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Facile synthesis of [1]benzothieno[3,2-*b*]benzothiophene from *o*-dihalostilbenes

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ABSTRACT

A convenient one-pot synthesis of [1]benzothieno[3,2-*b*]benzothiophene from readily available *o*-dihalostilbenes using combined reagents of sodium sulfide nonahydrate ($Na_2S{\cdot}9H_2O$) or sodium hydrosulfide hydrate ($NaSH{\cdot}nH_2O$) and sulfur is described along with plausible reaction paths in this intriguing reaction.

Benzo[*b*]thiophene (BT) is an important structural component in the development of organic optoelectronic materials, including organic photovoltaics[1] and field-effect transistors.[2] For these applications, the BT moiety is often incorporated into further π-extended molecular systems, which can be classified into several types. One of these includes compounds where two or more thiophene rings are fused onto a benzene or a naphthalene core, for example, benzo[1,2-*b*:4,5-*b*′]dithiophene (BDT),[3] benzo[1,2-*b*:3,4-*b*′:5,6-*b*″]trithiophene (BTT),[4] or naphtho[1,2-*b*:5,6-*b*′]dithiophene (NDT)[5] (Class I in Fig. 1). Another class is compounds with two BT units fused at the thiophene *b*-bonds, for example, [1]benzothieno[3,2-*b*]benzothiophene (BTBT)[6] and dinaphtho[2,3-*b*:2′,3′-*f*]thieno[3,2-*b*]thiophene (DNTT)[7] (Class II in Fig. 1).

For the synthesis of the compounds in Class I, we recently developed a convenient one-pot procedure from readily available *o*-halo-substituted ethynylbenzenes (Scheme 1).[8] The procedure only requires heating of the substrate with sodium sulfide nonahydrate ($Na_2S{\cdot}9H_2O$) in *N*-methyl-2-pyrrolidone (NMP) at 180 °C and is applicable to the synthesis of not only simple BT derivatives but also the BDT, BTT,[8] and NDT derivatives.[5]

With this successful development of the facile synthetic procedure for the Class I compounds, we preliminarily tested a similar reaction for the synthesis of BTBT using $Na_2S{\cdot}9H_2O$ as a reagent and *o*-dichlorostilbene as a substrate, the latter of which is easily available via a low-valent titanium-mediated coupling reaction of *o*-chlorobenzaldehyde (Scheme 2, entry 1 in Table 1).[9] However, the major product of this reaction was not the desired compound, BTBT, but dibenzo[*b*,*f*]thiepin (**1**),[10] with the sulfur-containing seven-membered ring, in 44% isolated yield. This result indicates that the aromatic nucleophilic substitution (S_NAr) reaction on the dichlorostilbene substrate took place, but the amount of sulfur source was not sufficient and/or that the intramolecular S_NAr reaction favorably occurs in combination with the isomerization from *trans*- to *cis*-form to afford **1**.

With these experimental results and considerations, we then attempted a similar reaction by using a mixed reagent of an equimolar amount of $Na_2S{\cdot}9H_2O$ and elemental sulfur in NMP at 180 °C (entry 2 in Table 1).[11] The isolated products after purification with

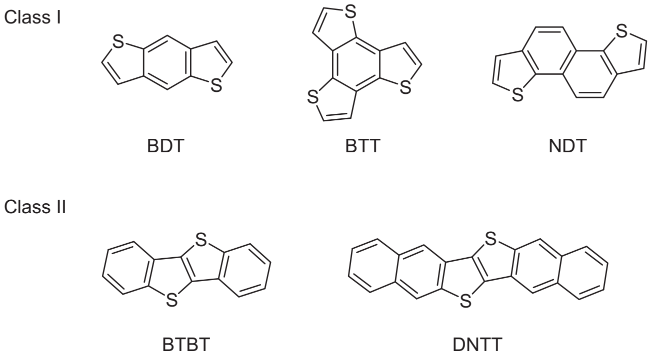
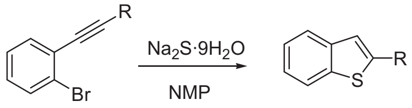


Figure 1. Two classes of π-extended BT structures.



Scheme 1. One-pot synthesis of BT derivatives from *o*-halo-substituted ethynylbenzenes.

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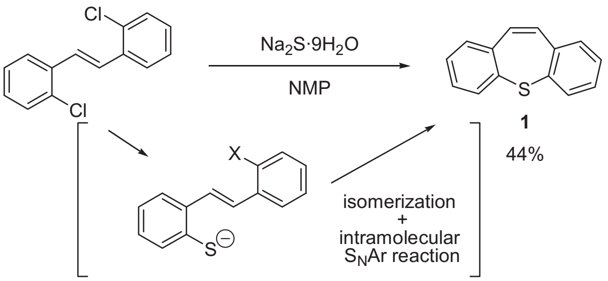
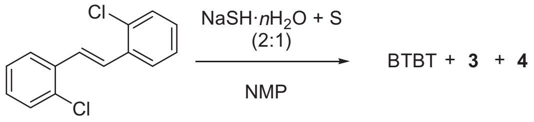


Scheme 2. Reaction of *o*-dichlorostilbene with $Na_2S·9H_2O$.

gel-permeation chromatography (JAI-GEL 1H, 2H column assembly) included desired BTBT (16% yield, $R_v = 250$ mL), **1** (12% yield, $R_v = 240$ mL), and 2-pheneylbenzo[*b*]thiophene (**2**, 13% yield, $R_v = 245$ mL). Together with these well-characterized products, substantial amount of ill-characterized byproducts with relatively high molecular weight judged from EI-MS spectra ($m/z = 450$) and the retention volume of gel-permeation chromatography ($R_v = 205$ mL) was obtained and thus the material balance including the byproduct seemed to be relatively good (>70%). When the same reaction conditions were applied to *trans*-*o*-dibromostilbene[12] as the substrate, BTBT was isolated in 30% yield (entry 3) indicating higher reactivity of the bromo compound than that of the chloro compound. These experimental results indicate that the sodium sulfide-based reagent is useful for the synthesis of BTBT from *o*-dihalostilbene via the direct S_NAr-type reaction, cyclization, and dehydrogenation to form the central thieno[3,2-*b*]thiophene moiety.

We then tested sodium hydrosulfide hydrate ($NaSH·nH_2O$) instead of $Na_2S·9H_2O$ in a similar cyclization reaction from *o*-dichlorostilbene (Table 1, entries 4–8). Without the addition of elemental sulfur (entry 4), only small amount of BTBT was obtained (3%) together with dihydro-BT derivative (**3**, 41%) as the major product. Addition of elemental sulfur (entry 4)[11] altered the product distribution: BTBT (17%), **3** (13%), and other minor products with large amounts of the ill-defined byproduct. In this reaction, one half of elemental sulfur added was recovered after purification and then the amount of sulfur was reduced to half of $NaSH·nH_2O$ (entry 6), which gave almost the same yield of BTBT. Interestingly, when a reaction with the same reagents was carried out under ambient air conditions, the yield of BTBT was improved significantly up to 33% (entry 7). Under the identical reaction conditions, *o*-dibromostilbene as the substrate gave BTBT in 44% isolated yield (entry 8), which is fairly better than the previously reported yield of BTBT from (dichloromethyl)benzene (33%).[13] It should also be noted that the reactions of $NaSH·nH_2O$-based reagents (entries 4–8) did not afford dibenzothiepin (**1**), which means that the intramolecular S_NAr-type reaction does not occur with these reagents.

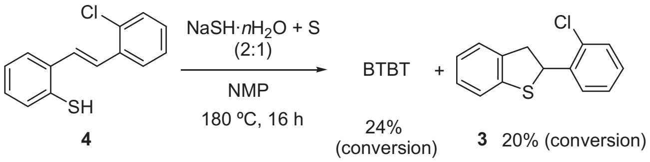
Table 2
Reaction of *o*-dichlorostilbene with $NaSH·nH_2O$ + S (2:1) at various temperatures[a]



Entry	Temp (°C)	Time (h)	Yield (%)		
			BTBT	**3**	**4**
1[b]	100	16	—	—	—
2	120	16	23	—	42
3	120	48	22	25	19

[a] All the reactions were carried out using 1.0 mmol *o*-dichlorostilbene under ambient air conditions.

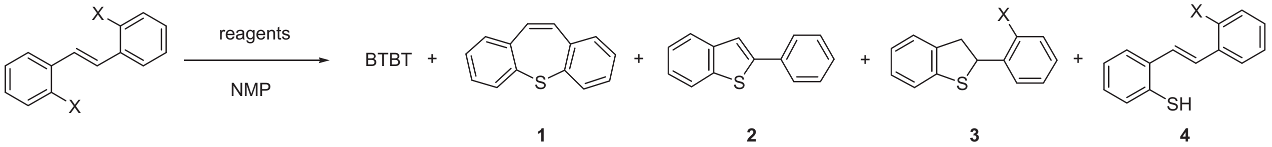
[b] The substrate was recovered (84%).



Scheme 3. Reaction of **4** with $NaSH·nH_2O$ + S (2:1).

The experimental results summarized in Table 1 clearly indicated that the combined reagents of $Na_2S·9H_2O$/S or $NaSH·nH_2O$/S in situ generating the sodium oligosulfide reagents (Na_2S_n) can be a good nucleophile in the S_NAr-type-reaction on *o*-dihalostilbene to afford BTBT in moderate yields (up to 44%). The formation of BTBT must involve the initial S_NAr reaction of the sodium oligosulfide nucleophile, subsequent cyclization onto the central double bond, and final aromatization. To investigate the reaction path to BTBT from *o*-dichlorostilbene, we then carried out the reactions at a lower

Table 1
Reaction of *trans*-*o*-dihalostilbene with various reagents[a]

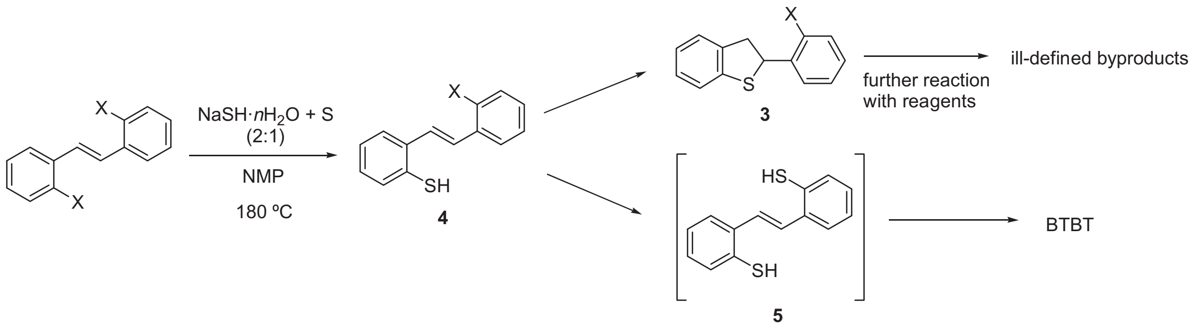


Entry	X	Reagent(s)	Temp (°C)	Time (h)	Yield (%)				
					BTBT[c]	**1**[c]	**2**[c]	**3**[c]	**4**[c]
1	Cl	$Na_2S·9H_2O$	180	16	—	44	—	18	6
2	Cl	$Na_2S·9H_2O$ + S (1:1)	180	16	16	12	13	—	—
3	Br	$Na_2S·9H_2O$ + S (1:1)	180	16	30	6	7	—	—
4	Cl	$NaSH·nH_2O$	180	16	3	—	3	41	6
5	Cl	$NaSH·nH_2O$ + S (1:1)	180	16	17	—	6	13	16
6	Cl	$NaSH·nH_2O$ + S (2:1)	180	16	18	—	Trace	10	Trace
7	Cl	$NaSH·nH_2O$ + S (2:1)[b]	180	4	33	—	9	10	9
8	Br	$NaSH·nH_2O$ + S (2:1)[b]	180	4	44	—	Trace	Trace	Trace

[a] All the reactions were carried out using 1.0 mmol *trans*-*o*-dihalostilbene under nitrogen atmosphere unless otherwise noted. All the products were isolated by gel-permeation chromatography on a LC-9204 (Japan Analytical Industry Co. Ltd) with a JAI-GEL 1H, 2H column assembly eluted with chloroform.

[b] The reaction was carried out under ambient conditions.

[c] BTBT, **1**, and **2** were characterized by comparing the authentic samples. Compounds **3** and **4** were fully characterized by means of spectroscopic analyses.



Scheme 4. Plausible reaction paths from *o*-dihalostilbene with NaSH·nH$_2$O and elemental sulfur.

temperature (Table 2). At 100 °C or at a much lower temperature no reaction took place, and most of the substrate was recovered (entry 1), whereas the reaction at 120 °C gave 2-chloro-2′-mercaptostilbene (**4**, 42% isolated yield) as the major product together with BTBT (23% isolated yield) (entry 2). Since the former compound, which was most likely formed through the initial S_NAr reaction on one benzene ring was thought to be an intermediate for BTBT, the longer reaction time at the same temperature was examined. However, the yield of BTBT was not increased instead the yield of **3** was increased (25%) with decreased yield of **4** (entry 3) suggesting that the intramolecular addition of the thiol moiety of **4** to the olefine took place almost exclusively.

By using isolated and purified **4** as the substrate, we then tested the reactions under the identical conditions in entries 7 and 8 in Table 1 (Scheme 3). Unexpectedly, nearly half of **4** was recovered in this reaction and BTBT and **3** were obtained in 24% and 20% conversion yields, respectively, together with the byproducts. These results indicate that **4** is indeed an important intermediate in the formation of BTBT, although the second S_NAr reaction on **4** with the thiolate anion is relatively slow and the intramolecular addition of the thiol moiety to the olefine part affording **3** is competing. Furthermore, we tested the reaction of **3** under the identical conditions. However, this reaction afforded only the ill-defined byproducts described above. Thus, we concluded that BTBT does not form via **3**.

Considering the results from all the reactions, we propose a plausible reaction path from *trans*-*o*-dihalostilbene to BTBT as shown in Scheme 4. The key intermediate **4** produced by the initial S_NAr-type reaction has two reaction paths: one is a further reaction with the reagent to produce *o*-dimercaptostilbene (**5**, not isolated) that smoothly cyclizes and aromatizes to BTBT.[14] The other is the intramolecular addition of the thiol moiety to the olefine part to produce **3**, further reaction of which finally gives the ill-defined byproducts. From the proposed reaction path, it is clear that the formation of *o*-dimercaptostilbene (**5**) from *o*-dihalostilbene via **4** is critical for the formation of BTBT. However, there are two reaction paths from **4** as mentioned above and these two paths compete under the present reaction condition, which would be the major reason for the low to moderate yields of BTBT. This consideration is supported by the fact that the reactive substrate in the S_NAr-type-reaction, *o*-dibromostilbene gave a better yield (44% yield) than the chloro counterpart did (33% yield). In addition, an improved yield of BTBT (39%) from *o*-dichlorostilbene when the reaction was carried out in hexamethylphosphoramide (HMPA), a solvent that accelerates the S_NAr-type reaction,[15] also supports this consideration.

In summary, we found that the combined reagents of $Na_2S{\cdot}9H_2O$/S or NaSH·nH$_2$O/S can be a good nucleophile in the S_NAr-type reaction on *o*-dihalostilbene to give BTBT. Since the yield is better than the previously reported yield (33%) of BTBT from (dichloromethyl)benzene,[13] the present reaction gives a new convenient method for the synthesis of BTBT. Furthermore, since the compounds with *o*-dihalostilbene substructure can be readily prepared from the corresponding aldehyde, the present reaction will be a useful method for the synthesis of the Class II compound in Figure 1. In fact, preliminary reactions under similar conditions using *trans*-1,2-bis(3-chloronaphth-2-yl)ethane as the substrate afforded DNTT, a superior OFET material recently utilized in various applications.[16] Optimization of the DNTT synthesis as well as the applications to the synthesis of other compounds is now actively conducted in our group.

Acknowledgments

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Supplementary data

Supplementary data (experimental details and spectroscopic characterizations of new compounds (**3** and **4**, X = Cl)) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.152.

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