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Palladium Catalyzed Direct Carbonylative Thiomethylation of Aryldiazonium Salts and Amines with 4-(Methylthio)-2-Butanone as (Methylthio) Transfer Agent

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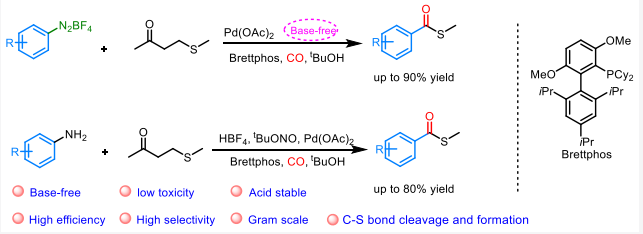
ABSTRACT: Herein, an interesting palladium-catalyzed procedure for the direct carbonylative thiomethylation of aromatic amine derivatives with 4-methylthio-2-butanone is developed. Using 4-methylthio-2-butanone as (methylthio) transfer agent, a variety of corresponding thioesters are obtained with moderate to good yields under base-free condition. In addition, good functional group tolerance can be observed.



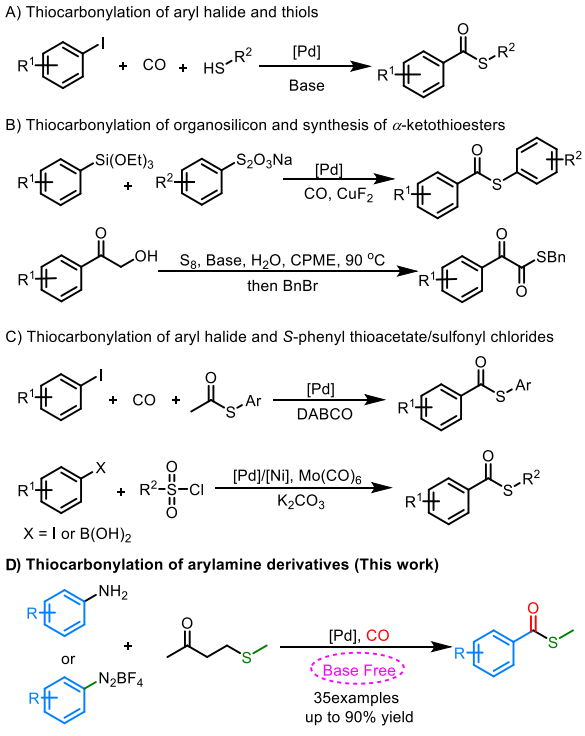
INTRODUCTION

Thioesters are extremely important in biochemistry due to their expedient biological properties.[1] Since they are more active than esters due to mesomeric effects based on inferior orbital overlap,[2] thioesters are also used as building blocks in many reactions.[3] Consequently, the development of new catalytic protocols for the preparation of thioesters has attracted continuous interest in organic synthesis.[4]

Transition metal-catalyzed carbonylation presents an efficient and direct way for the synthesis of carbonyl-containing moieties.[5] Using carbonylative reaction for the preparation of thioesters is attractive. In fact, a lot of metal-catalyzed thiocarbonylations have been reported in the past decade.[6] However, the majority of the reported thiocarbonylations rely on thiols as the nucleophiles. Therefore, the challenges brought by the unpleasant odor and poisonous catalyst properties of thiols still remain.[7] In 2016, Jiang et al. described the Pd-catalyzed thiocarbonylation using sodium sulfinates as the thiol surrogate (Scheme 1B).[8a] Later, the same group reported a practical protocol for the straightforward construction of α-ketothioesters available to be used as a stable and convenient 1,2-dicarbonyl reagent.[8b] In 2018, Lee et al. reported a Pd-catalyzed carbonylation of thioacetates and aryl iodides (Scheme 1C).[9] In 2020, Wu et al. reported a Ni-catalyzed thiocarbonylation reaction of arylboronic acids with sulfonyl chlorides as the sulfur precursor.[10] Recently, our group has also reported the palladium-catalyzed intermolecular transthioetherification of aryl halides with thioethers using KO^{t}Bu as the base.[11] However, most of these protocols require a stoichiometric amount of bases to promote the thiocarbonylation, which leads to not only narrow substrate scopes but also a stoichiometric amount of waste of the reaction.

4-Methylthio-2-butanone is used as a food chemical additive.[12] However, the use of 4-methylthio-2-butanone as a

Scheme 1. Previous Reports and the Present Strategy



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methylthio transfer reagent rather than additive or solvent in modern synthetic methodology is still rare. As methyl mercaptan is a flammable and toxic gas, the direct use of 4-methylthio-2-butanone as a methylthio source would be an attractive choice.

With all these considerations in mind, in this paper, we would like to report the first Pd-catalyzed methylthiocarbonylation of tetrafluoroaryl diazonium salts or aromatic amines using 4-methylthio-2-butanone as a reliable methylthio transfer reagent under base-free condition.

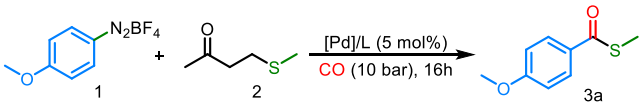
RESULTS AND DISCUSSION

At the beginning of our study, 4-methoxybenzenediazonium tetrafluoroborate (**1**) and 4-methylthio-2-butanone (**2**) were selected as a model substrate. First, the effect of palladium salts was tested (as shown in Table 1). $Pd(OAc)_2$ showed the best result, and gave the desired product 3a with 65% GC yield (Table 1, Entry 5). Interestingly, heterogeneous catalyst Pd/C can be also used in this catalytic protocol, which gave the desired product with a 43% yield (Table 1, Entry 6). Screening of different phosphine ligands revealed that brettphos is the most effective ligand for delivering the desired thioester product. Subsequently, the amount of ^{t}BuOH was studied. When 1 mL of ^{t}BuOH was used, the yield was increased to 74% (Table 1, Entry 11). Reducing the amount of solvent can increase the effective collision among molecules, which is conductive to the reaction. Interestingly, the reaction at 60 °C produced the highest yield of desired product **3a** (Table 1, Entry 13). And decreasing yields were obtained at low or high temperature (80 °C, 50 °C; Table 1, Entries 11, 12). Considering the solubility of the organic salt, different solvents were tested. When the reaction was carried out in DMSO, DME, or ^{i}PrOH, the yield of the desired product **3a** decreased (Table 1, Entries 14, 15, and 16). Furthermore, in the absence ligand, only trace amounts of the desired product were observed (Table 1, Entry 17). This may be due to that the ligand can make the catalyst more stable and accelerate the reduction and elimination. Finally, the amount of 4-methylthio-2-butanone was also studied, and when 1 equiv of 4-methylthio-2-butanone was used, **3a** was observed in 59% yield (Table 1, Entry 19). Overall, it was found that the use of 5 mol % of $Pd(OAc)_2$ and brettphos under CO atmosphere (10 bar) at 60 °C gave **3a** in 83% yield.

Considering that arenediazoniumtetrafluoroborates are one of the aromatic amine derivatives,[13] we decided to examine carbonylative thiomethylation reactions with aromatic amine directly. To our delight, when 1 equiv of HBF_4 and 1.5 equiv of ^{t}BuONO were used as additives, 13% of the desired product could be obtained (Table 2, Entry 1). The yield was improved to 63% when HBF_4 was increased to 3 equiv (Table 2, Entry 2). When 5 equiv of HBF_4 was applied, the yield decreased to 26% (Table 2, Entry 6). This may be due to the instability of the thioester under acidic conditions. Next, the effect of temperature was studied, but no better yield was obtained. Especially, when the reaction was conducted at 100 °C, only a trace amount of desired products was obtained (Table 2, Entry 5). It is possible that aryldiazonium salts and the desired product thioesters are not stable under high-temperature condition, especially under acid condition.

In order to examine the scope of this method, different aryl tetrafluoroborate diazonium salts were evaluated for direct carbonylative thiomethylation (as shown in Scheme 2). First, electron-donating substrates were tested under the optimized conditions. Both methyl- and *tert*-butyl- substituted aryl tetrafluoroborate diazonium salts reacted smoothly and provided the corresponding thioesters in 86% and 69% yield, respectively (Scheme 2, **3b** and **3c**). Simultaneously, the

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	ligand	solvent	yield (%)[b]
1	$Pd(MeCN)_2Cl_2$	L1	^{t}BuOH	30
2	$Pd_2(dba)_2$	L1	^{t}BuOH	44
3	$Pd(ally)Cl_2$	L1	^{t}BuOH	46
4	$Pd(TFA)_2$	L1	^{t}BuOH	61
5	$Pd(OAc)_2$	L1	^{t}BuOH	65
6	Pd/C	L1	^{t}BuOH	43[c]
7	$Pd(OAc)_2$	L2	^{t}BuOH	66
8	$Pd(OAc)_2$	L3	^{t}BuOH	61
9	$Pd(OAc)_2$	L4	^{t}BuOH	58
10	$Pd(OAc)_2$	L5	^{t}BuOH	53
11	$Pd(OAc)_2$	L1	^{t}BuOH	74[c]
12	$Pd(OAc)_2$	L1	^{t}BuOH	75[d]
13	$Pd(OAc)_2$	L1	^{t}BuOH	83[e]
14	$Pd(OAc)_2$	L1	DMSO	25[e]
15	$Pd(OAc)_2$	L1	DME	69[e]
16	$Pd(OAc)_2$	L1	^{i}PrOH	74[e]
17	$Pd(OAc)_2$	–	^{t}BuOH	trace[e]
18	–	L1	^{t}BuOH	trace[e]
19	$Pd(OAc)_2$	L1	^{t}BuOH	59[f]

[a]Reaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), Pd salt (5.0 mol %), solvent (2.0 mL), CO (10 bar), 80 °C, 16 h. [b]Yield determined by GC using *n*-dodecane as an internal standard. [c]Solvent (1.0 mL). [d]Solvent (1.0 mL), 50 °C. [e]Solvent (1.0 mL), 60 °C. [f]Solvent (1.0 mL), **2** (0.2 mmol), 60 °C.

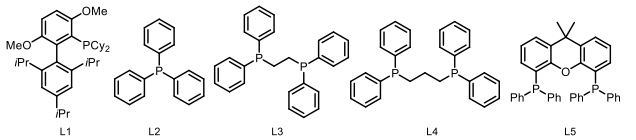
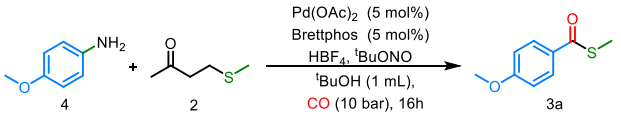


Table 2. Optimization of Reaction Conditions of Aniline and 4-Methylthio-2-butanone[a]



entry	HBF_4 (equiv)	temp (°C)	yield (%)[b]
1	1	60	13
2	3	60	63
3	3	25	20
4	3	80	41
5	3	100	trace
6	5	60	26

[a]Reaction conditions: **4** (0.2 mmol), **2** (0.6 mmol), HBF_4 (0.2–1.0 mmol), ^{t}BuONO (0.3 mmol), $Pd(OAc)_2$ (5 mol %), brettphos (5 mol %), CO (10 bar), ^{t}BuOH (1 mL), 25–100 °C, 16 h. [b]Yield determined by GC using *n*-dodecane as an internal standard.

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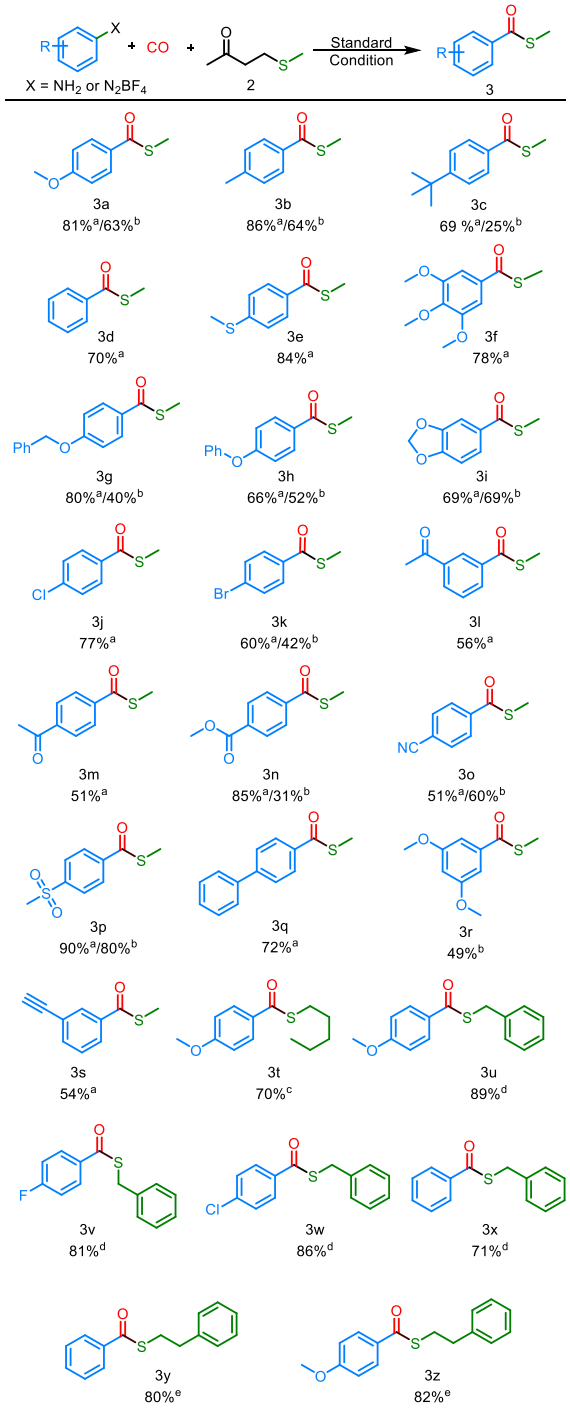
Scheme 2. Substrate Scope of Diazonium Tetrafluoroborate and Aromatic Amine



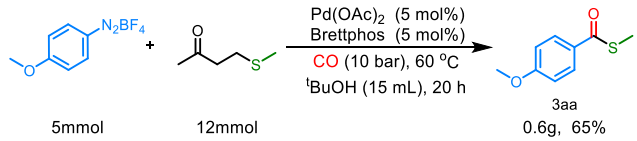
[a]Reaction conditions: **1** (0.2 mmol), **2** (0.6 mmol), $Pd(OAc)_2$ (5 mol %), Brettphos (5 mol %), ^{t}BuOH (1 mL), CO (10 bar), 60 °C, 16 h. Yields refer to the isolated products. [b]Reaction conditions: **4** (0.2 mmol), **2** (0.6 mmol), HBF_4 (0.6 mmol), ^{t}BuONO (0.3 mmol), $Pd(OAc)_2$ (5 mol %), brettphos (5 mol %), CO (10 bar), ^{t}BuOH (1 mL), 60 °C, 16 h, isolated yield. [c]Reaction conditions: **1** (0.2 mmol), 1-(pentylthio)hexan-3-one (0.6 mmol), $Pd(OAc)_2$ (5 mol %), Brettphos (5 mol %), ^{t}BuOH (1 mL), CO (10 bar), 60 °C, 16 h. [d]Reaction conditions: **1** (0.2 mmol), 4-(benzylthio) pentan-2-one (0.6 mmol), $Pd(OAc)_2$ (5 mol %), Brettphos (5 mol %), ^{t}BuOH (1 mL), CO (10 bar), 60 °C, 16 h. [e]Reaction conditions: **1** (0.2 mmol), 4-(phenethylthio) pentan-2-one (0.6 mmol), $Pd(OAc)_2$ (5 mol %), Brettphos (5 mol %), ^{t}BuOH (1 mL), CO (10 bar), 60 °C, 16 h.

substrates containing heteroatom substituents (S, O) also reacted well, and gave the desired products with moderate to good yields (66−84% yield, Scheme 2, **3e**−**3i**). Interestingly, chloro and bromo groups can also be tolerated by the employed reaction conditions, with no observable competitive byproducts detected by GC-MS (Scheme 2, **3j** and **3k**). Electron-withdrawing groups can also be tolerated and gave the corresponding products, such as 3-acetylbenzene-diazonium and 4-acetylbenzene-diazonium (Scheme 2, **3l** and **3m**). Furthermore, substrates containing −CN and $-SO_2Me$ can react smoothly (Scheme 2, **3o** and **3p**). Notably, Alkynes can also be tolerated in this system (Scheme 2, **3s**). In order to prove the synthetic potential of this methodology, testing of different 4-(methylthio)-2-butanone derivatives were also conducted under our standard conditions. As shown in Scheme 2, good yield of the desired thioester can be produced by reacting 4-methoxybenzenediazonium tetrafluoroborate with 1-(pentylthio) hexan-3-one (Scheme 2, **3t**). Similarly, when 4-(benzylthio) pentan-2-one and 4-(phenethylthio) pentan-2-one substituted 4-(methylthio)-2-butanone were employed, good yields of the desired thioester can be obtained from the corresponding diazonium salt, and **3u** and **3z** were obtained in 89% and 82% yields, respectively.

Next we turned our attention to evaluating the scope of the aromatic amines carbonylative thiomethylation. As shown in Scheme 2, the use of aromatic amines instead of aryldiazonium salts as precursors affords thioesters. The reaction showed a good functional group tolerance, for example, −Br (**3k**), −CN (**3o**), $-CO_2Me$ (**3n**), and $-SO_2Me$ (**3p**) can be tolerated, which provides the possibility for further synthetic transformations.

To demonstrate the practical utility, the reaction of 4-methoxybenzenediazonium tetrafluoroborate and 4-methylthio-2-butanone was performed at the 5 mmol scale. As illustrated in Scheme 3, the desired *S*-methyl-4-methoxy benzothioate was formed in 65% yield.

Scheme 3. Gram Scale Experiment



To prove the synthetic practicability of this method, three reactions have been exemplified to build C−N, C−C, C−O bonds (see the Supporting Information). Related amides, ketones, and carboxylic acids were efficiently obtained using thioesters as the starting substrates under relatively mild reaction conditions.

To gain insight into the reaction mechanism, control experiments were conducted under different reaction conditions (see the Supporting Information). When 4-methylthio-2-butanone was under the catalyst-free condition, no methyl vinyl ketone was observed. However, when 4-methylthio-2-butanone was applied under the standard reaction conditions, methyl vinyl ketone was observed with the NMR yield of 8%. Furthermore, increasing the loading of $Pd(OAc)_2$ to 50 mol %, the yield of the expected methyl vinyl ketone was improved to

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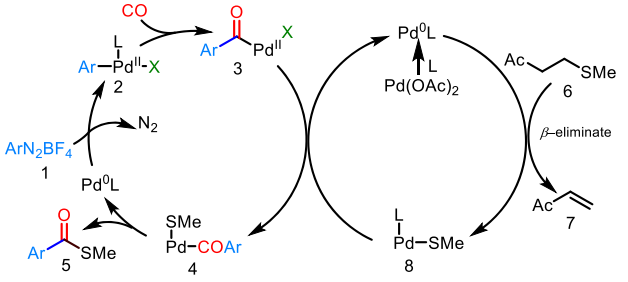
50%. The results indicated that the palladium salt plays an important role in this C−S bond cleavage process.

On the basis of the above investigations and references, a tentative mechanism for this carbonylative thiomethylation chemistry is depicted in Scheme 4.[14] We propose that the

Scheme 4. Possible Mechanism for the Carbonylative Thiomethylation



mechanism involves two catalytic cycles. Initially, the catalyst precursor could be reduced to Pd(0) species in the presence of CO and brettphos ligand. Then, Pd(0)L insert into the carbon diazonium bond to give the intermediate **2**, which is followed by CO insertion for the formation of acyl intermediate **3**. In addition, the organometallic nucleophile **8** is formed via the *β*-elimination of 4-methylthio-2-butanone. Next, intermediate **4** could be formed through the transmetalation between intermediate **3** and the organometallic nucleophile **8**. Finally, the desired thioester product **5** could be formed by classic reductive elimination of intermediate **4** and regenerate Pd(0)L.

CONCLUSIONS

In conclusion, an interesting palladium-catalyzed procedure for the direct carbonylative thiomethylation of various arenediazonium tetrafluoroborates has been developed with a good functional group compatibility. A variety of desired thioesters can be produced with moderate to excellent yields using 4-methylthio-2-butanone as methylthio transfer agent. In addition, the use of aromatic amines instead of aryldiazonium salts as precursors also affords thioesters in moderate to good yields.

EXPERIMENTAL SECTION

General Information. Most of the chemicals were purchased from Aladdin, TCI, Alfa Aesar, Energy-Chemical and used as such unless stated otherwise. Solvents (anhydrous and under inert atmosphere) were collected from the solvent purification system by MBRAUN and used under standard Schlenk technique. NMR spectra were recorded on Bruker Avance 600 and Bruker ARX 400 spectrometers. Chemical shifts (ppm) are given relative to solvent: references for $CDCl_3$ were 7.26 ppm (^{1}H NMR) and 77.00 ppm (^{13}C NMR). Multiplets were assigned as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), dd (doublet of doublet), m (multiplet), and br. s (broad singlet). GC-yields were calculated using isooctane as internal standard. All measurements were carried out at room temperature unless otherwise stated. GC-MS analysis was performed on a Shimadzu 2010 instrument and Rtx-5 capillary column. High resolution mass spectra (HRMS) were recorded on Agilent 6210. The data are given as mass units per charge (m/z). Gas chromatography analysis was performed on a Shimadzu 2010 instrument with an FID detector and Rtx-5 capillary column. The products were isolated from the reaction mixture by column chromatography on silica gel 60, 0.063−0.2 mm, 70−230 mesh (Merck). The arenediazonium salts and 4-methylthio-2-butanone derivative were all synthesized as described preciously.

General Procedure of Diazonium Salt Carbonylative Thiomethylation. A 4 mL screw-cap vial was charged with ArN_2BF_4 (0.2 mmol), Brettphos (5.36 mg, 5 mol %), $Pd(OAc)_2$ (2.24 mg, 5 mol %), and an oven-dried stirring bar. Then **2** (0.6 mmol) and ^{t}BuOH (1 mL) were injected by syringe. The vial was closed by a Teflon septum and a phenolic cap and connected to the atmosphere through a needle. Then the vial was fixed in an alloy plate and put into a Parr 4560 series autoclave (300 mL). At room temperature, the autoclave was flushed with carbon monoxide for three times and 10 bar of carbon monoxide was charged. The autoclave was placed on a heating plate equipped with magnetic stirring and an aluminum block. The reaction was heated at 60 °C for 16 h. Afterward, the autoclave was cooled to room temperature and the pressure was carefully released. After removal of solvent under reduced pressure, pure product was obtained by column chromatography on silica gel (eluent: pentane/EA = 500−30:1).

General Procedure of Aromatic Amine Carbonylative Thiomethylation. A 4 mL screw-cap vial was charged with aromatic amine (0.2 mmol), Brettphos (5.36 mg, 5 mol %), $Pd(OAc)_2$ (2.24 mg, 5 mol %), and an oven-dried stirring bar. Then HBF_4 (50 wt %, 0.6 mmol), 4-(methylthio)-2-butanone (70.8 mg, 0.6 mmol), ^{t}BuOH (1 mL), and ^{t}BuONO (0.3 mmol) were injected by syringe. The vial was closed by a Teflon septum and a phenolic cap and connected to the atmosphere through a needle. Then the vial was fixed in an alloy plate and put into a Parr 4560 series autoclave (300 mL). At room temperature, the autoclave was flushed with carbon monoxide for three times and 10 bar of carbon monoxide was charged. The autoclave was placed on a heating plate equipped with magnetic stirring and an aluminum block. The reaction was heated at 60 °C for 16 h. Afterward, the autoclave was cooled to room temperature and the pressure was carefully released. After removal of solvent under reduced pressure, pure product was obtained by column chromatography on silica gel (eluent pentane/EA = 500−30:1).

General Procedure of Gram Scale Experiment. A 25 mL screw-cap vial was charged with 4-methoxybenzene-diazonium tetrafluoroborate (1.1 g, 5.0 mmol), Brettphos (134.0 mg, 5 mol %), $Pd(OAc)_2$ (56.0 mg, 5 mol %), and an oven-dried stirring bar. Then 4-(methylthio)-2-butanone (1.44 mg, 2.4 mmol) and ^{t}BuOH (15 mL) were injected by syringe. The vial was closed by a Teflon septum and a phenolic cap and connected to the atmosphere through a needle. Then the vial was fixed in an alloy plate and put into a Parr 4560 series autoclave (300 mL). At room temperature, the autoclave was flushed with carbon monoxide for three times and 10 bar of carbon monoxide was charged. The autoclave was placed on a heating plate equipped with magnetic stirring and an aluminum block. The reaction was heated at 60 °C for 16 h. Afterward, the autoclave was cooled to room temperature and the pressure was carefully released. After removal of solvent under reduced pressure, pure product was obtained by column chromatography on silica gel (eluent: pentane/EA = 100−30:1) to obtain the product **3aa** as colorless liquid (600.0 mg, yield 65%).

*Synthesis of N-Benzyl-4-methoxybenzamide (**3ab**).* A mixture of *S*-methyl 4-methoxybenzothioate (58.0 mg, 0.31 mmol), phenylmethanamine (100 mg, 0.9 mmol), K_2CO_3 (171.0 mg, 1.2 mmol), and DMF (4 mL) was stirred in a 100 mL round-bottom flask at 120 °C under reflux for 12 h. Afterward, the autoclave was cooled to room temperature, and then a saturated solution of NaCl (25 mL) was added. The aqueous phase was extracted with EA (4 × 10 mL) and dried over anhydrous Na_2SO_4 and concentrated in a vacuum with silica gel added. The residue was purified by flash chromatography (PE/EA = 20:1) to obtain the product as a white solid (42.0 mg, yield 53%).

*Synthesis of Benzophenone (**3ac**).* A mixture of *S*-methyl benzothioate (45.6 mg, 0.3 mmol), trimethoxy(phenyl)silane (89.1 mg, 0.45 mmol), $Pd(PPh_3)_4$ (17.0 mg, 5 mol %), CuI (57.0 mg, 0.3 mmol), TBAF (15.7 mg, 20 mol %), and THF (4 mL) was stirred in a 25 mL tube at 60 °C under reflux for 0.5 h. Afterward, the autoclave was cooled to room temperature, and then the residue was purified by flash chromatography (PE/EA = 20:1) to obtain the product as a white solid (26.0 mg, yield 49%)

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*Synthesis of 4-(Benzyloxy)benzoic acid (**3ad**).* A mixture of *S*-methyl 4-(benzyloxy)benzothioate (77.4 mg, 0.3 mmol), KOH (672.0 mg, 12.0 mmol), and EtOH (10 mL) was stirred in a 100 mL round-bottom flask at 80 °C under reflux for 30 h. Afterward, the autoclave was cooled to room temperature, and then a solution of HCl (1 mol/L, 25 mL) was added. The aqueous phase was extracted with EA (4 × 10 mL) and dried over anhydrous Na_2SO_4 and concentrated in a vacuum with silica gel added. The residue was purified by flash chromatography (PE/EA = 10:1) to obtain the product as a white solid (38.0 mg, yield 56%).

*S-Methyl 4-methoxybenzothioate (**3a**).*[11] Purified by column chromatography (PE). Yield = 29.5 mg (81%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.93 (dd, J = 9.3, 2.4, 2H), 6.90 (t, J = 5.9, 2H), 3.84 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 190.89, 163.64, 130.00, 129.21, 113.71, 55.43, 11.52. GC-MS (EI, 70 ev) m/z (%) = 182 (M^+, 5), 135 (100), 92 (17), 77 (25), 50 (7).

*S-Methyl 4-methylbenzothioate (**3b**).*[14] Purified by column chromatography (PE). Yield = 28.6 mg (86%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.86 (d, J = 8.2, 2H), 7.28−7.18 (m, 2H), 2.45 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.97, 144.01, 134.59, 129.19, 127.15, 21.58, 11.55. GC-MS (EI, 70 ev) m/z (%) = 166 (M^+, 8), 119 (100), 91 (55), 65 (21), 51 (4).

*S-Methyl 4-(tert-butyl)benzothioate (**3c**).*[11] Purified by column chromatography (PE). Yield = 28.7 mg (69%). White solid, mp 64−66 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.90 (d, J = 8.4, 2H), 7.45 (d, J = 8.4, 2H), 2.46 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.98, 157.00, 134.48, 126.99, 125.49, 35.10, 31.04, 11.55. GC-MS (EI, 70 ev) m/z (%) = 208 (M^+, 3), 161 (100), 146 (15), 118 (16), 91 (16), 77 (9), 51 (6).

*S-Methyl benzothioate (**3d**).*[11] Purified by column chromatography (PE). Yield = 21.3 mg (70%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99−7.93 (m, 2H), 7.56 (m, 1H), 7.48−7.41 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.38, 137.08, 133.20, 128.55, 127.09, 11.66. GC-MS (EI, 70 ev) m/z (%) = 152 (M^+, 7), 105 (100), 77 (68), 51 (30).

*S-Methyl 4-(methylthio)benzothioate (**3e**).*[11] Purified by column chromatography (PE). Yield = 33.3 mg (84%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.86 (d, J = 8.6, 2H), 7.26−7.21 (m, 2H), 2.50 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.28, 146.03, 133.37, 127.43, 125.05, 14.81, 11.55. GC-MS (EI, 70 ev) m/z (%) = 198 (M^+, 14), 151 (100), 123 (14), 108 (13), 79 (12), 50 (8).

*S-Methyl 3,4,5-trimethoxybenzothioate (**3f**).* Purified by column chromatography (PE). Yield = 37.8 mg (78%). White solid, mp 53−56 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.22 (s, 2H), 3.89 (dd, J = 10.6, 4.7, 9H), 2.46 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.41, 153.09, 142.66, 132.29, 104.57, 60.94, 56.14, 11.81. GC-MS (EI, 70 ev) m/z (%) = 242 (M^+, 18), 195 (100), 152 (9), 122 (8), 109 (9), 66 (12). HRMS (ESI) calcd for $C_{11}H_{15}O_4S$ $[M + H]^+$: 243.0686, found 243.0691.

*S-Methyl 4-(benzyloxy)benzothioate (**3g**).*[11] Purified by column chromatography (PE). Yield = 41.3 mg (80%). White solid, mp 65−68 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.07−7.79 (m, 2H), 7.38 (m, 5H), 7.04−6.83 (m, 2H), 5.12 (s, 2H), 2.45 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 190.84, 162.81, 136.15, 130.22, 129.25, 128.65, 128.19, 127.41, 114.61, 70.18, 11.54. GC-MS (EI, 70 ev) m/z (%) = 258 (M^+, 2), 211 (40), 91 (100), 65 (14).

*S-Methyl 4-phenoxybenzothioate (**3h**).*[11] Purified by column chromatography (PE). Yield = 32.2 mg (66%). White solid, mp 35−37 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02−7.85 (m, 2H), 7.45−7.34 (m, 2H), 7.19 (m, 1H), 7.09−7.03 (m, 2H), 7.01−6.92 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.91, 162.12, 155.48, 131.64, 130.01, 129.25, 124.58, 120.11, 117.33, 11.62. GC-MS (EI, 70 ev) m/z (%) = 244 (M^+, 6), 197 (100), 141 (18), 115 (21), 77 (17), 51 (9).

*S-Methyl benzo[d][1,3]dioxole-5-carbothioate (**3i**).*[15] Purified by column chromatography (PE). Yield = 27.0 mg (69%). White solid, mp 70−72 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.59 (d, J = 8.2, 1H), 7.40 (s, 1H), 6.82 (d, J = 8.2, 1H), 6.03 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 190.58, 151.86, 148.00, 131.66, 123.10, 107.96, 107.13, 101.86, 11.70. GC-MS (EI, 70 ev) m/z (%) = 196 (M^+, 14), 149 (100), 121 (37), 91 (9), 65 (30), 53 (5).

*S-Methyl 4-chlorobenzothioate (**3j**).*[15] Purified by column chromatography (PE). Yield = 28.6 mg (77%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96−7.82 (m, 2H), 7.44−7.36 (m, 2H), 2.47 (d, J = 1.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.15, 139.61, 135.38, 128.86, 128.43, 11.73. GC-MS (EI, 70 ev) m/z (%) = 186 (M^+, 8), 141 (30), 139 (100), 111 (47), 75 (32), 50 (15).

*S-Methyl 4-bromobenzothioate (**3k**).*[16] Purified by column chromatography (PE). Yield = 27.8 mg (60%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94−7.65 (m, 2H), 7.65−7.50 (m, 2H), 2.47 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.33, 135.80, 131.85, 128.54, 128.24, 11.73. GC-MS (EI, 70 ev) m/z (%) = 232 (M^+, 10), 183 (100), 155 (38), 75 (45), 50 (40).

*S-Methyl 3-acetylbenzothioate (**3l**).* Purified by column chromatography (PE). Yield = 21.7 mg (56%). White solid, mp 30−33 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.68−8.35 (m, 1H), 8.24−8.04 (m, 2H), 7.54 (m, 1H), 2.73−2.59 (m, 3H), 2.54−2.43 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 196.92, 191.71, 137.47, 132.47, 131.29, 129.02, 126.89, 26.60, 11.78. GC-MS (EI, 70 ev) m/z (%) = 194 (M^+, 4), 147 (100), 119 (18), 91 (35), 76 (19), 50 (12). HRMS (ESI) calcd for $C_{10}H_{11}O_2S$ $[M + H]^+$: 195.0480, found 195.0475.

*S-Methyl 4-acetylbenzothioate (**3m**).* Purified by column chromatography (PE). Yield = 19.8 mg (51%). White solid, mp 27 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.02 (q, J = 8.2, 4H), 2.63 (d, J = 0.9, 3H), 2.50 (d, J = 1.0, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 197.21, 191.75, 140.36, 140.24, 128.47, 127.30, 26.79, 11.85. GC-MS (EI, 70 ev) m/z (%) = 194 (M^+, 6), 147 (100), 119 (19), 91 (26), 76 (17), 50(12). HRMS (ESI) calcd for $C_{10}H_{11}O_2S$ $[M + H]^+$: 195.0474, found 195.0480.

*Methyl 4-((methylthio)carbonyl)benzoate (**3n**).* Purified by column chromatography (PE). Yield = 35.7 mg (85%). White solid, mp 59−62 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.14−8.05 (m, 2H), 8.05−7.90 (m, 2H), 3.93 (d, J = 4.3, 3H), 2.50 (d, J = 4.9, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.79, 166.06, 140.31, 134.09, 129.80, 127.00, 52.38, 11.81. GC-MS (EI, 70 ev) m/z (%) = 210 (M^+, 3), 163 (100), 135 (25), 120 (8), 103 (18), 76 (20), 50 (14). HRMS (ESI) calcd for $C_{10}H_{11}O_3S$ $[M + H]^+$: 211.0423, found 211.0425.

*S-Methyl 4-cyanobenzothioate (**3o**).* Purified by column chromatography (PE). Yield = 18.1 mg (51%). White solid, mp 54−56 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.04 (d, J = 8.3, 2H), 7.75 (d, J = 8.3, 2H), 2.51 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.01, 140.09, 132.45, 127.54, 117.74, 116.56, 11.91. GC-MS (EI, 70 ev) m/z (%) = 177 (M^+, 7), 130 (100), 102 (45), 75 (18), 50 (9). HRMS (ESI) calcd for C_9H_8NOS $[M + H]^+$: 178.0321, found 178.0327.

*S-Methyl 4-(methylsulfonyl)benzothioate (**3p**).* Purified by column chromatography (PE/EtOAc 30:1). Yield = 41.4 mg (90%). White solid, mp 142−144 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.21−8.08 (m, 2H), 8.03 (d, J = 8.5, 2H), 3.07 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.11, 144.38, 141.09, 127.96, 127.78, 44.30, 11.96. GC-MS (EI, 70 ev) m/z (%) = 230 (M^+, 4), 183 (100), 121 (55), 104 (18), 76 (35), 50 (20). HRMS (ESI) calcd for $C_9H_{11}O_3S_2$ $[M + H]^+$: 231.0144, found 231.0150.

*S-Methyl [1,1′-biphenyl]-4-carbothioate (**3q**).*[11] Purified by column chromatography (PE). Yield = 32.8 mg (72%). White solid, mp 100−101 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.04 (d, J = 8.3, 2H), 7.67 (d, J = 8.3, 2H), 7.62 (d, J = 7.8, 2H), 7.47 (t, J = 7.6, 2H), 7.40 (t, J = 7.4, 1H), 2.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ = 191.88, 146.01, 139.81, 135.79, 128.92, 128.20, 127.65, 127.21, 127.20, 11.68. GC-MS (EI, 70 ev) m/z (%) = 228 (M^+, 7), 182 (15), 181 (100), 152 (48), 127 (6), 76 (13).

*S-Methyl 3,5-dimethoxybenzothioate (**3r**).*[11] Purified by column chromatography (PE). Yield = 20.8 mg (49%). White solid, mp 50−54 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.10 (d, J = 2.3 Hz, 2H), 6.64 (d, J = 2.2 Hz, 1H), 3.82 (s, 6H), 2.46 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.27, 160.81, 139.00, 105.65, 104.88, 55.57, 11.82. GC-MS (EI, 70 ev) m/z (%) = 212 (M^+, 35), 165 (100), 137 (48), 122 (43), 107 (25), 73 (29), 51 (15).

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*S-Methyl 3-ethynylbenzothioate (**3s**).*[17] Purified by column chromatography (PE). Yield = 19.0 mg (54%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J = 1.7 Hz, 1H), 7.92 (ddd, J = 7.9, 1.9, 1.1 Hz, 1H), 7.66 (dt, J = 7.8, 1.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 1H), 3.13 (s, 1H), 2.48 (d, J = 0.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.57, 137.21, 136.43, 130.72, 128.64, 127.21, 122.83, 82.38, 78.39, 11.74. GC-MS (EI, 70 ev) m/z (%) = 176 (M^+, 9), 129 (100), 101 (55), 75 (37), 51 (13).

*S-Pentyl 4-methoxybenzothioate (**3t**).*[18] Purified by column chromatography (PE). Yield = 33.3 mg (70%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05−7.84 (m, 2H), 6.99−6.84 (m, 2H), 3.86 (d, J = 1.3 Hz, 3H), 3.04 (t, J = 7.3 Hz, 2H), 1.66 (p, J = 7.4 Hz, 2H), 1.44−1.31 (m, 4H), 0.90 (t, J = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.65, 163.61, 130.23, 129.27, 113.67, 55.44, 31.06, 29.35, 28.86, 22.20, 13.88. GC-MS (EI, 70 ev) m/z (%) = 238 (M^+, 3), 135 (10), 92 (8), 77 (14).

*S-Benzyl 4-methoxybenzothioate (**3u**).*[19] Purified by column chromatography (PE). Yield = 46.0 mg (89%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, J = 8.9 Hz, 2H), 7.40−7.34 (m, 2H), 7.34−7.28 (m, 2H), 7.27−7.21 (m, 1H), 6.94−6.88 (m, 2H), 4.30 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.69, 163.81, 137.74, 129.70, 129.45, 128.93, 128.58, 127.19, 113.78, 55.46, 33.20. GC-MS (EI, 70 ev) m/z (%) = 258 (M^+, 4), 135 (100), 77 (16).

*S-Benzyl 4-fluorobenzothioate (**3v**).*[19] Purified by column chromatography (PE). Yield = 40.0 mg (81%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03−7.95 (m, 2H), 7.37 (d, J = 7.0 Hz, 2H), 7.32 (t, J = 7.7 Hz, 2H), 7.29−7.20 (m, 1H), 7.11 (t, J = 8.6 Hz, 2H), 4.32 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$,) δ 189.70, 165.93 (J_{C-F} = 255.2 Hz), 137.29, 133.19, 129.81 (J_{C-F} = 9.0 Hz), 128.93, 128.64, 127.36, 115.73 (J_{C-F} = 21.1 Hz), 33.45. ^{19}F NMR (564 MHz, $CDCl_3$) δ −104.61. GC-MS (EI, 70 ev) m/z (%) = 246 (M^+, 10), 123 (100), 95 (25).

*S-Benzyl 4-chlorobenzothioate (**3w**).*[20] Purified by column chromatography (PE). Yield = 45.0 mg (86%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, J = 8.7 Hz, 2H), 7.41 (d, J = 8.6 Hz, 2H), 7.39−7.35 (m, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 2.7 Hz, 1H), 4.32 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.05, 139.80, 137.16, 135.16, 128.93, 128.91, 128.65, 128.60, 127.39, 33.47. GC-MS (EI, 70 ev) m/z (%) = 262 (M^+, 14), 139 (100), 111 (25), 91 (20).

*S-Benzyl benzothioate (**3x**).*[21] Purified by column chromatography (PE). Yield = 32.4 mg (71%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (m, 2H), 7.58−7.53 (m, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.37 (d, J = 7.1 Hz, 2H), 7.31 (m, 2H), 7.25 (s, 1H), 4.32 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.75, 140.04, 137.17, 133.26, 128.60, 128.54, 128.49, 127.18, 126.49, 35.90, 30.39. GC-MS (EI, 70 ev) m/z (%) = 228 (M^+, 12), 105 (100), 77 (36), 51 (14).

*S-Phenethyl benzothioate (**3y**).*[22] Purified by column chromatography (PE). Yield = 38.7 mg (80%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99−7.93 (m, 2H), 7.59−7.54 (m, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.29−7.26 (m, 2H), 7.23 (d, J = 7.1 Hz, 1H), 3.32 (m, 2H), 2.97 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.75, 140.04, 137.17, 133.26, 128.60, 128.54, 128.49, 127.18, 126.49, 35.90, 30.39. GC-MS (EI, 70 ev) m/z (%) = 242 (M^+, 5), 105 (100), 77 (50), 51 (18).

*S-Phenethyl 4-methoxybenzothioate (**3z**).*[19] Purified by column chromatography (PE). Yield = 45.0 mg (82%). Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, J = 8.9 Hz, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.30−7.26 (m, 2H), 7.23 (m, 1H), 6.97−6.89 (m, 2H), 3.85 (s, 3H), 3.34−3.26 (m, 2H), 2.97 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.24, 163.74, 140.19, 130.08, 129.34, 128.60, 128.47, 126.45, 113.74, 55.46, 36.07, 30.27. GC-MS (EI, 70 ev) m/z (%) = 272 (M^+, 3), 168 (22), 135 (100), 77 (18).

*N-Benzyl-4-methoxybenzamide (**3ab**).*[23] Purified by flash chromatography (PE/EA = 20:1). Yield = 42.0 mg (53%). White solid, mp 128−131 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (m, 2H), 7.34 (d, J = 3.8 Hz, 3H), 7.29 (q, J = 4.2 Hz, 1H), 7.25 (d, J = 3.4 Hz, 1H), 6.94−6.87 (m, 2H), 6.35 (s, 1H), 4.62 (m, 2H), 3.83 (d, J = 3.2 Hz, 3H).

*Benzophenone (**3ac**).*[24] Purified by flash chromatography (PE). Yield = 26.0 mg (49%). White solid, mp 46−48 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84−7.76 (m, 4H), 7.58 (dd, J = 10.6, 4.2 Hz, 2H), 7.48 (t, J = 7.7 Hz, 4H).

*4-(Benzyloxy)benzoic acid. (**3ad**).*[25] Purified by flash chromatography (PE/EA = 10:1). Yield = 38.0 mg (56%). White solid, mp 173−175 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.76−7.66 (m, 2H), 7.42 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 6.85−6.76 (m, 2H), 5.05 (s, 2H).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00665.

^{1}H and ^{13}C NMR spectra for all new compounds (PDF)

FAIR data, including the primary NMR FID files, for compounds **3a**−**3z**, **3ab**, **3ac**, and **3ad** (ZIP)

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Notes

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REFERENCES

(1) (a) Dawson, P.; Muir, T.; Clark-Lewis, I; Kent, S. Synthesis of proteins by native chemical ligation. *Science* **1994**, *266*, 776−779. (b) Staunton, J.; Weissman, K. J. Polyketide biosynthesis: a millennium review. *Nat. Prod. Rep.* **2001**, *18*, 380−416. (c) Fisher, B. F. S.; Hong, H.; Gellman, S. H. Propensities of amino acid residues via thioester exchange. *J. Am. Chem. Soc.* **2017**, *139*, 13292−13295. (d) Joyce, N. I.; Eady, C. C.; Silcock, P.; Perry, N. B.; Klink, J. W. Fast phenotyping of LFS-silenced (tearless) onions by desorption electrospray ionization mass spectrometry (DESI-MS). *J. Agric. Food Chem.* **2013**, *61*, 1449−1456. (e) Feng, M.-H.; Tang, B.-Q.; Liang, S. H.; Jiang, X.-F. Sulfur containing scaffolds in drugs: synthesis and application in medicinal chemistry. *Curr. Top. Med. Chem.* **2016**, *16*, 1200−1216. (f) Wang, N.-Z.; Saidhareddy, P. S.; Jiang, X.-F. Construction of sulfur-containing moieties in the total synthesis of natural products. *Nat. Prod. Rep.* **2020**, *37*, 246−275.

(2) Hirschbeck, V.; Gehrtz, P. H.; Fleischer, I. Regioselective thiocarbonylation of vinyl arenes. *J. Am. Chem. Soc.* **2016**, *138*, 16794−16799.

(3) (a) Fausett, B. W.; Liebeskind, L. S. Palladium-catalyzed coupling of thiol esters with aryl and primary and secondary alkyl organoindium reagents. *J. Org. Chem.* **2005**, *70*, 4851−4853. (b) Prokopcová, H.; Kappe, C. O. The liebeskind-srogl C-C cross-coupling reaction. *Angew. Chem., Int. Ed.* **2009**, *48*, 2276−2286. (c) Fuwa, H.; Ichinokawa, N.; Noto, K.; Sasaki, M. Stereoselective synthesis of 2,6-cis-substituted tetrahydropyrans: bronsted acid-catalyzed intramolecular oxa-conjugate cyclization of α,β-unsaturated ester surrogates. *J. Org. Chem.* **2012**, *77*, 2588−2607. (d) Burhardt, M. N.; Taaning, R. H.; Skrydstrup, T. Pd-catalyzed thiocarbonylation with stoichiometric carbon monoxide: scope and applications. *Org. Lett.* **2013**, *15*, 948−951. (e) Kobayashi, H.; Eickhoff, J. A.; Zakarian, A. Synthesis of 2-aminoazoles from thioesters via α-heterosubstituted ketones by copper-mediated cross-coupling. *J. Org. Chem.* **2015**, *80*, 9989−9999. (f) Sun, F.; Li, M.; He, C.-F.; Wang, B.; Li, B.; Sui, X.-W.; Gu, Z.-H. Cleavage of the C(O)-S bond of thioesters by palladium/norbornene/copper cooperative catalysis: an efficient synthesis of 2-(arylthio)aryl ketones. *J. Am. Chem. Soc.* **2016**, *138*, 7456−7459.

(4) (a) Zhao, B.; Fu, Y.; Shang, R. Oxalic acid monothioester for palladium-catalyzed decarboxylative thiocarbonylation and hydrothiocarbonylation. *Org. Lett.* **2019**, *21*, 9521−9526. (b) Jabarullah, N. H.; Jermsittiparsert, K.; Melnikov, P. A.; Maseleno, A.; Hosseinian, A.; Vessally, E. Methods for the direct synthesis of thioesters from aldehydes: a focus review. *J. Sulfur Chem.* **2020**, *41*, 96−115. (c) Xu, T.-X.; Cao, T.-P.; Yang, M.-C.; Xu, R.-T.; Nie, X.-L.; Liao, S.-H. Decarboxylative thiolation of redox-active esters to thioesters by merging photoredox and copper catalysis. *Org. Lett.* **2020**, *22*, 3692−3696. (d) Feng, Y.-X.; Yang, S.-M.; Zhao, S.; Zhang, D.-P.; Li, X.-J.; Liu, H.; Dong, Y.-H.; Sun, F.-G. Nickel-catalyzed reductive aryl thiocarbonylation of alkene via thioester group transfer strategy. *Org. Lett.* **2020**, *22*, 6734−6738.

(5) For selected examples on carbonylation: (a) Liu, Q.; Zhang, H.; Lei, A. Oxidative carbonylation reactions: organometallic compounds (R-M) or hydrocarbons (R-H) as nucleophiles. *Angew. Chem., Int. Ed.* **2011**, *50*, 10788−10799. (b) Wu, X. - F.; Neumann, H.; Beller, M. Synthesis of heterocycles via palladium-catalyzed carbonylations. *Chem. Rev.* **2013**, *113*, 1−35. (c) Burhardt, M. N.; Ahlburg, A.; Skrydstrup, T. Palladium-catalyzedthiocarbonylation of aryl,vinyl, and benzylbromides. *J. Org. Chem.* **2014**, *79*, 11830−11840. (d) Zhao, H.-Y.; Du, H.-Y.; Yuan, X.-R.; Wang, T.-J.; Han, W. Iron-catalyzed carbonylation of aryl halides with arylborons using stoichiometric chloroform as the carbon monoxide source. *Green Chem.* **2016**, *18*, 5782−5787.

(6) For selected examples on thiocarbonylation: (a) Xiao, W.-J.; Vasapollo, G.; Alper, H. Highly regioselective palladium-catalyzed thiocarbonylation of allenes with thiols and carbon monoxide. *J. Org. Chem.* **1998**, *63*, 2609−2612. (b) Hu, Y.-H.; Liu, J.; Lü, Z.-X.; Luo, X.-C.; Zhang, H.; Lan, Y.; Lei, A. Base-induced mechanistic variation in palladium-catalyzed carbonylation of aryliodides. *J. Am. Chem. Soc.* **2010**, *132*, 3153−3158. (c) Nakaya, R.; Yorimitsu, H.; Oshima, K. Bis(cyclopentadienyl- dicarbonyliron) as a convenient carbon monoxide source in palladium-catalyzed carbonylative coupling of aryl iodides with amines, alcohols, and thiols. *Chem. Lett.* **2011**, *40*, 904−906. (d) Islam, S. M.; Molla, R. A.; Roy, A. S.; Ghosh, K. Polymer supported Pd catalyzed thioester synthesis via carbonylation of aryl halides under phosphine free conditions. *RSC Adv.* **2014**, *4*, 26181−26192.

(7) Fernandez-Rodriguez, M. A.; Shen, Q.; Hartwig, J. F. Highly efficient and functional-group-tolerant catalysts for the palladium-catalyzedcoupling of aryl chlorides with thiols. *Chem. - Eur. J.* **2006**, *12*, 7782−7796.

(8) (a) Qiao, Z.-J.; Jiang, X.-F. Ligand-controlled divergent cross-coupling involving organosilicon compounds for thioether and thioester synthesis. *Org. Lett.* **2016**, *18*, 1550−1553. (b) Wang, M.; Dai, Z.; Jiang, X.-F. Design and application of α-ketothioesters as 1,2-dicarbonyl-forming reagents. *Nat. Commun.* **2019**, *10*, 2661.

(9) Kim, M.; Yu, S.; Kim, J. G.; Lee, S. Palladium-catalyzed carbonylation of thioacetates and aryl iodides for the synthesis of saryl thioesters. *Org. Chem. Front.* **2018**, *5*, 2447−2452.

(10) (a) Qi, X.-X.; Bao, Z.-P.; Wu, X.-F. Palladium-catalyzed carbonylative transformation of aryl iodides and sulfonyl chlorides: convenient access to thioesters. *Org. Chem. Front.* **2020**, *7*, 885−889. (b) Qi, X.-X.; Bao, Z.-P.; Yao, X.-T.; Wu, X.-F. Nickel-catalyzed thiocarbonylation of arylboronicacids with sulfonyl chlorides for the synthesis of thioesters. *Org. Lett.* **2020**, *22*, 6671−6676.

(11) Li, Y.; Bao, G.; Wu, X.-F. Palladium-catalyzed intermolecular transthioetherification of aryl halides with thioethers and thioesters. *Chem. Sci.* **2020**, *11*, 2187−2192.

(12) (a) Wrona, M.; Vera, P.; Pezo, D.; Nerin, C. Identification and quantification of odours from oxobiodegradable polyethylene oxidised under a free radical flow by headspace solid-phase microextraction followed by gas chromatography-olfactometry-mass spectrometry. *Talanta* **2017**, *172*, 37−44. (b) Baoguo, S. Household chemical dictionary (in chinese). *Chem. Ind. Press* **2002**, 288.

(13) Colleville, A. P.; Horan, R. A. J.; Tomkinson, N. C. O. Aryldiazonium tetrafluoroborate salts as green and efficient coupling partners for the suzuki-miyaurareaction: from optimization to mole scale. *Org. Process Res. Dev.* **2014**, *18*, 1128−1136.

(14) Abbasi, M.; Khalifeh, R. One-pot odourless synthesis of thioesters via in situ generation of thiobenzoic acids using benzoic anhydrides and thiourea. *Beilstein J. Org. Chem.* **2015**, *11*, 1265−1273.

(15) Harrowven, D. C.; Lucas, M. C.; Howes, P. D. A simple and direct method for converting thioamides into thioesters. *Tetrahedron* **1999**, *55*, 1187−1196.

(16) He, J.; Man, Z.-M.; Shi, Y.-P.; Li, C.-Y. Synthesis of β-amino-α,β-unsaturated Ketone derivatives via sequential rhodium-catalyzed sulfurylide formation/ rearrangement. *J. Org. Chem.* **2015**, *80*, 4816−4823.

(17) Ube Industries, Ltd. Substituted phenylethynyl gold-nitrogenated heterocyclic carbene complex. EP.2042506A1, 2009.

(18) Chung, J. Y.; Seo, U. R.; Chun, S.; Chung, Y. K. Poly (3,4-dimethyl-5-vinylthiazolium)/dbu-catalyzed thioesterification of aldehydes with thiols. *ChemCatChem* **2016**, *8*, 318−321.

(19) Chou, Y.-L.; Jhong, Y.; Swain, S. P.; Hou, D.-R. Microwave-assisted direct thioesterification of carboxylic acids. *J. Org. Chem.* **2017**, *82*, 10201−10208.

(20) Zhu, X.-B.; Shi, Y.; Mao, H.-B.; Cheng, Y.-X.; Zhu, C.-G. Tetraethylammonium bromide-catalyzed oxidative thioesterification of aldehydes and alcohols. *Adv. Synth. Catal.* **2013**, *355*, 3558−3562.

(21) Steemers, L.; Wijsman, L.; Maarseveen, J. H. V. Regio- and stereoselective chan-lam-evans enol esterification of carboxylic acids with alkenylboroxines. *Adv. Synth. Catal.* **2018**, *360*, 4241.

(22) Qi, X.-X.; Bao, Z.-P.; Yao, X.-T.; Wu, X.-F. Nickel-catalyzed thiocarbonylation of arylboronic acids with sulfonyl chlorides for the synthesis of thioesters. *Org. Lett.* **2020**, *22*, 6671−6676.

(23) Kosal, A. D.; Wilson, E. E.; Ashfeld, B. L. Phosphine-based redox catalysis in the direct traceless staudinger ligation of carboxylic acids and azides. *Angew. Chem., Int. Ed.* **2012**, *51*, 12036−12040.

https://doi.org/10.1021/acs.joc.1c00665
J. Org. Chem. 2021, 86, 8797−8804

(24) Seo, S.; Taylor, J. B.; Greaney, M. F. Protode carboxylation of benzoic acids under radical conditions. *Chem. Commun.* **2012**, *48*, 8270−8272.
(25) Bhunia, S. K.; Das, P.; Nandi, S.; Jana, R. Carboxylation of aryl triflates with CO_2 merging palladium and visible-light-photoredox catalysts. *Org. Lett.* **2019**, *21*, 4632−4637.

https://doi.org/10.1021/acs.joc.1c00665
J. Org. Chem. 2021, 86, 8797−8804