Synthesis M. Hayakawa et al. Paper

# Integration of a Four-Step Reaction into One-Pot under the Coexistence of Silica-Gel-Supported Acid and Base Reagents: Synthesis of Benzo- and Naphthothiophenes Using $NaHSO_4/SiO_2$ and $Na_2CO_3/SiO_2$

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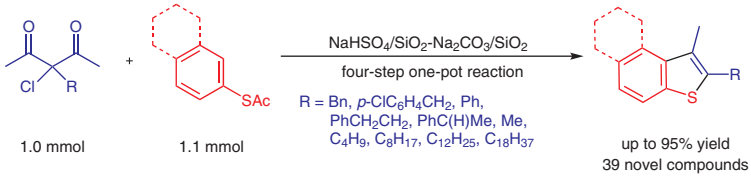


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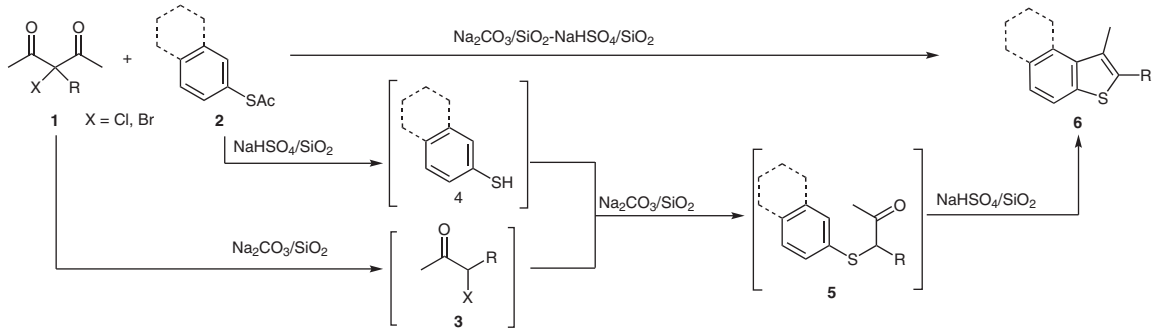
**Abstract** A four-step synthesis of benzo- and naphthothiophenes that have biological importance and application in material science was integrated into a one-pot reaction by using silica gel-supported acid and base reagents, $NaHSO_4/SiO_2$ and $Na_2CO_3/SiO_2$. The supported reagents provided acid and base environments on the surface of the supports without neutralization and worked separately in the same medium. The four-step reaction comprises (i) deacetylation of 3-halo-2,4-pentanediones to α-halo ketones, (ii) deacetylation of *S*-aryl thioacetates to arenethiols, (iii) coupling of α-halo ketones and arenethiols to give α-sulfanyl ketones, and (iv) cyclization of sulfanyl ketones to benzo- and naphthothiophenes. The steps (i) and (iii) proceeded by $Na_2CO_3/SiO_2$, and (ii) and (iv) by $NaHSO_4/SiO_2$. The four-step reaction proceeded efficiently by introduction of starting materials and reagents in a single reaction vessel. The starting materials were very easy to handle and unpleasant smell of aryl thiols that were used in conventional methods could be avoided. Novel thirty-nine benzo- and naphthothiophenes were synthesized by this method in excellent to fair yields.

**Key words** benzothiophenes, one-pot synthesis, 3-halo-2,4-pentanediones, *S*-aryl thioacetates, silica-gel-supported reagents

One of the goal in organic synthesis is to obtain maximum yield with minimum synthetic steps, thus reducing consumption of chemicals and laborious isolation and purification procedures in syntheses. One of the solutions to minimize synthetic steps is to conduct reactions in one pot but some combination of reactions cannot be conducted in one pot. Consecutive acid and base reactions is one of such reactions because of their neutralization. However, we have shown that consecutive acid and base reactions can proceed efficiently by using solid-supported acid and base reagents, which was applied to a two-step synthesis of benzo- and naphthothiophenes.[1]

Benzo[*b*]thiophene and its derivatives are very important because of their biological activities and applications in material science.[2] Therefore, many new and convenient syntheses of benzo[*b*]thiophenes have been developed. The usual methods for the synthesis of benzo[*b*]thiophenes are coupling cyclization reaction using *o*-bromoalkynylbenzenes and various thiols[3] and annulation of alkynylbenzenes.[4]

However, these methods require severe reaction conditions or expensive starting materials, and complicated procedures. Recently, simple and efficient synthesis using metal catalysts have been reported[5] but they often use expensive transition metal catalysts such as Pd.[6] Previously we have developed a one-pot two-step synthesis of benzo[*b*]thiophenes and naphtho[2,1-*b*]thiophenes from α-halo ketones and arenethiols by using silica gel-supported polyphosphoric acid ($PPA/SiO_2$) and sodium carbonate ($Na_2CO_3/SiO_2$) (**3** + **4** → [**5**] → **6** in Scheme 1),[1] in which the acid and base did not neutralize but worked separately in the same medium.[7] However, limitation in the commercially available α-halo ketones and odious smell of arenethiols, such as benzene and toluene thiols, are two major disadvantages in this reaction. To obtain various α-halo ketones, many synthetic method from corresponding carbonyl compounds have been reported but many of them suffers from the formation of dihalogenated compounds[8] and only one selective preparation of monohalogenated ketones **3** has been reported by deacylation of α-halo-1,3-dicarbonyls **1**




**Scheme 1** One-pot four-step reaction leading to benzo- and naphthothiophenes

under basic conditions.[7a,9] To avoid odious smell of arenethiols **4**, they can be easily prepared in situ from *S*-aryl thioacetates **2** under acidic conditions.[10]

To decrease the load of the synthesis, instead of synthesizing α-halo ketones separately, and to avoid odious smell of arenethiols at the same time, we report here an efficient four-step one-pot reaction of benzo- and naphthothiophenes **6** from **1** and **2**, by integrating the reactions **1** → **3** and **2** → **4** to **3** + **4** → [**5**] → **6** using silica-gel-supported acid and base reagents (Scheme 1).

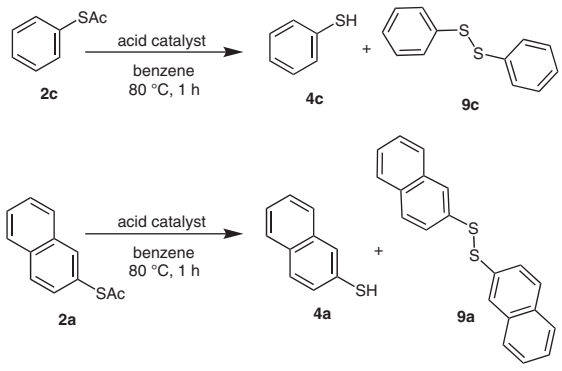
## Deacetylation of Aryl Thioacetates 2 to Aryl Thiols 4

First, we have screened different solid acids for the conversion of *S*-phenyl (**2c**) and *S*-2-naphthyl (**2a**) thioacetates into the corresponding arenethiols **4a** and **4c**, whose results are summarized in Table 1. As shown in Table 1, PPA/$SiO_2$, which was an efficient acid for converting **5** to **6**,[6] only gave 15% yield of **4c** and 50% yield of diphenyl disulfide (**9c**) from **2c** (Table 1, entry 1). $SiO_2$, silica sulfuric acid (SSA), and $ZnCl_2/SiO_2$ did not give **4c** at all (entries 2, 3, and 6) and alumina sulfuric acid (ASA) only gave a low yield of **4c** (entry 4). However, we found that silica-gel-supported perchloric acid ($HClO_4/SiO_2$)[10] and sodium hydrogen sulfate ($NaHSO_4/SiO_2$) were effective acid for obtaining **4c** (entries 5 and 7). By using these two acids, deacetylation of *S*-2-naphthyl thioacetate (**2a**) also proceeded efficiently (entries 8 and 9).

## Optimization of the Reaction Conditions Using 1a and 2a

As we found optimum reaction conditions for each of the four steps [the first step **1** → **3** using $Na_2CO_3/SiO_2$,[7a] the second step **2** → **4** using $HClO_4/SiO_2$ (vide supra), the third and fourth steps **3** + **4** → [**5**] → **6** using $Na_2CO_3/SiO_2$ and PPA/$SiO_2$,[6] respectively], we have integrated the four reactions in one pot using **1** and **2** (Scheme 1). First, the reaction was tested by using 3-benzyl-3-bromo-2,4-pentanedione (**1a'**) and *S*-2-naphthyl thioacetate (**2a**) in the presence of $HClO_4/SiO_2$ and $Na_2CO_3/SiO_2$ at 80 °C. However, only 2-(2-naphthalenylthio)-3-phenyl-1-propanone (**5a**) was formed in 17% yield without formation of the desired 2-benzyl-1-

**Table 1** Optimization of Solid Acid for the Deacetylation of Aryl Thioacetates **2**[a]



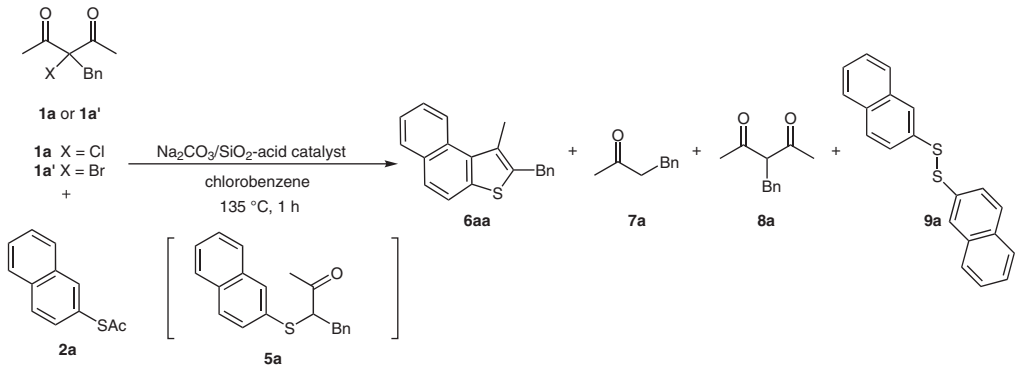

| Entry | 2 | Acid | Yield (%)[b] | |
|---|---|---|---|---|
| | | | 4 | 9 |
| 1 | **2c** | PPA/$SiO_2$[c] | 15[d] | 50[d] |
| 2 | **2c** | $SiO_2$ | N.D | N.D |
| 3 | **2c** | silica sulfuric acid (SSA)[e] | N.D | 100 |
| 4 | **2c** | alumina sulfuric acid (ASA)[e] | 30 | 70 |
| 5 | **2c** | $HClO_4/SiO_2$[f] | 100 | N.D |
| 6 | **2c** | $ZnCl_2/SiO_2$[g] | N.D | N.D |
| 7 | **2c** | $NaHSO_4/SiO_2$[h] | 65 | 7 |
| 8 | **2a** | $HClO_4/SiO_2$[f] | 100[d] | N.D |
| 9 | **2a** | $NaHSO_4/SiO_2$[h] | 70[d] | 8[d] |

[a] A mixture of **2c** (1.0 mmol) and acid reagent (1.0 g) was stirred in benzene (10 mL) at 80 °C for 1.0 h.
[b] GC yield. Yields are based on **2**; N.D. = not detected.
[c] PPA/$SiO_2$ (30 wt%, 1.0 g).
[d] Isolated yield.
[e] SSA, ASA (33.3 mmol/g).
[f] $HClO_4/SiO_2$ (0.06 mmol/g).
[g] $ZnCl_2/SiO_2$ (1.83 mmol/g).
[h] $NaHSO_4/SiO_2$ (2.1 mmol/g).

methylnaphtho[2,1-*b*]thiophene (**6aa**) (Table 2, entry 1). The product **6aa** was not formed either when the reaction time was extended to 12 hours, but **6aa** was obtained in 5% by increasing the reaction temperature up to 135 °C (entries 2 and 3). Several solid acids were tested for this reaction. Reactions using SSA[11] and $NaHSO_4/SiO_2$ gave **6aa** without **5a** but significant amount of side-products **7a**, **8a**, and **9a** were formed at the same time (entries 4 and 5). When the amount of $NaHSO_4/SiO_2$ was reduced to 1/2, it needed 3 hours for complete consumption of the starting materials (entry 6); the yield of **6aa** increased with that of **9a**. Reactions using reduced amount of **2a** gave **6aa** over 60% with low yields of **8a** (entries 7 and 8). When 3-benzyl-3-chloropentane-2,4-dione (**1a**) was used in place of **1a'**, a drastic increase in the formation of **6aa** and decrease of **5a**, **7a**, **8a**, and **9a** was observed (entries 9–11). When 1.2 equivalents of **2a** was used, expected **6aa** was obtained in 94% yield along with 14% of **9a** and without formation of **7a** and **8a** (entry 9). The use of an equivalent of **2a** also gave **6aa** in 92% yield but without **9a**, and the reaction using 1.1 equivalents of **2a** gave **6aa** in the highest yield of 95% (entries 10 and 11).

In order to make clear that both the acid- and base-supported reagents existing in the same vessel are able to function as an acid and a base, respectively, the reaction was conducted by using either $Na_2CO_3/SiO_2$ or $NaHSO_4/SiO_2$. But **6aa** was not observed in the reaction mixture (Table 3). For instance, when the reaction was conducted in the presence of $Na_2CO_3/SiO_2$, **5a** was obtained as the main product along with 2-naphthalenethiol and **9a** (Table 3, entry 2). On the other hand, reaction using $NaHSO_4/SiO_2$ recovered **1a** quantitatively and **2a** in moderate along with the formation of 2-naphthalenethiol and **9a** (entry 3). The reaction using both granular $Na_2CO_3$ and $NaHSO_4$ did not promote at all (entry 4).

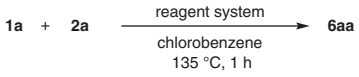
**Table 2** Optimization of the Reaction of **1a**/**1a**′ and **2a**[a]




| Entry | Acid[b] | X | **2a** (mmol) | Temp (°C) | Time (h) | Yield (%)[c] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | **5a** | **6aa** | **7a** | **8a** | **9a** |
| 1 | $HClO_4/SiO_2$ | Br | 1.5 | 80 | 1 | 17 | N.D. | – | 14 | 21 |
| 2 | $HClO_4/SiO_2$ | Br | 1.5 | 80 | 12 | 80 | N.D. | – | 20 | N.D. |
| 3 | $HClO_4/SiO_2$ | Br | 1.5 | 135 | 1 | 60 | 5 | 5 | 16 | 15 |
| 4 | SSA | Br | 1.5 | 135 | 1 | N.D. | 15 | 14 | 41 | 60 |
| 5 | $NaHSO_4/SiO_2$ | Br | 1.5 | 135 | 1 | N.D. | 34 | 2 | 19 | 30 |
| 6[d] | $NaHSO_4/SiO_2$ | Br | 1.5 | 135 | 3 | 4 | 48 | 4 | 16 | 40 |
| 7[d] | $NaHSO_4/SiO_2$ | Br | 1.2 | 135 | 3 | 5 | 67 | 6 | 6 | 30 |
| 8[d] | $NaHSO_4/SiO_2$ | Br | 1.0 | 135 | 2 | N.D. | 60 | 9 | 4 | 20 |
| 9[d] | $NaHSO_4/SiO_2$ | Cl | 1.2 | 135 | 1 | N.D. | 94 | N.D. | N.D. | 14 |
| 10[d] | $NaHSO_4/SiO_2$ | Cl | 1.1 | 135 | 1 | N.D. | 95 | N.D. | N.D. | 10 |
| 11[d] | $NaHSO_4/SiO_2$ | Cl | 1.0 | 135 | 1 | N.D. | 92 | N.D. | N.D. | N.D. |

[a] A mixture of **1** (1.0 mmol), **2a**, acid reagent (1.0 g), and $Na_2CO_3/SiO_2$ (1.5 mmol/g, 2.0 g) was stirred in chlorobenzene (10 mL, 135 °C) or in benzene (10 mL, 80 °C).
[b] $HClO_4/SiO_2$: 0.06 mmol/g; SSA: 3.33 mmol/g; $NaHSO_4/SiO_2$: 2.1 mmol/g.
[c] Isolated yield. Yields are based on **1**; N.D. = not detected.
[d] $NaHSO_4/SiO_2$: 0.5 g.

**Table 3** Synthesis of **6aa** Using Various Reagent Systems[a]




| Entry | Reagent system | | Yield (%) of **6aa** |
|---|---|---|---|
| 1 | $Na_2CO_3/SiO_2$ | $NaHSO_4/SiO_2$ | 95 |
| 2 | $Na_2CO_3/SiO_2$ | – | N.D |
| 3 | – | $NaHSO_4/SiO_2$ | N.D |
| 4 | $Na_2CO_3$ | $NaHSO_4$ | no reaction |

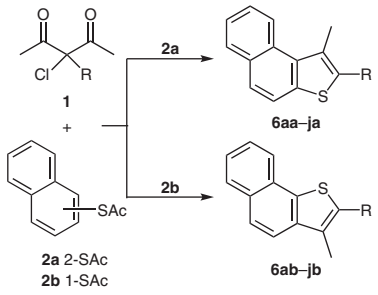
[a] A mixture of **1** (1.0 mmol), **2a** (1.1 mmol), and acid and base reagents were stirred in chlorobenzene (10 mL) at 135 °C; N.D. = not detected.

## Reaction of Various 3-Substituted 3-Chloropentane-2,4-diones 1 and Thioacetates 2a–e

To investigate the scope of the reaction, first, we have conducted reactions using various **1** and thioacetates **2a**,**b** (Table 4). Both alkyl- and aryl-substituted **1** gave excellent to good yields for the formation of **6aa–ja** with *S*-2-naphthyl thioacetate (**2a**), except for the sterically hindered **1e**. However, long alkyl substituent, **1j**, required longer reaction time.

A similar trend was observed when *S*-1-naphthyl thioacetate (**2b**) was used in place of **2a**. Similarly, **1a** was reacted with phenyl (**2c**), *o*-tolyl (**2d**), and *p*-tolyl (**2e**) thioacetates (Table 5). The reaction of **1a** and **2c** did not give the corresponding **6ac** under the same reaction condition as those in Table 4. However, when the reaction time was prolonged to 24 hours, **6ac** was formed in 32% yield (Table 5, entry 1). By increasing the reaction temperature to 180 °C, a large increase in the yield of **6ac** was observed (entry 2). In the reaction using *o*-tolyl thioacetate (**2d**), **6ad** was obtained in 77% at 135 °C after 24 hours, and at 180 °C, the reaction was completed in 3 hours and gave **6ad** in 87% yield (entries 3 and 4). On the other hand, the reactions using *p*-tolyl thioacetate (**2e**) was not much affected by reaction temperature (entries 5 and 6). According to our previous work,[11] the rate-determining step of the reaction is the intramolecular cyclization of **5** to **6**, which depends on the reactivity of aromatic ring of **2**. Higher reactivity of the tolyl groups (**2d**,**e**) to phenyl group (**2c**) in this reaction can be rationalized by an electron-donating nature of the methyl groups to the phenyl moieties in **2**. Based on these results, various 3-substituted 3-chloropentane-2,4-diones **1a–j** were reacted at 180 °C for 24 hours with **2c**,**e** and 3 hours with **2d**, whose results are summarized in Scheme 2. In the case of reaction using **2c**, the corresponding **6** were obtained in 40–73% yields except for the reactions of **1e** and **1f** that gave **6ec** and **6fc** in 26 and 21%, respectively (Scheme 2, first line).

**Table 4** Reaction of **1a–j** with **2a**,**b**[a]



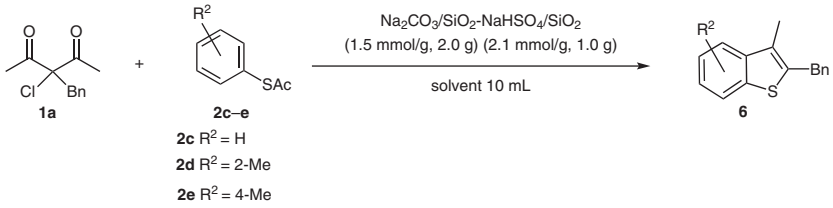

| Entry | 1 | R | 2 | Yield of **6** (%)[b] | |
|---|---|---|---|---|---|
| 1 | **1a** | Bn | **2a** | **6aa** | 95 |
| 2 | **1b** | *p*-$ClC_6H_4CH_2$ | **2a** | **6ba** | 84 |
| 3 | **1c** | Ph | **2a** | **6ca** | 76 |
| 4 | **1d** | $PhCH_2CH_2$ | **2a** | **6da** | 90 |
| 5 | **1e** | PhC(H)Me | **2a** | **6ea** | 50 |
| 6 | **1f** | Me | **2a** | **6fa** | 70 |
| 7 | **1g** | $C_4H_9$ | **2a** | **6ga** | 89 |
| 8 | **1h** | $C_8H_{17}$ | **2a** | **6ha** | 88 |
| 9 | **1i** | $C_{12}H_{25}$ | **2a** | **6ia** | 81 |
| 10[c] | **1j** | $C_{18}H_{37}$ | **2a** | **6ja** | 76 |
| 11 | **1a** | Bn | **2b** | **6ab** | 93 |
| 12 | **1b** | *p*-$ClC_6H_4CH_2$ | **2b** | **6bb** | 90 |
| 13 | **1c** | Ph | **2b** | **6cb** | 76 |
| 14 | **1d** | $PhCH_2CH_2$ | **2b** | **6db** | 92 |
| 15 | **1e** | PhC(H)Me | **2b** | **6eb** | 53 |
| 16 | **1f** | Me | **2b** | **6fb** | 35 |
| 17 | **1g** | $C_4H_9$ | **2b** | **6gb** | 85 |
| 18 | **1h** | $C_8H_{17}$ | **2b** | **6hb** | 66 |
| 19 | **1i** | $C_{12}H_{25}$ | **2b** | **6ib** | 60 |
| 20[d] | **1j** | $C_{18}H_{37}$ | **2b** | **6jb** | 91 |

[a] A mixture of **1** (1.0 mmol), **2** (1.1 mmol), $NaHSO_4/SiO_2$ (2.1 mmol/g, 0.5 g), and $Na_2CO_3/SiO_2$ (1.5 mmol/g, 2.0 g) was stirred in chlorobenzene (10 mL) for 1 h at 135 °C.
[b] Isolated yields are based on **1**.
[c] The reaction mixture was stirred for 3 h.
[d] The reaction mixture was stirred for 2 h.

The reactions using **2d** gave expected compounds **6ad–jd** in high yields in 3 hours (Scheme 2, second line). However, the yield of **6ed**, using sterically hindered **1e** was lower than the others. Although the reactivity of **2e** was higher at 135 °C, the reactivity with **1a–j** was similar to that of **2c** at 180 °C, which needed 24 hours for completion (Scheme 2, third line). The reaction using **1e** also gave **6ee** in low yield but other products were obtained in moderate yields.

In summary, a simple and efficient four-step one-pot synthesis of naphtho- and benzothiophens was developed by using solid-supported reagents $NaHSO_4/SiO_2$ and $Na_2CO_3/SiO_2$. The four-step synthesis comprises, (i)

**Table 5** Reaction of **1a** with **2c–e**[a]

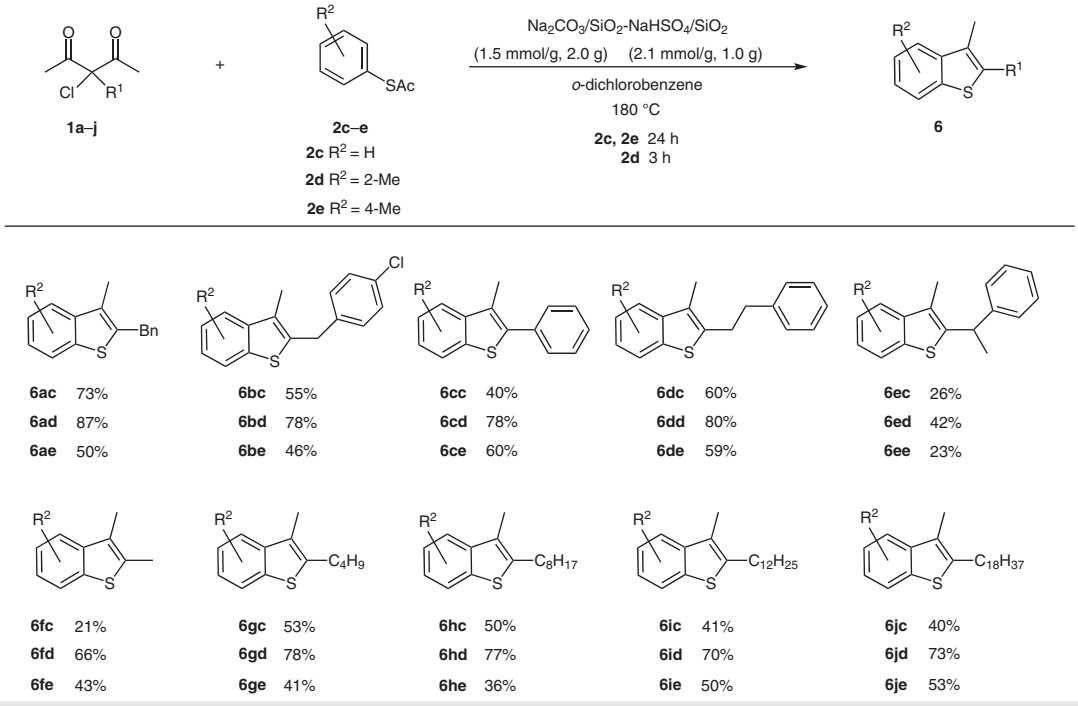



| Entry | 2 | Solvent | Temp (°C) | Time (h) | Product | Yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | **2c** | chlorobenzene | 135 | 24 | **6ac** | 32 |
| 2 | **2c** | *o*-dichlorobenzene | 180 | 24 | **6ac** | 73 |
| 3 | **2d** | chlorobenzene | 135 | 24 | **6ad** | 77 |
| 4 | **2d** | *o*-dichlorobenzene | 180 | 3 | **6ad** | 87 |
| 5 | **2e** | chlorobenzene | 135 | 24 | **6ae** | 43 |
| 6 | **2e** | *o*-dichlorobenzene | 180 | 24 | **6ae** | 50 |

[a] A mixture of **1** (1.0 mmol), **2** (1.1 mmol), $Na_2CO_3/SiO_2$ (1.5 mmol/g, 2.0 g), and $NaHSO_4/SiO_2$ (2.1 mmol/g, 1.0 g) was stirred in solvent (10 mL).
[b] Isolated yields are based on **1a**.

deacetylation of 3-halo-2,4-pentanediones **1** to α-halo ketones **3**, (ii) deacetylation of *S*-aryl thioacetates **2** to arenethiols **4**, (iii) coupling of **3** and **4** to give α-sulfanyl ketones **5**, and (iv) cyclization of **5** to benzo- and naphthothiophenes **6**. The steps (i) and (iii) were carried out with $Na_2CO_3/SiO_2$ and (ii) and (iv) with $NaHSO_4/SiO_2$. All solid supported reagents were easily removed from the reaction mixture by simple filtration. In total, 39 novel naphtho- or benzothiophens have been synthesised in excellent to fair yields.

NMR spectra were recorded on JEOL JNM-ECX400 spectrometer. TMS (δ = 0) and $CDCl_3$ (δ = 77.0) were used as internal standards for $^1H$ and $^{13}C$ NMR measurements, respectively. High-resolution mass analyses were performed on an Agilent G1969 LC/MDS TOF mass spectrometer




**Scheme 2** Reaction of **1a** with **2c–e**; isolated yields given are based on **1**

or JEOL GCmate. Elemental analyses were performed on a j-Science Lab Micro Corder JM-10 instrument. IR spectra were recorded on a FT/IR-6100 or Thermo Electron Nicolet 380 spectrometer. Melting points were determined on Yanako micro-melting point apparatus or on a Büchi Melting Point B-540 apparatus.

The preparation of benzo- and naphthothiophenes **6aa–ja** is given below. For the preparation of the rest of the benzo- and naphthothiophenes, see the Supporting Information.

### $NaHSO_4/SiO_2$

To a 200 mL of eggplant-shaped flask was added a solution of $NaHSO_4·H_2O$ (15 mmol, 1.59 g) in distilled $H_2O$ (100 mL) and silica gel [Wakogel C-200 (Wako Pure Chemical Ind. Ltd.), 10 g], and then the mixture was stirred at r.t. for 0.5 h. The $H_2O$ was removed by a rotary evaporator under reduced pressure, and the resulting solid was dried in vacuo (10 mmHg) at 120 °C for 5 h.

### $Na_2CO_3/SiO_2$

To a 200 mL of eggplant-shaped flask was added a solution of $Na_2CO_3·H_2O$ (30 mmol, 4.14 g) in distilled $H_2O$ (100 mL) and silica gel [Wakogel C-200 (Wako Pure Chemical Ind. Ltd.), 8.41 g], and then the mixture was stirred at r.t. for 0.5 h. The $H_2O$ was removed by a rotary evaporator under reduced pressure, and the resulting solid was dried in vacuo (10 mmHg) at r.t. for 5 h.

### General Procedure for the Synthesis of 6

To a 30 × 20 cm cylindrical reaction vessel of organic synthesizer process station PPS-25A was added the respective 3-chloro-2,4-pentandione **1** (1 mmol), thioacetate **2** (1.1 mmol), $NaHSO_4/SiO_2$ (2.1 mmol/g, 0.5–1 g), $Na_2CO_3/SiO_2$ (1.5 mmol/g, 2 g), and chlorobenzene (10 mL) or *o*-dichlorobenzene (10 mL). The mixture was stirred at 135 °C (chlorobenzene) or at 180 °C (*o*-dichlorobenzene) for the appropriate time in the organic synthesizer process station PPS-25A, and then the solid reagents were removed by filtration. The solvent was removed from the filtrate by a rotary evaporator to give the crude product, which was purified by silica gel column chromatography (hexane/EtOAc) to obtain the desired pure **6**.

### 2-Benzyl-1-methylnaphtho[2,1-*b*]thiophene (6aa)[1]

Yield: 274 mg (95%); white solid; mp 98–100 °C (*n*-hexane).

IR (neat): 2978, 1601, 713, 801 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 2.81 (s, 3 H), 4.30 (s, 2 H), 7.22–7.32 (m, 5 H), 7.48–7.59 (m, 2 H), 7.66 (d, *J* = 8.5 Hz, 1 H), 7.75 (d, *J* = 8.5 Hz, 1 H), 7.93 (d, *J* = 7.8 Hz, 1 H), 8.71 (d, *J* = 8.5 Hz, 1 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 16.9, 34.5, 120.7, 123.3, 124.5, 124.7, 125.8, 126.5, 128.5, 128.6, 129.0, 130.4, 130.5, 132.1, 134.7, 136.5, 137.6, 139.9.

HRMS (TOF-CI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{17}S$: 289.1050; found: 289.1059.

Anal. Calcd for $C_{20}H_{16}S$: C, 83.29; H, 5.59. Found: C, 83.24; H, 5.47.

### 2-(4-Chlorobenzyl)-1-methylnaphtho[2,1-*b*]thiophene (6ba)

Yield: 271 mg (84%); colorless needles; mp 113–114 °C (*n*-hexane).

IR (neat): 2926, 1506, 1435, 802, 736 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 2.79 (s, 3 H), 4.25 (s, 2 H), 7.16 (d, *J* = 8.5 Hz, 2 H), 7.26 (d, *J* = 8.5 Hz, 2 H), 7.49–7.60 (m, 2 H), 7.67 (d, *J* = 8.5 Hz, 1 H), 7.76 (d, *J* = 8.5 Hz, 1 H), 7.94 (d, *J* = 8.0 Hz, 1 H), 8.70 (d, *J* = 8.5 Hz, 1 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 16.9, 33.8, 120.7, 123.3, 124.6, 124.9, 125.9, 128.7, 129.0, 129.7, 130.5, 130.6, 132.1, 132.3, 134.7, 136.5, 136.7, 138.3.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{16}ClS$: 323.0661; found: 323.0665.

Anal. Calcd for $C_{20}H_{15}ClS$: C, 74.40; H, 4.68. Found: C, 74.81; H, 4.63.

### 1-Methyl-2-phenylnaphtho[2,1-*b*]thiophene (6ca)[1]

Yield: 208 mg (76%); white solid; mp 125–127 °C (*n*-hexane).

IR (neat): 3051, 1597, 1442, 795, 756 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 2.87 (s, 3 H), 7.37–7.61 (m, 7 H), 7.71 (d, *J* = 8.5 Hz, 1 H), 7.83 (d, *J* = 8.5 Hz, 1 H), 7.96 (d, *J* = 8.0 Hz, 1 H), 8.76 (d, *J* = 8.5 Hz, 1 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 17.9, 120.6, 123.4, 124.7, 125.3, 125.9, 127.8, 128.5, 129.0, 130.2, 130.4, 130.8, 132.2, 134.8, 134.9, 137.3, 138.7.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{15}S$: 275.0894; found: 275.0889.

Anal. Calcd for $C_{19}H_{14}S$: C, 83.17; H, 5.14. Found: C, 83.47; H, 5.15.

### 1-Methyl-2-phenethylnaphtho[2,1-*b*]thiophene (6da)

Yield: 272 mg (90%); colorless needles; mp 118–120 °C (*n*-hexane).

IR (neat): 3045, 1508, 1454, 800, 750 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 2.67 (s, 3 H), 3.03 (t, *J* = 7.8 Hz, 2 H), 3.25 (t, *J* = 7.8 Hz, 2 H), 7.20–7.30 (m, 5 H), 7.49–7.57 (m, 2 H), 7.67 (d, *J* = 8.5 Hz, 1 H), 7.79 (d, *J* = 8.5 Hz, 1 H), 7.94 (d, *J* = 7.8 Hz, 1 H), 8.68 (d, *J* = 8.5 Hz, 1 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 16.7, 31.0, 38.0, 121.0, 123.6, 124.7, 124.7, 125.9, 126.4, 128.6, 128.7, 129.1, 130.1, 130.7, 132.3, 134.9, 136.2, 138.5, 141.1.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{19}S$: 303.1207; found: 303.1209.

Anal. Calcd for $C_{21}H_{18}S$: C, 83.40; H, 6.00. Found: C, 83.48; H, 5.94.

### 1-Methyl-2-(1-phenylethyl)naphtho[2,1-*b*]thiophene (6ea)

Yield: 151 mg (50%); yellow solid; mp 65–66 °C (*n*-hexane).

IR (neat): 2979, 1600, 1506, 801, 698 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.79 (d, *J* = 7.3 Hz, 3 H), 2.76 (s, 3 H), 4.70 (q, *J* = 7.3 Hz, 1 H) 7.19–7.33 (m, 5 H), 7.47–7.57 (m, 2 H), 7.66 (d, *J* = 8.5 Hz, 1 H), 7.79 (d, *J* = 8.5 Hz, 1 H), 7.92 (d, *J* = 8.2 Hz, 1 H), 8.68 (d, *J* = 8.5 Hz, 1 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 17.0, 23.2, 39.0, 120.8, 123.5, 124.5, 124.5, 125.8, 126.4, 127.3, 128.5, 128.9, 129.5, 130.5, 132.1, 134.8, 136.1, 144.6, 145.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{19}S$: 303.1207; found: 303.1215.

Anal. Calcd for $C_{21}H_{18}S$: C, 83.40; H, 6.00. Found: C, 83.68; H, 5.39.

### 1,2-Dimethylnaphtho[2,1-*b*]thiophene (6fa)[1]

Yield: 148 mg (70%); white solid; mp 99–101 °C (*n*-hexane).

IR (neat): 2917, 1612, 1506, 802, 740 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3 H), 2.76 (s, 3 H), 7.47–7.58 (m, 2 H), 7.64 (d, *J* = 8.5 Hz, 1 H), 7.76 (d, *J* = 8.5 Hz, 1 H), 7.92 (d, *J* = 8.0 Hz, 1 H), 8.70 (d, *J* = 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 14.2, 16.5, 120.6, 123.3, 124.3, 124.4, 125.7, 128.9, 129.8, 130.3, 132.1, 133.5, 134.7, 135.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}S$: 213.0737; found: 213.0732.

**2-Butyl-1-methylnaphtho[2,1-*b*]thiophene (6ga)**

Yield: 226 mg (89%); yellow crystals; mp 43–45 °C (*n*-hexane).

IR (neat): 2950, 1509, 1464, 1370, 798 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.5 Hz, 3 H), 1.45 (sext, *J* = 7.5 Hz, 2 H), 1.72 (quint, *J* = 7.5 Hz, 2 H), 2.78 (s, 3 H), 2.94 (t, *J* = 7.5 Hz, 2 H), 7.47–7.58 (m, 2 H), 7.65 (d, *J* = 8.5 Hz, 1 H), 7.78 (d, *J* = 8.5 Hz, 1 H), 7.93 (d, *J* = 8.2 Hz, 1 H), 8.70 (d, *J* = 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 13.9, 16.7, 22.4, 28.4, 33.7, 120.7, 123.4, 124.3, 124.4, 125.7, 128.9, 129.2, 130.4, 132.1, 134.8, 135.8, 139.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{19}S$: 255.1207; found: 255.1217.

Anal. Calcd for $C_{17}H_{18}S$: C, 80.26; H, 7.13. Found: C, 80.56; H, 7.16.

**1-Methyl-2-octylnaphtho[2,1-*b*]thiophene (6ha)**

Yield: 273 mg (88%); colorless needles; mp 54–55 °C (*n*-hexane).

IR (neat): 2927, 2851, 1465, 802, 733 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.1 Hz, 3 H), 1.23–1.46 (m, 10 H), 1.73 (quint, *J* = 7.8 Hz, 2 H), 2.78 (s, 3 H), 2.94 (t, *J* = 7.8 Hz, 2 H), 7.47–7.58 (m, 2 H), 7.65 (d, *J* = 8.5 Hz, 1 H), 7.78 (d, *J* = 8.2 Hz, 1 H), 7.93 (d, *J* = 8.2 Hz, 1 H), 8.72 (d, *J* = 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 14.1, 16.7, 22.7, 28.7, 29.3, 29.3, 29.4, 31.6, 31.9, 120.7, 123.4, 124.3, 124.4, 125.7, 128.9, 129.2, 130.4, 132.1, 134.8, 135.8, 139.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{27}S$: 311.1827; found: 311.1827.

Anal. Calcd for $C_{21}H_{26}S$: C, 81.23; H, 8.44. Found: C, 81.36; H, 8.42.

**2-Dodecyl-1-methylnaphtho[2,1-*b*]thiophene (6ia)**

Yield: 297 mg (81%); colorless needles; mp 69–71 °C (*n*-hexane).

IR (neat): 2915, 1466, 802, 733 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.26–1.45 (m, 18 H), 1.73 (quint, *J* = 7.6 Hz, 2 H), 2.78 (s, 3 H), 2.94 (t, *J* = 7.6 Hz, 2 H), 7.48–7.59 (m, 2 H), 7.65 (d, *J* = 8.5 Hz, 1 H), 7.79 (d, *J* = 8.5 Hz, 1 H), 7.93 (d, *J* = 8.1 Hz, 1 H), 8.72 (d, *J* = 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 14.1, 16.7, 22.7, 28.7, 29.3, 29.4, 29.5, 29.6, 29.7, 29.7, 29.7, 31.5, 31.9, 120.7, 123.4, 124.3, 124.4, 125.7, 128.9, 129.2, 130.4, 132.0, 134.8, 135.8, 139.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{35}S$: 367.2459; found: 367.2451.

Anal. Calcd for $C_{25}H_{34}S$: C, 81.91; H, 9.35. Found: C, 81.76; H, 9.46.

**1-Methyl-2-octadecylnaphtho[2,1-*b*]thiophene (6ja)**

Yield: 342 mg (76%); white solid; mp 84–85 °C (*n*-hexane).

IR (neat): 2953, 1466, 802, 734 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.6 Hz, 3 H), 1.25–1.44 (m, 30 H), 1.73 (quint, *J* = 7.6 Hz, 2 H), 2.78 (s, 3 H), 2.94 (t, *J* = 7.8 Hz, 2 H), 7.47–7.59 (m, 2 H), 7.65 (d, *J* = 8.5 Hz, 1 H), 7.78 (d, *J* = 8.5 Hz, 1 H), 7.93 (d, *J* = 7.8 Hz, 1 H), 8.72 (d, *J* = 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 14.1, 16.7, 22.7, 28.7, 29.3, 29.4, 29.5, 29.6, 29.7, 29.7 (overlap), 31.6, 31.9, 120.7, 123.4, 124.3, 124.4, 125.7, 128.9, 129.2, 130.4, 132.0, 134.8, 135.8, 139.9.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{47}S$: 451.3398; found: 451.3407.

Anal. Calcd for $C_{31}H_{46}S$: C, 82.60; H, 10.29. Found: C, 82.22; H, 10.16.

## Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610866.

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