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Efficient synthesis of benzothiophenes by [4+1] cycloaddition of 2-mercaptobenzaldehyde derivatives with isocyanides

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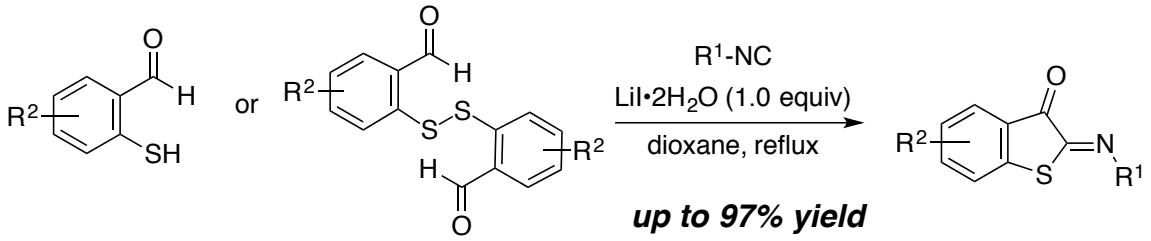
O
H
R2
SH
or
O
H
R2
S
S
H
O
R2
R1-NC
LiI•2H2O (1.0 equiv)
dioxane, reflux
up to 97% yield
O
R2
S
N
R1

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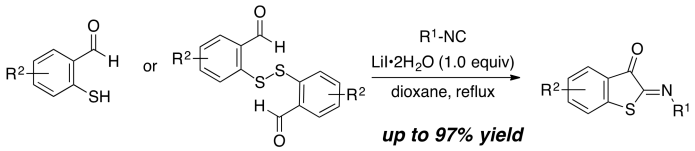

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ABSTRACT

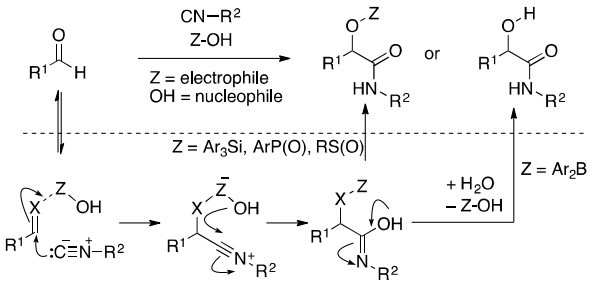
We developed a [4+1] cycloaddition reaction of isocyanides with 2-mercaptobenzaldehydes and/or their disulfide derivatives, promoted by LiI·2H$_2$O, to afford benzothiophene derivatives in moderate to good yields. Isocyanides, 2-mercaptobenzaldehydes and disulfide derivatives of various types were used successfully in the reaction.

1. Introduction

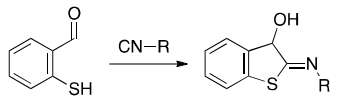
The Passerini reaction is one of the oldest multicomponent reactions, and has been found to be useful in the construction of multifunctional α-acyloxyamides.[1] It is probably the best method for producing α-acyloxyamide in a highly convergent manner, and a large number of biologically active substances can be accessed quickly in this way.[2] The Passerini reaction generally requires a carboxylic acid, which activates an aldehyde and traps a nitrilium cation to form an acyloxylated intermediate; subsequent acyl transfer leads to the corresponding α-acyloxy amides. The requirement for a carboxylic acid limits the application of this reaction to the construction of a particular range of molecules. To overcome this limitation, we reasoned that a compound Z–X, composed of an electrophile Z and a nucleophilic group X, could essentially perform the same function as the carboxylic acid in the Passserini reaction. Based on this hypothesis, we previously developed *O*-silylative, *O*-phosphinative, and *O*-sulfinative Passerini reactions as well as borinic acid-catalyzed α-addition of isocyanide (Scheme 1).[3] In addition, we expanded this concept to intramolecular trapping of a nitrilium intermediate in an Ugi-type reaction. Thus, when a molecule contains both an electrophile (such as C=N) and a potential nucleophilic group (Nu$^-$), intramolecular trapping of the nitrilium intermediate should be readily achieved in a manner similar to the intermolecular version of the reaction.[4] Based on these investigations, we focused on the utility of 2-mercaptobenzaldehyde for effective synthesis of benzothiophene derivatives (Scheme 2).

Benzothiophene derivatives have been the subject of much attention and are frequently found in pharmaceuticals.[5] They are also useful as building blocks in materials science.[6] Owing to these unique properties, various methods of synthesizing benzothiophene derivatives have been investigated, and a number of combinatorial techniques have recently been developed, including one using Friedel-Crafts type aroylation,[7] and an electrophilic cyclization.[8] These methods can only be used with a limited number of substrates; however, benzothiophene derivatives are not readily accessed through existing preparative methods. To address this deficiency, we herein report [4+1] cycloaddition of isocyanides to 2-mercaptobenzaldehyde derivatives promoted by a lithium iodide to afford various benzothiophene derivatives.

Scheme 1 *O*-Silylative Passerini reaction, *O*-phosphinative Passerini reaction, *O*-sulfinative Passerini reaction, and borinic-acid-catalyzed α-addition of an isocyanide.



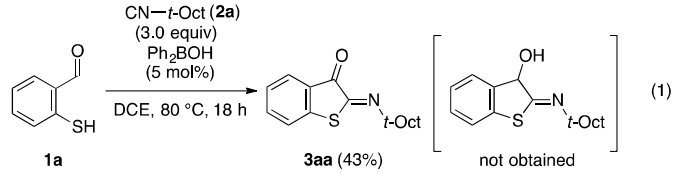
Scheme 2 Working hypothesis



[4+1] cycloaddition?

2. Results and Discussion

First, we examined whether 2-mercaptobenzaldehyde (**1a**) was capable of participating in a Passerini-type reaction to afford the corresponding benzothiophene derivatives. For this, we used a combination of 2-mercaptobenzaldehyde (**1a**) and *tert*-octyl isocyanide (**2a**, 3.0 equiv) in the presence of a catalytic amount of phenylborinic acid, which has been shown to be useful in catalyzing α-addition of isocyanide,[3d] in dichloroethane (DCE) at 80 °C. Once the starting material had been consumed after 18 h, the reaction mixture was purified and characterized. ^{1}H-NMR, ^{13}C-NMR, IR and HRMS spectroscopies revealed that the structure of the product was different from what was expected: the hydroxy group had been oxidized during the reaction, giving the benzothiophene-3(*2H*)-one derivative **3aa** (eq 1).



(1)

Based on these results, we optimized the reaction conditions (Table 1). When 2-mercaptobenzaldehyde (**1a**) was refluxed in dioxane with *tert*-octyl isocyanide (**2a**) (1.5 equiv), the starting material **1a** was consumed after 1 h and the desired **3aa** was obtained in 62% yield (entry 1). Chlorotrimethylsilane (TMSCl) and diphenylborinic acid, which are useful Lewis acids for the isocyanide-based reactions,[3d, 4d] were not effective in this reaction, affording the product in lower yields (entries 2 and 3). LiI·2H$_2$O was found to be a good promotor in this reaction system, giving the product in 72% yield (entry 4). Anhydrous LiI was less effective (entry 5), but NaI and KI were relatively effective (entries 6 and 7). In the case of LiBr and LiCl, the reactions proceeded at much lower rate, affording the product in 60% and 46% yields, respectively (entries 8 and 9). Since it was evident that the solvent influenced the efficiency of the reaction, we next examined LiI·2H$_2$O-promoted [4+1] cycloaddition using different solvents. When toluene was used as a solvent, the reaction proceeded smoothly to afford the product **3aa** in 74% yield, although the reaction system has slightly complicated compared with the use of dioxane as a solvent (entry 10). Dichloroethane (DCE) and propionitrile were not particularly effective, affording the product only in moderate yields (entries 11 and 12).

Next, we attempted to expand the range of isocyanides **2** and 2-mercaptobenzaldehyde derivatives **1** that can be used in the Passerini-type [4+1] cycloaddition reaction with LiI·2H$_2$O as a promoter, as detailed in Table 2. The reaction of aliphatic isocyanides **2a** and **2b** (R^2 = *t*-Oct and *t*-Bu) with **1a** in the presence of LiI·2H$_2$O gave the products in good yields (entries 1 and 2), while the secondary and primary aliphatic isocyanides **2c** and **2d** were not applicable to the reaction (entries 3 and 4). However, isocyanides **2e**–**2h** reacted with **1a** to afford the desired products (entries 5–8). We also investigated substituted 2-mercaptobenzaldehyde derivatives bearing an electron-donating or an electron-withdrawing group on the aromatic ring (entries 9–11). The reactions proceeded to afford the corresponding benzothiophene derivatives **3ba–3da** in moderate to good yields. The structure of the product was confirmed by X-ray crystallographic analysis of a single crystal of **3af**. The structure of **3af** is shown in Figure 1.

Figure 1 X-ray structure of **3af**

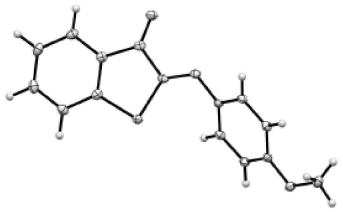
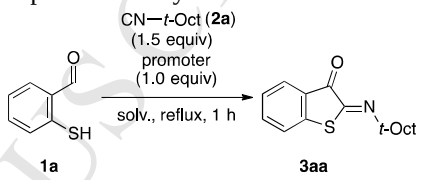


Table 1 Results of Passerini-type [4+1] cycloaddition reaction using 2-mercaptobenzaldehyde under various conditions.



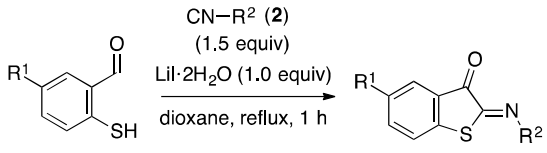
Entry	Promoter	Solv.	Yield / %
1	-	dioxane	62
2	TMSCl	dioxane	22
3	Ph_2BOH	dioxane	48
4	LiI·2H$_2$O	dioxane	72
5	LiI	dioxane	41
6	NaI	dioxane	69
7	KI	dioxane	64
8	LiBr	dioxane	60
9	LiCl	dioxane	46
10	LiI·2H$_2$O	toluene	74
11	LiI·2H$_2$O	DCE	50
12	LiI·2H$_2$O	propionitrile	59

As mentioned above, 2-mercaptobenzaldehyde derivatives **1** were good substrates for [4+1] cycloaddition of isocyanides, but these have an unpleasant smell, are unstable, and are difficult to be isolated in good yields. Therefore, we decided to use the corresponding disulfide compounds **4**, which are easier to store, as substrates.

We examined whether the disulfide derivative **4a** was capable of participating in a Passerini-type reaction with *t*-octyl isocyanide (**2a**) in the presence of $MgCl_2$, $ZnCl_2$ and other metal halides in refluxing toluene (Table 3). Although trace amounts of product were observed in the absence of any promoter, the desired **3aa** was obtained in low yield in the presence of MgI_2, ZnI_2, and CuI (entries 1–4). When LiI·2H$_2$O was used as a promoter, the substrate was consumed in 3 h, affording the

product in 84% yield (entry 5). Anhydrous LiI was also effective in this reaction, although NaI and KI were not (entries 6–8). When LiBr or LiCl was used, the reaction proceeded very slowly to afford the product in 70% or 17% yield, respectively, after 48 h (entries 9 and 10). We found that NIS, NBS, and NCS were not effective as promoters (entries 11–13). The reaction proceeded efficiently in toluene and dioxane to afford **3aa** in high yields (entries 6 and 14). The use of DMF, dichloroethane (DCE), or propionitrile as a solvent was less effective, resulting in the formation of **3aa** in yields of 20, 37, and 66%, respectively (entries 15–17).

Table 2 Range of isocyanides and 2-mercaptobenzaldehyde derivatives applicable to the Passerini-type [4+1] cycloaddition reaction.



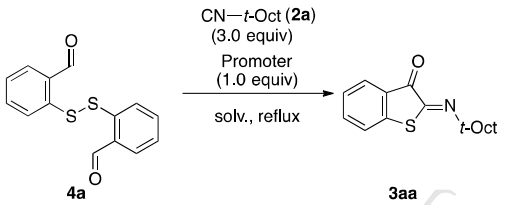
1 **3**

Entry	R^1	R^2	Yield / %
1	H (**1a**)	*t*-Oct (**2a**)	72 (**3aa**)
2	H (**1a**)	*t*-Bu (**2b**)	54 (**3ab**)
3	H (**1a**)	*c*-Hex (**2c**)	-[a]
4	H (**1a**)	Bn (**2d**)	-[a]
5	H (**1a**)	Ph (**2e**)	51 (**3ae**)
6[b]	H (**1a**)	4-$MeOC_6H_4$ (**2f**)	27 (**3af**)
7	H (**1a**)	4-$Me_2NC_6H_4$ (**2g**)	66 (**3ag**)
8	H (**1a**)	4-BrC_6H_4 (**2h**)	31 (**3ah**)
9	*t*-Bu (**1b**)	*t*-Oct (**2a**)	77 (**3ba**)
10	MeO (**1c**)	*t*-Oct (**2a**)	47 (**3ca**)
11	Cl (**1d**)	*t*-Oct (**2a**)	51 (**3da**)

[a] Complex mixture. [b] The reaction was quenched after 20 h.

We subsequently attempted to expand the range of isocyanides and disulfide derivatives that could be used in the [4+1] cycloaddition reaction, using LiI·$2H_2O$ in all cases, as detailed in Table 4. In these reactions, optimal molar quantities of disulfide derivatives **4a**, **4e**, and **4c** (1.0 equiv) and isocyanides **2a–g** (3.0 equiv) were used in the presence of 1.0 equiv of LiI·$2H_2O$ under reflux in dioxane. The reaction of aliphatic isocyanides **2a** and **2b** (R^2 = *t*-Oct, *t*-Bu) with **4a** in the presence of LiI·$2H_2O$ gave the products in good to high yield (entries 1–2). In the case of secondary and primary aliphatic isocyanides **2c** and **2d**, the product mixture was complex and the desired benzothiophene derivatives **3** were not obtained (entries 3–4). Aromatic isocyanides were also investigated, but they showed very low reactivity (entries 5–7). Even aromatic isocyanides bearing an electron-donating group at the *para* position exhibited low reactivity, with low product yield (entry 7). We also investigated substituted disulfide derivatives bearing an electron-donating group. In the case of disulfide **4e**, which has a methyl group at the 3-position, the reaction proceeded efficiently to afford the product in high yield (entry 8). Lower reactivity was observed when disulfide **5c**, which has a methoxy group at the 3-position, was used, giving the product in 6% yield (entry 9).

Table 3 Results of Passerini-type [4+1] cycloaddition reaction under various conditions



4a **3aa**

Entry	Promoter	solv.	Time / h	Yield / %
1	-	toluene	23	trace
2	MgI_2	toluene	15	23
3	ZnI_2	toluene	24	31
4	CuI	toluene	24	35
5	LiI·$2H_2O$	toluene	3	84
6	LiI	toluene	3	69
7	NaI	toluene	24	nr
8	KI	toluene	24	nr
9	LiBr	toluene	48	70
10	LiCl	toluene	48	17
11	NIS	toluene	24	-[b]
12	NBS	toluene	24	-[b]
13	NCS	toluene	24	-[b]
14	LiI·$2H_2O$	dioxane	24	94
15[a]	LiI·$2H_2O$	DMF	24	20
16	LiI·$2H_2O$	DCE	24	37
17	LiI·$2H_2O$	propionitrile	1	66

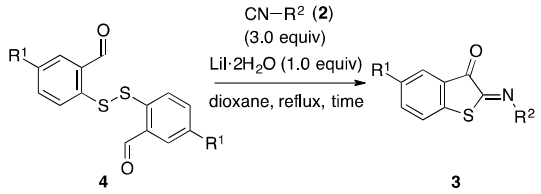
[a] Reaction was carried out at 100 °C. [b] Complex mixture.

To gain a mechanistic insight into this reaction, a series of control experiments were rationally designed and performed. When the reaction of 2-mercaptobenzaldehyde (**1a**) with *tert*-octyl isocyanide (**2a**) was carried out in the presence of TEMPO as a radical scavenger, disulfide **4a** was obtained in 75% yield as a major product and the desired **3aa** was obtained only in 7% yield (eq 2). In the case of disulfide **4a** with **2a** in the presence of TEMPO, the reaction was sluggish, affording **3aa** in 33% yield (eq 3). In addition, homolytic cleavage of the S-S bond was observed in refluxing dioxane. Thus, when the mixture of **4a** and **4d** was heated in dioxane, the heterocoupling disulfide **4e** was obtained in 67% yield (eq 4). Since the desired product was not obtained from aldehydes in the absence of LiI·$2H_2O$, it was concluded that Li^+ acts as a Lewis acid to activate the carbonyl group (Table 1, entry 1).

Based on these results, reaction mechanisms were proposed for the Passerini-type [4+1] cycloaddition reaction from the two substrates **1** and **4**, as shown in Scheme 2. In the case of 2-mercaptobenzaldehyde **1**, Li^+ acts as a Lewis acid, coordinating to the aldehyde. Passerini-type nucleophilic attack of the isocyanide generates the nitrilium intermediate **A**. This

intermediate is subsequently trapped by the thiol to afford adduct **B**. Finally, aerobic oxidation of the resulting alcohol proceeds to afford the corresponding benzothiophene derivative **3** (*path 1*). When **4** is used as a substrate, thermal homolytic cleavage of S-S bond is initiated to afford the thiyl radical **C**,[9] which intramolecularly abstracts the hydrogen of the aldehyde, giving the acyl radical **D**. The other generated thiyl radical **C** abstracts the hydrogen from the thiol group of **D** to afford the biradical **E** and 2-mercaptobenzaldehyde **1**. [4+1] Cycloaddition between **E** and isocyanide **2** proceeds via radical reaction to afford the desired benzothiophene derivative **3** (*path 2-A*), and product **1** reacts with isocyanide in a similar way to *Path 1* (*Path 2-B*).

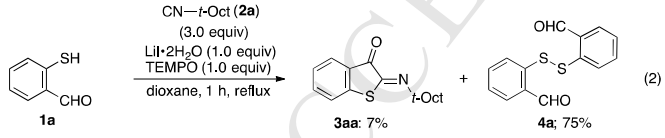
Table 4 Range of isocyanides and disulfide derivatives

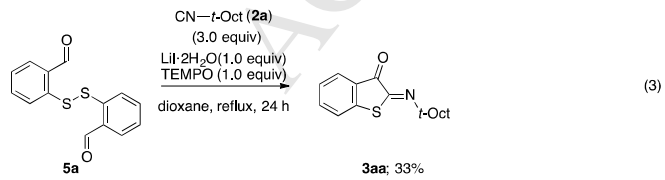


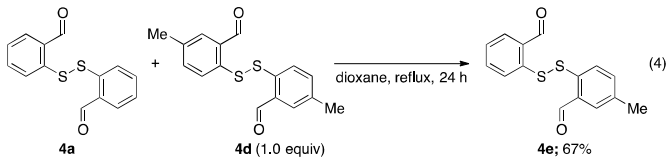
applicable to the Passerini-type [4+1] cycloaddition reaction

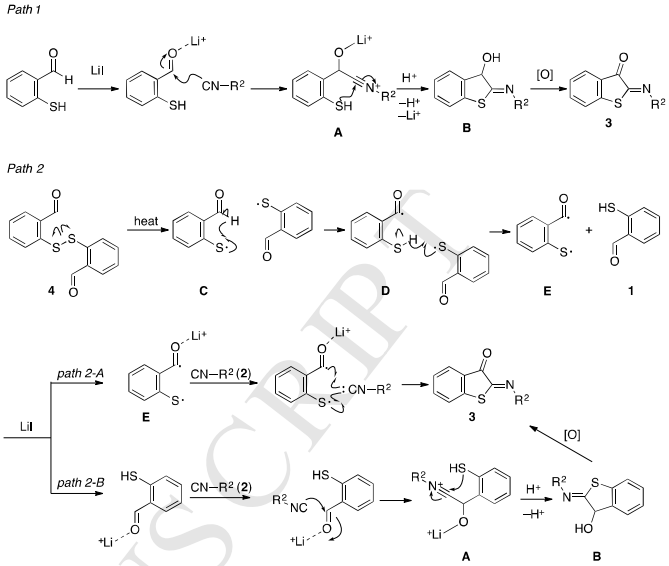
Entry	R^1	R^2	Time / h	Yield / %
1	H (**4a**)	*t*-Oct (**2a**)	24	94 (**3aa**)
2	H (**4a**)	*t*-Bu (**2b**)	20	72 (**3ab**)
3	H (**4a**)	*c*-Hex (**2c**)	24	-[a]
4	H (**4a**)	Bn (**2d**)	24	-[a]
5	H (**4a**)	Ph (**2e**)	24	nr
6	H (**4a**)	4-$MeOC_6H_4$ (**2f**)	24	nr
7	H (**4a**)	4-$Me_2NC_6H_4$ (**2g**)	22	6 (**3ag**)
8	Me (**4e**)	*t*-Oct (**2a**)	24	97 (**3da**)
9	MeO (**4c**)	*t*-Oct (**2a**)	44	6 (**3ca**)

[a] Complex mixture.









3. Conclusion

We developed a [4+1] cycloaddition reaction of isocyanides with 2-mercaptobenzaldehydes and their disulfide derivatives, promoted by $LiI \cdot 2H_2O$, which affords benzothiophene derivatives in moderate to good yields. Various types of isocyanides, 2-mercaptobenzaldehydes and disulfide derivatives were used successfully in the reaction.

4. Experimental Section

^1H NMR spectra were recorded on a 400 MHz NMR spectrometer. Chemical shifts δ are reported in ppm using TMS as an internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (*J*) and integration. ^{13}C NMR spectra were recorded on 100 MHz NMR spectrometer. The chemical shifts were determined in the δ-scale relative to $CDCl_3$ (δ = 77.0 ppm). The wave numbers of maximum absorption peaks of IR spectroscopy are presented in cm^{-1}. HRMS (FAB positive, DART) was measured with a quadrupole mass spectrometer and TOF mass spectrometers. All melting points were measured using a micro melting point apparatus. Dehydrated solvents were purchased for the reactions and used without further desiccation.

General procedure (Table 2)

To a solution of **1** (0.3 mmol) and **2** (0.45 mmol) in dioxane (3.0 mL), $LiI \cdot 2H_2O$ (0.3 mmol) was added and the whole was stirred at 110 °C. After reaction completion (monitored by TLC), the solvent was removed *in vacuo*. The crude was purified by silica gel column chromatography.

In the case of Table 4, **4** (0.3 mmol) and **2** (0.9 mmol) were used as substrates.

(*Z*)-2-((2,4,4-trimethylpentan-2-yl)imino)benzo[*b*]thiophen-3(2*H*)-one (3aa) (Table 4, entry 1)

Silica gel column chromatography (hexane/diethyl ether = 10/1) gave **3aa** (155 mg, 94% yield) as a brown oil. ^{1}H NMR ($CDCl_3$): 0.89 (s, 9H), 1.42 (s, 6H), 1.79 (s, 2H), 7.20 (m, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.51 (m, 1H), 7.80 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): 28.7, 31.5, 32.0, 54.5, 62.5, 124.4, 126.1, 127.2, 127.5, 136.5, 144.9, 147.3, 185.6. IR (KBr): 2950, 1710, 1630, 1590, 1450, 1390, 1280, 1070, 1030 cm^{-1}. HRMS–FAB (*m/z*): Calcd for $C_{16}H_{22}NOS$ $[M+H]^+$: 276.1422. Found: 276.1422.

(*Z*)-2-(*tert*-butylimino)benzo[*b*]thiophen-3(2*H*)-one (3ab) (Table 4, entry 2)

Silica gel column chromatography (hexane/diethyl ether = 10/1) gave **3ab** (95 mg, 72% yield) as a brown oil. ^{1}H NMR ($CDCl_3$): 1.42 (s, 9H), 7.21 (m, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.52 (m, 1H), 7.82 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$): 28.5, 58.6, 124.4, 126.1, 127.1, 127.4, 136.6, 144.5, 149.1, 185.8. IR (KBr): 2970, 1720, 1620, 1590, 1450, 1390, 1360, 1280, 1230, 1070, 1030 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{12}H_{14}NOS$ $[M+H]^+$: 220.0796. Found: 220.0793.

(*Z*)-2-(phenylimino)benzo[*b*]thiophen-3(2*H*)-one (3ae) (Table 2, entry 5)

Silica gel column chromatography (hexane/diethyl ether = 6/1) gave **3ae** (36 mg, 51% yield) as a pale orange solid of mp = 151–152 °C (hexane/ethyl acetate). ^{1}H NMR ($CDCl_3$): 7.23–7.62 (m, 8H), 7.94 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): 121.0, 124.9, 126.7, 127.3, 127.8, 129.3, 136.9, 144.5, 149.6, 156.4, 185.4. IR (KBr): 2970, 1710, 1620, 1600, 1450, 1290, 1220 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{14}H_{10}NOS$ $[M+H]^+$: 240.0483. Found: 240.0481.

(*Z*)-2-((4-methoxyphenyl)imino)benzo[*b*]thiophen-3(2*H*)-one (3af) (Table 2, entry 6)

Silica gel column chromatography (hexane/diethyl ether = 6/1) gave **3af** (22 mg, 27% yield) as a pale orange solid of mp = 146–147 °C (hexane/ethyl acetate). ^{1}H NMR ($CDCl_3$): 3.85 (s, 3H), 7.00 (d, *J* = 9.2 Hz, 2H), 7.34 (m, 1H), 7.41 (d, *J* = 9.2 Hz, 2H), 7.43 (m, 1H), 7.58 (m, 1H), 7.95 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): 55.5, 114.5, 124.6, 124.8, 126.6, 127.6, 127.8, 136.6, 141.3, 144.5, 152.5, 159.5, 185.7. IR (KBr): 2850, 1700, 1600, 1560, 1500, 1460, 1290, 1260, 1180, 1040 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{15}H_{12}NO_2S$ $[M+H]^+$: 270.0589. Found: 270.0592.

(*Z*)-2-((4-(dimethylamino)phenyl)imino)benzo[*b*]thiophen-3(2*H*)-one (3ag) (Table 2, entry 7)

Silica gel column chromatography (hexane/ethyl acetate = 3/1~1/1) gave **3ag** (56 mg, 66% yield) as a brown solid of mp = 172–173 °C (hexane/ethyl acetate). ^{1}H NMR ($CDCl_3$): 3.07 (s, 6H), 6.79 (d, *J* = 8.8 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): 40.2, 112.0, 124.6, 126.2, 126.7, 127.3, 128.2, 135.8, 135.9, 144.5, 146.8, 150.6, 186.0. IR (KBr): 2960, 1700, 1640, 1530, 1380, 1290, 1240, 1180, 1020 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{16}H_{15}N_2OS$ $[M+H]^+$: 283.0905. Found: 283.0897.

(*Z*)-2-((4-bromophenyl)imino)benzo[*b*]thiophen-3(2*H*)-one (3ah) (Table 2, entry 5)

Silica gel column chromatography (hexane/diethyl ether = 6/1) gave **3ah** (29 mg, 31% yield) as a glay solid of mp = 150–151 °C (hexane/ethyl acetate). ^{1}H NMR ($CDCl_3$): 7.08 (d, *J* = 8.0 Hz, 2H), 7.27–7.36 (m, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), (m, 1H), 7.57 (m, 1H), 7.91 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): 120.8, 122.7, 124.9, 126.9, 127.6, 127.9, 132.5, 137.1, 144.0, 148.2, 157.1, 185.2. IR (KBr): 2960, 1700, 1650, 1560, 1480, 1300, 1280, 1070 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{14}H_9BrNOS$ $[M+H]^+$: 317.9588. Found: 317.9591.

(*Z*)-5-(*tert*-butyl)-2-((2,4,4-trimethylpentan-2-yl)imino)benzo[*b*]thiophen-3(2*H*)-one (3ba) (Table 2, entry 9)

Silica gel column chromatography (hexane/diethyl ether = 10/1) gave **3ba** (76 mg, 77% yield) as a brown oil. ^{1}H NMR ($CDCl_3$): 0.91 (s, 9H), 1.27 (s, 9H), 1.44 (s, 6H), 1.80 (s, 2H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.57 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.84 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): 28.8, 31.1, 31.5, 32.0, 34.7, 54.3, 62.5, 124.0, 124.2, 126.9, 134.3, 141.2, 148.2, 149.7, 185.9. IR (KBr): 2960, 1700, 1640, 1490, 1360, 1280, 1190, 1030 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{20}H_{30}NOS$ $[M+H]^+$: 332.2048. Found: 332.2036.

(*Z*)-5-methoxy-2-((2,4,4-trimethylpentan-2-yl)imino)benzo[*b*]thiophen-3(2*H*)-one (3ca) (Table 2, entry 10)

Silica gel column chromatography (hexane/diethyl ether = 3/1) gave **3ca** (51 mg, 47% yield) as a brown oil. ^{1}H NMR ($CDCl_3$): 0.96 (s, 9H), 1.47 (s, 6H), 1.84 (s, 2H), 3.82 (s, 3H), 7.17 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): 28.7, 31.5, 31.9, 54.3, 55.7, 62.5, 109.7, 125.1, 125.5, 127.9, 136.4, 148.4, 158.3, 185.7. IR (KBr): 2960, 1710, 1620, 1570, 1480, 1360, 1300, 1280, 1080, 1030 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{17}H_{24}NO_2S$ $[M+H]^+$: 306.1528. Found: 306.1516.

(*Z*)-5-chloro-2-((2,4,4-trimethylpentan-2-yl)imino)benzo[*b*]thiophen-3(2*H*)-one (3da) (Table 2, entry 11)

Silica gel column chromatography (hexane/diethyl ether = 10/1) gave **3da** (48 mg, 51% yield) as a brown oil. ^{1}H NMR ($CDCl_3$): 0.98 (s, 9H), 1.45 (s, 6H), 1.79 (s, 2H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 2.4, 8.4 Hz, 1H), 7.79 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): 28.7, 31.6, 32.0, 54.6, 62.7, 125.6, 127.2, 128.2, 132.4, 136.4, 143.0, 146.7, 184.5. IR (KBr): 2950, 1720, 1630, 1590, 1560, 1450, 1360, 1290, 1250, 1220, 1080 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{16}H_{21}ClNOS$ $[M+H]^+$: 310.1032. Found: 310.1023.

(*Z*)-5-methyl-2-((2,4,4-trimethylpentan-2-yl)imino)benzo[*b*]thiophen-3(2*H*)-one (3ea) (Table 2, entry 8)

Silica gel column chromatography (hexane/diethyl ether = 10/1) gave **3ea** (90 mg, 97% yield) as a pale yellow solid of mp = 79–80 °C (hexane/ethyl acetate). ^{1}H NMR ($CDCl_3$): 0.96 (s, 9H), 1.45 (s, 6H), 1.84 (s, 2H), 2.35 (s, H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.68 (s, 1H). ^{13}C NMR ($CDCl_3$): 20.6, 28.5, 31.4, 31.7, 54.2, 62.2, 124.0, 126.9, 127.3, 136.0, 137.4, 141.5, 147.8, 185.5. IR (KBr): 2950, 1710, 1630, 1600, 1570,

1470, 1380, 1300, 1280, 1230, 1160, 1080 cm^{-1}. HRMS–DART (*m/z*): Calcd for $C_{17}H_{24}NOS$ $[M+H]^+$: 290.1579. Found: 290.1570.

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Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.

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