Journal of Fluorine Chemistry 273 (2024) 110231

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Deoxygenative perfluoroalkylthiolation of carboxylic acids with benzothiazolium reagents

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ARTICLE INFO

This paper is dedicated to Prof. Dr. Beate Koksch, the recipient of the 2021 ACS Award for Creative Work in Fluorine Chemistry.

Keywords:
Fluorine
Thioesters
Benzothiazolium reagents
Perfluoroalkyl groups
Deoxygenative reactions
Carboxylic acids

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 C_6F_{13}. A survey of carboxylic acid substrates with the pentafluoroethylthiolating reagent BT-SC_2F_5 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 (SCF_3) 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 SCF_3 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 SC_2F_5, S(*n*-C_3F_7) and S(*n*-C_4F_9) could also find roles in these fields[19,20]. Direct comparisons of drug molecules featuring CF_3 and C_2F_5 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-SCF_3 as an easily accessible and practical reagent for conducting nucleophilic trifluoromethylthiolation reactions [42,43]. Moreover, by employing longer chain perfluoroalkyl iodides in place of CF_3I 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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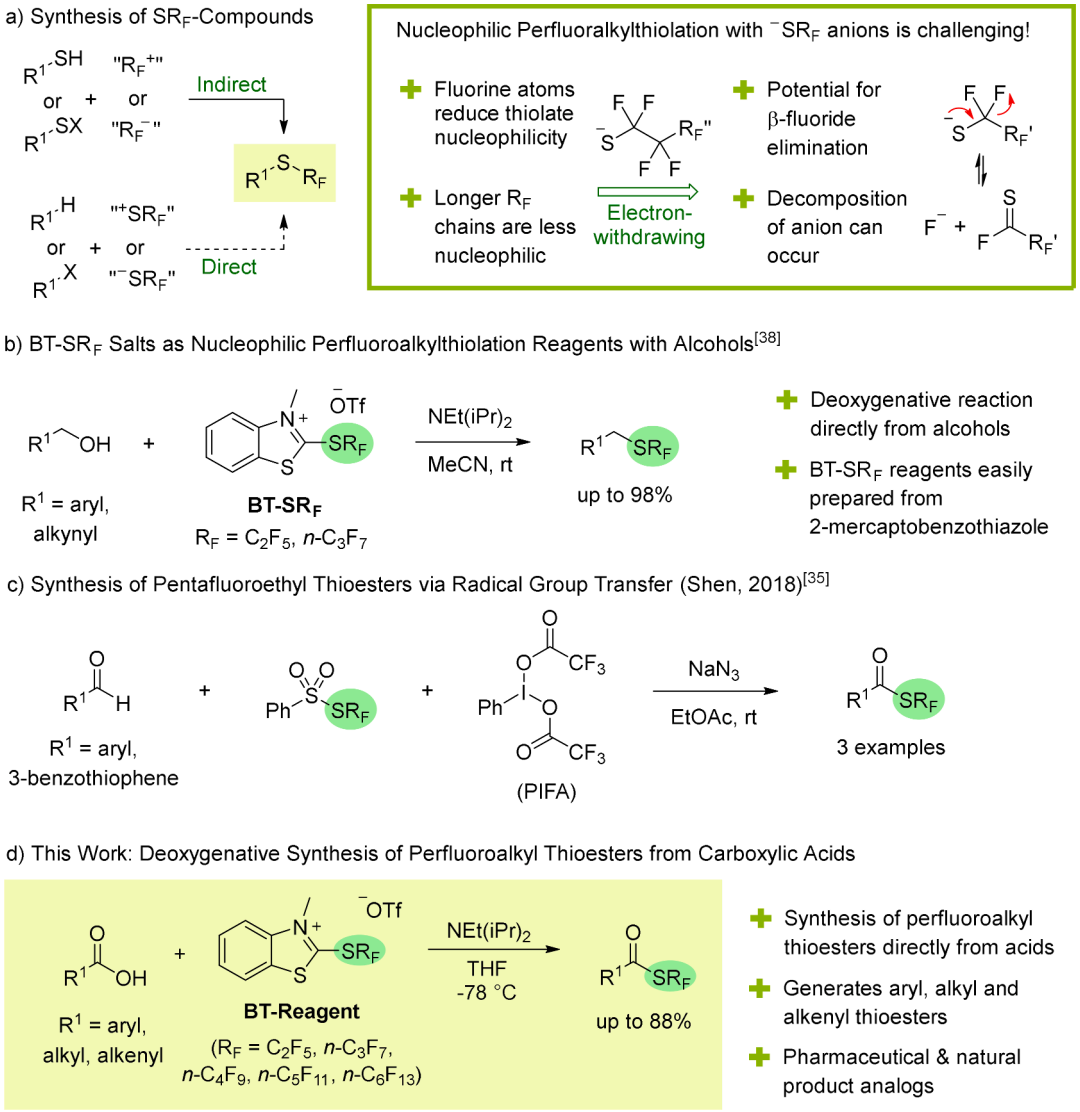
https://doi.org/10.1016/j.jfluchem.2023.110231
Received 1 November 2023; Received in revised form 24 November 2023; Accepted 24 November 2023
Available online 1 December 2023

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-SCF_3 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 $PhSO_2SC_2F_5$ as an SC_2F_5 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 SC_2F_5 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).

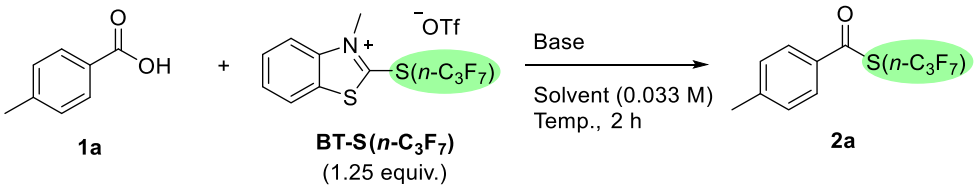
2. Results and discussion

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*-C_3F_7), 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-SCF_3 previously developed by our group (Table 1, Entry 1): **1a** (1.0 equiv.), BT-S(*n*-C_3F_7) (1.25 equiv.), NaH (3.0 equiv.), THF (0.03 M), −78 °C, 2 h). Disappointingly, ^{1}H and ^{19}F 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 % ^{19}F NMR yield (internal standard: $PhCF_3$, 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 perfluoroalkythiolation 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*-Pr)$_2$ (1 equiv.)	THF	rt	22 %
4	NEt(*i*-Pr)$_2$ (1 equiv.)	THF	−78 °C	55 %
5[c]	NEt(*i*-Pr)$_2$ (1 equiv.)	THF	−78 °C	63 %
6[c]	NEt(*i*-Pr)$_2$ (1 equiv.)	1,4-Dioxane	−78 °C	15 %
7[c]	NEt(*i*-Pr)$_2$ (1 equiv.)	Et_2O	−78 °C	32 %
8[c,d]	NEt(*i*-Pr)$_2$ (1 equiv.)	THF	−78 °C	81 % (50 %)

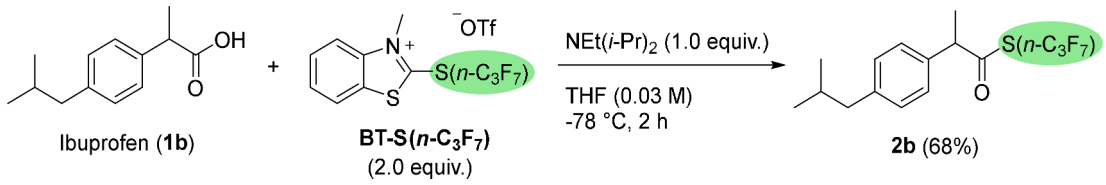
[a] Conditions: **1a** (0.1 mmol, 1.0 equiv.), BT-SR$_F$ (0.125 mmol, 1.25 equiv.) and base (0.1–0.3 mmol, 1.0–3.0 equiv.) stirred in the designated solvent (3.0 mL) for 2 h at the stated temperature.
[b] ^{19}F NMR yields determined using $PhCF_3$ as an internal standard.
[c] Solution of **1a** and NEt(*i*-Pr)$_2$ in THF (1.5 mL) added slowly to solution of BT-S(*n*-C_3F_7) in THF (1.5 mL) over 15 mins.
[d] 2 equiv. of BT-S(n-C_3F_7).

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*-C_3F_7) 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 unambigiously 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, ^{19}F 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).

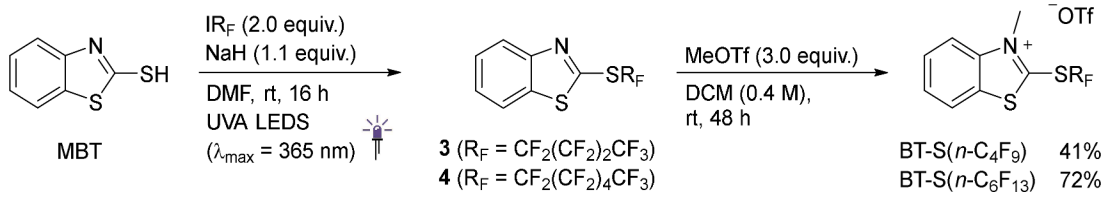
As the first nucleophilic and first deoxygenative route to perfluoroalkyl thioesters with R_F groups longer than CF_3, we next sought to investigate the generality of the approach for accessing novel thioesters with different perfluoroalkyl chains. As a result, six additional benzothiazolium reagents alongside BT-S(*n*-C_3F_7) were selected; five linear BT-SR$_F$ derivatives (BT-SC_2F_5, BT-S(*n*-C_4F_9), BT-S(*n*-C_5F_{11}), BT-S(*n*-C_6F_{13}) and BT-(*n*-SC_8F_{17})) and the heptafluoroisopropyl species BT-S(*i*-C_3F_7), 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*-C_4F_9) and BT-(*n*-C_6F_{13}) 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 synthesized 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 ^{19}F 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 ^{19}F NMR yield of thioesters generally decreasing with longer perfluoroalkyl chains. For example, while the SC_2F_5 compound **5b** was formed in 79 % ^{19}F NMR yield, the S(*n*-C_6F_{13})-containing thioester **8b** was obtained in only 58 % ^{19}F NMR yield. The reaction with BT-S(*n*-C_8F_{17}) 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*-C_4F_9) 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*-C_3F_7) 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 Me_4NSCF_3 by Schoenebeck and co-

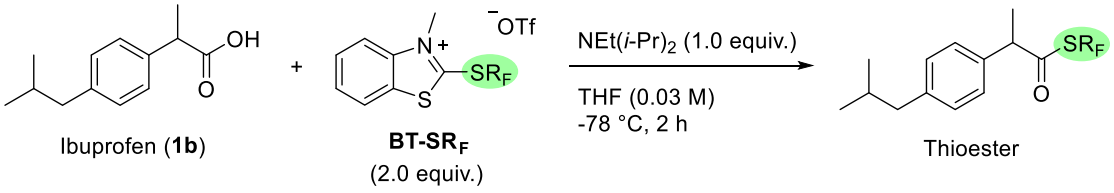


Scheme 2. Synthesis of heptafluoropropyl thioester 2b from ibuprofen 1b. (Conditions from Table 1, Entry 8).



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

Table 2
Deoxygenative perfluoroalkythiolation of ibuprofen **1b** with different BT-SR_F reagents.

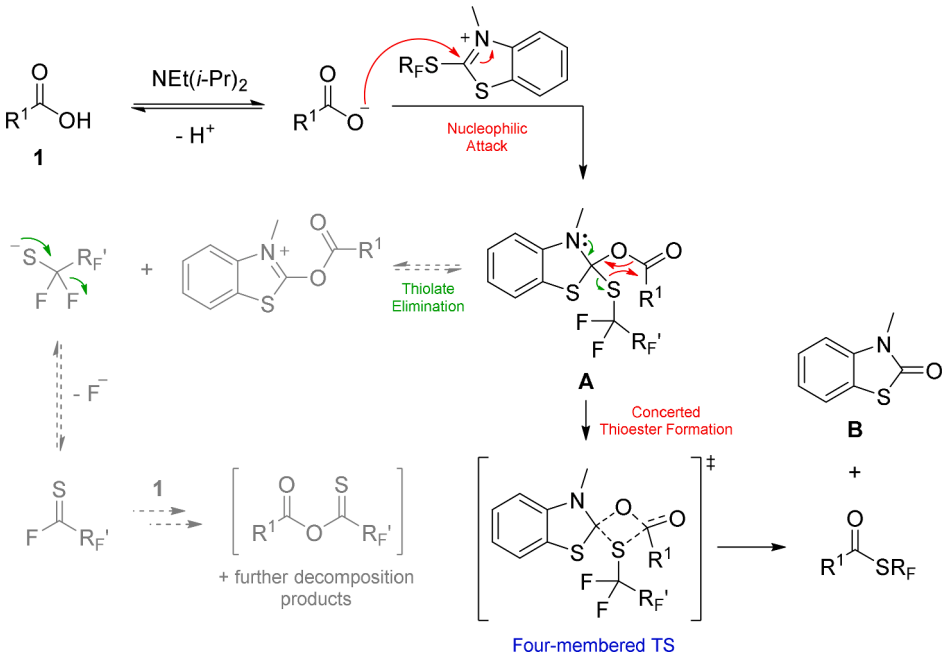


Entry[a]	R_F	Thioester[b]
1	CF_2CF_3	**5b**: 79 %
2	$CF_2CF_2CF_3$	**2b**: 76 %
3	$CF_2(CF_2)_2CF_3$	**6b**: 61 %
4	$CF_2(CF_2)_3CF_3$	**7b**: 51 %
5	$CF_2(CF_2)_4CF_3$	**8b**: 58 %
6	$CF_2(CF_2)_6CF_3$	Traces
7	$CF(CF_3)_2$	Traces

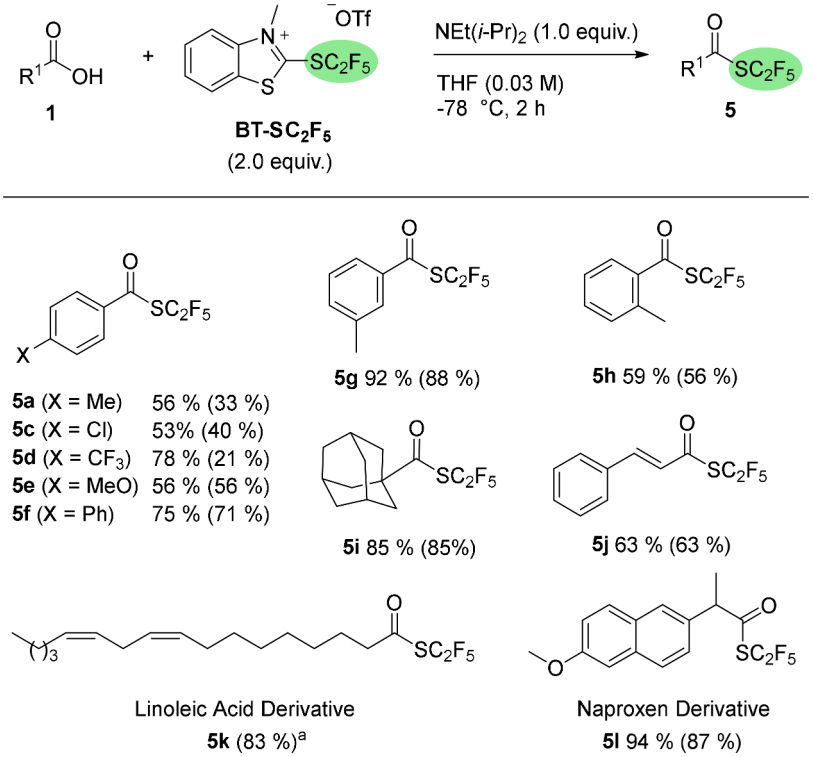
[a] Conditions: **1b** (0.1 mmol, 1.0 equiv.) and NEt(*i*-Pr)$_2$ (0.1 mmol, 1.0 equiv.) in THF (1.5 mL) added slowly over 15 mins to solution of BT-SR_F (0.2 mmol, 2.0 equiv.) in THF (1.5 mL) at −78 °C. Mixture stirred for 2 h.
[b] ^{19}F NMR yields determined using $PhCF_3$ as an internal standard.

workers were often observed as minor by-products while ^{19}F NMR signals consistent with thioic acid anhydride species were also observed. Notably, the reaction between ibuprofen **1b** and BT-(*n*-SC_8F_{17}) 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 SC_2F_5 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-SC_2F_5 (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*-C_3F_7), deoxypentafluoroethythiolation of 4-methylbenzoic acid **1a** proceeded smoothly in 56 % ^{19}F 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 ^{13}C 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, ^{13}C peaks consistent with the thioester products **5** were always observed, with ^{1}H and ^{19}F 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-SC_2F_5. 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 °C. Mixture stirred for 2 h. ^{19}F NMR yield (internal standard: $PhCF_3$), isolated yields after column chromatography in parentheses. [a] ^{19}F NMR yield not measured.

chromatography[1]. Benzoic acid derivatives featuring the more electron-donating groups -OMe and -pH at the *para*-position were seemingly 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 5 g (88 %) and 5 h (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

[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.

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-SC_2F_5. 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 C_6F_{13} while a scope and limitations study with BT-SC_2F_5 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 F_{254} and aluminium oxide 60 F_{254} 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).

^{1}H, ^{19}F and ^{13}C 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). CD_3CN or $CDCl_3$ were used as deuterated solvents and the residual solvent signals were used as references in the ^{1}H and ^{13}C NMR spectra. ^{19}F NMR spectra were not calibrated by an internal reference. ^{19}F 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 $MgSO_4$. 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*-C_4F_9) (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).

^{1}H NMR (300 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): 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*-C_6F_{13}) (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).

^{1}H NMR (700 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): 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). **^{13}C NMR** (176 MHz, $CDCl_3$): 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* CF_2 *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 $[C_{13}H_4F_{13}NS_2]^+$ ($[M]^+$): 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-C_4F_9))

BT-(*n*-SC_4F_9) was prepared according to General Procedure 2. BT-(*n*-SC_4F_9) (2.21 g, 4.0 mmol, 67%) was dried under reduced pressure and obtained as a white powder.

^{1}H NMR (700 MHz, CD_3CN) 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). **^{19}F NMR** (376 MHz, CD_3CN) δ [ppm] = −79.4, −81.6 (t, *J* = 10 Hz), −83.0 (t, *J* = 14 Hz), −119.7, −126.0. **^{13}C NMR** (176 MHz, CD_3CN): 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* CF_2 *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 $[C_{12}H_7F_9NS]^+$ ($[M-OTf]^+$): 399.9871, measured: 399.9876.

4.3.2. 3-Methyl-2-((perfluorohexyl)thio)benzo[d]thiazol-3-ium trifluoromethanesulfonate (BT-S(n-C_6F_{13}))

BT-S(*n*-C_6F_{13}) was prepared according to General Procedure 2. BT-S (*n*-C_6F_{13}) (2.81 g, 4.32 mmol, 87%) was dried under reduced pressure and obtained as a white powder.

^{1}H NMR (300 MHz, CD_3CN) 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). **^{19}F NMR** (282 MHz, CD_3CN) 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). **^{13}C NMR** (176 MHz, CD_3CN): 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* CF_2 *peaks are overlapping.* **IR (ATR)**: ṽ [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 $[C_{14}H_7F_{13}NS_2]^+$ ($[M-OTf]^+$): 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 ^{19}F 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*-SC_3F_7) (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.

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.78 (dt, J = 8.4, 2.0 Hz, 2H), 7.31 (dm, J = 8.4 Hz, 2H), 2.44 (s, 3H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −79.9 (t, J = 9 Hz), −90.0 (qt, J = 9, 3 Hz), −123.9 (m). **^{13}C NMR** (75 MHz, $CDCl_3$): 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)**: ṽ [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 $[C_8H_7O]^+$ ($[M\text{-}SC_3F_7]^+$): 119.0491, measured: 119.0495; calculated for $[C_3F_7S]^-$ ($[M\text{-}C_8H_7O]^-$): 200.9614, measured: 200.9627; calculated for $[C_8H_7OS]^-$ ($[M\text{-}C_3F_7]^-$): 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*-SC_3F_7) (0.30 g, 0.60 mmol) on a 0.3 mmol scale. ^{19}F 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.

^{1}H NMR (300 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −80.0 (t, J = 10 Hz), −90.5 (m), −124.1 (d, J = 3 Hz). **^{13}C NMR** (75 MHz, $CDCl_3$): 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* CF_2 *carbons could not be unambiguously identified.* **IR (ATR)**: ṽ [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 $[C_{16}H_{17}F_7OS]^+$ ($[M]^+$): 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-SC_2F_5 (0.36 g, 0.80 mmol) on a 0.40 mmol scale. ^{19}F 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.

^{1}H NMR (300 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −83.8 (t, J = 3 Hz), −94.0 (dq, J = 241, 3 Hz), −94.9 (dq, J = 241, 3 Hz). **^{13}C NMR** (101 MHz, $CDCl_3$): 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)**: ṽ [cm^{-1}]: 2958, 2872, 1743, 1467, 1320, 1210, 1108, 966, 909, 751, 649, 571, 548. **HRMS (APCI)** calculated for $[C_{15}H_{17}F_5OS]^+$ ($[M]^+$): 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*-C_4F_9) (0.33 g, 0.60 mmol) on a 0.3 mmol scale. ^{19}F 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.

^{1}H NMR (300 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −81.03 (tt, J = 10, 3 Hz), −89.7 (m), −120.6 (m), −125.7 (m). **^{13}C NMR** (75 MHz, $CDCl_3$): 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* CF_3 *and three* CF_2 *carbon could not be unambiguously identified.* **IR (ATR)**: ṽ [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 $[C_{17}H_{17}F_9OS]^+$ ($[M]^+$): 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*-C_5F_{11}) (0.36 g, 0.60 mmol) on a 0.3 mmol scale. ^{19}F 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: ^{1}H, ^{19}F & ^{13}C NMR peaks corresponding to **7b** reported, some peaks overlap with those of the impurity.* **^{1}H NMR** (700 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): 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). **^{13}C NMR** (176 MHz, $CDCl_3$): 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, 3, 22.43, 22.42, 17.9. **IR (ATR)**: ṽ [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 $[C_{15}H_{17}F_5OS]^+$ ($[M]^+$): 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*-C_6F_{13}) (0.39 g, 0.6 mmol) on a 0.3 mmol scale. ^{19}F 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: ^{1}H, ^{19}F & ^{13}C NMR peaks corresponding to **8b** reported, some peaks overlap with those of the impurity.* **^{1}H NMR** (300 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): 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). **^{13}C NMR** (126 MHz, $CDCl_3$): 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)**: ṽ [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 $[C_{19}H_{17}F_{13}OS]^+$ ($[M]^+$): 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-SC_2F_5 (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.

^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.77 (dm, *J* = 8.2 Hz, 2H), 7.30 (dm, *J* = 8.2 Hz, 2H), 2.44 (s, 3H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −83.5 (t, *J* = 3 Hz), −93.9 (q, *J* = 3 Hz). **^{13}C NMR** (101 MHz, $CDCl_3$): 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)**: ṽ [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 $[C_8H_7O]^+$ ($[M\text{-}SC_2F_5]^+$): 119.0491, measured: 119.0495; calculated for $[C_2F_5S]^-$ ($[M\text{-}C_8H_7O]^-$): 150.9646, measured: 150.9644; calculated for $[C_8H_7OS]^-$ ($[M\text{-}C_2F_5]^-$): 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-SC_2F_5 (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.

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.85 – 7.80 (m, 2H), 7.52 – 7.48 (m, 2H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −83.5 (t, *J* = 3 Hz), −93.8 (q, *J* = 3 Hz). **^{13}C NMR** (176 MHz, $CDCl_3$): 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)**: ṽ [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 $[C_7H_4ClO]^+$ ($[M\text{-}SC_2F_5]^+$): 138.9945, measured: 138.9953; calculated for $[C_7H_4ClOS]^-$ ($[M\text{-}C_2F_5]^-$): 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-SC_2F_5 (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.

^{1}H NMR (700 MHz, $CDCl_3$): δ [ppm] = 8.01 (dm, *J* = 8.1 Hz, 2H), 7.80 (dm, *J* = 8.1 Hz 2H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −63.5, −83.5 (t, *J* = 3 Hz), −93.9 (q, *J* = 3 Hz). **^{13}C NMR** (75 MHz, $CDCl_3$): 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)**: ṽ [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 $[C_8H_4F_3O]^+$ ($[M\text{-}SC_2F_5]^+$): 173.0209, measured: 173.0206; calculated for $[C_8H_4F_3OS]^-$ ($[M\text{-}C_2F_5]^-$): 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-SC_2F_5 (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.

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.86 (d, *J* = 9.1 Hz, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 3.89 (s, 3H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −83.5 (t, *J* = 3 Hz), −93.7 (q, *J* = 3 Hz). **^{13}C NMR** (176 MHz, $CDCl_3$): 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)**: ṽ [cm^{-1}]: 1707, 1599, 1509, 1316, 1267, 1207, 1167, 1099, 963, 877, 836, 751, 614. **HRMS (APCI)** calculated for $[C_{10}H_7F_5O_2S]^+$ ($[M]^+$): 287.0165, measured: 287.0158.

4.4.11. S-(Perfluoroethyl) [1,1′-biphenyl]−4-carbothioate 5f

Prepared according to General Procedure 3 using [1,1′-biphenyl]−4-carboxylic acid (0.079 g, 0.40 mmol) and BT-SC_2F_5 (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.

^{1}H NMR (300 MHz, $CDCl_3$): 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). **^{19}F NMR** (282 MHz, $CDCl_3$): 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-SC_2F_5 (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product 5 g 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.

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.72 – 7.66 (m, 2H), 7.49 (dm, *J* = 7.6 Hz, 1H), 7.39 (m, 1H), 2.43 (s, 3H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ [ppm] = −83.5 (t, *J* = 3 Hz), −94.0 (q, *J* = 3 Hz). **^{13}C NMR** (176 MHz, $CDCl_3$): 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)**: ṽ [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 $[C_8H_7O]^+$ ($[M\text{-}SC_2F_5]^+$): 119.0491, measured: 119.0495; calculated for $[C_2F_5S]^-$ ($[M\text{-}C_8H_7O]^-$): 150.9646, measured: 150.9644; calculated for $[C_8H_7OS]^-$ ($[M\text{-}C_2F_5]^-$): 151.0223, measured: 151.0232.

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

Prepared according to General Procedure 3 using 2-methylbenzoic acid (0.041 g, 0.30 mmol) and BT-SC_2F_5 (0.27 g, 0.60 mmol) on a 0.3 mmol scale. Perfluorinated thioester product 5 h 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.

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.75 (m, 1H), 7.50 (m, 1H), 7.24 (m, 2H), 7.35 – 7.28 (m, 2H), 2.53 (s, 3H). **^{19}F 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)**: ṽ [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 $[C_8H_7O]^+$ ($[M\text{-}SC_2F_5]^+$): 119.0491, measured: 119.0496. Calculated for $[C_2F_5S]^-$ ($[M\text{-}C_8H_7O]^-$): 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.

^{1}H 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)**: ṽ [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 $[C_{10}H_{15}]^+$ ($[M\text{-}SC_3OF_5]^+$): 135.1168, measured: 135.1172; calculated for $[C_2F_5S]^-$ ($[M\text{-}C_{11}H_{15}O]^-$): 150.9646, measured: 150.9644; calculated for $[C_{11}H_{15}OS]^-$ ($[M\text{-}C_2F_5]^-$): 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.

^{1}H 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)**: ṽ [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 $[C_9H_7O]^+$ ($[M\text{-}SC_2F_5]^+$): 131.0491, measured: 131.0506. Calculated for $[C_2F_5S]^-$ ($[M\text{-}C_9H_7O]^-$): 150.9646, measured: 150.9644; calculated for $[C_9H_7OS]^-$ ($[M\text{-}C_2F_5]^-$): 163.0223, measured: 163.0223.

4.4.16. S-(Perfluoroethyl) (9Z,12Z)-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 **5n** 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.

^{1}H 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)**: ṽ [cm^{-1}]: 3009, 2926, 2855, 1709, 1459, 1217, 1170, 1104, 965, 751, 724, 599. **HRMS (APCI)** calculated for $[C_{20}H_{31}F_5OS]^+$ ($[M]^+$): 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.

^{1}H 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)**: ṽ [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 $[C_{16}H_{13}F_5O_2S]^+$ ($[M]^+$): 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.

Acknowledgments

This work was funded by Newcastle University (PhD studentship to AH) and the Studienstiftung des deutschen Volkes (PhD scholarship to MT). The authors thank Dr. A. Charlton and the NMR and mass spectrometry services at Newcastle University for analytical support.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2023.110231.

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