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Synthesis and Crystal Structure of a Tubular Sexithiophene

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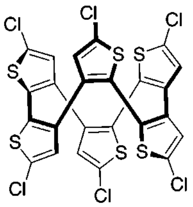
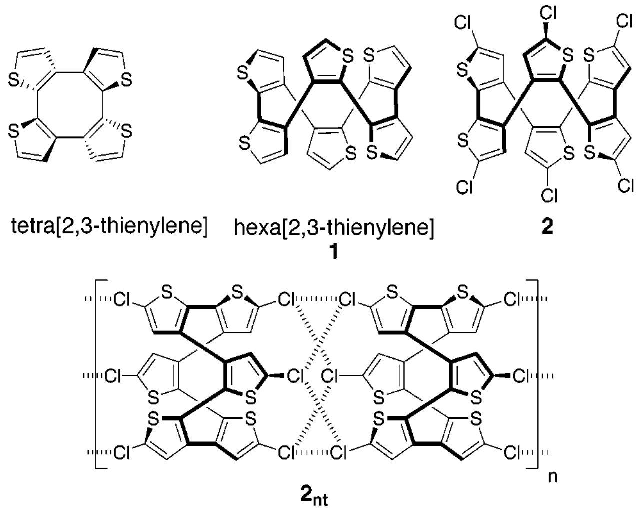
ABSTRACT



The synthesis of a rigid, tubular sexithiophene is reported. Close intermolecular Cl⋯Cl interactions play a significant role in defining the crystal structure.

In 1978, Kauffmann reported the synthesis of both tetra[2,3-thienylene] and hexa[2,3-thienylene] (24% and 4% isolated yield, respectively; see Figure 1) via the $CuCl_2$-promoted oxidative homocoupling of 3,3′-dilithio-2,2′-bithiophene.[1] Despite their novel structure, these cyclic oligothiophenes disappeared from the literature for almost 20 years. During this hiatus, the interest in π-conjugated materials with novel topologies increased dramatically.[2] Beginning in 1999, we focused our attention on the aforementioned cyclic oligothiophenes, having reported tetra[2,3-thienylene] as a building block for both molecular electromechanical actuators ("molecular muscles")[3] and extended double helices.[4] In addition, Iyoda recently reported the synthesis of planar variants of tetra[2,3-thienylene].[5] Although tetra[2,3-thienylene] is conformationally analogous to its parent [8]annulene, cyclooctatetraene, expansion of the macrocycle by one extra bithiophene unit yields the rigid



tetra[2,3-thienylene]   hexa[2,3-thienylene] **1**   **2**

$\mathbf{2_{nt}}$

Figure 1. Three cyclic oligothiophenes and the hypothetical self-assembled nanotube, compound $\mathbf{2_{nt}}$.

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and tubular hexa[2,3-thienylene], compound **1**. Herein we report the synthesis and crystal structure of the hexachloro derivative of compound **1**, compound **2**.

Our impetus for pursuing the hexachloro derivative of compound **1** came, in part, from the desire to investigate how intermolecular Cl$\cdots$Cl interactions would dictate solid-state packing, as such interactions traditionally play a significant role in determining crystal structures.[6,7] In the case of compound **2**, each of the two ends of the tubular molecule possess three coplanar chlorine atoms that should act to orient adjacent molecules. In one possible scenario, Cl$\cdots$Cl interactions could linearly align the long molecular axis of **2** along the imaginary line formed by joining the centroid of each molecule. As depicted in Figure 1 by the hypothetical supramolecular assembly, $\mathbf{2}_{\mathbf{nt}}$, this interaction would yield a supramolecular nanotube motif.[8] Alternatively, C$-$Cl$\cdots$Cl$-$C interactions may radiate in an approximately linear sense (with respect to the C$-$Cl bond) to yield a zigzag-type arrangement (Figure 2). In this report, the latter of the two motifs is observed.

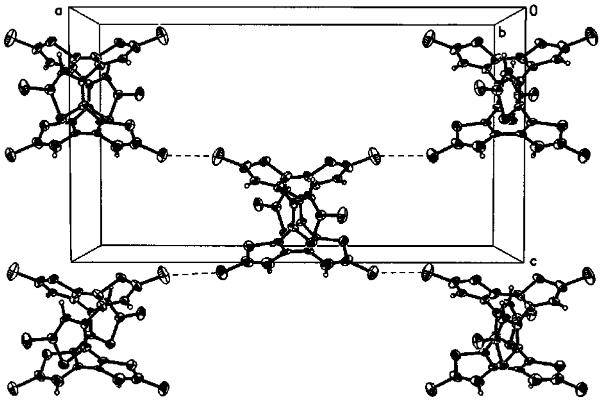
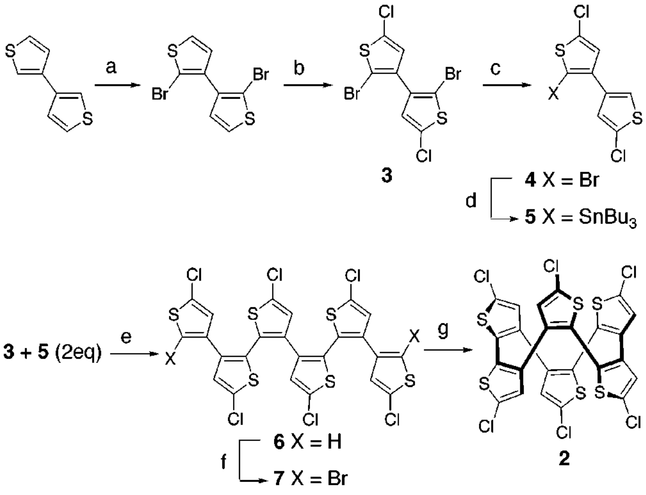


Figure 2. X-ray crystal structure of compound **2** showing 3.452 Å Cl$\cdots$Cl interactions (dashed lines). Disordered THF has been omitted for clarity.

Given the low reported yield of compound **1**, we wished to pursue an alternative synthetic strategy. In analogy to our synthesis of regioregular tetra[2,3-thienylene]s via cyclization of the corresponding linear tetrathiophene,[3] we envisioned synthesizing compound **2** via its parent linear sexithiophene. The synthesis of compound **2** is shown in Scheme 1 and is built on the following three premises: (1) the α-thienyl position is more reactive than the β-thienyl position toward electrophillic attack[9] and Pd(0) insertion (oxidative addition);[10] (2) aryl bromides, but not aryl chlorides, undergo facile lithium$-$halogen exchange;[11] and (3) arylbromides typically undergo palladium- and nickel-catalyzed cross-coupling faster than aryl chlorides.[12,13] With specific regard to premise 1, the reactivity of 3,3′-bithiophene toward electrophillic attack follows the order $2 = 2' > 5 = 5' > 4 = 4'$.[3] Thus, bromination of 3,3′-bithiophene with 2 equiv of NBS, followed by chlorination with 2 equiv of NCS, yields the key building block, compound **3**. Compound **3** serves as both the central bithiophene unit of linear hexathienylene, compound **7**, as well as the precursor to the two terminal bithiophene moieties, compound **5** (Scheme 1).

Scheme 1[a]



[a] Reagents: (a) 2.1 equiv of NBS, DMF, 84%; (b) 2.4 equiv of NCS, DMF, 80 °C, 90%; (c) (i) 1.05 equiv of *n*-BuLi, THF, −78 °C, (ii) *i*-PrOH, −78 °C, 76%; (d) (i) 2.1 equiv of *n*-BuLi, Et$_2$O, −78 °C, (ii) Bu$_3$SnCl; (e) Pd(PPh$_3$)$_4$, toluene, 27%; (f) 2.15 equiv of NBS, DMF, 60 °C, 98%; (g) (i) 2.0 equiv of *n*-BuLi, Et$_2$O, −78 °C, (ii) CuCl$_2$, Et$_2$O, 20%.

Unlike the numerous reports demonstrating facile cross-coupling of α,α′-oligo- and polythiophenes,[14−16] the assembly of hexathienylene **6** via the cross-coupling of **3** and **5** was troublesome. In our hands, the optimized procedure (27% yield of **6**[17]) entailed a Stille-type cross-coupling using toluene as solvent and Pd(PPh$_3$)$_4$ as catalyst (premise 3, Scheme 1). Of the many conditions screened during this optimization, it is interesting to note that although zerovalent

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(17) **Compound 6.** A room-temperature toluene solution (12 mL) of compound **5** (2.45 mmol), compound **3** (1.22 mmol), and Pd(Ph$_3$P)$_4$ (0.049 mmol) was stirred for 1 h and then heated to 100 °C for 12 h. The reaction mixture was cooled and extracted with brine/Et$_2$O. Compound **6** was isolated from the crude by drying the organic extract over MgSO$_4$, filtering, removing volatile components under reduced pressure, and purifying by silica gel column chromatography (hexane). Compound **6** was isolated as a yellow

nickel cross-coupling between 2- or 3-thienylmagnesiumbromide and 2- or 3-bromothiophene gives nearly quantitative yield of the corresponding bithiophene,[18−20] the analogous reaction to prepare compound **6** is unproductive.

As a final step, compound **2**[21] was prepared in 20% isolated yield (racemic) by lithium−halogen exchange of the two bromines of compound **7**[22] (achiral) with butyllithium (premise 2), followed by oxidative coupling with $CuCl_2$. In agreement with Kauffmann's observations, product **2** could not be obtained when Fe^{3+} oxidants ($FeCl_3$ or $Fe(acac)_3$) were used.[1]

Compound **2** is a colorless solid (onset of absorption at 320 nm), indicating poor π-orbital overlap within the [12]-annulene equator of the macrocycle. This is commensurate with the experimentally determined 102.7° average value of the S−C−C−S dihedral angle (determined by X-ray crystallography). Unlike tetra[2,3-thienylene], this angle is relatively fixed in a twisted *s-trans* conformation. Compound **2** exhibits relatively good solubility in chlorinated solvents and in THF. X-ray crystallographic data for single crystals of compound **2** grown in CCl_4 and CH_2Cl_2 could not be sufficiently refined but did show unequivocal evidence of solvent inclusion via Cl···Cl interactions between solvent and substrate. In general, it was found that the crystal morphology of compound **2** varied dramatically as a function of solvent, and only crystallization from THF consistently provided plates suitable for X-ray analysis.

Figure 2 shows the crystal structure of compound **2.** Note that included molecules of disordered THF have been omitted for clarity. The dashed lines in Figure 2 represent 3.452 Å Cl···Cl interactions, of which there are four per molecule. With respect to these interactions, compound **2** interacts with four nearest neighbors to yield the aforementioned zigzag motif, as depicted in Figure 2. The remaining two Cl···Cl interactions (not shown) extend along the *b*-axis of the unit cell, at a length of 3.706 Å. Having established that intermolecular Cl···Cl interactions in this system are significant directing entities, we attempted to obtain an alternative packing motif by avoiding solvent inclusion and thus performed a sublimation of compound **2**. Although compound **2** sublimed without degradation, it did not yield crystals of X-ray quality. Our investigations into other polymorphs of compound **2** continue.

In addition to influencing solid-state structure, the placement of a chlorine at each of the six peripheral α-thienyl positions of compound **2** was also pursued in an effort to provide reactive sites for further synthetic transformations, such as covalent extension of the macrocycle via cross-coupling chemistry.[23−25] Furthermore, the synthesis established herein should be readily modified to prepare the parent hexa[2,3-thienylene], compound **1**. In this regard, it is worth noting that compound **1** serves to hold three (twisted) *s-trans* bithiophene units rigidly in three-dimensional space. The electrochemical polymerization of such a building block should result in a highly rigid, porous, and cross-linked polythiophene; ideally providing a polymer network somewhat analogous to that observed in the crystal structure of **2**. Such studies are currently under investigation.

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Supporting Information Available: Details of X-ray determination. This material is available free of charge via the Internet at http://pubs.acs.org.

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powder in 27.0% yield. ^1H NMR ($CDCl_3$) δ 6.75 (s, 2H), 6.59 (d, 2H, J = 1.54 Hz), 6.41 (d, 2H, J = 2.05), 6.27 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 134.86, 134.15, 133.77, 132.33, 131.03, 130.88, 129.01, 128.61, 128.10, 127.48, 126.19, 121.33. HRMS calcd 697.7081, obsd 697.7057.

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[21] **Compound 2**. To a solution of compound **7** (0.499 g, 0.581 mmol) in diethyl ether (29 mL) was added dropwise *n*-butyllithium (0.75 mL of 1.58 M solution, 1.18 mmol) at −65 °C. After the mixture was stirred at −40 °C for 1 h, the cold solution was cannulated slowly (0.3 mL/min) to a stirred, room-temperature solution of $CuCl_2$ in diethyl ether (29 mL). After 20 h of stirring at room temperature, the mixture was quenched with water and filtered over Celite. The two layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with water and brine solution and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude was purified by fractional recrystallization (CH_2Cl_2/hexanes) to provide compound **2** as a white powder in 20.0% yield. ^1H NMR ($CDCl_3$) δ 6.70 (s, 6H). Crystal structure is shown in Figure 2, and crystallographic data has been deposited in the Cambridge Crystallographic Data Centre Database.

[22] **Compound 7**. ^1H NMR ($CDCl_3$) δ 6.90 (s, 2H), 6.20 (s, 2H), 6.13 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 134.80, 133.65, 132.29, 131.65, 131.45, 130.14, 129.77, 128.71, 128.35, 127.68, 127.37, 107.62. HRMS calcd 855.5271, obsd 855.5297.

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