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Microwave-assisted direct thioesterification of carboxylic acids

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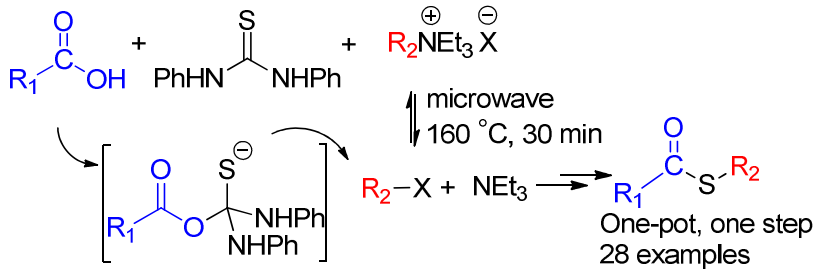


ABSTRACT. A one-pot synthesis of thioesters directly from carboxylic acids, *N,N*'-diphenylthiourea, triethylamine and primary alkyl halides is described. Microwave-assisted heating and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) further improved the yields. Both aromatic and aliphatic carboxylic acids were converted to the corresponding thioesters, and many functional groups were compatible with this reaction. Several possible reaction intermediates were investigated, and the quaternary ammonium salts, derived from alkyl halides and tertiary amines, were the intermediates to yield thioesters. A new reaction mechanism for this thioesterification is proposed.

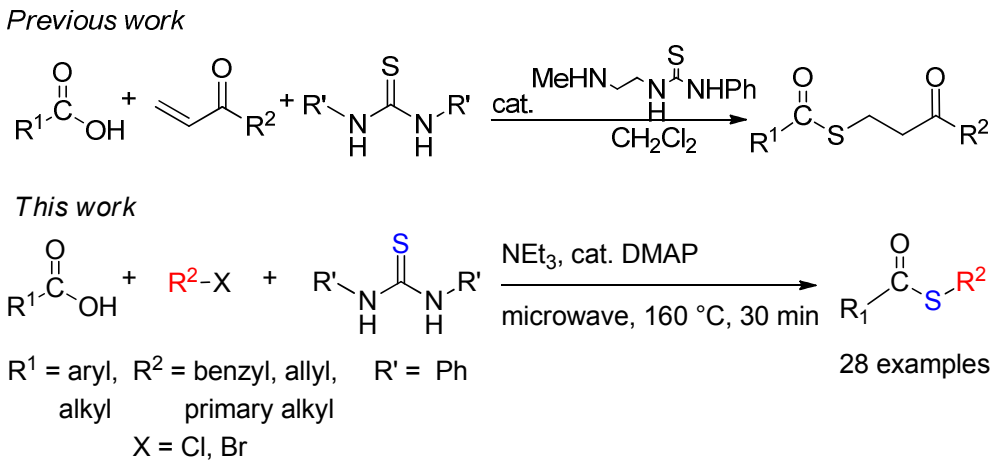
Introduction

Thioesters (thiol esters) are useful synthetic building blocks and often considered as activated carboxylic acids or acyl transfer agents for various nucleophiles.[1,2] For example, acetyl-CoA is the most common thioester in cells and an acetyl donor to oxaloacetate in the citric acid cycle.[3] Thioesters are also precursors to the formation of radicals and activate olefins for 1,4-conjugate addition.[4,5] Recently, the synthesis of thioesters has received chemists' attention because a C-terminal peptide thioester is essential for native chemical ligation (NCL), an important chemical method for synthesizing proteins.[6]

Conventional methods for preparing thioesters often require the activation of carboxylic acids by converting them to various acyl compounds amenable to subsequent acyl substitution with thiols.[7] Alternatively, the substitution reactions of alkyl halides with thiocarboxylic acids[8] and acid-catalyzed condensation reaction of carboxylic acids and thiols also yield thioesters.[9] Various metal-catalyzed or organocatalyzed coupling reactions such as oxidative coupling reactions between aldehydes and thiols have also become a useful tool for preparing thioesters.[10,11] These reports indicate the interest in developing methods for synthesizing thioesters and the potential for discovering new and interesting chemistry of thioesters.

Recently, we reported an amine-catalyzed, one-pot synthesis of thioesters directly from carboxylic acids, thioureas, and Michael acceptors.[12] Here, we describe a new microwave-assisted thioesterification of carboxylic acids that features use of an activating agent and a new source of the thiolate group, *i.e.*, primary alkyl halides and *N,N*'-diphenylthiourea, thereby not requiring use of a foul-smelling thiol (Scheme 1).[13] Our studies also suggest a new reaction mechanism for this thioesterification.

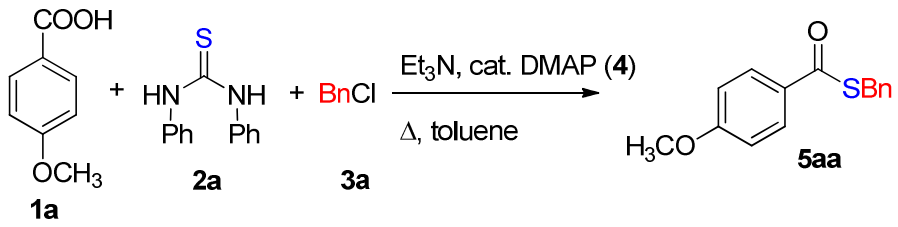
Scheme 1. Synthesis of thioesters using thiourea.



Results and Discussion

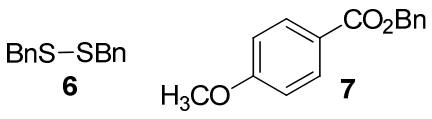
The results derived from our initial screening for the conversion of 4-methoxybenzoic acid (**1a**) to *S*-benzyl 4-methoxybenzothioate (**5aa**) are summarized in Table 1. Conducting the reaction in refluxing toluene only yielded 18% of the thioester (entry 1). Many conventional methods to promote this reaction, such as heating in DMF (entry 2), have been attempted; however, the formation of the desired thioester remained poor. We found that the conversion improved significantly when the reaction mixture was heated by microwave in toluene. When the boiling point of toluene (110 °C) was chosen as the reaction temperature, the microwave-assisted reaction (40 min) provided a yield twice of that from conventional heating (entry 3).[14] Under pressurized conditions, the reaction temperatures could be further elevated, and the yields (35–66%) were better than those resulted from conventional heating (entries 4–11). However, the products derived from these microwave-assisted reactions were often contaminated with 3% of dibenzyl disulfide (**6**) and 3% benzyl 4-methoxybenzoate (**7**). After screening of the reaction conditions, the optimized reaction temperature and microwave-irradiation time, 160 °C and 30 min (entry 8), were chosen for our subsequent studies.

Table 1. Reaction conditions for thioesterification.



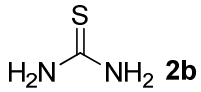
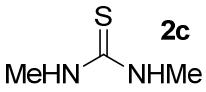
entry[a]	heating	temp (°C)	time	yield (%)[b]
1	oil bath	110	16 h	18
2	oil bath	110	16 h	13[c]
3	microwave	110	40 min	35
4	microwave	130	40 min	35
5	microwave	150	40 min	66
6	microwave	150	60 min	47
7	microwave	160	40 min	44
8	microwave	160	30 min	66(61)[d]
9	microwave	160	20 min	47
10	microwave	170	30 min	55
11	microwave	170	20 min	59

[a]Starting materials (**1a**-**3a**, 0.4 mmol each), triethylamine (0.4 mmol), DMAP (0.04 mmol), and toluene (2 mL) were combined in a pressure tube and heated by microwave (250 W, monitored by IR temperature sensor). [b]Yields determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [c]DMF as the solvent. [d]Isolated yield.



Several factors for influencing this multicomponent reaction were also examined, and the results are shown in Table 2. Compared to the standard condition (entry 1), using thiourea (**2b**) and *N*,*N*'-dimethylthiourea (**2c**) did not yield the thioester due to their limited solubility in toluene (entries 2 and 3, respectively). Very little thioester resulted from the reaction without triethylamine (entry 4), which suggests that the base was essential for the reaction. On the other hand, a catalytic amount of 4-(dimethylamino)pyridine (DMAP, **4**) raised the yield, but its use also increased the formation of by-products **6** and **7** (entry 1 *vs.* entry 5). Raising the amount of DMAP to 20 mol% did not further improve the yield (entry 6). Benzyl chloride yielded almost twice amount of thioester **5aa** than benzyl bromide (entry 1 *vs*. entry 7), and more by-products (**6** and **7)** were generated while using benzyl bromide.

Table 2. Reagents for thioesterification

entry[a]	reactant **2**	reactant **3**	base	DMAP (mol%)	yield (%)[b]
1	**2a**	BnCl	Et_3N	10	66
2	 **2b**	BnCl	Et_3N	10	0
3	 **2c**	BnCl	Et_3N	10	0
4	**2a**	BnCl	-	10	2
5	**2a**	BnCl	Et_3N	0	48[c,d]
6	**2a**	BnCl	Et_3N	20	44

7	**2a**	BnBr	Et_3N	10	37

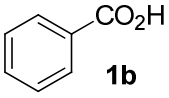
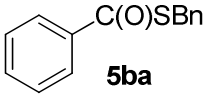
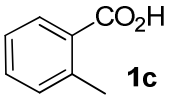
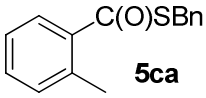
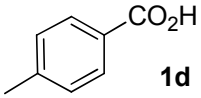
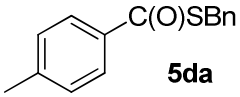
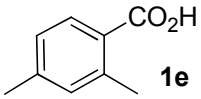
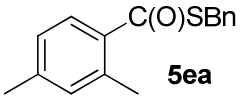
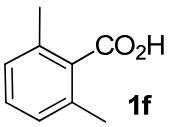
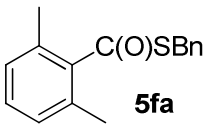
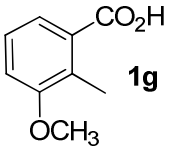
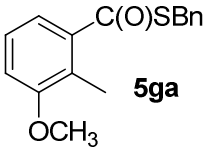
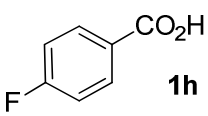
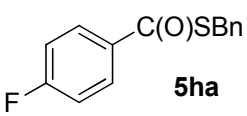
[a]Reactions conducted in toluene, microwave-assisted heating (250 W), 160 °C, 30 min. [b]Yields of **5aa** determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard. [c]Reactions conducted in toluene, microwave-assisted heating (250 W), 150 °C, 40 min. [d]By-products **6** and **7** were not detected.

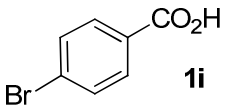
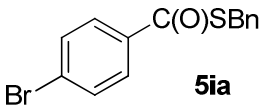
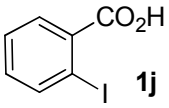
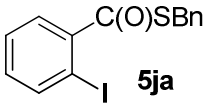
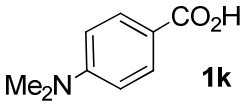
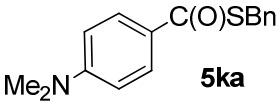
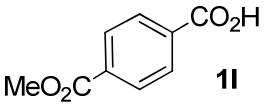
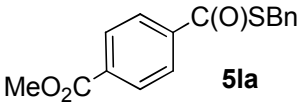
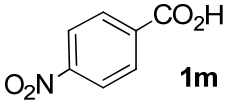
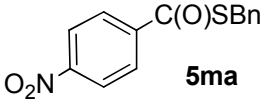
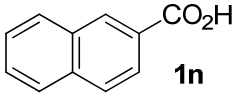
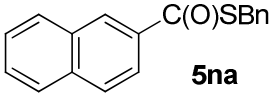
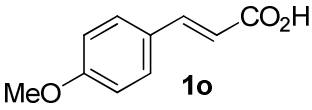
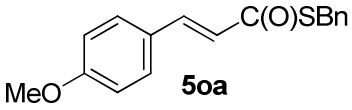
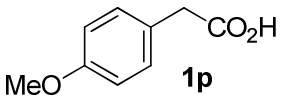
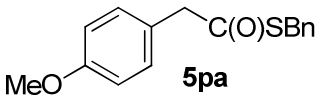
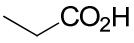
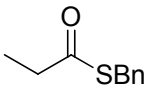
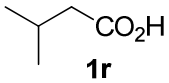
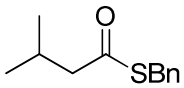
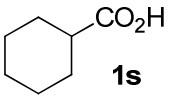
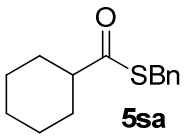
This direct thioesterification was applied to prepare other thioesters (Table 3). As we had observed in the previous studies,[12] some thioesters were unstable and often lost during the purification, so the reported yields were determined by ^{1}H NMR analysis of the crude products with an internal standard (1,3,5-trimethoxybenzene); isolated yields, shown in parentheses, were obtained after column chromatography. Benzoic acid (**1b**) gave a very similar yield of the corresponding thioester (64%, entry 1) as did **1a**. Slightly lower yields were obtained with the methyl-substituted benzoic acids (**1c**–**1f**), and the difference in yields for the benzoic acids bearing an *ortho*- or *para*-methyl group was minor (within 10%, entries 2–5). *S*-Benzyl 3-methoxy-2-methylbenzothioate (**5ga**), derived from a di-substituted benzoic acid **1g**, was isolated in 52% yield (entry 6). Halogen substituents (**1h-1j,** entries 7–9) did not impede the reaction, and 2-iodobenzoic acid provided the best yield (74%) among the substrates screened. Both electron-donating (-NMe_2 in **1k**) and electron-withdrawing groups (-CO_2Me and -NO_2 in **1l** and **1m**, respectively) were compatible with this process (entries 10–12).

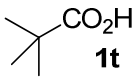
The reaction is not limited to benzoic acid and its derivatives since both 2-naphthoic acid (**1n**) and 4-methoxycinnamic acid (**1o**) were converted to the corresponding thioesters **5na** and **5oa** (entries 13 and 14, respectively). However, the yield of the thioester **5pa** derived from 4-methoxyphenylacetic acid (**1p**) was poor (entry 15). Aliphatic carboxylic acids **1q**–**1t** also yielded the corresponding thioesters **5qa**–**5ta**; however, their yields were moderate at most

(entries 16–19). The yields of the aliphatic thioesters improved with increased steric hindrance around the carboxyl group, *i.e.*, the degree of substitution at the □-carbon increases from 2°, to 3°, to 4° in **1r**, **1s**, and **1t** (entries 17–19). This may be related to the relative stability of the generated thioesters under the reaction conditions (*vide infra*).

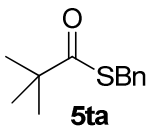
Table 3. Thioesterification with various carboxylic acids.

entry[a]	carboxylic acid	thioester	yield (%)[b]
1	 **1b**	 **5ba**	64(60)
2	 **1c**	 **5ca**	48
3	 **1d**	 **5da**	55
4	 **1e**	 **5ea**	53
5	 **1f**	 **5fa**	58
6	 **1g**	 **5ga**	56(52)
7	 **1h**	 **5ha**	50(49)

8	 **1i**	 **5ia**	54(51)
9	 **1j**	 **5ja**	74(66)
10	 **1k**	 **5ka**	38(42)
11	 **1l**	 **5la**	60
12	 **1m**	 **5ma**	51(44)
13	 **1n**	 **5na**	63(60)
14	 **1o**	 **5oa**	37(32)
15	 **1p**	 **5pa**	21(13)
16	 **1q**	 **5qa**	19(10)
17	 **1r**	 **5ra**	24
18	 **1s**	 **5sa**	28



1t



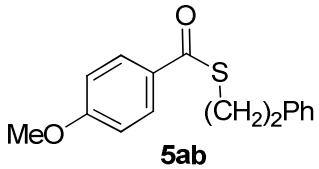
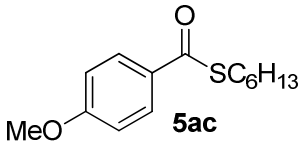
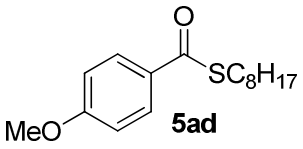
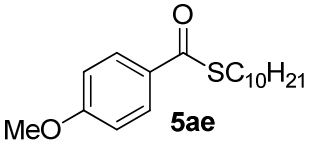
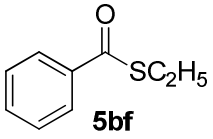
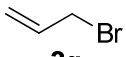
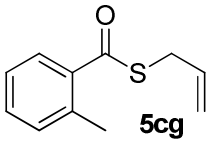
5ta

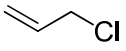
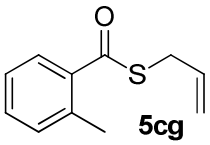
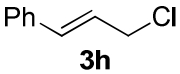
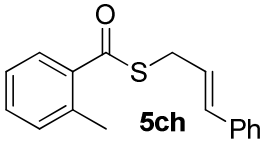
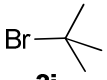
[a]Reactions conducted in toluene, microwave-assisted heating (250 W), 160 °C, 30 min. [b]Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard; isolated yields shown in parentheses.

In addition to benzyl halides, other alkyl bromides were also applicable in the thioesterification (Table 4). Thioester **5ab** was prepared from **1a** and 2-phenylethyl bromide (**3b**) in 46% yield. For primary bromides (**3c**-**3f**), better yields were obtained from those with a medium-length alkyl chain, such as *n*-hexyl bromide (**3c**) and *n*-octyl bromide (**3d)**, entries 2 and 3, respectively. On the other hand, the substrate with an ethyl group (**3f**) or a long *n*-decyl group (**3e**) gave lower yields (entries 4 and 5, respectively). The reactivity of alkyl bromides toward to nucleophiles is known to be reduced as the alkyl chain is lengthened.[15] Similarly, the generated thioesters bearing a long alkyl chain could be more inert to further acyl substitution reactions. The compromise of these factors may justify the results that better yields were obtained from the C6 and C8 alkyl halides. A much lower yield was observed for the reaction using 1-chlorooctane (entry 6 *vs.* entry 3), which is consistent with the results using quaternary ammonium salts (*vide infra*). Unlike the substantial difference in yields observed from the thioesterifications using benzyl bromide and benzyl chloride (Table 2), both allyl bromide and allyl chloride gave low yields of the allyl thioester (**5cg**) (entries 7 and 8). In addition to the issue of stability in **5cg**, the loss of the volatile allyl halides during high-temperature reactions may also account for the low yields. Indeed, the thioesterification using cinnamyl chloride (**3h**) provided better yields of **5ch** (entries 9 and 10). No thioester could be isolated when secondary or tertiary alkyl bromides (**3i**

and **3j**, entries 11 and 12, respectively) were used. The dominance of elimination reactions for the 2° and 3° alkyl bromides thwarted the substitution reaction to form the sulfur-carbon bond and the thioesters that would result.

Table 4. Thioesterification with various alkyl halides.

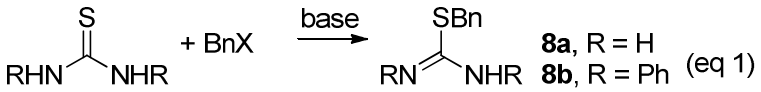
entry[a]	RCO_2H	alkyl halide	thioester	yield (%)[b]
1	**1a**	$Ph(CH_2)_2Br$ **(3b)**	 **5ab**	46
2	**1a**	*n*-$C_6H_{13}Br$ **(3c)**	 **5ac**	44(37)
3	**1a**	*n*-$C_8H_{17}Br$ **(3d)**	 **5ad**	52(41)
4	**1a**	*n*-$C_{10}H_{21}Br$ **(3e)**	 **5ae**	35(29)
5	**1b**	C_2H_5Br **(3f)**	 **5bf**	28(8)
6	**1a**	*n*-$C_8H_{17}Cl$	**5ad**	12
7	**1c**	 **3g**	 **5cg**	29(27)

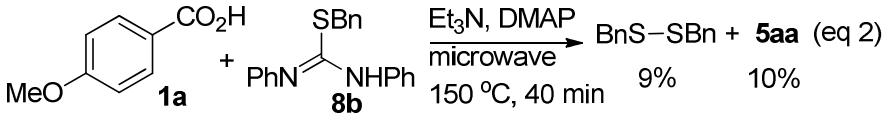
8	**1c**		 **5cg**	25
9	**1c**	 **3h**	 **5ch**	41
10	**1c**	**3h**	**5ch**	63(61)[c]
11	**1a**	 **3i**	-	0
12	**1a**	 **3j**	-	0

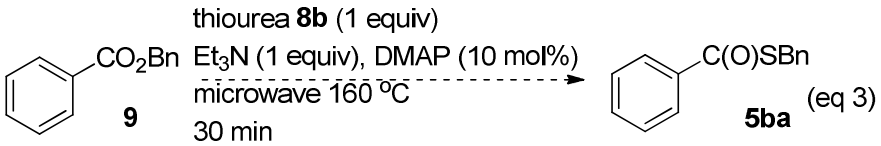
[a]Reactions conducted in toluene, microwave-assisted heating (250 W), 160 °C, 30 min. [b]Yields determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as the internal standard; isolated yields shown in parentheses. [c]Reactions conducted in toluene, microwave-assisted heating (250 W), 180 °C, 30 min.

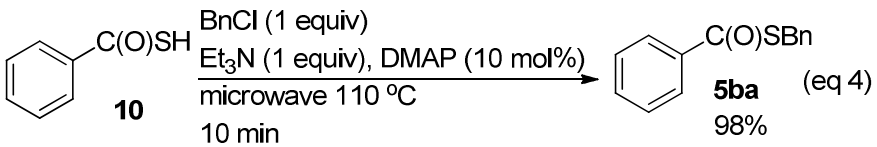
We initially thought that the mechanism for thioesterification of carboxylic acids using alkyl halides might resemble our previous report using Michael acceptors, in which Michael adducts derived from thioureas and α,β-unsaturated ketones or esters were generated as reaction intermediates.[12] In addition, benzyl carbamimidothioate (**8a**) has been proposed as the reaction intermediate and the source of benzylthiolate under basic, aqueous conditions.[13, 16] However, we found that the corresponding benzyl *N,N'*-diphenylcarbamimidothioate (**8b**), separately prepared from benzyl bromide and diphenylthiourea (**2a**, eq 1),[17] was a very poor reagent for this thioesterification (eq 2). Thus, **8b** is unlikely to be the key intermediate here. Other possible

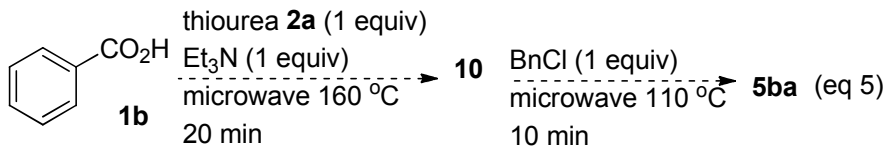
intermediates, such as benzyl benzoate (**9**) were also considered, but **9** also failed to yield any thioester under our reaction conditions (eq 3). Although the benzylation of thiobenzoic acid (**10**) provided thioester **5ba** in excellent yield under much milder conditions (eq 4), we did not observe thioester **5ba** when we divided our one-pot, one-step reaction into a two-step process, *i e.,* belated addition of BnCl (eq 5). Here, we assumed that thiobenzoic acid (**10)** could be generated from benzoic acid and thiourea **2a** and that its subsequent benzylation could generate the desired thioester. Formation of thiobenzoic acid (**10**) could not be detected, however. Instead *N*-phenylbenzamide (**11**) was isolated (eq 6) and was often observed as a minor by-product in our thioesterifications.

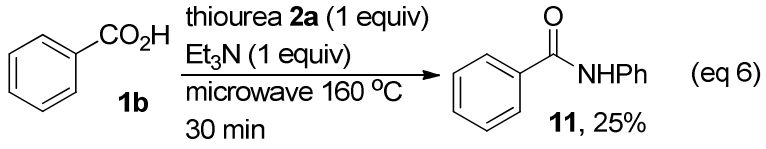






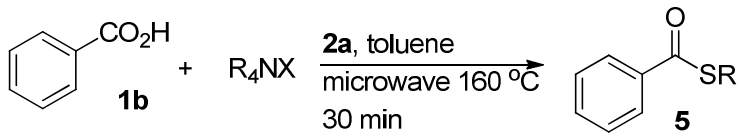


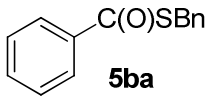
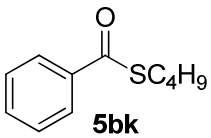




After excluding these potential intermediates and considering the high reaction temperature required for this process, we suspected that the reaction may go through quaternary ammonium salts. Indeed, the direct thioesterification of carboxylic acids was also achieved using quaternary ammonium salts and diphenylthiourea **2a** (Table 5). Both benzyltriethylammonium chloride and bromide provided thioester **5ba,** and their yields were comparable with those obtained from using the benzyl halides and triethylamine (entries 1 and 2, Table 5 *vs.* entries 1 and 7, Table 2). Tetrabutylammonium iodide, bromide, and chloride all gave butyl thioester **5bk** (entries 3–5). However, the tetrabutylammonium salts of bisulfate and tetrafluoroborate (**17** and **18**, respectively) failed to form the thioester (entries 6 and 7). The difference in the yields as a function of the counterions is consistent with their difference in nucleophilicity according to the hard-soft-acid-base (HSAB) concept, in which a soft anion such as iodide functions more as a nucleophile than a base that would remove a proton and yield an elimination product.[18] The addition of DMAP was not helpful for the reaction using quaternary ammonium salts (entry 8).

Table 5. Thioesterification using quaternary ammonium salts.



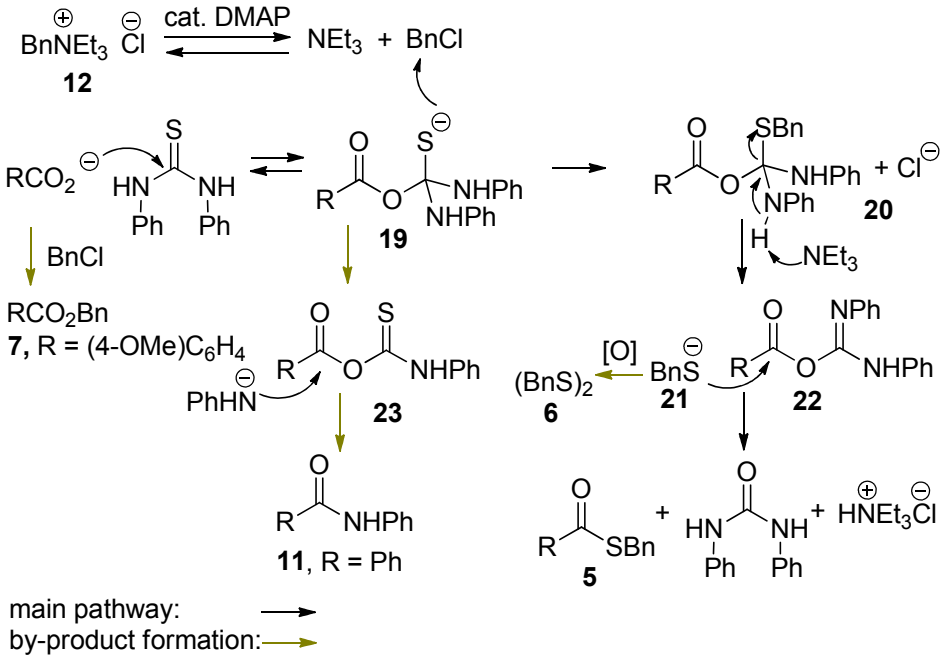
entry[a]	ammonium salt	thioester	yield (%)[b]
1	$BnNEt_3^{\oplus}\ Cl^{\ominus}$ **(12)**	 **5ba**	41
2	$BnNEt_3^{\oplus}\ Br^{\ominus}$ **(13)**	**5ba**	25
3	$Bu_4N^{\oplus}\ I^{\ominus}$ **(14)**	 **5bk**	58 (40)
4	$Bu_4N^{\oplus}\ Br^{\ominus}$ **(15)**	**5bk**	43 (31)
5	$Bu_4N^{\oplus}\ Cl^{\ominus}$ **(16)**	**5bk**	17 (8)
6	$Bu_4N^{\oplus}\ HSO_4^{\ominus}$ **(17)**	**5bk**	0
7	$Et_4N^{\oplus}\ BF_4^{\ominus}$ **(18)**	**5bf**	0
8	$Bu_4N^{\oplus}\ I^{\ominus}$ **(14)**	**5bk**	53 (33)[c]

[a] Starting materials (**1b** and **2a**, 0.4 mmol each), quaternary ammonium salt (0.4 mmol) and toluene (2 mL) placed in a reaction tube and heated by microwave (250 W). [b]Yields determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard; isolated yields shown in parentheses. [c]Addition of DMAP (0.04 mmol).

On the basis of the above results, a plausible reaction mechanism for direct thioesterification of carboxylic acids using thiourea **2a**, benzyl chloride, and triethylamine is shown Scheme 2. At high temperatures, the formation of the quaternary ammonium salt **12** is facilitated by DMAP and is reversible.[19] Since both compounds **8** and **9**, derived from the benzylation of thiourea or carboxylic acid, did not lead to the product and thiobenzoic acid (**10**) as the reaction intermediate was unlikely, benzyl mercaptan anion (**21**) should come from the benzylation of the intermediate **19** to generate **20** and the following base-assisted fragmentation. The acylation of **21** was

achieved with carbamimidic anhydride **22** to give the thioester **5**. The oxidation of benzyl mercaptan to give disulfide **6** as one of the by-products was well-documented.[20] In the absence of BnCl, the intermediate **19** will give carbamothioic anhydride **23** and aniline anion, which lead to amide **11** as we observed in eq 6.

Scheme 2. Proposed mechanism for the thioesterification.



Conclusions

In summary, a microwave-assisted, direct thioesterification of carboxylic acids was achieved using primary alkyl halides, amines, and *N,N*-diphenylthiourea. There are several advantages in this process: a one-pot procedure, short reaction time, and the absence of metals, foul-smelling reagents, or costly reagents to activate carboxylic acids. This reaction supplements our previous method of thioesterification, which was limited to using Michael acceptors to form the thiolate

moiety of thioesters. The formation of the thiolate group from quaternary ammonium salts and the adducts of carboxylates and thiourea provides a new pathway for thioesterification.

Experimental Section

General information: Thin-layer chromatography (TLC) spots were examined under UV light or revealed by $KMnO_4$ solution. Dichloromethane was distilled from calcium hydride; tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone. Reagents were purchased from commercial sources and used without further purification. Chemical shifts for ^{1}H-NMR and ^{13}C NMR spectra are reported in δ units (parts per million) with reference to residual solvent peaks. The multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, td = triplet of doublets. Assignments of ^{1}H and ^{13}C resonances for complex structures were confirmed by extensive 2D experiments (COSY, HMQC, and HMBC). TLC was conducted using pre-coated silica gel 60 F254 plates containing a fluorescent indicator; purification by chromatography was conducted using silica gel (230-400 mesh). Microwave-assisted reactions were performed in a CEM Discover single-mode microwave reactor using a sealed reaction vessel (10 mL, max. pressure: 30 bar), equipped with a vertically-focused IR temperature sensor; controlled temperature, power and time settings were used for all reactions. High-resolution mass spectrometry (HRMS) data were recorded on a JMS-700 quadrupole mass spectrometer.

Typical Procedure for the Synthesis of Thioesters

A solution of 4-methoxybenzoic acid (**1a**, 60.9 mg, 0.40 mmol), *N,N*'-diphenylthiourea (**2a**, 91.3 mg, 0.40 mmol), benzyl chloride (**3a**, 46.0 μL, 0.40 mmol), triethylamine (56.0 μL, 0.40 mmol), DMAP (**4**, 4.9 mg, 0.04 mmol), and toluene (2 mL) was placed in a pressure tube that

was heated to 160 °C (250 W, monitored by IR temperature sensor) and maintained at this temperature for 30 min. After cooling to rt, 1,3,5-trimethoxybenzene (6.7 mg, 39.8 μmol) was added to the reaction mixture which was then concentrated. The yield of thioester **5aa** was calculated according to the ^{1}H NMR spectrum of the crude product. Thioester **5aa** (63.1 mg, 0.24 mmol, 61%) was also isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.15). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.84 (s, 3H), 4.29 (s, 2H), 6.90 (d, J = 8.9 Hz, 2H), 7.23 (t, J = 7.4 Hz, 1H), 7.28–7.31 (m, 2H), 7.36 (d, J = 7.4 Hz, 2H), 7.94 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.2, 55.5, 113.8, 127.2, 128.6, 128.9, 129.4, 129.6, 137.7, 163.8, 189.7. The spectroscopic data are consistent with the reported values.[10a]

***S*-Benzyl benzothioate (5ba)**.[13] The standard procedure for the thioesterification was followed. Starting with **1b** (48.8 mg, 0.40 mmol), thioester **5ba** (55.0 mg, 0.24 mmol, 60%) was isolated after column chromatography (SiO_2, hexanes, R_f 0.18). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.31 (s, 2H), 7.22–7.25 (m, 1H), 7.30 (t, J = 7.8 Hz, 2H), 7.34–7.37 (m, 2H), 7.43 (t, J = 7.8 Hz, 2H), 7.53–7.56 (m, 1H), 7.94–7.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.3, 127.2, 128.6, 128.9, 133.4, 136.7, 137.4, 191.2.

***S*-Benzyl 2-methylbenzothioate (5ca)**.[10a] The standard procedure for the thioesterification was followed. Starting with **1c** (54.5 mg, 0.40 mmol), thioester **5ca** (46.1 mg, 0.19 mmol, 48%) was produced according to ^{1}H NMR. Compound **5ca** was purified by column chromatography (SiO_2, hexanes, R_f 0.15) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.49 (s, 3H), 4.27 (s, 2H), 7.19–7.39 (m, 8H), 7.75 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6, 33.9, 125.7, 127.2, 128.5, 128.6, 128.9, 131.6, 131.7, 136.9, 137.1, 137.6, 193.6.

***S*-Benzyl 4-methylbenzothioate (5da).**[13] The standard procedure for the thioesterification was followed. Starting with **1d** (54.5 mg, 0.40 mmol), thioester **5ea** (52.9 mg, 0.22 mmol, 55%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5da** was purified by column chromatography (SiO_2, hexanes, R_f 0.17) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.40 (s, 3H), 4.32 (s, 2H), 7.23–7.40 (m, 7H), 7.88 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 33.2, 127.2, 127.3, 128.6, 128.9, 129.3, 134.3, 137.6, 144.3, 190.9.

***S*-Benzyl 2,4-dimethylbenzothioate (5ea).** The standard procedure for the thioesterification was followed. Starting with **1e** (60.1 mg, 0.40 mmol), thioester **5ea** (54.1 mg, 0.21 mmol, 53%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5ea** was purified by column chromatography (SiO_2, hexanes, R_f 0.17) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.34 (s, 3H), 2.50 (s, 3H), 4.28 (s, 2H), 7.02–7.05 (m, 2H), 7.23–7.40 (m, 5H), 7.73 (d, J = 7.8 Hz, 1H); ^{13}C NMR (CDCl3, 75 MHz) δ 20.7, 21.3, 33.8, 126.3, 127.1, 128.6, 128.9, 132.4, 134.2, 137.2, 137.7, 142.3, 192.9; HRMS (APCI) calcd for $[M + H]^+$ ($C_{16}H_{17}OS$) 257.1000, found 257.0994.

***S*-Benzyl 2,6-dimethylbenzothioate (5fa).** The standard procedure for the thioesterification was followed. Starting with **1e** (60.1 mg, 0.40 mmol), thioester **5fa** (59.4 mg, 0.23 mmol, 58%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5fa** was purified by column chromatography (SiO_2, hexanes, R_f 0.17) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 6H), 4.31 (s, 2H), 6.98–7.00 (m, 2H), 7.14–7.19 (m, 1H), 7.25–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.0, 33.8, 127.3, 127.7, 128.6, 128.9, 129.4, 133.8, 137.6, 139.8, 197.0; HRMS (APCI) calcd for $[M + H]^+$ ($C_{16}H_{17}OS$) 257.1000, found 257.1001.

***S*-Benzyl 3-methoxy-2-methylbenzothioate** (**5ga**). The standard procedure for the thioesterification was followed. Starting with **1g** (66.5 mg, 0.40 mmol), thioester **5ga** (59.4 mg, 0.23 mmol, 58%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ga** (56.3 mg, 0.21 mmol, 52%) was isolated after column chromatography (SiO_2, hexanes, R_f 0.10) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.30 (s, 3H), 3.83 (s, 3H), 4.28 (s, 2H), 6.94 (d, J = 8.1 Hz, 1H), 7.18 (t, J = 7.9 Hz, 1H), 7.23–7.26 (m, 2H), 7.29–7.32 (m, 2H), 7.36–7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 12.3, 34.1, 55.7, 113.0, 119.9, 125.1, 126.3, 127.2, 128.6, 128.9, 137.5, 139.2, 158.0, 194.2; HRMS (APCI) calcd for $[M + H]^+$ ($C_{16}H_{17}O_2S$) 273.0949, found 273.0951.

***S*-Benzyl 4-fluorobenzothioate** (**5ha**). The standard procedure for the thioesterification was followed. Starting with **1h** (56.0 mg, 0.40 mmol), thioester **5ha** (49.3 mg, 0.20 mmol, 50%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ha** (48.2 mg, 0.19 mmol, 50%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.21). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.31 (s, 2H), 7.08–7.12 (m, 2H), 7.23–7.26 (m, 1H), 7.31 (t, J = 7.7 Hz, 2H), 7.35–7.37 (m, 2H), 7.96–8.00 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.4, 115.7 ($J_{C\text{-}F}$ = 22.1 Hz), 127.4, 128.7, 128.9, 129.8 ($J_{C\text{-}F}$ = 9.3 Hz), 133.1, 137.3, 165.9 ($J_{C\text{-}F}$ = 253.5 Hz), 189.8; HRMS (APCI) calcd for $[M + H]^+$ ($C_{14}H_{12}FOS$) 247.0593, found 247.0591.

***S*-Benzyl 4-bromobenzothioate** (**5ia**).[21] The standard procedure for the thioesterification was followed. Starting with **1i** (80.4 mg, 0.40 mmol), thioester **5ia** (66.3 mg, 0.22 mmol, 54%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ia** (62.5 mg, 0.20 mmol, 51%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.20). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.30 (s, 2H), 7.23–7.26 (m, 1H), 7.29–7.32 (m,

2H), 7.35–7.36 (m, 2H), 7.56 (d, J = 8.5 Hz, 2H), 7.81 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.4, 127.4, 128.5, 128.7, 128.7, 128.9, 131.9, 135.5, 137.1, 190.3.

***S*-Benzyl 2-iodobenzothioate** (**5ja**). The standard procedure for the thioesterification was followed. Starting with **1j** (99.2 mg, 0.40 mmol), thioester **5ja** (105.5 mg, 0.30 mmol, 74%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ja** (95.8 mg, 0.27 mmol, 66%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.15). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.32 (s, 2H), 7.13 (dt, J = 7.7 Hz, J = 1.6 Hz, 1H), 7.24–7.40 (m, 6H), 7.57 (dd, J = 7.7 Hz, J = 1.6 Hz, 1H), 7.92 (dd, J = 7.9 Hz, J = 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.4, 91.3, 127.4, 127.9, 128.7, 128.8, 129.0, 132.4, 137.0, 140.8, 142.3, 193.4; HRMS (ESI) calcd for $[M + Na]^+$ ($C_{14}H_{11}ONaSI$) 376.9473, found 376.9465.

***S*-Benzyl 4-(dimethylamino)benzothioate** (**5ka**).[22] The standard procedure for the thioesterification was followed. Starting with **1k** (66.1 mg, 0.40 mmol), thioester **5ka** (40.8 mg, 0.15 mmol, 38%) was produced according to ^{1}H NMR analysis of the reaction mixture.Thioester **5ka** (46.0 mg, 0.17 mmol, 42%) was isolated as a light-yellow solid after column chromatography (SiO_2, hexanes, R_f 0.10). Mp 103.0–104.0 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.02 (s, 6H), 4.28 (s, 2H), 6.61 (d, J = 9.2 Hz, 2H), 7.20–7.23 (m, 1H), 7.27–7.30 (m, 2H), 7.36–7.37 (m, 2H), 7.87 (dd, J = 9.1 Hz, J = 1.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 32.9, 40.0, 110.6, 124.3, 127.0, 128.5, 128.9, 129.4, 138.3, 153.7, 188.9.

Methyl 4-(benzylthiocarbonyl)benzoate (**5la**).[23] The standard procedure for the thioesterification was followed. Starting with **1l** (72.1 mg, 0.40 mmol), thioester **5la** (68.5 mg, 0.24 mmol, 60%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5la** was purified by column chromatography (SiO_2, hexanes, R_f 0.13) as a light-

yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.92 (s, 3H), 4.32 (s, 2H), 7.24–7.37 (m, 5H), 7.99 (d, J = 8.4 Hz, 2H), 8.08 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 33.5, 52.5, 127.2, 127.5, 128.7, 129.0, 129.8, 134.2, 137.0, 140.0, 166.1, 190.7.

***S*-Benzyl 4-nitrobenzothioate (5ma)**.[23] The standard procedure for the thioesterification was followed. Starting with **1m** (66.8 mg, 0.40 mmol), thioester **5ma** (56.0 mg, 0.21 mmol, 51%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ma** (48.1 mg, 0.18 mmol, 44%) was isolated as a light-yellow solid after column chromatography (SiO_2, hexanes, R_f 0.23). Mp 80.5–82.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.35 (s, 2H), 7.24–7.37 (m, 5H), 8.09 (d, J = 8.7 Hz, 2H), 8.28 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.8, 123.9, 127.6, 128.3, 128.8, 129.0, 136.6, 141.3, 150.5, 189.7.

***S*-Benzyl naphthalene-2-carbothioate (5na)**.[22] The standard procedure for the thioesterification was followed. Starting with **1n** (68.9 mg, 0.40 mmol), thioester **5na** (70.5 mg, 0.25 mmol, 63%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5na** (67.1 mg, 0.24 mmol, 60%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.18). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.38 (s, 2H), 7.25–7.27 (m, 1H), 7.31–7.34 (m, 2H), 7.41–7.42 (m, 2H), 7.52–7.55 (m, 1H), 7.57–7.60 (m, 1H), 7.84–7.88 (m, 2H), 7.93 (d, J = 7.8 Hz, 1H), 7.98–8.00 (m, 1H), 8.53 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.5, 123.1, 126.9, 127.3, 127.5, 127.8, 128.5, 128.7, 128.7, 129.0, 129.5, 132.4, 134.1, 135.8, 137.5, 191.2.

(*E*)-*S*-Benzyl 3-(4-methoxyphenyl)prop-2-enethioate (5oa). The standard procedure for the thioesterification was followed. Starting with **1o** (71.3 mg, 0.40 mmol), thioester **5oa** (41.8 mg, 0.15 mmol, 37%) was produced according to ^{1}H NMR analysis of the reaction mixture..

Thioester **5oa** (36.6 mg, 0.13 mmol, 32%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.21). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.82 (s, 3H), 4.24 (s, 2H), 6.58 (d, J = 15.7 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 7.21–7.22 (m, 1H), 7.27–7.33 (m, 4H), 7.47 (d, J = 8.8 Hz, 2H), 7.59 (d, J = 15.7 Hz, 1H); ^{13}C NMR (CDCl3, 125 MHz) δ 33.1, 55.4, 114.4, 122.3, 126.7, 127.2, 128.6, 128.9, 130.1, 137.8, 140.7, 161.7, 189.0; HRMS (APCI) calcd for $[M + H]^+$ ($C_{17}H_{17}O_2S$) 285.0949, found 285.0946.

***S*-Benzyl 2-(4-methoxyphenyl)ethanethioate** (**5pa**).[24] The standard procedure for the thioesterification was followed. Starting with **1p** (66.5 mg, 0.40 mmol), thioester **5pa** (23.1 mg, 0.08 mmol, 21%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5pa** (14.1 mg, 0.05 mmol, 13%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.10). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.76 (s, 2H), 3.78 (s, 3H), 4.07 (s, 2H), 6.85 (d, J = 8.7 Hz, 2H), 7.18 (d, J = 8.7 Hz, 2H), 7.21–7.27 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.6, 49.4, 55.2, 114.1, 125.4, 127.2, 128.6, 128.8, 130.7, 137.3, 159.0, 197.3.

***S*-Benzyl propanethioate (5qa)**. The standard procedure for the thioesterification was followed. Starting with **1q** (29.6 mg, 0.40 mmol), thioester **5qa** (13.7 mg, 0.076 mmol, 19%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5qa** (7.5 mg, 0.042 mmol, 10%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.14). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.13 (t, J = 7.5 Hz, 3H), 2.53 (q, J = 7.5 Hz, 2H), 4.06 (s, 2H), 7.17–7.24 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 9.6, 33.0, 37.1, 127.2, 128.6, 128.8, 137.7, 199.5; HRMS (EI) calcd for M^+ ($C_{10}H_{12}OS$) 180.0609, found 180.0602.

***S*-Benzyl 3-methylbutanethioate** (**5ra**). The standard procedure for the thioesterification was followed. Starting with **1r** (40.9 mg, 0.40 mmol), thioester **5ra** (19.8 mg, 0.095 mmol, 24%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5ra** was purified by column chromatography (SiO_2, hexanes, R_f 0.12) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (d, J = 6.7 Hz, 6H), 2.17 (m, J = 6.7 Hz, 1H), 2.43 (d, J = 7.1 Hz, 2H), 4.11 (s, 2H), 7.20–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.3, 26.5, 33.1, 52.6, 127.1, 128.6, 128.7, 137.8, 198.2; HRMS (EI) calcd for M^+ ($C_{12}H_{16}OS$) 208.0922, found 208.0922.

***S*-Benzyl cyclohexanecarbothioate** (**5sa**).[25] The standard procedure for the thioesterification was followed. Starting with **1s** (51.3 mg, 0.40 mmol), thioester **5sa** (26.1 mg, 0.11 mmol, 28%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5sa** was purified by column chromatography (SiO_2, hexanes, R_f 0.15) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.15–1.33 (m, 3H), 1.40–1.53 (m, 2H), 1.60–1.67 (m, 1H), 1.73–1.80 (m, 2H), 1.88–1.93 (m, 2H), 2.48 (tt, J = 11.4, J = 3.5 Hz, 1H), 4.08 (s, 2H), 7.15–7.30 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.5, 25.6, 29.5, 32.8, 52.4, 127.1, 128.6, 128.8, 137.8, 202.4.

***S*-Benzyl 2,2-dimethylpropanethioate** (**5ta**).[26] The standard procedure for the thioesterification was followed. Starting with **1t** (40.9 mg, 0.40 mmol), thioester **5ta** (29.3 mg, 0.14 mmol, 35%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5ta** was purified by column chromatography (SiO_2, hexanes, R_f 0.22) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 (s, 9H), 4.07 (s, 2H), 7.20–7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.4, 33.0, 46.4, 127.1, 128.5, 128.8, 137.7, 206.1.

***S*-Phenethyl 4-methoxybenzothioate (5ab).**[27] The standard procedure for the thioesterification was followed. Starting with **1a** (60.9 mg, 0.40 mmol) and (2-

bromoethyl)benzene (**3b**, 74.0 mg, 0.40 mmol), thioester **5ab** (49.6 mg, 0.18 mmol, 46%) was produced according to ^{1}H NMR analysis of the reaction mixture. Compound **5ab** was purified by column chromatography (SiO_2, hexanes, R_f 0.12) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.93–2.98 (m, 2H), 3.26–3.31 (m, 2H), 3.85 (s, 3H), 6.91 (d, J = 8.9 Hz, 2H), 7.19–7.33 (m, 5H), 7.94 (d, J = 8.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.3, 36.1, 55.5, 113.7, 126.5, 128.5, 128.6, 129.4, 130.0, 140.2, 163.7, 190.3.

***S*-Hexyl 4-methoxybenzothioate** (**5ac**). The standard procedure for the thioesterification was followed. Starting with **1a** (60.9 mg, 0.40 mmol) and 1-bromohexane (**3c**, 56.1 μL, 0.40 mmol), thioester **5ac** (44.0 mg, 0.17 mmol, 44%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ac** (37.0 mg, 0.15 mmol, 37%) was isolated as a light yellow-liquid after column chromatography (SiO_2, hexanes, R_f 0.20). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.87 (t, J = 6.9 Hz, 3H), 1.27–1.30 (m, 4H), 1.39–1.43 (m, 2H), 1.61–1.67 (m, 2H), 3.02 (t, J = 7.4 Hz, 2H), 3.83 (s, 3H), 6.89 (d, J = 9.0 Hz, 2H), 7.93 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.0, 22.5, 28.6, 28.9, 29.6, 31.3, 55.4, 113.7, 129.3, 130.2, 163.6, 190.7; HRMS (APCI) calcd for $[M + H]^+$ ($C_{14}H_{21}O_2S$) 253.1262, found 253.1255.

***S*-Octyl 4-methoxybenzothioate** (**5ad**).[28] The standard procedure for the thioesterification was followed. Starting with **1a** (60.9 mg, 0.40 mmol) and 1-bromooctane (**3d**, 69.0 μL, 0.40 mmol), thioester **5ad** (58.5 mg, 0.21 mmol, 52%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ad** (46.0 mg, 0.16 mmol, 41%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.20). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.86 (t, J = 6.8 Hz, 3H), 1.25–1.31 (m, 8H), 1.37–1.42 (m, 2H), 1.61–1.67 (m, 2H), 3.02 (t, J = 7.5 Hz, 2H), 3.84 (s, 3H), 6.89 (d, J = 8.9 Hz, 2H), 7.93 (d, J = 8.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 22.6, 28.9, 28.9, 29.1, 29.2, 29.7, 31.8, 55.5, 113.7, 129.3, 130.2, 163.6, 190.7.

***S*-Decyl 4-methoxybenzothioate (5ae).**[29] The standard procedure for the thioesterification was followed. Starting with **1a** (60.9 mg, 0.40 mmol) and 1-bromodecane (**3e,** 83.0 μL, 0.40 mmol), thioester **5ae** (43.3 mg, 0.14 mmol, 35%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ae** (36.4 mg, 0.12 mmol, 29%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.20). ^{1}H NMR ($CDCl_3$, 500 MHz) δ0.86 (t, J = 6.8 Hz, 3H), 1.24–1.31 (m, 12H), 1.37–1.43 (m, 2H), 1.61–1.67 (m, 2H), 3.02 (t, J = 7.4 Hz, 2H), 3.84 (s, 3H), 6.89 (d, J = 8.9 Hz, 2H), 7.93 (d, J = 9.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.1, 22.7, 28.9, 28.9, 29.2, 29.3, 29.5, 29.5, 29.7, 31.9, 55.4, 113.7, 129.3, 130.2, 163.6, 190.6.

***S*-Ethyl benzothioate (5bf).**[27] The standard procedure for the thioesterification was followed. Starting with **1b** (48.8 mg, 0.40 mmol) and 1-bromoethane (**3f,** 30.0 μL, 0.40 mmol), thioester **5bf** (18.8 mg, 0.11 mmol, 28%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5bf** (5.3 mg, 0.03 mmol, 8%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.15). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.33 (t, J = 7.4 Hz, 3H), 3.06 (q, J = 7.4 Hz, 2H), 7.42 (t, J = 8.2 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.93–7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 14.7, 23.4, 127.1, 128.5, 133.2, 137.2, 192.1.

***S*-Allyl 2-methylbenzothioate (5cg).** The standard procedure for the thioesterification was followed. Starting with **1c** (54.5 mg, 0.40 mmol) and allyl bromide (**3f,** 34.6 μL, 0.40 mmol), thioester **5cg** (22.3 mg, 0.12 mmol, 29%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5cg** (20.7 mg, 0.11 mmol, 27%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.17). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.47 (s, 3H), 3.68 (d, J = 6.9 Hz, 2H), 5.13 (dd, J = 9.9 Hz, J = 0.9 Hz, 1H), 5.30 (dq, J = 17.0 Hz, J = 1.4 Hz, 1H), 5.89 (qt, J = 10.0 Hz, J = 7.0 Hz, 1H), 7.21–7.24 (m, 2H), 7.35–7.38 (m, 1H), 7.74–

7.76 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.5, 32.5, 117.9, 125.7, 128.4, 131.5, 131.6, 133.1, 136.8, 137.4, 193.6; HRMS (APCI) calcd for $[M + H]^+$ ($C_{11}H_{13}OS$) 193.0687, found 193.0690.

***S*-Cinnamyl 2-methylbenzothioate** (**5ch**). The standard procedure for the thioesterification was followed except the reaction temperature (180 °C). Starting with **1c** (54.5 mg, 0.40 mmol) and cinnamyl chloride (**3h,** 55.7 μL, 0.40 mmol), thioester **5ch** (67.6 mg, 0.24 mmol, 63%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5ch** (65.5 mg, 0.24 mmol, 61%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.14). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.50 (s, 3H), 3.87 (dd, J = 7.2 Hz, J = 1.2 Hz, 2H), 6.27 (dt, J = 15.6 Hz, J = 7.2 Hz 1H), 6.65 (dd, J = 15.6 Hz, J = 1.2 Hz, 1H), 7.20–7.41 (m, 8H), 7.77–7.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6, 32.2, 117.6, 124.5, 125.7, 126.4, 127.1, 127.6, 128.5, 129.1, 131.6, 131.7, 133.2, 136.7, 193.6; HRMS (FAB) calcd for $[M]^+$ ($C_{17}H_{16}OS$) 268.0922, found 268.0914.

***S*-Butyl benzothioate** (**5bk**).[30] A solution of benzoic acid (**1b**, 60.9 mg, 0.40 mmol), *N,N*'-diphenylthiourea (**2a**, 91.3 mg, 0.40 mmol), tetrabutylammonium iodide (147.7 mg, 0.40 mmol) and toluene (2 mL) was placed in a pressure tube that was heated to 160 °C and maintained at this temperature for 30 min. After cooling to rt, the reaction mixture was added with 1,3,5-trimethoxybenzene (10.1 mg, 60.1 μmol) and concentrated. Thioester **5bk** (44.3 mg, 0.23 mmol, 40%) was produced according to ^{1}H NMR analysis of the reaction mixture. Thioester **5bk** (30.6 mg, 0.16 mmol, 40%) was isolated as a light-yellow liquid after column chromatography (SiO_2, hexanes, R_f 0.15). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.93 (t, J = 7.4 Hz, 3H), 1.40–1.48 (m, 2H), 1.61–1.67 (m, 2H), 3.06 (t, J = 7.4 Hz, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.52–7.55 (m, 1H), 7.94–7.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.6, 22.0, 28.7, 31.6, 127.1, 128.5, 133.1, 137.3, 192.1.

Benzyl *N,N'*-diphenylcarbamimidothioate (8b). Benzyl bromide (57.3 μL. 0.48 mmol) was added to a solution of *N,N'*-diphenylthioura (100.0 mg, 0.44 mmol) and methanol (2 mL) at 0 °C. The reaction mixture was stirred at rt for 3 h, quenched with sat $NaHCO_{3(aq)}$ (0.5 mL) and extracted with ethyl acetate (4 mL × 3). The combined organic layers were dried over sodium sulfate, filtered and concentrated to give **8b** (138.5 mg, 0.43 mmol, 99%) as a light-yellow liquid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.03 (s, 2H), 7.05–7.10 (m, 2H), 7.14–77.17 (m, 4H), 7.28–77.35 (m, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 36.1, 121.5, 123.6, 127.6, 128.7, 128.9, 129.0, 137.1; IR (neat) 3400, 3059, 3028, 1623, 1285, 1490, 1434, 1309, 1220, 1128, 912, 758, 694 cm^{-1}; HRMS (ESI) calcd for $[M + H]^+$ ($C_{20}H_{19}N_2S$) 319.1269, found 319.1264.

Supporting Information. NMR spectra for the synthesized thioesters.

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