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PIFA-Mediated Synthesis of Acylsulfenic Acid Alkyl Esters and Benzoyl Alkyl Disulfides from Thioacids

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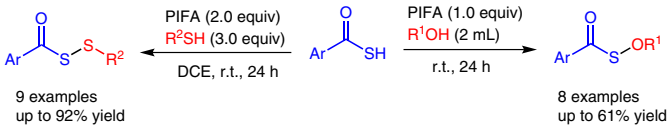

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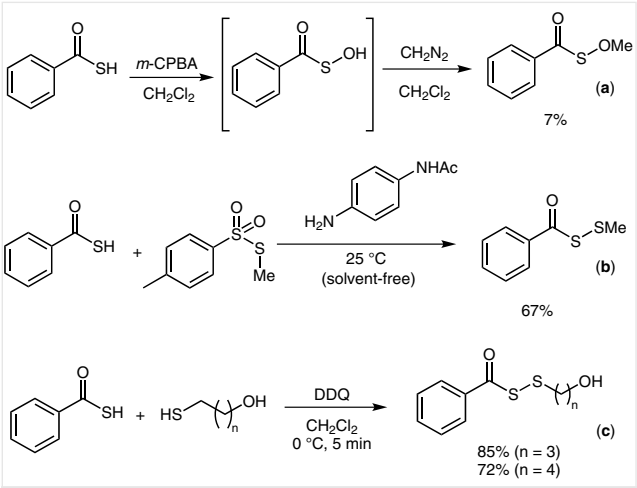
Abstract A simple and convenient approach for the synthesis of acylsulfenic acid alkyl esters and benzoyl alkyl disulfides from thiobenzoic acids is described. This reaction uses commercially available [bis(trifluoroacetoxy)iodo]benzene (PIFA) as an oxidant under mild reaction conditions.

Key words thioacids, alcohols, thiols, oxidations, PIFA, acylsulfenic acid alkyl esters, disulfides

Acylsulfenic acids [compounds with the general formula RC(O)SOH] are known as metabolic intermediates for the transformation of COOH to COSH,[1] and derivatives of acylsulfenic acids, especially methyl esters, were found in a culture medium of *Pseudomonas putida*.[2–4] Hubner and co-workers[5] developed a method for the synthesis of alkyl esters of acylsulfenic acids by treatment of diazomethane with acylsulfenic acid, which in turn was prepared by oxidation of thioacid in the presence of *m*-CPBA (Scheme 1, a). However, this method has substantial disadvantages, such as low yield and the use of toxic diazomethane as the alkylating agent.

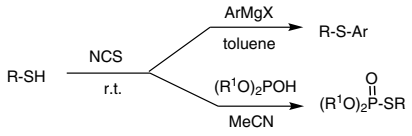
Alkyl or acyl disulfides play a particularly vital role in chemistry and biology.[6] Acyl disulfides, in particular monoacyl disulfides, have come into use as mediators for peptide bond formation between unprotected peptide segments.[7] Generally, alkyl or acyl disulfides can be synthesized by the oxidation of thiols or thiocarboxylates under controlled conditions.[8] Alkyl disulfides are generally synthesized by using 2,2′-dithiobis(benzothiazole),[9] where the benzothiazole is the resultant fragment in the products. In other methods, dithio compounds are synthesized from symmetrical disulfides by oxidative coupling by using rhodium metal,[10] with sulfenic acid and thiosulfenate intermediates as precursors.[11] Tajbakhsh and co-workers[12] demonstrated the synthesis of alkyl or acyl disulfides from the corresponding alkyl or acyl halides by using sulfur and quaternary diammonium borohydrides as reagents under mild conditions. All these methods are limited to the synthesis of either symmetrical or unsymmetrical dialkyl or diacyl disulfides. However, alkyl acyl disulfides have received less attention in literature. Fujiki et al.[13] reported the synthesis of alkyl benzoyl disulfides from thiobenzoic acids and alkyl aryl thiosulfonates under solvent-free conditions (Scheme 1, b). The main drawback of this reaction is the use of commercially unavailable alkyl aryl thiosulfonates. Later, Wang and co-workers[14] synthesized alkyl benzoyl disulfides from thiobenzoic acids and thiols by using DDQ as an oxidant



Scheme 1 Previous methods for the construction of S–O and S–S bonds

(Scheme 1, c). However, this method was generalized to dialkyl disulfides, but not to alkyl benzoyl disulfides (only two examples were reported).

Recently, our research group developed the syntheses of aryl sulfides[15] and thiophosphates[16] by treatment of thiols with NCS, followed by quenching with Grignard reagents and dialkyl phosphites, respectively (Scheme 2). As part of our research interest in sulfur coupling,[17] herein we report a novel approach for the synthesis of acylsulfenic acid alkyl esters and alkyl benzoyl disulfides via oxidative coupling of thioacids with alcohols or alkyl sulfides in the presence of [bis(trifluoroacetoxy)iodo]benzene (PIFA).



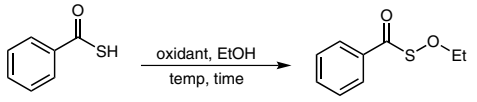
Scheme 2 NCS-mediated syntheses of aryl sulfides and thiophosphates

For the optimization, we examined the feasibility of using thiobenzoic acid (**1a**) as substrate to react with an alcohol, to form the S–O bond (Table 1). Firstly, when thiobenzoic acid (**1a**) was treated with ethanol in the presence of NBS, the reaction failed to form the S–O bond (entry 1). When we treated thiobenzoic acid with ethanol in the presence of NCS or NIS instead of NBS, this also failed to give S–O bond formation (entries 2 and 3). Fortunately, when (diacetoxyiodo)benzene (PIDA) was used as coupling reagent, the desired product, benzoylsulfenic acid ethyl ester (**2a**), was obtained at room temperature in a 50% isolated yield (entry 4). Increasing the temperature of the reaction or the amount of PIDA did not improve the yield of the product (entries 5, 6, and 7). Best results were obtained when thiobenzoic acid (1 mmol) was treated with ethanol (2 mL) in the presence of PIFA (1.0 equiv) at room temperature for 24 hours to afford the product in 61% isolated yield (entry 8). No improvements were observed by leaving the reaction to run for a longer time (entry 9). Other oxidants such as DDQ, $AgNO_3$, PCC and CAN failed to give the desired product (entries 10–13). The decrease in yield of product or failure of the reaction is due to the formation of undesired ethyl benzoate as byproduct.

With these optimized reaction conditions in hand, we treated thiobenzoic acid (**1a**) with different types of alcohols in the presence of PIFA at ambient temperature and obtained the corresponding products (**2a–h**) in moderate to good yields (Scheme 3). Alcohols such as ethylene glycol, ethanolamine, and phenols failed to give the desired products.

Next, our attention was focused on the synthesis of disulfides (Table 2). For the optimization, we chose thiobenzoic acid (**1a**) as the substrate to react with the alkanethiol.

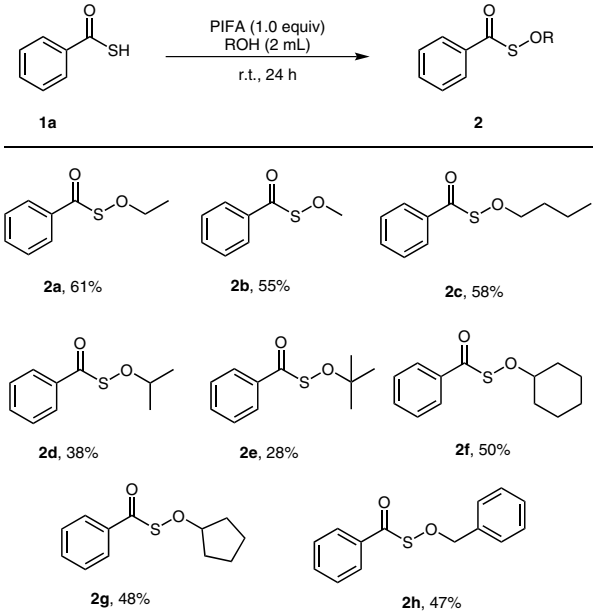
Table 1 Optimization of the Reaction Conditions[a]



1a **2a**

Entry	Oxidant (equiv)	Temp	Time (h)	Yield (%)[b,c]
1	NBS (1.0)	r.t.	24	n.d.[c]
2	NCS (1.0)	r.t.	24	n.d.[c]
3	NIS (1.0)	r.t.	24	n.d.[c]
4	PIDA (1.0)	r.t.	24	50
5	PIDA (1.0)	50 °C	24	49
6	PIDA (1.0)	70 °C	24	36
7	PIDA (2.0)	r.t.	24	49
8	**PIFA (1.0)**	**r.t.**	**24**	**61**
9	PIFA (1.0)	r.t.	48	59
10	DDQ (1.0)	r.t.	24	n.d.[c]
11	$AgNO_3$	r.t.	24	n.d.[c]
12	PCC	r.t.	24	n.d.[c]
13	CAN	r.t.	24	n.d.[c]

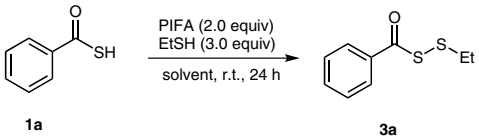
[a] Reaction conditions: **1a** (1.0 mmol), oxidant (1.0 equiv), EtOH (2.0 mL), temp, time, under N_2.
[b] Isolated yield; n.d. = not detected.
[c] Ethyl benzoate was detected by GC-MS analysis.



Scheme 3 Scope of the S–O bond formation. *Reagents and conditions*: **1a** (1.0 mmol), PIFA (1.0 equiv), ROH (2.0 mL), r.t., 24 h, under N_2; isolated yields are given.

To afford the S–S bonds, the amount of alkanethiol used in the reaction was minimized, due to the unpleasant smell of thiols. Thus, we treated thiobenzoic acid (**1a**) with ethanethiol (3.0 equiv) in the presence of PIFA (1.0 equiv) in DCE at room temperature for 24 hours, to yield the desired benzoyl ethyl disulfide (**3a**) in 36% isolated yield (entry 1). The use of 2.0 equivalents of PIFA as oxidant and 3.0 equivalents of ethanethiol in this coupling reaction afforded benzoyl ethyl disulfide (**3a**) in 92% yield (entry 2). Several other common solvents such as diethyl ether, THF, DMF, ethyl acetate, 1,4-dioxane, MTBE, and CH_2Cl_2 were also tested in the S–S coupling (entries 4–10), but, unfortunately, all of them gave less satisfactory results. We also detected diethyl disulfide as byproduct by GC-MS analysis.

Table 2 Optimization of the S–S Bond Formation[a]

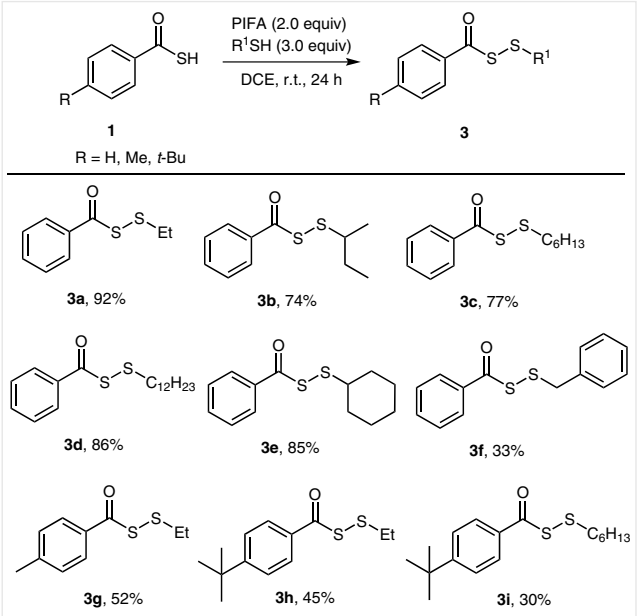


1a **3a**

Entry	Solvent	Yield (%)[b]
1	DCE	36[c]
2	**DCE**	**92**
3	DCE	86[d]
4	CH_2Cl_2	53
5	Et_2O	65
6	THF	11
7	DMF	20
8	1,4-dioxane	21
9	EtOAc	30
10	MTBE	38

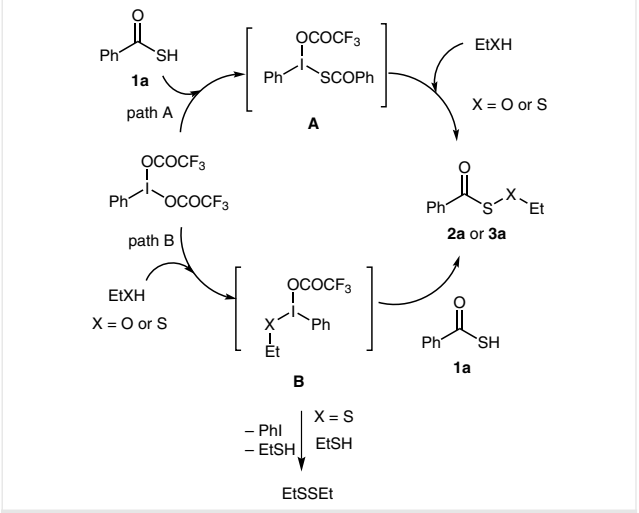
[a] Reaction conditions: **1a** (1.0 mmol), PIFA (2.0 equiv), EtSH (3.0 equiv), solvent, r.t., 24 h, under N_2.
[b] Isolated yield.
[c] PIFA (1.0 equiv) used.
[d] After 48 h.

With these promising results in hand, we chose a variety of linear and branched alkanethiols to react with thiobenzoic acid (**1a**) in the presence of PIFA to obtain the corresponding disulfides **3a–e** in very good yields (Scheme 4). We also identified the formation of dialkyl disulfides as byproducts in the reaction. When phenylmethanethiol was used, the corresponding disulfide **3f** was produced in moderate yield (Scheme 4), the decrease in yield due to the ease of formation of dibenzyl disulfide as a major byproduct. To increase the scope of the reaction, we also used other thioacids such as 4-methylthiobenzoic acid (**1b**) and 4-*tert*-butylthiobenzoic acid (**1c**) to react with alkanethiols, and obtained disulfides **3g–i** in moderate to good yields (Scheme 4). On the other hand, prop-2-ene-1-thiol and the aromatic thiol benzenethiol failed to give the corresponding acyl allyl and acyl aryl disulfides; the failure of these reactions are due to the formation of diallyl and diaryl sulfides.



Scheme 4 Scope of the S–S bond formation. *Reagents and conditions*: **1** (1.0 mmol), PIFA (2.0 equiv), R^1SH (3.0 equiv), DCE (3.0 mL), r.t., 24 h, under N_2; isolated yields are given.

While the exact mechanism of this oxidative coupling is not clear at this stage, the results seem to be consistent with the proposed coupling shown in Scheme 5. This coupling is likely to be initiated by PIFA to form either transient species **A** (path A) or **B** (path B) via nucleophilic attack of thioacid or alcohol or alkanethiol with PIFA. Alcohol or alkanethiol will react with intermediate **A** affording product



Scheme 5 Plausible mechanism

2 or **3** upon removal of iodobenzene. On the other hand, alcohol or alkanethiol or thioacid can react with species **B** to give either the desired product or the homocoupling product (ethyl disulfide in this case).

In summary, we have developed a simple and convenient protocol for the synthesis of acylsulfenic acid alkyl esters and benzoyl alkyl disulfides in moderate to good yields at ambient temperatures, by using thioacids with commercially available alcohols or alkanethiols and PIFA. We anticipate that this strategy of oxidative coupling may lead to a wide range of applications in synthetic chemistry.

Chemicals were purchased from commercial suppliers and used without further purification. All reactions were carried out under an inert atmosphere. Flash chromatography was performed on Merck silica gel 60 (230–400 mesh). NMR spectra were recorded on a Varian Unity Inova-600 or a Varian Mercury-400 instrument; $CDCl_3$ was used as solvent. Chemical shifts are reported in parts per million (ppm) and referenced to the residual solvent resonance. GC-MS analyses were performed on an HP 5890 GC instrument equipped with HP 5972 MS. High-resolution mass spectra were carried out on a Jeol JMS-HX 110 spectrometer by the services at the National Chung Hsing University.

Benzoylsulfenic Acid Alkyl Esters 2; General Procedure

An oven-dried Schlenk tube was charged with PIFA (0.430 g, 1.0 mmol) and alcohol (2 mL). To this stirred solution was added thiobenzoic acid (**1a**; 1.0 mmol) at r.t., and the mixture was stirred for 24 h. After completion of the reaction, low volatiles were removed under vacuum. The residue was purified by column chromatography (silica gel, hexane–EtOAc) to afford **2**.

Benzoylsulfenic Acid Ethyl Ester (2a)

Colorless liquid; yield: 111.2 mg (61%); R_f = 0.51 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.4 Hz, 2 H), 7.45–7.52 (m, 1 H), 7.34–7.40 (m, 2 H), 3.97 (q, *J* = 7.2 Hz, 2 H), 1.31 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 134.0, 133.8, 128.9, 125.9, 75.6, 15.7.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_9H_{10}O_2S$: 182.0402; found: 182.0396.

Benzoylsulfenic Acid Methyl Ester (2b)[5]

Colorless liquid; yield: 92.5 mg (55%); R_f = 0.49 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.2 Hz, 2 H), 7.55–7.62 (m, 1 H), 7.42–7.48 (m, 2 H), 3.93 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1, 133.9, 133.9, 129.0, 125.9, 66.8.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_8H_8O_2S$: 168.0245; found: 168.0246.

Benzoylsulfenic Acid *n*-Butyl Ester (2c)

Colorless liquid; yield: 122.0 mg (58%); R_f = 0.51 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 6.8 Hz, 2 H), 7.56–7.62 (m, 1 H), 7.42–7.48 (m, 2 H), 4.01 (t, *J* = 6.8 Hz, 2 H), 1.71–1.77 (m, 2 H), 1.44–1.49 (m, 2 H), 0.94 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 134.0, 133.7, 128.9, 125.8, 79.9, 32.2, 18.8, 13.7.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{11}H_{14}O_2S$: 210.0715; found: 210.0711.

Benzoylsulfenic Acid Isopropyl Ester (2d)

Colorless liquid; yield: 74.5 mg (38%); R_f = 0.50 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.0 Hz, 2 H), 7.55–7.62 (m, 1 H), 7.42–7.48 (m 2 H), 4.00–4.07 (m, 1 H), 1.38 (d, *J* = 8.8 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 134.1, 133.7, 128.9, 125.9, 82.6, 22.3.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{10}H_{12}O_2S$: 196.0558; found: 196.0550.

Benzoylsulfenic Acid *tert*-Butyl Ester (2e)

Colorless liquid; yield: 60.0 mg (28%); R_f = 0.52 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.6 Hz, 2 H), 7.56–7.60 (m, 1 H), 7.42–7.49 (m, 2 H), 1.40 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.8, 134.3, 133.6, 128.9, 126.0, 84.6, 27.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{14}NaO_2S$: 233.0612; found: 233.0611.

Benzoylsulfenic Acid Cyclohexyl Ester (2f)

Colorless liquid; yield: 118.4 mg (50%); R_f = 0.50 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.6 Hz, 2 H), 7.57–7.61 (m, 1 H), 7.40–7.46 (m, 2 H), 3.72–3.77 (m, 1 H), 2.10–2.14 (m, 2 H), 1.77–1.81 (m, 2 H), 1.51–1.60 (m, 3 H), 1.22–1.37 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 134.1, 133.7, 128.9, 125.9, 87.4, 32.3, 25.3, 23.8.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{13}H_{16}O_2S$: 236.0871; found: 236.0866.

Benzoylsulfenic Acid Cyclopentyl Ester (2g)

Colorless liquid; yield: 106.7 mg (48%); R_f = 0.48 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.4 Hz, 2 H), 7.56–7.60 (m, 1 H), 7.42–7.46 (m, 2 H), 4.43 (m, 1 H), 1.99–2.04 (m, 2 H), 1.76–1.85 (m, 4 H), 1.57–1.63 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 134.1, 133.7, 128.9, 125.9, 91.8, 33.2, 23.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{15}O_2S$: 223.0793; found: 223.0777.

Benzoylsulfenic Acid Benzyl Ester (2h)

Colorless liquid; yield: 115.0 mg (47%); R_f = 0.49 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.74 (m, 2 H), 7.56–7.60 (m, 1 H), 7.36–7.56 (m, 7 H), 4.98 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0, 136.2, 133.9, 129.6, 129.0, 128.8, 128.5, 128.3, 125.9, 80.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{12}NaO_2S$: 267.0456; found: 267.0455.

Benzoyl Alkyl Disulfides 3; General Procedure

A dry Schlenk tube was charged with PIFA (0.860 g, 2.0 mmol) and DCE (3 mL). To the stirred solution was added thiobenzoic acid (0.125 mL, 1.0 mmol) and the thiol (3.0 mmol) at r.t., and the mixture was

stirred for 24 h. After completion of the reaction, low volatiles were removed under vacuum. The resulting residue was purified by column chromatography (silica gel, hexane–EtOAc) to afford **3**.

Benzoyl Ethyl Disulfide (3a)

Colorless liquid; yield: 182.2 mg (92%); R_f = 0.50 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.2 Hz, 2 H), 7.49–7.55 (m, 1 H), 7.35–7.40 (m, 2 H), 2.71 (q, *J* = 7.6 Hz, 2 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.4, 135.7, 133.9, 128.8, 127.6, 32.6, 14.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_9H_{11}OS_2$: 199.0251; found: 199.02454.

Benzoyl *sec*-Butyl Disulfide (3b)

Colorless liquid; yield: 167.3 mg (74%); R_f = 0.51 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.4 Hz, 2 H), 7.56–7.62 (m, 1 H), 7.41–7.49 (m, 2 H), 2.84–2.96 (m, 1 H), 1.64–1.78 (m, 1 H), 1.52–1.60 (m, 1 H), 1.31 (d, *J* = 6.4 Hz, 3 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.4, 135.6, 133.7, 128.7, 127.5, 48.1, 28.8, 19.7, 11.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{15}OS_2$: 227.0564; found: 227.0555.

Benzoyl *n*-Hexyl Disulfide (3c)

Colorless liquid; yield: 196.0 mg (77%); R_f = 0.49 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 6.4 Hz, 2 H), 7.56–7.62 (m, 1 H), 7.42–7.52 (m, 2 H), 2.78 (t, *J* = 7.6 Hz, 2 H), 1.64–1.71 (m, 2 H), 1.26–1.45 (m, 6 H), 0.88 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.4, 135.7, 133.9, 128.8, 127.6, 38.7, 31.3, 28.9, 28.1, 22.5, 14.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{19}OS_2$: 255.0877; found: 255.0826.

Benzoyl *n*-Dodecyl Disulfide (3d)

Colorless liquid; yield: 290.8 mg (86%); R_f = 0.50 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.0 Hz, 2 H), 7.56–7.62 (m, 1 H), 7.40–7.48 (m, 2 H), 2.77 (t, *J* = 6.4 Hz, 2 H), 1.61–1.69 (m, 2 H), 1.40 (t, *J* = 6.8 Hz, 2 H), 1.25 (br s, 16 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.0, 135.6, 133.7, 128.6, 127.5, 38.6, 31.7, 29.48, 29.47, 29.42, 29.3, 29.2, 29.0, 28.8, 28.3, 22.5, 14.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{31}OS_2$: 339.1816; found: 339.1801.

Benzoyl Cyclohexyl Disulfide (3e)[13]

Colorless liquid; yield: 214.4 mg (85%); R_f = 0.50 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.0 Hz, 2 H), 7.57–7.61 (m, 1 H), 7.43–7.49 (m, 2 H), 2.82–2.89 (m, 1 H), 2.02–2.06 (m, 2 H), 1.76–1.81 (m, 2 H), 1.56–1.60 (m, 1 H), 1.35–1.45 (m, 2 H), 1.18–1.33 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.4, 135.6, 25.3, 133.7, 128.6, 127.5, 49.4, 32.4, 25.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{17}OS_2$: 253.0721; found: 253.0710.

Benzoyl Benzyl Disulfide (3f)[13]

White solid; mp 53–54.0 °C; yield: 86.0 mg (33%); R_f = 0.47 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.2 Hz, 2 H), 7.56–7.60 (m, 1 H), 7.40–7.48 (m, 2 H), 7.23–7.38 (m, 5 H), 3.98 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.8, 136.0, 135.6, 133.9, 129.4, 128.8, 128.5, 127.6, 127.6, 42.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}OS_2$: 261.0408; found: 261.0395.

Ethyl 4-Methylbenzoyl Disulfide (3g)

Colorless liquid; yield: 110.3 mg (52%); R_f = 0.51 (5% EtOAc in hexanes).

^{1}H NMR (400 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* = 7.2 Hz, 2 H), 2.39 (s, 3 H), 1.34 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.6, 144.0, 134.7, 129.1, 127.1, 23.3, 21.6, 14.8.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{10}H_{12}OS_2$: 212.0330; found: 212.1172.

4-*tert*-Butylbenzoyl Ethyl Disulfide (3h)

Colorless liquid; yield: 114.2 mg (45%); R_f = 0.50 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.4 Hz, 2 H), 7.45 (d, *J* = 8.4 Hz, 2 H), 3.06 (q, *J* = 7.6 Hz, 2 H), 1.26–1.36 (m, 12 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.6, 156.9, 134.6, 127.0, 125.4, 31.1, 29.7, 23.3, 14.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{19}OS_2$: 255.0877; found: 255.0863.

4-*tert*-Butylbenzoyl *n*-Hexyl Disulfide (3i)

Colorless liquid; yield: 93.4 mg (30%); R_f = 0.51 (5% EtOAc in hexanes).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.6 Hz, 2 H), 7.44 (d, *J* = 8.6 Hz, 2 H), 3.05 (t, *J* = 7.2 Hz, 2 H), 1.62–1.70 (m, 2 H), 1.26–1.48 (m, 15 H), 0.89 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.5, 156.8, 134.6, 127.1, 125.4, 35.0, 31.3, 31.0, 29.6, 28.8, 28.5, 22.5, 14.0.

HRMS (ESI): *m*/*z* [M – H]$^-$ calcd for $C_{17}H_{25}OS_2$: 309.1347; found: 309.1737.

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Supporting Information

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