (m, 2H), 4.47 (s, 3H). ¹⁹F NMR (282 MHz, CD₃CN) δ [ppm] = -79.4, -81.5 (t, *J* = 10 Hz), -82.6 (t, *J* = 14 Hz), -118.7, -121.7, -123.1, -126.5 (m). ¹³C NMR (176 MHz, CD₃CN): δ [ppm] = 158.4, 143.9, 134.7, 132.6, 131.8, 125.3, 123.1 (tt, *J* = 301, 35 Hz), 122.1 (q, *J* = 32 Hz), 119.6, 118.0 (qt, *J* = 288, 33 Hz), 113.5–107.5 (m), 40.2. Note: Four CF₂ peaks are overlapping. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3102, 1789, 1695, 1575, 1514, 1491, 1461, 1434, 1386, 1361, 1316, 1281, 1249, 1220, 1197, 1143, 1125, 1099, 1066, 1053, 1030, 963, 881, 861, 816, 767, 756, 745, 723, 695, 666, 636, 603, 593, 572, 563, 544, 528, 515, 421, 407. HRMS (ESI) calculated for [C₁₄H₇F₁₃NS₂]⁺ ([M-OTf]⁺): 499.9807, measured: 499.9815.

4.4. Synthesis of perfluorinated thioesters 2,5,6,7 and 8

General Procedure 3: The carboxylic acid substrate (1, 0.3 or 0.4 mmol, 1.0 equiv.) and NEt(*i*-Pr)₂ (0.3 or 0.4 mmol, 1.0 equiv.) in THF (1.5 or 2.0 mL) were added slowly over 15 mins to a solution of the BT-SR_F reagent (0.6–0.8 mmol, 2.0 equiv.) in THF (1.5 or 2.0 mL) at -78 °C. The mixture was stirred for 2 h. The solvent was then removed under reduced pressure. The crude mixture was separated using column chromatography to afford the thioester products (2,5,6,7 or 8). Where noted, crude yields were measured using ¹⁹F NMR spectroscopy with α,α,α-trifluorotoluene as an internal standard.

4.4.1. S-(Perfluoropropyl) 4-methylbenzothioate 2a

Prepared according to General Procedure 3 using 4-methylbenzoic acid (0.041 g, 0.30 mmol) and BT-(*n*-SC₃F₇) (0.30 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product 2a was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 50% yield (48 mg, 0.15 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.78 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.31 (dm, *J* = 8.4 Hz, 2H), 2.44 (s, 3H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -79.9 (t, *J* = 9 Hz), -90.0 (qt, *J* = 9, 3 Hz), -123.9 (m). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 181.4, 146.7, 133.0, 130.0, 128.1, 122.9 (tt, *J* = 295, 35 Hz), 117.8 (qt, *J* = 288, 34 Hz), 113.0–107.0 (m), 21.9. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2926, 1714, 1605, 1575, 1408, 1337, 1312, 1203, 1174, 1166, 1115, 1028, 870, 846, 820, 780, 751, 742, 714, 684, 638, 616, 535, 470, 419. HRMS (APCI) Note: a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for [C₈H₇O]⁺ ([M-SC₃F₇]⁺): 119.0491, measured: 119.0495; calculated for [C₃F₇S]⁻ ([M-C₈H₇O]⁻): 200.9614, measured: 200.9627; calculated for [C₈H₇OS]⁻ ([M-C₃F₇]⁻): 151.0223, measured: 151.0220.

4.4.2. S-(Perfluoropropyl) 2-(4-isobutylphenyl)propanethioate 2b

Prepared according to General Procedure 3 using 2-(4-isobutylphenyl)propanoic acid (0.062 g, 0.30 mmol) and BT-(*n*-SC₃F₇) (0.30 g, 0.60 mmol) on a 0.3 mmol scale. ¹⁹F NMR analysis of the crude mixture indicated an initial yield of 2b of 76%. Perfluorinated thioester product 2b was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 68% yield (80 mg, 0.20 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.22–7.14 (m, 4H), 3.87 (q, *J* = 7.1 Hz, 1H), 2.50 (d, *J* = 7.2 Hz, 2H), 1.88 (nonet, *J* = 7.2 Hz, 1H), 1.58 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 6H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -80.0 (t, *J* = 10 Hz), -90.5 (m), -124.1 (d, *J* = 3 Hz). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 191.1, 142.5, 134.3, 130.1, 128.3, 122.6 (tt, *J* = 296, 35 Hz), 55.8, 45.2, 30.3, 22.5, 17.9. Note: Peaks for two CF₂ carbons could not be unambiguously identified. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3386, 2958, 1743, 1708, 1661, 1510, 1466, 1384, 1336, 1208, 1186, 1114, 1044, 919, 858, 844, 801, 741, 682, 607, 570, 535, 490.

HRMS (APCI) calculated for [C₁₆H₁₇F₇OS]⁺ ([M]⁺): 390.0888, measured: 390.0876.

4.4.3. S-(Perfluoroethyl) 2-(4-isobutylphenyl)propanethioate 5b

Prepared according to General Procedure 3 using 2-(4-isobutylphenyl)propanoic acid (0.083 g, 0.40 mmol) and BT-SC₂F₅ (0.36 g, 0.80 mmol) on a 0.40 mmol scale. ¹⁹F NMR analysis of the crude mixture indicated an initial yield of 5b of 79%. Perfluorinated thioester product 5b was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 71% yield (97 mg, 0.28 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.18 (d, *J* = 1.1 Hz, 4H), 3.87 (q, *J* = 7.1 Hz, 1H), 2.50 (d, *J* = 7.2 Hz, 2H), 1.57 (dt, *J* = 7.1 Hz, 3H), 1.28 (s, 1H), 0.92 (d, *J* = 6.6 Hz, 6H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -83.8 (t, *J* = 3 Hz), -94.0 (dq, *J* = 241, 3 Hz), -94.9 (dq, *J* = 241, 3 Hz). ¹³C NMR (101 MHz, CDCl₃): δ [ppm] = 191.2, 142.5, 134.3, 130.1, 128.4, 120.1 (tq, *J* = 294, 42 Hz), 118.2 (qt, *J* = 287, 35 Hz), 55.8, 45.2, 30.3, 22.5, 17.9. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2958, 2872, 1743, 1467, 1320, 1210, 1108, 966, 909, 751, 649, 571, 548. HRMS (APCI) calculated for [C₁₅H₁₇F₅OS]⁺ ([M]⁺): 340.0920, measured: 340.0905.

4.4.4. S-(Perfluorobutyl) 2-(4-isobutylphenyl)propanethioate 6b

Prepared according to General Procedure 3 using 2-(4-isobutylphenyl)propanoic acid (0.062 g, 0.30 mmol) and BT-S(*n*-C₄F₉) (0.33 g, 0.60 mmol) on a 0.3 mmol scale. ¹⁹F NMR analysis of the crude mixture indicated an initial yield of 6b of 61%. Perfluorinated thioester product 6b was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 55% yield (73 mg, 0.17 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.24–7.10 (m, 4H), 3.87 (q, *J* = 7.0 Hz, 1H), 2.49 (d, *J* = 7.2 Hz, 2H), 1.88 (nonet, *J* = 6.7 Hz, 1H), 1.57 (d, *J* = 7.1 Hz, 3H), 0.92 (d, *J* = 6.6 Hz, 6H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -81.03 (tt, *J* = 10, 3 Hz), -89.7 (m), -120.6 (m), -125.7 (m). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 191.1, 142.5, 134.3, 130.1, 128.3, 55.8, 45.2, 30.3, 22.5, 17.9. Note: Peaks for one CF₃ and three CF₂ carbon could not be unambiguously identified. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2957, 2871, 1745, 1707, 1513, 1464, 1421, 1384, 1367, 1347, 1232, 1207, 1136, 1093, 1022, 999, 919, 860, 824, 798, 790, 745, 728, 694, 650, 636, 574, 537. HRMS (APCI) calculated for [C₁₇H₁₇F₉OS]⁺ ([M]⁺): 440.0856, measured: 440.0843.

4.4.5. S-(Perfluoropentyl) 2-(4-isobutylphenyl)propanethioate 7b

Prepared according to the general procedure using 2-(4-isobutylphenyl)propanoic acid (0.062 g, 0.30 mmol) and BT-S(*n*-C₅F₁₁) (0.36 g, 0.60 mmol) on a 0.3 mmol scale. ¹⁹F NMR analysis of the crude mixture indicated an initial yield of perfluorinated thioester product 7b of 51%. Significant decomposition was observed upon purification via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and 7b was isolated in an inseparable mixture together with an impurity with NMR signals consistent with the corresponding acid fluoride (71 mg) as a pale yellow oil.

Note: ¹H, ¹⁹F & ¹³C NMR peaks corresponding to 7b reported, some peaks overlap with those of the impurity. ¹H NMR (700 MHz, CDCl₃): δ [ppm] = 7.23–7.14 (m, 4H), 3.88 (q, *J* = 7.0 Hz, 1H), 2.50 (d, *J* = 7.3 Hz, 2H), 1.89 (nonet, *J* = 6.7 Hz, 1H), 1.58 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 6H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = -89.0 (dtm, *J* = 245, 15 Hz), -90.0 (dtm, *J* = 245, 15 Hz), -119.9 (m), -122.4 (m), -126.3 (m). ¹³C NMR (176 MHz, CDCl₃): δ [ppm] = 190.1, 142.5, 134.3, 130.1, 128.3, 123.4 (tt, *J* = 297, 35 Hz), 117.4 (qt, *J* = 289, 33 Hz), 112.6–106.5 (m), 55.8, 45.2, 30.3, 22.43, 22.42, 17.9. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2959, 2873, 1744, 1710, 1513, 1466, 1357, 1232, 1203, 1143, 1109, 1085, 1060, 998, 977, 914, 846, 812, 770, 734, 720, 690, 655, 601, 574, 532, 422. HRMS (APCI) calculated for [C₁₅H₁₇F₅OS]⁺ ([M]⁺): 340.0920, measured: 340.0905.

4.4.6. *S*-(Perfluorohexyl) 2-(4-isobutylphenyl)propanethioate 8b

Prepared according to General Procedure 3 using 2-(4-isobutylphenyl)propanoic acid (0.062 g, 0.30 mmol) and BT-*S*-(*n*-C₆F₁₃) (0.39 g, 0.6 mmol) on a 0.3 mmol scale. ¹⁹F NMR analysis of the crude mixture indicated an initial yield of perfluorinated thioester product **8b** of 58%. Significant decomposition was observed upon purification via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and **8b** was isolated in an inseparable mixture together with an impurity with NMR signals consistent with the corresponding acid fluoride (94 mg) as a pale yellow oil.

Note: ¹H, ¹⁹F & ¹³C NMR peaks corresponding to **8b** reported, some peaks overlap with those of the impurity. ¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.16 – 6.99 (m, 4H), 3.87 (q, *J* = 7.1 Hz, 1H), 2.50 (d, *J* = 7.0 Hz, 2H), 1.88 (nonet, *J* = 6.7 Hz, 1H), 1.57 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 6H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –80.9 (tm, *J* = 10 Hz), –89.1 (ddm, *J* = 245, 15 Hz), –89.9 (ddm, *J* = 245, 15 Hz), –119.7 (m), –121.6 (m), –122.8 (m), –126.2 (m). ¹³C NMR (126 MHz, CDCl₃): δ [ppm] = 191.1, 142.5, 134.3, 130.1, 128.3, 123.4 (tt, *J* = 297, 32 Hz), 117.3 (qt, *J* = 289, 33 Hz), 114.5 – 107.6 (m), 55.8, 45.2, 30.3, 3, 22.5, 18.0. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2959, 2873, 1745, 1709, 1513, 1466, 1361, 1236, 1198, 1146, 1123, 1093, 1042, 1020, 997, 918, 886, 846, 800, 775, 735, 721, 691, 669, 635, 598, 562, 532, 417. HRMS (APCI) calculated for [C₁₉H₁₇F₁₃OS]⁺ ([M]⁺): 540.0792, measured: 540.0811.

4.4.7. *S*-(Perfluoroethyl) 4-methylbenzothioate 5a

Prepared according to General Procedure 3 using 4-methylbenzoic acid (0.041 g, 0.30 mmol) and BT-SC₂F₅ (0.27 g, 0.30 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5a** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 33% yield (27 mg, 0.10 mmol) as a pale yellow oil.

¹H NMR (400 MHz, CDCl₃): δ [ppm] = 7.77 (dm, *J* = 8.2 Hz, 2H), 7.30 (dm, *J* = 8.2 Hz, 2H), 2.44 (s, 3H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –83.5 (t, *J* = 3 Hz), –93.9 (q, *J* = 3 Hz). ¹³C NMR (101 MHz, CDCl₃): δ [ppm] = 181.5, 146.7, 133.0, 130.0, 128.1, 120.4 (tq, *J* = 294, 42 Hz), 118.3 (qt, *J* = 288, 35 Hz), 21.9. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2930, 1808, 1759, 1714, 1606, 1575, 1451, 1409, 1319, 1204, 1177, 1131, 1100, 1037, 962, 877, 838, 819, 803, 783, 751, 714, 653, 639, 617, 594, 552, 528, 514, 469, 444, 430, 417. HRMS (APCI) *Note:* a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for [C₈H₇O]⁺ ([M-SC₂F₅]⁺): 119.0491, measured: 119.0495; calculated for [C₂F₅S]⁻ ([M-C₈H₇O]⁻): 150.9646, measured: 150.9644; calculated for [C₈H₇OS]⁻ ([M-C₂F₅]⁻): 151.0223, measured: 151.0220.

4.4.8. *S*-(Perfluoroethyl) 4-chlorobenzothioate 5c

Prepared according to General Procedure 3 using 4-chlorobenzoic acid (0.047 g, 0.30 mmol) and BT-SC₂F₅ (0.27 g, 0.30 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5c** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 40% yield (35 mg, 0.12 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.85 – 7.80 (m, 2H), 7.52 – 7.48 (m, 2H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –83.5 (t, *J* = 3 Hz), –93.8 (q, *J* = 3 Hz). ¹³C NMR (176 MHz, CDCl₃): δ [ppm] = 180.9, 180.8, 142.0, 133.8, 129.8, 129.2, 120.2 (tq, *J* = 295, 42 Hz), 118.2 (qt, *J* = 287, 35 Hz). IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2928, 1710, 1587, 1572, 1487, 1400, 1319, 1202, 1176, 1136, 1104, 1090, 1014, 963, 875, 835, 751, 728, 718, 652, 634, 600, 572, 552, 472, 443, 427. HRMS (APCI) *Note:* a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for [C₇H₄ClO]⁺ ([M-SC₂F₅]⁺): 138.9945, measured: 138.9953; calculated for [C₇H₄ClOS]⁻ ([M-C₂F₅]⁻): 170.9677, measured: 170.9676.

4.4.9. *S*-(Perfluoroethyl) 4-(trifluoromethyl)benzothioate 5d

Prepared according to General Procedure 3 using 4-(trifluoromethyl)benzoic acid (0.057 g, 0.30 mmol) and BT-SC₂F₅ (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5d** was purified via

column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 21% yield (20 mg, 0.060 mmol) as a pale yellow oil.

¹H NMR (700 MHz, CDCl₃): δ [ppm] = 8.01 (dm, *J* = 8.1 Hz, 2H), 7.80 (dm, *J* = 8.1 Hz, 2H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –63.5, –83.5 (t, *J* = 3 Hz), –93.9 (q, *J* = 3 Hz). ¹³C NMR (75 MHz, CDCl₃): δ [ppm] = 181.3, 138.2, 136.5 (q, *J* = 33 Hz), 128.3, 126.5 (q, *J* = 4 Hz), 123.3 (q, *J* = 273 Hz), 120.1 (tq, *J* = 295, 42 Hz), 118.3 (qt, *J* = 287, 35 Hz). IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 2924, 1699, 1410, 1323, 1176, 1137, 1067, 850, 772. HRMS (APCI) *Note:* a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for [C₈H₄F₃O]⁺ ([M-SC₂F₅]⁺): 173.0209, measured: 173.0206; calculated for [C₈H₄F₃OS]⁻ ([M-C₂F₅]⁻): 204.9940, measured: 204.9951.

4.4.10. *S*-(Perfluoroethyl) 4-methoxybenzothioate 5e

Prepared according to General Procedure 3 using 4-methoxybenzoic acid (0.061 g, 0.40 mmol) and BT-SC₂F₅ (0.36 g, 0.80 mmol) on a 0.4 mmol scale. Perfluorinated thioester product **5e** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 56% yield (64 mg, 0.22 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.86 (d, *J* = 9.1 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 3.89 (s, 3H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –83.5 (t, *J* = 3 Hz), –93.7 (q, *J* = 3 Hz). ¹³C NMR (176 MHz, CDCl₃): δ [ppm] = 180.2, 165.3, 130.5, 128.2, 120.4 (tq, *J* = 295, 42 Hz), 118.3 (qt, *J* = 286, 35 Hz), 114.6, 55.9. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 1707, 1599, 1509, 1316, 1267, 1207, 1167, 1099, 963, 877, 836, 751, 614. HRMS (APCI) calculated for [C₁₀H₇F₅O₂S]⁺ ([M]⁺): 287.0165, measured: 287.0158.

4.4.11. *S*-(Perfluoroethyl) [1,1'-biphenyl]-4-carbthioate 5f

Prepared according to General Procedure 3 using [1,1'-biphenyl]-4-carboxylic acid (0.079 g, 0.40 mmol) and BT-SC₂F₅ (0.36 g, 0.80 mmol) on a 0.4 mmol scale. Perfluorinated thioester product **5f** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 71% yield (94 mg, 0.28 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.96 (dt, *J* = 8.7, 2.0 Hz, 2H), 7.73 (dt, *J* = 8.8, 2.0 Hz, 2H), 7.66 – 7.60 (m, 2H), 7.54 – 7.40 (m, 3H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –83.4 (t, *J* = 3 Hz), –93.8 (q, *J* = 3 Hz).

The data agree with literature precedents [41].

4.4.12. *S*-(Perfluoroethyl) 3-methylbenzothioate 5g

Prepared according to General Procedure 3 using 3-methylbenzoic acid (0.041 g, 0.30 mmol) and BT-SC₂F₅ (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5g** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 88% yield (71 mg, 0.26 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.72 – 7.66 (m, 2H), 7.49 (dm, *J* = 7.6 Hz, 1H), 7.39 (m, 1H), 2.43 (s, 3H). ¹⁹F NMR (282 MHz, CDCl₃): δ [ppm] = –83.5 (t, *J* = 3 Hz), –94.0 (q, *J* = 3 Hz). ¹³C NMR (176 MHz, CDCl₃): δ [ppm] = 182.1, 139.5, 136.1, 135.5, 129.2, 128.4, 125.2, 120.3 (tq, *J* = 294, 42 Hz), 118.3 (qt, *J* = 287, 35 Hz), 21.4. IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3577, 3925, 2855, 1712, 1603, 1585, 1457, 1381, 1320, 1243, 1214, 1148, 1101, 967, 940, 925, 813, 793, 773, 751, 692, 669, 650, 631, 524, 482, 439. HRMS (APCI) *Note:* a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for [C₈H₇O]⁺ ([M-SC₂F₅]⁺): 119.0491, measured: 119.0495; calculated for [C₂F₅S]⁻ ([M-C₈H₇O]⁻): 150.9646, measured: 150.9644; calculated for [C₈H₇OS]⁻ ([M-C₂F₅]⁻): 151.0223, measured: 151.0232.

4.4.13. *S*-(Perfluoroethyl) 2-methylbenzothioate 5h

Prepared according to General Procedure 3 using 2-methylbenzoic acid (0.041 g, 0.30 mmol) and BT-SC₂F₅ (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5h** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 59% yield (48 mg, 0.18 mmol) as a pale yellow oil.

¹H NMR (300 MHz, CDCl₃): δ [ppm] = 7.75 (m, 1H), 7.50 (m, 1H), 7.24 (m, 2H), 7.35 – 7.28 (m, 2H), 2.53 (s, 3H). ¹⁹F NMR (282 MHz,

CDCl_3): δ [ppm] = -83.5 (t, $J = 3$ Hz), -94.6 (q, $J = 3$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ [ppm] = 183.0, 138.8, 135.1, 133.7, 132.4, 129.0, 126.4, 120.4 (tq, $J = 294$, 42 Hz), 118.4 (qt, $J = 287$, 35 Hz), 20.9. IR (ATR): $\tilde{\nu}$ [cm^{-1}]: 2923, 2853, 1723, 1458, 1378, 1318, 1217, 1190, 1102, 965, 876, 764, 751, 719, 673, 647, 481. HRMS (APCI) Note: a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for $[\text{C}_8\text{H}_7\text{O}]^+$ ($[\text{M}-\text{SC}_2\text{F}_5]^+$): 119.0491, measured: 119.0496. Calculated for $[\text{C}_2\text{F}_5\text{S}]^-$ ($[\text{M}-\text{C}_8\text{H}_7\text{O}]^-$): 150.9646.

4.4.14. *S*-(Perfluoroethyl)adamantane-1-carbothioate 5i

Prepared according to General Procedure 3 using 1-adamantanecarboxylic acid (0.054 g, 0.30 mmol) and BT- SC_2F_5 (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5i** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 83% yield (78 mg, 0.25 mmol) as a pale yellow oil.

^1H NMR (300 MHz, CDCl_3): δ [ppm] = 2.14–2.06 (br s, 3H), 1.93 (d, $J = 2.8$ Hz, 6H), 1.81–1.65 (m, 6H). ^{19}F NMR (282 MHz, CDCl_3): δ [ppm] = -83.8 (t, $J = 3$ Hz), -94.6 (q, $J = 3$ Hz). ^{13}C NMR (176 MHz, CDCl_3): δ [ppm] = 195.6, 120.6 (tq, $J = 294$, 42 Hz), 118.3 (qt, $J = 287$, 35 Hz), 51.0, 38.7, 36.2, 28.1. IR (ATR): $\tilde{\nu}$ [cm^{-1}]: 2909, 2855, 1739, 1698, 1453, 1345, 1318, 1208, 1130, 1101, 963, 942, 910, 819, 786, 750, 668, 645, 631, 537, 526, 445, 410. HRMS (APCI) Note: a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for $[\text{C}_{10}\text{H}_{15}]^+$ ($[\text{M}-\text{SC}_3\text{OF}_5]^+$): 135.1168, measured: 135.1172; calculated for $[\text{C}_2\text{F}_5\text{S}]^-$ ($[\text{M}-\text{C}_{11}\text{H}_{15}\text{O}]^-$): 150.9646, measured: 150.9644; calculated for $[\text{C}_{11}\text{H}_{15}\text{OS}]^-$ ($[\text{M}-\text{C}_2\text{F}_5]^-$): 195.0849, measured: 195.0848.

4.4.15. *S*-(Perfluoroethyl) (*E*)-3-phenylprop-2-enethioate 5j

Prepared according to General Procedure 3 using cinnamic acid (0.044 g, 0.30 mmol) and BT- SC_2F_5 (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5j** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 63% yield (53 mg, 0.19 mmol) as a pale yellow oil.

^1H NMR (300 MHz, CDCl_3): δ [ppm] = 7.67 (d, $J = 15.8$ Hz, 1H), 7.63–7.52 (m, 2H), 7.51–7.39 (m, 3H), 6.61 (d, $J = 15.8$ Hz, 1H). ^{19}F NMR (282 MHz, CDCl_3): δ [ppm] = -83.6 (t, $J = 3$ Hz), -93.4 (q, $J = 3$ Hz). ^{13}C NMR (176 MHz, CDCl_3): δ [ppm] = 179.5, 145.5, 133.1, 132.0, 129.4, 129.1, 120.2 (tq, $J = 294$, 42 Hz), 118.3 (qt, $J = 286$, 35 Hz). IR (ATR): $\tilde{\nu}$ [cm^{-1}]: 3064, 1699, 1612, 1577, 1496, 1450, 1322, 1279, 1206, 1128, 1095, 1032, 1017, 999, 948, 878, 843, 747, 687, 647, 630, 614, 566, 504, 478, 412. HRMS (APCI) Note: a molecular ion peak could not be identified; diagnostic fragments are reported: calculated for $[\text{C}_9\text{H}_7\text{O}]^+$ ($[\text{M}-\text{SC}_2\text{F}_5]^+$): 131.0491, measured: 131.0506. Calculated for $[\text{C}_2\text{F}_5\text{S}]^-$ ($[\text{M}-\text{C}_9\text{H}_7\text{O}]^-$): 150.9646, measured: 150.9644; calculated for $[\text{C}_9\text{H}_7\text{OS}]^-$ ($[\text{M}-\text{C}_2\text{F}_5]^-$): 163.0223, measured: 163.0223.

4.4.16. *S*-(Perfluoroethyl) (9*Z*,12*Z*)-octadeca-9,12-dienethioate 5k

Prepared according to General Procedure 3 using linoleic acid (0.084 g, 0.30 mmol) and BT- SC_2F_5 (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5k** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 83% yield (103 mg, 0.25 mmol) as a pale yellow oil.

^1H NMR (300 MHz, CDCl_3): δ [ppm] = 5.45–5.27 (m, 4H), 2.77 (t, $J = 6.0$ Hz, 2H), 2.64 (t, $J = 7.4$ Hz, 2H), 2.05 (q, $J = 6.8$ Hz, 4H), 1.76–1.64 (m, 2H), 1.42–1.23 (m, 14H), 1.89 (t, $J = 6.9$ Hz, 3H). ^{19}F NMR (282 MHz, CDCl_3): δ [ppm] = -83.9 (t, $J = 3$ Hz), -94.0 (q, $J = 3$ Hz). ^{13}C NMR (75 MHz, CDCl_3): δ [ppm] = 188.7, 130.4, 130.0, 128.3, 128.0, 120.2 (tq, $J = 294$, 42 Hz), 118.2 (qt, $J = 286$, 35 Hz), 45.5, 31.7, 29.7, 29.5, 29.14, 29.08, 28.8, 27.4, 27.3, 25.8, 24.9, 22.7, 14.2. IR (ATR): $\tilde{\nu}$ [cm^{-1}]: 3009, 2926, 2855, 1709, 1459, 1217, 1170, 1104, 965, 751, 724, 599. HRMS (APCI) calculated for $[\text{C}_{20}\text{H}_{31}\text{F}_5\text{OS}]^+$ ($[\text{M}]^+$): 414.2016, measured: 414.2014.

4.4.17. *S*-(Perfluoroethyl) 2-(6-methoxynaphthalen-2-yl)propanethioate 5l

Prepared according to General Procedure 3 using Naproxen (0.069 g, 0.30 mmol) and BT- SC_2F_5 (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product **5l** was purified via column chromatography (Petroleum ether (40:60): ethyl acetate, 20:1) and isolated in 87% yield (95 mg, 0.26 mmol) as a pale yellow oil.

^1H NMR (700 MHz, CDCl_3): δ [ppm] = 7.79 (d, $J = 8.6$ Hz, 1H), 7.76 (d, $J = 8.9$ Hz, 1H), 7.70 (br s, 1H), 7.34 (dm, $J = 8.6$ Hz, 1H), 7.17 (m, 1H), 4.03 (q, $J = 7.0$ Hz, 1H), 3.94 (s, 3H), 1.67 (d, $J = 7.0$ Hz, 3H). ^{19}F NMR (282 MHz, CDCl_3): δ [ppm] = -83.7 (t, $J = 3$ Hz), -94.0 (dq, $J = 240$, 3 Hz), -94.9 (dq, $J = 240$, 3 Hz). ^{13}C NMR (75 MHz, CDCl_3): δ [ppm] = 191.2, 158.4, 134.6, 132.0, 129.6, 129.0, 128.1, 127.9, 126.3, 120.1 (tq, $J = 294$, 42 Hz), 119.7, 118.2 (qt, $J = 286$, 35 Hz), 105.8, 56.1, 55.4, 17.8. IR (ATR): $\tilde{\nu}$ [cm^{-1}]: 2989, 2941, 1743, 1713, 1631, 1605, 1533, 1505, 1486, 1459, 1438, 1419, 1391, 1319, 1268, 1210, 1175, 1160, 1106, 1073, 1030, 968, 959, 926, 906, 854, 824, 751, 734, 692, 676, 647, 630, 590, 548, 522, 423, 473. HRMS (APCI) calculated for $[\text{C}_{16}\text{H}_{13}\text{F}_5\text{O}_2\text{S}]^+$ ($[\text{M}]^+$): 364.0556, measured: 364.0541.

CRediT authorship contribution statement

Alex Haswell: Investigation, Methodology, Validation, Visualization, Writing – review & editing. **Matteo Tironi**: Conceptualization, Project administration, Supervision, Writing – review & editing. **Haoyue Wang**: Investigation, Methodology, Validation, Writing – review & editing. **Matthew N. Hopkinson**: Conceptualization, Funding acquisition, Project administration, Supervision, Visualization, Writing – original draft.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Matthew N. Hopkinson has patent #EP19150201 pending to Freie Universität Berlin. Matthew N. Hopkinson has patent #PCT/EP2020/050,031 pending to Freie Universität Berlin.

Data availability

Data will be made available on request.

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Supplementary materials

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