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COMMUNICATION

Studies on the stereochemical behaviors of winding vine-shaped molecular wire of bithiophene dimer with molecular asymmetry

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Multiple ring-closing metathesis of oligomeric bithiophene smoothly formed the winding vine-shaped oligomer with molecular asymmetry. Stereochemical studies suggested that the dimeric 1:1 of meso and racemic stereochemical mixture showed the conversion to the meso-enriched product upon standing under the solid state, while the obtained meso compound reverted to the meso and racemic mixture upon heating the solution in chloroform at 50 °C for 30 min. On the other hand, heating of the meso isomer in the solid state at 80 °C for 3 days did not lead to isomerization.

The reversible switching of organic molecules has recently attracted much interest in the design of a computing system. A switching of functional group is a possible model for molecular computing if the information triggered by the structural change can be successfully converted into an electrical signal.[1–6] Chirality is a suitable candidate as a digitizing unit by interpreting the detectable absolute configuration into a digital signal. Molecular asymmetry that exhibits chirality, without a chiral carbogenic center, is capable of switching the absolute configuration by a conformational change without the forming and breaking of chemical bonds. It is therefore an interesting possibility for the design of a linear linkage of molecular asymmetric chirality leading to a suitable oligomer.[7–15] We have been investigating a new class of organic compounds, winding vine-shaped (hetero)biaryls, that show molecular asymmetry.[16-18] We also learned that the isomerization barrier of bithiophene shown in Fig. 1 was quite low (ca. 100 kJmol^{-1}) and that racemization occurred at room temperature ($t_{1/2}$ = ca. 7 h) within a reasonable time scale.[19–22] We planned to synthesize the molecular wire[6,23,24] of bithiophene, in which the linkage of each chirality unit consists of molecular asymmetry and its chirality is detectable spectroscopically as a diastereomer. Herein, we report our initial efforts as a study of the isomerization behavior of winding vine-shaped bithiophene wire, which showed a unique diastereomeric change between meso and racemic forms in solution and solid states.

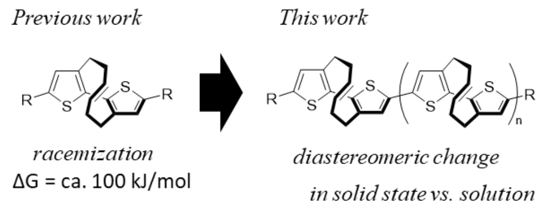

Fig. 1 Winding vine-shaped bithiophene with molecular asymmetry (ref 19) into its molecular wire

First, the side-chain structure of the bithiophene moiety was chosen as an aliphatic alchohol of silyl ether to improve the solubility of the bithiophene wire to an organic solvent. Alkynyl alchohol **2** was employed to undergo the smooth bond fromation with the thiophene moiety at the terminal alkyne. Introduction of an end group at the 5-position of bithiophene to winding vine-shaped bithiophene **1** was thus performed by the Sonogashira coupling with terminal alkyne **2**.[25,26] Excess amount of bithiophene to **2** was employed to avoid the functionalization at the both ends of bithiophene. The coupling product **3** was obtained in 41% yield with recovery of 39% of starting bithiophene, which can be employed for an additional use. Terminal hydroxy group of **3** was then protected by TBS (*t*-butyldimethylsilyl) group leading to silyl ether **4** in a quantitative yield. The obtained product was subjected to the dimerization by the treatment of *n*-butyllithium to undergo halogen–metal exchange followed by oxidative dimerization with $CuCl_2$ to afford dimer **5** in 52% yield.[27] (Scheme 1)

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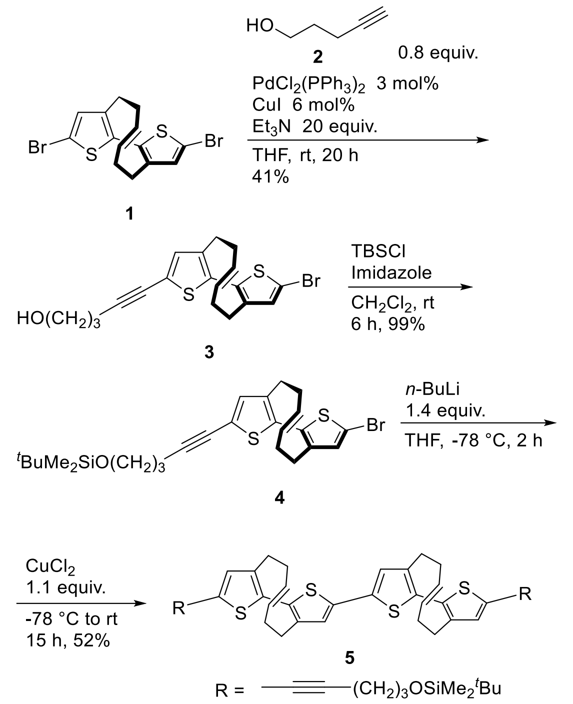


Scheme 1 Synthesis of winding vine-shaped bithiophene dimer **5**

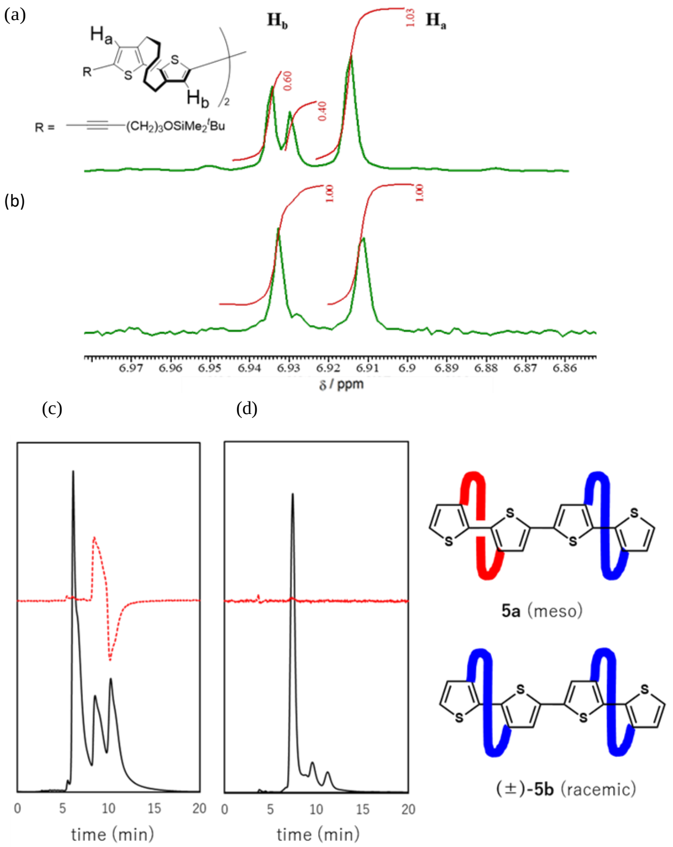


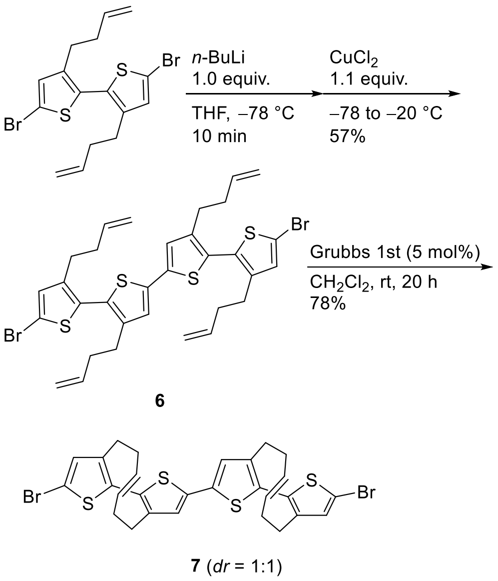
Fig. 2. (a) ^1H NMR spectra of **5** as prepared, (b) after standing a few months at –20 °C, (c) HPLC profile of **5** by UV (lower) and CD (upper red) detectors as prepared, and (d) after standing

The measurement of ^1H NMR spectrum of **5** suggested to afford a mixture of two diastereomers at ca. 6.93 ppm derived from the molecular asymmetry of the vine-shaped bithiophene unit as shown in Figure 2a. HPLC analysis with a chiral column (DAICEL Chiralpak IF) exhibited three peaks of ca. 2:1:1 intensities, which suggest the first elute as meso isomer **5a** and the following two as racemic **5b** and *ent*-**5b**. The HPLC profile by CD detection showed positive and negative peaks corresponding to the latter two while no signal at the earliest one. (Figure 2c) The result also supported the separation of each enantiomer **5b** and *ent*-**5b** as well as that of diastereomer **5a** and **5b**.

We have also found that the obtained mixture of meso and racemic **5** changes to meso-enriched **5a** upon standing the solid of **5** in the freezer (ca. –20 °C for several months) as shown in the HPLC profile of Figure 2d,[28] where the increment of the earliest peak along with disappearance of the racemic ones was observed and almost no signal was found by the CD detection. The measurement of ^1H NMR spectrum also supported that the 1:1 mixture changed to meso-enriched **5** as shown in Figure 2b. We thus attempted to observe the isomerization rate of **5** at –20 °C in the solid state, however we learned that such isomerization was sluggish to observe the change of the diastereomeric ratio of **5a**:**5b** from 50:50 to 58:42 after 30 days.

We next envisaged to synthesize other derivatives of winding vine-shaped bithiophene dimers. Synthesis of bithiophene dimer bearing a bromine atom at both ends was performed as summarized in Scheme 2. Bithiophene dimer bearing 3-buten-1-yl side chain on each thiophene ring **6** was synthesized by the copper-mediated dimerization.[27] Thus obtained **6** was then subjected to double ring-closing metathesis with 5 mol% of Grubbs 1st generation catalyst. The reaction successfully proceeded to afford **7** in 78% yield after stirring at room temperature for 20 h in dichloromethane. The obtained ring-closed dimer **7** was revealed to be a ca. 6:4 mixture of meso and racemic diastereomers, which was confirmed by ^1H NMR analysis as shown in Fig 3a (top). The separation of characteristic two signals, which were assigned as H_a at the β-position of the thiophene ring, was observed δ = 6.93 ppm as meso and racemic isomers, while no separation was shown in the signal at δ = 6.85 ppm assigned as β-proton H_b. However, attempted HPLC analysis with a chiral column resulted to be unsuccessful.

The isomerization study of **7** in the solid state[29] was then examined in a similar manner to that of **5** and found that the transformation of (±)–**7b** to meso **7a** proceeded much faster than that of **5**. When the solid bithiophene dimer **7** was kept at –20 °C, slow isomerization took place to observe the ratio of *meso*–**7a** : (±)-**7b** = 69:31 after 16 days and 71:29 after 22 days, respectively. (Fig 3a)



Scheme 2 Synthesis of winding vine-shaped bithiophene dimer through multiple ring-closing metathesis

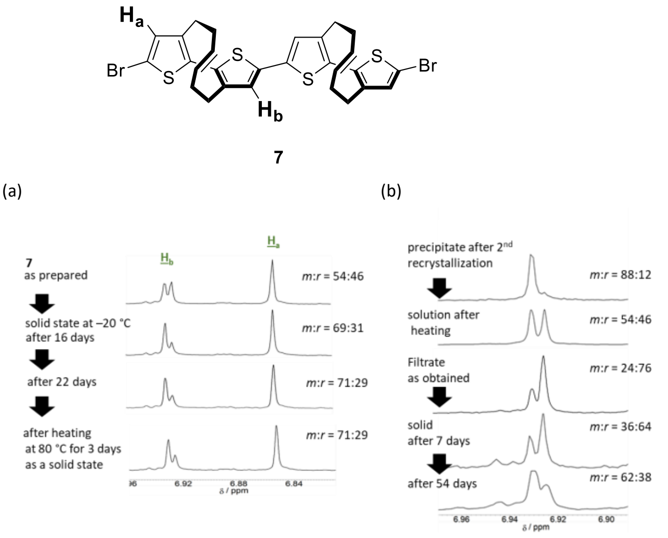


Fig. 3 Isomerization study of winding vine-shaped bithiophene dimer **7** by ^{1}H NMR measurement: (a) with as prepared product; (b) from recrystallization crops

Measurements of X-ray difraction of meso-enriched and ca. 1:1 diastereomeric mixture of **7** were then carried out. As shown in Fig 4(a), it was found that the meso-enriched bithiophene dimer indicated several characteristic sharp peaks, while little remarkable peak was observed in the meso and racemic mixture (Fig 4(b)). The results suggest that the meso form of **7** shows crystalline characteristics in the solid state, while racemic **7** in the solid state favors conversion to a more stable meso form. We also performed DSC analysis of meso-enriched and 1:1 meso/racemic mixture **7**. Both of those showed little peak suggesting phase transition until the exotherm at 268 °C (meso-rich) and 243 °C (meso:racemic = ca. 1:1) was observed in the first heating suggesting that decomposition took place. (See Supporting Information)

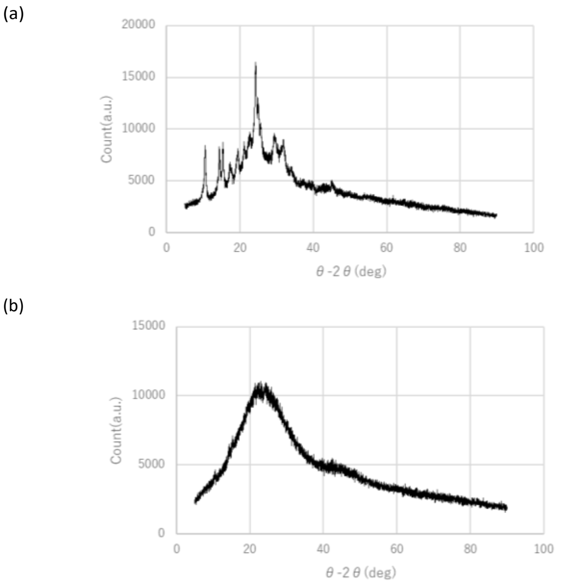
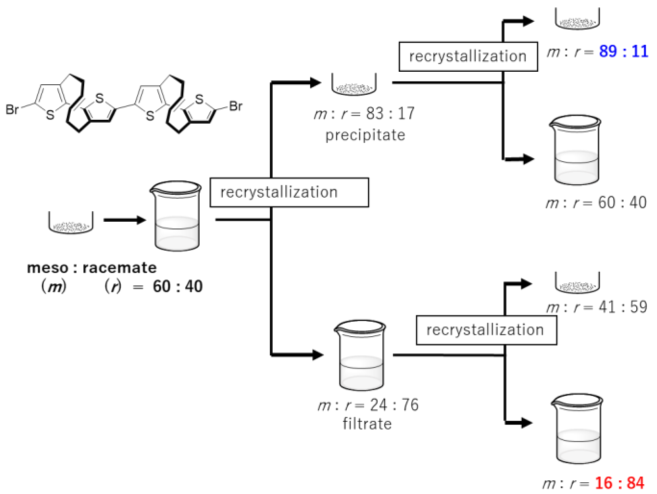


Fig. 4 (a) XRD profile of meso-enriched **7** (b) meso and racemic ca. 1:1 mixture of **7**

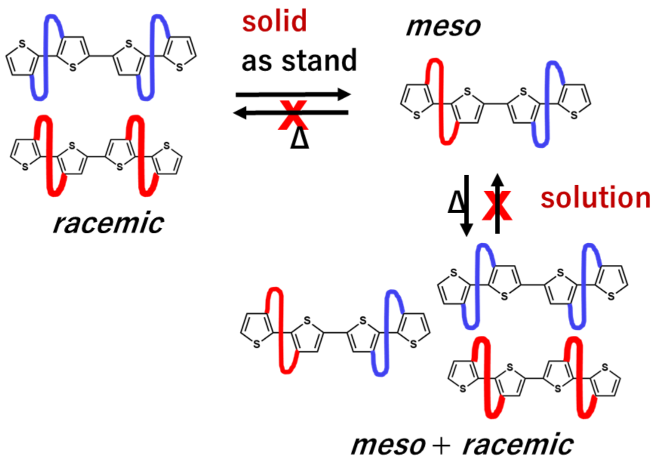
It was also found that separation of diastereomers of **7** can be performed by sequential recrystallization with a mixed solution of hexane and chloroform. As depicted in Scheme 3, a diastereomeric mixture of **7a** and **7b** in the solution afforded precipitation containing 83:17 of meso **7a** and racemic **7b**, respectively, accompanied by 24:76 (Fig3b 3rd) of the filtrate. The second recrystallization of thus formed meso-enriched solid afforded 88:12 (Fig3b top) of the diastereomer with 60:40 of the filtrate. The racemate-enriched filtrate was obtained from the second recrystallization of the initial filtrate (**7a**:**7b** = 24:76) to afford 16:84 of the corresponding filtrate accompanied by the formation of a precipitate (**7a**:**7b** = 41:59).



Scheme 3 Separation of diastereomers *meso*-**7a** and racemic (±)-**7b** by sequential recrystallization of bithiophene dimer **7**

Fig 3b shows the 1H NMR analyis of thus obtained meso-enriched **7**. It was confirmed that a solution of meso-enriched **7a** with the ratio of 88:12 (top) isomerized rapidly to ca. 1:1 mixture (2 nd) after heating the $CDCl_3$ solution at 50 °C for 30 min. In contrast, when the racemate-enriched bithiophene dimer **7** (*m* : *r* =24:76: middle) was stand as a solid state, sluggish isomerization took place at –20 °C for 7 days and 54 days. The isomerization was observed to show the ratio to *m*:*r* = 36:64 and 62:38, respectively.

Based on the above studies, the isomerization behavior of winding vine-shaped bithiophene wire is summarized as shown in Scheme 4. The diastereomeric mixture of meso and racemic bithiophene dimer **5** and **7** converts to the meso-enriched form upon standing in the solid state even at low temperature, but heating of the resulting solid of meso bithiophene dimer hardly epimerizes.[30,31] In contrast, a solution of meso **5a** (**7a**) is rapidly transformed into the ca. 1:1 meso and racemic mixture upon gentle heating. The result is similar to our previous studies on the racemization behavior of vine-shaped **1** composed of a singular bithiophene unit that undergo slow racemization even at room temperature.[20,21] However, the solution of a mixture of meso and racemic bithiophene dimers does not convert to the meso enriched form.



Scheme 4 Isomerization behaviors of winding vine-shaped bithiophene dimer in solid/solution state

Conclusions

In summary, we have synthesized winding vine-shaped bithiophene dimer by the dimerization of corresponding bithiophene with molecular asymmetry in each bithiophene unit. The preparation was successfully proceeded through the dimerization of ring-closed derivative of **1** or alternatively multiple ring-closing metathesis composed of four thiophene units **6**. The bithiophene wire **5** and **7** was afforded as a 1:1 mixture of meso and racemic isomers**.** Isomerization studies of the resulting **5** and **7** revealed to show different behaviors in solid and solution states. Although the results are initial efforts with a simplified model as a small molecule and more rapid isomerization with further amounts of bithiophene unit is required, such findings involving the switching of reversible absolute configuration can potentially be applied for the encoding of the stereochemical information into digital signals combined with a detection protocol of the stereochemistry along with isomerization induced by an external stimulus.

Author Contributions

A. M. conceived the ideas and designed the project. K. H. Y. N. and K. T. performed experimental works. K. O and M. H. contributed the interpretation of experimental results. A. M. wrote the manuscript with contributions from all authors.

Conflicts of interest

There are no conflicts to declare.

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