Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Synthesis of thioesters through copper-catalyzed coupling of aldehydes with thiols in water

Chih-Lun Yi,[a] Yu-Ting Huang[a] and Chin-Fa Lee*[a]

Received (in XXX, XXX) XthXXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

A copper-catalyzed C-S bond formation between aldehydes and thiols in the presence of TBHP as an oxidant is described. Functional groups including chloro, trifluoromethyl, bromo, iodo, nitrile, ester and thiophene are all tolerated by the reaction conditions employed. This reaction is performed in water without the use of a surfactant. Both aryl and alkyl aldehydes couple suitably with aryl- and alkyl thiols, affording the corresponding thioesters in moderate to good yields.

Introduction

Thioesters are important building blocks for organic synthesis,[1] and they have been utilized in acyl transfer reactions as the intermediates. Thioesters are also play an important role in biology.[2] The traditional preparation of thioesters relied on the condensation reaction of carboxylic acids with thiols or metal thiolates in the presence of an activating reagent.[3] However, some limitations remain using this protocol. First, some starting materials such as acyl chlorides are moisture-sensitive and need to be prepared in situ. Second, this method sometimes produces an equal amount of halide anion when acyl chlorides were used. As a result, the direct coupling of aldehydes with thiol surrogates serves as an attractive route to access thioesters. Since the discovery of this approach in 1976 by Takagi et al., through a photo-induced reductive acylation of disulfides with aldehydes,[4] several synthetic limitations have been observed using this approach. First, the reaction is not applicable to substituted aromatic aldehydes. Second, the reaction needs a specific photo-reactor. Third, a diluted reaction concentration is required. Recently, Takemoto et al. reported the carbene-catalyzed coupling of aldehydes with thiols in THF,[5] however, some drawbacks are observed in this method, as well. First, the carbenes used in this work are expensive. Second, alkyl aldehydes are less reactive than aromatic aldehydes, and more electron-rich carbenes are required. Bandgar and co-workers described the Dess-Martin periodinane-promoted synthesis of thioesters, however, 6 equiv of Dess-Martin periodinane in combination with 6 equiv of NaN_3 are required to give the desired thioesters. Moreover, the substrates are limited to aryl thiols.[6] Water is one of the most attractive medium for chemical transformations.[7] Interestingly, Kita et al. reported the preparation of thioesters from aldehydes and dipentafluorophenyl disulfide in water through a radical pathway.[8] However, many limitations remained in this work. First, 1 equiv of water soluble initiator is necessary. Second, the scope of the substrate is limited to dipentafluorophenyl disulfide and low yields were observed when simple phenyl disulfides were used; moreover, no alkyldisulfides were presented in this system. Third, cetyltrimethyl-ammonium bromide was required as a surfactant. Therefore, the development of a general method for preparing thioesters from aldehydes and thiols in water is highly desirable. Transition-metal-catalyzed C-H functionalization has emerged as an efficient strategy for introducing carbon-carbon and carbon-heteroatom bonds.[9] Herein we report that the catalytic amount of CuCl is an active catalyst for the coupling of aldehydes with thiols in the presence of TBHP as an oxidant in water without the need for surfactant.

Results and discussion

Initially, benzaldehyde and 1-dodecanethiol were selected as the model substrates to determine the optimized reaction conditions and the results are summarized in Table 1. We first examined the source of oxidant (Table 1, entries 1-5), and TBHP was found to be superior to the others (Table 1, entry 1). The effect of solvent was then studied (Table 1, entries 6-9), and to our delight, water afforded the target in a 50% isolated yield (Table 1, entry 9). A 61% yield was obtained when the reaction was performed at 100 ^{o}C (Table 1, entry 10), however, a lower yield was determined at 110 ^{o}C (Table 1, entry 11). Interestingly, a similar result was obtained when the copper salt was reduced to 2.5 mol% (Table 1, entry 12). However, a low yield (51%) was observed when 1.0 mol% of copper salt was used (Table 1, entry 13). Notably, a 75% yield was obtained when TBHP was decreased to 1 mmol (Table 1, entry 13). We then examined the influence of copper sources (Table 1, entries 15-20), and found that CuCl was superior to $Cu(OTf)_2$, CuO, Cu_2O, CuBr and CuI. The control experiment showed that the product was obtained with only a 13% yield when the reaction was carried out in the absence of a

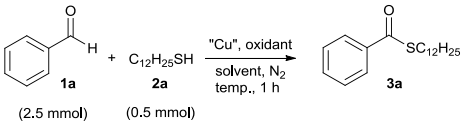
Department of Chemistry, NationalChungHsingUniversity, Taichung, Taiwan 402, R.O.C

E-mail: cfalee@dragon.nchu.edu.tw; Fax: +886 4 2286-2547; Tel: +886 4 2284-0411 ext. 810

† Electronic Supplementary Information (ESI) available: Experimental details, spectral data for new products. See DOI:10.1039/b000000x/

copper salt (Table 1, entry 21). When the aldehyde was reduced to 1.5 mmol, only 76% yield was obtained (Table 1, entry 22). A 72% yield resulted when the reaction was performed under an air atmosphere (Table 1, entry 23). Shorter reaction times reduced the product yield to 76% yield (Table 1, entry 24).

Table 1 Optimize the reaction conditions[a]

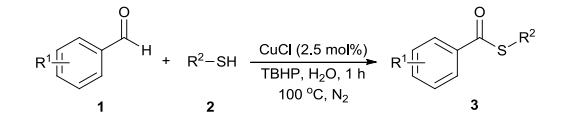


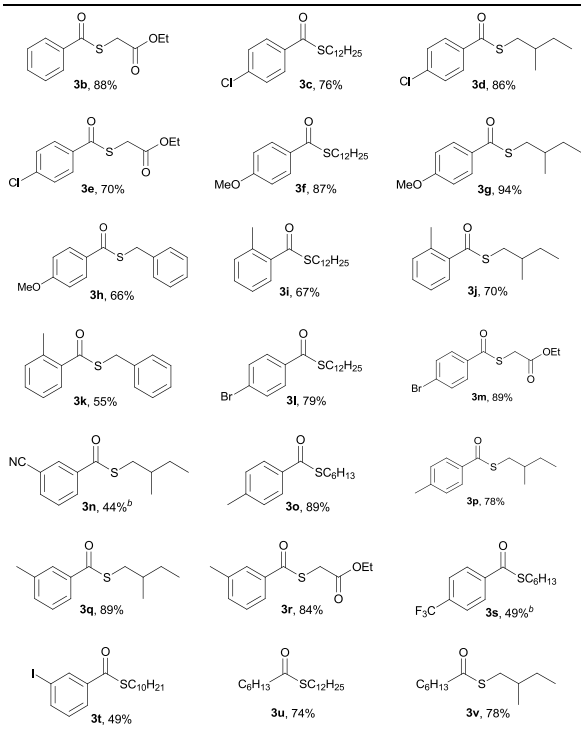
Entry	"Cu" (mol%)	Oxidant (mmol)	Temp.	Solvent	Yield(%)[b]
1	$Cu(OAc)_2$ (14)	TBHP (2.5)	80	toluene	22
2	$Cu(OAc)_2$ (14)	BPO (2.5)	80	toluene	12
3	$Cu(OAc)_2$ (14)	AcOOH (2.5)	80	toluene	3
4	$Cu(OAc)_2$ (14)	DTBP (2.5)	80	toluene	-
5	$Cu(OAc)_2$ (14)	H_2O_2 (2.5)	80	toluene	-
6	$Cu(OAc)_2$ (14)	TBHP (2.5)	80	CH_3CN	29
7	$Cu(OAc)_2$ (14)	TBHP (2.5)	80	THF	20
8	$Cu(OAc)_2$ (14)	TBHP (2.5)	80	DCE	25
9	$Cu(OAc)_2$ (14)	TBHP (2.5)	80	H_2O	50
10	$Cu(OAc)_2$ (14)	TBHP (2.5)	100	H_2O	61
11	$Cu(OAc)_2$ (14)	TBHP (2.5)	110	H_2O	43
12	$Cu(OAc)_2$ (2.5)	TBHP (2.5)	100	H_2O	60
13	$Cu(OAc)_2$ (1)	TBHP (2.5)	100	H_2O	51
14	$Cu(OAc)_2$ (2.5)	TBHP (1.0)	100	H_2O	75
15	$Cu(OTf)_2$ (2.5)	TBHP (1.0)	100	H_2O	69
16	CuO (2.5)	TBHP (1.0)	100	H_2O	73
17	Cu_2O (2.5)	TBHP (1.0)	100	H_2O	76
18	CuCl (2.5)	TBHP (1.0)	100	H_2O	89
19	CuBr (2.5)	TBHP (1.0)	100	H_2O	60
20	CuI (2.5)	TBHP (1.0)	100	H_2O	69
21	-	TBHP (1.0)	100	H_2O	13
22[c]	CuCl (2.5)	TBHP (1.0)	100	H_2O	76
23[d]	CuCl (2.5)	TBHP (1.0)	100	H_2O	72
25[e]	CuCl (2.5)	TBHP (1.0)	100	H_2O	76

[a] Reaction conditions: Cu source (0.0125 mmol, 2.5 mol%), oxidant (1.0 mmol), thiol (0.5 mmol), benzaldehyde (2.5 mmol) under a nitrogen atmosphere in solvent (1.5 mL) for 1 h. [b] Isolated yield. [c] Benzaldehyde (1.5 mmol). [d] Under air atmosphere. [e] 30 min. TBHP = *tert*-butyl hydroperoxide. BPO = benzoyl peroxide. AcOOH = peracetic acid. DTBP = di-*tert*-butyl peroxide.

With these optimized reaction conditions in hand, the scope of the substrates was then studied. The results are summarized in Table 2. A variety of alkyl thiols were conducted with aromatic- and alkyl aldehydes, to afford the corresponding thioesters in moderate to good yields. Aromatic aldehydes bearing electron-donating and electron-withdrawing substituents are all suitable for catalysis. It is important to note that this system shows good functional group tolerance; ester (Table 2, products **3b**, **3e**, **3m** and **3r**), chloro (Table 2, products **3c**, **3d** and **3e**), bromo (Table 2, products **3l** and **3m**), nitrile (Table 2, product **3n**), iodo (Table 2, product **3t**) and trifluoromethyl (Table 2, product **3s**) are all tolerated by the reaction conditions employed. Furthermore, sterically demanding substituted aryl aldehydes also underwent the cross-coupling with thiols to afford the desired products in 55-70% yields (Table 2, products **3i**, **3j** and **3k**). Alkyl thiols were also reacted with alkyl aldehydes to give the corresponding thioesters ((Table 2, products **3u** and **3v**).

Table 2 Copper-catalyzed coupling reaction of aldehydes with alkyl thiols[a]

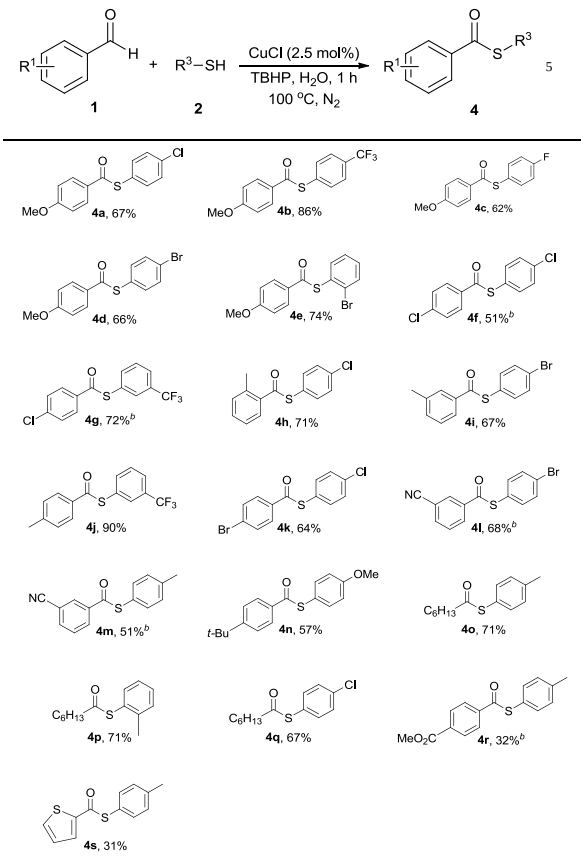




[a] Reaction conditions unless otherwise stated: CuCl (0.0125 mmol, 2.5 mol%), TBHP (1.0 mmol), thiol (0.5 mmol), aldehyde (2.5 mmol) under a nitrogen atmosphere in H_2O (1.5 mL) for 1 h. [b] 5 mol% of CuCl was used.

Based on the promising results for alkyl thiols, we next turned our attention to aryl thiols. Aryl thiols bearing electron-donating and electron-withdrawing substituents underwent cross-coupling with aryl- and alkyl ((Table 3, products **4o**, **4p** and **4q**) aldehydes to provide the corresponding thioesters in 31-90% yields. Functional groups including chloro (Table 3, products **4a**, **4f**, **4g**, **4h**, **4k** and **4q**), trifluoromethyl (Table 3, product **4b**), fluoro (Table 3, product **4c**), bromo (Table 3, products **4d**, **4e**, **4i** and **4l**), nitrile (Table 3, products **4l** and **4m**), ester (Table 3, product **4r**) and thiophene (Table 3, product **4s**) are tolerated by the reaction conditions.

Table 3 Copper-catalyzed synthesis of thioesters through coupling of aldehydes with aryl thiols[a]



[a] Reaction conditions unless otherwise stated: CuCl (0.0125 mmol, 2.5 mol%), TBHP (1.0 mmol), thiol (0.5 mmol), aldehyde (2.5 mmol) under a nitrogen atmosphere in H_2O (1.5 mL) for 1 h. [b] 5 mol% of CuCl was used.

Conclusions

In conclusion, we have developed a general method for preparing thioesters by using 2.5 mol% of CuCl as a catalyst and TBHP as an oxidant. It is important to note that the reactions were carried out in water without any surfactant. Aryl- and alkyl aldehydes were coupled with aryl- and alkyl thiols, giving the corresponding thioesters in 31-94% yields. This system shows good functional group tolerance. Additionally, sterically demanding substrates were also shown good activity for catalysis. Mechanistic studies and applications of this catalytic system are currently underway in our laboratory

Experimental

General information

All chemicals were purchased from commercial suppliers and used without further purification. NMR spectra were recorded on a Varian Unity Inova-600 or a Varian Mercury-400 instrument using $CDCl_3$ as solvent. Chemical shifts are reported in parts per million (ppm) and referenced to the residual solvent resonance. Coupling constant (*J*) are reported in hertz (Hz). Standard abbreviations indicating multiplicity were used as follows: s = singlet, d = doublet, t = triplet, dd = double doublet, tt = triplet triplet, td = triplet doublet, dt = doublet triplet, q = quartet, m = multiplet, b = broad. Melting points (m.p.) were determined using a Büchi 535 apparatus and are reported uncorrected. High resolution mass spectra (HRMS) were performed on an electron ionization time-of-flight (EI-TOF) mass spectrometer or LCMS with an APCI source by the services at the National Chung Hsing University.

General procedure for Table 1

A Schlenk tube equipped with a magnetic stirrer bar was charged with copper salt (0.0125 mmol) in a nitrogen-filled glove box. The Schlenk tube was then covered with a rubber septum and removed from the glove box. Under a nitrogen atmosphere, 1-dodecanethiol (0.5 mmole), benzaldehyde (2.5 mmol), oxidant (1.0 mmol), solvent (1.5 mL) was added via syringe, and the Schlenk tube was connected to a nitrogen-filled balloon and heated at 100 ℃ in an oil bath. After stirring at this temperature for 1 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was directly filtered through a pad of silica gel then washed with ethyl acetate (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to yield **3a**.

Representative example of Table 1. *S*-Dodecyl benzothioate (entry 18, 3a).[10] Following the general procedure for Table 1, using CuCl (1.3 mg, 0.0125 mmol), benzaldehyde (0.26 mL, 2.5 mmol), 1-dodecanethiol (0.125 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3a** as a yellow oil (136 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.6 Hz, 3 H), 1.26-1.44 (m, 18 H), 1.63-1.71 (m, 2H), 3.06 (t, *J* = 7.4 Hz, 2 H), 7.43 (t, *J* = 7.8 Hz, 2 H), 7.55 (t, *J* = 7.4 Hz, 1 H), 7.97 (d, *J* = 4.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 28.9, 29.0, 29.1, 29.3, 29.5, 29.5, 29.6, 29.6, 29.6, 31.9, 127.1, 128.5, 133.1, 137.2, 192.1.

General procedure for Table 2

A Schlenk tube equipped with a magnetic stirrer bar was charged with CuCl (1.3 mg, 0.0125 mmol) in a nitrogen-filled glove box. The Schlenk tube was then covered with a rubber septum and removed from the glove box. Under a nitrogen atmosphere, thiol (0.5 mmole), aldehyde (2.5 mmol), TBHP (0.14 mL, 1.0 mmol), H_2O (1.5 mL) was added via syringe, and the Schlenk tube was connected to a nitrogen-filled balloon and heated at 100 ℃ in an oil bath. After stirring at this temperature for 1 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was directly filtered through a pad of silica gel then washed with ethyl acetate (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to yield **3**.

Ethyl 2-(benzoylthio)acetate (3b).[3b] Following the general procedure for

Table 2, using CuCl (1.3 mg, 0.0125 mmol), benzaldehyde (0.26 mL, 2.5 mmol), ethyl 2-mercaptoacetate (0.056 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **3b** as a colorless oil (99 mg, 88% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.2 Hz, 3 H), 3.88 (s, 2 H), 4.23 (q, *J* = 7.2 Hz, 3 H), 7.46 (t, *J* = 7.8 Hz, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.97 (d, *J* = 4.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 31.3, 61.8, 127.3, 128.6, 133.7, 136.0, 168.7, 190.0.

***S*-Dodecyl 4-chlorobezothioate (3c).**[10] Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-chlorobenzaldehyde (359 mg, 2.5 mmol), 1-dodecanethiol (0.125 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3c** as a yellow oil (130 mg, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.26-1.43 (m, 18 H), 1.63-1.70 (m, 2 H), 3.06 (t, *J* = 7.4 Hz, 2 H), 7.40-7.43 (m, 2 H), 7.89-7.92 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 28.9, 29.1, 29.2, 29.3, 29.5, 29.5, 29.6, 29.6, 29.6, 31.9, 128.5, 128.8, 135.6, 139.5, 191.0.

***S*-(2-Methyl-1-butyl) 4-chlorobenzothioate (3d).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-chlorobenzaldehyde (359 mg, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to afford **3d** as a yellow oil (105 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.4 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 1.24-1.31 (m, 1 H), 1.47-1.54 (m, 1 H), 1.67-1.72 (m, 1 H), 2.95 (dd, *J* = 7.2, 12.8 Hz, 1 H), 3.13 (dd, *J* = 5.6, 12.8 Hz, 1 H), 7.40-7.44 (m, 2 H), 7.91-7.94 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.8, 28.7, 34.9, 35.7, 128.5, 128.8, 135.6, 139.5, 190.9; HRMS-EI calcd. for $C_{12}H_{15}ClOS$: 242.0532, found: 242.0541.

Ethyl 2-((4-chlorobenzoyl)thio)acetate (3e). Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-chlorobenzaldehyde (359 mg, 2.5 mmol), ethyl 2-mercaptoacetate (0.056 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **3e** as a white solid (90 mg, 70% yield). M.p.: 55-56 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, *J* = 7.0 Hz, 3 H), 3.89 (s, 2 H), 4.23 (q, *J* = 7.1 Hz, 2 H), 7.44 (dd, *J* = 2.0, 6.8 Hz, 2 H), 7.92 (dd, *J* = 2.0, 6.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 31.4, 61.9, 128.7, 129.0, 134.4, 140.1, 168.5, 188.9; HRMS-EI calcd. for $C_{11}H_{11}ClO_3S$: 258.0117, found: 258.0115.

***S*-Dodecyl 4-methoxybenzothioate (3f).**[10] Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 1-dodecanethiol (0.125 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **3f** as a yellow oil (147 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3 H), 1.26-1.43 (m, 18 H), 1.64-1.67 (m, 2 H), 3.04 (t, *J* = 7.4 Hz, 2 H), 3.85 (s, 3 H), 6.9 (dd, *J* = 2.0, 6.8 Hz, 2 H), 7.95 (dd, *J* = 2.0, 6.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 28.9, 28.9, 29.1, 29.3, 29.5, 29.6, 29.6, 29.6, 29.7, 31.9, 55.4, 113.6, 129.3, 130.1, 163.5, 190.6.

***S*-(2-Methyl-1-butyl) 4-methoxybenzothioate (3g).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **3g** as a yellow oil (112 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.4 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 1.23-1.30 (m, 1 H), 1.47-1.54 (m, 1 H), 1.64- 1.69 (m, 1 H), 2.93 (dd, *J* = 7.2, 12.8 Hz, 1 H), 3.11 (dd, *J* = 6.0, 13.2 Hz, 1 H), 3.86 (s, 3 H), 6.90-6.94 (m, 2 H), 7.95-7.99 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.8, 28.7, 35.1, 35.4, 55.5, 113.6, 129.3, 130.1, 163.6, 190.6; HRMS-EI calcd. for $C_{13}H_{18}O_2S$: 238.1028, found: 238.1035.

***S*-Benzyl 4-methoxybenzothioate (3h).**[5] Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), phenylmethanethiol (0.060 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **3h** as a yellow solid (86 mg, 66% yield). M.p.: 50-51 ℃ (lit.[5] m.p.: 51-52 ℃). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3 H), 4.29 (s, 2 H), 6.90 (dd, *J* = 2.0, 6.8 Hz, 2 H), 7.23-7.38 (m, 5 H), 7.94 (dd, *J* = 2.0, 6.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.1, 55.4, 113.7, 127.2, 128.6, 128.9, 129.4, 129.5, 137.7, 163.7, 189.7.

***S*-Dodecyl 2-methylbenzothioate (3i).**[10] Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 2-methylbenzaldehyde (0.30 mL, 2.5 mmol), 1-dodecanethiol (0.125 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3i** as a colorless oil (107 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.26-1.44 (m, 18 H), 1.63-1.70 (m, 2 H), 2.48 (s, 3 H), 3.03 (t, *J* = 7.2 Hz, 2 H), 7.22-7.26 (m, 2 H), 7.35-7.39 (m, 1 H), 7.76 (dd, *J* = 1.6, 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.5, 22.7, 28.9, 29.2, 29.3, 29.5, 29.6, 29.6, 29.6, 29.6, 31.9, 125.7, 128.3, 131.4, 131.5, 136.6, 137.8, 194.6.

***S*-(2-Methyl-1-butyl) 2-methylbenzothioate (3j).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 2-methylbenzaldehyde (0.30 mL, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3j** as a

yellow oil (77 mg, 70% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.6 Hz, 3 H), 1.01 (d, *J* = 6.4 Hz, 3 H), 1.24-1.31 (m, 1 H), 1.48-1.55 (m, 1 H), 1.67-1.72 (m, 1 H), 2.47 (s, 3 H), 2.93 (dd, *J* = 7.2, 13.2 Hz, 1 H), 3.09 (dd, *J* = 6.0, 13.2 Hz, 1 H), 7.23 (t, *J* = 7.4 Hz, 2 H), 7.33-7.39 (m, 1 H), 7.78 (dd, *J* = 1.6, 7.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.8, 20.5, 28.7, 35.0, 36.0, 125.6, 128.3, 131.4, 131.4, 136.5, 137.9, 194.6; HRMS-EI calcd. for $C_{13}H_{18}OS$: 222.1078, found: 222.1072.

***S*-Benzyl 2-methylbenzothioate (3k).**[3b] Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 2-methylbenzaldehyde (0.30 mL, 2.5 mmol), phenylmethanethiol (0.060 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to give **3k** as a yellow oil (67 mg, 55% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (s, 3 H), 4.28 (s, 2 H), 7.22-7.27 (m, 3 H), 7.30-7.39 (m, 5 H), 7.76 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) 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, 193.5.

***S*-Dodecyl 4-bromobenzothioate (3l).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-bromobenzaldehyde (467 mg, 2.5 mmol), 1-dodecanethiol (0.125 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to obtain **3l** as a white solid (152 mg, 79% yield). M.p.: 31-32 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.25-1.43 (m, 18 H), 1.64-1.68 (m, 2 H), 3.06 (t, *J* = 7.4 Hz, 2 H), 7.57 (d, *J* = 8.4 Hz, 2 H), 7.82 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 28.9, 29.1, 29.1, 29.3, 29.4, 29.5, 29.5, 29.6, 29.6, 31.9, 128.2, 128.6, 131.8, 135.9, 191.0; HRMS-EI calcd. for $C_{19}H_{29}BrOS$: 384.1122, found: 384.1115.

Ethyl 2-((4-bromobenzoyl)thio)acetate (3m). Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-bromobenzaldehyde (467 mg, 2.5 mmol), ethyl 2-mercaptoacetate (0.056 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to afford **3m** as a yellow solid (135 mg, 89% yield). M.p.: 41-42 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, *J* = 7.2 Hz, 3 H), 3.80 (s, 2 H), 4.14 (q, *J* = 7.1 Hz, 2 H), 7.51 (dd, *J* = 1.6, 6.8 Hz, 2 H), 7.74 (dd, *J* = 1.6, 6.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 31.4, 61.9, 128.7, 128.8, 131.9, 134.7, 168.4, 189.0; HRMS-EI calcd. for $C_{11}H_{11}BrO_3S$: 301.9612, found: 301.9604.

***S*-(2-Methyl-1-butyl) 3-cyanobenzothioate (3n).** Following the general procedure for Table 2, using CuCl (2.5 mg, 0.025 mmol), 3-formylbenzonitrile (331 mg, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **3n** as a yellow oil (52 mg, 44% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.4 Hz, 3 H), 1.01 (t, *J* = 6.4 Hz, 3 H), 1.24-1.35 (m, 1 H), 1.47-1.69 (m, 1 H), 1.70-1.74 (m, 1 H), 3.00 (dd, *J* = 7.2, 13.2 Hz, 1 H), 3.17 (dd, *J* = 6.0, 13.6 Hz, 1 H), 7.58-7.62 (m, 1 H), 7.83-7.86 (m, 1 H), 8.18-8.21 (m, 1 H), 8.26-8.27 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 18.8, 28.7, 34.8, 35.9, 113.0, 117.8, 129.6, 130.8, 131.1, 136.0, 138.0, 190.2; HRMS-EI calcd. for $C_{13}H_{15}NOS$: 233.0874, found: 233.0879.

***S*-Hexyl 4-methylbenzothioate (3o).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-methylbenzaldehyde (0.30 mL, 2.5 mmol), 1-hexanethiol (0.0725 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to give **3o** as a yellow oil (105 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.0 Hz, 3 H), 1.25-1.44 (m, 6 H), 1.62-1.68 (m, 2 H), 2.40 (s, 3 H), 3.05 (t, *J* = 7.4 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.87 (dd, *J* = 1.6, 6.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 21.6, 22.5, 28.6, 28.9, 29.5, 31.3, 127.2, 129.2, 134.7, 144.0, 191.7; HRMS-EI calcd. for $C_{14}H_{20}OS$: 236.1235, found: 236.1228.

***S*-(2-Methyl-1-butyl) 4-methylbenzothioate (3p).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 4-methylbenzaldehyde (0.30 mL, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3p** as a yellow oil (86 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.4 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 1.24-1.31 (m, 1 H), 1.48-1.54 (m, 1 H), 1.66-1.71 (m, 1 H), 2.41 (s, 3 H), 2.94 (dd, *J* = 7.2, 13.6 Hz, 1 H), 3.11 (dd, *J* = 5.6, 13.2 Hz, 1 H), 7.22-7.26 (m, 2 H), 7.87-7.90 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.8, 21.6, 28.8, 35.0, 35.4, 127.2, 129.2, 134.7, 144.0, 191.8; HRMS-EI calcd. for $C_{13}H_{18}OS$: 222.1078, found: 222.1085.

***S*-(2-Methyl-1-butyl) 3-methylbenzothioate (3q).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 3-methylbenzaldehyde (0.30 mL, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3q** as a yellow oil (99 mg, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.4 Hz, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 1.24-1.31 (m, 1 H), 1.44-1.54 (m, 1 H), 1.68-1.70 (m, 1 H), 2.94 (dd, *J* = 7.6, 13.6 Hz, 1 H), 3.13 (dd, *J* = 6.0, 13.6 Hz, 1 H), 7.30-7.38 (m, 2 H), 7.78-7.79 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.8, 21.3, 28.7, 35.0, 35.5, 124.4, 127.6, 128.4, 133.9, 137.3, 138.4, 192.2; HRMS-EI calcd. for $C_{13}H_{18}OS$: 222.1078, found: 222.1072.

Ethyl 2-((3-methylbenzoyl)thio)acetate (3r).[3b] Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 3-methylbenzaldehyde (0.30 mL, 2.5 mmol), ethyl 2-mercaptoacetate (0.056 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3r** as

a yellow oil (101 mg, 85% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, *J* = 7.2 Hz, 3 H), 2.40 (s, 3 H), 3.87 (s, 2 H), 4.22 (q, *J* = 7.2 Hz, 2 H), 7.31-7.40 (m, 2 H), 7.76-7.78 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 21.1, 31.3, 61.7, 124.5, 127.7, 128.5, 134.4, 136.0, 138.5, 168.7, 190.1.

***S*-Hexyl 4-(trifluoromethyl)benzothioate (3s).** Following the general procedure for Table 2, using CuCl (2.5 mg, 0.025 mmol), 4-(trifluoromethyl)benzaldehyde (0.35 mL, 2.5 mmol), 1-hexanethiol (0.0725 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3s** as a colorless oil (72 mg, 49% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.90 (t, *J* = 6.9 Hz, 3 H), 1.31-1.34 (m, 4 H), 1.41-1.46 (m, 2 H), 1.66-1.71 (m, 2 H), 3.10 (t, *J* = 7.2 Hz, 2 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 8.07 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.0, 22.5, 28.6, 29.3, 29.7, 31.3, 123.5 (q, *J* = 271.1 Hz), 125.6, 125.6, 127.5, 134.5 (q, *J* = 32.4 Hz), 139.9, 191.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.7 (s); HRMS-EI calcd. for $C_{14}H_{17}F_3OS$: 290.0952, found: 290.0954.

***S*-Decyl 3-iodobenzothioate (3t).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), 3-iodobenzaldehyde (592 mg, 2.5 mmol), 1-decanethiol (0.1075 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3t** as a white solid (99 mg, 49% yield). M.p.: 44-45 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.26-1.43 (m, 14 H), 1.62-1.70 (m, 2 H), 3.06 (t, *J* = 7.4 Hz, 2 H), 7.17 (t, *J* = 7.8 Hz, 1 H), 7.86-7.93 (m, 2 H), 8.27 (t, *J* = 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 28.9, 29.1, 29.2, 29.3, 29.4, 29.5, 29.5, 31.8, 94.2, 126.3, 130.1, 135.9, 138.8, 141.8, 190.6; HRMS-APCI calcd. for $C_{17}H_{26}OIS[M + H]^+$: 405.07436, found: 405.07428.

***S*-Dodecyl heptanethioate (3u).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), heptaldehyde 0.37 mL, 2.5 mmol), 1-dodecanethiol (0.125 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3u** as a colorless oil (116 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.26-1.34 (m, 24 H), 1.54-1.57 (m, 2 H), 1.63-1.67 (m, 2 H), 2.53 (t, *J* = 7.6 Hz, 2 H), 2.86 (t, *J* = 7.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 22.4, 22.7, 25.7, 28.6, 28.8, 28.8, 29.1, 29.3, 29.5, 29.6, 29.6, 29.6, 29.6, 31.4, 31.9, 44.1, 199.8; HRMS-APCI calcd. for $C_{19}H_{39}OS[M + H]^+$: 315.2716, found: 315.2724.

***S*-(2-Methyl-1-butyl) heptanethioate (3v).** Following the general procedure for Table 2, using CuCl (1.3 mg, 0.0125 mmol), heptaldehyde 0.37 mL, 2.5 mmol), 2-methyl-1-butanethiol (0.065 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **3v** as a colorless oil (84 mg, 78% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86-0.94 (m, 9 H), 1.17-1.34 (m, 7 H), 1.39-1.46 (m, 1 H), 1.55-1.67 (m, 3 H), 2.55 (t, *J* = 7.4 Hz, 2 H), 2.75 (dd, *J* = 7.2, 12.4 Hz, 1 H), 2.92 (dd, *J* = 6.0, 12.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 14.0, 18.7, 22.4, 25.7, 28.6, 28.6, 31.4, 35.0, 35.3, 44.2, 199.8; HRMS-APCI calcd. for $C_{12}H_{25}OS[M + H]^+$: 217.16206, found: 217.16198.

General procedure for Table 3

A Schlenk tube equipped with a magnetic stirrer bar was charged with CuCl (1.3 mg, 0.0125 mmol) in a nitrogen-filled glove box. The Schlenk tube was then covered with a rubber septum and removed from the glove box. Under a nitrogen atmosphere, thiol (0.5 mmole), aldehyde (2.5 mmol), TBHP (0.14 mL, 1.0 mmol), H_2O (1.5 mL) was added via syringe, and the Schlenk tube was connected to a nitrogen-filled balloon and heated at 100 ℃ in an oil bath. After stirring at this temperature for 1 h, the heterogeneous mixture was cooled to room temperature and diluted with ethyl acetate (20 mL). The resulting solution was directly filtered through a pad of silica gel then washed with ethyl acetate (20 mL) and concentrated to give the crude material which was then purified by column chromatography (SiO_2, hexane) to yield **4**.

***S*-(4-Chlorophenyl) 4-methoxybenzothioate (4a).**[11] Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 4-chlorobenzenethiol (0.074 g, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4a** as a white solid (93 mg, 67% yield). M.p.: 96-97 ℃ (lit.[11] m.p.: 98-101 ℃). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3 H), 6.94 (d, *J* = 9.2 Hz, 2 H), 7.41 (t, *J* = 1.0 Hz, 4 H), 7.98 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 113.9, 126.1, 128.9, 129.3, 129.7, 135.7, 136.3, 164.0, 187.9.

***S*-(4-(Trifluoromethyl)phenyl) 4-methoxybenzothioate (4b).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 4-(trifluoromethyl)benzenethiol (0.071 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4b** as a white solid (134 mg, 86% yield). M.p.: 105-106 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.86 (s, 3 H), 6.95 (dd, *J* = 2.4, 7.2 Hz, 2 H), 7.63 (d, *J* = 7.8 Hz, 2 H), 7.68 (d, *J* = 8.4 Hz, 2 H), 7.99 (dd, *J* = 2.4, 7.2 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.5, 114.0, 123.8 (q, *J* = 270.9 Hz), 125.8, 125.8, 128.8, 129.8, 131.1 (q, *J* = 32.6 Hz), 132.5, 135.2, 164.2, 187.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s); HRMS-APCI calcd. for $C_{15}H_{12}O_2F_3S[M + H]^+$: 313.0505, found: 313.0513.

***S*-(4-Fluorophenyl) 4-methoxybenzothioate (4c).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 4-fluorobenzenethiol (0.054 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then

purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4c** as a white solid (81 mg, 62% yield). M.p.: 89-90 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.86 (s, 3 H), 6.95 (dd, *J* = 2.4, 7.2 Hz, 2 H), 7.12-7.15 (m, 2 H), 7.46-7.48 (m, 2 H), 7.99 (dd, *J* = 2.4, 7.2 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 55.5, 113.9, 116.3, 116.4, 122.8, 122.8, 129.0, 129.6, 137.1, 137.2, 162.6, 164.0, 164.3, 188.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.9 (s); HRMS-APCI calcd. for $C_{14}H_{12}O_2FS[M + H]^+$: 263.0537, found: 263.0544.

***S*-(4-Bromophenyl) 4-methoxybenzothioate (4d).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 4-bromobenzenethiol (0.099 g, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4d** as a white solid (107 mg, 66% yield). M.p.: 103-104 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3 H), 6.94 (d, *J* = 9.2 Hz, 2 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.55 (d, *J* = 8.4 Hz, 2 H), 7.97 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 113.9, 124.0, 126.7, 128.9, 129.7, 132.2, 136.5, 164.0, 187.7; HRMS-APCI calcd. for $C_{14}H_{12}O_2BrS[M + H]^+$: 322.9736, found: 322.9748.

***S*-(2-Bromophenyl) 4-methoxybenzothioate (4e).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-methoxybenzaldehyde (0.31 mL, 2.5 mmol), 2-bromobenzenethiol (0.062mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4e** as a white solid (120 mg, 74% yield). M.p.: 79-80 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3 H), 6.95 (dd, *J* = 2.0, 6.8 Hz, 2 H), 7.29 (td, *J* = 1.6, 8.0 Hz, 1 H), 7.37 (td, *J* = 1.6, 7.6 Hz, 1 H), 7.61 (dd, *J* = 2.0, 7.6 Hz, 1 H), 7.72 (dd, *J* = 1.6, 8.0 Hz, 1 H), 8.01 (dd, *J* = 2.0, 6.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 113.9, 127.9, 129.0, 129.4, 129.8, 130.0, 131.1, 133.5, 137.6, 164.1, 186.7; HRMS-APCI calcd. for $C_{14}H_{12}O_2BrS[M + H]^+$: 322.9736, found: 322.9750.

***S*-(4-Chlorophenyl) 4-chlorobenzothioate (4f).[12]** Following the general procedure for Table 3, using CuCl (2.5 mg, 0.025 mmol), 4-chlorobenzaldehyde (359 mg, 2.5 mmol), 4-chlorobenzenethiol (74 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4f** as a white solid (72 mg, 51% yield). M.p.: 136-137 ℃ (lit.[12] m.p.: 136-138 ℃). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 4 H), 7.46 (d, *J* = 8.4 Hz, 2 H), 7.94 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.3, 128.8, 129.1, 129.6, 134.6, 136.1, 136.2, 140.3, 188.5.

***S*-(3-(Trifluoromethyl)phenyl) 4-chlorobenzothioate (4g).** Following the general procedure for Table 3, using CuCl (2.5 mg, 0.025 mmol), 4-chlorobenzaldehyde (359 mg, 2.5 mmol), 3-(trifluoromethyl)benzenethiol (0.070mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4g** as a yellow solid (114 mg, 72% yield). M.p.: 51-52 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (dt, *J* = 2.4, 9.0 Hz, 2 H), 7.59 (t, *J* = 7.8 Hz, 1 H), 7.70 (dd, *J* = 7.8, 13.8 Hz, 2 H), 7.78 (s, 1 H), 7.96 (dt, *J* = 2.4, 8.4 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 123.5 (q, *J* = 271.1 Hz), 126.4 (q, *J* = 3.6 Hz), 128.3, 128.8, 128.9, 129.0, 129.1, 129.2, 129.7, 131.7 (q, *J* = 32.6 Hz), 131.7 (q, *J* = 3.9 Hz), 134.4, 138.4, 140.5, 187.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s); HRMS-APCI calcd. for $C_{14}H_9OClF_3S[M + H]^+$: 317.00092, found: 317.00103.

***S*-(4-Chlorophenyl) 2-methylbenzothioate (4h).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 2-methylbenzaldehyde (0.30 mL, 2.5 mmol), 4-chlorobenzenethiol (74 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4h** as a white solid (94 mg, 71% yield). M.p.: 90-91 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 3 H), 7.25-7.31 (m, 2 H), 7.40-7.44 (m, 5 H), 7.92 (dd, *J* = 1.6, 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 125.9, 126.6, 128.6, 129.4, 131.8, 132.2, 135.8, 136.1, 136.2, 137.5, 191.4; HRMS-APCI calcd. for $C_{14}H_{12}OClS[M + H]^+$: 263.0292, found: 263.0294.

***S*-(4-Bromophenyl) 3-methylbenzothioate (4i).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 3-methylbenzaldehyde (0.30 mL, 2.5 mmol), 4-bromobenzenethiol (99 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4i** as a yellow solid (103 mg, 67% yield). M.p.: 66-67 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 7.34-7.42 (m, 4 H), 7.55-7.58 (m, 2 H), 7.79-7.82 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 124.1, 124.7, 126.5, 127.9, 128.6, 132.4, 134.6, 136.3, 136.5, 138.7, 189.5; HRMS-APCI calcd. for $C_{14}H_{12}OBrS[M + H]^+$: 306.9787, found: 306.9795.

***S*-(3-(Trifluoromethyl)phenyl) 4-methylbenzothioate (4j).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-methylbenzaldehyde (0.30 mL, 2.5 mmol),3-(trifluoromethyl)benzenethiol (0.070 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4j** as a yellow solid (134 mg, 90% yield). M.p.: 62-63 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 7.28 (d, *J* = 7.8 Hz, 2 H), 7.56 (t, *J* = 9.6 Hz, 1 H), 7.69 (d, *J* = 7.8 Hz, 2 H), 7.78 (s, 1 H), 7.91 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.7, 123.6 (q, *J*= 271.1 Hz), 126.1 (q, *J* = 3.5 Hz), 127.6, 129.0, 129.3, 129.3, 129.5, 129.7, 131.5 (q, *J* = 32.4 Hz), 131.7 (q, *J* = 3.9 Hz), 133.5, 138.5, 145.1, 188.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.2 (s); HRMS-APCI calcd. for $C_{15}H_{12}OF_3S[M + H]^+$: 297.0555, found: 297.0563.

***S*-(4-Chlorophenyl) 4-bromobenzothioate (4k).[13]** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-bromobenzaldehyde (467 mg, 2.5 mmol), 4-chlorobenzenethiol (74 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified

by column chromatography (SiO_2, hexane) to provide **4k** as a white solid (106 mg, 64% yield). M.p.: 144-145 ℃ (lit.[13] m.p.: 145-146 ℃). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 4 H), 7.62 (d, *J* = 8.4 Hz, 2 H), 7.86 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 125.2, 128.9, 128.9, 129.5, 132.1, 135.0, 136.1, 136.2, 188.7.

S-(4-Bromophenyl) 3-cyanobenzothioate (4l). Following the general procedure for Table 3, using CuCl (2.5 mg, 0.025 mmol), 3-formylbenzonitrile (331 mg, 2.5 mmol), 4-bromobenzenethiol (99 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4l** as a white solid (108 mg, 68% yield). M.p.: 150-151 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 2 H), 7.60-7.67 (m, 3 H), 7.90 (d, *J* = 7.6 Hz, 1 H), 8.22 (d, *J* = 8.0 Hz, 1 H), 8.28 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.3, 117.5, 124.7, 125.1, 129.8, 131.0, 131.3, 132.6, 136.3, 136.6, 137.1, 187.8; HRMS-EI calcd. for $C_{14}H_8BrNOS$: 316.9510, found: 316.9518.

***S*-*p*-Tolyl 3-cyanobenzothioate (4m).** Following the general procedure for Table 3, using CuCl (2.5 mg, 0.025 mmol), 3-formylbenzonitrile (331 mg, 2.5 mmol), 4-methylbenzenethiol (63 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4m** as a white solid (65 mg, 51% yield). M.p.: 100-101 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.62 (t, *J* = 8.0 Hz, 1 H), 7.86 (d, *J* = 7.6 Hz, 1 H), 8.22 (d, *J* = 8.0 Hz, 1 H), 8.28 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 113.2, 117.6, 122.4, 129.7, 130.2, 130.9, 131.3, 134.8, 136.3, 137.4, 140.3, 188.9; HRMS-EI calcd. for $C_{15}H_{11}NOS$: 253.0561, found: 253.0566.

***S*-(4-Methoxyphenyl) 4-(tert-butyl)benzothioate (4n).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 4-(*tert*-butyl)benzaldehyde (0.44 mL, 2.5 mmol),4-methoxylbenzenethiol (0.063 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4n** as a white solid (85 mg, 57% yield). M.p.: 88-89 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (s, 9 H), 3.82 (s, 3 H), 6.97 (d, *J* = 8.8 Hz, 2 H), 7.41 (d, *J* = 9.2 Hz, 2 H), 7.48 (d, *J* = 8.4 Hz, 2 H), 7.96 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.0, 35.1, 55.3, 114.8, 118.0, 125.6, 127.3, 133.9, 136.6, 157.3, 160.6, 190.5; HRMS-EI calcd. for $C_{18}H_{20}O_2S$: 300.1184, found: 300.1177.

***S*-*p*-Tolyl heptanethioate (4o).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), heptaldehyde (0.37 mL, 2.5 mmol),4-methylbenzenethiol (63 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4o** as a yellow oil (84 mg, 71% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.8 Hz, 3 H), 1.26-1.37 (m, 6 H), 1.67-1.71 (m, 2 H), 2.35 (s, 3 H), 2.62 (t, *J* = 7.6 Hz, 2 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 2.0, 6.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 21.2, 22.4, 25.5, 28.5, 31.4, 43.5, 124.3, 129.9, 134.3, 139.4, 197.9; HRMS-APCI calcd. for $C_{14}H_{21}OS$ $[M + H]^+$: 237.1308, found: 237.1313.

***S*-*o*-Tolyl heptanethioate (4p).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), heptaldehyde (0.37 mL, 2.5 mmol), 2-methylbenzenethiol (0.06 mL, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4p** as a yellow oil (85 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.8 Hz, 3 H), 1.26-1.40 (m, 6 H), 1.67-1.74 (m, 2 H), 2.33 (s, 3 H), 2.64 (t, *J* = 7.4 Hz, 2 H), 7.17-7.21 (m, 1 H), 7.28-7.30 (m, 2 H), 7.38 (d, *J* = 8.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 20.6, 22.4, 25.6, 28.5, 31,4, 43.6, 126.4, 127.3, 129.9, 130.6, 135.8, 141.8, 197.1; HRMS-EI calcd. for $C_{14}H_{20}OS$: 236.1235, found: 236.1239.

***S*-(4-Chlorophenyl) heptanethioate (4q).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), heptaldehyde (0.37 mL, 2.5 mmol), 4-chlorobenzenethiol (74 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4q** as a colorless oil (87 mg, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.2 Hz, 3 H), 1.26-1.38 (m, 6 H), 1.68-1.72 (m, 2 H), 2.65 (t, *J* = 7.6 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 7.28 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.4, 25.5, 28.6, 31.4, 43.7, 126.3, 129.4, 135.7, 197.0; HRMS-EI calcd. for $C_{13}H_{17}ClOS$: 256.0689, found: 256.0688.

Methyl 4-((*p*-tolylthio)carbonyl)benzoate (4r). Following the general procedure for Table 3, using CuCl (2.5 mg, 0.025 mmol), methyl 4-formylbenzoate (415 mg, 2.5 mmol), 4-methylbenzenethiol (63 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane/EtOAc, 100:1) to provide **4r** as a white solid (45 mg, 32% yield). M.p.: 113-114 ℃. ^{1}H NMR (400 MHz, $CDCl_3$)δ 2.41 (s, 3 H), 3.95 (s, 3 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 7.39 (d, *J* = 8.0 Hz, 2 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 8.14 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 52.5, 123.1, 127.3, 129.9, 130.2, 134.2, 134.8, 139.9, 140.0, 166.0, 190.1; HRMS-EI calcd. for $C_{16}H_{14}O_3S$: 286.0664, found: 286.0667.

***S*-*p*-Tolyl thiophene-2-carbothioate (4s).** Following the general procedure for Table 3, using CuCl (1.3 mg, 0.0125 mmol), 2-thiophenecarboxaldehyde (0.24 mL, 2.5 mmol), 4-methylbenzenethiol (63 mg, 0.5 mmol) and TBHP (0.14 mL, 1.0 mmol) in H_2O (1.5 mL), then purified by column chromatography (SiO_2, hexane) to provide **4s** as a yellow oil (37 mg, 31% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 7.14 (t, *J* = 4.4 Hz, 1 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.64 (d, *J* = 4.8 Hz, 1 H), 7.89 (d, *J* = 3.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 123.3, 127.9, 130.1, 131.5, 133.1, 135.0, 139.9, 141.4, 182.5; HRMS-EI calcd. for $C_{12}H_{10}OS_2$: 234.0173, found: 234.0165.

Acknowledgements

The National Science Council, Taiwan (NSC 101-2113-M-005-008-MY3), the National Chung Hsing University and the Center of Nanoscience and Nanotechnology (NCHU) are gratefully acknowledged for financial support. We also thank Prof. Fung-E Hong (NCHU) for sharing his GC-MS instruments. C.F.L. is a Golden-Jade Fellow of Kenda Foundation, Taiwan.

References

1 (*a*) S. Rossi, M. Benaglia, F. Cozzi, A. Genoni and T. Benincori, *Adv. Synth. Catal.*, 2011, **353**, 848-854; (*b*) D. Crich and I. Sharma, *Angew. Chem., Int. Ed.*, 2009, **48**, 2355-2358; (*c*) D. Crich and K. Sasaki, *Org. Lett.*, 2009, **11**, 3514-3517; (*d*) M. Benaglia, M. Cinquini and F. Cozzi, *Eur. J. Org. Chem.*, 2000, 563-572; (*e*) K. Matsuo and M. Sindo, *Org. Lett.*, 2010, **12**, 5346-5349; (*f*) S. Iimura, K. Manabe and S. Kobayashi, *Org. Lett.*, 2003, **5**, 101-103; (*g*) T. Fukuyama and H. Tokuyama, *Aldrichimica Acta*, 2004, **37**, 87-96; (*h*) H. Yang, H. Li, R. Wittenberg, M. Egi, W. Huang and L. S. Liebeskind, *J. Am. Chem. Soc.*, 2007, **129**, 1132-1140; (*i*) H. Li, H. Yang and L. S. Liebeskind, *Org. Lett.*, 2008, **10**, 4375-4378; (*j*) K. Kunchithapatham, C. C. Eichman and J. P. Stambuli, *Chem. Commun.*, 2011, **47**, 12679-12681; (*k*) J. M. Yost, G. Zhou and D. M. Coltart, *Org. Lett.*, 2006, **8**, 1503-1506; (*l*) N. Utsumi,S. Kitagaki and C. F. Barbas III, *Org. Lett.*, 2008, **10**, 3405-3408; (*m*) D. A. Alonso, S. Kitagaki, N. Utsumi and C. F. Barbas III, *Angew. Chem., Int. Ed.*, 2008, **47**, 4588-4591; (*n*) A. Iida, J. Osada,R. Nagase, T. Misaki and Y. Tanabe, *Org. Lett.*, 2007, **9**, 1859-1862.

2 J. Staunton and K. J. Weissman, *Nat. Prod. Rep.*, 2001, **18**, 380-416.

3 (*a*) S. Magens and B. Plietker, *Chem.–Eur. J.*, 2011, **17**, 8807-8809; (*b*) A. R. Katritzky, A. A. Shestopalov and K. Suzuki, *Synthesis*, 2004, 1806-1813; (*c*) S. limura, K. Manabe and S. Kobayashi, *Chem. Commun.*, 2002, 94-95; (*d*) S. Ahmad and J. Iqbal, *Tetrahedron Lett.*, 1986, **27**, 3791-3794; (*e*) G. O. Spessard, W. K. Chan and S. Masamune, *Org. Synth.*, 1982, **61**, 134-141; (*f*) S. Ahmad and J. Iqbal, *Tetrahedron Lett.*, 1986, **27**, 3791-3794; (*g*) C. C. Silveira, A. L. Braga and E. L. Larghi, *Organometallics*, 1999, **18**, 5183-5186; (*h*) H. M. Meshram G. S. Reddy, K. H. Mindu and J. S. Yadav, *Synlett*, 1998, 877-878.

4 (*a*) M. Takagi, S. Goto and T. Matsuda, *J. Chem. Soc., Chem. Commun.*, 1976, 92-93; (*b*) M. Takagi, S. Goto, M. Tazaki and T. Matsuda, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1982-1987.

5 T. Uno, T. Inokuma and Y. Takemoto, *Chem. Commun.*, 2012, **48**, 1901-1903.

6 S. B. Bandgar, B. P. Bandgar, B. L. Korbad and S. S. Sawant, *Tetrahedron Lett.*, 2007, **48**, 1287-1290.

7 (*a*) C.-J. Li, *Chem. Rev.*, 2005, **105**, 3095-3165; (*b*) C.-J. Li and L. Chen, *Chem. Soc. Rev.*, 2006, **35**, 68–82; (*c*) C. I. Herrerías, X. Yao, Z. Li and C.-J. Li, *Chem. Rev.*, 2007, **107**, 2546-2562; (*d*) M.-O. Simon and C.-J. Li, *Green Techniques for Organic Synthesis and Medicinal Chemistry*, 2012, 263-295; (*e*) S. Kobayashi, P. Xu; T. Endo, M. Ueno and T. Kitanosono, *Angew. Chem., Int. Ed.*, 2012, **51**, 12763-12766; (*f*) C.-Q. Ren, C.-H. Di, Y.-U. Zhao and J.-P. Zhang, *Tetrahedron Lett.*, 2013, **54**, 1478-1481; (*g*) S. Xu, Y. Zhou, J. Xu, H. Jiang and H. Liu, *Green Chem.*, 2013, **15**, 718-726; (*h*) Y.-C. Teo, F.-F. Yong, I. K. Ithnin, S.-H. Yio and Z. Lin, *Eur. J. Org. Chem.*, 2013, 515-524.

8 (*a*) H. Nambu, K. Hata, M. Matsugi and Y. Kita, *Chem. Commun.*, 2002, 1082-1083; (*b*) H. Nambu, K. Hata, M. Matsugi and Y. Kita, *Chem. Eur. J.*, 2005, **11**, 719-727.

9 For representative reviews, please see: (*a*) S. Murai, *Activation of Unreactive Bonds and Organic Synthesis*; Springer: Berlin, Germany, 1999; pp 48; (*b*) G. Dyker, *Handbook of C-H Transformations. Applications in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2005; (*c*) I. A. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy and J. F. Hartwig, *Chem. Rev.*, 2010, **110**, 890-931; (*d*) T. W. Lyons and M. S. Sanford, *Chem. Rev.*, 2010, **110**, 1147-1169; (*e*) J. C. Lewis, R. G. Bergman and J. A. Ellman, *Acc. Chem. Res.*, 2008, **41**, 1013-1025; (*f*) Y. J. Park, J. W. Park and C. H. Jun, *Acc. Chem. Res.*, 2008, **41**, 222-234; (*g*) M. M. Díaz-Requejo and P. J. Pérez, *Chem. Rev.*, 2008, **108**, 3379-3394; (*h*) D. A. Colby, R. G. Bergman and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624-655.

10 Y. Hu, J. Liu, Z. Lü, X. Luo, H. Zhang, Y. Lan and A. Lei, *J. Am. Chem. Soc.*, 2010, **132**, 3153-3158.

11 B. C. Ranu and T. Mandal, *J. Org. Chem.*, 2004, **69**, 5793-5795.

12 G. Sumrell, M. Zief, E. J. Huber, G. E. Ham and C. H. Schramm, *J. Am. Chem. Soc.*, 1959, **81**, 4313-4315.

13 B. W. Fausett and L. S. Liebeskind, *J. Org. Chem.*, 2005, **70**, 4851-4853.