A ONE-POT SYNTHESIS OF SUBSTITUTED THIENO[3,2-*b*]THIOPHENES AND SELENOLO[3,2-*b*]SELENOPHENES

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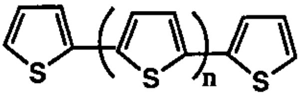
Abstract - Heating a mixture of 2,5-dimethyl-3-hexyne-2,5-diol (**3a**) with elemental sulfur in benzene at 190-200 °C in an autoclave affords 3,6-dimethylthieno[3,2-*b*]thiophene (**5a**) in 26% yield. The reaction provides a practical one-pot synthesis of several gram quantities of **5a**, even if the yield is moderate, since **3a** is commercially available and inexpensive. The reaction proceeds *via* 2,5-dimethyl-1,5-hexadiene-3-yne (**4a**) as one of probable intermediates, which is produced by dehydration of **3a**. Addition of *p*-toluenesulfonic acid promotes the dehydration of **3a** and thus can lower the reaction temperature. In addition, the reaction of **4a**, prepared from **3a** independently, with sulfur affords **5a** in a somewhat improved yield (33%). The reaction of **3a** with elemental selenium also provides a one-pot synthesis of 3,6-dimethylselenolo[3,2-*b*]selenophene (**9a**) in 16% yield. Reactions of some other acetylenic diols with elemental sulfur and selenium are also described.

INTRODUCTION

We have been investigating the synthesis[1] and properties[2] of thiophene oligomers (**1**) in recent several years. In the extention of these studies, we have planned the preparation of thieno[3,2-*b*]thiophene oligomers (**2**) in which thieno[3,2-*b*]thiophene units are connected at the 2- and 5-positions so that they can conjugate with each other most effectively. A literature survey reveals, however, that no practical short-step synthesis of the parent thieno[3,2-*b*]thiophene[3] and substitued thieno[3,2-*b*]thiophenes[4] in which their most reactive 2- and 5-positions still remain unsubstituted for the subsequent manipulations, are available. Synthetic methods for selenolo[3,2-*b*]selenophenes are much more limited: only several selenolo[3,2-*b*]selenophenes including the parent compound have been known.[5] We report here a practical one-pot synthesis of thieno[3,2-*b*]thiophenes and selenolo[3,2-*b*]selenophenes.



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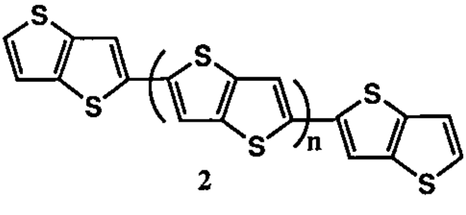

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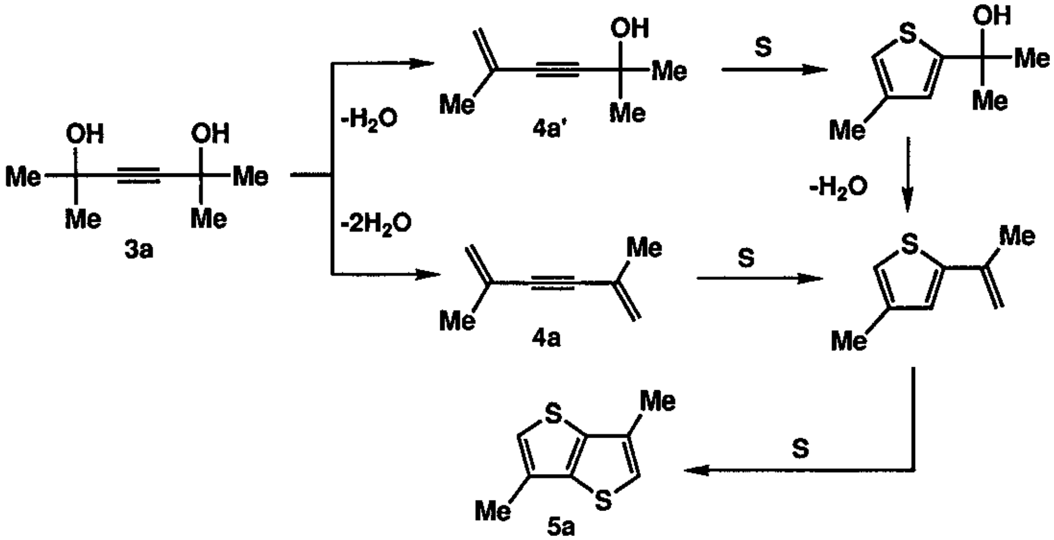
RESULTS AND DISCUSSION

Preparation of Thieno[3,2-*b*]thiophenes

In 1955 Teste and Lozac'h found that the reaction of 2,5-dimethyl-3-hexyne-2,5-diol (**3a**) with elemental sulfur or with elemental sulfur/phosphorus trisulfide affords 3,6-dimethylthieno-[3,2-*b*]thiophene (**5a**) though in very low yields.[6] Although this reaction seemed to be of no practical use,[4b] it is very attractive since it provides **5a** in a single step from commercially available, inexpensive **3a**.

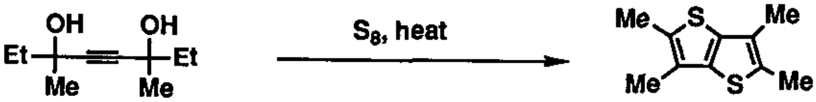
We therefore re-examined this reaction under a wide variety of conditions, and found that heating a mixture of **3a** and sulfur in benzene in an autoclave provides **5a** in a reasonable yield. Thus, heating a mixture of **3a** (8.52 g) and sulfur (4.76 g) in benzene (50 ml) at 190-200 °C for 12 h in an autoclave affords 2.60 g (26%) of **5a**. The reaction was carried out many times and gave **5a** reproducibly in 20-30% yields. The present reaction probably proceeds through the reaction pathways shown below. If so, the addition of an acid catalyst such as *p*-toluenesulfonic acid (TsOH) would facilitate the formation of **4a** and **4a'** and thus could lower the reaction temperature. In fact, the reaction of **3a** (8.52 g) with sulfur (4.76 g) in the presence of TsOH (145 mg) proceeded at 150-170 °C to give 2.73g (27%) of **5a**, although the yield of **5a** was not improved. Next, we examined the reaction of **4a**, prepared from **3a** independently,[7] with sulfur to confirm the involvement of **4a** as one of the intermediates. Heating **4a** (6.36 g) and sulfur (4.76 g) in benzene (50 ml) at 170-175 °C gave **5a** in a slightly improved yield (3.40 g, 33%). Apart from the mechanism, the present reaction provides a very practical synthesis of **5a** whose reactive 2- and 5-positions remain unsubstituted for the subsequent manipulations which lead to a new type of thienothiophene oligomers and polymers.[8]



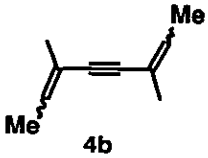
3,6-Dimethyl-4-octyne-3,6-diol (**3b**) also reacted with sulfur to give 2,3,5,6-tetramethylthieno-[3,2-*b*]thiophene (**5b**)[6] (6%). The reaction in the presence of TsOH gave **5b** in 11% yield. The reaction of the ynediene (**4b**), prepared by dehydration of **3b**,[9] with sulfur gave **5b** in a slightly improved yield (13%) along with the bithiophene **6**[10] (2%).

The reaction of the ynediol (**3c**) with sulfur gives the dibenzothienothiophene (**5c'**)[11] (8%) and the benzothiophene (**7**)[12] (17%). The dibenzothienothiophene (**5c'**) would be formed mostly *via* dehydrogenation of the initially-formed **5c** by sulfur, while the benzothiophene (**7**) would be formed by dehydration and dehydrogenation of **8**.

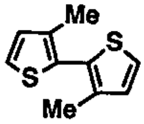
The reaction of the ynediol (**3d**) with sulfur gives acetophenone (34%) as the major product, the desired thienothiophene (**5d**)[13] being obtained in very low yield (3%). This indicates that decomposition of **3d** to acetophenone and acetylene predominates over dehydration to the ynediene which can react with sulfur to give **5d**.



3b **5b**



4b



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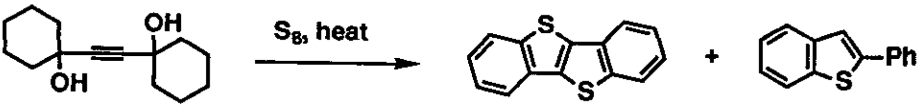
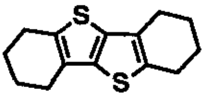
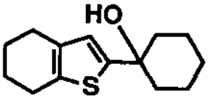


3c **5c'** **7**



5c



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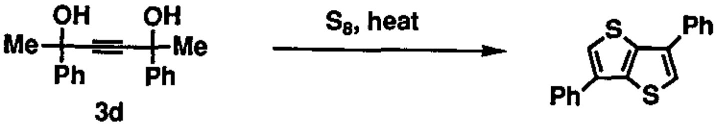
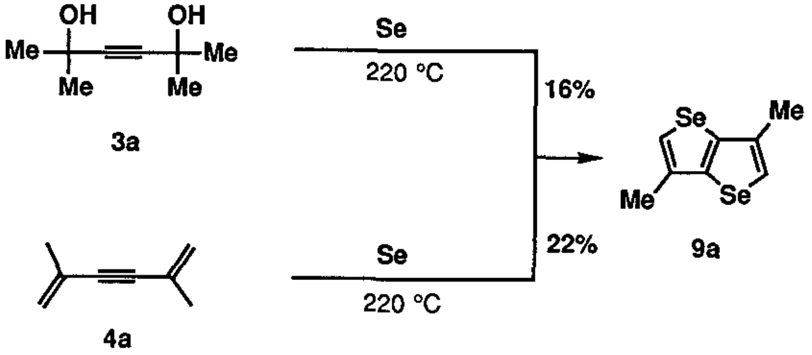


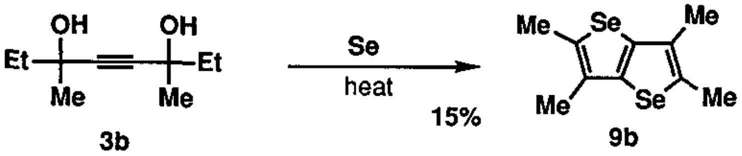
3d **5d**

Preparation of Selenolo[3,2-*b*]selenophenes

The reactions of 3 with selenium generally require more forcing conditions (higher temperatures) than those with sulfur, but reproducibly afford selenolo[3,2-*b*]selenophenes (**9**) in moderate yields, thus providing a convenient one-pot synthesis of these rather novel heterocycles which are otherwise difficult to prepare.[5] Heating a mixture of the ynediol (**3a**) and elemental selenium in benzene at 220 °C in an autoclave affords 3,6-dimethylselenolo[3,2-*b*]selenophene (**9a**) in 16% yield. The use of the ynediene (**4a**) affords **9a** in an improved yield (22%). Similarly, the reaction of **3b** with selenium at 220 °C affords 2,3,5,6-tetramethylselenolo[3,2-*b*]selenophene (**9b**) in 15% yield.

The moderate to very low yields of the desired products and the low material balance observed throughout this work are mainly due to the formation of considerable amounts of tarry materials.





EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were determined on a Bruker AM-400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) in $CDCl_3$ using tetramethylsilane as an internal standard, unless otherwise stated. The ynediols (**3a**) and (**3b**) were purchased from Tokyo Kasei and used without further purifications, and **3c** and **3d** were prepared according to the literature method.[14] Column chromatography was carried out using silica gel 60 (E. Merck, 70-230 mesh ASTM). Elemental sulfur and selenium were used as purchased from Wako Pure Chemical Industries.

Reaction of 3a with Sulfur. A mixture of 8.52 g (60 mmol) of **3a** and 4.76 g of elemental sulfur in 50 ml of benzene was heated at 190-200 °C for 12 h in a stainless steel autoclave. The dark brown mixture was evaporated and the residue was triturated with hot hexane (200 ml) and the insoluble material was filtered off. The filtrate was evaporated and chromatographed on a column of silica gel (150 g). Elution with hexane gave the excess sulfur and then 2.60 g (26%) of 3,6-dimethylthieno[3,2-*b*]thiophene (**5a**), mp 89-90 °C (from hexane) (lit.,[6] mp 89-90 °C): ^{1}H nmr δ 2.33 (s, 6H), 6.92 (s, 2H); ^{13}C nmr δ 14.61, 121.77, 130.31, 140.03.

Reaction of 3a with Sulfur in the Presence of TsOH. A mixture of 8.52 g (60 mmol) of **3a**, 4.77 g of sulfur, and 145 mg of TsOH in 50 ml of benzene was heated at 150-170 °C for 24 h in an autoclave. The mixture was treated as described above to give 2.73 g (27%) of **5a**.

Reaction of 4a with Sulfur. A mixture of 6.36 g (60 mmol) of **4a**[7] and 4.77 g of sulfur in 50 ml of benzene was heated at 170-175 °C for 17 h in an autoclave. The mixture was treated as described above to give 3.40 (33%) of **5a**.

Reaction of 3b with Sulfur. A mixture of 1.70 g (10 mmol) of **3b** and 2.56 g of sulfur in 80 ml of benzene was heated at 170-180 °C for 15 h in an autoclave. The mixture was evaporated and chromatographed on a column of silica gel with hexane as the eluent to give 2,3,5,6-tetramethylthieno[3,2-*b*]thiophene (**5b**) contaminated with **6**, which was recrystallized from ethanol to give 122 mg (6%) of pure **5b**, mp 137-137.5 °C

Reaction of 3b with Sulfur in the Presence of TsOH. A mixture of 1.70 g (10 mmol) of **3b**, 2.56 g of sulfur, and 0.38 g of TsOH in 80 ml of benzene was heated at 170-180 °C for 15 h in an autoclave. The mixture was treated as described above to give 223 mg (11%) of **5b**.

Reaction of 4b with Sulfur. A mixture of 670 mg (5 mmol) of **4b**[9] and 1.28 g of sulfur in 40 ml of benzene was heated at 155-160 °C for 8 h in an autoclave. The mixture was treated as described above to give 126 mg (13%) of **5b** and 20 mg (2%) of 3,3'-dimethyl-2,2'-bithiophene (**6**), bp 50 °C/1.5 mmHg (bulb-to-bulb distillation) (lit.,[10] bp 135 °C/16 mmHg); ^{1}H nmr δ 2.17 (s, 6H), 5.92 (d, *J*=5.2 Hz, 2H), 7.25 (d, *J*=5.2 Hz, 2H); ^{13}C nmr δ 14.65, 124.95, 129.35, 129.99, 136.48.

Reaction of 3c with Sulfur. A mixture of 444 mg (2 mmol) of **3c** and 512 mg of sulfur in 40 ml of benzene was heated at 175-180 °C for 12.5 h in an autoclave. The mixture was evaporated and the residue was purified by silica gel column chromatography with hexane as the eluent to give 37 mg (8%) of benzothieno-[3,2-*b*]benzothiophene (**5c'**), mp 215-216 °C (lit.,[11] mp 216 °C); ^{13}C nmr 121.59, 124.03, 124.86, 124.99, 133.10, 133.43, 142.26 and 72 mg (17%) of 2-phenylbenzo[*b*]thiophene (**7**), mp 175-176 °C (lit.,[12] mp 176°C); ^{13}C nmr δ 119.44, 122.56, 123.55, 124.30, 124.50, 126.49, 128.25, 128.94, 134.30, 139.50, 140.68, 144.24.

Reaction of 3d with Sulfur. A mixture of 532 mg (2 mmol) of **3d** and 512 mg of sulfur in 40 ml of benzene was heated at 190-200 °C for 15 h in an autoclave. The mixture was purified by silica gel column chromatography (hexane as the eluent) and then by repeated recrystallization from carbon tetrachloride to give 18 mg (3%) of 3,6-diphenylthieno[3,2-*b*]thiophene (**5d**), mp 210-211 °C (lit.,[13] mp 210-211 °C); ^{1}H nmr (DMSO-d_6) δ 7.41 (t, *ca.* J=8 Hz, 2H), 7.54 (t, *ca.* J=8 Hz, 4H), 7.82 (d, *ca.* J=8 Hz, 4H), 8.09 (s, 2H); ^{13}C nmr (DMSO-d_6) δ 123.84, 126.10, 127.90, 129.20, 133.76, 133.78, 137.40.

Reaction of 3a with Selenium. A mixture of 2.43 g (17 mmol) of **3a** and 4.82 g of elemental selenium in 100 ml of benzene was heated at 220 °C for 8 h in a stainless steel autoclave. The resulting mixture was filtered to remove the excess selenium and the filtrate was evaporated. The residue was chromatographed on a column of silica gel with hexane as the eluent to give 0.73 g (16%) of 3,6-dimethylselenolo[3,2-*b*]selenophene (**9a**), mp 94-94.5 °C (from hexane); ^{1}H nmr δ 2.34 (s, 6H), 7.45 (s, 2H); ^{13}C nmr δ 17.26, 123.68, 135.31, 141.63. Anal. Calcd for $C_8H_8Se_2$: C, 36.66; H, 3.08. Found: C, 36.85; H, 3.19.

Reaction of 4a with Selenium. A mixture of 2.25 g (21 mmol) of **4a** and 5.51 g of selenium in 60 ml of benzene was heated at 220 °C for 8 h in an autoclave. The mixture was treated as described above to give 1.24 g (22%) of **9a**.

Reaction of 3b with Selenium. A mixture of 1.72g of **3b** and 2.37 g of selenium in 80 ml of benzene was heated at 220 °C for 8 h in an autoclave. The mixture was treated as described above to give 0.45 g (15%) of 2,3,5,6-tetramethylselenolo[3,2-*b*]selenophene (**9b**), mp 156.5-157.5 °C (from ethanol); ^{1}H nmr δ 2.15 (s, 6H), 2.50 (s, 6H); ^{13}C nmr δ 14.49, 16.25, 130.23, 135.78, 137.60. Anal. Calcd for $C_{12}H_{12}Se_2$: C, 41.40; H, 4.17. Found: C, 41.17; H, 4.18.

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