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Stepwise Construction of Head-to-Tail-Type Oligothiophenes via Iterative Palladium-Catalyzed CH Arylation and Halogen Exchange

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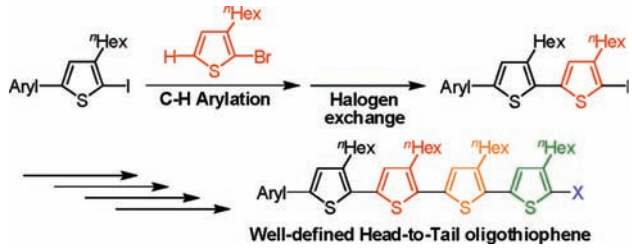
ABSTRACT



The well-defined head-to-tail oligothiophenes were synthesized via palladium-catalyzed CH arylation and halogen exchange sequentially through the 2-halothiophene derivatives.

As demand increases for oligothiophenes and polythiophenes as advanced electronic and photonic materials, such as organic TFT, liquid crystals, photovoltaic cells, etc.,[1,2] preparative methodologies of oligothiophenes have become a significant issue in organic synthesis.[3,4] We have recently shown that palladium-catalyzed homocoupling of bromothiophene derivatives, which occurs at the carbon−hydrogen bond of thiophene adjacent to the sulfur atom and the carbon−bromine bond is completely intact, is a highly efficient synthetic pathway for well-defined oligothiophenes, and indeed has prepared several oligomers bearing 2−8 thiophene units.[5] Although the method is effective for the head-to-head (HH) or tail-to-tail (TT) type oligomers, synthetic design of head-to-tail (HT) oligothiophene that

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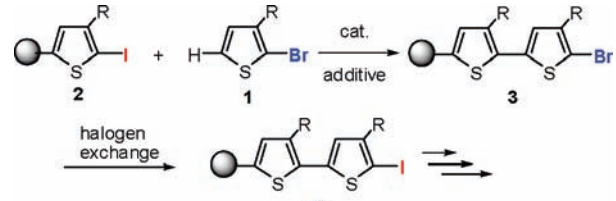
generally shows a higher performance than other regio isomers has been difficult.

On the other hand, transition metal-catalyzed C−H functionalization reactions are of great interest in organic synthesis since the reaction shows advantages in atom efficiency compared with related cross coupling with organometallic compounds.[6] The reaction of heteroaromatic compounds is particularly important because of their wide utilities in the synthesis of biologically active molecules and advanced organic materials.[7] The catalytic carbon−carbon bond-forming reaction via C−H functionalization has been achieved by the reaction of aryl halides.[8,9]

Thereby, a new synthetic strategy for HT oligothiophenes based on the CH coupling, which improves synthetic diversity efficiently, is intriguing.[10] In addition, recent progress of the HT-type oligothiophenes as materials for organic dye-sensitized[11,12] and thin-film[13] photovoltaic batteries as well as organic TFTs[1c] prompted us to develop facile synthetic strategies for such materials. We herein report stepwise synthesis of HT regioregular oligothiophenes via iterative palladium-catalyzed CH arylation and halogen exchange reactions leading to the oligomers bearing 2−4 thiophene units.

Synthesis of the HT-type oligothiophene based on the CH arylation of a 2-bromothiophene derivative at the CH bond is illustrated in Scheme 1. Since palladium-catalyzed CH arylation of heteroaromatic compounds we have shown selectively takes place with an aryl iodide, cross coupling of iodothiophene **2** and bromothiophene **1** forms HT bithiophene **3** bearing a C−Br bond. Halogen exchange of **3** into iodide **2′** and following coupling with **1** bring about an additional extension of a thiophene unit and the iterative reactions would lead to HT oligothiophenes.

Scheme 1



We first performed the synthesis of oligothiophene bearing a carbazole moiety at the end group. Introduction of the carbazole group was performed by the palladium-catalyzed CH arylation of 2-bromo-3-hexylthiophene **4** with *N*-ethyl-3-iodocarbazole **5** in the presence of silver nitrate/KF to obtain the corresponding product **6** in 75% yield. Transformation of the bromo group into iodide was carried out with

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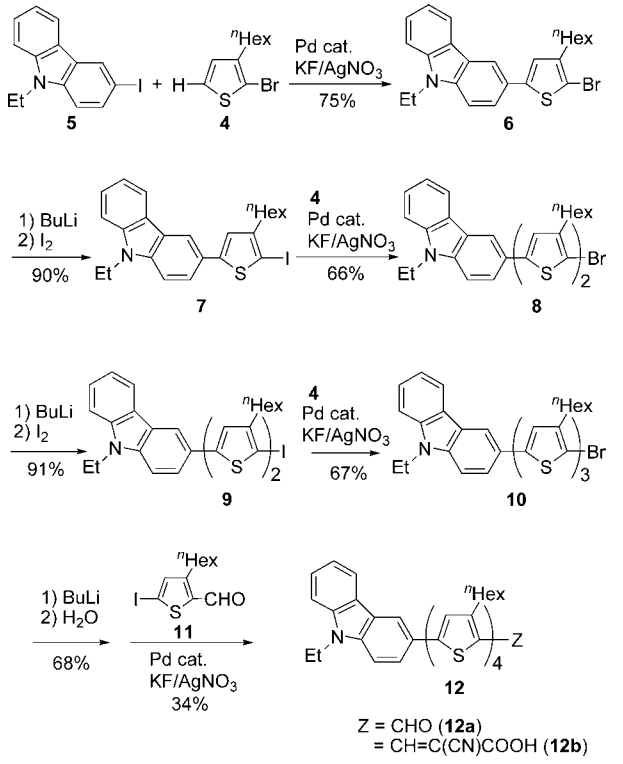
bromine−lithium exchange with butyllithium and following treatment of iodine at −78 °C afforded **7** in 90% yield.

The CH coupling reaction of thus obtained **7** with bromothiophene **4** was carried out in the presence of the palladium catalyst and $AgNO_3$/KF to obtain bithiophene **8** (66% yield). Transformation into the iodide of **8** similarly proceeded (91%).

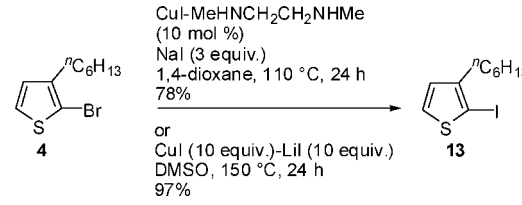
As shown in Scheme 2, further extension of the thiophene unit was similarly successful to afford up to the corresponding trimer **10**, which was subjected to protonolysis and CH arylation with thienyl aldehyde **11** to give the tetramer **12a**. The obtained **12a** was identical with a intermediate of the dye molecule **12b** available as a dye-sensitized solar cell on the electrode of titanium oxide nanoparticle, which showed remarkably high efficiency as an organic dye.[12] Transformation of **12a** was shown to be performed by Knoevenagel reaction of the formyl group with cyanoacetic acid lead to **12b** as reported.[11a] We then examined the synthesis of a head-to-tail oligothiophene bearing an ester moiety at the end group.

Scheme 2



Since strong base or nucleophile can not be employed for the halogen exchange reaction from bromine to iodine, a copper-mediated protocol reported by Buchwald[14] for halogen exchange was examined by using the reaction of 2-bromo-3-hexylthiophene **4** as a model study. When the reaction of **4** was carried out with 2 equiv. of NaI in the presence of a catalytic amount of CuI with several diamine derivatives, the exchange reaction proceeded in moderate to good yields to afford the corresponding iodide **13**. Although the reaction was efficient and facile, it was found to be difficult to achieve complete conversion of bromide **4** into iodide **13**, which caused troubles in chromatographic purification of **13** due to the similar polarity between bromide and iodide. The reaction with complete conversion was successful when the reaction with excess amounts of CuI/LiI was employed, which was a modified method reported by Yamashita (use of excess CuI in DMSO under heterogeneous conditions).[15] The reaction proceeded in a homogeneous manner in DMSO at 150 °C and resulted in almost complete conversion after stirring for 24 h. The corresponding iodide **13** was isolated in 97% yield (Scheme 3).

Scheme 3



Synthesis of HT-type oligothiophene bearing an ester group was carried out with palladium-catalyzed CH arylation and copper-mediated halogen exchange protocols. Scheme 4 shows the synthetic pathway of the head-to-tail oligothiophene bearing four thiophene units and (4-ethoxycarbonyl)phenyl group at the end group. The reaction of ethyl 4-iodobenzoate **14** with bromothiophene **4** in the presence of $PdCl_2(PPh_3)_2$ (5 mol %) and $AgNO_3$/KF proceeded smoothly to afford the bromothiophene bearing the aryl group **15** in an excellent yield. The obtained bromothiophene derivative was subjected to the halogen exchange reaction, whose conditions were optimized in the model study, to afford iodothiophene **16** in 91% yield. The CH arylation reaction of **16** with **4** was performed in a similar manner to the reaction of **14** to afford the corresponding HT bithiophene **17**. Since CH arylation with aryl iodide bearing an electron-donating substituent has been shown to proceed with inferior yield to that with electron-deficient arenes, thienyl iodide that is recognized as an electron-enriched substrate would result in a lower yield.[9d] Indeed, the arylation reaction of **16** under similar conditions to that for **14** resulted in a lower yield (26%). However, a slight modification of the conditions by reducing amount of the solvent and repeating addition of $AgNO_3$/KF improved the yield of **17** to 70%. By the iterative halogen-exchange reaction and palladium-catalyzed CH arylation in a similar manner, synthesis of HT-type oligothiophenes up to the tetramer **19** was successfully achieved.

In summary, we showed that the several well-defined head-to-tail oligothiophenes were synthesized efficiently with

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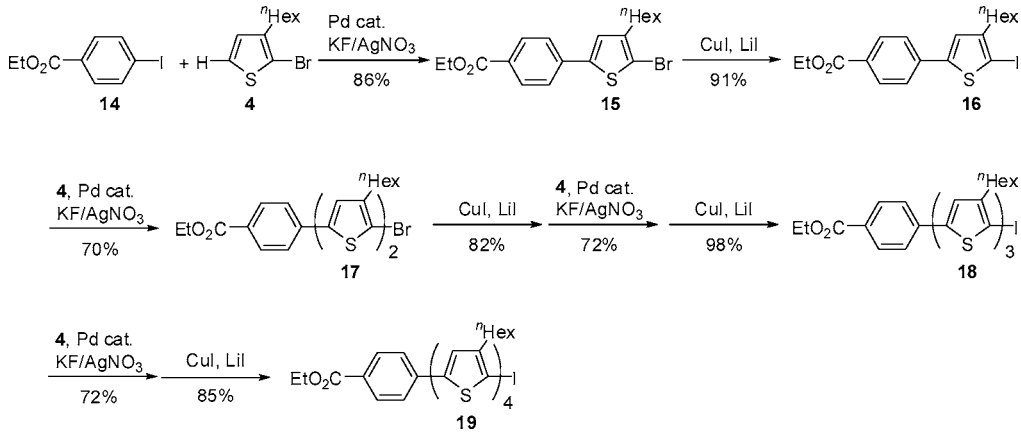
(16) The authors thank Nara Institute of Science and Technology, Kyoto-Advanced Nanotechnology Network, supported by MEXT for measurements of high resolution mass spectra.

Scheme 4



repeating palladium-catalyzed CH arylation and halogen exchange sequentially with 2-bromo-3-hexylthiophene. Further oligomers of well-defined structure would be prepared in a similar manner. With these methodologies, introduction of a thiophene unit bearing a different substituent would also be possible by the stepwise methodology.

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Supporting Information Available: Experimental details.[16] This material is available free of charge via the Internet at http://pubs.acs.org.

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