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Base-Catalyzed Transesterification of Thionoesters

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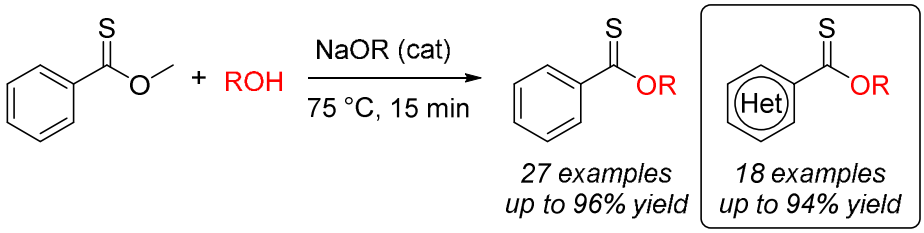
Supporting Information Placeholder[i]

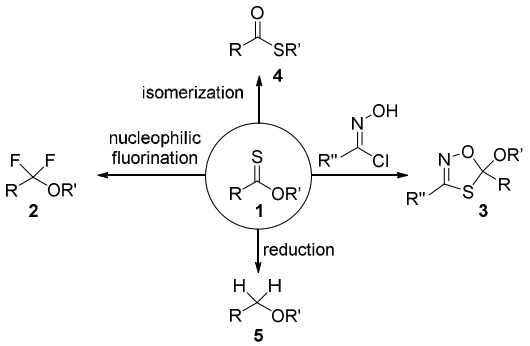


ABSTRACT: Here we report a convenient synthesis of thionoesters by base-catalyzed transesterification. Benzyl and alkyl thionobenzoates and thionoheterobenzoates were efficiently prepared using various alcohols catalyzed by the corresponding sodium alkoxide. This methodology features a broad substrate scope, good to excellent yields, short reaction times, while simultaneously driving the reaction towards completion through the removal of the methanol byproduct. We also report the conversion of a small collection of thionobenzoates into the corresponding α,α-difluorobenzyl ethers to demonstrate the conversion of alcohols into difluorobenzyl or difluoroheterobenzyl ethers, a process that could prove useful for lead optimization in medicinal chemistry.

Introduction

Thionoesters are the thiocarbonyl analogue of esters, and are of interest due to their unique reactivity. For example, thionoesters can be fluorinated by Deoxofluor®[1] to provide difluoroalkyl ethers or readily isomerized to the corresponding thioesters (Scheme 1).[2,3] Thionoesters also serve as ether precursors through reduction by the use of Raney Nickel[4] or tributyltin hydride.[5] Recently, it has been shown that thionoesters can be converted into 1,4,2-oxathiazoles,[6] which are of interest as motifs for drug discovery.[7]

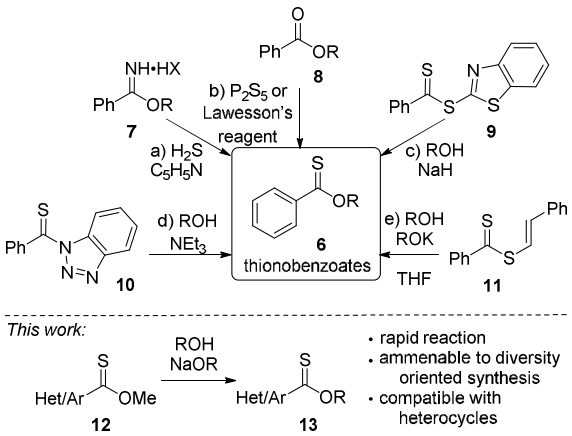
Scheme 1: Common reactions of thionoesters.



While historically thionoesters were accessed from a Pinner alkyl imidate, which is cleaved with H_2S and pyridine,[8,9] they are now generally prepared from their corresponding ester, through the aid of Lawesson's reagent (Scheme 2 b)).[10,11] While this process offers access to a wide range of thionoesters, application of this reaction to diversity oriented or library synthesis can be time-consuming and present challenges in isolation. For example, thionation of benzoyl esters requires 8 or more hours in refluxing xylene and up to 24 h in toluene.[12] Additionally, the purification of thionoester products often requires tedious precipitation of and extensive chromatography to completely remove Lawesson's reagent and reaction byproducts. While alternative and more convenient strategies for thionoester synthesis have been reported, these processes require additional synthetic steps in the preparation of activated precursors (Scheme 2 c)[13], d)[14], e)[15]).[16] It has also been shown that thionoesters can be prepared through the sulfhydrolysis of orthoesters[17] or from ferrocenyl carbene complexes.[18]

Curiously, while the synthesis of thioamides from thionoesters has been reported extensively, the use of alcohols as nucleophiles for the transesterification of thionoesters is extremely rare.[19,20,21] Early research involving transesterification of dithiobenzoyl acetic acid suggested to us that transesterification should provide a straightforward means to rapidly diversify thionoesters.[8,22] In addition, exchange reactions with dithioesters and alcohols have been reported.[23,24] It was also demonstrated that α-oxo-dithioesters will undergo transesterification yielding thionoesters.[16,25] One notable use of this strategy is in the total synthesis of clostrubin, where the resulting thionoester was a Barton-Kellogg olefination as a key step in the synthesis.[26]

Scheme 2: Synthesis of thionobenzoates.

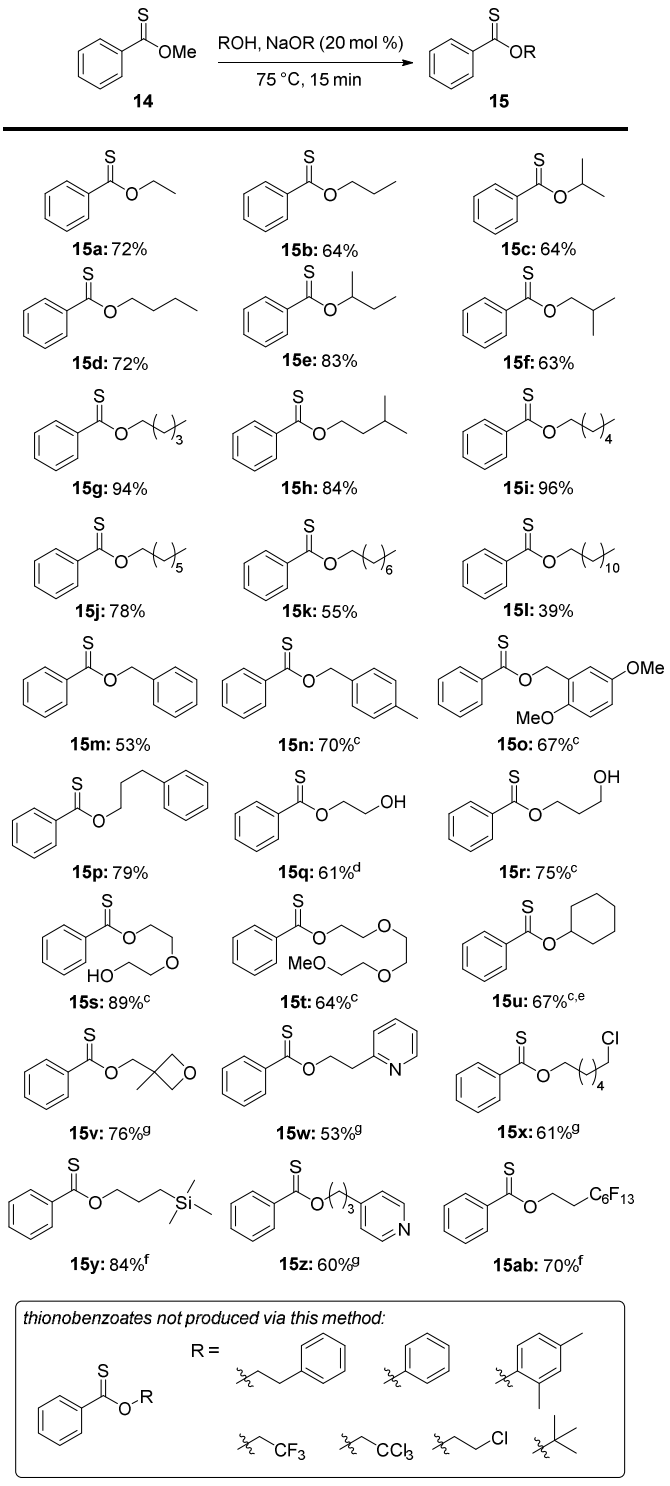


Considering the above, we envisioned a streamlined synthesis of structurally diverse thionoesters could be achieved through a straightforward transesterification reaction from a starting methyl thionoester. Here, transesterification would be promoted by the removal of methanol. While clearly products of transesterification of thionoesters could be accessed using one of the strategies outlined in Scheme 2 or reagents such as thiobenzoyl chloride[27], transesterification offers the advantage of being a mild reaction that involves no byproduct formation, and minimal required purification. To explore this process, we began by examining the transesterification of methylthionobenzoate (**14**).

Results and Discussion

As highlighted in Table 1, the transesterification of methylthionobenzoate is generally a rapid and robust reaction. Each reaction was carried out in a solution (~0.7 M) of the required alcohol with the addition of a catalytic amount of the corresponding alkoxide at 75 °C. In most cases we observed excellent conversion after only 15 minutes, with only small increases in yield with extended time. It should be noted that many thiocarbonyl compounds are sensitive to moisture or photooxidation. While thionoesters are more stable than thioketones or thioaldehydes, we observed the slow hydrolysis of thionoesters into the corresponding ester when stored as aqueous solutions for extended periods of time. As summarized in Table 1, a variety of primary and secondary alcohols (e.g., **15a-15ab**) were successfully transformed into their thionoester derivatives. The possibility of exploiting this transformation for more interesting substrates was also considered, and we were pleased to find that benzyl alcohols, cyclohexanol, as well as short-chain PEG alcohols were all compatible. Transesterification with diols also provided monomeric products (e.g., **15q**, **15r** and **15s**), which is useful for further derivatization. We note that tertiary alcohols, phenols, 2-haloethanols and 2-phenylethanol were all incompatible with this process. Despite these limitations, this straightforward and convenient reaction enabled the rapid assembly of wide range of functionally diverse thionoesters that may otherwise be incompatible with standard reagents used in the conversion of esters to thionoesters (e.g., Lawesson's reagent).

Table 1: Base-catalyzed transesterification of methylthionobenzoate[a,b]

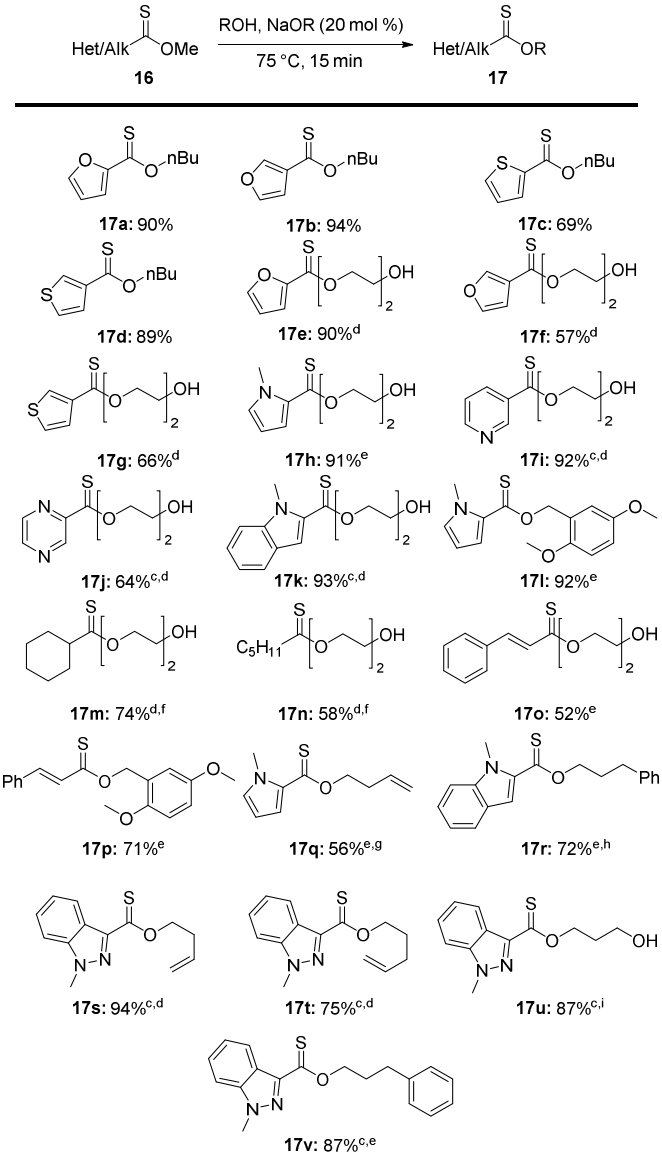


[a] Reaction conditions: methyl thionobenzoate (1.0 mmol) and the described alcohol (1.5 mL) were mixed and then treated with the corresponding sodium alkoxide (0.2 mmol) and heated at 75 °C for 15 min. [b] Isolated yields; [c] reaction time = 2 h; [d] reaction time

= 3 h; [e] reaction on 0.5 mmol scale; [f] reaction time = 30 min; [g] reaction time = 1 h.

Having established a wide scope of compatible alcohols, we next examined a range of alkyl, alkenyl and heteroaryl thionoesters (Table 2). Here, we found that the transformation of a variety of methyl thionoesters could be directly converted into a broad array of thionoesters using this convenient process. Of note, the reaction was compatible with furans, thiophenes, pyrroles, pyridines, pyrazines, indoles, indazoles, and cinnamates.

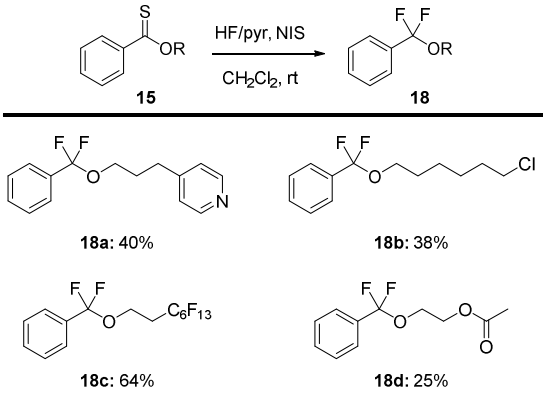
Table 2: Base-catalyzed transesterification of heteroaryl and alkyl thionoesters[a,b]



[a] Reaction conditions: a mixture of the thionoester (1.0 mmol) and the required alcohol (1.5 mL) was treated with the corresponding sodium alkoxide (0.2 mmol) and heated at 75 °C for 15 min; [b] isolated yields; [c] 0.2 mmol thionoester; [d] reaction time = 30 min; [e] reaction time = 1 h; [f] 0.5 mmol thionoester; [g] 2.0 mmol thionoester; [h] 0.1 mmol thionoester; [I] reaction time = 2.5 h.

Finally, in an effort to demonstrate the utility of this process, we examined the conversion of a small collection of readily available thionoesters into the corresponding α,α-difluorobenzyl ethers, as shown in Table 3. Thus, starting with methylthionobenzoate, transesterification followed by fluorination using reaction conditions reported by Kuroboshi,[28,29] we were able to rapidly access the difluorobenzylethers **18a-18d**. As such, this process may prove useful for the conversion of alcohols into difluorobenzyl or difluoroheterobenzyl ethers, a process that could prove useful for lead optimization in medicinal chemistry.[30–32]

Table 3: Synthesis of α,α-difluorobenzyl ethers.



In summary, we developed a convenient and rapid method of preparing thionoesters from primary and secondary alcohols through base-catalyzed transesterification with methyl thionoesters. This process is robust and tolerates a wide range of alcohols and thionoesters.

Experimental Section

General Information. All solvents, reagents and starting materials were purchased from Sigma Aldrich, Anachemia, Fisher Scientific, EMD, Alfa Aesar, AK Sci, or BDH and were used without further purification. Flash chromatography was carried out with Sigma Aldrich high-purity grade 60 Å silica gel (70-230 mesh), or Silicycles 60 Å silica gel (70-230 mesh) using a forced flow of eluent. All reported yields are isolated yields.

Bruker ASCEND III 400 MHz with Bruker AVANCE III 400 MHz running TopSpin 3.1.6 were employed as required for obtaining solution-state NMR data. Nuclear magnetic resonance (NMR) spectra were recorded using CDCl3 (CDCl3). Signal positions (δ) are given in parts per million from tetramethylsilane (δ 0). Coupling constants (J values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. ^{1}H NMR spectral data are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet), coupling constants, number of protons. High-resolution mass spectrometry was performed on an Agilent 6210 TOF LC/MS or a Bruker MaXis Impact TOF LC/MS.

O-Methyl benzothioate ***(14)***[12]**.** Methyl benzoate (13.602 g, 99 mmol) was refluxed with Lawesson's reagent (40.468 g, 100 mmol) in xylenes (150 mL) for 8 h. The crude solution appeared orange, and upon cooling, much of the Lawesson's

reagent precipitated out. The resulting solution was diluted with 150 mL of hexanes to precipitate any residual Lawesson's reagent. The Lawesson's solution was filtered, and residual solvent was evaporated. The resulting solution was purified by column chromatography on silica gel (100% hexane), to yield *O*-methyl benzothioate as an orange liquid (9.694 g, 64% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.5 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.8 Hz, 2H), 4.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 212.3, 138.2, 132.7, 128.8, 128.1, 59.3.

General Procedure for Synthesis of Thionobenzoates. 0.2 mmol of sodium metal was added to in 1.5 mL of the alcohol, and mixed until it had completely dissolved. To the solution was added *O*-methyl benzothioate (0.152 g, 1 mmol), and the mixture was heated at 75°C for 15 minutes, uncapped. Residual volatiles were evaporated, and the crude reaction mixture was purified by column chromatography on silica gel to obtain the pure product.

*O-Ethyl benzothioate (**15a**)*[6]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15a** as a yellow liquid (130 mg, 72% yield).^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 4.64 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 138.5, 132.7, 128.7, 128.1, 68.6, 13.8.

*O-Propyl benzothioate (**15b**)*[13]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15b** as a yellow liquid (116 mg, 64% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.3 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.8 Hz, 2H), 4.63 (q, J = 6.6 Hz, 2H), 1.94 (sext, J = 7.1 Hz, 2H), 1.09 (t, J = 7.4, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.5, 132.6, 128.7, 128.1, 74.3, 21.8, 10.7.

*O-(1-methylethyl) benzothioate (**15c**)*[13]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15c** as a yellow liquid (124 mg, 66% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 2H), 7.44 (t, J = 7.4 Hz, 1H), 7.30 (t, J = 7.3 Hz, 2H), 5.80 (sept, J = 6.2 Hz, 1H), 1.40 (d, J = 6.2 Hz, 6H);^{13}C NMR (101 MHz, $CDCl_3$) δ 210.8, 139.0, 132.5, 128.8, 128.0, 75.6, 21.2.

*O-butyl benzothioate (**15d**)*[13]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15d** as a yellow liquid (150 mg, 72% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.8 Hz, 2H), 4.67 (t, J = 6.5 Hz, 2H), 1.90 (quint, J = 7.1 Hz, 2H), 1.55 (m, 2H), 1.01 (t, J = 1.0, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.5, 132.6, 128.7, 128.1, 72.6, 30.4, 19.5, 13.8.

*O-(1-Methylpropyl) benzothioate (**15e**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15e** as a yellow liquid (156 mg, 83% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.4 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.7 Hz, 2H), (sext, J = 6.2 Hz, 1H), 1.96-1.74 (m, 2H), 1.42 (d, J = 6.2 Hz, 3H), 1.01 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.0, 139.0, 132.5, 128.8, 128.0, 80.2, 28.6, 18.6, 9.7; HRMS (ESI): calcd for $C_{11}H_{15}OS^+$ [M+H$^+$]: 195.0838, found **195.0838.**

*O-(2-Methylpropyl) benzothioate (**15f**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15f** as a yellow liquid (120 mg, 63% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.4 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 4.48 (d, J = 6.5 Hz, 2H), 2.37-2.23 (m, 1H), 1.13 (d, J = 6.7 Hz, 6H) ;^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 138.5, 132.7, 128.7, 128.1, 78.8, 27.8, 19.4; HRMS (ESI): calcd for $C_{11}H_{15}OS^+$ [M+H$^+$]: 195.0838, found **195.0839.**

*O-pentyl benzothioate (**15g**)*[33]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15g** as a yellow liquid (193 mg, 94% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.1 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H**),** 4.66 (t, J = 6.6 Hz, 2H), 1.92 (quint, J = 7.0 Hz, 2H), 1.53-1.37 (m, 2H), 0.95 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.5, 132.6, 128.7, 128.1, 72.9, 28.3, 28.0, 22.4, 14.0.

*O-(3-Methylbutyl) benzothioate (**15h**)*[34]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15h** as a yellow liquid (174 mg, 84% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.4 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.31 (t, J = 7.8 Hz, 2H**),** 4.63 (t, J = 6.5 Hz, 2H), 1.84-1.71 (m, 3H), 0.93 (t, J = 6.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 138.5, 132.6, 128.7, 128.1, 71.5, 37.0, 25.4, 22.6.

*O-hexyl benzothioate (**15i**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15i** as a yellow liquid (214 mg, 96% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 4.2 Hz, 2H), 7.44 (t, J = 7.4 Hz, 1H), 7.30 (t, J = 7.8 Hz, 2H**),** 4.58 (t, J = 6.7 Hz, 2H), 1.83 (quin, J = 7.1 Hz, 2H), 1.43 (quin, J = 7.5 Hz, 2H), 1.33-1.25 (m, 2H), 0.84 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 138.5, 132.6, 128.7, 128.1, 72.9, 31.5, 28.3, 25.9, 22.6, 14.0; HRMS (ESI): calcd for $C_{13}H_{19}OS^+$ [M+H$^+$]: 223.1151, found 223.1140.

*O-heptyl benzothioate (**15j**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15j** as a yellow liquid (186 mg, 78% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H**),** 4.70 (t, J = 6.6 Hz, 2H), 1.95 (quin, J = 7.1 Hz, 2H), 1.57-1.33 (m, 8H), 0.94 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 138.5, 132.6, 128.7, 128.1, 72.9, 31.6, 29.0, 28.3, 26.2, 22.6, 14.1; HRMS (ESI): calcd for $C_{14}H_{21}OS^+$ [M+H$^+$]: 237.1308, found 237.1289.

*O-octtyl benzothioate (**15k**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15k** as a yellow liquid (136 mg, 55% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H**),** 4.70 (t, J = 6.6 Hz, 2H), 1.94 (quin, J = 7.1 Hz, 2H), 1.57-1.29 (m, 10H), 0.93 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.6, 138.5, 132.6, 128.7, 128.1, 72.9, 31.8, 29.3, 29.2, 28.3, 26.2, 22.6, 14.1; HRMS (ESI): calcd for $C_{15}H_{23}OS^+$ [M+H$^+$]: 251.1464, found 251.1483.

*O-dodecyl benzothioate (**15l**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired

product **15l** as a yellow liquid (119 mg, 39% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.8 Hz, 2H), 4.69 (t, J = 6.6 Hz, 2H), 1.94 (quin, J = 7.1 Hz, 2H), 1.54-1.29 (m, 18H), 0.91 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.5, 132.6, 128.7, 128.1, 73.0, 31.9, 29.3, 29.7, 29.6, 29.5, 29.4, 29.3, 28.3, 26.2, 22.7, 14.1; HRMS (ESI): calcd for $C_{19}H_{31}OS^+$ [M+H$^+$]: 307.2090, found 307.2066.

*O-benzyl benzothioate (**15m**)*[13]. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15m** as a yellow liquid (122 mg, 53% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.48 (d, J = 7.8 Hz, 2H), 7.44-7.36 (m, 5H), 5.71 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.1, 138.3, 135.3, 132.9, 128.9, 128.7, 128.5, 128.4, 128.1, 74.1.

*O-(4-methylbenzyl) benzothioate (**15n**)*. Reaction continued for 2h. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15n** as a yellow liquid (172 mg, 70% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.4 Hz, 2H), 7.56 (t, J = 6.9 Hz, 1H), 7.40 (d, J = 7.5 Hz, 4H), 7.26 (d, J = 7.8 Hz, 2H), 5.70 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.2, 138.4, 138.3, 132.8, 132.3, 129.4, 128.9, 128.6, 128.1, 74.2, 21.3; HRMS (ESI): calcd for $C_{15}H_{15}OS^+$ [M+H$^+$]: 243.0838, found 243.0817.

*O-(2,5-dimethoxybenzyl) benzothioate (**15o**)*. Reaction continued for 2h. Purification by column chromatography on silica gel (100% pentane), afforded 15n as a yellow solid. Recrystallization out of pentane afforded yellow flakey crystals. Crystalline mp 69-71 °C; Amorphous mp 65-66 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.4 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.40 (d, J = 7.9 Hz, 2H), 7.06 (s, 1H), 7.40 (d, J = 7.9 Hz, 2H), 5.74 (s, 2H), 3.85 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.3, 153.5, 151.9, 138.5, 132.7, 128.9, 128.1, 124.7, 116.0, 113.9, 111.7, 69.7, 56.1, 55.8; HRMS (ESI): calcd for $C_{16}H_{17}O_3S^+$ [M+H$^+$]: 289.0893, found 289.0871.

*O-(3-Phenylpropyl) benzothioate (**15p**)*. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15p** as a yellow liquid (198 mg, 79% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.2 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 7.8 Hz, 2H), 7.32-7.28 (m, 2H), 7.24-7.19 (m, 2H), 4.68 (t, J = 6.4 Hz, 2H), 2.84 (t, J = 7.6 Hz, 2H), 2.28-2.21 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.5, 141.1, 138.4, 132.7, 128.7, 128.6, 128.5, 128.1, 126.1, 72.0, 32.5, 30.0; HRMS (ESI): calcd for $C_{16}H_{17}OS^+$ [M+H$^+$]: 257.0995, found 257.1015.

*O-(2-Hydroxyethyl) benzothioate (**15q**)*[17]. Reaction continued for 3h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **15q** as a yellow liquid (113 mg, 61% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.39 (d, J = 7.8 Hz, 2H), 4.80 (t, J = 4.6 Hz, 2H), 4.10 (br, 2H), 2.02 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.5, 138.2, 133.0, 128.8, 128.2, 73.6, 60.8.

*O-(2-Hydroxypropyl) benzothioate (**15r**)*[17]. Reaction continued for 2h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **15r** as a yellow liquid (159 mg, 75% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 7.8 Hz, 2H), 4.82 (t, J = 6.2 Hz, 2H), 3.85 (t, J = 6.2, 2H), 2.16 (quint, J = 6.2, 2H), 1.91 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.3, 132.8, 128.7, 128.1, 69.5, 59.5, 31.4.

*O-(2-(2-Hydroxyethoxy)ethyl) benzothioate (**15s**)*. Reaction continued for 2h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **15s** as a yellow liquid (198 mg, 89% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.4 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.39 (d, J = 7.8 Hz, 2H), 4.83 (t, J = 4.7 Hz, 2H), 3.98 (t, J = 4.7, 2H), 3.77 (br, 2H), 3.68 (t, J = 4.44, 2H), 2.15 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 138.2, 132.9, 128.8, 128.1, 72.5, 71.7, 71.4, 68.7, 61.8; HRMS (ESI): calcd for $C_{11}H_{15}O_3S^+$ [M+H$^+$]: 227.0736, found 227.0710.

*O-2-(2-(2-Methoxyethoxy)ethoxy)ethyl benzothioate (**15t**)*. Reaction continued for 2h. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15t** as a yellow liquid (198 mg, 89% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.4 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H), 7.31 (d, J = 7.8 Hz, 2H), 4.75 (t, J = 4.7 Hz, 2H), 3.90 (t, J = 4.7, 2H), 3.69-3.67 (m, 2H), 3.63-3.58 (m, 4H), 3.48-3.46 (m, 2H), 3.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 138.3, 132.8, 128.9, 128.1, 71.9, 71.6, 70.8, 70.7, 70.6, 68.8, 59.1; HRMS (ESI): calcd for $C_{14}H_{21}O_4S^+$ [M+H$^+$]: 285.1155, found 285.1129.

*O-Cyclohexyl benzothioate (**15u**)*[35]. Reaction continued for 2h. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **15u** as a yellow liquid (154 mg, 67% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.3 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.41 (d, J = 7.8 Hz, 2H), 5.73 (quint, J = 4.1 Hz, 1H), 2.12-2.04 (m, 2H), 1.89-1.73 (m, 4H), 1.67-1.43 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.6, 139.0, 132.5, 128.8, 128.0, 80.1, 30.8, 25.5, 23.6.

*O-((3-methyloxetan-3-yl)methyl) benzothioate (**15v**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (10:90 EtOAc/pentane), afforded the desired product **15v** as a dark green liquid (168 mg, 76% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.26 – 8.15 (m, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.9 Hz, 2H), 4.71 (s, 2H), 4.70 (d, J = 6.0 Hz, 2H), 4.53 (d, J = 6.0 Hz, 2H), 1.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 138.3, 133.1, 128.9, 128.4, 79.9, 77.2, 76.6, 39.6, 21.7; HRMS (ESI): calcd for $C_{12}H_{15}O_2S^+$ [M+H$^+$]: 223.0787, found **223.0788**.

*O-(2-(pyridin-2-yl)ethyl) benzothioate (**15w**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **15w** as a swamp green liquid (136 mg, 53% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.58 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 8.15 – 8.06 (m, 2H), 7.64 (td, J = 7.6, 1.8 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.27 (d, J = 7.7 Hz, 1H), 7.17 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 5.07 (t, J = 6.7 Hz, 2H),

3.40 (t, J = 6.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 158.0, 149.8, 138.5, 136.6, 132.8, 128.8, 128.2, 123.5, 121.9, 77.2, 71.6, 37.2.HRMS (ESI): calcd for $C_{14}H_{14}NOS^+$ [M+H$^+$]: 244.0791, found **244.0791**.

*O-(6-chlorohexyl) benzothioate (**15x**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **15x** as a dark orange liquid (164 mg, 61% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.18 (dd, J = 8.5, 1.3 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.40 (dd, J = 8.5, 7.2 Hz, 2H), 4.67 (t, J = 6.5 Hz, 2H), 3.56 (t, J = 6.6 Hz, 2H), 1.94 (p, J = 6.9 Hz, 2H), 1.83 (p, J = 7.0 Hz, 2H), 1.55 (p, J = 3.6 Hz, 4H);^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.5, 132.8, 128.8, 128.2, 77.2, 72.7, 45.1, 32.6, 28.3, 26.7, 25.7. HRMS (ESI): calcd for $C_{13}H_{18}ClOS^+$ [M+H$^+$]: 257.0761, found **257.0759**.

*O-(3-(trimethylsilyl)propyl) benzothioate (**15y**)*. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **15y** as a yellow liquid (206 mg, 84% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.26 – 8.12 (m, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.39 (dd, J = 8.4, 7.2 Hz, 2H), 4.64 (t, J = 6.9 Hz, 2H), 1.98 – 1.85 (m, 2H), 0.69 – 0.60 (m, 2H), 0.05 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.7, 138.7, 132.8, 128.8, 128.2, 77.2, 75.4, 23.1, 12.8, -1.6; HRMS (ESI): calcd for $C_{13}H_{21}OSSi^+$ [M+H$^+$]: 253.1077, found **253.1060**.

*O-(3-(pyridin-4-yl)ethyl) benzothioate (**15z**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (gradient elution from 10:90 to 70:30 EtOAc/pentane), afforded the desired product **15z** as an amber-colored liquid (159 mg, 60% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.53 (d, J = 5.1 Hz, 2H), 8.20 – 8.08 (m, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.17 (d, J = 5.9 Hz, 2H), 4.69 (t, J = 6.3 Hz, 2H), 2.85 (d, J = 7.7 Hz, 2H), 2.33 – 2.21 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 211.4, 150.1, 150.0, 138.3, 133.0, 128.8, 128.3, 124.0, 77.2, 71.5, 32.0, 29.0. HRMS (ESI): calcd for $C_{15}H_{16}NOS^+$ [M+H$^+$]: 258.0947, found **258.0950**.

*O-(1H,1H,2H,2H-perfluoro-1-octyl) benzothioate (**15ab**)*. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (10:90 Et_2O/petroleum ether), afforded the desired product **15ab** as a black-green liquid (300 mg, 70% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.18 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.40 (dd, J = 8.3, 7.4 Hz, 2H), 4.99 (t, J = 6.3 Hz, 2H), 2.76 (tq, J = 18.2, 6.3 Hz, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 210.6, 137.8, 133.1, 128.8, 128.2, 120.7 – 107.5 (m), 63.6 (t, J = 4.0 Hz), 30.3 (t, J = 21.8 Hz); ^{19}F NMR (376 MHz, CDCl3) δ -80.8 (tt, J = 9.9, 2.6 Hz), -112.7 – -113.5 (m), -121.4 – -122.1 (m), -122.4 – -123.1 (m), -123.2 – -123.8 (m), -125.6 – -126.6 (m); HRMS (ESI): calcd for $C_{15}H_9F_{13}OS^+$ [M+H$^+$]: 485.0239, found **485.0237.**

General Procedure for Synthesis of Methyl Heteraryl thionoesters. 0.2 mmol of sodium metal was added to in 1.5 mL of the alcohol, and mixed until it had completely dissolved. To the solution was added *O*-methyl benzothioate (0.152 g, 1 mmol), and the mixture was heated at 75°C for 15 minutes. Residual volatiles were evaporated, and the crude reaction mixture was purified by column chromatography on silica gel to obtain the pure product.

Ester (10 mmol) was mixed with Lawesson's reagent (10 mmol, 4.045 g) in xylenes (9 mL) and heated at 150°C, until conversion to the thionoester slowed to a halt, as monitored by TLC and/or GC-MS. Upon cooling, much of the Lawesson's reagent precipitated out. The resulting solution was diluted with 10 mL of hexanes (or 10 mL of ethyl acetate if the starting ester was insoluble in hexanes) to precipitate any residual Lawesson's reagent. The resulting solution was filtered through a cotton plug, and residual solvent was evaporated. The resulting solution was purified by column chromatography on silica gel, to yield the pure product.

*O-methyl furan-2-carbothioate (**16a**)*. Reaction continued for 3h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **16a** as an orange liquid (0.696 g, 48% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.52 (br, 1H), 7.16 (d, J = 3.5 Hz, 1H), 6.42 (dd, J = 3.0 Hz, 1.6 Hz, 1H), 4.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 153.0, 146.8, 116.7, 112.6, 57.9.

O-methyl furan-3-carbothioate (**16b**)[5]. *Reaction continued for 3h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **16b** as an orange liquid (0.871 g, 62% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, J = 1.5 Hz, 0.7 Hz, 1H), 7.28 (t, J = 1.7 Hz, 1H), 6.75 (dd, J = 1.8 Hz, 0.6 Hz, 1H), 4.10 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.6, 145.7, 143.6, 129.6, 110.2, 58.0; HRMS (ESI): calcd for $C_6H_7O_2S^+$ [M+H$^+$]: 143.0161, found **143.0155.***

O-methyl thiophene-2-carbothioate (**16c**)[36]. *Reaction continued for 3h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **16c** as an orange liquid (1.518 g, 99% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 3.8 Hz, 1.3 Hz, 1H), 7.54 (dd, J = 5.0 Hz, 1.3 Hz, 1H), 7.06 (m, 1H), 4.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.5, 144.9, 133.7, 131.9, 128.1, 58.6.*

O-methyl thiophene-3-carbothioate (**16d).** Reaction continued for 3h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **16d** as an orange liquid (0.975 g, 62% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 3.1 Hz, 1.2 Hz, 1H), 7.67(dd, J = 5.1 Hz, 1.2 Hz, 1H), 7.23 (dd, J = 5.1 Hz, 3.1 Hz, 1H), 4.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.8, 142.9, 130.4, 128.5, 125.5, 58.5; HRMS (ESI): calcd for $C_6H_7O_1S_2^+$ [M+H$^+$]: 158.9933, found **158.9927.**

*O-methyl 1-methyl-1H-pyrrole-2-carbothioate (**16e**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **16d** as a yellow liquid (0.873 g, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (dd, J = 4.1, 1.9 Hz, 1H), 6.80 (t, J = 2.1 Hz, 1H), 6.09 (dd, J = 4.1, 2.5 Hz, 1H), 4.16 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 200.4, 133.6, 131.8, 120.1, 108.4, 57.1, 38.8. HRMS (ESI): calcd for $C_7H_{10}NOS^+$ [M+H$^+$]: 156.0478, found **156.0472.**

*O-methyl pyridine-3-carbothioate (**16f**)*[37]. Reaction continued for 3h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **16f** as a dark orange liquid (0.154 g, 10% yield). Low yields occur

with unprotected N-heterocycles. ^{1}H NMR (400 MHz, CDCl3) δ 9.35 (dd, *J* = 2.2, 0.7 Hz, 1H), 8.79 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.56 – 8.42 (m, 1H), 7.38 (ddd, *J* = 8.1, 4.9, 0.7 Hz, 1H), 4.32 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 209.1, 152.0, 148.5, 137.1, 133.9, 123.2, 59.5.

*O-methyl pyrazine-2-carbothioate (**16g**).* Reaction continued for 1h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **16g**, which was concentrated in vacuo, and placed in the freezer to facilitate crystallization, affording a dark brown waxy crystalline solid (0.100g, 7% yield). mp 115-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (d, *J* = 1.4 Hz, 1H), 8.74 (d, *J* = 2.4 Hz, 1H), 8.67 (dd, *J* = 2.4, 1.5 Hz, 1H), 4.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.3, 148.5, 146.5, 145.4, 143.5, 60.0. HRMS (ESI): calcd for $C_6H_7N_2OS^+$ [M+H$^+$]: 155.0274, found **155.0270.**

*O-methyl 1-methyl-1H-indole-2-carbothioate (**16h**).* Reaction was conducted on a 2 mmol scale. Reaction continued for 1h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **16h** as a yellow crystalline solid (0.079 g, 18% yield). Additional thionoester was contaminated with starting ester in later fractions, and was abandoned. mp 70-72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 1H), 7.47 (s, 1H), 7.39 – 7.31 (m, 2H), 7.13 (ddd, *J* = 7.9, 5.7, 2.2 Hz, 1H), 4.27 (s, 3H), 4.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.5, 140.6, 138.2, 125.8, 125.6, 122.8, 120.8, 111.5, 110.5, 58.0, 32.9. HRMS (ESI): calcd for $C_{11}H_{12}NOS^+$ [M+H$^+$]: 206.0634, found **206.0626.**

*O-methyl cyclohexanecarbothioate (**16i**)[38].* Reaction continued for 2h. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **16i** as a yellow liquid (0.619 g, 33% yield). ^{1}H NMR (400 MHz, CDCl3) δ 4.06 (s, 3H), 2.68 (tt, *J* = 11.7, 3.4 Hz, 1H), 1.96 – 1.89 (m, 2H), 1.79 (dt, *J* = 11.8, 2.9 Hz, 2H), 1.70 – 1.64 (m, 1H), 1.57 – 1.45 (m, 2H), 1.33 – 1.18 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 229.4, 58.7, 54.7, 32.4, 25.8.

*O-methyl hexanethioate (**16j**)*[36]. Reaction continued for 2h. Purification by column chromatography on silica gel (100% pentane), afforded the desired product **16j** as a light-brown liquid (0.337 g, 25% yield). The product is volatile, and should be used within a few days of preparation, as it slowly decomposes and will fume in air. ^{1}H NMR (400 MHz, CDCl3) δ 4.07 (s, 3H), 2.73 (t, *J* = 7.6 Hz, 2H), 1.74 (p, *J* = 7.5 Hz, 2H), 1.35 – 1.29 (m, 4H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 225.4, 58.9, 46.7, 31.0, 28.4, 22.4, 13.9.

*O-ethyl (E)-3-phenylprop-2-enethioate (**16k**)[39].* Reaction continued for 30 minutes. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **16k** as a dark red/orange liquid (0.753 g, 39% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ* 7.69 (d, *J* = 15.8 Hz, 1H), 7.55 (m, 2H), 7.37 (m, 3H), 7.01 (d, *J* = 15.8 Hz, 1H), 4.63 (t, *J* = 7.09 Hz, 2H), 1.47 (q, *J* = 7.09 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 210.4, 140.4, 134.8, 130.3, 129.0, 128.4, 68.9, 13.9.

*Methyl 1-methyl-1H-indazole-3-carboxylate (**8**)*[40]. Methyl-1H-indazole-3-carboxylate (0.922 g, 5.2 mmol) was dissolved in 8 mL of DMF with K_2CO_3 (4.674 g, 33.8 mmol), and to it was added 1.5 mL of iodomethane (24 mmol). The solution was magnetically stirred and heated at 60°C for 4 hours. The resulting solution was diluted in water and extracted with ethyl acetate. The resulting organic layers were combined, and washed twice with water, and dried over sodium sulfate. The resulting solution was filtered, concentrated, and white crystals of **8** slowly formed from the resulting solution over the next few days (0.834 g, 84% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.2 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.5 – 7.4 (m, 2H), 7.3 (dt, *J* = 7.9, 3.9 Hz, 1H), 4.2 (s, 3H), 4.0 (s, 3H);^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 141.2, 134.6, 127.1, 123.9, 123.3, 122.3, 109.6, 77.2, 52.2, 36.5.

*O-methyl 1-methyl-1H-indazole-3-carbothioate (**16l**).* Reaction was conducted on a 3 mmol scale. Reaction continued for 2h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), but the resulting product was contaminated with Lawesson's reagent. The columned product was dissolved in 10 mL of methanol, filtered, and concentrated. The resulting residue was filtered through a plug of silica with 50/50 DCM/pentane, and concentrated, affording yellow crystalline **16l** (0.297 g, 47% yield). mp 54-56 °C. ^{1}H NMR (400 MHz, CDCl3) δ 8.5 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.5 – 7.4 (m, 2H), 7.4 (dt, *J* = 8.0, 3.9 Hz, 1H), 4.4 (s, 3H), 4.2 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.9, 142.4, 141.4, 127.0, 124.0, 123.6, 123.4, 109.6, 77.2, 58.2, 36.6; (ESI): calcd for $C_{10}H_{11}N_2OS^+$ [M+H$^+$]: 207.0587, found **207.0580.**

General Procedure for Transesterification of Heteroaryl Thionoesters. 0.2 mmol of sodium metal was added to in 1.5 mL of the alcohol, and mixed until it had completely dissolved. To the solution was added the heteroaryl thionoester (1 mmol), and the mixture was heated at 75°C for 15 minutes, uncapped. The crude reaction mixture was purified by column chromatography on silica gel to obtain the pure product.

*O-butyl furan-2-carbothioate (**17a**.).* Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **17a** as a yellow liquid (154 mg, 90% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ* 7.60 (dd, *J* = 1.7 Hz, 0.8 Hz, 1H), 7.23 (dd, *J* = 3.6 Hz, 0.7 Hz, 1H), 6.50 (dd, *J* = 3.5 Hz, 1.7 Hz, 1H), 4.63 (t, *J* = 6.6 Hz, 2H), 1.85 (quin; *J* = 7.1 Hz, 2H), 1.50 (sext, *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 197.4, 153.2, 146.8, 116.3, 112.5, 71.3, 30.3, 19.3, 13.8; HRMS (ESI): calcd for $C_9H_{13}O_2S^+$ [M+H$^+$]: 185.0631, found **185.0620.**

*O-butyl furan-3-carbothioate (**17b**.).* Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **17b** as a yellow liquid (193 mg, 94% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ* 8.04 (dd, *J* = 1.4 Hz, 0.6 Hz, 1H), 7.36 (t, *J* = 1.8 Hz, 1H), 6.83 (dd, *J* = 1.8 Hz, 0.6 Hz, 1H), 4.59 (t, *J* = 6.6 Hz, 2H), 1.83 (quin; *J* = 7.1 Hz, 2H), 1.49 (sext, *J* = 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 205.1, 145.6, 143.5, 129.9, 110.1, 71.3, 30.3, 19.4, 13.8; HRMS (ESI): calcd for $C_9H_{13}O_2S^+$ [M+H$^+$]: 185.0631, found **185.0627.**

*O-butyl thiophene-2-carbothioate (**17c**.).* Purification by column chromatography on silica gel (5:95 EtOAc/pentane), af-

forded the desired product **17c** as a yellow liquid (143 mg, 69% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 3.8 Hz, 1.3 Hz, 1H), 7.53 (dd, J = 5.0 Hz, 1.2 Hz, 1H), 7.05 (dd, J = 5.0 Hz, 3.8 Hz, 1H), 4.62 (t, J = 6.5 Hz, 2H), 1.85 (quin; J = 7.0 Hz, 2H), 1.51 (sext, J = 7.5 Hz, 2H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.0, 145.3, 133.5, 131.5, 128.1 72.0, 30.3, 19.4, 13.8; HRMS (ESI): calcd for $C_9H_{13}OS_2^+$ [M+H$^+$]: 201.0402, found **201.0394**.

*O-butyl thiophene-3-carbothioate (**17d**.)*. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **17d** as a yellow liquid (178 mg, 89% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 3.1 Hz, 1.2 Hz, 1H), 7.67 (dd, J = 5.1 Hz, 1.2 Hz, 1H), 7.23 (dd, J = 5.1 Hz, 3.1 Hz, 1H), 4.61 (t, J = 6.6 Hz, 2H), 1.86 (quin; J = 7.1 Hz, 2H), 1.51 (sext, J = 7.5 Hz, 2H), 1.00 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.2, 143.2, 130.2, 128.4, 125.4 71.8, 30.4, 19.4, 13.8; HRMS (ESI): calcd for $C_9H_{13}OS_2^+$ [M+H$^+$]: 201.0402, found **201.0383**.

*O-(2-(2-hydroxyethoxy)ethyl) furan-2-carbothioate (**17e**)*. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17e** as a yellow liquid (194 mg, 90% yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.71 – 7.43 (m, 1H), 7.28 (d, J = 3.6 Hz, 1H), 6.51 (dd, J = 3.6, 1.7 Hz, 1H), 5.01 – 4.57 (m, 2H), 3.98 – 3.90 (m, 1H), 3.82 – 3.70 (m, 2H), 3.70 – 3.64 (m, 2H), 2.18 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8, 153.0, 147.0, 117.1, 112.7, 72.5, 70.1, 68.6, 61.7.; HRMS (ESI): calcd for $C_9H_{13}O_4S^+$ [M+H$^+$]: 217.0529, found **217.0507**.

*O-(2-(2-hydroxyethoxy)ethyl) furan-3-carbothioate (**17f**)*. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17f** as a yellow liquid (135 mg, 57% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 1.5 Hz, 0.7 Hz, 1H), 7.37 (t, J = 1.7 Hz, 1H), 6.85 (dd, J = 2.0 Hz, 0.6 Hz, 1H), 4.66 (t, J = 4.7 Hz, 2H), 4.76 (t; J = 4.7 Hz, 2H), 3.92 (t, J = 4.7 Hz, 2H), 3.76 (t, J = 4.4 Hz, 2H), 3.66 (t, J = 4.5 Hz, 2H), 2.17 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.7, 145.9, 143.6, 129.6, 110.2, 72.5, 70.2, 68.7, 61.7.; HRMS (ESI): calcd for $C_9H_{13}O_4S^+$ [M+H$^+$]: 217.0529, found **217.0504**.

*O-(2-(2-hydroxyethoxy)ethyl) thiophene-3-carbothioate (**17g**)*. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17g** as a yellow liquid (159 mg, 66% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, J = 3.1 Hz, 1.1 Hz, 1H), 7.68 (dd, J = 5.1 Hz, 1.1 Hz, 1H), 7.24 (dd, J = 5.1 Hz, 3.1 Hz, 1H), 4.66 (t, J = 4.7 Hz, 2H), 3.94 (t; J = 4.6 Hz, 2H), 3.67 (m, 2H), 3.66 (t, J = 4.5 Hz, 2H), 2.15 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 142.9, 130.6, 128.5, 125.6, 72.5, 70.7, 68.7, 61.8; HRMS (ESI): calcd for $C_9H_{13}O_3S_2^+$ [M+H$^+$]: 233.0301, found **233.0292.**

*O-(2-(2-hydroxyethoxy)ethyl)-1-methyl-1H-pyrrole-2-carbothioate (**17h**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17h** as a yellow liquid (208 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 4.1, 1.9 Hz, 1H), 6.81 (dd, J = 2.1 Hz, 1H), 6.10 (dd, J = 4.1, 2.5 Hz, 1H), 4.75 (t, J = 4.7 Hz, 2H), 3.96 (s, 3H), 3.90 (t, J = 4.7 Hz, 2H), 3.77 – 3.72 (m, 2H), 3.64 (t, J = 4.2 Hz, 2H), 2.09 (br, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.4, 133.7, 132.1, 121.0, 108.8, 77.2, 72.4, 69.2, 69.0, 61.9, 38.9. HRMS (ESI): calcd for $C_{10}H_{16}NO_3S^+$ [M+H$^+$]: 230.0845, found **230.0853**.

*O-(2-(2-hydroxyethoxy)ethyl) pyridine-3-carbothioate (**17i**)*. Reaction conducted on a 0.22 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (100% EtOAc), afforded the desired product **17i** as a yellow liquid (46 mg, 92% yield). ^{1}H NMR (400 MHz, CDCl3) δ 9.35 (dd, J = 2.2, 0.7 Hz, 1H), 8.79 (dd, J = 4.9, 1.7 Hz, 1H), 8.56 – 8.42 (m, 1H), 7.38 (ddd, J = 8.1, 4.9, 0.7 Hz, 1H), 4.32 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ 209.1, 152.0, 148.5, 137.1, 123.2, 59.5. HRMS (ESI): calcd for $C_{10}H_{14}NO_3S^+$ [M+H$^+$]: 228.0689, found **228.0691.**

*O-(2-(2-hydroxyethoxy)ethyl) pyrazine-2-carbothioate (**17j**)*. Reaction conducted on a 0.23 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (100% EtOAc), afforded the desired product **17j** as an orange/brown oil (33 mg, 64% yield). ^{1}H NMR (400 MHz, CDCl3) δ 9.42 (d, J = 1.4 Hz, 1H), 8.71 (d, J = 2.5 Hz, 1H), 8.66 – 8.57 (m, 1H), 4.91 – 4.80 (m, 2H), 4.06 – 3.97 (m, 2H), 3.78 – 3.75 (m, 2H), 3.70 – 3.66 (m, 2H), 2.02 (br, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.7, 148.6, 147.0, 146.8, 145.7, 143.6, 77.2, 72.8, 72.4, 68.3, 61.8. HRMS (ESI): calcd for $C_9H_{13}N_2O_3S^+$ [M+H$^+$]: 229.0641, found **229.0631.**

*O-(2-(2-hydroxyethoxy)ethyl) 1-methyl-1H-indole-2-carbothioate (**17k**.)*. Reaction conducted on a 0.21 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17k.** as a yellow liquid (56 mg, 93% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 4.1, 1.9 Hz, 1H), 6.81 (dd, J = 2.1 Hz, 1H), 6.10 (dd, J = 4.1, 2.5 Hz, 1H), 4.75 (t, J = 4.7 Hz, 2H), 3.96 (s, 3H), 3.90 (t, J = 4.7 Hz, 2H), 3.77 – 3.72 (m, 2H), 3.64 (t, J = 4.2 Hz, 2H), 2.09 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.6, 140.6, 138.2, 125.9, 125.8, 122.8, 120.9, 112.3, 110.6, 72.4, 70.2, 68.7, 61.8, 33.0. HRMS (ESI): calcd for $C_{14}H_{18}NO_3S^+$ [M+H$^+$]: 280.1002, found **280.1001.**

*O-(2-(2-hydroxyethoxy)ethyl)-1-methyl-1H-pyrrole-2-carbothioate (**17l**)*. Reaction continued for 1h. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **17l** as a yellow liquid (266 mg, 92% yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.28 – 7.21 (m, 1H), 7.02 – 6.94 (m, 1H), 6.86 – 6.84 (m, 1H), 6.78 (t, J = 2.2 Hz, 1H), 6.08 (dd, J = 4.1, 2.5 Hz, 1H), 5.64 (s, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.4, 153.4, 152.0, 133.7, 131.6, 125.1, 120.9, 116.2, 114.0, 111.5, 108.5, 67.7, 56.0, 55.8, 38.7. HRMS (ESI): calcd for $C_{15}H_{18}NO_3S^+$ [M+H$^+$]: 292.1002, found **292.0992.**

*O-(2-(2-hydroxyethoxy)ethyl) cyclohexanecarbothioate (**17m**)*. Reaction conducted on a 0.52 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product

17m as a yellow liquid (90 mg, 74% yield). ^{1}H NMR (400 MHz, CDCl3) δ 4.54 (t, *J* = 4.7 Hz, 2H), 3.78 (t, *J* = 4.7 Hz, 2H), 3.72 – 3.63 (m, 2H), 3.60 – 3.52 (m, 2H), 2.62 (tt, *J* = 11.6, 3.4 Hz, 1H), 2.03 (s, 1H), 1.91 – 1.82 (m, 2H), 1.72 (td, *J* = 12.0, 2.9 Hz, 2H), 1.64 – 1.58 (m, 1H), 1.45 (qd, *J* = 12.3, 3.1 Hz, 2H), 1.32 – 1.05 (m, 4H).^{13}C NMR (101 MHz, $CDCl_3$) δ 228.7, 72.3, 70.7, 68.6, 61.7, 54.7, 32.5, 25.8, 25.7. $C_{11}H_{21}O_3S^+$ [M+H$^+$]: 233.1206, found **233.1200**.

*O-(2-(2-hydroxyethoxy)ethyl) hexanethioate (**17n**).* Reaction conducted on a 0.58 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17n** as a yellow liquid (74 mg, 58% yield). ^{1}H NMR (400 MHz, CDCl3) δ 4.61 (t, *J* = 4.7 Hz, 2H), 3.85 (t, *J* = 4.7 Hz, 2H), 3.81 – 3.71 (m, 2H), 3.68 – 3.57 (m, 2H), 2.75 (t, *J* = 7.7 Hz, 2H), 2.11 (s, 1H), 1.75 (p, *J* = 9.8, 7.3 Hz, 2H), 1.37 – 1.29 (m, 4H), 0.92 – 0.87 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 224.6, 72.4, 71.0, 68.5, 61.7, 46.9, 31.0, 28.4, 22.3, 13.9. $C_{10}H_{21}O_3S^+$ [M+H$^+$]: 221.1206, found **221.1205**.

*O-(2-(2-hydroxyethoxy)ethyl)-(Z)-3-phenylprop-2-enethioate (**17o**).* Reaction continued for 1h. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17o** as a dark red/orange liquid (120 mg, 52% yield). ^{1}H-NMR (400 MHz, $CDCl_3$) *δ* 7.75 (d, *J* = 15.8 Hz, 1H), 7.56 (m, 2H), 7.38 (m, 3H), 7.05 (d, *J* = 15.8 Hz, 1H), 4.75 (t, *J* = 4.7 Hz, 2H), 3.93 (t, *J* = 4.7 Hz, 2H), 3.78 (t, *J* = 4.5 Hz, 2H), 3.67 (t, *J* = 4.5 Hz, 2H), 2.04 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 210.3, 141.5, 134.7, 130.4, 129.0, 128.6, 72.4, 70.7, 68.8, 61.8, 53.4; HRMS (ESI): calcd for $C_{13}H_{17}O_3S^+$ [M+H$^+$]: 253.0893, found **253.0860.**

*O-(2,5-dimethoxybenzyl) (E)-3-phenylprop-2-enethioate (**17p**).* Reaction continued for 1h. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product **17p** as a dark red/orange liquid (252 mg, 71% yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.73 (d, *J* = 15.8 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.41 – 7.34 (m, 3H), 7.07 (d, *J* = 15.8 Hz, 1H), 7.04 – 6.96 (m, 1H), 6.92 – 6.83 (m, 2H), 5.63 (s, 2H), 3.83 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.2, 153.5, 151.9, 141.0, 134.8, 130.3, 128.9, 128.9, 128.4, 124.8, 116.0, 114.0, 111.7, 69.0, 56.2, 55.8. HRMS (ESI): calcd for $C_{18}H_{19}O_3S^+$ [M+H$^+$]: 315.1049, found **315.1036.**

*O-(but-3-en-1-yl) 1-methyl-1H-pyrrole-2-carbothioate (**17q**)* Reaction conducted on a 2.19 mmol scale. Reaction continued for 1h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **17q** as a yellow liquid (241 mg, 56% yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.23 (dd, *J* = 4.1, 2.0 Hz, 1H), 6.79 (dd, *J* = 2.0 Hz, 1H), 6.09 (dd, *J* = 4.1, 2.0 Hz, 1H), 5.88 (ddt, *J* = 17.0, 10.3, 6.6 Hz, 1H), 5.18 (dq, *J* = 17.0, 1.6 Hz, 1H), 5.12 (dd, *J* = 10.3, 1.6 Hz, 1H), 4.65 (t, *J* = 6.6 Hz, 2H), 3.94 (s, 3H), 2.61 (qt, *J* = 6.6, 1.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7, 134.3, 133.8, 131.6, 120.8, 117.3, 108.6, 69.6, 38.9, 32.9. HRMS (ESI): calcd for $C_{10}H_{14}NOS^+$ [M+H$^+$]: 196.0791, found **196.0785.**

*O-(3-phenylpropyl) 1-methyl-1H-indole-2-carbothioate (**17r**).* Reaction conducted on a 0.46 mmol scale. Reaction continued for 1h. Purification by column chromatography on silica gel (5:95 EtOAc/pentane), afforded the desired product **17r** as a yellow crystalline solid (103 mg, 72% yield). mp 57-58 °C. ^{1}H NMR (400 MHz, CDCl3) δ 7.71 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.49 (s, 1H), 7.43 – 7.31 (m, 4H), 7.30 – 7.24 (m, 3H), 7.17 (ddd, *J* = 8.0, 5.8, 2.1 Hz, 1H), 4.73 (t, *J* = 6.4 Hz, 2H), 4.11 (s, 3H), 2.88 (dd, *J* = 8.6, 6.8 Hz, 2H), 2.35 – 2.21 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.8, 141.0, 140.6, 138.4, 128.6, 128.4, 126.2, 125.8, 125.7, 122.8, 120.8, 111.5, 110.5, 70.9, 33.0, 32.6, 30.1. HRMS (ESI): calcd for $C_{19}H_{20}NOS^+$ [M+H$^+$]: 310.1260, found **310.1254.**

*O-(but-3-en-1-yl) 1-methyl-1H-indazole-3-carbothioate (**17s**).* Reaction conducted on a 0.18 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **17s** as a yellow crystalline solid (43 mg, 94% yield). mp 34-35 °C. ^{1}H NMR (400 MHz, CDCl3) δ 8.3 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.4 – 7.3 (m, 2H), 7.3 (dtd, *J* = 8.0, 3.9, 0.9 Hz, 1H), 5.9 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.2 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.1 (dd, *J* = 10.2, 1.5 Hz, 1H), 4.8 (t, *J* = 6.8 Hz, 2H), 4.1 (s, 3H), 2.7 (dt, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.8, 142.8, 141.4, 134.0, 126.9, 123.8, 123.4, 122.3, 117.8, 109.6, 77.2, 70.6, 36.7, 32.9; HRMS (ESI): calcd for $C_{13}H_{15}N_2OS^+$ [M+H$^+$]: 247.0900, found **247.0904**.

*O-(pent-4-en-1-yl) 1-methyl-1H-indazole-3-carbothioate (**17t**).* Reaction conducted on a 0.18 mmol scale. Reaction continued for 30 minutes. Purification by column chromatography on silica gel (20:80 EtOAc/pentane), afforded the desired product **17t** as an orange liquid (35 mg, 75% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.4 (d, *J* = 8.2 Hz, 1H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 1H), 5.9 (ddt, *J* = 16.9, 10.1, 6.6 Hz, 1H), 5.1 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.0 (dq, *J* = 10.2, 1.3 Hz, 1H), 4.8 (t, *J* = 6.8 Hz, 2H), 4.2 (s, 3H), 2.3 (td, *J* = 7.5, 6.1 Hz, 2H), 2.1 (p, *J* = 6.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.9, 142.8, 141.4, 137.5, 126.9, 123.9, 123.4, 122.5, 115.7, 109.6, 77.2, 71.0, 36.7, 30.4, 27.7; HRMS (ESI): calcd for $C_{14}H_{17}N_2OS^+$ [M+H$^+$]: 261.1056, found **261.1059.**

*O-(3-hydroxypropyl) 1-methyl-1H-indazole-3-carbothioate (**17u**).* Reaction conducted on a 0.22 mmol scale. Reaction continued for 2.5h. Purification by column chromatography on silica gel (50:50 EtOAc/pentane), afforded the desired product, which was still contained 1,3-propanediol which was extracted with a several small portions with water, from a solution in diethyl ether. The solution was dried over sodium sulfate, filtered, and concentrated in vacuo, affording the desired product **17u** as a yellow oil, which crystallized after several days (48 mg, 87% yield). mp 89-90 °C. ^{1}H NMR (400 MHz, CDCl3) δ 8.5 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.5 – 7.5 (m, 2H), 7.4 (dt, *J* = 8.0, 3.9 Hz, 1H), 5.0 (t, *J* = 6.1 Hz, 2H), 4.2 (s, 3H), 3.9 – 3.9 (m, 4H), 2.4 (s, 1H), 2.3 (q, *J* = 6.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.3, 142.4, 141.5, 127.0, 124.0, 123.4, 123.1, 109.7, 77.2, 69.2, 60.3, 36.7, 31.6; HRMS (ESI): calcd for $C_{12}H_{15}N_2O_2S^+$ [M+H$^+$]: 251.0849, found **251.0852.**

*O-(3-phenylpropyl) 1-methyl-1H-indazole-3-carbothioate (**17v**)*. Reaction conducted on a 0.23 mmol scale. Reaction continued for 1h. Purification by column chromatography on silica gel (15:85 EtOAc/pentane), afforded the desired product **17v** as a yellow oil, which crystallized after several days (63 mg, 87% yield). mp 109-111 °C. ^{1}H NMR (400 MHz, CDCl3) δ 8.4 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.5 – 7.4 (m, 2H), 7.4 – 7.3 (m, 3H), 7.3 – 7.2 (m, 2H), 4.8 (t, *J* = 6.7 Hz, 2H), 4.2 (s, 3H), 2.9 (dd, *J* = 8.7, 6.7 Hz, 2H), 2.4 – 2.3 (m, 2H);^{13}C NMR (101 MHz, $CDCl_3$) δ 203.8, 142.8, 141.5, 141.2, 128.7, 128.6, 127.0, 126.3, 123.9, 123.3, 122.5, 109.7, 77.2, 70.9, 36.7, 32.5, 30.1; HRMS (ESI): calcd for $C_{18}H_{19}N_2OS^+$ [M+H$^+$]: 311.1213, found **311.1211.**

General Procedure for Oxidative Fluorodesulfuration of Thionoesters. Thionoester (0.2 mmol) was dissolved in 1 mL of DCM, and to the solution was added HF/pyridine(70/30, 0.05 mL) was subsequently added. The solution was magnetically stirred until homogenous, and N-iodosuccinimide was added in one portion (0.5 mmol). The solution quickly turned black and was allowed to stir at room temperature for 15 minutes. The resulting solution neutralized dropwise with NaHCO_3 sat'd water until slightly basic, and the iodine liberated in the reaction was quenched with sodium thiosulfate. The organic layer was separated, and the aqueous layer was extracted with 3x1 mL of dichloromethane. The organic layers were combined, dried over sodium sulfate, filtered, and the solvent was evaporated in vacuo. The crude reaction mixture was purified by column chromatography on silica gel to yield the desired product.

*4-(3-(difluoro(phenyl)methoxy)propyl)pyridine (**18a**)*. Purification by column chromatography on silica gel (Gradient elution from 20:80 to 50/50 EtOAc/pentane), afforded the desired product **18a** as a colorless liquid (21 mg, 40% yield). ^{1}H NMR (400 MHz, CDCl3) δ 8.5 (d, *J* = 4.9 Hz, 2H), 7.7 – 7.6 (m, 2H), 7.5 – 7.4 (m, 3H), 7.1 (d, *J* = 6.1 Hz, 2H), 4.1 (t, *J* = 6.2 Hz, 2H), 2.8 (t, *J* = 7.7 Hz, 2H), 2.1 – 2.0 (m, 2H); ^{13}C NMR (101 MHz, CDCl3) δ 150.5, 149.9, 134.3 (t, *J* = 32.6 Hz), 130.7, 128.5, 125.5 (t, *J* = 3.7 Hz), 124.1, 62.9 (t, *J* = 5.9 Hz), 31.6, 29.9; HRMS (ESI): calcd for $C_{15}H_{16}F_2NO^+$ [M+H$^+$]: 264.1194, found **264.1197.**

*(((6-chlorohexyl)oxy)difluoromethyl)benzene (**18b**)*. Purification by column chromatography on silica gel (5:95 Et_2O/pentane), afforded the desired product **18b** as a colorless liquid (13 mg, 38% yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.65 – 7.58 (m, 2H), 7.50 – 7.38 (m, 3H), 4.04 (t, *J* = 6.5 Hz, 2H), 3.55 (t, *J* = 6.7 Hz, 2H), 1.80 (p, *J* = 6.7 Hz, 2H), 1.73 (p, *J* = 6.6 Hz, 2H), 1.53 – 1.43 (m, 4H). ^{13}C NMR (101 MHz, CDCl3) δ 134.4 (t, *J* = 32.8 Hz), 130.4, 128.3, 125.4 (t, *J* = 3.7 Hz), 122.9, 63.7 (t, *J* = 5.9 Hz), 45.0, 32.5, 29.1, 26.5, 25.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -69.2. HRMS (ESI): calcd for $C_{13}H_{17}ClF_2ONa^+$ [M+Na$^+$]: 285.0828, found **285.0819.**

*((1H,1H,2H,2H-perfluoro-1-octyl)difluoromethyl)benzene (**18c**)*. Purification by column chromatography on silica gel (5:95 Et_2O/pentane), afforded the desired product **18c** as a colorless liquid (60 mg, 64 % yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.7 – 7.6 (m, 2H), 7.6 – 7.3 (m, 3H), 4.4 (t, *J* = 6.7 Hz, 2H), 2.6 (tt, *J* = 18.1, 6.6 Hz, 2H). ^{13}C NMR (101 MHz, CDCl3) δ 133.5 (t, *J* = 31.8 Hz), 130.7, 128.4, 125.3 (t, *J* = 3.7 Hz), 122.8, 121.6 – 106.3 (m, $CF_2CF_2CF_2CF_2CF_2CF_3$), 56.0 (t, *J* = 5.9 Hz), 31.3 (t, *J* = 21.8 Hz); ^{19}F NMR (376 MHz, CDCl3) δ -70.3 (s), -80.8 (tt, *J* = 10.1, 2.6 Hz), -120.3 – -106.0 (m), -121.9 (t, *J* = 14.4 Hz), -122.6 – -123.1 (m), -123.3 – -123.8 (m), -125.8 – -126.4 (m). HRMS (ESI): calcd for $C_{15}H_9F_{15}ONa^+$ [M+Na$^+$]: 513.0306, found **513.0308.**

*2-((phenylcarbonothioyl)oxy)ethyl acetate (**17w**)*. ***15q*** was dissolved in 1 mL of dichloromethane to which acetic anhydride was added (0.104 g, 1.02 mmol), followed by the addition of a catalytic amount of 4-dimethylamino-pyridine (2 mg, 0.016 mmol). The mixture was stirred at room temperature for 15 minutes, and the crude reaction mixture was filtered through a plug of silica, eluted with 20/80 ethyl acetate pentane. The solvent was removed in vacuo, yielding **17w** as a yellow liquid (59 mg, 91% yield). In a test experiment without the dimethylaminopyridine, no reaction was observed by TLC even after 3 hours. ^{1}H NMR (400 MHz, CDCl3) δ 8.19 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 4.88 – 4.81 (m, 2H), 4.58 – 4.53 (m, 2H), 2.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.1, 170.8, 138.0, 133.0, 128.9, 128.1, 70.0, 61.7, 20.9; HRMS (ESI): calcd for $C_{11}H_{13}O_3S^+$ [M+H$^+$]: 225.0580, found **225.0580.**

*2-(difluoro(phenyl)methoxy)ethyl acetate (**18d**)*. Purification by column chromatography on silica gel (5:95 Et_2O/pentane), afforded the desired product **18d** as a colorless liquid (11 mg, 25% yield). ^{1}H NMR (400 MHz, CDCl3) δ 7.7 – 7.6 (m, 2H), 7.5 – 7.4 (m, 3H), 4.4 – 4.3 (m, 2H), 4.2 – 4.2 (m, 2H), 2.1 (s, 3H).^{13}C NMR (101 MHz, CDCl3) δ 171.0, 133.9 (t, *J* = 32.1 Hz), 130.8, 128.5, 125.6 (t, *J* = 3.7 Hz), 123.0, 62.7, 62.0 (t, *J* = 6.0 Hz), 21.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -69.4; HRMS (ESI): calcd for $C_{11}H_{12}F_2NaO_3^+$ [M+Na$^+$]: 253.0647, found **253.0641.**

ASSOCIATED CONTENT

Supporting Information

(The Supporting Information is available free of charge on the ACS Publications website.

^{1}H-,^{13}C-, and ^{19}F-NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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