Synthesis of 2-Nitrothiophenes *via* Tandem Henry Reaction and Nucleophilic Substitution on Sulfur from β-Thiocyanatopropenals

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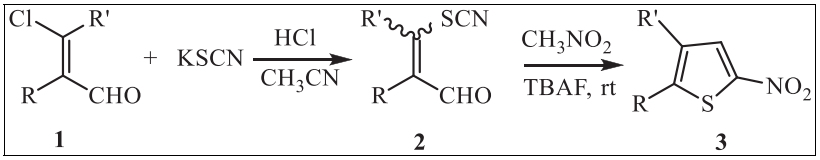

A new synthetic route of 2-nitrothiophenes was described through a tetra-*n*-butylammonium fluoride-promoted or diisopropylethylamine-promoted tandem Henry reaction and nucleophilic substitution of nitromethane with 3-thiocyanatopropenals, which were conveniently prepared by the replacement reaction of 3-chloropropenals with potassium thiocyanate under a mild acidic condition.

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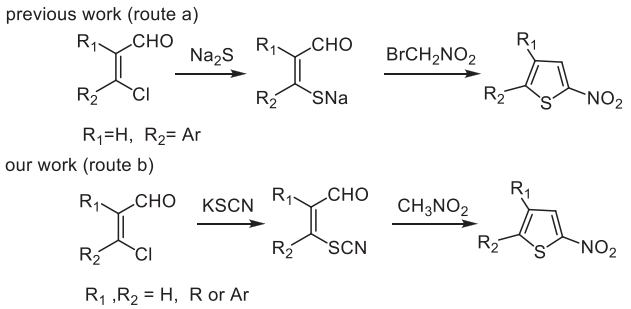
INTRODUCTION

The structural motif of thiophene widely exists as a key unit in naturally occurring products, pharmaceuticals, some of the top-selling marketed drugs (Plavix, Spriva, raloxifene, zileuton, and clopidogrel) [1–4], and functional materials [5–9] owing to their structural rigidity and specific electronic properties. Accordingly, a variety of synthetic methodologies have been developed for functionalized thiophenes [10,11]. Among these, the representative method is classical Paal−Knorr reaction [12,13], which involves sulfuration of the corresponding 1,4-dicarbonyl precursors using reagents such as H_2S/HCl, P_2S_5, and Lawesson's reagent. In addition, the Gewald reaction is applied to synthesis of 2-aminothiophenes *via* a multicomponent condensation between sulfur, an α-methylene carbonyl compound, and an α-cyanoester [14–16]. An alternative method to access substituted thiophenes involves the use of inorganic sulfide salts as the sulfur source. For example, Xi's group described an approach to variously substituted thiophenes through copper-catalyzed tandem *S*-alkenylation of potassium sulfide with 1,4-diiodo-1,3-dienes [17]. Jiang and co-workers reported a CuI-catalyzed synthesis of 2,5-disubstituted thiophenes from haloalkynes or 1,3-diynes in the presence of excessive $Na_2S{\cdot}9H_2O$ [18]. Additionally, several diversely substituted thiophenes were prepared by the reaction of substituted 1,3-dienyl bromides with K_2S in the presence of iodine without using any metal [19]. In addition, Kirsch and co-workers reported a transition metal-free method for the synthesis of 2-nitrothiophene (Scheme 1a), in which Na_2S, 3-chloroenals, and bromonitromethane were employed [20]. Recently, we developed a simple protocol to generate cyclic dienolates from cyclic β-haloenals under mild conditions [21,22] and fluoride-promoted tandem reaction between cyclic β-thiocyanatoenals and terminal electron-deficient alkenes [23]. In this work, we designed an alternative synthesis route of nitrothiophene through a tandem Henry reaction and nucleophilic substitution on sulfur of thiocyanate as outlined in Scheme 1b.

RESULTS AND DISCUSSION

In the beginning, a model reaction of 3-chloro-3-phenylpropenal **1a** (1.0 mmol) with potassium thiocyanate (1.5 mmol) was performed in typical polar solvents at room temperature in view of the solubility of potassium thiocyanate. The reaction was followed by thin-layer chromatography (TLC), and almost no substitution product **2a** was provided in CH_3OH, acetone, dimethylformamide, CH_3CN, or dimethyl sulfoxide after 24 h (Table 1, entries 1–5). In contrast, the reaction in glacial acetic acid underwent readily, affording the desired product, 3-phenyl-3-thiocyanatopropenal (**2a**) in moderate yield (Table 1, entry 6). This result encouraged us to evaluate the effect of acidic additives on the replacement reaction. Accordingly, a surprisingly big acceleration to the earlier substitution was achieved when 2.0 mmol of 1 *M* aqueous HCl solution was added into the reaction mixture, and the replacement product **2a** was produced in all the used solvents, despite of the different yields (Table 1, entries 1–5). The highest yield of **2a** was isolated in the case of CH_3CN (Table 1, entry 4). Estimation of the effect of amount of HCl on the reaction clearly showed that addition of 2.0 mmol of HCl was the best choice (entries 7–9). In addition, the weakly acidic

Scheme 1. Synthesis of 2-nitrothiophenes from 3-chloroenals.

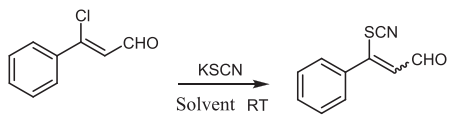


benzoic acid almost cannot improve the reaction yield (Table 1, entry 10).

Based on the optimized reaction parameters, a variety of 3-thiocyanatoenals were prepared in moderate-to-high yields under the optimized conditions. The chemical structures and yields of the substitution products are summarized in Table 2. It should be noted that both the geometric isomers are simultaneously generated in the cases of **2a–e** during the reaction, despite of the initial geometric configuration of 3-haloenals **1a–e**. This observation in stereochemistry clearly indicates that the replacement of chloro group by thiocyanate followed a stepwise process, namely, nucleophilic addition and 1,2-elimination.

Table 1

Optimized preparation of 3-thiocyanatoenal **2a**.[a]



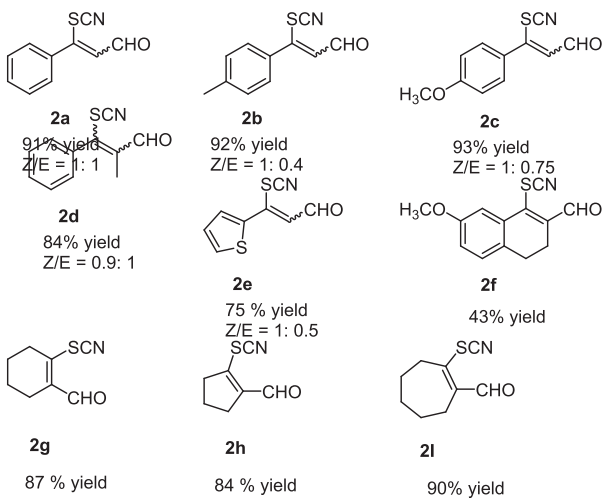
1a **2a**

Entry	Solvent	Additive	Yield (%)
1	CH_3OH	None	Trace
		1 *M* HCl (2 mmol)	76
2	Acetone	None	Trace
		1 *M* HCl (2 mmol)	65
3	DMF	None	Trace
		1 *M* HCl (2 mmol)	22
4	CH_3CN	None	Trace
		1 *M* HCl (2 mmol)	91
5	DMSO	None	Trace
		1 *M* HCl (2 mmol)	46
6	AcOH	None	54
7	CH_3CN	None	Trace
		1 *M* HCl (1 mmol)	68
8	CH_3CN	None	Trace
		1 *M* HCl (2 mmol)	91
9	CH_3CN	None	Trace
		1 *M* HCl (4 mmol)	70
10	CH_3CN	PhCOOH	<10

KSCN, potassium thiocyanate; RT, room temperature; DMF, dimethylformamide; DMSO, dimethyl sulfoxide.
[a]Reaction was conducted by mixing **1a** (1.0 mmol) and KSCN (1.5 mmol) in 3 mL of the given solvent and stirred at room temperature for 24 h.

Table 2

Preparation of 3-thiocyanatoenals from 3-haloenals and KSCN.



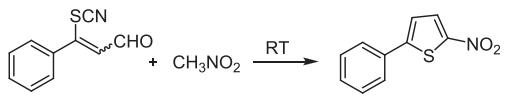
KSCN, potassium thiocyanate.

After optimizing preparation of 3-thiocyanatoenals, we started to investigate their Henry reactions with nitromethane in the presence of a commonly used base. The initial reaction was performed between 3-phenyl-3-thiocyanatopropenal (**2a**, 0.2 mmol, *Z*/*E* = 1:1), nitromethane (1.0 mL), and tetra-*n*-butylammonium fluoride (0.2 mmol) at room temperature. The reaction was followed by TLC and almost completed within 4 h. Product analysis showed that the earlier reaction furnished 35% yield of the desired product **3a**, as well as a certain amount of 2-nitro alcohol (Table 3, entry 1). Then some common inorganic and organic bases involving NaOH, Cs_2CO_3, 4-(*N*,*N*-dimethylamino) pyridine, *N*-methylmorpholine, 1,8-diazabicyclo[5.4.0] undec-7-ene, triethylamine, and diisopropylethylamine (DIPEA) were assessed; unfortunately, the product yields cannot be improved well in all the cases (Table 3, entries 2–8). The dosage of base has also little effect on the product yield (Table 3, entries 9–10).

Under the earlier reaction conditions, the reaction of different 3-thiocyanatoenals **2b–i** with nitromethane was next studied. The results listed in Table 4 showed that all the 3-thiocyanatoenals prepared earlier could undergo the tandem reaction, giving moderate yields of 2-nitrothiophenes. A good yield of product **3f** was isolated in the case of **2f** with only *Z*-isomer. To our delight, the use of sterically bulky DIPEA could improve the reaction yields of cyclic 3-thiocyanatoenals **2g–i** to a considerable extent. For example, the yield of product **3g** was raised from 44 to 71%.

Table 3

Tandem reaction between **2a** and nitromethane.[a]



2a **3a**

Entry	Base	Base: **2a**	Yield (%)[b]
1	TBAF	1:1	35
2	NaOH	1:1	20
3	Cs_2CO_3	1:1	30
4	DMAP	1:1	26
5	NMM	1:1	Trace
6	DBU	1:1	30
7	TEA	1:1	12
8	DIPEA	1:1	31
9	DIPEA	2:1	32
10	TBAF	2:1	35

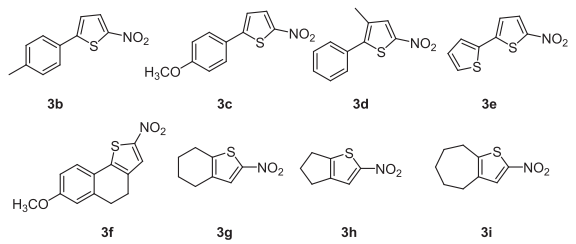
RT, room temperature; TBAF, tetra-*n*-butylammonium fluoride; DMAP, 4-(*N*,*N*-dimethylamino)pyridine; NMM, *N*-methylmorpholine; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; TEA, triethylamine; DIPEA, diisopropylethylamine.

[a]Reaction between 3-phenyl-3-thiocyanatoenal (*Z*/*E* = 1:0.75, 0.2 mmol), nitromethane (1 mL), and TBAF (0.2 mmol) was carried out at RT for 4 h.

[b]Isolated yields.

Table 4

Tandem reaction between **2a–i** and nitromethane.[a]



3b **3c** **3d** **3e**

3f **3g** **3h** **3i**

Entry	Enal **2**	*Z*/*E* ratio	Product	Yield (%)[b]
1	**2a**	1:1	**3a**	33
2	**2b**	1:0.4	**3b**	54
3	**2c**	1:0.75	**3c**	48
4	**2d**	1:0.9	**3d**	42
5	**2e**	1:0.5	**3e**	34
6	**2f**	1:0	**3f**	65
7	**2g**	1:0	**3g**	44 (71)[c]
8	**2h**	1:0	**3h**	45 (50)[c]
9	**2i**	1:0	**3i**	50 (65)[c]

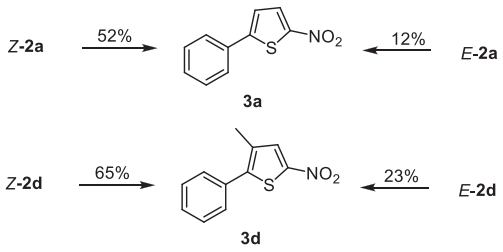
[a]Reaction between 3-thiocyanatoenals (0.2 mmol), nitromethane (1 mL), and tetra-*n*-butylammonium fluoride (0.2 mmol) was carried out at room temperature for 4 h.

[b]Isolated yields.

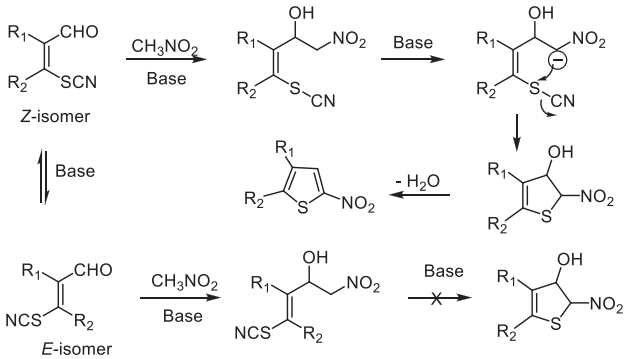
[c]Yields in parentheses using diisopropylethylamine as the base.

The remaining issue for the replacement reaction is how the configuration of 3-thiocyanatoenals affected the reaction and product yield. To solve this problem, we carefully separated *Z*-isomer from *E*-isomer of both **2a** and **2d** by silica gel column chromatography and then conducted their tandem reactions individually. As a consequence, the reaction of *Z*-**2a** afforded 52% yield of the desired product **3a**, whereas that of *E*-**2a** afforded only 12% yield of **3a** under the earlier condition. Similar results were also observed in the cases of *Z*-**2d** and *E*-**2d**, where 65 and 23% yields of **3d** were isolated, respectively (Scheme 2).

Scheme 2. Effect of configuration of 3-thiocyanatoenals on the reaction.



Scheme 3. A possible mechanism for the formation of 2-nitrothiophene.



Obviously, *Z*-isomer greatly favored the formation of 2-nitrothiophenes in comparison with *E*-isomer. To understand the earlier phenomenon well, we further investigated the side product formed in the reaction of *E*-**2a**. Besides the desired 2-nitrothiophene **3a**, 34% yield of the 2-nitro alcohol was also produced, as well as some complicated side products with high polarity. This result demonstrated that the configuration of 3-thiocyanatoenals has a crucial influence on nucleophilic attack on sulfur of the 2-nitro alcohol. A possible mechanism was supposed and depicted in Scheme 3.

CONCLUSIONS

In conclusion, we have developed a convenient synthetic way of 2-nitrothiophenes through a tandem nitroaldol reaction–nucleophilic substitution on sulfur of thiocyanate between 3-thiocyanatoenals and nitromethane promoted by fluoride or DIPEA under mild reaction conditions. This tandem reaction realized the synthesis of

2,5-disubstituted and 2,4,5-trisubstituted thiophenes with high regioselectivity.

EXPERIMENTAL

Reactions were monitored by TLC analysis using silica gel 60 Å F-254 thin-layer plates. Flash column chromatography was performed on silica gel 60 Å, 10–40 μm. ^{1}H-NMR spectra were recorded on a Bruker instrument (400 MHz, Bruker AV, Switzerland). Chemical shifts are reported in parts per million from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; and m; multiplet), coupling constants (Hz), and integration. ^{13}C-NMR spectra were recorded on a Bruker instrument (101 MHz) with complete proton decoupling. Chemical shifts are reported in parts per million from the TMS with the solvent resonance as internal standard. IR spectra were recorded on a Bruker Fourier transform infrared spectroscopy spectrometer. High-resolution mass spectrometry was measured on a Waters Micromass GCT (Milford, Massachusetts, USA) Premier with an electron impact source.

General procedure for the preparation of 3-thiocyanatoenals. Dissolved potassium thiocyanate (102 mg, 1.5 mmol) into acetonitrile (6.0 mL) and into the solution 3-chloroenal (1.0 mmol) was added with magnetic stirring at room temperature. After the mixture was stirred for 10 min, 2.0 mL of 1 *M* aqueous HCl solution was added with continuous stirring, and the reaction mixture was kept at room temperature for 24 h. The solvent was evaporated under reduced pressure, and into the residue, 5 mL of water was added. The mixture was extracted with dichloromethane for three times (3 × 6 mL). The combined organic phase was washed with dilute aqueous solution of $NaHCO_3$ and water and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was isolated by silica gel column chromatography using petroleum ether/ether (8:1 v/v) to give the desired product **2**. The spectroscopic data for the prepared 3-thiocyanatoenals are listed in the following.

(Z/E)-3-Phenyl-3-thiocyanatoacrylaldehyde (2a). Yellow oil; *Z/E* ratio = 1/1 (from ^{1}H-NMR); for (*Z*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.88 (d, *J* = 2.8 Hz, 1H), 7.57–7.46 (m, 5H), 6.71 (d, *J* = 2.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.44, 152.85, 136.06, 132.02, 129.73, 129.06, 128.45, 109.04. For (*E*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.40 (d, *J* = 7.2 Hz, 1H), 7.57–7.46 (m, 5H), 6.68 (d, *J* = 7.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): 188.38, 150.35, 131.50, 131.12, 129.39, 128.35, 126.71, 106.84; IR (film): ν 3059, 2923, 2853, 2748, 2161, 1723, 1672, 1557, 1116, 761, 696 cm^{-1}.

(Z/E)-3-(4-Methylphenyl)-3-thiocyanatoacrylaldehyde (2b). Yellow oil; *Z/E* ratio = 1/0.4 (from ^{1}H-NMR); for (*Z*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.77 (d, *J* = 3.2 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 6.62 (d, *J* = 3.2 Hz, 1H), 2.35 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.63, 149.45, 142.15, 130.05, 129.73, 128.41, 128.01, 109.37, 21.48. For (*E*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.34 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.57 (d, *J* = 7.6 Hz, 1H), 2.37 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.45, 153.11, 142.80, 133.19, 129.78, 128.78, 126.96, 107.29, 21.51; IR (film): ν 2922, 2856, 2159, 1671, 1550, 1506, 1447, 1226, 1117, 1017, 815, 771 cm^{-1}.

(Z/E)-3-(4-Methoxyphenyl)-3-thiocyanatoacrylaldehyde (2c). Yellow oil; *Z/E* ratio = 1/0.75 (from ^{1}H-NMR); for (*Z*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.89 (d, *J* = 3.6 Hz, 1H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.64 (d, *J* = 3.6 Hz, 1H), 3.86 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.41, 162.45, 149.42, 130.20, 127.81, 126.74, 114.54, 109.16, 55.56. For (*E*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.40 (d, *J* = 7.2 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.61 (d, *J* = 7.2 Hz, 1H), 3.87 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.68, 162.67, 152.96, 131.63, 127.99, 123.23, 114.79, 107.26, 55.63; IR (film): ν 3035, 2967, 2932, 2840, 2157, 1666, 1599, 1554, 1503, 1459, 1252, 1173, 1112, 1020, 992, 825, 793 cm^{-1}.

(Z/E)-2-Methyl-3-phenyl-3-thiocyanatoacrylaldehyde (2d). Yellow oil; *Z/E* ratio = 0.90/1 (from ^{1}H-NMR); for (*Z*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 7.53–7.47 (m, 3H), 7.34–7.31 (m, 2H), 1.93 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 190.63, 143.18, 136.09, 135.12, 130.30, 129.15, 128.41, 109.24, 16.41. For (*E*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.27 (s, 1H), 7.53–7.47 (m, 3H), 7.40–7.37 (m, 2H), 2.05 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.50, 148.67, 137.88, 132.75, 130.93, 130.25, 128.99, 107.08, 13.31; IR (film): ν 3059, 2920, 2857, 2742, 2161, 1675, 1589, 1486, 1443, 1390, 1254, 1214, 1022, 902, 857, 762, 711 cm^{-1}.

(Z/E)-3-Thiocyanato-3-(thiophen-2-yl)acrylaldehyde (2e). Yellow oil; *Z/E* ratio = 1/0.5 (from ^{1}H-NMR); for (*Z*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.06 (d, *J* = 4.8 Hz, 1H), 7.68 (d, *J* = 4.0 Hz, 1H), 7.62 (d, *J* = 5.2 Hz, 1H), 7.20 (dd, *J* = 5.2 Hz, 4.0 Hz, 1H), 6.75 (d, *J* = 4.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.55, 139.23, 133.05, 132.07, 128.98, 128.45, 108.30. For (*E*)-isomer, ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.70 (d, *J* = 7.2 Hz, 1H), 7.69 (d, *J* = 5.2 Hz, 1H), 7.44 (d, *J* = 4.0 Hz, 1H), 7.21 (dd, *J* = 5.2 Hz, 4.0 Hz, 1H), 6.67 (d, *J* = 7.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.14, 138.19, 132.40, 131.66, 128.82, 128.69, 106.95; IR (film): ν 3105, 2921, 2851, 2161, 1667, 1571, 1509, 1415, 1232, 1112, 848, 772, 719 cm^{-1}.

7-Methoxy-1-thiocyanato-3,4-dihydronaphthalene-2-carbaldehyde (2f). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.42 (s, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 6.90 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H), 6.79 (d, *J* = 2.4 Hz, 1H), 3.85 (s, 3H), 2.81 (m, 2H), 2.66 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 188.12, 161.53, 140.35, 139.11, 136.40, 128.46, 122.61, 113.44, 111.37, 108.06, 54.54, 26.03, 21.89; IR (film): ν 2965, 2938, 2866, 2836, 2158, 1649, 1596, 1543, 1490, 1450, 1381, 1310, 1249, 1182, 1104, 909, 866, 827, 799 cm^{-1}.

2-Thiocyanatocyclohex-1-enecarbaldehyde (2g). Yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 2.79–2.75 (m, 2H), 2.55–2.50 (m, 2H), 1.89–1.83 (m, 2H), 1.79–1.74 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 190.78, 141.59, 134.26, 109.73, 33.29, 26.58, 22.98, 21.06; IR (film): ν 2940, 2863, 2756, 2154, 1730, 1677, 1564, 1419, 1126, 987, 744, 698 cm^{-1}.

2-Thiocyanatocyclopent-1-enecarbaldehyde (2h). This compound was obtained as yellow liquid; ^{1}H-NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ 9.69 (s, 1H), 3.07–3.02 (m, 2H), 2.90–2.85 (m, 2H), 2.22–2.14 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 187.66, 144.11, 138.21, 109.07, 39.59, 31.69, 22.25; IR (film): ν 2966, 2930, 2880, 2158, 1657, 1549, 1465, 1111, 979, 727 cm^{-1}.

2-Thiocyanatocyclohept-1-enecarbaldehyde (2i). Yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 9.73 (s, 1H), 3.03–3.00 (m, 2H), 2.71–2.68 (m, 2H), 1.91–1.85 (m, 2H), 1.76–1.70 (m, 2H), 1.60–1.54 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 190.18, 147.90, 140.74, 110.15, 37.99, 31.47, 28.91, 25.52, 24.90; IR (film): ν 2925, 2884, 2847, 2147, 1670, 1655, 1531, 1398, 1212, 1106, 952, 826, 770 cm^{-1}.

General procedure for synthesis of 2-nitrothiophenes. 3-Phenyl-3-thiocyanatoenal **2a** (*Z*/*E* = 1:1, 0.2 mmol), nitromethane (1.0 mL), and tetra-*n*-butylammonium fluoride (0.2 mmol) were added to a 10-mL flask equipped with a magnetic stirring bar. The solution was stirred for 2 h at room temperature, and the reaction progress was monitored by TLC. After 4 h, the reaction was completed. The reaction mixture was evaporated under reduced pressure, and the residue was purified by flash chromatography on silica gel eluting with petroleum ether/ethyl acetate (5:1 v/v) to give a yellow solid product **3a**. The other 2-nitrothiophenes were prepared according to the earlier procedure.

2-Nitro-5-phenylthiophene (3a). Yellowish crystals; mp 123–124°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 4.4 Hz, 1H), 7.64–7.62 (m, 2H), 7.46–7.44 (m, 3H), 7.24 (d, *J* = 4.4 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 152.05, 132.14, 130.10, 129.70, 129.42, 126.33, 122.38; IR (film): ν 3106, 3064, 2960, 2924, 1725, 1600, 1580, 1536, 1499, 1446, 1427, 1331, 1224, 1041, 955, 904, 813, 757, 729, 683 cm^{-1}.

*2-Nitro-5-***p***-tolylthiophene (3b).* Yellowish crystals; mp 86–87°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 4.4 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 4.4 Hz, 1H), 2.40 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 152.42, 140.54, 130.07, 129.74, 126.21, 121.82, 21.37; IR (film): ν 3115, 3095, 2918, 2853, 1602, 1534, 1510, 1486, 1421, 1355, 1328, 1251, 1039, 953, 803, 728 cm^{-1}.

2-(4-Methoxyphenyl)-5-nitrothiophene (3c). Yellowish crystals; mp 129–131°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.89–7.88 (d, *J* = 4.0 Hz, 1H), 7.58–7.56 (d, *J* = 8.8 Hz, 2H), 7.13 (d, *J* = 4.0 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 161.25, 152.43, 129.95, 127.79, 124.83, 121.22, 114.82, 55.51; IR (film): ν 3099, 3013, 2959, 2928, 2831, 1601, 1534, 1509, 1477, 1427, 1355, 1319, 1256, 1202, 1174, 1055, 1027, 956, 813, 732 cm^{-1}.

3-Methyl-5-nitro-2-phenylthiophene (3d). Yellowish crystals; mp 73–74°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.48–7.44 (m, 5H), 2.33 (s, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 146.48, 133.51, 132.27, 131, 79, 129.28, 129.01, 15.12; IR (film): ν 3100, 3055, 2964, 2923, 1624, 1600, 1538, 1483, 1444, 1410, 1390, 1325, 1239, 1073, 1008, 969, 872, 806, 765, 729, 695 cm^{-1}.

5-Nitro-2,2′-bithiophene (3e). Brown crystals; mp 113–113.5°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 4.0 Hz, 1H), 7.41 (dd, *J* = 5.2 Hz, 0.4 Hz, 1H), 7.36 (dd, *J* = 3.6 Hz, 0.4 Hz, 1H), 7.10 (dd, *J* = 5.2 Hz, 3.6 Hz, 1H), 7.09 (d, *J* = 4.0 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 145.15, 134.96, 129.69, 128.56, 127.93, 126.63, 122.45; IR (film): ν 3084, 2922, 2851, 1635, 1595, 1543, 1512, 1485, 1434, 1374, 1328, 1220, 1033, 892, 838, 804, 718 cm^{-1}.

*8-Methoxy-2-nitro-4,5-dihydronaphtho[1,2-***b***]thiophene (3f).* Yellowish crystals; mp 130–131°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.35–7.26 (m, 1H), 6.79–6.78 (m, 1H), 3.84 (s, 3H), 2.96–2.93 (t, 2H), 2.82–2.78 (t, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 160.98, 147.42, 145.13, 138.19, 134.84, 129.45, 125.44, 122.29, 114.34, 112.73, 55.46, 28.83, 23.46; IR (film): ν 2932, 2835, 1607, 1571, 1529, 1479, 1437, 1388, 1322, 1308, 1277, 1242, 1172, 1117, 1028, 977, 869, 836, 800, 733 cm^{-1}.

*2-Nitro-4,5,6,7-tetrahydrobenzo[***b***]thiophene (3g).* Yellowish crystals; mp 73°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 2.80–2.77 (t, *J* = 7.6 Hz, 2H), 2.64–2.61 (t, *J* = 7.6 Hz, 2H), 1.90–1.81 (m, 4H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 145.73, 135.86, 129.34, 25.46, 25.27, 22.69, 22.18; IR (film): ν 3096, 3073, 2946, 2898, 2867, 1546, 1496, 1435, 1344, 1326, 1299, 1133, 1083, 859, 804, 732 cm^{-1}.

*2-Nitro-5,6-dihydro-4***H***-cyclopenta[***b***]thiophene (3h).* Yellowish crystals; mp 48–50°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 2.98 (t, *J* = 7.7 Hz, 2H), 2.80 (t, *J* = 7.7 Hz, 2H), 2.45 (m, *J* = 7.7 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 151.47, 145.30, 124.49, 30.03,

28.44, 28.03; IR (film): ν 3110, 2924, 2851, 1562, 1531, 1493, 1439, 1392, 1333, 1299, 1152, 857, 733 cm^{-1}.

2-Nitro-5,6,7,8-tetrahydro-4H-cyclohepta[b]thiophene (3i). Yellowish crystals; mp 51–53°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 2.84–2.81 (m, 2H), 2.71–2.69 (m, 2H), 1.91–1.86 (m, 2H), 1.76–1.70 (m, 2H), 1.67–1.62 (m, 2H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 150.37, 145.84, 141.61, 131.32, 32.06, 30.81, 27.81, 27.41; IR (film): ν 3095, 3072, 2960, 2928, 2847, 1541, 1498, 1405, 1335, 1136, 1075, 950, 887, 826, 799, 738 cm^{-1}.

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