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"Fibonacci's Route" to Regioregular Oligo(3-hexylthiophene)s

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S *Supporting Information*

ABSTRACT: We describe a new synthetic approach to regioregular monodisperse oligo(3-alkylthiophene)s allowing for simple separation of regioregular material in gram quantities. The number of repeat units follows the Fibonacci numbers up to a length of 21. In a small adaption of this approach, introduction of a protecting group was used to synthesize an oligo(3-hexylthiophene) with 36 repeating units, the longest regioregular 3-hexylthiophene oligomer synthesized to date.

Within the class of conjugated polymeric materials, poly(3-hexylthiophene) (P3HT) has been one of the most widely investigated materials because of its relative ease of synthesis combined with good processability and promising performance in a range of applications. The synthesis of P3HT has been reported by a number of routes, mainly based around transition-metal-catalyzed cross-coupling methodologies.[1,2] However, despite this interest, the molecular-weight dependence of the characteristics of P3HT and its structure−property relationships are still not fully understood. As is the case more often than not, this is due to, among other things, regioirregularity of the solubilizing hexyl group, polydispersities not equal to 1, inconsistent end-group chemistry, and ill-defined processing schemes.

The availability of precisely defined oligomers is well-known to enable the development of structure−property studies to understand and control the crystal structure, self-assembly, and performance of these materials. Previous work has demonstrated the relevance of this approach, with molecularly defined oligomers being produced to study, for instance, various crystal structures and the onset of chain folding in poly(ethylene), among other materials.[3,4]

In the synthesis of well-defined oligomers of monomers with C_{2v} symmetry, as in the case of 3,3′-dihexyl-2,2′-bithiophene, the major challenges to overcome are selective monofunctionalization and the separation of side products with similar molecular weights to yield monodisperse materials.[5] Oligomers of such C_{2v}-symmetric monomers with up to 96 repeating units have already been prepared.[6]

For monomers with C_s symmetry such as 3-hexylthiophene, the synthesis is far more challenging because of the additional issue of regioregularity.[7] Most approaches have been based on an iterative synthesis involving stepwise extension of the oligomer by one or two monomer units per cross-coupling step followed by activation of the newly formed chain end. Often a protecting group is used to block one oligomer end and enforce regioselective functionalization.[8−11] Immobilization of the growing oligomer on a solid-phase support has also been reported to simplify purification,[8,9,11−13] enabling the synthesis of a dodecamer with high regioregularity, albeit on the milligram scale.[8] A major drawback of these approaches for long oligomers is the growth by only one or two thiophene units per cross-coupling step, necessitating numerous steps. Into the bargain, the separation of oligomers with length *n* from unreacted oligomers with length *n* − 1 or *n* − 2 is increasingly difficult for longer chains.

An alternative approach is based upon sequential dimerizations to afford a geometric sequence of oligomers. This can afford reasonable quantities of long oligomers in a short number of steps and is well-suited to monomers of C_{2v} symmetry. However, for oligomers of C_s symmetry based upon 3-alkylthiophenes, it has been reported that significant amounts of regioirregular byproducts are formed by oxidative dimerization[14] or homocoupling that occurs during cross-coupling.[15] Such byproducts are very difficult to remove, as the regioregular and irregular materials have the same molecular weight and molecular weight makes the highest impact on purification properties in oligomers. For example, in our own attempts to make the octamer of 3-hexylthiophene by geometric Stille coupling of the brominated and stannylated mono-, di-, and tetramers, the undesired byproducts with tail-to-tail miscoupling were consistently formed in 5−15% yield. These could be separated from the desired head-to-tail product only by preparative-recycling gel-permeation chromatography (GPC) after a few tens of cycles (ca. 45 h runtime) on the milligram scale (Figure S1 in the Supporting Information). The significant impact that regioirregular impurities can have on the physical properties is apparent from a simple examination of the melting points. The purely regioregular hexadecamer has a sharp melting point at 126 °C,[16] while that of the impure material is ca. 50 °C lower (78 °C).[15]

A synthetic strategy leading to high-purity monodisperse regioregular oligo(3-hexylthiophene)s in useful quantities should therefore avoid the need to separate regioirregular isomers of the same molar mass. Our solution, as described forthwith, is based upon the coupling of oligomers having different molecular weights following the Fibonacci sequence. We found that such an approach allows the facile separation of the regioirregular side

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products formed by homocoupling or oxidative dimerization of educts as a result of the significant difference in molecular weight relative to that of the desired product, allowing the synthesis of highly regioregular oligomers with up to 36 repeating units.

To allow easy identification of the discussed materials, the nomenclature for oligo(3-hexylthiophene) derivatives shown in Figure 1 will be used. A substituent at the so-called “2-position” (or “head position”) is given as a prefix, as in Br-(3HT)$_n$. A substituent at the “5-position” (or “tail position”) is given as a suffix, as in (3HT)$_n$-SnBu$_3$.

Figure 1. Nomenclature for oligo(3-hexylthiophene)s (3HT)$_n$ and substituted derivatives thereof.

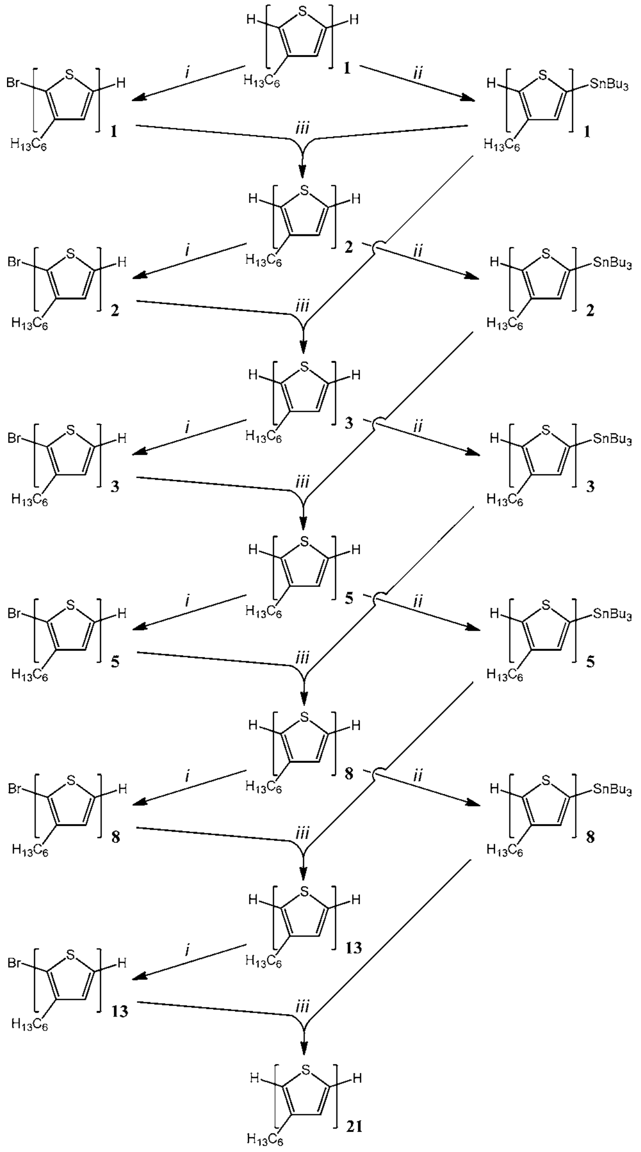
The synthetic strategy is shown in Scheme 1. It is based on the cross-coupling of regioselectively brominated and metalated oligomers in solution. Bromination of the oligomers at the “2-position” was readily achieved using *N*-bromosuccinimide (NBS) at reduced temperature,[8,10] while the “5-position” was selectively stannylated by treatment with lithium diisopropylamide (LDA) at cryogenic temperature followed by addition of tributyltin chloride.[17]

Thus, 3,4′-dihexyl-2,2′-bithiophene, (3HT)$_2$, was synthesized in good yield by cross-coupling of 2-bromo-3-hexylthiophene with 5-tributylstannyl-3-hexylthiophene using tetrakis(triphenylphosphine)palladium according to the reported protocol (Scheme 1).[18] Here the resulting regioirregular side products originating from homocoupling and oxidative dimerization were removed by vacuum distillation.[15] The dimer was subsequently brominated or stannylated to yield Br-(3HT)$_2$ and (3HT)$_2$-SnBu$_3$, respectively. Coupling of Br-(3HT)$_2$ with the shorter (3HT)-SnBu$_3$ afforded (3HT)$_3$ in a yield of 73%. The resulting homocoupled products, 3,4′,3″,3‴-tetrahexyl-2,2′:5′,2″:5″,2‴-terthiophene [*HH*-(3HT)$_4$] and 4,4′-dihexyl-2,2′-bithiophene [*TT*-(3HT)$_2$], with higher and lower molecular weight, respectively, relative to the desired *HT*-(3HT)$_3$, were readily removed by column chromatography on a large scale, since the influence of molecular weight on the retention factor exceeds the influence of regioregularity.

Similarly following analogous reactions for subsequent steps, the trimer was brominated and subsequently cross-coupled with (3HT)$_2$-SnBu$_3$ to yield (3HT)$_5$ in 77% yield following chromatographic purification. Following Scheme 1, Br-(3HT)$_5$ and (3HT)$_3$-SnBu$_3$ were reacted to give (3HT)$_8$, and Br-(3HT)$_8$ and (3HT)$_5$-SnBu$_3$ were combined to give (3HT)$_{13}$. Finally, Br-(3HT)$_{13}$ and (3HT)$_8$-SnBu$_3$ reacted to give (3HT)$_{21}$, the longest regioregular oligo(3-hexylthiophene) reported to date.

In general, then, the synthesis of the oligomer (3HT)$_{n_i}$ is achieved by the coupling of Br-(3HT)$_{n_{i-1}}$ and (3HT)$_{n_{i-2}}$-SnBu$_3$. The progression of the oligomer length can be described by $n_i = n_{i-1} + n_{i-2}$. Therewith, the presented synthetic strategy follows the Fibonacci numbers, yielding (3HT)$_n$ with n = (1,) 1, 2, 3, 5, 8, 13, and 21.

Scheme 1. “Fibonacci’s Route” to (3HT)$_n$^{a}



^{a}Conditions: (*i*) NBS, −20 °C to rt; (*ii*) THF, LDA, Bu$_3$SnCl, −78 °C; (*iii*) Pd(PPh$_3$)$_4$, toluene, 90 °C.

The progress of the oligomer growth in this presented strategy is slower than in a geometric sequence (i.e., coupling of oligomers of equal length). In the latter, the synthesis of (3HT)$_8$ is achieved in nine steps from 3HT, whereas the “Fibonacci synthesis” requires 11 steps. However, the significantly easier purification for high regioregularity and monodispersity is clearly worth the additional effort. This strategy allows the synthesis of (3HT)$_8$ in large quantities (e.g., 5 g) and easy purification by reprecipitation from CHCl$_3$/acetone and column chromatography. Admittedly, the purification of longer oligomers by column chromatography becomes more difficult but can readily be performed by simple preparative GPC without excessive run times.

The synthesized oligomers were pure with respect to molecular weight [polydispersity index (PDI) = 1.00], as evidenced by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF-MS) measurements (Figure 2), clearly indicating their “monodispersity”. In comparison, typical “low-molecular-weight polymers” prepared by Kumada polycondensation have PDIs of 1.15−1.25[19] and show a broad distribution over the different chain lengths in

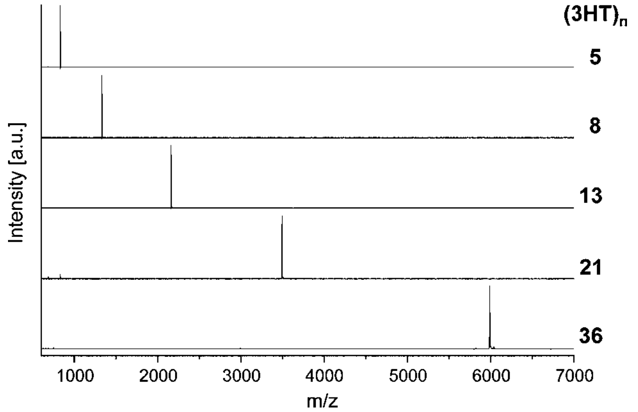


Figure 2. MALDI-TOF mass spectra of oligo-3-hexylthiophenes. $(3HT)_n$ with $n > 8$ feature minor signals in the low-molecular-weight regime up to m/z 1000 due to fragments and aggregates of the matrix employed.

MALDI-TOF-MS (Figure S2). To be able to appreciate the meaning of such a PDI in the low-molecular-weight regime, a simple example is illustrative. A theoretical sample containing the same number of molecules of each oligomer $(3HT)_n$ with $n = 5$, 6, ... 21 would have a number-average molecular weight (M_n) of 2.16 kg/mol with a PDI of 1.14 and generally would be considered nearly "monodisperse".

The >99% regioregularity of the oligomers and the regioselectivity of the bromination and stannylation were proven by NMR spectroscopy. The signals in the ^{1}H NMR spectrum were assigned to a regioregular oligomer in accordance with the literature, as shown in Figure 3 for $(3HT)_8$.[12,20,21] Regioregular oligomers can be discerned from regio-irregular ones by both the aromatic and benzylic ^{1}H signals. In the *HH* configuration, benzylic methylene signals occur at 2.45−2.55 ppm, whereas in *TT* they are at 2.57−2.61 ppm. For the aromatic protons, the four possible triads *HT*−*HT* (6.98 ppm), *TT*−*HT* (7.00 ppm), *HT*−*HH* (7.02 ppm), and *TT*−*HH* (7.05 ppm) can be distinguished.[21] The NMR spectra of all oligomers showed no such signals of significant intensity.

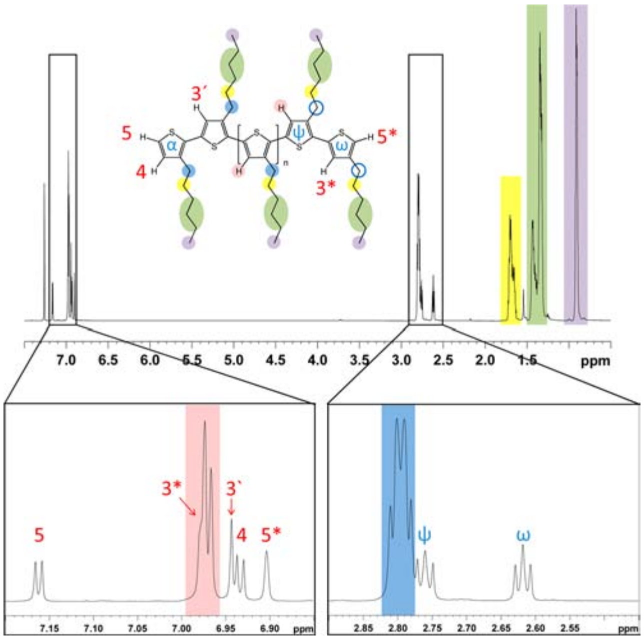


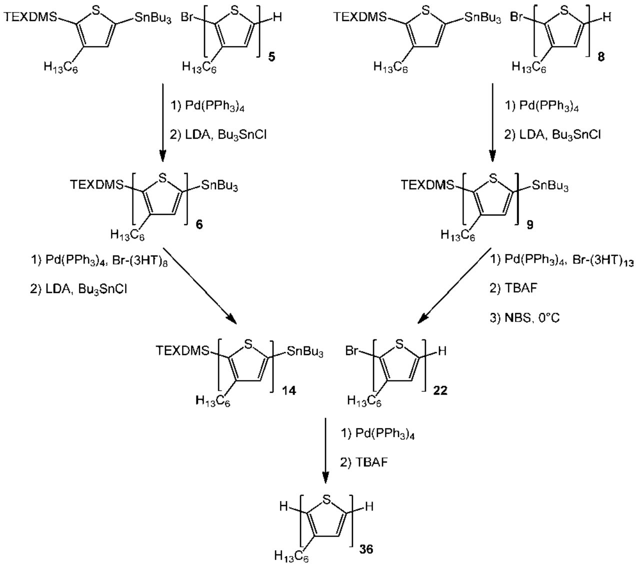
Figure 3. Assignment of the signals in the ^{1}H NMR spectrum (700 MHz, $CDCl_3$) of $(3HT)_8$. indicating high isomeric purity.

The attempted synthesis of oligomers longer than $(3HT)_{21}$ was complicated because of the low solubility of $(3HT)_{13}$ in tetrahydrofuran (THF) at −78 °C. The solubility of $(3HT)_8$ was found to be quite poor already, requiring low concentrations in the metalation step. The isomerization of thienyllithium derivatives between the 2- and 5-position at elevated temperature[22,23] prohibited performing the reaction at higher temperatures (e.g., room temperature) where improved solubility in THF was observed.

Therefore, to allow for regioselective metalation of $(3HT)_{13}$ and longer oligomers, a bulky silyl protecting group was introduced at the 2-position of the oligothiophene. We found this to force deprotonation to occur solely in the corresponding unprotected 5-position. This additionally allowed for the use of excess LDA to drive the reaction to completion. A number of different silyl derivatives were explored. As reported previously by Spivey et al.,[13] the trimethylsilyl (TMS) and triethylsilyl (TES) groups were quite labile and therefore not suitable as a first choice.[13] By contrast, the *tert*-butyldimethylsilyl (TBDMS) and (2,3-dimethylbutan-2-yl)dimethylsilyl (TEXDMS) groups were both very stable under the required reaction and purification conditions and could easily be cleaved off afterward with tetra-*n*-butylammonium fluoride (TBAF). We favored the TEXDMS group over the TBDMS group because its steric demand is slightly higher and it could also conveniently be removed using TBAF in THF at room temperature.

The synthesis of the longer oligomers utilizing the protecting group is shown in Scheme 2. The silyl group was introduced into the oligomers by Stille coupling of TEXDMS-(3HT)-$SnBu_3$ with Br-$(3HT)_5$ and Br-$(3HT)_8$ to yield TEXDMS-$(3HT)_6$ and TEXDMS-$(3HT)_9$, respectively, which were subsequently regioselectively stannylated. The resulting stannyl monomers were both contaminated with significant amounts of starting materials and were used crude in both cases. We note that the impurities were readily removed following cross-coupling as a result of the significant differences in molecular weight relative to

Scheme 2. Introduction of a Silyl Protecting Group at the Stage of $(3HT)_5$ and $(3HT)_8$ Followed by the Synthesis of $(3HT)_n$, n = 14, 22, 36



the desired product. TEXDMS-$(3HT)_6$-$SnBu_3$ was cross-coupled with Br-$(3HT)_8$ to yield TEXDMS-$(3HT)_{14}$, which was then regioselectively stannylated at 0 °C. The crude TEXDMS-$(3HT)_9$-$SnBu_3$ was cross-coupled with Br-$(3HT)_{13}$ to yield TEXDMS-$(3HT)_{22}$ and, after deprotection and bromination, Br-$(3HT)_{22}$. Finally, the reaction of Br-$(3HT)_{22}$ and TEXDMS-$(3HT)_{14}$-$SnBu_3$ under $Pd(PPh_3)_4$ catalysis yielded $(3HT)_{36}$ in 34% yield after deprotection and purification.

The conjugation of the P3HT backbone is often thought to cause a semistiff conformation, resulting in an increased hydrodynamic radius and therefore an overestimation of the molecular weight in GPC in comparison with polystyrene standards.[6,24] As the synthesized oligomers were monodisperse and had a precise molecular weight, they allowed verification of this molecular-weight overestimation by comparison of MALDI-TOF-MS and GPC data (Figure 4). In agreement with measurements reported by other authors, the GPC molecular weight was overestimated by a factor of 1.67 relative to the ones measured by MALDI-TOF-MS[6] and NMR spectroscopy.[23]

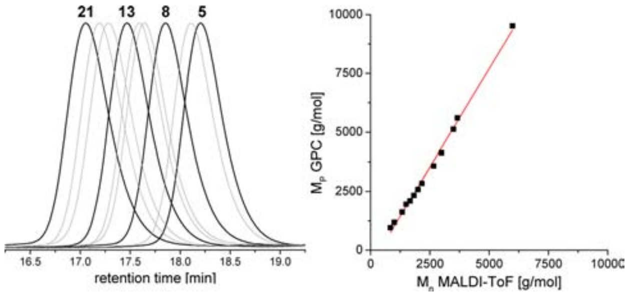


Figure 4. (left) Overlay of GPC traces of oligomers $n = 5$ to 21, shown in black for the ones following the Fibonacci numbers (5, 8, 13, 21) and in gray for some intermediate oligomers (6, 10, 11, 16, 18). (right) Comparison of the molecular weights determined by MALDI-TOF-MS (M_n) and GPC peak molecular weights (M_p) calibrated with polystyrene standards.

In conclusion, the approach presented in this work, to synthesize regioregular oligo(3-hexylthiophene)s via "Fibonacci's route", allows for the synthesis of large quantities of long $(3HT)_n$ [e.g., >1 g for $(3HT)_{13}$] with high regioregularity. This route requires a marginally higher number of synthetic steps to reach a certain oligomer length compared with an approach following, for example, a geometric sequence, but it simplifies the purification significantly. With the presented method, regioregular oligomers up to a length of 21 repeat units were synthesized. A small adaption of this method, namely, the introduction of a silyl protecting group at the oligomers' "2-position", allowed stannylation of, for example, $(3HT)_{14}$ by enforcing deprotonation selectively in the "5-position". By these means, a regioregular oligomer with 36 repeat units was successfully synthesized. The thermal and structural characteristics of the compounds synthesized are described in an accompanying paper.[16]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and additional data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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