JOC The Journal of Organic Chemistry

Article

Air-Tolerant Direct Thiols Esterification with Carboxylic Acids Using Hydrosilane Via Simple Inorganic Base Catalysis

Maojie Xuan, Chunlei Lu, Meina Liu, and Bo-Lin Lin

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b00500 • Publication Date (Web): 29 May 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

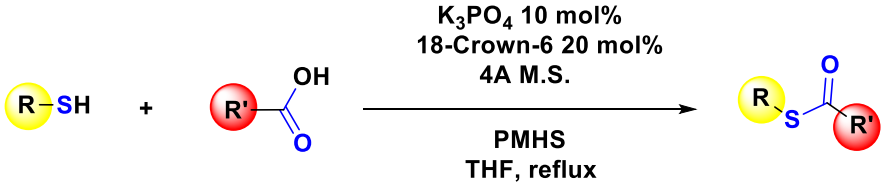
Air-Tolerant Direct Thiols Esterification with Carboxylic Acids Using Hydrosilane Via Simple Inorganic Base Catalysis

Maojie Xuan,[†,‡] Chunlei Lu,[‡,§] Meina Liu,[*,†] and Bo-Lin Lin[*,‡,§]

[†]School of Chemical and Environmental Engineering, Shanghai Institute of Technology, Shanghai 201418, People's Republic of China

[‡]School of Physical Science and Technology (SPST), ShanghaiTech University, Shanghai 201210, People's Republic of China

[§]Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, People's Republic of China



- transition metal free
- air tolerant
- gram scale
- 42 examples, yields up to 100%
- high functional group tolerance

ABSTRACT: Direct thioesterification of carboxylic acids with thiols using nontoxic activation agent is highly desirable. Herein, an efficient and practical protocol using safe and inexpensive industrial waste PMHS (poly(methylhydrosiloxane)) as the activation agent and K_3PO_4 with 18-crown -6 as a catalyst is described. Various functional groups on carboxylic acid and thiol substituents can be tolerated by the present system to afford thioesters in yields of 19 to 100%.

INTRODUCTION

The development of synthetic methods for C-S bond constructions with mild, inexpensive, and easy-to-operate reaction conditions has been attracting widespread interests[1-2] owing to the prevalence of sulfur element in natural products, bioactive molecules and materials[1]. In particular, thioester is an important structural fragment of many physiologically active drugs and natural products[3], such as topical effective corticosteroids, Fluticasone furoate and Fluticasone propionate for anti-allergic reactions, Stepronin for liver disease adjuvant, Butyrylthiocholine for detection of pseudocholinesterase, Thiolactomycin for sensitive bacterial infection, cough expectant Erdosteine, diuretic Spirocolactone, and signal transduction pathway kinase inhibitor Dalciperib, *etc.* (**Figure 1**). Furthermore, activation of carboxylic acid via the formation of thioester intermediate has also attracted a great deal of attention in synthetic chemistry[4], allowing for facile preparations of various functional groups, such as esters[5], amides[6], aldehydes[7], and ketones[7a, 8], due to the weaker p-π orbital overlap of thioesters relative to esters[9]. The acetyl form of coenzyme A also takes advantage over such a strategy to efficiently transfer acetyl groups in living organisms[10].

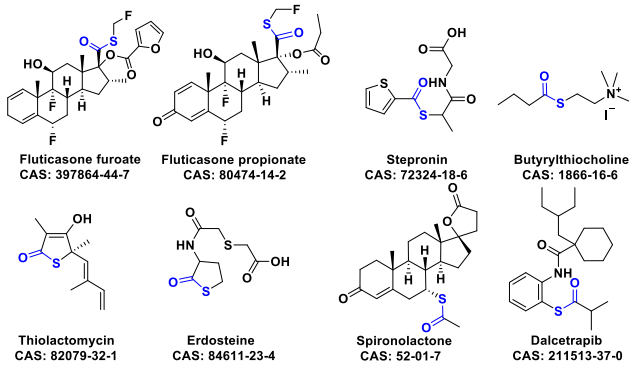
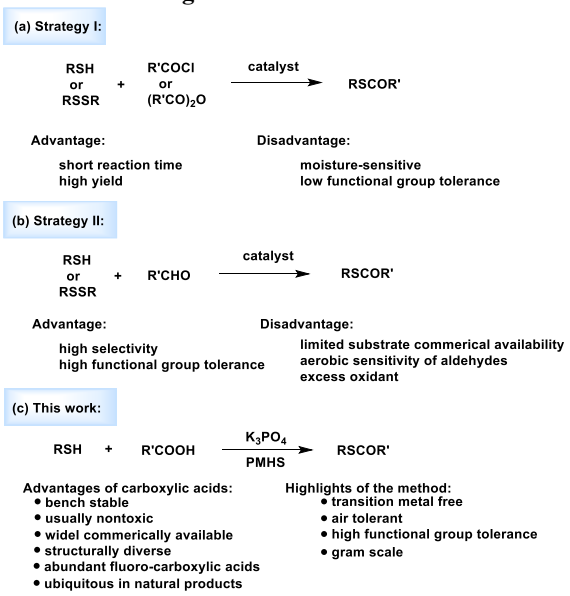


Figure 1. Representative thioester structure

Given the significance of thioesters, a few synthetic methods have been developed over the past few decades[11]. The esterification[12] of thiols is one of the most commonly-used reactions[11, 13]. However, the reactions typically use moisture-sensitive acid chlorides[14] or acid anhydrides[14c, 14d, 15] as the acylation agent and transition metals, such as zinc[14a], nickel[15a], titanium[15c] and copper[16], as the catalyst (**Scheme 1a**). New methods using aldehyde[17] have been developed recently to convert thiol or disulfide to thioester under oxidative conditions (**Scheme 1b**). In 2013, Zhu *et al.* reported a method for the synthesis of thioesters by oxidative coupling of aldehydes with thiols or disulfides using $K_2S_2O_8$ as the oxidant[17g]. Subsequently, Lee *et al.* reported the use of TBHP[17a] (*tert*-butyl hydroperoxide) or DTBP[17f] (di-*tert*-butyl peroxide) as the oxidant for the reaction. However, these oxidative methods suffer from drawbacks such as the limited availability and aerobic sensitivity of aldehydes.

Scheme 1. Strategies for Thioester Construction

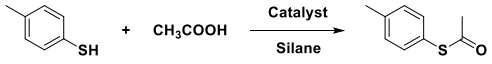


RESULTS AND DISCUSSION

Alternative method to form thioesters directly from carboxylic acid and thiol is still highly desirable. The unfavorable thermodynamic barrier represents a core challenge for intermolecular thioesterification of carboxylic acids with thiols[18]. To overcome such a barrier, strategies including activation of carboxylic acid by a stoichiometric amount of toxic carbodiimides or continuous removal of the water side product under azeotropic refluxing conditions[18a] have been developed. Recently, several reports on N-alkylation or acylation have demonstrated that hydrosilanes can be used to activate carboxylic acids or CO_2 via the formation of silyl esters[19]. We postulated that such a strategy may also be used to active carboxylic acid, enabling direct intermolecular thioesterification of carboxylic acids with thiols. Herein, we report that potassium phosphate (K_3PO_4) catalyzes the intermolecular direct thioesterification of carboxylic acids with thiols using hydrosilane (**Scheme 1c**), especially polymethylhydrosiloxane (PMHS)—a side product of silicon industry, as the activation agent.

Initially, we chose *p*-toluenethiol and acetic acid as the model substrates. A series of organic and inorganic bases were screened as the potential catalyst in the presence of PMHS. To our delight, thioester was observed upon refluxing a mixture of the substrates in THF for 12 hours (h) in the presence of a 10 mol% loading of catalyst with 20 mol% loading of 18-crown-6 and 12 equivalents of Si-H bond with 10 mg 4A molecular sieve (4A M.S.) (**Table 1**, entries 1-6). K_3PO_4 was found to be the best one, leading to a quantitative formation of the desired product (**Table 1**, entry 6). Control experiments confirmed that K_3PO_4, 18-crown-6 and 4A M.S. are all necessary for the quantitative yield (**Table 1**, entries 7-9). 18-crown-6 is presumably a phase-transfer agent that enhances the solubility of the salt. It's worth mentioning that all the experiments were performed under air.

Table 1. Catalyst Screening and Condition Optimization[a]



1 2a 3a

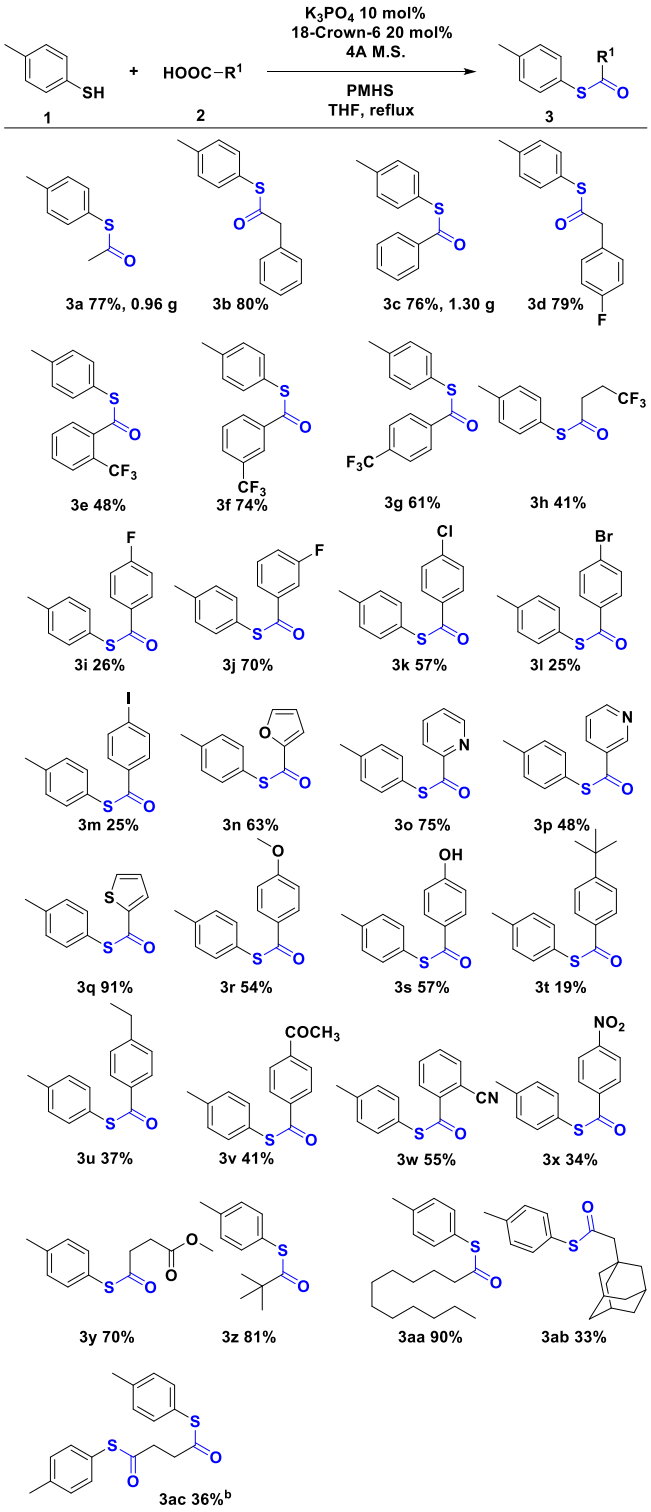
Entry	Cat.	Silane	Solvent	Yield (%)
1[b]	DBU	PMHS	THF	14
2[b]	Et_3N	PMHS	THF	2
3[b]	DMAP	PMHS	THF	4
4	K_2CO_3	PMHS	THF	31
5	KOH	PMHS	THF	97
6	K_3PO_4	PMHS	THF	>99
7[b]	K_3PO_4	PMHS	THF	26
8	-	PMHS	THF	-
9[c]	K_3PO_4	PMHS	THF	91
10	K_3PO_4	$PhSiH_3$	THF	>99
11[d]	K_3PO_4	$PhSiH_3$	THF	71
12	K_3PO_4	Ph_2SiH_2	THF	96
13	K_3PO_4	Ph_3SiH	THF	-
14	K_3PO_4	$(EtO)_3SiH_3$	THF	2
15	K_3PO_4	PMHS	DMF	28
16	K_3PO_4	PMHS	CH_3CN	65
17	K_3PO_4	PMHS	Toluene	38
18	K_3PO_4	PMHS	1,4-dioxane	66
19[e]	**K_3PO_4**	**PMHS**	**THF**	**92**

[a]Reaction conditions: It was carried out on a 0.25 mmol scale. *p*-Toluenethiol (1 eq), catalyst (10 mol%), 18-Crown-6 (20 mol%), 4A molecular sieve (10 mg), with acetic acid(4.6 eq) and silane(12 eq Si-H bond) under air in the solvent (1.6 mL) , at reflux overnight. Determined by GC analysis of the reaction mixture using anisole as internal standard. [b]No 18-Crown-6. [c]No 4A molecular sieve. [d]Room temperature. [e]Acetic acid (3 eq) and PMHS (6 eq Si-H bond).

Subsequent studies indicated that the reaction is highly sensitive to the hydrosilane. The yield follows the order of PMHS~$PhSiH_3$ > Ph_2SiH_2 > $(EtO)_3SiH$ > Ph_3SiH (**Table 1**,

entries 10, 12-14), indicating that steric hindrance of hydrosilanes may have a great influence on the reaction. It was worth mentioning that a 71% yield was obtained with $PhSiH_3$ even at room temperature (RT) (**Table 1**, entry 11). A screening of solvents showed that THF is the best one (**Table 1**, entries 15-18). Finally, an excess amount of carboxylic acid is needed (**Table 1**, entries 6, 19).

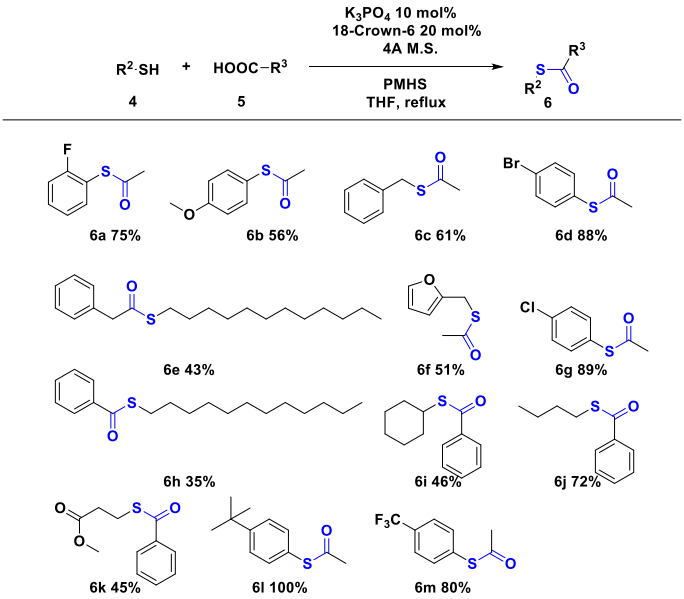
Table 2. Scope of Carboxylic Acids[a]



[a]Reaction conditions: It was carried out on a 0.25 mmol scale. *p*-Toluenethiol (1 eq), K_3PO_4 (10 mol%), 18-C-6 (20 mol%), 4A M.S. (10 mg), with carboxylic acid (3 eq) and PMHS (6 eq Si-H bond) under air in the solvent (1.6 mL) over night. [b]Succinic acid (1.5 eq)

With the optimal reaction conditions in hand, we next explored the scope of carboxylic acids for the present system (**Table 2**). Carboxylic acids with either an electron-donating or electron-withdrawing group could be converted to the desired products. A wide scope of aromatic carboxylic acids with various functional groups, such as fluoro (**3d**, **3i**, **3j**), chloro (**3k**), bromo (**3l**), iodo (**3m**), methoxyl (**3r**), *tert*-butyl (**3t**, **3z**, **3ab**), trifluoromethyl (*o/m/p*: **3e-3g**), **ethyl** (**3u**), carbonyl (**3v**), nitrile (**3w**) and nitro (**3x**), are suitable substrates. Notably, hydroxyl group is well tolerated, which is particularly challenging for other methods. The present methodology can also be extended to other aliphatic carboxylic acids (**3b**, **3h**, **3y-3ac**), including a substrate with an ester group (**3y**) and a dicarboxylic acid (**3ac**). Two natural carboxylic acids, nicotinic acid (**3p**) and lauric acid (**3aa**), could also directly react with a thiol to obtain the corresponding thioesters. In addition, heteroaryl carboxylic acids also furnished corresponding thioesters in good to excellent yields (**3n-3q**). Furthermore, good yields were successfully obtained for two gram-scale reactions (**3a**, **3c**), clearly proving the excellent scalability of the present protocol.

Table 3. Scope of Thiols[a]



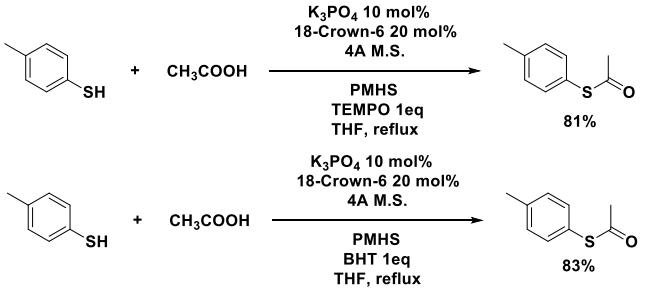
[a]Reaction conditions: It was carried out on a 0.25 mmol scale. Thiols (1 eq), K_3PO_4 (10 mol%), 18-C-6 (20 mol%), 4A M.S. (10 mg), with carboxylic acid (3 eq) and PMHS (6 eq Si-H bond) under air in the solvent (1.6 mL) over night.

We next studied the scope of thiols (**Table 3**). In general, thiols reacted with benzoic acid or acetic acid to offer the corresponding thioesters in 35–100% yields under the present catalytic conditions. Functional groups including fluoro (**6a**), chloro (**6g**), bromo (**6d**), furan (**6f**), trifluoromethyl (**6m**), ester (**6k**), methoxyl (**6b**) and *tert*-butyl (**6l**) are tolerated. Aliphatic thiols with a linear (**6e**, **6h**, **6j**), branched (**6k**) or cyclic (**6i**) chain are all suitable substrates.

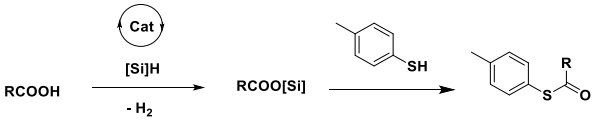
A radical pathway has been proposed for previous C-S coupling reactions to form thioesters[17b, 17f, 20]. To test whether a

similar mechanism is also involved in the present system, we performed control experiments in the presence of a radical inhibitor (**Scheme 2**). It was found that the reaction was virtually unaltered by the addition of TEMPO or dibutylhydroxytoluene (BHT), suggesting a non-radical mechanism. As discussed earlier, previous literatures[19a, 19b, 19h, 21-22] indicate that hydrosilane and carboxylic acid may undergo dehydrogenative coupling to form silyl esters, which can subsequently react with thiol to form the thioester (**Scheme 3**).

Scheme 2. Control Experiment Suggesting A Non-radical Mechanism



Scheme 3. Possible Mechanism



CONCLUSIONS

In summary, we developed a convenient catalytic approach for direct thioesterification of thiols with excess carboxylic acids using inexpensive industrial waste PMHS as the activation agent. The simplicity and the wide substrate scopes of the catalytic system indicate that ubiquitous carboxylic acids may be pursued as a new type of useful and general acylation agents for the construction of C-S bonds under transition metal-free and air-tolerant conditions.

EXPERIMENTAL SECTION

General Methods. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance 500 MHz and 400 MHz spectrometer at ambient temperature in $CDCl_3$ unless otherwise noted. Data for ^{1}H-NMR are reported as follows: chemical shift (δ ppm), multiplicity, integration, and coupling constant (Hz). Data for ^{13}C-NMR are reported in terms of chemical shift (δ ppm), multiplicity, and coupling constant (Hz). GC-MS analysis was performed on Thermo Scientific Ultimate 3000 GC-MS System. Gas chromatographic (GC) analyses were performed on a Jiedao GC-1620 series GC system equipped with a flame-ionization detector using anisole as an internal standard. Glove box (Mikrouna Germany) was used for the set-up of the reactions. Flash column chromatographic purification of the products was accomplished using forced-flow chromatography on Silica Gel (200-300 mesh).

General procedure for the esterification of thiol using carboxylic acids with PMHS and analytical data of compounds. In a glovebox, K_3PO_4 (10 mol %, 5.3 mg), 18-Crown-6 (20 mol %, 13.2 mg) , 4A M.S. (10 mg), and 1.6 mL tetrahydrofuran were added into a Schlenk tube equipped with a stir bar, then PMHS (1.5 mmol Si-H bond, 121 μL), thiol (0.25 mmol) and carboxylic acid (0.75 mmol) were added on the outside under an air atmosphere. The reaction mixture was stirred refluxing overnight (450 rpm). To isolate the products, the reaction mixture was diluted with EtOAc, filtered through a short silica gel column. The resultant solution was concentrated and purified by silica gel column chromatography with EtOAc and petroleum ether as the eluent to give the corresponding thioester.

S-(p-tolyl) ethanethioate (**3a**): Colorless liquid (0.96 g, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 7.9 Hz, 2H), 2.33 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.71, 139.78, 134.47, 130.09, 124.45, 30.14, 21.38.

S-(p-tolyl) 2-phenylethanethioate (**3b**): Colorless liquid (48.4 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.20 (m, 5H), 7.17 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 3.81 (s, 2H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.91, 139.74, 134.46, 133.43, 130.05, 129.73, 128.75, 127.55, 124.27, 50.07, 21.39. HRMS (ESI) for $C_{15}H_{14}OS$ $[M+H]^+$: calcd 243.0838, found 243.0833.

*S-(p-tolyl) benzothioate (***3c**): White solid (1.30 g, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 7.7 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.7 Hz, 2H), 7.31 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.64, 139.87, 136.74, 135.09, 133.64, 130.17, 128.78, 127.52, 123.80, 21.45.

S-(p-tolyl) 2-(4-fluorophenyl)ethanethioate (**3d**): Colorless liquid (51.4 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 4H), 7.10 (d, J = 8.0 Hz, 2H), 6.94 (t, J = 8.6 Hz, 2H), 3.77 (s, 2H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.48 (s), 162.64 (d, J = 248.5 Hz), 140.04 (s), 138.59 (d, J = 6.7 Hz), 134.90 (s), 130.35 (d, J = 7.7 Hz), 130.16 (s), 123.20 (s), 123.17 (s), 120.48 (d, J = 21.4 Hz), 114.25 (d, J = 23.0 Hz), 21.35 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -114.89. HRMS (ESI) for $C_{15}H_{13}FOS$ $[M+H]^+$: calcd 235.0246, found 235.0241.

S-(p-tolyl) 2-(trifluoromethyl)benzothioate (**3e**): White solid (35.5 mg, 48%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, J = 15.6, 7.2 Hz, 2H), 7.59 – 7.51 (m, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.73 (s), 140.27 (s), 137.53 (q, J = 1.6 Hz), 134.58 (s), 131.79 (s), 131.17 (s), 130.32 (s), 128.42 (s), 127.27 (q, J = 32.8 Hz), 127.06 (q, J = 5.1 Hz), 123.65 (s), 123.26 (q, J = 274.0 Hz), 21.43 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -58.53 (s). HRMS (ESI) for $C_{15}H_{11}F_3OS$ $[M+H]^+$: calcd 297.0555, found 297.0549.

S-(p-tolyl) 3-(trifluoromethyl)benzothioate (**3f**): Colorless liquid (54.8 mg ,74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.52 (s), 140.19 (s), 137.27 (s), 134.89 (s), 131.33 (q, J = 33.0 Hz), 130.56 (s), 130.23 (s), 129.90 (q, J = 3.6 Hz), 129.40 (s), 124.27 (q, J = 3.9 Hz), 123.78 (q, J = 272.2 Hz), 122.89 (s), 21.35 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.77 (s). HRMS (ESI) for $C_{15}H_{11}F_3OS$ $[M+H]^+$: calcd 297.0555, found 297.0550.

S-(p-tolyl) 4-(trifluoromethyl)benzothioate (**3g**): White solid (45.1 mg, 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.83 (s), 140.22 (s), 139.46 (s), 134.88 (s), 134.82 (q, J = 32.8 Hz), 130.24 (s), 127.77 (s), 125.78 (q, J = 3.7 Hz), 124.44 (q, J = 273.4 Hz), 122.93 (s), 21.37 (s). ^{19}F NMR (471

MHz, $CDCl_3$) δ -63.10 (s). HRMS (ESI) for $C_{15}H_{11}F_3OS$ $[M+H]^+$: calcd 297.0555, found 297.0548.

S-(p-tolyl) 4,4,4-trifluorobutanethioate (**3h**): Colorless liquid (25.4 mg, 41%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.84 – 2.78 (m, 2H), 2.46 – 2.35 (m, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.21 (s), 140.14 (s), 134.45 (s), 130.17 (s), 125.72 (q, *J* = 275.94 Hz), 123.22 (s), 35.63 (q, *J* = 2.8 Hz), 29.21 (q, *J* = 30.3 Hz), 21.32 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -66.62 (s). HRMS (ESI) for $C_{11}H_{11}F_3OS$ $[M+H]^+$: calcd 249.0555, found 249.0548.

S-(p-tolyl) 4-fluorobenzothioate (**3i**): White solid (16.0 mg, 26%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.00 – 7.96 (m, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.11 – 7.07 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.19 (s), 166.01 (d, *J* = 255.4 Hz), 139.97 (s), 135.01 (s), 132.98 (d, *J* = 3.0 Hz), 130.15 (s), 130.02 (d, *J* = 9.4 Hz), 123.42 (s), 115.87 (d, *J* = 22.2 Hz), 21.38 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -104.32 (s). HRMS (ESI) for $C_{14}H_{11}FOS$ $[M+H]^+$: calcd 247.0587, found 247.0583.

S-(p-tolyl) 3-fluorobenzothioate (**3j**): White solid (43.1 mg, 70%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 9.1 Hz, 1H), 7.37 (td, *J* = 8.0, 5.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.23 – 7.17 (m, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.48 (s), 162.64 (d, *J* = 248.5 Hz), 140.04 (s), 138.59 (d, *J* = 6.7 Hz), 134.90 (s), 130.35 (d, *J* = 7.7 Hz), 130.16 (s), 123.20 (s), 123.17 (s), 120.48 (d, *J* = 21.4 Hz), 114.25 (d, *J* = 23.0 Hz), 21.35 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -111.33 (s). HRMS (ESI) for $C_{14}H_{11}FOS$ $[M+H]^+$: calcd 247.0587, found 247.0581.

S-(p-tolyl) 4-chlorobenzothioate (**3k**): White solid (37.3 mg, 57%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.6 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.49 (s), 140.01 (s), 139.95 (s), 135.00 (s), 134.95 (s), 130.16 (s), 129.01 (s), 128.79 (s), 123.28 (s), 21.37 (s).

S-(p-tolyl) 4-bromobenzothioate (**3l**): White solid (19.1 mg, 25%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 9.1 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.72 (s), 140.03 (s), 135.44 (s), 134.95 (s), 132.00 (s), 130.18 (s), 128.89 (s), 128.63 (s), 123.24 (s), 21.38 (s).

S-(p-tolyl) 4-iodobenzothioate (**3m**): White solid (22.1 mg, 25%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.70 (s), 139.71 (s), 137.67 (s), 135.69 (s), 134.63 (s), 129.85 (s), 128.44 (s), 122.90 (s), 101.03 (s), 21.07 (s). HRMS (ESI) for $C_{14}H_{11}IOS$ $[M+H]^+$: calcd 354.9648, found 354.9644.

S-(p-tolyl) furan-2-carbothioate (**3n**): White solid (34.3 mg, 63%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 0.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.19 – 7.16 (m, 3H), 6.48 (dd, *J* = 3.5, 1.7 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.08 (s), 150.36 (s), 146.35 (s), 139.94 (s), 135.04 (s), 130.07 (s), 122.48 (s), 116.10 (s), 112.34 (s), 21.33 (s). HRMS (ESI) for $C_{12}H_{10}O_2S$ $[M+H]^+$: calcd 219.0474, found 219.0469.

S-(p-tolyl) pyridine-3-carbothioate (**3p**): Colorless liquid (27.5 mg, 48%). ^1H NMR (500 MHz, $CDCl_3$) δ 9.17 (s, 1H), 8.75 (d, *J* = 2.7 Hz, 1H), 8.19 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.36 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.29 (s), 153.89 (s), 148.58 (s), 140.23 (s), 134.88 (s), 134.72 (s), 132.33 (s), 130.23 (s), 123.60 (s), 122.60 (s), 21.36 (s). HRMS (ESI) for $C_{13}H_{11}NOS$ $[M+H]^+$: calcd 230.0634, found 230.0627.

S-(p-tolyl) pyridine-2-carbothioate (**3o**): White solid (42.9 mg, 75%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.5 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.78 (td, *J* = 7.7, 1.5 Hz, 1H), 7.48 – 7.44 (m, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.29 (s), 151.66 (s), 149.07 (s), 139.59 (s), 137.31 (s), 134.80 (s), 130.00 (s), 127.99 (s), 124.46 (s), 120.69 (s), 21.32 (s). HRMS (ESI) for $C_{13}H_{11}NOS$ $[M+H]^+$: calcd 230.0634, found 230.0627.

S-(p-tolyl) thiophene-2-carbothioate (**3q**): White solid (53.2 mg, 91%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 3.7, 0.7 Hz, 1H), 7.54 (dd, *J* = 4.9, 0.7 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 7.9 Hz, 2H), 7.04 (dd, *J* = 4.7, 4.1 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.42 (s), 141.34 (s), 139.89 (s), 134.92 (s), 133.04 (s), 131.43 (s), 130.03 (s), 127.91 (s), 123.23 (s), 21.31 (s). HRMS (ESI) for $C_{12}H_{10}OS_2$ $[M+H]^+$: calcd 235.0246, found 235.0239.

S-(p-tolyl) 4-methoxybenzothioate (**3r**): White solid (34.8 mg, 54%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.02 (s), 163.86 (s), 139.60 (s), 135.08 (s), 129.99 (s), 129.63 (s), 129.40 (s), 123.97 (s), 113.82 (s), 55.49 (s), 21.34 (s). HRMS (ESI) for $C_{15}H_{14}O_2S$ $[M+H]^+$: calcd 259.0787, found 259.0780.

S-(p-tolyl) 4-hydroxybenzothioate (**3s**): White solid (34.8 mg, 57%). ^1H NMR (500 MHz, DMSO-d6) δ 10.63 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 187.90 (s), 163.44 (s), 139.78 (s), 135.54 (s), 130.42 (s), 130.14 (s), 127.48 (s), 124.10 (s), 116.22 (s), 21.32 (s). HRMS (ESI) for $C_{14}H_{12}O_2S$ $[M+H]^+$: calcd 245.0631, found 245.0624.

S-(p-tolyl) 4-(tert-butyl)benzothioate (**3t**): White solid (13.5 mg, 19%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 5.9 Hz, 2H), 2.33 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.17 (s), 157.41 (s), 139.68 (s), 135.04 (s), 134.03 (s), 130.04 (s), 127.37 (s), 125.66 (s), 123.93 (s), 35.19 (s), 31.07 (s), 21.37 (s). HRMS (ESI) for $C_{18}H_{20}OS$ $[M+H]^+$: calcd 285.1308, found 285.1304.

S-(p-tolyl) 4-ethylbenzothioate (**3u**): White solid (23.7 mg, 37%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.18 (s), 150.63 (s), 139.67 (s), 135.03 (s), 134.29 (s), 130.03 (s), 128.18 (s), 127.62 (s), 123.91 (s), 28.98 (s), 21.35 (s), 15.19 (s). HRMS (ESI) for $C_{16}H_{16}OS$ $[M+H]^+$: calcd 257.0995, found 257.0989.

S-(p-tolyl) 4-acetylbenzothioate (**3v**): White solid (27.7 mg, 41%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.3 Hz, 2H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 2.58 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.29 (s), 190.12 (s), 140.50 (s), 140.12 (s), 139.93 (s), 134.86 (s), 130.20 (s), 128.57 (s), 127.63 (s), 123.11 (s), 26.88 (s), 21.37 (s). HRMS (ESI) for $C_{16}H_{14}O_2S$ $[M+H]^+$: calcd 271.0787, found 271.0782.

S-(p-tolyl) 2-cyanobenzothioate (**3w**): White solid (34.8 mg, 55%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.4 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.64 (tdd, *J* = 15.1, 10.8, 4.2 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 2.33 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 188.64 (s), 140.37 (s), 139.04 (s), 135.09 (s), 134.79 (s), 132.77 (s), 132.61 (s), 130.25 (s), 129.11 (s), 122.55 (s), 117.11 (s), 110.34 (s), 21.36 (s). HRMS (ESI) for $C_{15}H_{11}NOS$ $[M+H]^+$: calcd 254.0634, found 254.0628.

S-(p-tolyl) 4-nitrobenzothioate (**3x**): White solid (23.2 mg, 34%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.7 Hz, 2H), 8.10 (d, *J* = 8.7 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 189.32 (s), 150.58 (s), 141.32 (s), 140.48 (s), 134.80 (s), 130.34 (s), 128.45 (s), 123.96 (s), 122.52 (s), 21.40 (s). HRMS (ESI) for $C_{14}H_{11}NO_3S$ $[M+H]^+$: calcd 274.0532, found 274.0525.

methyl 4-oxo-4-(p-tolylthio)butanoate (**3y**): Colourless liquid (41.7 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 3.61 (s, 3H), 2.91 (t, *J* = 6.9 Hz, 2H), 2.60 (t, *J* = 6.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.67 (s), 172.29 (s), 139.76 (s), 134.46 (s), 130.00 (s), 123.71 (s), 51.89 (s), 37.89 (s), 28.86 (s), 21.27 (s). HRMS (ESI) for $C_{12}H_{14}O_3S$ $[M+H]^+$: calcd 239.0736, found 239.0731.

S-(p-tolyl) 2,2-dimethylpropanethioate (**3z**): White solid (42.1 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.29 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.05 (s), 139.26 (s), 134.85 (s), 129.88 (s), 124.46 (s), 46.81 (s), 27.39 (s), 21.28 (s).

S-(p-tolyl) dodecanethioate (**3aa**): Colourless liquid (68.9 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.29 (s, 3H), 1.65 – 1.58 (m, 2H), 1.29 – 1.18 (m, 16H), 0.81 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.04 (s), 139.45 (s), 134.39 (s), 129.92 (s), 124.38 (s), 43.57 (s), 31.86 (s), 29.55 (s), 29.37 (s), 29.29 (s), 29.21 (s), 28.92 (s), 25.58 (s), 22.65 (s), 22.03 (s), 21.27 (s), 14.08 (s).

S-(p-tolyl)2-((3r,5r,7r)-adamantan-1-yl)ethanethioate (**3ab**): Colourless liquid (24.8 mg, 33%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 2.33 (s, 2H), 2.30 (s, 3H), 1.90 (s, 3H), 1.59 (d, *J* = 16.5 Hz, 12H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.78 (s), 139.46 (s), 134.27 (s), 129.92 (s), 124.98 (s), 57.17 (s), 42.39 (s), 36.65 (s), 33.97 (s), 28.59 (s), 21.32 (s). HRMS (ESI) for $C_{19}H_{24}OS$ $[M+H]^+$: calcd 301.1621, found 301.1616.

S,S-di-p-tolyl butanebis(thioate) (**3ac**): White solid (29.7 mg, 36%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.1 Hz, 4H), 7.14 (d, *J* = 8.0 Hz, 4H), 2.95 (s, 4H), 2.30 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.27 (s), 139.86 (s), 134.51 (s), 130.07 (s), 123.69 (s), 37.93 (s), 21.33 (s). HRMS (ESI) for $C_{18}H_{18}O_2S_2$ $[M+H]^+$: calcd 331.0821, found 331.0815.

S-(2-fluorophenyl) ethanethioate (**6a**): Colourless liquid (31.9 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 2H), 7.14 – 7.08 (m, 2H), 2.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.07 (s), 162.02 (d, *J* = 249.5 Hz), 136.57 (s), 132.14 (d, *J* = 8.2 Hz), 124.64 (d, *J* = 3.8 Hz), 116.21 (d, *J* = 22.8 Hz), 115.26 (d, *J* = 18.6 Hz), 30.04 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -106.70 (s). HRMS (ESI) for C_8H_7FOS $[M+H]^+$: calcd 171.0274, found 171.0272.

S-(4-methoxyphenyl) ethanethioate (**6b**): Colourless liquid (25.5 mg, 56%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.20 (s), 160.62 (s), 136.04 (s), 118.62 (s), 114.83 (s), 55.30 (s), 29.90 (s).

S-benzyl ethanethioate (**6c**): Colourless liquid (25.3 mg, 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.21 (m, 5H), 4.12 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.11 (s), 137.54 (s), 128.76 (s), 128.59 (s), 127.23 (s), 33.39 (s), 30.29 (s).

S-(4-bromophenyl) ethanethioate (**6d**): White solid (50.6 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.31 (s), 135.87 (s), 132.40 (s), 126.91 (s), 124.11 (s), 30.22 (s).

S-dodecyl 2-phenylethanethioate (**6e**): Colourless liquid (34.4 mg, 43%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.19 (m, 5H), 3.74 (s, 2H), 2.77 (t, *J* = 7.4 Hz, 2H), 1.49 – 1.44 (m, 2H), 1.21 – 1.16 (m, 18H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.56 (s), 133.79 (s), 129.50 (s), 128.60 (s), 127.30 (s), 50.53 (s), 31.89 (s), 29.61 (s), 29.60 (s), 29.53 (s), 29.44 (s), 29.35 (s), 29.33 (s), 29.25 (s), 29.06 (s), 28.81 (s), 22.67 (s), 14.11 (s). HRMS (ESI) for $C_{20}H_{32}OS$ $[M+H]^+$: calcd 321.2247, found 321.2239.

S-(furan-2-ylmethyl) ethanethioate (**6f**): Light yellow liquid (19.9 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 1H), 6.29 (s, 1H), 6.22 (s, 1H), 4.15 (s, 2H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.57 (s), 150.39 (s), 142.20 (s), 110.58 (s), 107.85 (s), 30.33 (s), 25.84 (s).

S-(4-chlorophenyl) ethanethioate (**6g**): Colourless liquid (41.4 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.43 (s), 135.78 (s), 135.61 (s), 129.39 (s), 126.25 (s), 30.15 (s).

S-dodecyl benzothioate (**6h**): Colourless liquid (26.8 mg, 35%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.29 (s, 3H), 1.65 – 1.58 (m, 2H), 1.29 – 1.18 (m, 16H), 0.81 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.04 (s), 139.45 (s), 134.39 (s), 129.92 (s), 124.38 (s), 43.57 (s), 31.86 (s), 29.55 (s), 29.37 (s), 29.29 (s), 29.21 (s), 28.92 (s), 25.58 (s), 22.65 (s), 22.03 (s), 21.27 (s), 14.08 (s).HRMS (ESI) for $C_{19}H_{30}OS$ $[M+H]^+$: calcd 307.2090, found 307.2092.

S-cyclohexyl benzothioate (**6i**): Colourless liquid (25.3 mg, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 3.73 (s, 1H), 2.03 (d, *J* = 8.9 Hz, 2H), 1.80 – 1.73 (m, 2H), 1.63 (d, *J* = 12.7 Hz, 2H), 1.51 (dd, *J* = 17.5, 9.4 Hz, 4H), 1.38 – 1.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.90 (s), 137.44 (s), 133.11 (s), 128.50 (s), 127.13 (s), 42.52 (s), 33.15 (s), 26.01 (s), 25.60 (s).

S-butyl benzothioate (**6j**): Colourless liquid (34.9 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 3.08 (t, *J* = 7.3 Hz, 2H), 1.67 (dd, *J* = 14.8, 7.3 Hz, 2H), 1.46 (dd, *J* = 14.9, 7.4 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.19 (s), 137.22 (s), 133.19 (s), 128.53 (s), 127.15 (s), 31.59 (s), 28.72 (s), 22.04 (s), 13.62 (s).

methyl 3-(benzoylthio)propanoate (**6k**): Colourless liquid (25.2 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 3.72 (s, 3H), 3.32 (t, *J* = 6.9 Hz, 2H), 2.75 (t, *J* = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.50 (s), 172.18 (s), 136.78 (s), 133.48 (s), 128.60 (s), 127.20 (s), 51.86 (s), 34.25 (s), 24.00 (s). HRMS (ESI) for $C_{11}H_{12}O_3S$ $[M+H]^+$: calcd 225.0580, found 225.0576.

S-(4-(tert-butyl)phenyl) ethanethioate (**6l**): Colourless liquid (52.0 mg, 100%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* =

8.3 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 2.40 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.52 (s), 152.60 (s), 134.02 (s), 126.30 (s), 124.43 (s), 34.71 (s), 31.15 (s), 30.08 (s). HRMS (ESI) for $C_{12}H_{16}OS$ $[M+H]^+$: calcd 209.0995, found 209.0995.

S-(4-(trifluoromethyl)phenyl) ethanethioate (**6m**): White solid (44.0 mg, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.54 (s), 134.46 (s), 132.49 (q, J = 1.3 Hz), 131.31 (q, J = 32.8 Hz), 125.95 (q, J = 3.8 Hz), 123.76 (q, J = 272.3 Hz), 30.37 (s). ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.90 (s). HRMS (ESI) for $C_9H_7F_3OS$ $[M+H]^+$: calcd 221.0242, found 221.0240.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra (PDF)

AUTHOR INFORMATION

Corresponding Author

* E-mail for M.N.L.: meina.liu@sit.edu.cn
* E-mail for B.-L.L.: linbl@shanghaitech.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We acknowledged the financial support by the National Science Foundation of China (NSFC U1532135).

REFERENCES

(1) （a）Fontecave, M.; Ollagnier-de-Choudens, S.; Mulliez, E. Biological Radical Sulfur Insertion Reactions. *Chem. Rev.* **2003**, *103*, 2149-2166; （b）Schaumann, E. Sulfur is more than the fat brother of oxygen. An overview of organosulfur chemistry. *Top. Curr. Chem.* **2007**, *274*, 1-34.

(2) Dunbar, K. L.; Scharf, D. H.; Litomska, A.; Hertweck, C. Enzymatic carbon–sulfur bond formation in natural product biosynthesis. *Chem. Rev.* **2017**, *117*, 5521-5577.

(3) （a）Dawson, P.; Muir, T.; Clark-Lewis, I.; Kent, S. Synthesis of proteins by native chemical ligation. *Science* **1994**, *266*, 776-779; （b）Dawson, P. E.; Kent, S. B. Synthesis of native proteins by chemical ligation. *Annu. Rev. Biochem.* **2000**, *69*, 923-960.

(4) Singh, P.; Peddinti, R. K. Harnessing the catalytic behaviour of 1, 1, 1, 3, 3, 3-hexafluoro-2-propanol (HFIP): An expeditious synthesis of thioesters. *Tetrahedron Lett.* **2017**, *58*, 1875-1878.

(5) Os'kina, I. A.; Vlasov, V. M. Activation parameters of the reactions of 4-nitrophenyl benzoates and S-phenyl benzothioate with 4-chlorophenol in dimethylformamide in the presence of potassium carbonate. *Russ. J. Org. Chem.* **2009**, *45*, 523-527.

(6) Burhardt, M. N.; Taaning, R. H.; Skrydstrup, T. Pd-Catalyzed Thiocarbonylation with Stoichiometric Carbon Monoxide: Scope and Applications. *Org. Lett.* **2013**, *15*, 948-951.

(7) （a）Fukuyama, T.; Miyazaki, T.; Han-ya, Y.; Tokuyama, H. New odorless protocols for the synthesis of aldehydes and ketones from thiol esters. *Synlett.* **2004**, 477-480; （b）Tokuyama, H.; Yokoshima, S.; Yamashita, T.; Lin, S. C.; Li, L. P.; Fukuyama, T. Facile palladium-mediated conversion of ethanethiol esters to aldehydes and ketones. *J. Braz. Chem. Soc.* **1998**, *9*, 381-387.

(8) （a）Sun, F.; Li, M.; He, C.; Wang, B.; Li, B.; Sui, X.; Gu, Z. Cleavage of the C(O)-S bond of thioesters by palladium/norbornene/copper cooperative catalysis: an efficient synthesis of 2-(Arylthio) aryl ketones. *J. Am. Chem. Soc.* **2016**, *138*, 7456-7459; （b）Prokopcova, H.; Kappe, C. O. The Liebeskind-Srogl C-C Cross-Coupling Reaction. *Angew. Chem. Int. Ed.* **2009**, *48*, 2276-2286; （c）Kobayashi, H.; Eickhoff, J. A.; Zakarian, A. Synthesis of 2-Aminoazoles from Thioesters via α-Heterosubstituted Ketones by Copper-Mediated Cross-Coupling. *J. Org. Chem.* **2015**, *80*, 9989-9999; （d）Villalobos, J. M.; Srogl, J.; Liebeskind, L. S. A New Paradigm for Carbon−Carbon Bond Formation: Aerobic, Copper-Templated Cross-Coupling. *J. Am. Chem. Soc.* **2007**, *129*, 15734-15735; （e）Fausett, B. W.; Liebeskind, L. S. Palladium-catalyzed coupling of thiol esters with aryl and primary and secondary alkyl organoindium reagents. *J. Org. Chem.* **2005**, *70*, 4851-4853; （f）Wittenberg, R.; Srogl, J.; Egi, M.; Liebeskind, L. S. Ketone synthesis under neutral conditions. Cu(I) diphenylphosphinate-mediated, palladium-catalyzed coupling of thiol esters and organostannanes. *Org. Lett.* **2003**, *5*, 3033-3035; （g）Liebeskind, L. S.; Srogl, J. Thiol ester−boronic acid coupling. A mechanistically unprecedented and general ketone synthesis. *J. Am. Chem. Soc.* **2000**, *122*, 11260-11261; （h）Tokuyama, H.; Yokoshima, S.; Yamashita, T.; Fukuyama, T. A novel ketone synthesis by a palladium-catalyzed reaction of thiol esters and organozinc reagents. *Tetrahedron Lett.* **1998**, *39*, 3189-3192.

(9) Hirschbeck, V.; Gehrtz, P. H.; Fleischer, I. Regioselective Thiocarbonylation of Vinyl Arenes. *J. Am. Chem. Soc.* **2016**, *138*, 16794-16799.

(10) （a）Mishra, P. K.; Drueckhammer, D. G. Coenzyme A analogues and derivatives: Synthesis and applications as mechanistic probes of coenzyme A ester-utilizing enzymes. *Chem. Rev.* **2000**, *100*, 3283-3310; （b）Staunton, J.; Weissman, K. J. Polyketide biosynthesis: a millennium review. *Nat. Prod. Rep.* **2001**, *18*, 380-416.

(11) Kazemi, M.; Shiri, L. Thioesters synthesis: recent adventures in the esterification of thiols. *J. Sulfur Chem.* **2015**, *36*, 613-623.

(12) （a）Ishihara, K.; Ohara, S.; Yamamoto, H. Direct condensation of carboxylic acids with alcohols catalyzed by hafnium (IV) salts. *Science* **2000**, *290*, 1140-1142; （b）Junzo, O. In Search of Practical Esterification. *Angew. Chem. Int. Ed.* **2001**, *40*, 2044-2045; （c）Manabe, K.; Sun, X. M.; Kobayashi, S. Dehydration reactions in water. Surfactant-type Brønsted acid-catalyzed direct esterification of carboxylic acids with alcohols in an emulsion system. *J. Am. Chem. Soc.* **2001**, *123*, 10101-10102.

(13) Sprecher, M.; Nov, E. The Preparation of Thiol Formates. *Synth. Commun.* **1992**, *22*, 2949-2954.

(14) （a）Bandgar, B. P.; More, P. E.; Kamble, V. T.; Sawant, S. S. Convenient and efficient synthesis of thiol esters using zinc oxide as a heterogeneous and eco-friendly catalyst. *Aust. J. Chem.* **2008**, *61*, 1006-1010; （b）Basu, B.; Paul, S.; Nanda, A. K. Silica-promoted facile synthesis of thioesters and thioethers: a highly efficient, reusable and environmentally safe solid support. *Green Chem.* **2010**, *12*, 767-771; （c）Massah, A. R.; Kalbasi, R. J.; Toghiani, M.; Hojati, B.; Adibnejad, M. Hydrotalcite as an Efficient and Reusable Catalyst for Acylation of Phenols, Amines and Thiols Under Solvent-free Conditions. *E-J. Chem.* **2012**, *9*, 2501-2508; （d）Ranu, B. C.; Dey, S. S.; Hajra, A. Highly efficient acylation of alcohols, amines and thiols under solvent-free and catalyst-free conditions. *Green Chem.* **2003**, *5*, 44-46.

(15) （a）Hajipour, A. R.; Karimi, H.; Kohi, A. Highly efficient and recyclable acetylation of phenols and alcohols by nickel zirconium phosphate under solvent-free conditions. *J. Iran. Chem. Soc.* **2015**, *13*, 55-64; （b）Prajapti, S. K.; Nagarsenkar, A.; Babu, B. N. Tris (pentafluorophenyl) borane catalyzed acylation of alcohols, phenols, amines, and thiophenols under solvent-free condition. *Tetrahedron Lett.* **2014**, *55*, 1784-1787; （c）Qiu, R.; Zhang, G.; Ren, X.; Xu, X.; Yang, R.; Luo, S.; Yin, S. Air-stable titanocene bis (perfluorooctanesulfonate) as a new catalyst for acylation of alcohols, phenols, thiols, and amines under solvent-free condition. *J. Organomet. Chem.* **2010**, *695*, 1182-1188; （d）Temperini, A.; Annesi, D.;

Testaferri, L.; Tiecco, M. A simple acylation of thiols with anhydrides. *Tetrahedron Lett.* **2010**, *51*, 5368-5371.

(16) Saravanan, P.; Singh, V. K. An efficient method for acylation reactions. *Tetrahedron Lett.* **1999**, *40*, 2611-2614.

(17) （a）Huang, Y. T.; Lu, S. Y.; Yi, C. L.; Lee, C. F. Iron-catalyzed synthesis of thioesters from thiols and aldehydes in water. *J. Org. Chem.* **2014**, *79*, 4561-4568; （b）Nambu, H.; Hata, K.; Matsugi, M.; Kita, Y. Efficient synthesis of thioesters and amides from aldehydes by using an intermolecular radical reaction in water. *Chem. Eur. J.* **2005**, *11*, 719-727; （c）Takagi, M.; Goto, S.; Matsuda, T. Photoreaction of lipoic acid and related organic disulphides: reductive acylation with aldehydes. *J. Chem. Soc., Chem. Commun.* **1976**, 92-93; （d）Uno, T.; Inokuma, T.; Takemoto, Y. NHC-catalyzed thioesterification of aldehydes by external redox activation. *Chem. Commun.* **2012**, *48*, 1901-1903; （e）Yi, C.-L.; Huang, Y.-T.; Lee, C.-F. Synthesis of thioesters through copper-catalyzed coupling of aldehydes with thiols in water. *Green Chem.* **2013**, *15*, 2476-2484; （f）Zeng, J.-W.; Liu, Y.-C.; Hsieh, P.-A.; Huang, Y.-T.; Yi, C.-L.; Badsara, S. S.; Lee, C.-F. Metal-free cross-coupling reaction of aldehydes with disulfides by using DTBP as an oxidant under solvent-free conditions. *Green Chem.* **2014**, *16*, 2644-2652; （g）Zhu, X.; Shi, Y.; Mao, H.; Cheng, Y.; Zhu, C. Tetraethylammonium Bromide-Catalyzed Oxidative Thioesterification of Aldehydes and Alcohols. *Adv. Synth. Catal.* **2013**, *355*, 3558-3562; （h）Tingoli, M; Temperini, A; Testaferri, L; Tiecco, M. A Useful Preparation of S-Phenyl Carbothioates, Se-Phenyl Carboselenoates from Aldehydes and Mixed (O, S; O, Se) Acetals from Dialkyl Ether. *Synlett* **1995**, *1995*, 1129-1130.

(18) （a）Iimura, S.; Manabe, K.; Kobayashi, S. Direct thioesterification from carboxylic acids and thiols catalyzed by a Brønsted acid. *Chem. Commun.* **2002**, 94-95; （b）Rouhi-Saadabad, H.; Akhlaghinia, B. Direct, rapid and convenient synthesis of esters and thioesters using PPh_3/N-chlorobenzotriazole system. *J. Braz. Chem. Soc.* **2014**, *25*, 253-263; （c）Imamoto, T.; Kodera, M.; Yokoyama, M. A convenient method for the preparation of thiol esters. *Synthesis* **1982**, *1982*, 134-136; （d）Movassagh, B.; Balalaie, S.; Shaygana, P. A new and efficient protocol for preparation of thiol esters from carboxylic acids and thiols in the presence of 2-(1H-benzotriazole-1-yl)-1, 1, 3, 3-tetramethyluronium tetrafluoroborate (TBTU). *Arkivoc.* **2007**, 47-52; （e）Iranpoor, N.; Firouzabadi, H.; Khalili, D.; Motevalli, S. Easily prepared azopyridines as potent and recyclable reagents for facile esterification reactions. An efficient modified Mitsunobu reaction. *J. Org. Chem.* **2008**, *73*, 4882-4887; （f）El-Azab, A. S.; Abdel-Aziz, A. A. M. An efficient synthesis of thioesters via tfa-catalyzed reaction of carboxylic acid and thiols: remarkably facile C–S bond formation. *Phosphorus, Sulfur, and Silicon and the Related Elements* **2012**, *187*, 1046-1055; （g）Moon, H. K.; Sung, G. H.; Kim, B. R.; Park, J. K.; Yoon, Y.-J.; Yoon, H. J. One for Many: A Universal Reagent for Acylation Processes. *Adv. Synth. Catal.* **2016**, *358*, 1725-1730.

(19) （a）Andrews, K. G.; Faizova, R.; Denton, R. M. A practical and catalyst-free trifluoroethylation reaction of amines using trifluoroacetic acid. *Nat. Commun.* **2017**, *8*, 15913; （b）Andrews, K. G.; Summers, D. M.; Donnelly, L. J.; Denton, R. M. Catalytic reductive N-alkylation of amines using carboxylic acids. *Chem. Commun.* **2016**, *52*, 1855-1858; （c）Augurusa, A.; Mehta, M.; Perez, M.; Zhu, J.; Stephan, D. W. Catalytic reduction of amides to amines by electrophilic phosphonium cations via FLP hydrosilylation. *Chem. Commun.* **2016**, *52*, 12195-12198; （d）Fu, M. C.; Shang, R.; Cheng, W. M.; Fu, Y. Boron-Catalyzed N-Alkylation of Amines using Carboxylic Acids. *Angew. Chem. Int. Ed.* **2015**, *54*, 9042-9046; （e）Minakawa, M.; Okubo, M.; Kawatsura, M. Ruthenium-catalyzed direct N-alkylation of amines with carboxylic acids using methylphenylsilane as a hydride source. *Tetrahedron Lett.* **2016**, *57*, 4187-4190; （f）Qiao, C.; Liu, X. F.; Liu, X.; He, L. N. Copper(II)-Catalyzed Selective Reductive Methylation of Amines with Formic Acid: An Option for Indirect Utilization of CO_2. *Org. Lett.* **2017**, *19*, 1490-1493; （g）Sorribes, I.; Junge, K.; Beller, M. Direct catalytic N-alkylation of amines with carboxylic acids. *J. Am. Chem. Soc.* **2014**, *136*, 14314-14319; （h）Fang, C.; Lu, C.; Liu, M.; Zhu, Y.; Fu, Y.; Lin, B.-L. Selective formylation and methylation of amines using carbon dioxide and hydrosilane catalyzed by alkali-metal carbonates. *ACS Catal.* **2016**, *6*, 7876-7881.

(20) Yan, K.; Yang, D.; Wei, W.; Zhao, J.; Shuai, Y.; Tian, L.; Wang, H. Catalyst-free direct decarboxylative coupling of α-keto acids with thiols: a facile access to thioesters. *Org. Biomol. Chem.* **2015**, *13*, 7323-7330.

(21) Revunova, K.; Nikonov, G. I. Base-Catalyzed Hydrosilylation of Ketones and Esters and Insight into the Mechanism. *Chem. Eur. J.* **2014**, *20*, 839-845.

(22) （a）Liu, X. F.; Ma, R.; Qiao, C.; Cao, H.; He, L. N. Fluoride-Catalyzed Methylation of Amines by Reductive Functionalization of CO_2 with Hydrosilanes. *Chem. Eur.J.* **2016**, *22*, 16489-16493; （b）Liu, X.-F.; Qiao, C.; Li, X.-Y.; He, L.-N. Carboxylate-promoted reductive functionalization of CO_2 with amines and hydrosilanes under mild conditions. *Green Chem.* **2017**, *19*, 1726-1731; （c）Nishimoto, Y.; Okita, A.; Yasuda, M.; Baba, A. Indium Tribromide Catalyzed Cross-Claisen Condensation between Carboxylic Acids and Ketene Silyl Acetals Using Alkoxyhydrosilanes. *Angew. Chem. Int. Ed.* **2011**, *50*, 8623-8625.