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Oligomerization

Unprecedented Demonstration of Regioselective S_EAr Reaction giving Unsymmetrical Regioregular Oligothiophenes

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Abstract: Aromatization of 4-cyano-3-oxotetrahydrothiophene by sulfuryl chloride gives the new building block 4-cyano-3-pyrrolidylthiophene, which forms unsymmetrical regioregular oligothiophenes with a strict alternation of the donor and acceptor groups along the conjugated system. The self-coupling reactions that form the oligomers are shown to proceed by a regioselective electrophilic aromatic substitution mechanism involving a stabilized Wheland intermediate.

Thiophene-based oligomers are among the most widely investigated classes of conjugated materials for the development of electronic plastics.[1] Careful modifications on the oligothiophene backbone by the insertion of substituents on the β and β′ positions of the thiophene units with electron-donating (D) or electron-acceptor (A) character enable a control of the energy levels of the HOMO and LUMO frontier orbitals.[2] Fine-tuning the band gap and energy levels of the conjugated materials are crucial to control the electronic properties, such as absorption and emission properties, ionization potential, and electronic affinity. Within the class of conjugated materials, donor–acceptor (D–A) materials, mixing both electron donor and electron acceptor blocks along the conjugated backbone, are currently among the most widely investigated materials that present moderate or low band gap and broad absorption bands.[3] In this context, we have developed new D–A building blocks in which the D and A groups are grafted onto the 3- and 4-positions of a thiophene ring.[4] Due to the asymmetric electronic distribution, the reactivity at the 2- and 5-positions of the thiophene are different, thus allowing the regioselective building of designed D–A structures. The electronic properties of the D–A derivatives strongly depend on the distribution of the D and A group along the conjugated backbone.[5] Thus from 3-alkoxy-4-cyanothiophene, various symmetrical D–A–D (for small molecules) or $(D–A)_n$ structures (for polymers) were synthesized (Figure 1) and used as donor materials in organic photovoltaic devices.[6] The unsymmetrical structure (Figure 1) built with a strict alternation of the D and A groups grafted at the 3- and 4-positions of thiophene represents a new D–A structure, for which different electronic properties are expected.[4a] Nevertheless, the synthesis of such D–A structures has been less developed. Indeed, the regioselective syntheses of unsymmetrical oligomers presenting an alternating D–A structure require several steps with similar difficulties encountered for the regioregular head-to-tail (H–T) structures for the coupling of β-substituted thiophenes.[7] Unsymmetrical bithiophenes with H–T structures are generally obtained in three steps by organometallic coupling of the corresponding halogenated and metallated thiophenes.[8] Some examples of regioselective metal-free coupling reactions to produce regioregular 3-alkylthiophenes through C–H activation or regioregular bithiophenes by hypervalent iodine reagents have also been described.[9] The synthesis of longer oligomers, built step by step, requires a high number of steps (at least 5 steps for the trimer and 6 or 7 steps for the tetramer), necessitating laborious purification by chromatography after each coupling reaction.[7b,10]

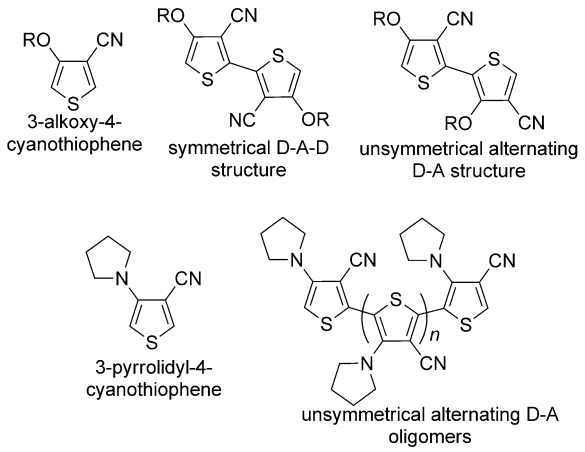

Figure 1. Various D–A structures in 3-donor-4-cyanothiophene series.

As a further step in our approach to these alternating D–A structures, we have investigated the influence of electron-donating ability on the reactivity of the D–A monomer by grafting a pyrrolidino group that exhibits a strong donor character.[11] We have explored the synthesis of oligomers based on the new 3-pyrrolidyl-4-cyanothiophene building block and found that chlorination induces an unprecedented regioselec-

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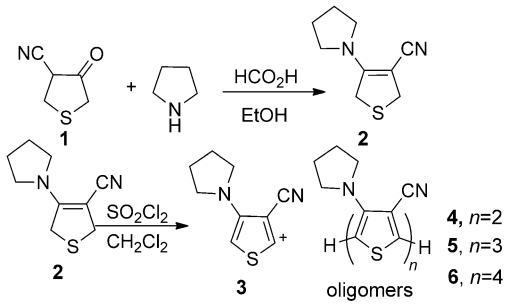
tive coupling leading to strictly D–A-alternated regioregular oligomers (Figure 1).

The synthesis of 3-pyrrolidyl-4-cyanothiophene **3** and oligomers was realized in two steps from the readily accessible 4-cyano-3-oxotetrahydrothiophene **1**[12] (Scheme 1). For the first step, the addition of pyrrolidine to **1** was realized by using



Scheme 1. Synthesis of 3-pyrrolidyl-4-cyanothiophene **3** and oligomers.

formic acid in ethanol to give **2** in 87% yield.[13] Aromatization of **2** was carried out with various oxidants, such as 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) or quinone, to give thiophene **3** in yields that did not exceed 65%.[14] By using an excess of the oxidant, a symmetrical bithiophene derivative was formed with pyrrolidyl groups at the internal positions (see the Supporting Information, Scheme S3). Aromatization by using sulfuryl chloride (SO_2Cl_2) at 0 °C in methylene chloride[15]afforded **3** in 88% yield. Moreover, when a slight excess (1.1 equiv) of SO_2Cl_2 was employed, several oligomers were also isolated and identified by MALDI-TOF mass spectrometry and NMR spectroscopy as being the dimer **4**, the trimer **5**, and the tetramer **6**. ^{1}H NMR spectra of **4**, **5**, and **6** include a singlet at $\delta = 7.8$–7.9 ppm for the proton adjacent to the electron-withdrawing cyano (A) group and a broad singlet at $\delta = 5.8$–5.9 ppm for the proton close to the donor pyrrolidyl (D) group, indicating the presence of only one isomer and suggesting the formation of alternating oligomers. For each isolated oligomer, ^{13}C NMR also confirmed the presence of only one unsymmetrical isomer. The strict D–A-alternated structures for the three oligomers were confirmed by X-Ray diffraction of single crystals (see below). To our knowledge, the direct formation of regioregular oligomers following the aromatization step has never been described. To further elucidate this reaction and to test whether the oligomerization process takes place during or after the aromatization, the reaction was examined with various amounts of SO_2Cl_2 (Table 1).

With less than 1 equivalent of oxidant, conversion of **2** into **3** (Table 1, entries 1 and 2) was not complete but corresponded to the exact amount of SO_2Cl_2 engaged for aromatization. When 1.1 equivalents were used at 0 °C, monomer **3** formed as the major product in 78% yield and the dimer **4**, trimer **5** and tetramer **6** were isolated in 8, 4, and 2% yields, respectively (Table 1, entry 3). When using 1.1 equivalents of SO_2Cl_2 at reflux in $CHCl_3$ (Table 1, entry 4), the amount of monomer decreased while the quantities of oligomers increased. However,

Table 1. Aromatization of **2** with various amounts of SO_2Cl_2.[a]

Entry	SO_2Cl_2 [equiv]	T	Products (conversion[b] or yield[c] [%])
1	0.5	RT	**3** (50)[b]
2	0.9	RT	**3** (90)[b]
3	1.1	0 °C	**3** (78), 4 (8), 5 (4) 6 (2)[c]
4	1.1	reflux	**3** (58), **4** (8-12), **5** (4-6), **6** (4)[c]
5	1.5	reflux	oligomers
6	2	reflux	oligomers

[a] Solvent = $CHCl_3$; [b] conversion based on NMR signals of non-isolated compounds **2** and **3**; [b] yields of isolated compounds.

the yields of isolated oligomers were not well reproducible and could vary even without modification of the parameters of the reaction (e.g., time of reflux or initial concentration of **2**). Increasing the amount of SO_2Cl_2 to 1.5 or 2 equivalents led to a complete disappearance of the monomer **3**, alongside an increase in the yield of oligomers (not quantified; Table 1, entries 5 and 6). MALDI-TOF mass spectrometry indicated the formation of the tetramer, pentamer, hexamer, and heptamer (see the Supporting Information, Figure S14). These results clearly show that the oligomerization process takes place after the aromatization and is brought about by the excess of SO_2Cl_2. Although SO_2Cl_2 is a well-known halogenating agent in electrophilic aromatic substitution (S_EAr) reactions, the reaction performed with 0.2 equivalents of SO_2Cl_2 directly on the monomer **3** at 0 °C did not allow isolation of the chlorinated derivative **3-Cl**. TLC showed the disappearance of **3**, but the reactional medium became dark quickly and we were unable to isolate **3-Cl**, while the formation of oligomers was also observed. Notably, the yields of isolated dimer and trimer were inferior to those obtained when using 1.1 equivalents of SO_2Cl_2 on dihydrothiophene **2**. To better understand how the excess of SO_2Cl_2 works in the oligomerization, the reaction was monitored directly in an NMR tube at 20 °C by adding 0.5, 1, and 1.5 equivalents of SO_2Cl_2 solution in $CDCl_3$ to the dihydrothiophene **2** in $CDCl_3$ (Figure 2). The solutions in each NMR tube were neutralized with sodium bicarbonate to facilitate NMR spectroscopy, because the pyrrolidyl group is partially protonated due to HCl emission in the course of the reaction.

With 0.5 equivalents of SO_2Cl_2, only aromatization took place and **3** was formed in around 50% yield. When the amount of SO_2Cl_2 was increased to1 equivalent, the signals associated to **3** remained predominant, thus conforming the quasi-complete aromatization reaction. However, a signal at $\delta = 3.81$ ppm, indicating the presence of a small quantity of **2**, is always present, and a small signal is detected at $\delta = 7.57$ ppm. When 1.5 equivalents of SO_2Cl_2 were used, the signal at $\delta = 3.81$ ppm disappeared, whereas that at $\delta = 7.57$ ppm increased in intensity and new signals corresponding to the pyrrolidyl protons appeared at $\delta = 3.65$ and 1.95 ppm. These signals would correspond to chlorinated **3-Cl**, obtained by regioselective chlorination of **3**. Signals corresponding to dimer **4** ($\delta = 7.85$ ppm) and traces of longer oligomers (small signal at $\delta = 7.90$ ppm) were also detected, showing that the oligomers were formed to the detriment of **3-Cl**. When the NMR tube was left for several

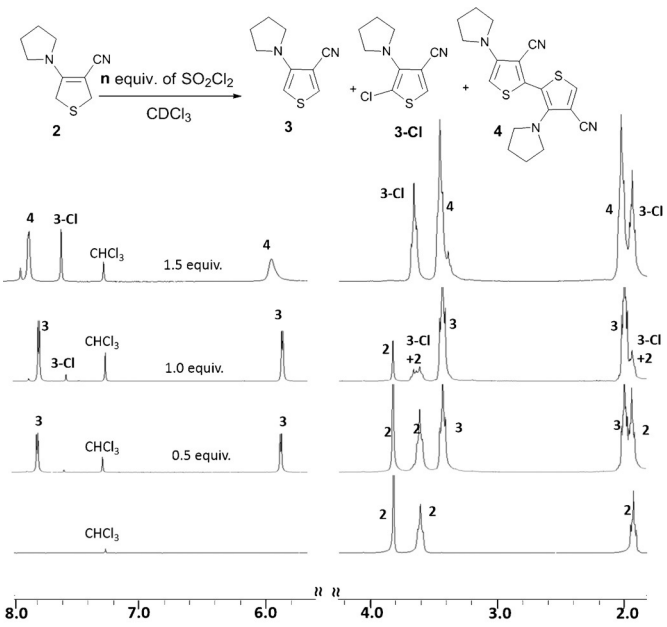


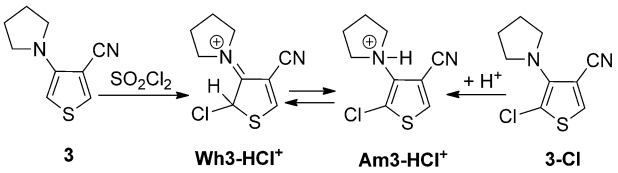
Figure 2. ^{1}H NMR analysis in $CDCl_3$ of dihydrothiophene **2** in the presence of different amount of SO_2Cl_2.

hours at room temperature, the orange solution became dark red and analysis showed complete disappearance of **3-Cl** and formation of numerous compounds, which were difficult to identify. Moreover, the reactional medium is again acidic, indicating that the chlorinated compound had eliminated HCl.

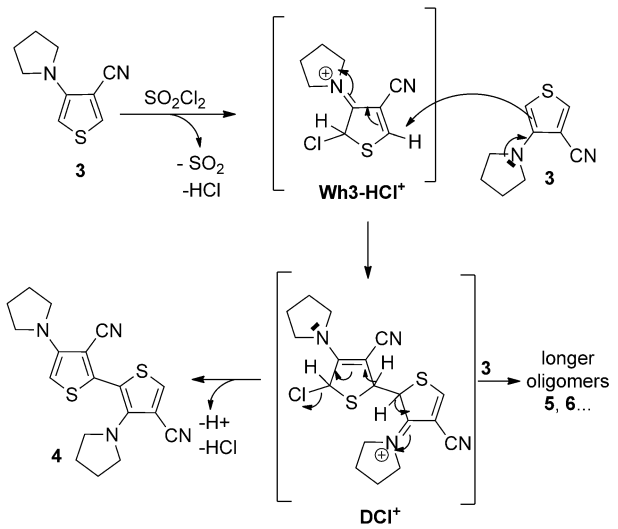
To test the formation of chlorinated derivatives suppressed by the presence of excess SO_2Cl_2 during the aromatization process, the reaction was carried out with 4-cyano-3-hexyloxy-2,5-dihydrothiophene (see the Supporting information, Scheme S6). The experiment showed the expected regioselective chlorination of the thiophene derivative and the chlorinated thiophene compound was isolated in 90% yield from the dihydrothiophene with 2.5 equivalents of SO_2Cl_2. The formation of oligomers of 4-cyano-3-hexyloxythiophene was not observed.

The difference in behavior of 4-cyano-3-pyrrolidylthiophene and 4-cyano-3-hexyloxythiophene towards S_EAr with SO_2Cl_2, leading to the formation of oligomers to the detriment of the chlorinated derivative for **3**, can be explained by the difference in stability between the Wheland intermediates (cationic σ-complexes). The study by Forlani and co-workers on 1,3,5-triaminobenzene showed that piperidyl or pyrrolidyl groups strongly stabilized Wheland σ-complexes as the mesomeric iminium form.[16] This stabilization of the amino cationic σ-complex intervenes during the chlorination of **3** but also corresponds to the protonated form of **3-Cl**. Indeed, as presented on Scheme 2, there are two possible tautomeric forms for the protonation of **3-Cl**; direct protonation of the nitrogen atom to give aminium derivative **Am3-HCl$^+$** or protonation of the carbon atom to give **Wh3-HCl$^+$**, which corresponds to the Wheland intermediate.

Recently De Rosa and Arnold demonstrated for 3-aminopyrrole that the iminium tautomer was favored.[17] Theoretical calculations of the two forms were performed at the ab initio density functional level with the Gaussian 09 package (see the Supporting Information, Figure S1).[18] The aminium form incorporates a bond length of the heterocycle that is compatible with the aromatic thiophene ring, whereas the C–N bond between the thiophene and pyrrolidyl rings corresponds to a single bond. For the iminium form, the sulfur heterocyle has lost its aromatic character but the C–N bond length with the pyrrolidyl group (130 pm) is as expected for a connection with an iminium bond. Nevertheless, the comparison of the calculated energy for the two forms shows that iminium form **Wh3-HCl$^+$** is slightly more stable than the aminium **Am3-HCl$^+$** with a difference of energy $\Delta E = 1.95$ kcal mol^{-1}. Due to the stabilization of the σ-complex **Wh3-HCl$^+$**, its reaction with a good nucleophile, such as **3**, can become competitive in comparison to the loss of proton leading to the formation of **3-Cl**. Thus, after aromatization, the action of SO_2Cl_2 on **3** starts with the formation of **Wh3-HCl$^+$**, which acts as electrophile to react with monomer **3** to give an intermediate dimer **DCl$^+$** (Scheme 3). This dimer undergoes elimination of HCl and H^+ to re-aromatize and afford dimer **4**. Chloride ion is a good leaving group allowing the easy formation of HCl. The reaction proceeds regioselectively due to the important difference in site reactivity (nucleophilic vs. electrophilic), thus leading only to the D–A-alternated dimer. Stepwise reactions with **3** from **DCl$^+$** or after chlorination of the dimer **4** will lead to longer oligomers. The chlorination of dimer **4** has also been performed by using SO_2Cl_2 in stoichiometric amount (see the Sup-



Scheme 2. Tautomeric equilibrium between **Wh3-HCl$^+$** and **Am3-HCl$^+$**.



Scheme 3. Proposed mechanism for the formation of oligomers.

porting Information, Scheme S5). The chlorinated dimer **4-Cl** was isolated in 46% yield. Tetramer **6** was also isolated in 4% yield, whereas no trimer was detected by mass spectrometry. Thus, as in the S_EAr reaction of **4** with SO_2Cl_2, the formation of **4-Cl** by loss of H^+ from the Wheland complex **Wh4-HCl$^+$** competes with the reaction between **4** and **Wh4-HCl$^+$** leading to **6**. However, both the better stability of chlorinated **4-Cl** and the lower nucleophilic reactivity of dimer **4** disfavor the oligomerization process.

Single crystals suitable for X-ray diffraction analysis were obtained for trimer **5** and tetramer **6** by slow evaporation of a chloroform/ethanol solution. The two structures with strict alternation of the cyano and pyrrolidyl groups present a good planarity of the conjugated systems, with torsion angles between the thiophene rings of $<12^\circ$ (Figure 3). The thiophene

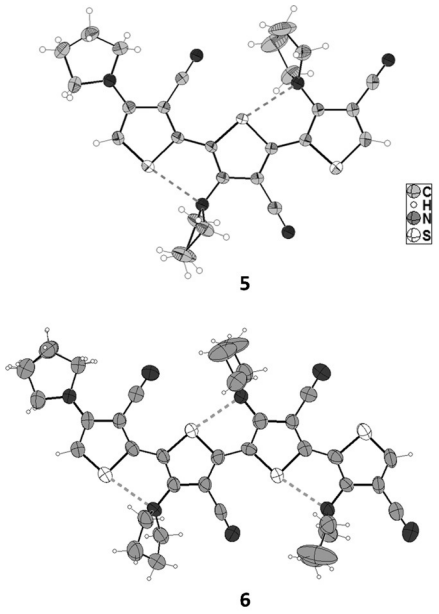


Figure 3. X-ray crystal structures of isolated oligomers **5** and **6**. Thermal ellipsoids are set at 50% level of probability.

rings adopt an *anti* orientation, whereas the internal pyrrolidyl groups have a quasi-orthogonal orientation to the conjugated backbone. These conformations limit the steric hindrance between the thiophene and pyrrolidyl rings. Moreover, the distances between the nitrogen atoms of the internal pyrrolidyl groups and the sulfur atoms of the adjacent thiophenes are small (Figure 3, gray dotted lines). The distances ranging from 276.6(5) pm to 282.6(2) pm are less than the sum of van der Waals radii (339 pm), thus indicating the occurrence of noncovalent intramolecular S–N interactions that participate to stabilize the planar conformation.

In summary, an effective synthesis of the new building block 3-cyano-4-pyrrolydylthiophene was realized and oligomers with strictly alternating D–A structures were isolated following aromatization with SO_2Cl_2. The formation of the oligomers took place in preference to the chlorination reaction. The proposed mechanism implies that the Wheland intermediate of the chlorinated derivative reacts as an electrophile with 3-cyano-4-pyrrolidylthiophene in an electrophilic aromatic substitution. A synergistic effect of pyrrolidyl and cyano groups induces the reaction. The electronic dissymmetry at the 2- and 5-positions of the thiophene ring is enhanced by the strong electron donor ability of the pyrrolidyl group, which increases the nucleophilic character of the thiophene derivative. The cyano group strengthens the electrophilic character of the Wheland complex stabilized by the pyrrolidyl group in the iminium form. The monomer and the dimer are useful for the synthesis of various oligomers with well-defined structures. The influence of the relative positions of the donor and acceptor groups along the conjugated chain on the electronic properties of the oligomers is under investigation and will be reported in future publications.

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