Simple Separation of an Isomeric Mixture of Dihexylbithiophenes with Head-to-head and Head-to-tail Orientations

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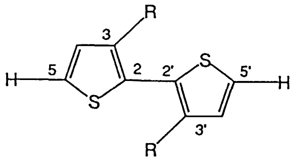
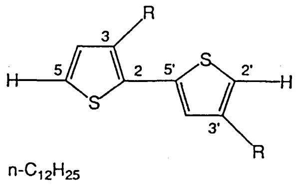
The isomeric mixture of 3,3'-dialkylbithiophenes with head-to-head (H-H) and head-to-tail (H-T) orientations was separated into each isomer by using preferential bromination of the H-T isomer. This separartion method proved to be useful for simultaneous preparation of the pure H-H and H-T bithiophenes which are inaccessable by other methods.

The oligo- and poly(3-alkylthiophene) derivatives have recently received considerable attention as a candidate of the new organic materials for the opto-electronic devices,[1] owing to the significant improvement of solubility and fusibility resulting from the grafting of flexible hydrocarbon chains on their conjugated thiophene backbones.[2] We previously reported the electronic and nonlinear optical properties of oligo(3-hexylthiophene)s with head-to-head (H-H) orientation, and showed that orientation of the 3-hexylthiophene ring greatly affects their electronic properties.[3]

3,3'-Dihexyl-2,2'-bithiophene (**1**), which is the starting material for the oligo- and poly(3-hexylthiophene) derivatives with H-H orientation,[4] was prepared by lithiation of 2-bromo-3-hexylthiophene (**3**) followed by an oxidative homo-coupling in the presence of iron(III) acetylacetonate ($\mathrm{Fe(acac)_3}$)[5] in much higher yield than that by the reported procedure.[6] However, in the coupling reaction an elevation of the reaction temperature and an increase of the reaction scale produced a considerable amount of 3,3'-dihexyl-2,5'-bithiophene (**2**) with head-to-tail (H-T) orientation along with the normal product, the isomer **1**. Separation of the isomer **1** from the isomer **2** in a mixture was very difficult by ordinary methods such as column chromatography, distillation, and GPC liquid chromatography since both isomers are viscous liquid substances and have almost the same Rf values in attempted elution on both silica gel ($\mathrm{SiO_2}$) and alumina ($\mathrm{Al_2O_3}$) and the similar molecular sizes, though each isomer could unambiguously be identified by ^{1}H NMR and UV spectra.[3b]

In this paper we present a convenient method for the separation of the isomeric bithiophenes **1** and **2**; this method would be applied for separation of other isomeric mixture of dialkylbithiophenes with H-H and H-T orientations.





R = n-$\mathrm{C_6H_{13}}$, n-$\mathrm{C_{12}H_{25}}$

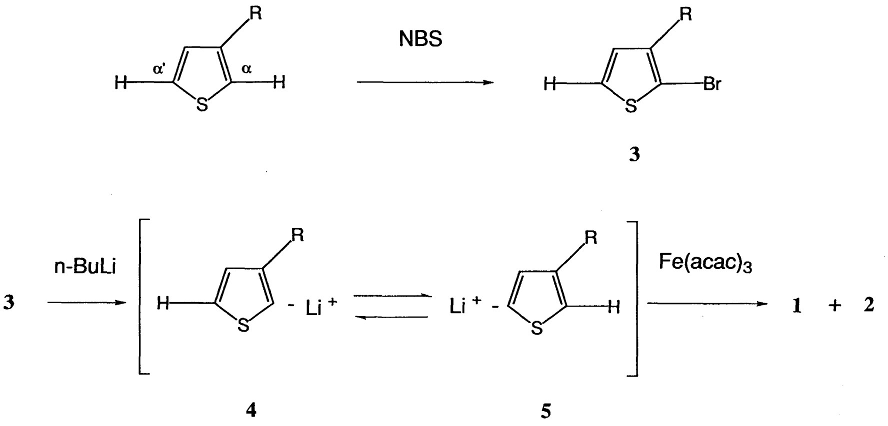
1 (H-H Isomer) 2 (H-T Isomer)

It is known that monobromination of 3-alkylthiophene with N-bromosuccinimide (NBS) in a mixture of acetic acid and chloroform gives the more crowded product, 3-alkyl-2-bromothiophene, in an almost quantitative yield.[7]

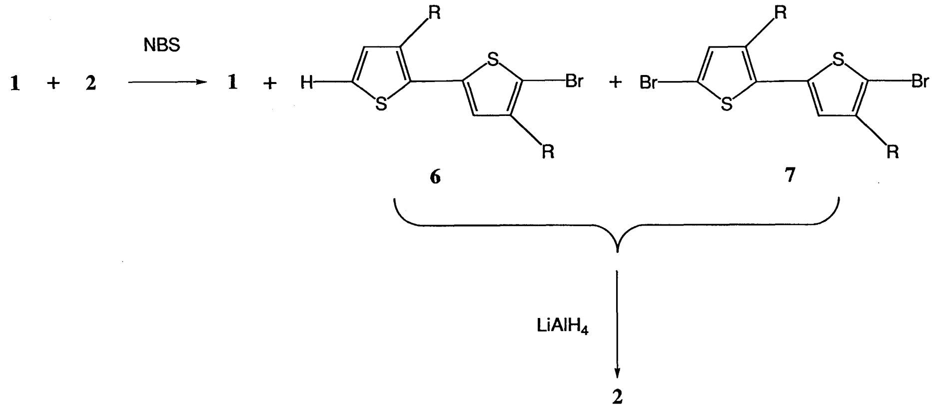
The species **4** generated from 2-bromo-3-hexylthiophene (**3**)[3b] (1 - 3 mmol) by reaction with butyllithium at - 80 °C was led to the H-H bithiophene **1** by addition of $\mathrm{Fe(acac)_3}$ at - 80 °C in 65 - 75% yield with the formation of the reduction product of **3**, 3-hexylthiophene, in 10 - 15% yield. However, when the reaction was carried out in a larger scale more than 10 mmol and $\mathrm{Fe(acac)_3}$ was added above - 40 °C, the isomeric mixture of H-H **1** and H-T **2** in a product ratio ranging from 7 : 1 to 3 : 1 was obtained in 60 - 70% yield along with 3-hexylthiophene.

These results suggest that an isomerization of the 2-lithiated species **4** to the more stable 5-lithiated species **5** which would be a counterpart for preparation of the H-T bithiophene **2** by the oxidative cross-coupling with **4**, occurred to some extent under the reaction conditions, as shown in Scheme 1.[8]

We carried out the separation of the isomeric mixture into each isomer of H-H and H-T bithiophenes as follows (Scheme



Scheme 1.



Scheme 2.

2). The content of H-T isomer in the mixture was determined by integral ratio of ^{1}H NMR signals (**1** : **2** = 5.5 : 1).[9] Addition of one molar NBS for the quantity of the H-T isomer **2** at room temperature produced a mixture of the brominated H-T bithiophene **6**,[10] the H-H bithiophene **1**, and a trace amount of the 5,2'-dibromo H-T bithiophene **7**.[10] All of these products were viscous liquid substances but could be easily separated to each compound by column chromatography on SiO_2 with hexane as the eluent. These eluted successively in the order of the dibromide **7**, the monobromide **6**, and the H-H bithiophene **1**. Then the pure H-T bithiophene **2** could be obtained by reducing the bromide **6** and/or the dibromide **7** with lithium aluminum hydride in a quantitative conversion yield.[11]

The preferential bromination of the H-T isomer **2** as compared with the H-H isomer **1** can be explained by considering the higher reactivity of the α-carbon at the 2-position of the 3-hexylthiophene ring than that of the α'-carbon at the 5-position in consequence of the electron-donating property of the hexyl substituent, though both α and α' carbons are adjacent to the sulfur atom.[7] It is obvious that the H-T isomer **2** has the more reactive α-carbon with the higher electron density because of the presence of the nearby hexyl group, while the H-H isomer **1** with C_2 symmetry has only the less reactive α'-carbons. Therefore bromination of the isomeric mixture of the 3,3'-dihexylbithiophenes with NBS occurred in the H-T isomer **2** preferably, leaving the H-H isomer unreacted.

Since separation of an isomeric mixture of the 3,3'-didodecylbithiophenes into each H-H and H-T isomer could be done completely in the similar manner for that of the mixture of **1** and **2**, the procedure would be applied for the separation of other 3,3'-dialkylbithiophenes with different orientations and present a route for simultaneous preparation of the pure dialkylbithiophenes with H-H and H-T orientations in good yields.

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References and Notes

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8 To a solution of 2-bromo-3-hexylthiophene (**3**) (250 mg, 1.01 mmol) in THF (20 cm^3) were added drops of butyllithium (1.6 mol dm^{-3} in hexane; 0.66 cm^3, 1.06 mmol) at - 80 ° C over 10 min. After being stirred for 15 min at - 80 °C or at - 40 °C, the solution was quenched with a mixture of D_2O and THF (1:1) at - 80 °C or at - 40 °C, respectively. Work-up afforded the mixture of 2-D (**4**) and 5-D-3-hexylthiophene (**5**) in more than 90% yield with ratios of 26 : 1 and 3 : 1 by quenching at - 80 °C and at - 40 °C, respectively.

9 The signals of the thiophene ring protons (2H) of the bithiophenes **1** and **2** appeared at δ_H 7.23 and 7.12, respectively, while those of the thienylmethylene protons at δ_H 2.50 (**1**: 4H) and 2.75 (**2**: 2H), respectively.[3b]

10 **6**: colorless oil; Mass *m/z* 412 and 414 (M^+ and M^++ 2, based on ^{79}Br); IR (neat) 2955, 2927, and 2856 cm^{-1} (CH); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.13 (2H, d, J=5 Hz, ThH), 6.88 (2H, d, J=5 Hz, ThH), 6.78 (2H, s, ThH), 2.72 (4H, t, J=7 Hz, ThC$\underline{H}_2$), 2.56 (4H, t, J=8 Hz, ThC$\underline{H}_2$), and 1.66 - 0.89 (22H, m, C_5H_{11}); UV λ_{max} (THF) 248 (ε 9100) and 303 nm (9460); Found: C, 58.06; H, 7.20%; Calcd for $C_{20}H_{29}BrS_2$: C, 58.10; H, 7.07%.
The structural assignment of **7** was made by examination of Mass and ^{1}H NMR spectra. Mass *m/z* 490, 492, and 494 (M^+, M^+ + 2, and M^+ + 4, based on ^{79}Br); ^{1}H NMR ($CDCl_3$, 90 MHz) δ 6.85 (1H, s, ThH), 6.72 (1H, s, ThH), 2.62 (2H, d, J=7 Hz, ThC$\underline{H}_2$), 2.54 (2H, d, J=7 Hz, ThC$\underline{H}_2$), and 1.80 - 0.75 (22H, m, C_5H_{11}).

11 Reduction of the bromide **6** was also carried out by lithiation at - 80 °C, followed by quenching with water at room temperature. The yield of the H-T bithiophene **2**, however, decreased to 85 - 90% owing to the formation of the butylated bithiophene as a by-product.