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Copper-Catalyzed Annulative Coupling of S,S-Disubstituted Enones with Diazo Compounds to Access Highly Functionalized Thiophene Derivatives

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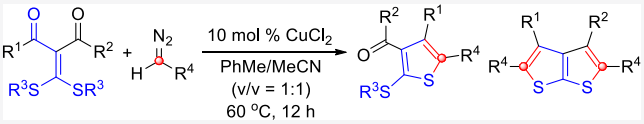
Supporting Information

ABSTRACT: An efficient protocol toward fully substituted thiophenes and thieno[2,3-*b*]thiophenes has been developed through $CuCl_2$-catalyzed annulative coupling of S,S-disubstituted enones with diazo compounds under mild conditions. Tetrasubstituted thiophenes and thieno[2,3-*b*]thiophenes were efficiently accessed by variation of the feed ratio of the reactants in good to excellent yields, respectively. The synthetic methodology has demonstrated the potential for the construction of diverse thiophene derivatives.



INTRODUCTION

Synthesis of thiophenes has been paid much attention because they represent an important class of sulfur-containing heterocycles, which are ubiquitous core structural motifs in many pharmaceuticals,[1,2] functional materials,[3] and transition-metal complexes.[4] For example, thiophene derivatives have been medically considered as the potent inhibitors of p38 kinase,[5a] IKKβ,[5b] and PTP1B[5c] (Figure 1). Thieno[2,3-*b*]thiophenes

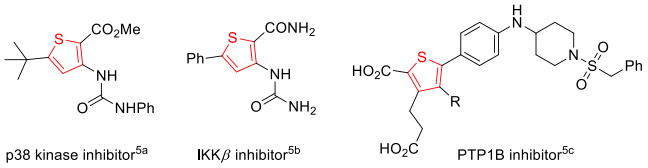


Figure 1. Selected bioactive thiophene derivatives.

are pharmaceutically used for inhibiting the growth of bacterial pathogens and treatment of bacterial infections.[5d] The general synthetic approaches to access such S-heterocycles involve either functionalization of the α- and β-positions of the preconstructed thiophene skeleton[5e,6] or construction of the thiophene ring from appropriately substituted open-chain precursors.[7] The latter approach is obviously more versatile and attractive but has been less developed. In this regard, Fiesselmann,[8] Gewald,[9] Paal,[10] and Hinsberg[11] reactions can be applied for the direct establishment of a thiophene ring in specific thiophene derivatives. Ketene *S*,*S*-acetals[12a] are known for the same purpose through transition-metal-catalyzed C−S bond cleavage and reconstruction.[12b] The traditional synthetic strategies for thieno[2,3-*b*]thiophenes are usually based on the cyclization of prefunctionalized organosulfur compounds.[13]

Although considerable advance has been achieved toward the synthesis of thiophene derivatives, concise and efficient methods are still highly desirable for the construction of functionalized thiophenes in order to overcome the limitations of the present synthetic protocols in terms of harsh conditions, low yields, expensive catalysts, and/or difficult purification.

Transition-metal-catalyzed reactions using diazo compounds[14] as the carbene precursors allow for the rapid assembly of useful complex molecules which cannot be readily accessed by other methods.[15] As versatile C1 synthons, diazo compounds are potentially used for the direct construction of cyclic architectures through cycloaddition or annulative coupling reactions.[16,17] Diazo compounds are amphiphilic, and the negatively polarized diazo carbon atom is nucleophilic, while the metal carbene species generated from a diazo compound has an electron-deficient carbene center.[18] Thus, diazo compounds can exhibit diverse reactivities. Based on this concept, Zhao, et al. very recently reported a copper(II)-catalyzed domino reaction to prepare polysubstituted thiophenes.[18b]

During the ongoing investigation of the reactivities of alkylthio-functionalized internal alkenes,[19] we found that α-oxo and thioxo-fuctionalized, N,S-substituted internal alkenes could efficiently react with the carbene precursor compounds, that is, ketone *N*-tosylhydrazones, under copper catalysis, affording five-membered 2-imino O- and S-heterocycles via carbene insertion into the olefinic C=C bond,[19c] whereas they underwent annulative coupling with aldehyde *N*-tosylhydrazones to give thiophene products under transition-metal-free

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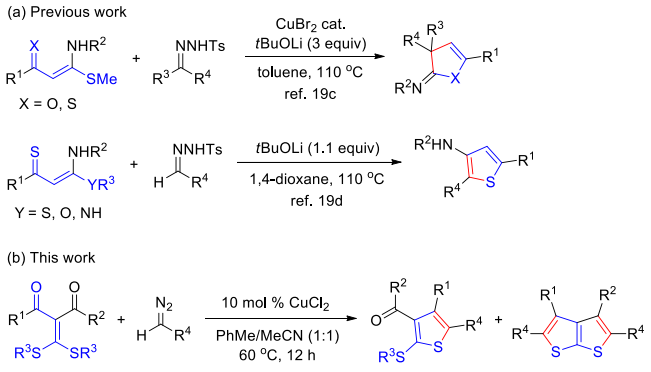
conditions[19d] (Scheme 1a). We conceived that the nucleophilicity/electrophilicity of the reaction intermediates generated in situ from *N*-tosylhydrazones, that is, the copper carbene species in the presence of a copper catalyst, and the diazo species under the transition-metal-free conditions, might be dramatically altered upon variation of the reactants and reaction conditions.[20] Nucleophilic attack of the thiocarbonyl sulfur at the diazo carbon atom may form a thiocarbonyl ylide, that is, a sulfur-centered 1,3-dipole, which can readily undergo 1,5-dipolar electrocyclization.[21] Thus, the sulfur atoms of a S,S-disubstituted enone were envisioned to interact with diazo compounds to form sulfur ylide intermediates which then cyclize to give S-heterocyclic compounds. Herein, we disclose the copper-catalyzed annulative coupling of S,S-disubstituted enones with diazo compounds for the chemoselective synthesis of highly functionalized thiophenes and thieno[2,3-*b*]-thiophenes (Scheme 1b).

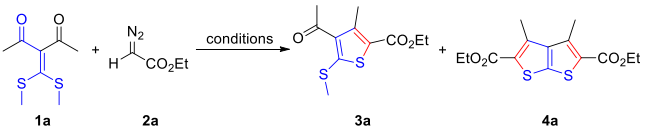
Scheme 1. Synthetic Strategies to Access Functionalized Thiophenes



RESULTS AND DISCUSSION

Initially, the reaction of S,S-disubstituted enone, that is, 3-(bis(methylthio)methylene)pentane-2,4-dione (**1a**) with ethyl diazoacetate (**2a**) was conducted to screen the reaction conditions (Table 1). In the presence of 10 mol % $Rh_2(OAc)_4$ as the catalyst, the reaction of **1a** and **2a** in a 1:2 molar ratio underwent in toluene at 80 °C for 12 h under a nitrogen atmosphere, forming the target thiophene product **3a** in 27% yield (Table 1, entry 1). Copper(II) salts $CuBr_2$ and $CuCl_2$ behaved more efficiently than the Rh(II) catalyst, and in the case of using 10 mol % $CuCl_2$ as the catalyst, **3a** was generated in 45−46% yields in toluene and trifluoromethylbenzene, respectively (Table 1, entries 2−4). In acetonitrile, the reaction proceeded less efficiently to produce **3a** in 27% yield (Table 1, entry 5). Lowering the temperature to 60 °C enhanced the yield of compound **3a** to 51% (Table 1, entry 6). An obvious solvent effect was demonstrated by using the mixed solvents of toluene and acetonitrile or toluene and $PhCF_3$ (1:1, v/v) at 60 °C, leading to **3a** in 79% isolated yield (Table 1, entries 7 and 8). In the absence of a catalyst, the reaction did not occur (Table 1, entry 9). An air atmosphere deteriorated the product yield to 31% from 76% under a nitrogen atmosphere (Table 1, entries 7 and 10). It is worth noting that in all of the above cases, thieno[2,3-*b*]thiophene **4a** could not be formed in a detectable amount. Unexpectedly, increasing the loading of diazo compound **2a** to 3 equiv led to a mixture of **3a** (45%) and **4a** (27%), and further increasing the amount of **2a** to 4 equiv selectively afforded **4a** in 85% isolated yield (Table 1, entries 11 and 12). It should be noted that the molecular structure of compound **3a** was confirmed by the X-ray single crystal crystallographic analysis (Figure 2, see the Supporting Information for details).

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	solvent	temp (°C)	yields[b] (%) 3a/4a
1	$Rh_2(OAc)_4$	PhMe	80	27/-
2	$CuBr_2$	PhMe	80	33/-
3	$CuCl_2$	PhMe	80	45/-
4	$CuCl_2$	$PhCF_3$	80	46/-
5	$CuCl_2$	MeCN	80	27/-
6	$CuCl_2$	PhMe	60	51/-
7	$CuCl_2$	PhMe/MeCN (1:1)	60	76 (79)[c]/-
8	$CuCl_2$	PhMe/$PhCF_3$ (1:1)	60	68/-
9		PhMe/MeCN (1:1)	60	0/0
10[d]	$CuCl_2$	PhMe/MeCN (1:1)	60	31/-
11[e]	$CuCl_2$	PhMe/MeCN (1:1)	60	45/27
12[f]	$CuCl_2$	PhMe/MeCN (1:1)	60	trace/(85)[c]

[a]Conditions: **1a** (0.3 mmol), **2a** (0.6 mmol), catalyst (10 mol %), solvent (2 mL), 0.1 MPa N_2, 12 h. [b]Determined by ^1H NMR analysis by using 1,3,5-trimethoxybenzene as the internal standard. [c]Isolated yields given in parentheses. [d]In air. [e]Using **2a** (0.9 mmol). [f]Using **2a** (1.2 mmol).

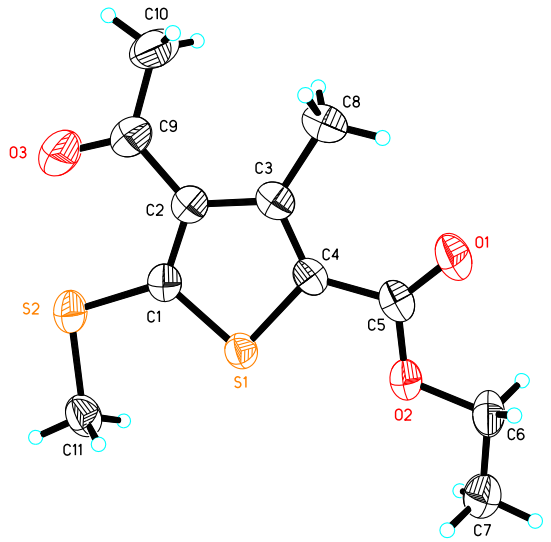


Figure 2. Perspective view of **3a** with thermal ellipsoids at the 30% probability level.

Under the optimal conditions, the scope of S,S-disubstituted enones (**1**) was explored (Table 2). Ethylthio, *n*-butylthio, and benzylthio-disubstituted enones (**1b−1d**) reacted with **2a** less efficiently than their methylthio analogue **1a** to give the target products **3b−3d** (71−75%). 2-Ester-functionalized di-(methylthio)-substituted enones **1e−1i** efficiently underwent the reaction to afford products **3e−3i** in 72−77% yields, exhibiting no obvious steric effect from the methyl, ethyl, isopropyl, and *tert*-butyl groups in the 2-ester functionalities. The amido group-functionalized enone substrates **1j** and **1k**

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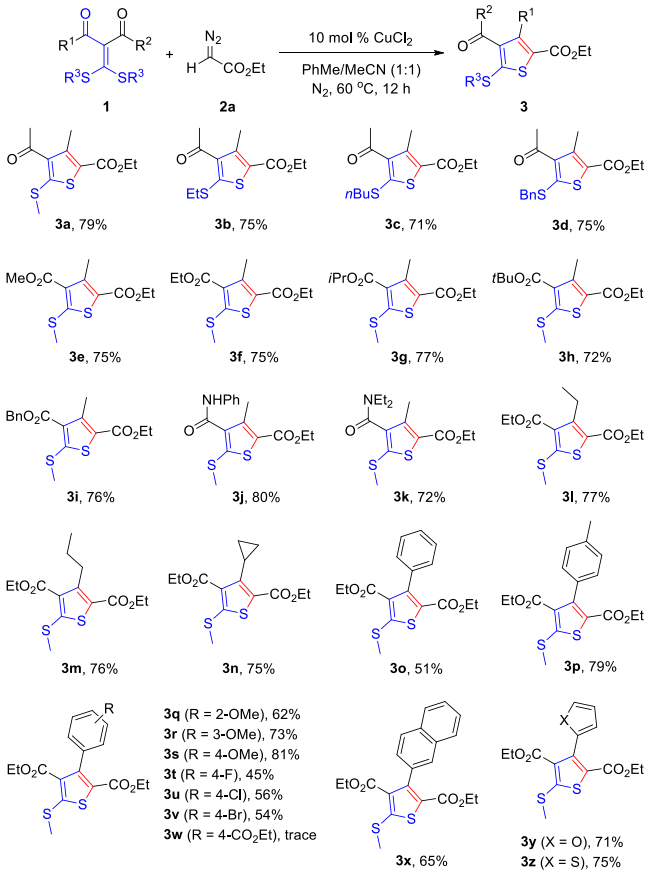
Table 2. Scope of S,S-Disubstituted Enones (1)[a]

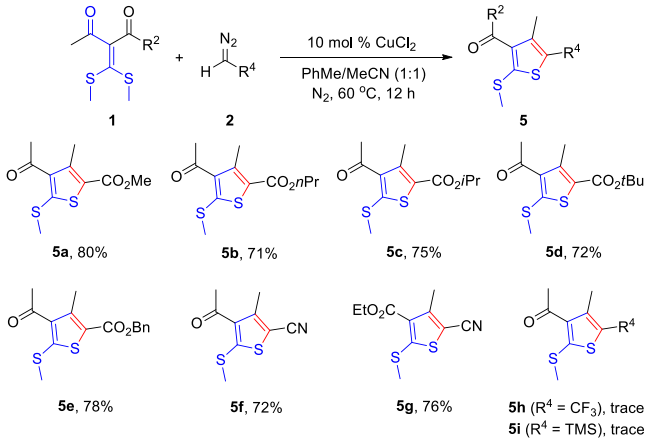


[a]Conditions: **1** (0.3 mmol), **2** (0.6 mmol), $CuCl_2$ (10 mol %), PhMe/MeCN (2 mL, v/v = 1:1), 0.1 MPa N_2, 12 h.

also reacted well with **2a** to yield **3j** (80%) and **3k** (72%), respectively. The short-chain alkyls such as ethyl and *n*-propyl and cyclopropyl in the alkanoyl functionalities of the enone substrates did not show an electronic or steric effect on the product yields for **3f** and **3l**−**3n** (75−77%). However, the substituents on the aryl groups in the aroyl functionalities of **1o**−**1w** exhibited obvious steric and electronic effects. The electron-donating methyl and methoxy groups facilitated the reaction to form **3p**−**3s** (62−81%), while the unsubstituted aryl enone **1o** reacted with **2a** to give **3o** in 51% yield. 2-Methoxy exhibited an obvious negative steric effect on the yield of **3q** (62%) among the methoxy-substituted substrates **1r** (73%) and **1s** (81%). The electron-withdrawing fluoro group diminished the yield of **3t** to 45%, and the ester group (CO_2Et) on the aryl moiety almost completely inhibited the reaction. 4-Chloro and 4-bromo groups slightly improved the reaction efficiency to give **3u** and **3v** (54−56%). The reaction of 2-naphthyl-functionalized enone **1x** produced **3x** in 65% yield. 2-Furyl and 2-thienyl-functionalized enones **1y** and **1z** reacted with **2a** under the same conditions, efficiently generating the corresponding heteroaryl-functionalized thiophene products **3y** (71%) and **3z** (75%), respectively. It is worth noting that 2-(bis(methylthio)methylene)cyclohexane-1,3-dione exhibited no reactivity to **2a** under the same conditions.

Next, the protocol generality was investigated by carrying out the reaction of enones **1** with various diazo compounds (**2**) (Table 3). Methyl diazoacetate (**2b**) reacted with S,S-

Table 3. Scope of Diazo Compounds (2)[a]

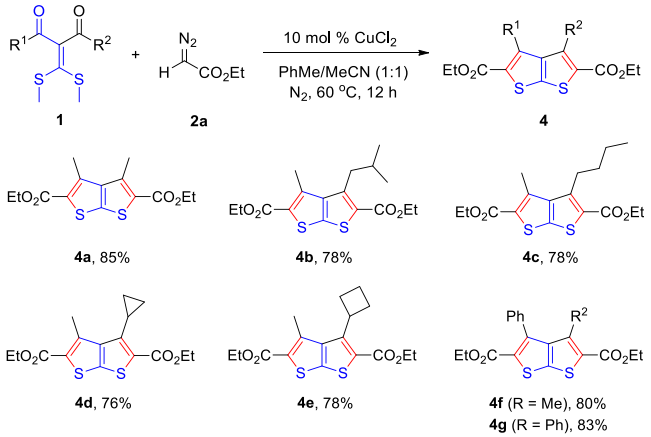


[a]Conditions: **1** (0.3 mmol), **2** (0.6 mmol), $CuCl_2$ (10 mol %), PhMe/MeCN (2 mL, v/v = 1:1), 0.1 MPa N_2, 12 h.

disubstituted enone **1a** to give the target thiophene product, that is, methyl 3-methyl-4-acetyl-5-(methylthio)thiophene-2-carboxylate (**5a**) in 80% yield. *n*-Propyl, isopropyl, *tert*-butyl, and benzyl diazoacetates also efficiently reacted with **1a** to form the corresponding thiophene products **5b**−**5e** (71−78%), only demonstrating slight electronic and steric effects. 2-Diazoacetonitrile (**2g**) reacted well with enones **1a** and **1f** to afford 2-cyano-functionalized thiophenes **5f** and **5g** in 72−76% yields, respectively, while CF_3 and TMS (trimethylsilyl)-functionalized diazo compounds **2h** and **2i** showed no reactivity to enone **1a** under the stated conditions.

Then, the protocol was applied for the synthesis of thieno[2,3-*b*]thiophene derivatives **4** (Table 4). 3-(Bis-

Table 4. Synthesis of Thieno[2,3-*b*]thiophenes (4)[a]



[a]Conditions: **1** (0.3 mmol), **2** (1.2 mmol), $CuCl_2$ (10 mol %), PhMe/MeCN (2 mL, v/v = 1:1), 0.1 MPa N_2, 12 h.

(methylthio)methylene)pentane-2,4-dione (**1a**) was reacted with 4 equiv of ethyl diazoacetate (**2a**) to give the target diethyl 3,4-dimethylthieno[2,3-*b*]thiophene-2,5-dicarbo-xylate (**4a**) in 85% yield under the standard conditions. Variation of the functional groups from methyl, isopropyl, *n*-butyl, cyclopropyl, to cyclobutyl in the 2-alkanoyl functionalities of the S,S-disubstituted enone substrates **1** also efficiently led to the corresponding target products **4b**−**4e** (76−78%). 2-Acetyl and 2-benzoyl-substituted aryl enones reacted with **2a** to give

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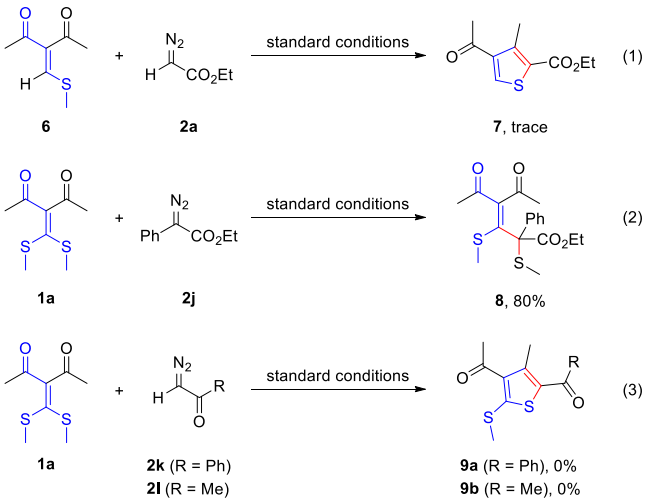
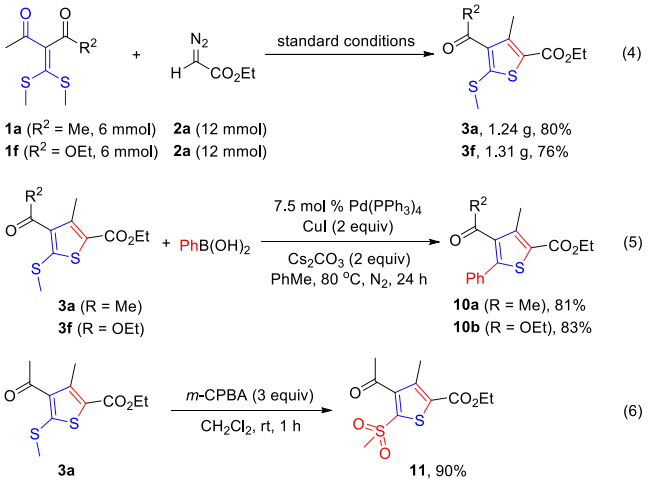
the corresponding products **4f** and **4g** in high yields (80–83%). These results have demonstrated a good substrate applicability of the present synthetic protocol.

Other types of S-substituted enones and diazo compounds were also employed in the synthesis of highly functionalized thiophene derivatives by the present synthetic methodology. The methylthio-monosubstituted enone (**6**) was treated with ethyl diazoacetate (**2a**) under the standard conditions; no detectable amount of the target thiophene product **7** was formed (eq 1). This result verifies the crucial role of the



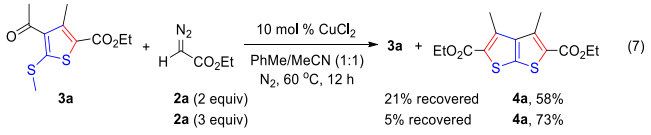
di(alkylthio) functionality at one terminus of the C=C backbone in the S,S-disubstituted enone substrates. Unexpectedly, the aryl diazo compound, that is, ethyl diazophenylacetic acid ester (**2j**) reacted with **1a** to give a new enone **8** (80%) which was generated by carbene insertion into the vinyl C–S bond[22] (eq 2). Neither of the two diazo compounds 2-diazo-1-phenyl-ethanone (**2k**) and 1-diazopropan-2-one (**2l**) could react with **2a** under the stated conditions, suggesting the necessity of an ester group in the diazo substrates (eq 3).

To demonstrate the applicability of the synthetic protocol, gram-scale preparation of the thiophene products **3a** (80%) and **3f** (76%) was performed by the reactions of **1a** and **1f** with **2a**, respectively (eq 4). 2-Arylthiophene-based functional



materials have been found to have broad applications in materials science.[5c] Thus, derivatization of thiophenes **3a** and **3f** was conducted by palladium-catalyzed Liebeskind–Srogl cross-coupling with phenylboronic acid, giving 5-phenylated tetrasubstituted thiophene derivatives **10a** and **10b** in 81–83% yields (eq 5). With *m*-chloroperoxybenzoic acid (*m*-CPBA) as the oxidant, the methylthio group in **3a** was readily oxidized to the corresponding sulfone **11** in 90% yield (eq 6), which may be used as a useful intermediate in organic synthesis.

Control experiments were performed to probe into the reaction mechanism. Under the standard conditions, thiophene **3a** reacted with two equivalents of diazo compound **2a** to give **4a** in 58% yield with compound **3a** partially recovered (21%), which suggests that **3a** is the possible intermediate to form thieno[2,3-*b*]thiophene **4a** (eq 7). Using 3 equiv of **2a** led to



4a in 73% yield with minor recovery of **3a** (5%). It was noted that compounds of type **4** could be observed as the minor products in some reactions to prepare compounds **3** and **5**. The reaction of **1a** with **2a** was conducted in the presence of two equivalents of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4-methyl-phenyl (BHT) under the standard conditions. These radical scavengers did not inhibit the annulative coupling reaction, and **3a** was formed in 65–73% yields which were comparable to that (79%) obtained under the standard conditions, excluding a radical reaction pathway.

A plausible mechanism is proposed in Scheme 2. The initial reaction of the copper catalyst and diazo compound **2** generates Cu(II)–carbene species **A** which then forms an adduct (**B**) with S,S-disubstituted enone **1a**. Regeneration of the catalytically active Cu(II) species leads to sulfur ylide **C**/**D**. Subsequent intramolecular annulation produces intermediate **E** which rearranges to yield the target thiophene product **3a** through elimination of methanol. Under the stated conditions using large excess of the diazo compound (4 equiv), thiophene **3a** further interacts with Cu(II)–carbene species **A** to generate adduct **F** from which the catalytically active Cu(II) species is regenerated with the formation of sulfur ylide intermediate **G**/**H**. A similar intramolecular annulation proceeds to yield species **I**, an analogue of species **E**. Elimination of methanol results in thieno[2,3-*b*]thiophene **4a**. It is worth noting that compound **8** can be obtained through carbene insertion into the vinyl C–S bond of the S,S-disubstituted enone substrate when an aryl diazo compound is used.

In conclusion, we have developed a concise and efficient copper(II)-catalyzed annulative coupling protocol of S,S-disubstituted enones and diazo compounds toward the synthesis of fully substituted thiophenes and thieno[2,3-*b*]thiophenes. Because of easy manipulations, readily available reactants, excellent chemoselectivity, and mild reaction conditions, this work offers a promising method to construct highly functionalized thiophene motifs.

EXPERIMENTAL SECTION

General Considerations. The solvents were dried and distilled prior to use by the literature methods. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on a Bruker DRX-400 spectrometer, and all chemical shift values refer to δ_{TMS} = 0.00 ppm or $CDCl_3$ ($\delta(^{1}H)$, 7.26 ppm and $\delta(^{13}C)$, 77.16 ppm). The HRMS (ESI) analysis was obtained on a Waters GC-TOF CA156 mass spectrometer. X-ray crystallographic

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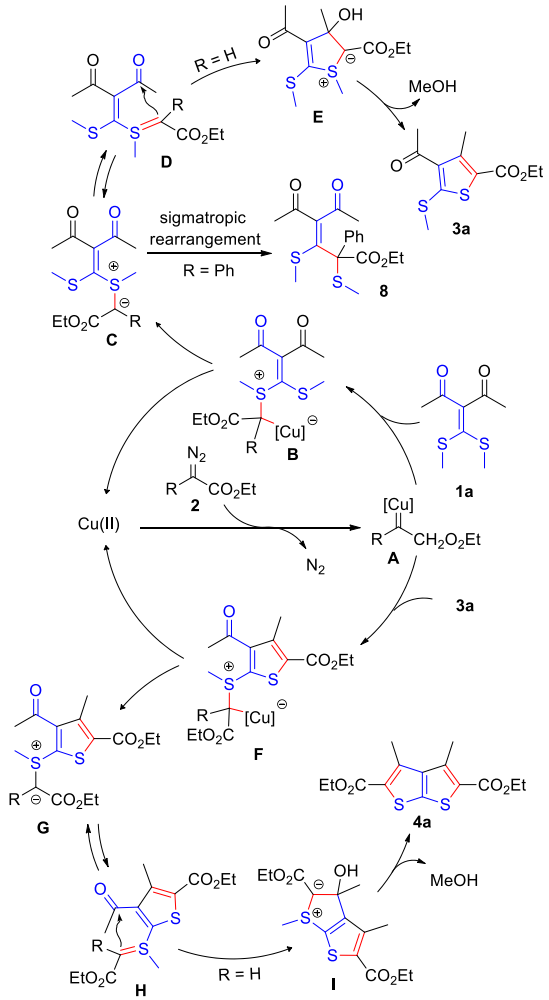
Scheme 2. Proposed Mechanism



analysis was achieved by the Analysis Center, Dalian Institute of Chemical Physics, Chinese Academy of Sciences. All chemical reagents were purchased from commercial sources and used as received unless otherwise indicated. The starting substrates **1a** and **1b**,[23a] **1c** and **1d**,[23b] **1e**−**1j**,[23a] **1k**,[23c] **1l**−**1z**,[23a] **1z5** and **1z6**,[23a] and diazo compounds **2a**,[19d] **2b**,[23d] **2c**,[23e] **2d**−**2g**,[19d] **2h** and **2i**,[23f] **2j**,[22] **2k** and **2l**,[19d] were known and prepared by the literature procedures, and their spectroscopic features are in good agreement with those reported in the literatures.

Preparation of S,S-Disubstituted Enones (1).[23a] *Typical Procedure for the Synthesis of S,S-Disubstituted Enones* ***1*** *—Synthesis of 3-(Bis(methylthio)methylene)pentane-2,4-dione* ***(1a)***. Iodomethane (1.6 g, 11 mmol) was added dropwise to a stirred mixture of acetylacetone (0.5 g, 5 mmol), K_2CO_3 (1.7 g, 12 mmol), and CS_2 (0.5 g, 6 mmol) in 10 mL DMF at 0 °C. The reaction was continued at 25 °C (oil bath) for 24 h. The resulting mixture was poured into 50 mL water and separated, and the aqueous phase was extracted with 10 mL CH_2Cl_2. The combined organic phase was washed with H_2O (3 × 10 mL), dried over anhydrous $MgSO_4$, and filtered, and it evaporated all the volatiles under reduced pressure. The resultant residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v] to afford **1a** as a yellow solid (800 mg, 81%).

3-(Bis(methylthio)methylene)-6-methylheptane-2,4-dione ***(1z1)***. Following the general procedure, compound **1z1** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v]. 880 mg, 72% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (d, J = 6.7 Hz, 2H), 2.37 (s, 6H), 2.32 (s, 3H), 2.14 (m, 1H), 0.90 (d, J = 6.7 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 200.0, 197.3, 151.4, 145.3, 51.8, 30.6, 24.3, 22.5, and 18.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{19}O_2S_2$, 247.0826; found, 247.0826.

3-(Bis(methylthio)methylene)octane-2,4-dione ***(1z2)***. Following the general procedure, compound **1z2** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v]. 923 mg, 75% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.59 (m, 2H), 2.35 (s, 6H), 2.29 (s, 3H), 1.55 (m, 2H), 1.34−1.23 (m, 2H), 0.84 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 201.0, 196.8, 151.7, 144.9, 42.9, 30.4, 26.0, 22.1, 18.0, and 13.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{19}O_2S_2$, 247.0826; found, 247.0824.

2-(Bis(methylthio)methylene)-1-cyclopropylbutane-1,3-dione ***(1z3)***. Following the general procedure, compound **1z3** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v]. 861 mg, 75% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 6H), 2.27 (s, 3H), 2.15 (m, 1H), 1.11 (m, 2H), 0.96 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 200.3, 196.5, 153.8, 144.0, 62.1, 30.4, 22.0, and 12.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{10}H_{15}O_2S_2$, 231.0513; found, 231.0513.

2-(Bis(methylthio)methylene)-1-cyclobutylbutane-1,3-dione ***(1z4)***. Following the general procedure, compound **1z4** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 20:1, v/v]. 842 mg, 69% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.53 (m, 1H), 2.37 (m, 6H), 2.28 (s, 3H), 2.22 (m, 2H), 2.04 (m, 2H), 1.95−1.69 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 201.6, 197.1, 152.7, 143.9, 45.6, 30.5, 25.3, 18.1, and 17.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{17}O_2S_2$, 245.0670; found, 245.0671.

Synthesis of Thiophenes 3 and 5. *Typical Procedure for the Synthesis of Thiophenes* ***3*** *and* ***5*** *—Synthesis of Ethyl 4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carboxylate* ***(3a)***. A mixture of 3-(bis(methylthio)methylene)pentane-2,4-dione (**1a**) (61 mg, 0.3 mmol), ethyl diazoacetate (**2a**) (68 mg, 0.6 mmol), and $CuCl_2$ (4 mg, 0.03 mmol) in PhMe/MeCN (2 mL, v/v = 1:1) was stirred at 60 °C (oil bath) for 12 h under a N_2 atmosphere. After **1a** was completely consumed by thin-layer chromatography (TLC) monitoring on silica gel, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/ethyl acetate = 50:1, v/v], affording **3a** (60 mg, 79%) as a pale yellow solid. mp 73−74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (q, J = 7.1 Hz, 2H), 2.64, 2.48, and 2.46 (s both, 3:3:3H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 194.8, 161.7, 156.7, 146.0, 137.6, 124.4, 60.9, 31.2, 18.5, 15.8, and 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{14}O_3S_2$, 259.0463; found, 259.0463.

Ethyl 4-Acetyl-5-(ethylthio)-3-methylthiophene-2-carboxylate ***(3b)***. Following the general procedure, compound **3b** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 82 mg, 75%; yellow solid, mp 67−68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31 (q, J = 7.1 Hz, 2H), 3.00 (q, J = 7.4 Hz, 2H), 2.65 and 2.54 (s both, 3:3H), 1.37 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.2, 161.9, 151.8, 145.6, 137.6, 140.2, 125.5, 61.1, 31.6, 30.4, 15.7, 14.4, and 13.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{12}H_{17}O_3S_2$, 273.0619; found, 273.0615.

Ethyl 4-Acetyl-5-(butylthio)-3-methylthiophene-2-carboxylate ***(3c)***. Following the general procedure, compound **3c** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 64 mg, 71%; yellow solid, mp 44−45 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25 (q, J = 7.1 Hz, 2H), 2.93 (q, J = 7.4 Hz, 2H), 2.60 and 2.49 (s both, 3:3H), 1.66 (dt, J = 15.1, 7.4 Hz, 2H), 1.42 (dd, J = 14.9, 7.4 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.1, 161.9, 152.4, 145.7, 140.0, 125.3, 61.1, 36.0, 31.6, 30.6, 22.1, 15.7, 14.5, and 13.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{21}O_3S_2$, 301.0932; found, 301.0932.

Ethyl 4-Acetyl-5-(benzylthio)-3-methylthiophene-2-carboxylate ***(3d)***. Following the general procedure, compound **3d** was obtained

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by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 75 mg, 75%; yellow solid, mp 46−47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−7.25 (m, 5H), 4.33 (q, J = 7.1 Hz, 2H), 4.18 (s, 2H), 2.66 and 2.49 (s both, 3:3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.3, 161.9, 150.3, 145.3, 141.0, 135.4, 126.2, 129.3, 128.9, 128.0, 61.2, 41.3, 31.5, 15.7, and 14.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{19}O_3S_2$, 335.0776; found, 335.0765.

*2-Ethyl 4-Methyl 3-Methyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3e**).* Following the general procedure, compound **3e** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 51 mg, 75%; yellow solid, mp 96−97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25 (q, J = 7.1 Hz, 2H), 3.81, 2.66, and 2.51 (s both, 3:3:3H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.2, 161.8, 158.6, 148.6, 126.8, 123.8, 61.0, 51.6, 18.0, 15.6, and 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{11}H_{15}O_4S_2$, 275.0412; found, 275.0419.

*Diethyl 3-Methyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3f**).* Following the general procedure, compound **3f** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 65 mg, 75%; yellow solid, mp 88−89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.27 (m, 4H), 2.67, and 2.51 (s both, 3:3H), 1.31 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.7, 161.8, 158.3, 148.7, 127.1, 123.8, 61.0, 60.9, 18.0, 15.6, 14.4, and 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{12}H_{17}O_4S_2$, 289.0568; found, 289.0568.

*2-Ethyl 4-Isopropyl 3-Methyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3g**).* Following the general procedure, compound **3g** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 70 mg, 77%; yellow solid, mp 77−78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.32−5.15 (m, 1H), 4.31 (q, J = 7.1 Hz, 2H), 2.74, and 2.58 (s both, 3:3H), 1.36 (m, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.3, 162.0, 158.0, 148.7, 127.5, 123.9, 68.9, 61.0, 22.2, 18.1, 15.7, and 14.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{13}H_{19}O_4S_2$, 303.0725; found, 303.0725.

*4-tert-Butyl 2-Ethyl 3-Methyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3h**).* Following the general procedure, compound **3h** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 68 mg, 72%; yellow solid, mp 86−87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (q, J = 7.1 Hz, 2H), 2.65 and 2.50 (s both, 3:3H), 1.52 (s, 9H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.9, 161.9, 157.0, 148.6, 128.7, 123.7, 82.3, 60.9, 28.5, 18.0, 15.7, and 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{21}O_4S_2$, 317.0881; found, 317.0875.

*4-Benzyl 2-Ethyl 3-Methyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3i**).* Following the general procedure, compound **3i** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 80 mg, 76%; yellow solid, mp 89−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.37 (m, 2H), 6.33−6.21 (m, 3H), 4.27 (s, 2H), 3.23 (q, J = 7.1 Hz, 2H), 1.66 and 1.48 (s both, 3:3H), 0.28 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.5, 161.8, 158.9, 148.7, 135.8, 126.7, 123.9, 128.7, 128.5, 128.4, 66.7, 61.0, 18.1, 15.8, and 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{19}O_4S_2$, 351.0725; found, 351.0724.

*Ethyl 3-Methyl-5-(methylthio)-4-(phenylcarbamoyl)thiophene-2-carboxylate (**3j**).* Following the general procedure, compound **3j** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 81 mg, 80%; yellow solid, mp 99−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (br, 1H), 7.56 (m, 2H), 7.28 (m, 2H), 7.08 (m, 1H), 4.24 (q, J = 7.1 Hz, 2H), 2.52 and 2.49 (s both, 3:3H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.2, 161.9, 146.1, 145.9, 137.7, 136.6, 126.4, 129.2, 124.9, 120.1, 61.2, 19.2, 14.9, and 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{18}NO_3S_2$, 336.0728; found, 336.0728.

*Ethyl 4-(Diethylcarbamoyl)-3-methyl-5-(methylthio)thiophene-2-carboxylate (**3k**).* Following the general procedure, compound **3k** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 68 mg, 72%; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (q, J = 7.1 Hz, 2H), 3.51 (m, 2H), 3.21−3.00 (m, 2H), 2.47 and 2.34 (s both, 3:3H), 1.29 (t, J = 7.1 Hz, 3H), 1.19 (t, J = 7.1 Hz, 3H), 1.01 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 165.3, 161.8, 143.9, 140.4, 139.7, 127.2, 60.9, 42.8, 39.1, 19.5, 14.4, 14.4, and 12.9. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{22}NO_3S_2$, 316.1041; found, 316.1041.

*Diethyl 3-Ethyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3l**).* Following the general procedure, compound **3l** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 70 mg, 77%; yellow solid, mp 74−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (m, 4H), 3.28 (q, J = 7.3 Hz, 2H), 2.58 (s, 3H), 1.38 (m, 6H), 1.18 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.6, 161.5, 158.6, 155.0, 126.6, 123.6, 61.0, 61.0, 22.2, 18.1, 15.0, 14.5, and 14.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{13}H_{19}O_4S_2$, 303.0725; found, 303.0725.

*Diethyl 5-(Methylthio)-3-propylthiophene-2,4-dicarboxylate (**3m**).* Following the general procedure, compound **3m** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 72 mg, 76%; yellow solid, mp 70−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.33 (m, 4H), 3.34−3.17 (m, 2H), 2.58 (s, 3H), 1.57 (m, 2H), 1.38 (m, 6H), 0.97 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.7, 161.7, 158.6, 153.5, 126.7, 123.9, 61.0, 61.0, 30.6, 24.2, 18.1, 14.4, and 14.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{21}O_4S_2$ [M + H]$^+$, 317.0881; found, 317.0881.

*Diethyl 3-Cyclopropyl-5-(methylthio)thiophene-2,4-dicarboxylate (**3n**).* Following the general procedure, compound **3n** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 71 mg, 75%; yellow solid, mp 104−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (m, 4H), 2.56 (s, 3H), 2.05 (m, 1H), 1.37 (m, 6H), 1.05−0.94 (m, 2H), 0.51 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.0, 161.2, 154.0, 151.7, 130.5, 127.8, 61.1, 18.2, 14.4, 14.4, 11.7, and 9.0. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{14}H_{19}O_4S_2$, 315.0725; found, 315.0726.

*Diethyl 5-(Methylthio)-3-phenylthiophene-2,4-dicarboxylate (**3o**).* Following the general procedure, compound **3o** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 54 mg, 51%; yellow solid, mp 74−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (m, 3H), 7.19 (m, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.99 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 1.09 (t, J = 7.1 Hz, 3H), 0.86 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.4, 161.1, 157.7, 149.7, 136.5, 127.6, 126.0, 128.7, 127.5, 127.3, 61.1, 60.6, 18.2, 14.0, and 13.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{19}O_4S_2$, 351.0725; found, 351.0725.

*Diethyl 5-(Methylthio)-3-(p-tolyl)thiophene-2,4-dicarboxylate (**3p**).* Following the general procedure, compound **3p** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 86 mg, 79%; yellow solid, mp 80−81 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (d, J = 7.9 Hz, 2H), 7.08 (d, J = 7.9 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 4.02 (q, J = 7.1 Hz, 2H), 2.65 and 2.38 (s both, 3:3H), 1.14 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.4, 161.0, 157.2, 150.2, 137.1, 133.3, 127.8, 125.6, 128.5, 128.1, 61.0, 60.7, 21.5, 18.2, 14.1, and 13.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{21}O_4S_2$, 365.0881; found, 365.0881.

*Diethyl 3-(2-Methoxyphenyl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3q**).* Following the general procedure, compound **3q** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 71 mg, 62%; yellow solid, mp 71−72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 1H), 7.09 (m, 1H), 7.03−6.83 (m, 2H), 4.14 (m, 2H), 4.09−3.97 (m, 2H), 3.74 and 2.68 (s both, 3:3H), 1.12 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.4, 161.1, 157.3, 156.8, 146.2, 127.6, 126.1, 125.8, 130.1, 129.1, 119.9, 110.3, 60.9, 60.4, 55.6, 18.1, 14.0, and 13.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{21}O_5S_2$, 381.0830; found, 381.0830.

*Diethyl 3-(3-Methoxyphenyl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3r**).* Following the general procedure, compound **3r** was obtained by column chromatography on silica gel [eluent:

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petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 83 mg, 73%; yellow solid, mp 79−80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, 1H), 691 (m, 1H), 6.81 (m, 1H), 6.76 (m, 1H), 4.14 (q, J = 7.1 Hz, 2H), 4.03 (q, J = 7.1 Hz, 2H), 3.81 and 2.67 (s both, 3:3H), 1.13 (t, J = 7.1 Hz, 3H), 0.92 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.4, 161.0, 158.9, 157.6, 149.3, 137.7, 127.6, 126.0, 128.3, 121.3, 114.5, 113.1, 61.1, 60.6, 55.3, 18.2, 14.0, and 13.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}O_5S_2$, 381.0830; found, 381.0830.

*Diethyl 3-(4-Methoxyphenyl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3s**).* Following the general procedure, compound **3s** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 92 mg, 81%; yellow solid, mp 82−83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20−7.06 (m, 2H), 6.94−6.83 (m, 2H), 4.14 (q, J = 7.1 Hz, 2H), 4.03 (q, J = 7.1 Hz, 2H), 3.83 and 2.64 (s both, 3:3H), 1.15 (t, J = 7.1 Hz, 3H), 0.95 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.5, 161.1, 159.2, 157.1, 149.7, 128.5, 128.0, 125.8, 130.0, 112.9, 61.1, 60.7, 55.4, 18.2, 14.1, and 13.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{21}O_5S_2$, 381.0830; found, 381.0832.

*Diethyl 3-(4-Fluorophenyl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3t**).* Following the general procedure, compound **3t** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 50 mg, 45%; yellow solid, mp 59−60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 (m, 2H), 7.05 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 4.02 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H), 0.93 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.7, 162.2 (d, J = 224.7 Hz), 161.3, 158.1, 148.6, 132.4 (d, J = 35.2 Hz), 127.4, 126.2, 130.4 (d, J = 81.4 Hz), 114.3 (d, J = 214.6 Hz), 61.2, 60.7, 18.2, 14.1, and 13.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}FO_4S_2$, 369.0631; found, 369.0631.

*Diethyl 3-(4-Chlorophenyl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3u**).* Following the general procedure, compound **3u** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 65 mg, 56%; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16 and 7.05 (m each, 2:2H), 4.12 (q, J = 7.1 Hz, 2H), 4.02 (q, J = 7.1 Hz, 2H), 2.65 (s both, 3H), 1.13 (t, J = 7.1 Hz, 3H), 0.93 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.1, 160.9, 158.4, 148.4, 135.5, 135.0, 133.5, 121.6, 130.5, 130.4, 130.1, 127.6, 61.2, 60.8, 18.2, 14.0, and 13.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}ClO_4S_2$, 385.0335; found, 385.0335.

*Diethyl 3-(4-Bromophenyl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3v**).* Following the general procedure, compound **3v** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 70 mg, 54%; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (m, 1H), 7.34 (m, 1H), 7.19−7.03 (m, 2H), 4.12 (q, J = 7.1 Hz, 2H), 4.02 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H), 0.93 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.1, 160.9, 159.2, 158.4, 148.3, 135.5, 135.0, 133.5, 121.6, 130.5, 130.4, 130.1, 127.6, 61.2, 60.8, 18.2, 14.0, and 13.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{18}BrO_4S_2$, 428.9830; found, 428.9832.

*Diethyl 5-(Methylthio)-3-(naphthalen-2-yl)thiophene-2,4-dicarboxylate (**3x**).* Following the general procedure, compound **3x** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 78 mg, 65%; yellow solid, mp 102−103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (m, 3H), 7.68 (s, 1H), 7.58−7.44 (m, 2H), 7.38 (m, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.95 (q, J = 7.1 Hz, 2H), 2.70 (s, 3H), 1.02 (t, J = 7.1 Hz, 3H), 0.69 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.4, 161.1, 157.8, 149.5, 134.0, 132.9, 132.8, 127.8, 126.2, 128.1, 127.8, 127.5, 127.3, 126.6, 126.0, 125.9, 61.1, 60.6, 18.2, 14.0, and 13.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{21}O_4S_2$, 401.0881; found, 401.0886.

*Diethyl 3-(Furan-2-yl)-5-(methylthio)thiophene-2,4-dicarboxylate (**3y**).* Following the general procedure, compound **3y** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 73 mg, 71%; yellow solid, mp 78−79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (m, 1H), 6.50 (m, 2H), 4.19 (m, 4H), 2.62 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.2, 160.6, 156.3, 146.1, 137.4, 128.3, 128.2, 142.0, 110.9, 110.9, 61.4, 61.0, 18.2, 14.2, and 14.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{17}O_5S_2$, 341.0517; found, 341.0517.

*Diethyl 5′-(Methylthio)-[2,3′-bithiophene]-2′,4′-dicarboxylate (**3z**).* Following the general procedure, compound **3z** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 80 mg, 75%; yellow solid, mp 86−87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (dd, J = 5.1, 1.0 Hz, 1H), 7.03 (dd, J = 5.0, 3.5 Hz, 1H), 6.91 (dd, J = 3.5, 1.0 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 4.08 (q, J = 7.1 Hz, 2H), 2.64 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.2, 160.7, 157.1, 141.4, 135.7, 128.5, 128.2, 127.5, 126.3, 125.8, 61.3, 60.8, 18.1, 14.1, and 13.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{17}O_4S_3$, 357.0289; found, 357.0281.

*Methyl 4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carboxylate (**5a**).* Following the general procedure, compound **5a** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 60 mg, 82%; yellow solid, mp 114−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86, 2.74, 2.57, and 2.56 (s both, 3:3:3:3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.0, 162.2, 157.1, 146.4, 137.7, 124.0, 52.0, 31.3, 18.6, and 16.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_{13}O_3S_2$, 245.0306; found, 245.0301.

*Propyl 4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carboxylate (**5b**).* Following the general procedure, compound **5b** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 58 mg, 71%; yellow solid, mp 95−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.22 (t, J = 6.6 Hz, 2H), 2.72, 2.56, and 2.54 (s both, 3:3:3H), 1.75 (dd, J = 14.2, 7.0 Hz, 2H), 1.00 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.0, 162.0, 156.7, 146.0, 137.9, 124.6, 66.6, 31.3, 22.2, 18.6, 15.9, and 10.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{17}O_3S_2$, 273.0619; found, 273.0619.

*Isopropyl 4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carboxylate (**5c**).* Following the general procedure, compound **5c** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 61 mg, 75%; yellow solid, mp 95−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.18 (m, 1H), 2.72, 2.57, 2.54, 1.35, and 1.33 (s both, 3:3:3:3:3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.2, 161.6, 156.5, 145.9, 138.0, 125.2, 68.8, 31.4, 22.1, 18.7, and 16.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_{17}O_3S_2$, 273.0619; found, 273.0619.

*tert-Butyl 4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carboxylate (**5d**).* Following the general procedure, compound **5d** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 62 mg, 72%; yellow solid, mp 117−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.68, 2.55, and 2.53 (s both, 3:3:3H), 1.55 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.2, 161.3, 155.8, 145.2, 138.0, 126.4, 82.2, 31.4, 28.4, 18.7, and 15.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{19}O_3S_2$, 287.0776; found, 287.0778.

*Benzyl 4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carboxylate (**5e**).* Following the general procedure, compound **5e** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 75 mg, 78%; yellow solid, mp 82−83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (m, 5H), 5.31 (s, 2H), 2.74, 2.56, and 2.55 (s both, 3:3:3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 195.1, 161.7, 157.2, 146.7, 138.0, 135.9, 124.1, 128.8, 128.4, 128.2, 66.7, 31.4, 18.7, and 16.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{17}O_3S_2$, 321.0619; found, 321.0610.

*4-Acetyl-3-methyl-5-(methylthio)thiophene-2-carbonitrile (**5f**).* Following the general procedure, compound **5f** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 46 mg, 72%; yellow solid, mp 110−111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60, 2.58, and 2.55 (s both, 3:3:3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 193.3, 159.8, 150.0, 135.0, 113.7, 103.6, 31.1, 18.9, and 17.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_9H_{10}NOS_2$, 212.0204; found, 212.0203.

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*Ethyl 5-Cyano-4-methyl-2-(methylthio)thiophene-3-carboxylate (**5g**).* Following the general procedure, compound **5g** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 55 mg, 76%; yellow solid, mp 117−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.35 (q, J = 7.1 Hz, 2H), 2.58, and 2.56 (s both, 3:3H), 1.38 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.7, 160.4, 152.3, 125.2, 113.7, 102.5, 61.3, 18.2, 17.4, and 14.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{10}H_{12}NO_2S_2$, 242.0309; found, 242.0309.

Synthesis of Thieno[2,3-*b*]thiophenes 4. *Typical Procedure for the Synthesis of Thieno[2,3-b]thiophenes **4**—Synthesis of Diethyl 3,4-Dimethylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4a**).* A mixture of 3-(bis(methylthio)methylene)pentane-2,4-dione (**1a**) (61 mg, 0.3 mmol), ethyl diazoacetate (**2a**) (136 mg, 1.2 mmol), $CuCl_2$ (4 mg, 0.03 mmol) in PhMe/MeCN (2 mL, v/v = 1:1) was stirred at 60 °C (oil bath) for 12 h under a N_2 atmosphere. After **1a** was completely consumed by TLC monitoring on silica gel, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/ethyl acetate = 50:1, v/v], affording **4a** (80 mg, 85%) as a pale yellow solid. mp 134−135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.35 (q, J = 7.1 Hz, 4H), 2.87 (s, 6H), 1.39 (t, J = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.7, 147.6, 145.1, 141.0, 129.9, 61.2, 14.5, and 14.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{14}H_{17}O_4S_2$, 313.0568; found, 313.0575.

*Diethyl 3-Isobutyl-4-methylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4b**).* Following the general procedure, compound **4b** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 83 mg, 78%; yellow solid, mp 121−122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.31 (q, J = 7.1 Hz, 4H), 3.21 (d, J = 7.2 Hz, 2H), 2.79 (s, 3H), 1.89 (m, 1H), 1.35 (m, 6H), 0.93 (d, J = 6.7 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.3, 162.2, 146.9, 145.3, 145.0, 140.5, 130.3, 129.9, 61.2, 60.9, 35.2, 30.8, 22.0, 14.3, 14.3, 14.1, and 14.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{23}O_4S_2$, 355.1038; found, 355.1040.

*Diethyl 3-Butyl-4-methylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4c**).* Following the general procedure, compound **4c** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 73 mg, 78%; yellow solid, mp 108−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.32 (q, J = 7.1 Hz, 4H), 3.33−3.16 (m, 2H), 2.81 (s, 3H), 1.65−1.53 (m, 2H), 1.46 (m, 2H), 1.37 (t, J = 7.2 Hz, 6H), 0.95 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.4, 162.1, 146.7, 146.1, 145.4, 140.4, 129.8, 129.6, 61.0, 61.0, 33.3, 27.3, 22.9, 14.2, 13.8, and 13.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{23}O_4S_2$, 355.1038; found, 355.1038.

*Diethyl 3-Cyclopropyl-4-methylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4d**).* Following the general procedure, compound **4d** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 77 mg, 76%; yellow solid, mp 111−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (m, 4H), 2.94 (s, 3H), 2.01 (m, 1H), 1.37 (m, 6H), 1.15 (m, 2H), 0.68 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.7, 161.9, 148.6, 144.9, 144.4, 141.3, 133.4, 129.9, 61.3, 61.1, 15.1, 14.4, 14.4, 10.1, and 10.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{19}O_4S_2$, 339.0725; found, 339.0727.

*Diethyl 3-Cyclobutyl-4-methylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4e**).* Following the general procedure, compound **4e** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 82 mg, 78%; yellow solid, mp 114−115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.51 (m, 1H), 4.34 (m, 4H), 2.89 (s, 3H), 2.72−2.56 (m, 2H), 2.41−2.27 (m, 2H), 2.12−1.89 (m, 2H), 1.38 (m both, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.6, 162.4, 147.6, 147.2, 144.7, 140.8, 131.0, 129.9, 61.5, 61.1, 33.9, 29.3, 17.8, 15.5, 14.4, and 14.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{21}O_4S_2$, 353.0881; found, 353.0888.

*Diethyl 3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4f**).* Following the general procedure, compound **4f** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 90 mg, 80%; yellow solid, mp 111−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 3H), 7.21 (m, 2H), 4.24 (q, J = 7.1 Hz, 2H), 4.06 (q, J = 7.1 Hz, 2H), 2.02 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 162.5, 161.8, 146.9, 144.8, 143.0, 141.2, 134.8, 132.1, 130.4, 129.1, 128.2, 128.0, 61.2, 14.4, 14.1, and 14.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}O_4S_2$, 375.0725; found, 375.0725.

*Diethyl 3,4-Diphenylthieno[2,3-b]thiophene-2,5-dicarboxylate (**4g**).* Following the general procedure, compound **4g** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 109 mg, 83%; yellow solid, mp 207−208 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.96 (m, 2H), 6.86 (m, 2H), 6.76 (m, 4H), 4.07 (q, J = 7.1 Hz, 4H), 1.03 (t, J = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.7, 145.9, 144.9, 143.4, 133.0, 132.2, 129.2, 127.2, 127.0, 61.2, and 14.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{21}O_4S_2$, 437.0881; found, 437.0878.

Carbene Insertion into the C−S Bond. *Typical Procedure for the Preparation of Ethyl 4-Acetyl-2,3-bis(methylthio)-5-oxo-2-phenylhex-3-enoate (**8**).* A mixture of 3-(bis(methylthio)methylene)-pentane-2,4-dione (**1a**) (61 mg, 0.3 mmol), ethyl 2-diazo-2-phenylacetate (**2j**) (114 mg, 0.6 mmol), and $CuCl_2$ (4 mg, 0.03 mmol) in PhMe/MeCN (2 mL, v/v = 1:1) was stirred at 60 °C (oil bath) for 12 h under a N_2 atmosphere. After **1a** was completely consumed by TLC monitoring on silica gel, all of the volatiles were evaporated under reduced pressure. The resultant residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/ethyl acetate = 50:1, v/v], affording **8** (88 mg, 80%) as a white solid. mp 109−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 and 7.33 (m each, 2:3H), 4.30−4.11 (m, 2H), 2.67, 2.14, 2.07, and 2.03 (s both, 3:3:3:3H), 1.27 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 200.0, 197.5, 168.8, 152.5, 145.5, 137.3, 129.8, 127.9, 65.8, 62.1, 30.5, 29.9, 22.4, 15.5, and 14.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{23}O_4S_2$, 367.1038; found, 367.1038.

Gram-Scale Synthesis of 3a. *Typical Procedure for the Gram-Scale Synthesis of Ethyl 4-Acetyl-3-methyl-5-(methylthio)-thiophene-2-carboxylate (**3a**).* Under a nitrogen atmosphere, a mixture of **1a** (1.22 g, 6 mmol), ethyl diazoacetate (**2a**) (1.36 g, 12 mmol), $CuCl_2$ (80 mg, 0.6 mmol) in PhMe/MeCN (40 mL, v/v = 1:1) was stirred at 60 °C (oil bath) for 12 h. After cooled to ambient temperature, CH_2Cl_2 (10 mL) was added, and the resultant mixture was filtered through a short pad of Celite, followed by rinsing with 10 mL CH_2Cl_2. The filtrate evaporated all the volatiles under reduced pressure. The resulting residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/ethyl acetate = 50:1, v/v] to afford **3a** as a yellow solid (1.24 g, 80%).

Derivatization of Compounds 3. *Typical Procedure for the Reaction of **3** with Phenylboronic Acid—Synthesis of Ethyl 4-Acetyl-3-methyl-5-phenylthiophene-2-carboxylate (**10a**).* Under a nitrogen atmosphere, a mixture of **3a** (78 mg, 0.3 mmol), phenylboronic acid (78 mg, 0.60 mmol), $Pd(PPh_3)_4$ (26 mg, 0.022 mmol), CuI (114 mg, 0.60 mmol), and Cs_2CO_3 (196 mg, 0.60 mmol) in 2 mL of 1,4-dioxane was stirred at 80 °C (oil bath) for 24 h. After cooled to ambient temperature, CH_2Cl_2 (10 mL) was added, and the resultant mixture was filtered through a short pad of Celite, followed by rinsing with 10 mL CH_2Cl_2. The filtrate evaporated all the volatiles under reduced pressure. The resulting residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/ethyl acetate = 50:1, v/v] to afford **10a** as a yellow solid (70 mg, 81%). mp 53−54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.28 (m, 5H), 4.28 (q, J = 7.1 Hz, 2H), 2.48 and 2.01 (s both, 3:3H), 1.30 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 200.8, 162.5, 148.7, 145.1, 141.5, 133.0, 129.6, 129.2, 129.0, 127.2, 61.1, 31.9, 14.6, and 14.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{17}O_3S$, 289.0898; found, 289.0895.

*Diethyl 3-Methyl-5-phenylthiophene-2,4-dicarboxylate (**10b**).* Following the general procedure, compound **10b** was obtained by column chromatography on silica gel [eluent: petroleum ether (60−90 °C)/EtOAc = 50:1, v/v]. 79 mg, 83%; yellow solid, mp 64−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−7.28 (m, 5H), 4.28 (q, J = 7.1 Hz, 2H), 4.10 (q, J = 7.1 Hz, 2H), 2.59 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ

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164.9, 162.3, 151.0, 146.0, 133.2, 131.9, 129.0, 128.8, 128.4, 126.8, 61.0, 61.0, 14.7, 14.3, and 13.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{19}O_4S$, 319.1004; found, 319.1006.

*Typical Procedure for the Synthesis of Ethyl 4-Acetyl-3-methyl-5-(methylsulfonyl)thiophene-2-carboxylate (**11**).* A mixture of **3a** (78 mg, 0.3 mmol) and *m*-CPBA (156 mg, 0.9 mmol) in 3 mL of CH_2Cl_2 was stirred at room temperature for 1 h. The resulting mixture was poured into 10 mL saturated aqueous Na_2CO_3 and extracted with dichloromethane (3 × 5 mL). The combined organic phase was washed with water (2 × 5 mL), dried over anhydrous Na_2SO_4, and filtered, and it evaporated all the volatiles under reduced pressure. The resultant residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/EtOAc = 5/1, v/v] to afford **11** (78 mg, 90%) as a yellow solid. mp 81−82 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.34 (q, J = 7.1 Hz, 2H), 3.41, 2.55, and 2.44 (s both, 3:3:3H), 1.32 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6): δ 200.4, 161.1, 148.4, 142.7, 141.1, 133.2, 62.3, 46.2, 32.4, 14.4, and 14.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{15}O_5S_2$, 291.0361; found, 291.0360.

Control Experiments. *TEMPO or BHT-Trapping Radical Experiments.* Under a nitrogen atmosphere, a mixture of 3-(bis(methylthio)methylene)pentane-2,4-dione (**1a**) (61 mg, 0.3 mmol), ethyl diazoacetate (**2a**) (68 mg, 0.6 mmol), $CuCl_2$ (4 mg, 0.03 mmol), and TEMPO or BHT (0.6 mmol) in PhMe/MeCN (2 mL, v/v = 1:1) was stirred at 60 °C (oil bath) for 12 h. In a fashion similar to the synthesis of compound **3a**, the reaction mixture was worked up to give **3a** in 65 and 73% yields, respectively. These radical-trapping reagents did not obviously inhibit the annulation reaction, which excludes a radical pathway.

*Synthesis of **4a** from **3a**.* A mixture of ethyl 4-acetyl-3-methyl-5-phenylthiophene-2-carboxylate (**3a**) (61 mg, 0.3 mmol), ethyl diazoacetate (**2a**) (68 mg, 0.6 mmol), $CuCl_2$ (4 mg, 0.03 mmol) in PhMe/MeCN (2 mL, v/v = 1:1) was stirred at 60 °C (oil bath) for 12 h under a nitrogen atmosphere. All of the volatiles were evaporated under reduced pressure. The resultant residue was purified by silica gel column chromatography [eluent: petroleum ether (60−90 °C)/ethyl acetate = 50:1, v/v], affording **4a** (50 mg, 58%) as a pale yellow solid and a portion of **3a** (13 mg, 21%) was recovered.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.9b02982.

NMR spectra of the substrates and products (PDF)

X-ray single crystal crystallographic data for compound **3a** (CIF)

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Notes

The authors declare no competing financial interest.

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