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A facile two-step synthesis of thiophene end-capped aromatic systems

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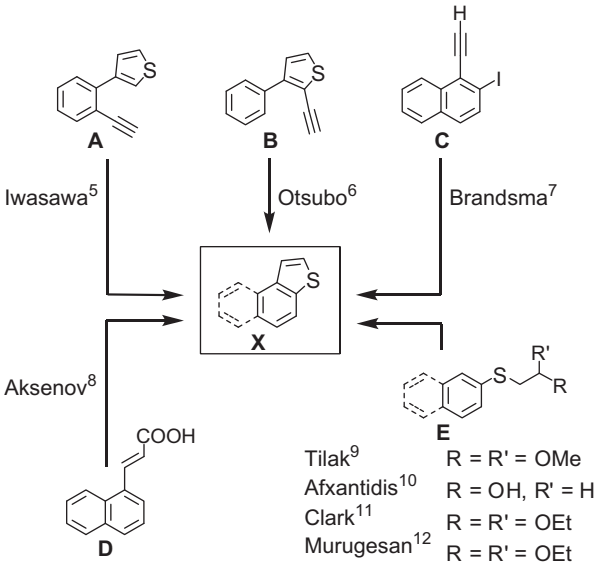
ABSTRACT

Thiophene end-capped aromatic analogues, that is, naphthothiophenes, naphthodithiophenes, pyrenothiophene, and benzotrithiophene, can be prepared from commercially available hydroxyarenes in two steps, including (1) a consecutive acid-mediated nucleophilic aromatic substitution of hydroxyarenes with 2-mercaptoethanol, followed by cyclization to form an arene-fused dihydrothiophene, and (2) oxidation of the dihydrothiophene unit to thiophene.

Thiophene, a sulfur-containing aromatic heterocycle, possesses remarkable electrochemical and optoelectrical properties. Due to their various potential applications in a wide range of the organic electronic devices,[1,2] thiophene derivatives have become major components or key precursors for the design and synthesis of novel materials.

Synthetic methods toward thiophene-fused polycyclic aromatic derivatives have been investigated extensively,[3] and the ease and efficiency of the procedures has played a key role in the development and applications of these materials in molecular devices.[4] However, only a limited number of literature reports describe the synthesis of thiophene-fused naphthalenes of type **X** and other related classes of aromatic compounds, as summarized in Scheme 1. Iwasawa and co-workers[5] reported $W(CO)_5$·THF-catalyzed electrocyclization of substrate **A** in the synthesis of naphtha[2,1-*b*]thiophene. Another approach was demonstrated by Otsubo's group[6] in which this naphthothiophene could be prepared by flash vacuum pyrolysis of monoethynyl thiophene **B**. In addition, Brandsma and co-workers[7] reported the synthesis of naphthothiophene (**X**) via the reaction of (1-naphthyl)acetylene **C** with the strong basic reagent, BuLi–*t*-BuOK, followed by the introduction of sulfur and then cyclization with *t*-BuOH. Aksenov's group[8] affected the synthesis, via oxidation, of *trans*-naphthylacrylic acid **D** with thionyl chloride in the presence of triethylbenzylammonium chloride.

Another possible route to construct thiophene analogues is via the cyclization of functionalized arylsulfides. For instance, Tilak



Scheme 1. Reported syntheses of naphtho[2,1-*b*]thiophene.

employed P_2O_5 and phosphoric acid for the cyclization of β-naphthyl ω-dimethoxyethyl sulfide **E** to furnish naphtho[2,1-*b*]thiophene.[9]

Related to Tilak's pioneering work, Afxantidis and co-workers[10] reported the use of aluminum orthophosphate catalyst and Pd on a solid support [Pd($AlPO_4$)] for the synthesis of benzothiophene.

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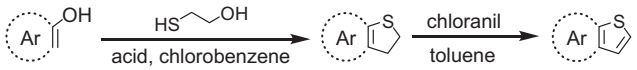


Scheme 2. Synthesis of thiophene end-capped aromatic compounds.

Clark and co-workers[11] employed the cyclization of phenylthioacetals over $ZnCl_2$-modified K10-montmorillonite. Similarly, Murugesan and co-workers reported that Zn^{2+} ion-exchanged beta zeolite catalyzed the cyclization of (phenylthio) acetaldehyde diethylacetal.[12] Recently, Takimiya et al. reported a one-pot synthesis of benzo[*b*]thiophenes via the cyclization of *o*-halo-ethynylbenzene and Na_2S.[13]

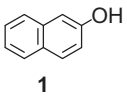
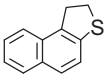
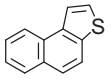
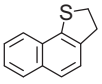
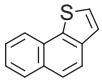
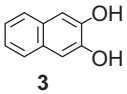
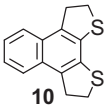
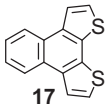
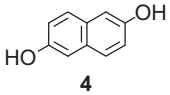
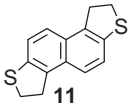
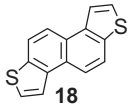
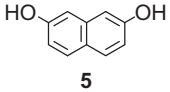
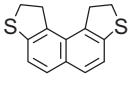
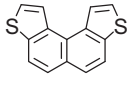
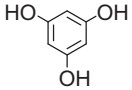
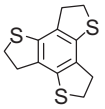
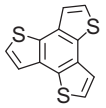
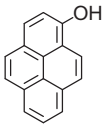
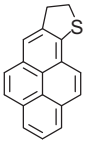
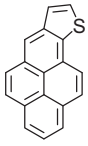
Our group is interested in acid-catalyzed nucleophilic aromatic substitutions for the synthesis of sulfur-containing aromatic systems.[14] The reaction effectively replaces the oxygen atom of hydroxyarenes with a sulfur atom from alkyl- or arylthiols to provide arylsulfides in variable yields depending on the reaction conditions.[14a,15] In this Letter, we report a convenient two-step route to thiophene end-capped aromatic analogues from commercially available hydroxyarenes. As shown in Scheme 2, the strategy involves: (1) construction of the dihydrothiophene derivative by a consecutive acid-mediated nucleophilic aromatic substitution between a hydroxyarene and 2-mercaptoethanol by exploiting the superior nucleophilicity of thiols over alcohols[16] to form a hydroxyethylarylsulfide, and a subsequent cyclization. (2) Oxidation of the corresponding dihydrothiophene to provide the corresponding thiophene end-capped aromatic analogue.

Following our reported procedure,[14a] *p*-toluenesulfonic acid (*p*-TsOH) was used as a mediator for dihydrothiophene formation. By using 2-naphthol (**1**) as the model starting material, the expected product **8** was obtained in a moderate yield (Table 1). However, when 2,3- and 2,7-dihydroxynaphthalenes were tested under the same reaction conditions (entries 3 and 5), the desired products were obtained in rather poor yields. Ultimately, all of these reactions gave insoluble by-products which were troublesome during the work-up procedure.[17] Therefore, we sought suitable conditions that would eliminate these difficulties and provide better yields.

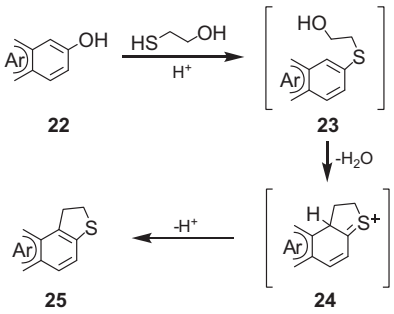
Nakazawa et al. reported an efficient use of trifluoromethanesulfonic acid (TfOH) to mediate the oxygen–sulfur replacement reaction.[15c] TfOH was thus used in our procedure and it was found to be a suitable acid since the yields were improved and the formation of the by-products after the work-up process was diminished.

As shown in Table 1, the cyclization reactions of mono- and dihydroxynaphthalenes **1**–**4** provided the corresponding dihydrothiophene- and tetrahydrodithiophene derivatives **8–11** in moderate yields.[18] The reaction of 2,7-dihydroxynaphthalene (**5**) gave a rather low yield of product possibly due to the steric hindrance on the concave side of the molecule. The reaction could also be applied to 1,3,5-trihydroxybenzene (**6**) and gave the desired product **13** in a 10% overall yield (one pot). This low yield is probably because of the high energy transition state that involved disruption of the

Table 1
Formation of thiophene end-capped aromatics from hydroxyarenes

Entry	Substrate	Hydrothiophene	Yield[a] (%)	Thiophene	Yield (%)
1	 **1**	 **8**	52 (54)	 **15**	86
2	 **2**	 **9**	29	 **16**	59
3	 **3**	 **10**	33 (22)	 **17**	78
4	 **4**	 **11**	37	 **18**	50
5	 **5**	 **12**	20 (12)	 **19**	57
6	 **6**	 **13**	10	 **20**	51
7	 **7**	 **14**	42	 **21**	64

[a] Yields in parenthesis are from the reaction mediated by *p*-TsOH.



Scheme 3. The proposed mechanism for the formation of dihydrothiophene derivatives.

aromaticity of the benzene ring. This procedure could also be applied to pyren-1-ol (**7**) to provide **14** in a 42% yield.

Subsequently, oxidation of the hydrothiophenes **8**–**14** with chloranil gave thiophene derivatives **15**–**21** in moderate to good yields.

A mechanism for dihydrothiophene formation can be proposed as follows. Nucleophilic aromatic substitution of hydroxyarene **22** takes place via keto-enol tautomerization of a hydroxyarene followed by the attack of the more nucleophilic sulfur to form a hemithioacetal which undergoes rearomatization.[14a,19] Subsequent intramolecular Friedel–Crafts type cyclization and rearomatization provided the dihydrothiophene **25** via intermediate **24** (Scheme 3).[20]

In summary, a synthetic strategy for the introduction of thiophene as end caps on aromatic systems has been established. The advantage of this method is the straightforward and efficient experimental methodology together with the ready availability of the starting materials. The method could be applied for the preparation of a variety of thiophene derivatives allowing a convenient access to naphthothiophenes, naphthodithiophenes, and terthienobenzene. This finding could accelerate the discovery of new applications in thiophene-based organic electronic devices.

Typical procedure for the synthesis of dihydrothiophene derivatives

Dihydrothiophene derivative 8

2-Mercaptoethanol (1.46 ml, 20.80 mmol) was added to a stirred solution of 2-naphthol (**1**) (0.50 g, 3.47 mmol) in chlorobenzene (15 mL). Next, TfOH (0.77 ml, 8.67 mmol) was added slowly at room temperature and the mixture was heated at reflux for 3 h. (It should be noted that a white solid started to form in the solution which gradually dissolved during heating.) The mixture was cooled to room temperature and quenched with 5% NaOH solution (50 mL), followed by extraction with CH_2Cl_2 (2×40 ml). The organic extract was dried over Na_2SO_4, filtered, and evaporated to dryness. The crude residue was purified by column chromatography to provide compound **8** (0.34 g, 52% yield) as a white solid.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2012.01.122.

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17. It is postulated that excess H_2O present in the reaction mixture might facilitate the formation of the unidentified solid by-product and thus should be avoided.
18. (a) Trace amounts of oxidized products were observed in the synthesis of compounds **8** and **9**. (b) Reaction between 2,3-dihydroxynaphthalene (**3**) and 1,2-ethanedithiol in the presence of TfOH provided 2,3-dihydronaphtho[2,3-*b*][1,4]dithiine. A similar transformation has been observed, see Ref. 14b.
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20. For another possible mechanism, see Ref. 10.