Regiospecifically Alkylated Oligothiophenes via Structurally Defined Building Blocks

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Abstract: We have developed a new synthetic protocol for the unsymmetrically alkylated and halogenated terthiophenes 5 and 10. To demonstrate their usefulness as building blocks for well-defined oligothiophenes, we synthesized a series of seven new sexi-, septi- and octithiophenes. Terthiophene 5 could be dimerized to the didecylderithiophene In6 and terthiophene 10 to sexithiophene Out6, respectively, by the use of nickel catalysis. Together with the bistannylated thiophenes 11 and 12, the septithiophenes In7 and Out7 as well as the octithiophenes In8 and Out8 could be obtained via Stille coupling methodology. We could also obtain the unsymmetrical sexithiophene Unsym6 by selective heterocoupling between one equivalent of terthiophene 5 and 10 each. All new sexi-, septi- and octithiophenes show high photoluminescence in solution, but the quantum yield drops sharply in thin films of the materials.

Key words: regioselectivity, halogenation, alkylations, coupling, oligothiophenes, luminescence

Oligomers and polymers of substituted thiophenes have received considerable attention in the last years owing to potential applications of both scientific and economic value.1 Alkyl substitution enhances molecular systems’ solubilities, thereby enabling the creation of applications that demand processability. The alkyl substitution can also alter the conjugation length of the thiophene chain by causing the thiophene units to assume separate planes from each other.2

The main application for oligo- and polythiophenes has traditionally been the electroactive component in light-emitting diodes (LEDs) and field-effect transistors (FETs). Thiophenes synthesized for FET-applications are typically substituted in the free peripheral α-positions,3 whereas LED-thiophenes have substituents in the β-positions.2 The latter substitution pattern opens up the possibility of different regioisomers, both in oligomers and polymers. While 3-alkylated thiophene monomers have been successfully polymerized regioselectively,4 there is a lack of synthetic procedures that generate regioselectively alkylated oligomers, both for use as such, and for further functionalization–polymerization.

Since the stability of a light-emitting diode depends on the number of coupling defects in the constituting polymer (among other things),5 it should be of interest to synthesize well-defined longer oligomers. Furthermore, as the diode efficiency is a function of several structural parameters, it should also be worthwhile to investigate different regioselectively alkylated oligomers, where different alkyl ‘dilutions’ of the π-system are possible. In addition to creating different conjugation lengths, different proportions of sp3-chains should also affect solubility, which previously has been proposed as a way of optimizing the photoluminescence yield.6

Terthiophenes can be considered key building blocks for oligothiophenes. We therefore anticipated that it should be valuable to develop synthetic routes to terthiophenes, with regioselective alkyl and halogen substitution, thereby facilitating further regioselective oligomerization–functionalization. We chose the unsymmetrically substituted terthiophenes 5 and 10 as useful, and until now, unknown targets for synthesis. We also chose a decyl group as the alkyl chain for our systems, since we thought it would be of sufficient length to solubilize the higher oligomers, and because starting materials are easily available.

Previous syntheses of terthiophenes have usually consisted of organometallic coupling of two thiophene subunits to one central substituted unit,7 or ring-closure of disubsti-

**Scheme 1** Reactions and conditions: i) Bromine, NBS or other brominating reagent
tuted 1,3-diacylene\textsuperscript{8} or 1,4-butadiene segments\textsuperscript{9} by different thionating reagents. None of these methods have been successful for the synthesis of \(\beta\)-alkylsubstituted terthiophenes with regioselective halogen attachment. Reported brominations of unsymmetrically alkylsubstituted terthiophenes have not been selective (Scheme 1).\textsuperscript{10}

We therefore anticipated that a useful synthesis must include a halogenated building block, which is assembled to the desired terthiophene without scrambling. Our synthesis is depicted in Scheme 2. 2-Bromothiophene (1) was acylated with \(n\)-dodecanoyl chloride in quantitative yield to give 2, which conveniently and quantitatively could be brominated to the ketone, with elemental bromine to give compound 3. We adopted the method of Kelin and Kulinkovich\textsuperscript{11} to transform 3 and 2-acetylthiophene to the corresponding unsymmetrically substituted 1,4-dithienylbutandione 4 in moderate yield (63%). The ring-closure of 4 to the corresponding thiophene proved a more demanding task than first expected. The common reagents for this transformation, like phosphorus pentasulfide or Lawesson’s reagent, gave high yields of debrominated, reduced terthiophene, despite claims in the literature that these reagents are inert toward aryl bromides.\textsuperscript{12} We are not sure if this debromination occurs before the cyclization, or whether it is the thionating reagent or one of its reaction products that is the active species in this undesired side-reaction. Noteworthy is however that reduction of the target terthiophenes (5 or 10) does not occur with either phosphorus pentasulfide or Lawesson’s reagent under similar conditions. In addition, we could somewhat suppress reduction by using very large excess of thionating reagent, leading to the assumption that the reduction is caused by one of the reaction products from the phosphorus reagent.

The desired non-reductive cyclization could, on the other hand, conveniently be carried out by the phosphorus-free procedure of Freeman et al. and Steliou et al.,\textsuperscript{13} where hexamethyldisilathiane is reacted with a 1,4-butanedione in the presence of boron trichloride (in situ creating borontrisulfide as the thionating reagent). This reaction afforded the target terthiophene 5 in 51\% yield of excellent purity. Analogously, the second target terthiophene 10 could be synthesized from thiophene (6).

Once we had created these valuable building blocks, we could proceed to synthesize a series of regio-defined oligothiophenes (Figure 1). Since the systematic names of these oligomers are rather inconvenient, we decided to give them more graphic acronyms than what is usual. The position of the alkyl chain is always at the second peripheral thiophene unit. Thus the position of the alkyl chain can be viewed as being either ‘In’ or ‘Out’ depending on its position on the thiophene. Accordingly, the word ‘In’ or ‘Out’ is followed by the number of thiophene units, making an acronym like In6 for the first oligothiophene in the series.

We synthesized the didecyl-substituted sexithiophene In6 via a nickel-catalyzed dimerization of 5 in the presence of 2,2’-bipyridine.\textsuperscript{14} It is interesting to note that zinc had to be added after the addition of the substrate 5 in order to get the reaction to proceed. Analogously the other regioisomeric sexithiophene Out6 could be obtained by dimerization of terthiophene 10.

Next, we were able to transform 5 to its corresponding trimethylstannyl derivative, and react it with 10 in a one-pot palladium-catalyzed procedure to yield the unsymmetri-
cally substituted sexithiophene Unsym6, with a very usual substitution pattern.

In order to obtain longer oligomers, we chose the tin-based Stille procedure, since the central bis-stannylated bridging units 11 and 12 (Figure 2) are easily obtainable.15 Terithiophene 5 and thiophene 11 conveniently gave sexithiophene In7. Analogously 10 and 11 could be assembled to give Out7. Additionally, bithiophene 12 could be reacted with terithiophene 5 to yield In8 and in a similar procedure with 10 to give Out8. We found this Stille methodology most useful as attempted syntheses of the same targets, employing boron-based procedures (such as Suzuki coupling) gave inconsistent and unsatisfactory results.

![Figure 2 Bis-stannylated building blocks](image)

Table: Optical Properties of Oligothiophenes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Absorption Maxima (nm)</th>
<th>Emission Maxima (nm)</th>
<th>PL Quantum Efficiency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Solution</td>
<td>Film</td>
<td>Solution</td>
</tr>
<tr>
<td>In6</td>
<td>415</td>
<td>445, 473, 613</td>
<td>515, 555</td>
</tr>
<tr>
<td>Out6</td>
<td>427</td>
<td>425, 501</td>
<td>515, 555</td>
</tr>
<tr>
<td>Unsym6</td>
<td>422</td>
<td>445, 473, 512</td>
<td>515, 555</td>
</tr>
<tr>
<td>In7</td>
<td>434</td>
<td>457, 482, 523</td>
<td>530, 570</td>
</tr>
<tr>
<td>Out7</td>
<td>444</td>
<td>438</td>
<td>530, 570</td>
</tr>
<tr>
<td>In8</td>
<td>444</td>
<td>476, 508, 554</td>
<td>545, 585</td>
</tr>
<tr>
<td>Out8</td>
<td>451</td>
<td>447</td>
<td>545, 585</td>
</tr>
</tbody>
</table>

All oligothiophenes were collected in 60–90% yield with these procedures. We could not distinguish any reliable trends in yields with respect to oligomer lengths or substitution patterns. However, we did observe that one crucial factor for high yields was the freshness of the stannylated building blocks. Although no deterioration of compounds 11 and 12 was detectable by NMR, oligomer yields were consistently higher when using freshly prepared material. The title compounds, terthiophenes 5 and 10, could on the other hand be stored at ambient temperature and atmosphere for several months without any detectable degradation or loss of reactivity.

All oligothiophenes were measured in a custom built integrating sphere made by Lab.

The title compounds, terthiophenes In7 and In8, could be assembled to give Out7. Additionally, bithiophene 12 could be reacted with terithiophene 5 to yield In8 and in a similar procedure with 10 to give Out8. We found this Stille methodology most useful as attempted syntheses of the same targets, employing boron-based procedures (such as Suzuki coupling) gave inconsistent and unsatisfactory results.

We investigated the optical properties of the new oligomers (Table) and found that all ‘Out’-oligomers show a small bathochromic shift compared to their ‘In’-isomers. All oligomers display high luminescence in chloroform solution, as expected for soluble thiophene oligomers. The emission wavelengths were identical for all oligomers of the same length, showing that the position of the alkyl group does not alter the emissive state’s energy levels. The photoluminescence efficiencies in solution are a few percent higher for the ‘Out’-isomers, compared to the corresponding ‘In’-isomers, meaning that the alkyl chain in the ‘Out’-isomers is more effective in hindering the interchain luminescence quenching. The photoluminescence efficiencies in films are only a few percent for all oligomers, which clearly shows that there is not enough ‘sp³-dilution’ of the π-system to prevent the interchain luminescence quenching in the solid state. The octimers In8 and Out8 are rather insoluble in chloroform, which clearly limits the measurements.

We have developed an efficient synthesis of two new versatile building blocks, terthiophenes 5 and 10. With these as starting materials, we have synthesized a series of new and hitherto unavailable sexi- sepi- and octithiophenes in high purity, useful on a preparative scale. All oligomers show high photoluminescence in solution, whereas interchain quenching drastically reduces the photoluminescence efficiency in the solid state. Further synthetic applications of building blocks 5 and 10 are now pursued in our laboratory and will be reported in due course.

All operations except where indicated were performed in ambient atmosphere, without any special care taken for the exclusion of air or moisture. 1H NMR and 13C NMR spectra were recorded at 400 and 100 MHz, respectively, on a Bruker AM 400. 13C NMR spectra could not be collected for the sexi-, sepi- or octithiophenes, even at prolonged experiment times (18 h), due to their relatively low solubility in CDCl3, or any other deuterated solvent. Mass spectra were recorded on a Finnigan SSQ 7000 (electron impact) and on a Perseptive Biosystems Voyager-De STR (MALDI-TOF). Elemental analyses were performed by Analytische Laboratorien GmbH, Germany. THF was freshly distilled from sodium benzophenone ketyl, and DMF was distilled from P2O5 and stored over molecular sieves. All other commercial reagents and solvents were used as received.

In the optical measurements, the oligomer was dissolved in CHCl3, with concentrations adjusted to give an optical density 0.2 or lower in a 10 mm optical glass cell. Thin films were spin-coated from CHCl3 solution, 5–10 mg/mL, on a 24 × 40 mm2 quartz substrate giving optical densities of 0.1–0.3. The optical absorption spectra of samples were measured on a Perkin Elmer Lambda 9 spectrometer, and the emission spectra were measured with an Oriel Instaspec IV diode matrix spectrometer. Photoluminescence (PL) yields and spectra were measured in a custom built integrating sphere made by Lab.
sphere, together with Oriel Instapect IV diode matrix spectrometer.

Exciting light was a chromatic beam and the beam wavelength was selected according to absorption spectra of each sample.

1-(5-Bromothien-2-yl)-dodecan-1-one (2)

2-Bromothiophene (1) (8.16 g, 50 mmol) and n-dodecanoyl chloride (13.67 g, 62.5 mmol) were dissolved in benzene (75 mL). AlCl\textsubscript{3} (8.33 g, 62.5 mmol) was added in portions, with stirring, over 10 min. The resulting black solution was refluxed for 30 min and left to cool to r.t.. The reaction was quenched by very cautious (excessive frothing!) addition of aq HCl (2 M; 75 mL), affording a yellow slurry that was rinsed into a separating funnel with benzene (50 mL) and aq HCl (2 M; 50 mL). The mixture was gently shaken and the phases separated. The organic phase was washed with aq HCl (2 M), affording a yellow product that was purified by flash chromatography (heptane) (R\textsubscript{f} 0.3) .

On evaporation, the pooled desired product was obtained. Yield: 47%; orange oil.

1-Thien-2-yl-dodecan-1-one (7)\textsuperscript{16}

Using the procedure for the synthesis of 2, with thiophene (6) substituted for 1, the desired product was obtained. Yield: quantitative; yellow oil.

2-Bromo-1-thien-2-yl-dodecan-1-one (8)

Using the procedure for the synthesis of 3, with the ketone 7 substituted for 2, the desired product was obtained. Yield: quantitative; orange oil.

4-(5-Bromothien-2-yl)-2-decyl-1-thienylbutane-1,4-dione (9)

Using the procedure for the synthesis of 4, with o-bromo ketone 8 substituted for 3 and with commercial 5-bromo-2-acythiophene instead of 2-acetyltiophene (more toluene was required to make a solution of these two reagents, compared to the synthesis of compound 4), the desired product was obtained. Yield: 47%; orange oil.

1\textsuperscript{13}C NMR (CDCl\textsubscript{3}): \( \delta = 14.5, 23.1, 27.8, 29.7, 29.8, 29.9, 30.0, 32.3, 33.4, 41.9, 43.1, 123.2, 128.6, 131.8, 132.6, 132.7, 134.3, 144.0, 146.1, 191.6, 195.4\)

5-Bromo-3-decyl-[2,2',5',2"]terthiophene (5)

The 1,4-butanodione 4 (7.04 g, 15 mmol) was dissolved in toluene (150 mL) and hexamethyldisilathiane (3.34 g, 30 mmol) was added in one portion at r.t., directly followed by BCl\textsubscript{3} (1 M in hexanes; 22.5 mL). After 1 h, TLC (EtOAc–heptane, 9:1) indicated total consumption of the starting material, and H\textsubscript{2}O (100 mL) was added. The organic phase was separated, washed with a further amount of H\textsubscript{2}O (2 \times 150 mL), dried (MgSO\textsubscript{4}) and evaporated to a dark crude product that was purified by flash chromatography (heptane) (R\textsubscript{f} 0.4). This afforded 5 of excellent purity.

Yield: 3.55 g (51%); yellowish crystalline product.

1\textsuperscript{1}H NMR (CDCl\textsubscript{3}): \( \delta = 0.88 \) (t, \( J = 6.4 \) Hz, 3 H); 1.22–1.39 (m, 14 H), 1.63 (q, \( J = 7.6 \) Hz, 2 H); 2.68 (t, \( J = 7.6 \) Hz, 2 H); 6.86 (d, \( J = 3.6 \) Hz, 1 H); 6.99 (s, 1 H); 7.00–7.02 (m, 2 H); 7.15 (dd, \( J = 3.6, 1.2 \) Hz, 1 H); 7.22 (dd, \( J = 4.8, 1.2 \) Hz, 1 H).

1\textsuperscript{13}C NMR (CDCl\textsubscript{3}): \( \delta = 14.9, 23.5, 30.0, 30.1, 30.2, 30.3, 30.3, 30.4, 31.4, 32.7, 112.5, 124.6, 125.4, 126.9, 127.2, 128.6, 129.3, 131.0, 136.5, 137.8, 138.2, 141.7.

MS (EI): \( m/z = 468, 466 \) (M\textsuperscript{+}, 100).

Anal. Calc. for C\textsubscript{32}H\textsubscript{56}Br\textsubscript{2}S: C, 56.51; H, 5.82. Found: C, 56.37; H, 5.97.
5-Bromo-4-Decyl-[2,2;5,2']-terthiophene (10)

Using the procedure for the synthesis of 5, with the 1,4-dione 9 substituted for 4, the desired product was obtained in slightly diminished yield (38%), as a yellow material, that required several days to crystallize.

1H NMR (CDCl3): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.20–1.39 (m, 14 H), 1.64 (q, J = 7.6 Hz, 2 H), 2.71 (t, J = 7.6 Hz, 2 H), 6.89 (d, J = 4 Hz, 1 H), 6.94 (s, 1 H), 6.96 (d, J = 4 Hz, 1 H), 7.06 (dd, J = 5.2, 3.6 Hz, 1 H), 7.12 (dd, J = 3.6, 1.0 Hz, 1 H), 7.31 (dd, J = 5.2, 1.0 Hz, 1 H).

MS (EI): m/z = 468, 466 (M+, 100).

Anal. Calcd for C52H58BrS2: C, 68.28; H, 7.02. Found: C, 68.32; H, 7.02.

Purification of the Sexi-, Septi- and Octithiophenes; General Procedure

After evaporation of the solvent, the crude product was treated with boiling Et2O (ca. 10 mL) and then rapidly cooled down to 0 °C by immersing the flask in an ice bath, whereupon the oligothiophene precipitated as flakes. Cold MeOH (a few mL) was added and the solids were collected by vacuum filtration and washed with a little cold MeOH and acetone. The solids were then adsorbed on -0.5 g silica gel and put on top of a dry silica column (1 cm diameter, 5 cm high). The column was then flushed with hexanes (50 mL) to remove non-polar byproducts, pumped dry, flushed with MeOH (50 mL) (to remove polar byproducts) and again pumped dry. The desired oligomer was then eluted with CH2Cl2 (sexithiophene) or THF (octithiophenes) and the analytically pure product was collected upon evaporation of the solvent, typically in 60–90% yield, in the form of a brick red amorphous solid.

4,3'-Didecyl-[2,2;5,2';5';2'';5'',2'''';5'''';2'''''';2''''''']sexithiophene

To a dry 25 mL 3-necked round-bottom flask, anhyd NiCl2 (13 mg, 0.1 mmol) in THF (5 mL), followed by a second portion of Pd(PPh3)4 (29 mg, 0.05 mmol) and Pd(OH)2 (30 mg, 0.5 mmol) were added. The system was flushed with argon for a few min, anhyd DMF (5 mL) was added and the solution stirred at 80 °C overnight. The product was precipitated by addition of cold MeOH (50 mL), collected by vacuum filtration and then purified according to the general purification procedure.

1H NMR (CDCl3): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.20–1.43 (m, 28 H), 1.62–1.72 (m, 4 H), 2.71–2.79 (m, 4 H), 7.00–7.05 (m, 4 H), 7.06–7.09 (m, 3 H), 7.11–7.14 (m, 2 H), 7.17 (d, J = 3.6 Hz, 1 H), 7.22 (d, J = 5.2 Hz, 1 H), 7.32 (d, J = 5.2 Hz, 1 H).

MS (MALDI-TOF): m/z = 856 (M+, 100).


3,4'-Didecyl-[2,2;5,2';5';2'';5'',2'''';5'''';2'''''';2''''''']septithiophene (In7)

To a dry 25 mL 3-necked round-bottom flask, terthiophene 5 (234 mg, 0.5 mmol), 2,5-bistributylstannylthiophene (Out6) (166 mg, 0.25 mmol) and Pd(PPh3)4 (58 mg, 0.50 mmol) were added. The system was flushed with argon for a few min, anhyd DMF (5 mL) was added and the solution stirred at 80 °C overnight. The product was precipitated by addition of cold MeOH (50 mL), collected by vacuum filtration and then purified according to the general purification procedure.

1H NMR (CDCl3): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.21–1.43 (m, 28 H), 1.68 (q, J = 7.6 Hz, 4 H), 2.77 (t, J = 7.6 Hz, 4 H), 7.00–7.05 (m, 6 H), 7.10 (s, 2 H), 7.13 (d, J = 4.0 Hz, 2 H), 7.17 (d, J = 3.6 Hz, 2 H), 7.22 (d, J = 4.8 Hz, 2 H).

MS (MALDI-TOF): m/z = 856 (M+, 100).


3,4'-Didecyl-[2,2;5,2';5';2'';5'',2'''';5'''';2'''''';2''''''']octithiophene (Out7)

The procedure for synthesis of In7, 16, with terthiophene 10 substituted for 5, afforded the desired product.

1H NMR (CDCl3): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.21–1.43 (m, 28 H), 1.66 (q, J = 7.6 Hz, 4 H), 2.73 (t, J = 7.6 Hz, 4 H), 7.02 (s, 2 H), 7.05–7.09 (m, 8 H), 7.13 (d, J = 3.6 Hz, 2 H), 7.32 (d, J = 5.2 Hz, 2 H).

MS (MALDI-TOF): m/z = 856 (M+, 100).


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