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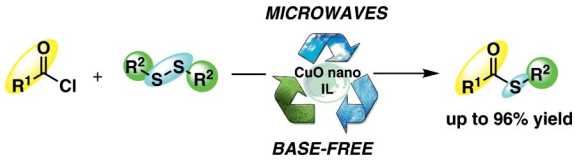
Organochalcogen Chemistry



We report an efficient, fast, and environmentally friendly method for the synthesis of thiol esters starting from diorganoyl disulfides and acyl chlorides, and using CuO nanoparticles and [pmim]Br as the reductive system. This approach gave good to excellent isolated yields of the desired products in only three minutes under microwave irradiation.

Keywords: Thiol esters / Ionic liquids / Sulfur / Nanoparticles / Microwave chemistry / Copper

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Synthesis of Thiol Esters Using Nano CuO/Ionic Liquid as an Eco-Friendly Reductive System Under Microwave Irradiation

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Keywords: Thiol esters / Ionic liquids / Sulfur / Nanoparticles / Microwave chemistry / Copper

We report an efficient, fast, and environmentally friendly method for the synthesis of a wide range of thiol esters using stable diorganoyl disulfides and acyl chlorides, using CuO nanoparticles and [pmim]Br as the reductive system. This method gave good to excellent isolated yields of the desired products after only three minutes of microwave irradiation. Furthermore, by using the same green approach, we were also able to synthesize thiocarbonates bearing interesting functionalities.

Introduction

The scope and applications of organochalcogen chemistry have increased tremendously, especially in relation to synthetic organic reactions, since sulfur-containing groups have been used as important auxiliary functional groups in several synthetic transformations.[1] Thiol esters are one of the most useful and powerful building blocks in organic chemistry. They have, for example, been used in C–C cross-coupling reactions,[2] in the synthesis of carbonyl compounds,[3] and in asymmetric transformations.[4] Furthermore, thiol esters have been used in native chemical ligation for peptide-bond formation,[5] and in the synthesis of natural products.[6] These compounds also have biological relevance, with applications in in-vivo tumor suppression[7] and as anti-HIV agents.[8]

Nowadays, the most convenient methods to incorporate a sulfur atom into an organic molecule generally involve the in situ generation of a nucleophilic sulfur species. This avoids the use of reagents with unpleasant odors such as thiols.[9] Most of the methods described for the reduction of S–S bonds use reagents such as hydroxide,[10] hydrazine,[11] sodium hydrogen telluride,[12] $[BnEt_3N]_2MoS_4$,[13] or expensive metals including indium salts.[14] The development of new synthetic strategies to improve these transformations is currently an area of great interest.

In this context, several methods for the synthesis of thiol esters under different reaction conditions have been described in the literature.[15] For example, they have been prepared from aldehydes using iBu$_2$AlSR,[16] from anhydrides using a base and thiol reagent combination,[17] and, more recently, from carboxylic acids using DCC.[18] However, the vast majority of reported methods have used acyl chlorides with nucleophilic sulfur species[19] such as $Hg(RS)_2$[20] or $RSSmI_2$.[21] Several other similar methods have been described that involve the generation of thiolate anions by the reductive cleavage of S–S bonds[22] or the deprotonation of thiols.[23] The reductive coupling of disulfides and acyl chlorides in an Rh/H_2 system has also been reported.[24] Nonetheless, it is well known that most of the reported protocols have their limitations, such as the use of toxic solvents, long reaction times, harsh conditions, or the problems associated with the handling of some thiols.

On the other hand, ionic liquids (ILs) have been used in recent years as an alternative reaction medium for a broad range of chemical transformations.[25] These solvents have certain features, such as nonvolatility, nonflammability, thermal stability, and recyclability, that make them an attractive medium for organic synthesis.[26] In this context, ionic liquids have also been used as effective solvents for the synthesis of thiol esters, either from thiols[27] or by reductive cleavage of S–S bonds by metals[28] or PPh_3.[29] We have also used a bimetallic system of $SnCl_2/CuBr_2$ for the synthesis of thiol esters,[30] using an excess of the bimetallic reagent as the reducing agent. The development of new catalytic methods for the preparation of thiol esters using environmentally friendly reductive systems under mild reaction conditions is highly desirable.

The catalysis of organic transformations by metallic nanostructures is currently an area of intensive research.[31] Generally, nanoscale copper catalysts in combination with ionic liquids provide more effective processes and allow great advances in relation to traditional methods.[32] In this context, CuO nanopowder, with its high surface area and

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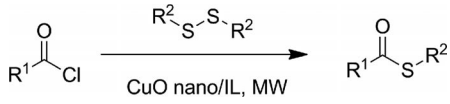
reactive morphology, has been studied as an effective catalyst for a wide range of reactions.[33]

Flash-heating by microwave (MW) irradiation for the acceleration of organic reactions is well established as a convenient method for accelerating reactions in the laboratory.[34] From a "green" point of view, the use of this kind of irradiation under solvent-free conditions or using an ionic liquid as a solvent is emerging as an environmentally benign alternative in organic synthesis.[35]

Bearing these factors in mind, and continuing our ongoing research into organochalcogen chemistry,[36] in this paper, we report a new method for the synthesis of thiol esters using an environmentally friendly reductive system under microwave irradiation (Scheme 1). With this method, we avoid the use of stoichiometric amounts of metals as well as strong reducing agents.

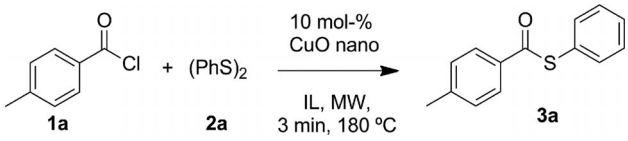


Scheme 1. General synthesis of thiol esters.

Results and Discussion

Initially, we focused our attention on the influence of different ionic liquids on the reaction (Table 1). To investigate this, we chose *p*-methylbenzoyl chloride (**1a**) and diphenyl disulfide (**2a**) as model substrates. We found that the nature of the ionic liquid was important for the success of the reaction. When [bmim]PF_6 was used as the solvent, thiol ester **3a** was obtained in only 45% yield (Table 1, entry 1). However, when [bmim]BF_4 was used, thiol ester **3a** was obtained in 52% yield (Table 1, entry 2). When an ionic liquid with a bromide counterion was used, a significant increase in the yield was obtained (Table 1, entries 3 and 4). For instance, the ionic liquid [bmim]Br gave the product in 87% yield (Table 1, entry 3). When [pmim]Br was used, the yield of the desired product was raised to 96% (Table 1, entry 4). This result highlights the influence of the length of alkyl chain of the imidazolium cation in this reaction, and also suggests that the counterion of the IL plays an important role in the reaction.

Table 1. Optimization of the ionic liquid used for the synthesis of thiol esters.[a]

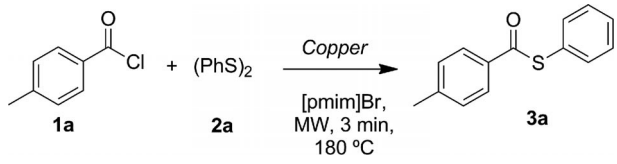


Entry	Ionic Liquid	Yield [%][b]
1	[bmim]PF_6	45
2	[bmim]BF_4	52
3	[bmim]Br	87
4	[pmim]Br	96

[a] Reaction conditions: *p*-methylbenzoyl chloride (0.5 mmol), diphenyl disulfide (0.25 mmol), nano CuO (10 mol-%), IL (0.5 mL), MW (100 W), 180 °C, 3 min. [b] Isolated yields.

Once we had established the best ionic liquid, we evaluated the amount of catalyst necessary to promote the reaction efficiently (Table 2). Initially, the reaction was performed with 2.5 mol-% of catalyst, and the desired product was formed in only 68% yield (Table 2, entry 1). When the amount of nano CuO was increased to 5.0 mol-%, the yield also increased significantly (Table 2, entry 2). Similarly, when 10 mol-% of nano CuO was used, the product was formed in 96% yield (Table 2, entry 3). Further increasing the amount of nano CuO to 20 mol-% did not affect the yield (Table 2, entry 4). The catalytic activity of bulk CuO was significantly lower than nano CuO, and it gave the desired product in only 41% yield (Table 2, entry 5). To examine the difference between this method and our previously reported method,[29] we tested $CuBr_2$ as a catalyst for the synthesis of thiol ester **3a**. However, this copper salt was not efficient as a catalyst for this transformation, and the desired product was formed in only 30% yield (Table 2, entry 6).

Table 2. Optimization of the amount of copper catalyst.[a]



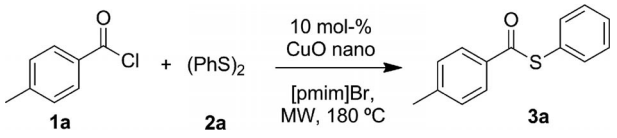
Entry	Copper source	Catalyst amount [mol-%]	Yield [%][b]
1	CuO_{nano}	2.5	68
2	CuO_{nano}	5	81
3	CuO_{nano}	10	96
4	CuO_{nano}	20	96
5	CuO	10	41
6	$CuBr_2$	10	30

[a] Reaction conditions: *p*-methylbenzoyl chloride (0.5 mmol), diphenyl disulfide (0.25 mmol), nano CuO, [pmim]Br (0.5 mL), MW (100 W), 3 min. [b] Isolated yields.

We then studied the influence of the reaction time (Table 3). Aiming to obtain an efficient method in terms of energy economy, we turned our attention to establishing the minimum reaction time associated with a good reaction rate. When the reaction was performed for only 1 min, a considerable decrease in the yield was observed (Table 3, entry 3). However, when the reaction time was increased to 2 min, thiol ester **3a** was obtained in 90% yield (Table 3, entry 2). Thus, 3 min was selected as the optimum reaction time.

Focusing on the influence of the microwave irradiation on the reaction, we carried out the reaction at lower power and also with conventional heating (Table 3, entries 4 and 5). When the power was decreased to 75 W, the yield decreased from 96 to 65% (Table 3, entry 4). When the reaction was carried out with conventional heating, even after 24 h, only a 24% yield of the desired product was obtained

Table 3. Optimization of the reaction conditions using *p*-methylbenzoyl chloride (**1a**) and diphenyl disulfide (**2a**).[a]

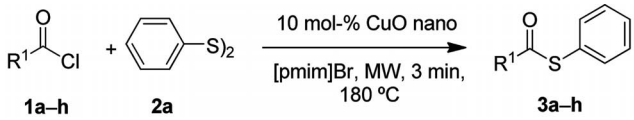


1a 2a 3a

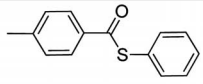
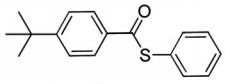
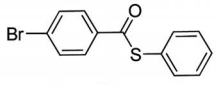
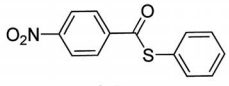
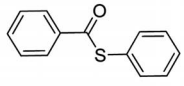
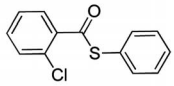
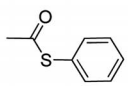
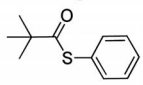
Entry	Power [W]	Time [min]	Yield [%][b]
1	100	3	96
2	100	2	90
3	100	1	55
4	75	3	65
5[c]	–	1440	24
6[d]	100	3	13

[a] Reaction conditions: *p*-methylbenzoyl chloride (0.5 mmol), diphenyl disulfide (0.25 mmol), nano CuO (10 mol-%), [pmim]Br (0.5 mL), MW (100 W), 180 °C, time. [b] Isolated yields. [c] The reaction was performed with conventional heating at 180 °C. [d] The reaction was performed using TEMPO (0.5 mmol).

Table 4. Synthesis of thiol esters using different acyl chlorides.[a]



1a–h 2a 3a–h

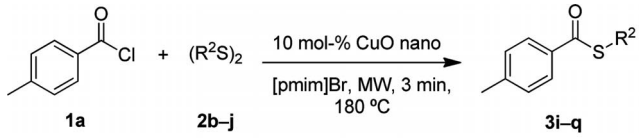
Entry	R^1	Product	Yield [%][b]
1	*p*-$CH_3C_6H_4$, **1a**	 **3a**	96
2	*p*-(*t*Bu)C_6H_4, **1b**	 **3b**	61
3	*p*-BrC_6H_4, **1c**	 **3c**	39
4	*p*-$NO_2C_6H_4$, **1d**	 **3d**	41
5	C_6H_5, **1e**	 **3e**	76
6	*o*-ClC_6H_4, **1f**	 **3f**	53
7	CH_3, **1g**	 **3g**	46
8	*t*-C_4H_9, **1h**	 **3h**	40

[a] Reaction conditions: acyl chloride (0.5 mmol), diphenyl disulfide (0.25 mmol), nano CuO (10 mol-%), MW (100 W), 180 °C, 3 min. [b] Isolated yields.

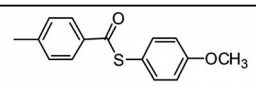
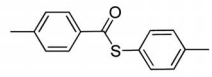
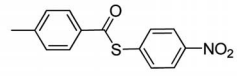
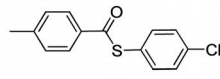
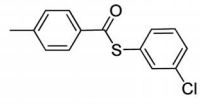
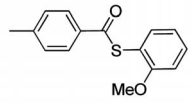
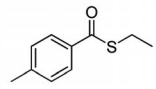
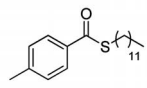
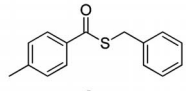
(Table 3, entry 5). To gain some insight into the mechanism, we evaluated the effect of a radical trap on the reaction outcome. When TEMPO was used, for example, the desired product was obtained in only 13% yield, which shows that a radical process might be operating (Table 3, entry 6).

We explored the generality of our method by combining other acyl chlorides **1b–f** with diphenyl disulfide (**2a**) (Table 4). With *p*-methylbenzoyl chloride, thiol ester **3a** was achieved in 96% yield (Table 4, entry 1). When a *tert*-butyl group was attached at the *para* position of the aromatic

Table 5. Scope and generality in the synthesis of thiol esters **3i–q** using *p*-methylbenzoyl chloride (**1a**) and disulfides **2b–j**.[a]



1a 2b–j 3i–q

Entry	R^2	Product	Yield [%][b]
1	*p*-$CH_3OC_6H_4$, **2b**	 **3i**	71
2	*p*-$CH_3C_6H_4$, **2c**	 **3j**	85
3	*p*-$NO_2C_6H_4$, **2d**	 **3k**	17
4	*p*-ClC_6H_4, **2e**	 **3l**	61
5	*m*-ClC_6H_4, **2f**	 **3m**	48
6	*o*-$CH_3OC_6H_4$, **2g**	 **3n**	41
7	CH_2CH_3, **2h**	 **3o**	88
8	$C_{12}H_{25}$, **2i**	 **3p**	31
9	$C_6H_4CH_2$, **2j**	 **3q**	49

[a] Reaction conditions: *p*-methylbenzoyl chloride (0.5 mmol), diorganoyl disulfide (0.25 mmol), nano CuO (10 mol-%), MW (100 W), 180 °C, 3 min. [b] Isolated yields.

ring, the corresponding product was obtained in moderate yield (Table 4, entry 2). When the aromatic ring had a mildly or strongly electron-withdrawing substituent, the corresponding products were formed in lower yields (Table 4, entries 3 and 4). With benzoyl chloride, the desired product was formed in 76% yield (Table 4, entry 5). With a chloride substitutent at the *ortho* position, thiol ester **3f** was formed in moderate yield (Table 4, entry 4). We were also able to prepare thiol esters starting from aliphatic acyl chlorides. The yield decreased to 46% for the reaction of acetyl chloride and diphenyl disulfide (Table 4, entry 7). When pivaloyl chloride, a more hindered group, was used, the desired product was formed in a lower yield (Table 4, entry 8).

We also investigated the reaction of *p*-methylbenzoyl chloride with a wide range of structurally diverse diorganoyl disulfides under our reaction conditions (Table 5, entries 1–10). When methoxy or methyl groups, both electron-donating groups, were attached at the *para* position of the aromatic ring, the corresponding thiol esters were obtained in 71 and 85% yields, respectively (Table 5, entries 1 and 2). However, a disulfide with a nitro group at the *para* position did not provide a very reactive nucleophile under the same conditions, and thiol ester **3k** was formed in poor yield (Table 5, entry 3). With an electron-withdrawing group at either the *para* or *meta* position, a slight decrease in the yield was observed (Table 5, entries 4 and 5). On the other hand, the disulfide with a methoxyphenyl substituent at the *ortho* position on the aromatic ring provided the desired product in moderate yield (Table 5, entry 6).

It is well known that aryl sulfides are more reactive than alkyl ones and also much more easily cleaved.[37] Using the same method, we also synthesized thiol esters starting from aliphatic disulfides (Table 5, entries 7–9). When diethyl disulfide was used as a nucleophile source, the desired product was formed in 88% yield (Table 5, entry 7). But when a long-chain disulfide was used, the yield of the corresponding product decreased dramatically (Table 5, entry 8). When we used dibenzyl disulfide, thiol ester **3l** was obtained in a satisfactory yield (Table 5, entry 9).

Due to our success in the preparation of thiol esters, we extended our method to the synthesis of thiocarbonates, which can act as versatile protecting groups for sulfur functionalities.[38] Thus, we attempted to synthesize different thiocarbonates containing interesting functional groups. When benzyl chloroformate (CbzCl; **1i**) and 9-fluorenylmethyl chloroformate (FmocCl; **1j**) were used as acylating agents, thiocarbonates **3r** and **3s** were obtained in 35 and 50% yields, respectively (Figure 1).

In addition, we evaluated the possibility of recycling the nano CuO/ionic liquid system used in our reactions (Figure 2). After the reaction was complete, the nano CuO/IL system was recovered and reused for further reactions. The CuO/IL system was very effective, even after the fourth run, giving thiol ester **3a** in 86% yield. Thus, we have shown that this method is greener and more efficient than that described in our previous report,[30] in which it was possible to recover and reuse only the ionic liquid. In this new protocol, it was possible to recycle and reuse, at the same time, both the catalyst and the ionic liquid components of the nano CuO/IL system.

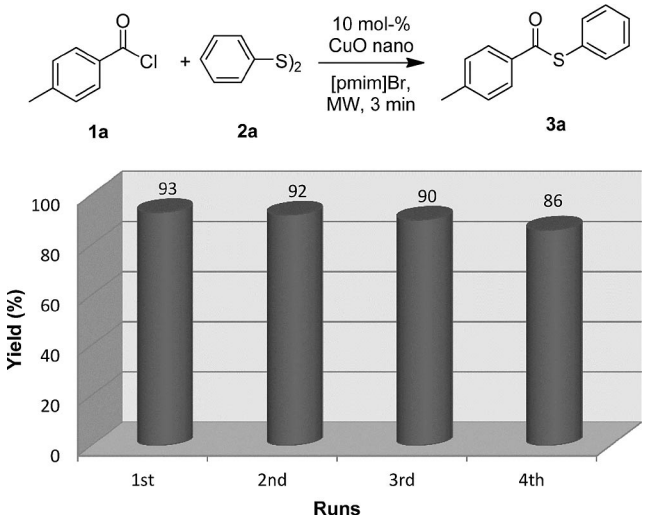


Figure 2. Reuse of nano CuO/[pmim]Br system in the synthesis of **3a**.

Conclusions

To summarize, we have described a new and rapid protocol for the synthesis of thiol esters using an environmentally friendly nano CuO/ionic liquid system under microwave ir-

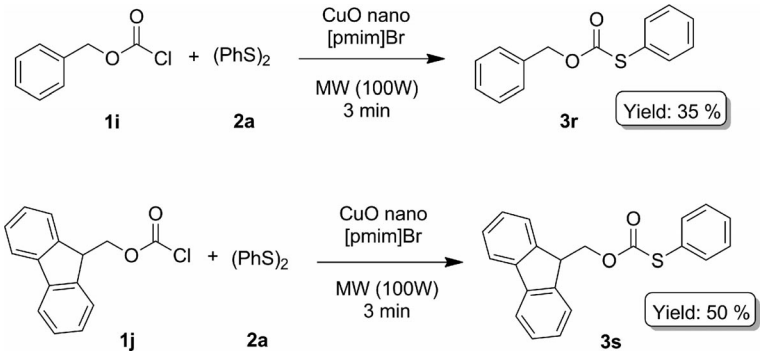


Figure 1. Synthesis of thiocarbonates.

radiation. In this way, we avoided the use of a base and reducing agents. This new method allowed the preparation of the desired products in good to excellent yields in very short reaction times. The catalytic system was used for the synthesis of thiol esters, and was easily recovered and reused for further reactions without loss of efficiency. Furthermore, we extended our method to the synthesis of thiocarbonates, which are also very important from a synthetic point of view. This shows the broad scope of the method. Studies to elucidate the mechanism of this reaction are in progress in our laboratory.

Experimental Section

General Remarks: ^{1}H (400 or 200 MHz) and ^{13}C (100 or 50 MHz) NMR spectra were recorded in $CDCl_3$. Chemical shifts (δ) are reported in ppm, and are calibrated to the TMS peak (^{1}H) or to the solvent peak (^{13}C). ESI-Q-TOF MS measurements were performed with a micrOTOF Q-II (Bruker Daltonics) mass spectrometer equipped with an automatic syringe pump from KD Scientific for sample injection. The ESI-Q-TOF mass spectrometer was running at 4.5 kV at a desolvation temperature of 180 °C, and was operating in the positive-ion mode. The standard electrospray (ESI) ion source was used to generate the ions. Samples were injected in an acetonitrile/methanol mixed solvent using a constant flow (3 μL/min). The ESI-Q-TOF MS instrument was calibrated in the range m/z = 50–3000 using an internal calibration standard (low-concentration tuning mix solution) supplied by Agilent Technologies. Data were processed using Bruker Data Analysis software version 4.0. Column chromatography was performed using Merck silica gel (230–400 mesh). Thin-layer chromatography (TLC) was performed using Merck silica gel GF_{254} plates (0.25 mm thickness). For visualization, TLC plates were placed under ultraviolet light and then stained using in acidic vanillin. The yields of the products given in all tables are isolated yields. The ionic liquids were prepared according to literature procedures.[39] All other solvents were used as received unless otherwise noted. All reactions were performed in 10 mL sealed tubes in a commercially available monomode reactor (CEM Discover) with IR monitoring and a non-invasive pressure transducer.

General Procedure for the Synthesis of Thiol Esters Under Microwave Irradiation: An oven-dried tube was allowed to cool to room temperature under argon, and then acyl chloride (0.5 mmol), CuO nanopowder (10 mol-%), diorganoyl disulfide (0.25 mmol), and [pmim]Br (1 mL) were added. The tube was sealed and placed into a CEM Discover microwave apparatus. Initially, a maximum irradiation power of 100 W and a temperature of 180 °C were applied for 3 min. When the reaction was complete, the product was extracted with diethyl ether. The solvent and volatiles were completely removed under vacuum to give the crude product. The compounds were purified by column chromatography over silica gel.

Recyclability Experiments: The nano CuO/[pmim]Br system was recycled without loss of activity. After completion of the reaction work-up, the catalyst/solvent mixture was washed with diethyl ether (5 × 5 mL), and then dried under vacuum for reuse in subsequent reactions.

***S*-Phenyl 4-Methylbenzothioate (3a):** Yield 0.194 g, 96%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, J = 4.0 Hz, 2 H), 7.54–7.52 (m, 2 H), 7.47–7.45 (m, 3 H), 7.29 (d, J = 4.0 Hz, 2 H), 2.40 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.5, 143.8, 135.1, 132.0, 129.2, 129.0, 126.3, 21.3 ppm. HRMS (ESI$^+$): calcd. for $C_{14}H_{13}OS$ [M + H]$^+$ 229.0682; found 229.0678.

***S*-Phenyl 4-*tert*-Butylbenzothioate (3b):** Yield 0.083 g, 61%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–8.12 (m, 5 H), 7.32–7.51 (m, 4 H), 1.35 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.5, 157.3, 130.2, 129.6, 126.4, 125.6, 125.4, 125.3, 36.2, 31.2 ppm. HRMS (ESI$^+$): calcd. for $C_{17}H_{19}OS$ [M + H]$^+$ 271.1151; found 271.1159.

***S*-Phenyl 4-Bromobenzothioate (3c):** Yield 0.057 g, 39%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.7 Hz, 2 H), 7.60 (d, J = 8.7 Hz, 2 H), 7.51–7.40 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 189.18, 135.50, 135.10, 132.13, 129.75, 129.31, 128.99, 128.81, 127.02 ppm. HRMS (ESI$^+$): calcd. for $C_{13}H_{10}BrOS$ [M + H]$^+$ 292.9630; found 292.9636.

***S*-Phenyl 4-Nitrobenzothioate (3d):** Yield 0.053 g, 41%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.34 (d, J = 9.1 Hz, 2 H), 8.17 (d, J = 9.1 Hz, 2 H), 7.60–7.45 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 188.90, 150.82, 141.46, 135.00, 130.17, 129.62, 128.60, 126.35, 124.11 ppm. HRMS (ESI$^+$): calcd. for $C_{13}H_{10}NO_3S$ [M + H]$^+$ 260.0376; found 260.0381.

***S*-Phenyl Benzothioate (3e):** Yield 0.081 g, 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12–8.00 (m, 2 H), 7.60–7.20 (m, 3 H), 7.53–7.45 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.1, 136.6, 135.0, 133.7, 133.6, 130.1, 129.5, 128.7, 128.4, 127.5 ppm. HRMS (ESI$^+$): calcd. for $C_{13}H_{11}OS$ [M + H]$^+$ 215.0525; found 215.0523.

***S*-Phenyl 2-Chlorobenzothioate (3f):** Yield 0,066 g, 53%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.60 (m, 1 H), 7.71–7.23 (m, 8 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.8, 136.8, 134.4, 132.2, 130.7, 129.5, 129.1, 128.9, 127.2, 126.5 ppm. HRMS (ESI$^+$): calcd. for $C_{13}H_{10}ClOS$ [M + H]$^+$ 249.0135; found 249.0132.

***S*-Phenyl Ethanethioate (3g):** Yield 0.034 g, 46%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.4 (s, 5 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.8, 134.3, 129.3, 129.0, 127.8, 30.0 ppm. HRMS (ESI$^+$): calcd. for C_8H_9OS [M + H]$^+$ 153.0369; found 153.0374.

***S*-Phenyl 2,2-Dimethylpropanethioate (3h):** Yield 0.038 g, 40%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.3 (s, 5 H), 1.31 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 204.4, 134.9, 129.0, 128.9, 128.0, 46.8, 27.3 ppm. HRMS (ESI$^+$): calcd. for $C_{11}H_{15}OS$ [M + H]$^+$ 195.0838; found 195.0835.

***S*-4-Methoxyphenyl 4-Methylbenzothioate (3i):** Yield 0.091 g, 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 8.0 Hz, 2 H), 7.41 (d, J = 9.0 Hz, 2 H), 7.25 (d, J = 7.0 Hz, 2 H), 6.98 (d, J = 8.0 Hz, 2 H), 3.84 (s, 3 H), 2.43 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.1, 161.2, 145.1, 138.9, 134.6, 129.8, 128.0, 118.6, 115.4, 55.8, 22.2 ppm. HRMS (ESI$^+$): calcd. for $C_{15}H_{15}O_2S$ [M + H]$^+$ 259.0787; found 259.0784.

***S*-*p*-Toluyl 4-Methylbenzothioate (3j):** Yield 0.103 g, 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, J = 8.1 Hz, 2 H), 7.38 (d, J = 8.1 Hz, 2 H), 7.26–7.23 (m, 4 H), 2.40 (s, 3 H), 2.38 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.5, 144.3, 139.6, 134.9, 134.1, 129.9, 129.3, 127.4, 123.9, 21.6, 21.3 ppm. HRMS (ESI$^+$): calcd. for $C_{15}H_{15}OS$ [M + H]$^+$ 243.0844; found 243.0838.

***S*-(4-Nitrophenyl) 4-Methylbenzothioate (3k):** Yield 0.023 g, 17%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.22 (d, J = 8.8 Hz, 2 H), 8.02 (d, J = 8.3 Hz, 2 H), 7.66 (d, J = 8.8 Hz, 2 H), 7.28 (d, J = 8.3 Hz, 2 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 187.20, 148.01, 145.34, 136.38, 133.32, 130.48, 129.50, 127.59, 123.68,

21.67 ppm. HRMS (ESI$^+$): calcd. for $C_{14}H_{12}NO_3S$ [M + H]$^+$ 274.0532; found 274.0530.

***S*-4-Chlorophenyl 4-Methylbenzothioate (3l):** Yield 0.079 g, 61%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, J = 8.1 Hz, 2 H), 7.425–7.421 (m, 4 H), 7.27 (d, J = 8.1 Hz, 2 H), 2.42 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.1, 144.8, 136.3, 135.8, 133.8, 129.44, 129.41, 127.5, 126.0 21.7 ppm. HRMS (ESI$^+$): calcd. for $C_{14}H_{12}ClOS$ [M + H]$^+$ 263.0297; found 263.0298.

***S*-3-Chlorophenyl 4-Methylbenzothioate (3m):** Yield 0.062 g, 48%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.89 (d, J = 8.2 Hz, 2 H), 7.50–7.34 (m, 4 H), 7.24 (d, J = 8.2 Hz, 2 H), 2.39 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 188.70, 144.92, 134.79, 134.72, 133.85, 133.23, 130.15, 129.60, 129.54, 127.65, 21.75 ppm. HRMS (ESI$^+$): calcd. for $C_{14}H_{11}ClOSNa$ [M + Na]$^+$ 285.0111; found 285.0115.

***S*-2-Methoxyphenyl 4-Methylbenzothioate (3n):** 0.053 g, 41%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70 (d, J = 8.3 Hz, 2 H), 7.24–7.14 (m, 2 H), 7.00 (d, J = 8.3 Hz, 2 H), 6.80–6.72 (m, 2 H), 3.58 (s, 3 H), 2.15 (s, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 188.89, 159.85, 144.36, 137.37, 134.37, 131.73, 129.37, 121.21, 115.78, 111.73, 56.10, 21.73 ppm. HRMS (ESI$^+$): calcd. for $C_{15}H_{15}O_2S$ [M + H]$^+$ 259.0787; found 259.0790.

***S*-Ethyl 4-Methylbenzothioate (3o):** Yield 0.079 g, 88%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.0 Hz, 2 H), 7.23 (d, J = 8.0 Hz, 2 H), 3.06 (q, J = 7.3 Hz, 2 H), 2.39 (s, 3 H), 1.34 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 191.7, 144.0, 134.7, 129.2, 127.2, 23.3, 21.6, 14.8 ppm. HRMS (ESI$^+$): calcd. for $C_{10}H_{13}OS$ [M + H]$^+$ 181.0682; found 181.0682.

S-Dodecyl 4-Methylbenzothioate (3p): Yield 0.049 g, 31%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.86 (d, J = 8.1 Hz, 2 H), 7.22 (d, J = 8.1 Hz, 2 H), 3.05 (t, J = 7.6 Hz, 2 H), 2.39 (s, 3 H), 170–1.59 (m, 2 H), 1.25 (br. s, 18 H), 0.88 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 191.62, 143.88, 134.75, 129.13, 127.18, 31.89, 29.62, 29.60, 29.56, 29.48, 29.32, 29.14, 28.93, 28.92, 14.07 ppm. HRMS (ESI$^+$): calcd. for $C_{20}H_{32}SONa$ [M + Na]$^+$ 343.2073; found 343.2069.

***S*-Benzyl 4-Methylbenzothioate (3q):** Yield 0.059 g, 49%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.83 (d, J = 8.2 Hz, 2 H), 7.34–7.17 (m, 5 H), 7.12 (d, J = 8.2 Hz, 2 H), 4.25 (s, 2 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 190.3, 143.9, 137.4, 134.0, 129.0, 128.9, 128.3, 127.0, 32.9, 21.4 ppm. HRMS (ESI$^+$): calcd. for $C_{15}H_{15}OS$ [M + H]$^+$ 243.0838; found 243.0839.

***O*-Benzyl *S*-Phenyl Carbonothioate (3r):** Yield 0.042 g, 35%. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.49–7.47 (m, 3 H), 7.32–7.28 (m, 7 H), 5.17 (s, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 169.3, 134.6, 129.3, 128.9, 128.3, 127.4, 69.0 ppm. HRMS (ESI$^+$): calcd. for $C_{14}H_{12}O_2SNa$ [M + Na]$^+$ 267.0450; found 267.0445.

***O*-(9*H*-Fluoren-9-yl)methyl *S*-Phenyl Carbonothioate (3s):** Yield 0.083 g, 50%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77–7.33 (m, 13 H), 4.54 (d, J = 7.6 Hz, 2 H), 4.28 (t, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.7, 142.3, 142.2, 128.8, 128.2, 127.3, 125.0, 120.2, 73.4, 46.1 ppm. HRMS (ESI$^+$): calcd. for $C_{21}H_{16}O_2SNa$ [M + Na]$^+$ 355.0763; found 355.0766.

Supporting Information (see footnote on the first page of this article): Experimental procedures, characterization data and copies of ^{1}H and ^{13}C NMR as well as mass spectra.

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