A Chiral Macrocyclic Oligothiophene with Broken Conjugation – Rapid Racemization through Internal Rotation

Kevin J. Weiland, a Nathalia Münch, a Wanja Gschwind, a Daniel Häussinger, a and Marcel Mayor a,b,c

a Department of Chemistry, University of Basel, St. Johanns-Ring 19, 4056 Basel, Switzerland, marcel.mayor@unibas.ch
b Institute for Nanotechnology (INT), Karlsruhe Institute of Technology (KIT), P. O. Box 3640, 76021 Karlsruhe, Germany
c Lehn Institute of Functional Materials, School of Chemistry, Sun Yat-Sen University, Guangzhou 510275, China

Dedication to Prof. François Diederich on the occasion of his retirement celebration.

A macrocyclic oligothiophene with an integrated pseudo-para substituted [2.2]paracyclophane has been achieved. The synthetic sequence relies on alternating steps of halogenation- and Suzuki-coupling conditions. By employing a modified Eglinton reaction under high dilution conditions, the macrocycle is closed and the obtained diacetylene is efficiently transferred to the corresponding thiophene. The molecule is fully characterized and its dynamic racemization is analysed by variable temperature NMR experiments. The racemization barrier hints with 38 kJ/mol at rapid enantiomerization at room temperature by Mislow’s “Euclidian rubber glove” enantiomerization process. Macrocycle formation results in red-shifted absorption and emission spectra, hinting at increased conjugation through the oligothiophene versus the enantiomer.

Keywords: Cyclophanes • Oligothiophenes • Macrocycles • Helical Chirality

Introduction

The ongoing miniaturization of electronic components approaches the nanometer scale, and novel concepts to fabricate objects in this range are a topic of high interest. One of the fabrication principles can be the bottom-up synthesis of molecules, profiting from the impressive achievements reported in the synthetic and macromolecular community. This assembly of tailor-made macromolecules from small reactive building blocks is approaching the nanoscale form the chemical features like their defined shapes and diameters, a high interest research directions develop at the interface between both approaches. Over the past decades, conjugated macrocycles have attracted high interest due to both, their structural integrity offering well-defined shapes and diameters, and their role as model compounds for infinitely conjugated π-systems. Furthermore their physical and chemical features like their optical, electrochemical, and encapsulation properties moved into the focus of interest. A synthetic milestone in the field of conjugated aromatic compounds was the synthesis and investigation of Kekulene by the young François Diederich in the labs of Heinz Staab.

Various molecular motifs have been reported as subunits of conjugated macrocyclic compounds, like e.g. pyridines, benzenes, acetylenes as well as five-membered aromatic heterocycles, like furans and thiophenes. We reported the assembly and investigation of a variety of macrocycles consisting of aromatic subunits in the past, among others structures comprising functional subunits like redox chromophores or optically addressable azo-benzenes. Macrocycles designed as single molecule switches or with pronounced π-stacking features, and giant macrocycles as model compounds for persistent ring currents. More recently, our focus moved to axial chiral systems like bicyclic “Geländert”-type structures or the macrocyclization of the ligands assembled in a M(II) terpyridine complex resulting in a helical macrocycle with an arrangement resembling a propeller.

Cyclo[n]thiophenes are an interesting class of conjugated macrocycles; they are model compounds for polythiophenes, with well-defined self-assembling and electronic features. Initially, the synthesis of macrocyclic oligothiophenes was performed by reacting on both sides ethynyl-terminated ter- and quinquethiophenes under oxidative acetylene coupling conditions in the presence of a copper catalyst. The resulting diethynyl linkers in the macrocycles were converted to thiophenes with sodium sulfide to form the corresponding cyclo[n]thiophenes. In this way, a library of macrocycles was obtained, where the smallest member of the series contained twelve thiophenes. In a later approach, strained oligothiophenic macrocycles were assembled, where only one diacetylene was formed oxidatively.

Figure 1. Series of oligothiophene macrocycles 2 a-c (left side) developed by Bäuerle et al. as basis for the design of the target structure 1 (right side). The eleven thiophene subunits of the macrocycle are separated by a step due to the pseudo-para substituted PC subunit (top) which disturbs the conjugation. The four peripheral bis-3,5-(tert-butyl)phenyl substituents provide the solubility required for wet chemical processing.

where the synthesis of the target structure was achieved through complexation of platinum followed by reductive elimination to obtain the corresponding catenanes, comprising the diethynyl link in their oligothiophene macrocycles.
The here presented structure is inspired by a split-ring resonator (SRR). This is the smallest possible realization of a circuit comprising a coil and a capacitor and thus displays interactions of electromagnetic fields of suitable wavelengths. As an example, a negative refractive index at microwave frequencies was reported for a large array of equally micrometer sized metallic SRRs.

The design of molecule 1 (Fig. 1) combines the conjugated periphery of an oligothiophene macrocycle with the conjugation altering pseudo-para (2.2)paracyclophane (PC). Using again the inspiring picture of a SRR, the macrocycle consisting of 2,5-interlinked thiophenes represent the “ring”, while the PC acts as the “split”. A particular appealing feature from the molecular design perspective is the helical chirality introduced by the step-like PC in the macrocycle, which might result in intriguing structural and chiroptical properties.

The step in the macrocycle is realized due to the 3D-structure of pseudo-para (2.2)paracyclophane (PC). It has attracted considerable attention due to the face-to-face orientation of its benzene rings, which are considerably closer than twice their individual van-der-Waals radii (typical ring distance: 3.09 Å), resulting in unusual optical, electronical and through-space charge-delocalization properties.

For example the comparison of annulene-PC hybrids with their benzannulene analogues displays typically a bathochromic shift in their absorption spectra, indicating an electronic conjugation through the PC building block. Also, electrochemical investigations of diethyl-substituted PC point at electronic coupling, as the oxidation wave is separated documenting the interdependence of both redox chromophores. Self assembled molecular rods comprising a central PC unit displayed very comparable electronic transport features compared with their benzene analogues, such that the limited control over the number of molecules in the crossed-wire junctions did not allow to trace the origin of the observed subtle variations.

Very recent single molecule experiments with molecular rods comprising a central PC subunit in a mechanically controlled break junction experiment even displayed mechanically triggered quantum interference in the junctions transport behavior.

Symmetrical dissubstitution of PC leads to four different region isomers. Pseudo-para and geminal dissubstitution leads to derivatives that are achiral due to internal symmetry elements. However, pseudo-ortho and meta dissubstitution leads to chiral products, separation of enantiomers of PCs with different substitution pattern have been accomplished. Notably, pseudo-ortho dissubstituted PC derivatives were incorporated in chiral thiophene-PC macrocycles, which showed pronounced chiroptical behavior.

Here we report a novel approach making the pseudo-para dissubstituted PC chiral by integrating it in the macrocyclic structure 1. In 1 the macrocycle is complemented by eleven 2,5-diyl-thiophene subunits, which are introduced pairwise in a sequential synthetic strategy at both ends of the open oligomer in order to identify the number of thiophene subunits required for a successful macrocyclization. In addition, four bis-3,5-(tert-butyl)phenyl substituents provide the solubility in organic solvents required to enable wet chemical processing of both, the precursors and the target structure. The unique integration of the PC substitution pattern in the macrocyclic structure 1 leads, to the best of our knowledge, to the first chiral pseudo-para symmetrically dissubstituted PC, as the introduction of the macrocycle leads to decreased symmetry. Interesting is the enantiomerization of 1, which due to its 3D PC building block follows Mislow’s “Euclidean rubber glove” mechanism. In other words, the molecule becomes its mirror image by rotations around single bonds without ever adapting a flat achiral conformation. The enantiomerization mechanism thus resembles the inversion of the chirality of a rubber glove, which is achieved by the complex movement of turning the glove inside out.

In this paper the stepwise assembly of the macrocycle 1 is reported together with its full characterization. The molecular dynamics of 1 are investigated by variable temperature NMR (VT-NMR) experiments shining light on its unique racemization behavior. The extent of electronic conjugation through macrocycle 1 and its precursors is qualitatively investigated by UV-Vis absorption and emission spectroscopy.

Results and Discussion

The synthesis of a complex structure as macrocycle 1 requires repetitive synthetic steps, mainly alternating halogenation and Pd-catalyzed carbon-carbon coupling reactions.

The linear and sequential synthetic strategy for macrocycle 1 involves a late stage macrocyclization and formation of a thiophene from the

Scheme 1. Synthetic strategy for the assembly of racemic macrocycle 1.
corresponding diacetylene, based on the linear protected intermediate 3. Precedence for this strategy exists, as the cyclization of alkyne substituted oligothiophenes under oxidative acetylene coupling conditions[44] was employed by Bäuerle et al. for the synthesis of phenanthroline containing cyclic oligothiophenes of similar ring diameters.[24] Based on this concept, chiral carbon-rich macrocycles were also obtained in the labs of François Diederich, who produced allen-acytlenic macrocycles with outstanding chiroptical properties.[45,46] The open-ring intermediate 3 is divided into two building blocks 4 and 5 which can be coupled in a Sonogashira reaction. This linear synthetic strategy allows for a step-by-step buildup of structure 4 through a series of halogenation and Suzuki coupling reactions without the need of excessive protecting-group strategies. Subunit 4 was assembled from highly functionalized building blocks 6, 7 and 8 in a repetitive halogenation, Pd-catalyzed coupling chemistry sequence. Building block 7 and 8 were introduced to achieve reasonable solubility for all relevant intermediates during the course of the synthesis. While building blocks 6 and 8 are already literature-known, a strategy to form 7 had to be developed.[36,41]

The synthesis of building block 7, that is introduced to increase the solubility, started from commercially available 3-bromothiophene (9) and literature-known 2-(3,5-di-tert-butylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (10).[48] The Suzuki coupling of both compounds afforded 11 in 88% yield and multigram amounts of 11 could be isolated after purification by silica gel chromatography. Next, 11 was reacted with one equivalent of N-bromosuccinimide (NBS) to selectively afford 12. Excess of NBS lead to bromination also in the 5-position of the thiophene. Compound 12 was, after isolation by column chromatography (CC) in 77% yield, reacted with n-butyllithium (n-BuLi) and 2-isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane to yield 7. During the course of the lithiation it is crucial that the temperature is kept at ~78 °C, as at higher temperatures, deprotonation of 12 at the 5-position was observed, leading to the corresponding 2-bromo-5-pinacolboronato thiophene after work up. After addition of 2-isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane and aqueous workup, 7 was isolated without purification in 90% yield as a yellow solid.

Having solubilizing building block 7 in hand, our focus moved towards the assembly of precursor 6. While its synthesis is already literature known, we aimed to develop a higher yielding procedure than the one published previously. Collard et al. reported a procedure relying on a Stille coupling which was efficient yet difficult to purify.[10] More recently, a procedure developed by Martin et al. was reported which utilized Suzuki coupling conditions, however working with 5-alkyl-thiophene boronic acids.[14] Therefore, a procedure utilizing Kumada reaction conditions as developed by Rozenberg et al. was adapted.[13] Commercially available 2-thienyl magnesium bromide (13) was added dropwise to a suspension of pseudo-para-dibromo-PC (14) and Pd(dppf)Cl2 in tetrahydrofuran (THF). After heating to 60 °C for two hours, building block 6 started to precipitate from the reaction mixture. Following aqueous workup and removal of the solvent, 6 could be isolated by washing the crude product with cyclohexane and cooled dichloromethane. Compound 6 was isolated in a yield of 87% as a white solid.

Subsequently, 6 was dibrominated with NBS in dimethylformamide (DMF), and after aqueous workup and filtration through a plug of celite, 15 was obtained as a white solid. 15 could only be dissolved in substantial amounts of toluene after heating the suspension to 60 °C. Thus, compounds 15 and 7 were reacted in a Suzuki reaction with Pd-PEPPSI-IrPyTM (PEPPSI: pyridine-enhanced precatalyst preparation stabilization and initiation, IPr: isopropyl) and K3CO3 in methanol (MeOH) and toluene in a procedure adapted from Nilsson et al.[15] The

Scheme 2. Synthesis of building block 7. Reagents and conditions: (a) Pd(PPh3)4, Na2CO3, DMF, H2O, 120 °C, 2 h, 88% (b) NBS, CHCl3, AcOH, 40 °C, 1 h, 77%. (c) n-BuLi, 2-isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, THF, -78 °C to room temp, 20 h, 90%.

Scheme 3. Synthesis of fragment 20. Reagents and conditions: (a) Pd(dppf)Cl2, THF, 60 °C, 2 h, 87%. (b) NBS, CHCl3, DMF, room temp, 20 h, 91%. (c) 7, Pd-PEPPSI-IrPyTM, K3CO3, toluene, MeOH, 70 °C, 15 min, 95%. (d) NBS, DMF, room temp, 20 h, 92%. (e) 8, Pd-PEPPSI-IrPyTM, K3CO3, toluene, MeOH, 70 °C, 20 min, 82%. (f) NIS, CHCl3, AcOH, room temp, 1.5 h, 99%. (g) 7, Pd-PEPPSI-IrPyTM, K3CO3, toluene, MeOH, 70 °C, 30 min, 83%.
reaction proceeded over the course of 15 minutes and 16 was obtained after CC in excellent yield as an off-white solid. To elongate the chain of thiophenes, 16 was brominated with NBS in DMF under exclusion of light. Aqueous work up and CC provided 17 as a yellow solid in 92% yield. Initial attempts to react 17 with thienylboronic acid led to the hexathiophenic building block of very limited solubility that prevented its separation from the byproducts of the synthesis. Therefore, 17 was reacted in a Pd-PEPPSI-IPr\(^{TM}\) catalyzed Suzuki reaction with trimethyl(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-y1)(thien-2-yl)silane (8) to ensure improved solubility due to the presence of TMS groups, that can be easily transferred to an iodine with N-iodosuccinimide (NIS).\(^{[41]}\)

After reacting 17 and 8 in a Pd-PEPPSI-IPr\(^{TM}\) catalyzed Suzuki reaction for 20 minutes, 18 could be isolated after aqueous workup and CC as a yellow amorphous solid. Next, 18 was readily interconverted to compound 19 by dissolving it in a 1:1 mixture of chloroform and acetic acid and treatment with NIS. During the reaction, compound 19 precipitated from the solution, but was soluble enough to be purified by CC and was isolated in quantitative yield as a yellow wax. Subsequently, 19 was reacted with building block 7 with Pd-PEPPSI-IPr\(^{TM}\) and K\(_2\)CO\(_3\) in toluene and MeOH. After a reaction time of 30 minutes, followed by aqueous work up, 20 was isolated in good yield of 83% after CC as a yellow amorphous solid.

Compound 20 was dibrominated with NBS in CHCl\(_3\) under the exclusion of light. After reacting the mixture for 20 hours, aqueous workup and CC lead to compound 21 in excellent yield as a yellow amorphous solid. Subsequently, 21 was reacted with building block 8 under the established Suzuki coupling conditions. Chromatography on silica gel and automated gel permeation chromatography (GPC) lead to the isolation of 4 in 72% yield. Unfortunately, all attempts to convert the TMS functionality of 4 to the corresponding dibromide or -iodide lead to a complex product mixture, which according to their MALDI-ToF MS analyses also contained mono- and trihalogenated species besides the desired material. Attempts to isolate the desired compound from those mixtures, either by silica gel chromatography or GPC were unsuccessful. Therefore, the mixture of bromides was directly reacted with CPDIPS acetylene in a Sonogashira reaction. The use of the polar protecting group introduced by Höger et al. lead to facile isolation of the desired protected diyne 3 by silica gel chromatography in toluene in 63% yield over two subsequent steps.\(^{[23]}\) Deprotection of 3 to diyne 22 with tetrabutylammonium fluoride in THF proceeded in excellent yield.

The macrocyclization of 22 to 23 was achieved through a modified Eglinton coupling as published by Scott et al.\(^{[26]}\) To facilitate selective formation of 23, a 0.55 mol solution of 22 in pyridine was added by a syringe pump over the course of 48 hours to a solution of 15 equivalents CuCl and 21 equivalents Cu(OAc)\(_2\) in 60 mL of pyridine. After aqueous workup, CC and size exclusion chromatography (BioBeads, SX-3) in toluene, the key intermediate 23 was isolated as a red amorphous solid in 33% yield. We also observed the twofold closed cyclic dimer of 22, which was removed easily by size exclusion chromatography. It is noteworthy that the macrocyclization of a similar molecule with eight thiophenes instead of ten exclusively resulted in the formation of its twofold closed dimer. The final cyclization step to form the target compound 1 was performed using a procedure of Bäuerle et al., where 23 was reacted with Na\(_2\)S \(\cdot\) 9 H\(_2\)O in a 1:1 mixture of DMF and 2-methoxyethanol.\(^{[52]}\) To our delight, MALDI-TOF analysis of the reaction mixture after 1.5 hours showed only the mass of the target compound 1. After acidic workup to remove excess reagent and solvent, and subsequent purification by CC, target compound 1 was isolated as a red amorphous solid in quantitative yield.

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**Scheme 4.** Synthesis of target molecule 1. Reagents and conditions: (a) NBS, CHCl\(_3\), room temp., 20 h, 90%. (b) 8, Pd-PEPPSI-IPr\(^{TM}\), K\(_2\)CO\(_3\), toluene, MeOH, 70 °C, 30 min, 72%. (c) NBS, CHCl\(_3\), AcOH, room temp., 15 min; then CPDIPS acetylene, Pd(PPh\(_3\))\(_2\), CuI, toluene, diisopropanolamine, 100 °C, 20 h, 63% (two steps). (d) TBAF, THF, room temp., 20 h, 97%. (e) CuCl, Cu(OAc)$_2$, pyridine, room temp., 48 h, 33%. (f) Na$_2$S · 9 H$_2$O, DMF, 2-methoxyethanol, 120 °C, 1.5 h, quant.
The identity of macrocycle 1 was fully corroborated by $^1$H and $^{13}$C NMR, as well as by 2D NMR spectroscopy, which enabled us to fully assign the observed resonances to the corresponding proton and carbon atoms. All recorded spectra of 1 are available in the supporting information (SI); its $^1$H NMR spectrum recorded at 600 MHz is displayed in figure 2 to demonstrate both, purity and identity of the isolated target structure. The elemental formula of 1 was confirmed by high-resolution matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (HR MALDI-TOF MS, displayed in figure S57 in the SI). The signal observed for 1 showed an isotopic pattern matching the one expected for its elemental composition (M$^+$ C$_{116}$H$_{116}$S$_{11}$).

The macrocyclization of 22 to 23 yields the product as a racemic mixture. Both enantiomers for macrocycles 23 and 1 can readily interconvert through a concerted rotation around the C-C bonds between the benzene rings of the PC and the thiophene building blocks on each adjacent side (see figure 3). We investigated the racemization dynamics for macrocycle 1. The rotation proceeds rapidly at room temperature, separation of the enantiomers by means of HPLC on a chiral stationary phase was not possible. It is worth to note that the racemization does not proceed through an achiral transition state, unlike in the cases of helicenes, twistacenes or banisteranes, as already demonstrated racemization kinetics that is fast on the $^1$H-NMR time scale. Depending on the concentration of the sample, the resonances appear as sharp resolved signals (c.f. figure 2) or, at higher concentration, stacking of the extended aromatic ring systems leads to broadening which is not related to a dynamic process originating in the racemization. When the temperature was lowered to 218 K, severe line broadening occurs and after coalescence at approximately 213 K a splitting into eight, partially overlapping signals was observed indicating slow interconversion of the enantiomers by the rubber glove mechanism (see figure 4). The activation barrier for the racemization was determined from the shift difference of 417 Hz for H-41/H-41a and the coalescence temperature (213 K) to be 38 kJ mol$^{-1}$. The barrier for racemization is considerably lower than the barrier for similar ferrocene-based macrocycles with smaller ring sizes. Further cooling of the sample to 183 K revealed a second dynamic process that is most likely related to rotational restrictions in the di-tert-butylphenyl units.

To investigate the change in through-space vs. through-bond conjugation by the introduced macrocycle, the optoelectronic properties of macrocycles 23 and 1 were investigated by UV/Vis absorption and emission spectroscopy and compared to linear building block 22 (figure 5). The terminal alkyn substiuted oligothiophene with a central PC subunit 22 has its absorption maximum at 438 nm. After macrocyclization, the absorption maxima of 23 and 1 are hypsochromically shifted with respect to 22. The absorption maximum of 23 is found at 413 nm and the absorption maximum of 1 is at 420 nm. Both absorption spectra of the macrocyclic compounds display additional shoulders, one is found around 450 nm, which is more pronounced in the case of 23, the other appears at wavelengths higher than 500 nm. The comparison of the absorption spectrum of 22 with reported electronic data from linear oligothiophenes points at through-space conjugation in the central PC subunit. Penta- and heptathiophenic oligomers have absorption maxima at 386 and 409 nm, respectively. The absorption maximum of 22, consisting of two pentathiophenes interlinked by PC, is at 438 nm. The bathochromic shift compared to the reported oligothiophenes confirms the through-space conjugation in the central PC subunit, as already reported for similar compounds. macrocyclic thiophenes of a given size have absorption maxima that correspond in energy to the absorption maxima of linear oligothiophenes of approximately half the number of thiophene subunits. The hypsochromic shift of the absorption maxima of the macrocycles 23 and 1 compared to linear 22 was thus not surprising. Also, the rather small values of 25 nm and 18 nm of the recorded shifts for 23 and 1 respectively can be rationalized by the
through-space conjugation in the central PC unit of the linear precursor 22. Compared with an oligomer of comparable length consisting exclusively of 2,5-interlinked thiophenes, the through-space conjugation is less effective than the delocalization in a thiophene, resulting in a larger separation of the frontier orbitals. The bathochromic shift of 7 nm of the absorption maximum of 1 compared to the signal of macrocycle 23 points at the increased delocalization through the sp² carbon atoms of the 2,5-diyl-thiophene linker in 1 (through-bond conjugation) compared with the sp centers of the diacetylene connection in 23.

The emission spectra of all three samples 22, 23, and 1 have an intense maximum with a more or less pronounced shoulder at about 648–649 nm in common. While the maximum of the emission of 22 is at 537 with a Stokes’ shift of 99 nm, the one of 23 is at 573 nm with a Stokes’ shift of 160 nm and the emission maximum of 1 is at 588 nm with a Stokes’ shift of 168 nm. Again, a bathochromic shift with increasing conjugation in the macromolecules’ subunits is observed in the order of the emission signals.

Initial attempts to measure the HOMO-LUMO gap electrochemically failed due to irreversible behavior of 1 in the cyclic voltammetry experiment. As approximations of the HOMO-LUMO gaps, the electronic transitions between the vibrational ground states of the absorption and emission spectra were compared. For the linear precursor 22, the absorption and emission bands intersect at 500 nm, corresponding to a transition energy of 2.48 eV. The intersection is bathochromically shifted to 528 nm (2.35 eV) for the cyclized 23 and shifts further to 542 nm (2.29 eV) upon replacing the diacetylene linkage with a thiophene subunit in 1. The decrease of transition energies further corroborates the trend of increasing conjugation in the subunits of the investigated series.

Conclusions

We present an efficient synthesis of chiral macrocycle 1 and its full characterization by ¹H, ¹³C and 2D NMR spectroscopy as well as high resolution mass spectrometry. Suitable precursors to incorporate PC as a key building block to break the conjugation of the macrocycle were designed and synthesized. The assembly of the achiral linear precursors is based on Pd-catalyzed coupling chemistry combined with halogenation sequences of the corresponding thiophenes. A linear synthetic strategy allowed to determine the required length of the precursor for a successful macrolization. The ring closing as key step of the synthesis provided the target molecule in reasonable yields, considering both its size and structural flexibility. The macrolization yielded a racemic mixture that could not be resolved due to the low racemization barrier at room temperature. The racemization barrier was investigated with VT-NMR experiments and was found to be 38 kJ mol⁻¹, indicating unhindered rotation of the central PC unit versus the oligothiophenic chain at room temperature. Investigation of the optical properties of the obtained macrocycles and comparison with the open-ring precursor allowed to determine the change of electronic features upon macrolization. All spectra of the macrocycles were considerably red-shifted compared to the open-ring precursor. We obtained rare insights into the through-space versus through-bond conjugation through the comparison of the considerable lowered transition energies between vibrational ground states.

In summary, two unique conjugated macrocycles have been prepared and investigated, elucidating the influence of a prochiral building block with broken conjugation on structural and electronic properties.

We are currently advancing the concept of helical chiral oligothiophene macrocycles comprising a PC subunit by designing model compounds of increased stability due to sterically hindered enantio- merization processes.

Experimental Section

General

Instruments, materials and methods are described in detail in the Supporting Information.

Previously Described Compounds

4,16-Dibromo[2,2]paracyclophane, trimethyl(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-yl)thien-2-yl)silane, 2-(3,5-di-tert-butylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane and CPDIPS-acetylene were prepared according to reported procedures.[47-48,51,57]

Experimental

3-(3,5-Di-tert-butylphenyl)thiophene (11): 2-(3,5-Di-tert-butylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane[46] (12.9 g, 40.7 mmol, 1.05 eq.), 3-bromothiophene (3.64 mL, 38.8 mmol, 1.00 eq.), Na₂CO₃ (20.5 g, 194 mmol, 5.00 eq.) and Pd(PPh₃)₄ (1.12 g, 970 μmol, 2.5 mol%) were suspended in a mixture of DMF (54 mL) and H₂O (6 mL). The reaction mixture was degassed by bubbling a stream of argon through the solution and was heated to 120 °C for two hours. The reaction was allowed to reach room temperature, toluene was added, and the organic phase was washed with 2 M HCl and dried over MgSO₄. The solvent was removed under reduced pressure and the crude was purified by column chromatography (pentane), yielding 11 as a colorless oil (9.35 g, 34.3 mmol, 88%). ¹H NMR (250 MHz, CDCl₃): δ = 7.47 – 7.38 (m, 6H), 1.37 (s, 18H) ppm. ¹³C NMR (101 MHz, CDCl₃): δ = 151.88, 135.76, 127.89, 127.29, 126.52, 122.00, 121.49, 120.56, 35.39, 31.79 ppm. MS (EI, 70 eV): m/z (%) = 272.20 (48.90), 257.20 (100), 57.10 (73.16). HRMS (EI): m/z calc. for C₁₉H₁₉S⁺ [M⁺]: 272.1594; found 272.1598.

2-Bromo-3-(3,5-di-tert-butylphenyl)thiophene (12): 3-(3,5-Di-tert-butylphenyl)thiophene (11) (9.33 g, 34.3 mmol, 1.00 eq.) was
dissolved in CHCl\(_3\) (100 mL) and AcOH (100 mL). To this was added, under exclusion of light, NBS (6.11 g, 34.3 mmol, 1.0 eq) and the reaction was heated to 40 °C for one hour. The reaction was allowed to reach room temperature. CHCl\(_3\) was added and the reaction was neutralized with sat. aq. NaHCO\(_3\). It was dried over MgSO\(_4\) and the solvent was removed in vacuo. The crude was purified by column chromatography (cyclohexane), yielding 12 as a colorless oil (9.27 g, 26.4 mmol, 77%). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.45\) (t, \(J = 1.8\) Hz, 1H), 7.41 (d, \(J = 1.8\) Hz, 2H), 7.35 (d, \(J = 5.6\) Hz, 1H), 7.08 (d, \(J = 5.6\) Hz, 1H), 1.37 (s, 18H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 151.48, 142.81, 134.60, 129.88, 126.45, 123.63, 122.17, 106.82, 35.45, 31.77\) ppm. MS (EI, 70 eV): \(m/z\% = 352.20, 285.15, 337.15, 75.23, 335.15, 75.10, 100\). C17H15BrS\(_2\): Calcd. C 64.4, H 5.0. Found: C 64.25, H 5.07.

2-(3-(3,5-di-tert-butylphenyl)thien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7): 2-Bromo-3-(3,5-di-tert-butylphenyl)thiophene (12) (3.45 g, 9.83 mmol, 1.0 eq). This was dissolved in THF (60 mL) and was degassed with argon. The reaction mixture was cooled to –78 °C and n-ButLi (1.6 M in hexane, 6.14 mL, 9.83 mmol, 1.0 eq.) was added dropwise. The reaction was stirred for two hours and 2-isoproxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.21 mL, 10.8 mmol, 1.10 eq.) was added dropwise. The reaction was allowed to reach room temperature and 2 mL HCl was added. The crude was suspended in toluene and filtered through a plug of celite. The solvent was removed, and the crude was washed with 2 mL HCl. It was dried over MgSO\(_4\) and the solvent was removed under reduced pressure. The crude was purified by column chromatography (cyclohexane/CHCl\(_3\) 4:1) and 16 was obtained as an off-white solid (557 g, 610 mg, 95%). M.p.: >250 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.44\) (t, \(J = 1.9\) Hz, 2H), 7.34 (d, \(J = 5.2\) Hz, 2H), 7.32 (d, \(J = 1.8\) Hz, 4H), 7.16 (d, \(J = 5.2\) Hz, 2H), 7.00 (d, \(J = 3.7\) Hz, 2H), 6.93 (d, \(J = 3.7\) Hz, 2H), 6.61 (dd, \(J = 7.8\) Hz, 1.9 Hz, 2H), 6.51 (d, \(J = 1.9\) Hz, 2H), 6.43 (d, \(J = 7.8\) Hz, 2H), 3.59 – 3.60 (m, 2H), 2.92 – 2.78 (m, 6H), 1.33 (s, 36H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 151.47, 144.82, 140.77, 140.69, 137.69, 136.65, 135.69, 134.94, 132.45, 132.40, 131.21, 131.77, 127.64, 124.40, 124.29, 121.50, 34.15, 34.48, 31.80 ppm. HRMS (MALDI TOF, DCTB): \(m/z\) calc. for C\(_{26}\)H\(_{24}\)Br\(_4\)S\(_2\): \(M^+ = 1322.4885\); found: 1322.4881.

4,16-Di-(3'-5,5'-di-tert-butylphenyl)tetraphenylethylene (17): Tetrathiophene (160 mg, 440 µmol, 1.00 eq.) was dissolved in DMF (25 mL) and this was added to the dark NBS (160 mg, 950 µmol, 2.05 eq.). The reaction was stirred at room temperature for 20 hours and toluene was added to the reaction mixture. The organic layer was washed with 2 mL HCl and was dried over MgSO\(_4\). The solvent was removed under reduced pressure and the crude product was purified by column chromatography (CHCl\(_3\)/cyclohexane 1:1). M.p.: 230 – 252 °C. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.44\) (t, \(J = 1.9\) Hz, 2H), 7.27 (d, \(J = 1.9\) Hz, 4H), 7.14 (s, 2H), 6.98 (d, \(J = 3.8\) Hz, 2H), 6.92 (d, \(J = 3.8\) Hz, 2H), 6.58 (dd, \(J = 7.8\) Hz, 1.9 Hz, 2H), 6.48 (d, \(J = 1.9\) Hz, 2H), 6.40 (d, \(J = 7.8\) Hz, 2H), 3.65 – 3.57 (m, 7H), 2.91 – 2.78 (m, 6H), 1.32 (s, 36H) ppm. \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta = 151.64, 145.36, 141.13, 110.70, 137.72, 135.48, 135.05, 134.82, 133.86, 136.65, 135.56, 131.92, 130.26, 129.79, 126.67, 126.17, 122.36, 110.97, 35.41, 34.75, 34.43, 31.77 ppm. HRMS (MALDI TOF, DCTB): \(m/z\) calc. for C\(_{17}\)H\(_{16}\)Br\(_4\)S\(_2\): \(M^+ = 908.2096\); found: 908.2095.
30.44, 34.16, 32.39, 31.24 ppm. HRMS (MALDI TOF, DCTB): m/z calcd for C_{48}H_{35}Na_{2}S_{2}: 1328.1573, found: 1328.1570.

4,16-Di-(3′,3′′-bis(3,5-di-tert-butylphenyl))-2,2′,5′-2″,5″-′′-quaterthienyl)-5-yl-[2,2′](paracyclophane 20: Diodio compound 19 (800 mg, 620 µmol, 1.0 eq.) and boronic ester 7 (982 mg, 2.46 mmol, 4.00 eq.) and KCO_{3} (511 mg, 3.70 mmol, 6.00 eq.) were suspended in toluene (30 mL) and MeOH (30 mL). The reaction mixture was degassed with argon and Pd-Peppi-IrH_{4}(42.6 mg, 61.6 µmol, 5 mol%) was added. The reaction mixture was placed in a preheated oil bath and the reaction was stirred at 70 °C for 30 minutes. The reaction was allowed to reach room temperature. When the organic layer was washed with 2 mL of water. It was dried over MgSO_{4} and the solvent was removed under reduced pressure.

The crude was purified by column chromatography (octathiohene/CHCl_{3}:4:1) and the resulting product was obtained as an orange wax (827 mg, 511 µmol, 83%). C NMR (500 MHz, CDCl_{3}) δ 7.52 (t, J = 1.8 Hz, 7H), 7.48 (t, J = 1.8 Hz, 2H), 7.38 – 7.34 (m, 10H), 7.20 (d, J = 5.2 Hz, 7H), 7.12 – 7.10 (m, 4H), 7.06 (d, J = 3.8 Hz, 2H), 7.04 (d, J = 3.8 Hz, 2H), 6.97 (d, J = 3.8 Hz, 2H), 6.65 (d, J = 7.8 Hz, 1H), 6.54 (d, J = 1.9 Hz, 2H), 6.46 (d, J = 7.8 Hz, 2H), 3.67 – 3.62 (m, 2H), 2.96 – 2.82 (m, 6H), 1.39 (s, 3H), 1.38 (s, 3H) ppm. 13C NMR (126 MHz, CDCl_{3}) δ = 151.10, 144.46, 142.86, 140.74, 140.09, 138.00, 137.12, 135.47, 134.91, 134.90, 134.53, 133.57, 133.07, 131.12, 129.64, 127.62, 127.01, 126.13, 125.21, 123.67, 127.02, 34.76, 34.16, 32.39, 31.24 ppm. HRMS (MALDI TOF, DCTB): m/z calcd for C_{48}H_{35}Na_{2}S_{2}: 1616.6524, found: 1616.6526.

4,16-Di-(5′′′-bromo-3′′′-bis(3,5-di-tert-butylphenyl))-2,2′,5′-2″,5″-′′′-quaterthienyl)-5-yl-[2,2′](paracyclophane 21: Octathiohene 20 (385 mg, 240 µmol, 1.0 eq.) was dissolved in CHCl_{3} (70 mL) and to this was added in the dark NBS (84.7 mg, 480 µmol, 2.00 eq.). The reaction was stirred at room temperature for 20 hours. The crude mixture was treated with 2 mL of water. It was dried over MgSO_{4} and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (CHCl_{3}/cyclohexane 1:9). 21 was isolated as an yellow wax (381 mg, 210 µmol, 90%). 1H NMR (400 MHz, CDCl_{3}) δ = 7.46 (t, J = 1.8 Hz, 2H), 7.43 (t, J = 1.8 Hz, 2H), 7.30 (d, J = 1.8 Hz, 4H), 7.25 (d, J = 1.8 Hz, 4H), 7.12 (s, 2H), 7.09 – 7.08 (m, 4H), 7.00 (d, J = 3.7 Hz, 2H), 6.96 (d, J = 3.8 Hz, 2H), 6.91 (d, J = 3.7 Hz, 2H), 6.88 (d, J = 7.8 Hz, 2H), 3.66 – 3.60 (m, 2H), 2.90 – 2.74 (m, 6H), 1.33 (s, 1H), 1.31 (s, 1H) ppm. 13C NMR (101 MHz, CDCl_{3}) δ = 160.51, 161.04, 144.94, 141.36, 141.36, 140.67, 138.75, 138.69, 136.20, 135.51, 135.47, 135.12, 130.00, 134.70, 134.37, 133.94, 133.63, 132.86, 132.11, 132.00, 128.33, 127.70, 127.52, 126.72, 124.25, 124.21, 124.20, 122.42, 122.26, 111.30, 35.43, 35.41, 34.74, 34.50, 31.80, 31.71 ppm. HRMS (MALDI TOF, DCTB): m/z calcd for C_{64}H_{41}Br_{2}S: [M+H]^{+}: 1772.4734, found: 1772.4743.

4,16-Di-(3′,3′′-bis(3,5-di-tert-butylphenyl))-5′′′-trimethylsilyl-2,2′-2″,5′-2″′-5″′′-quinque-5-yl-[2,2′](paracyclophane 4: Dibromide 21 (160 mg, 90.0 µmol, 1.00 eq.) and boronic ester 8 (153 mg, 540 µmol, 6.00 eq.) and KCO_{3} (74.8 mg, 540 µmol, 6.00 eq.) were suspended in toluene (10 mL) and MeOH (10 mL). The reaction mixture was degassed with argon and Pd-Peppi-IrH_{4}(6.15 mg, 9.02 µmol, 5 mol%) was added. The reaction mixture was placed in a preheated oil bath and the reaction was stirred at 70 °C for 30 minutes. The reaction was allowed to reach room temperature. When the organic layer was washed with 2 mL of HCl. It was dried over MgSO_{4} and the solvent was removed under reduced pressure. The crude was purified by column chromatography (cyclohexane/CHCl_{3}:4:1) as well as GPC. 4 was obtained as a yellow wax (125 mg, 65.0 µmol, 72%). 1H NMR (500 MHz, CDCl_{3}) δ = 7.46 (t, J = 1.8 Hz, 2H), 7.45 (t, J = 1.8 Hz, 2H), 7.32 – 7.30 (m, 10H), 7.21 (s, 2H), 7.20 (d, J = 3.5 Hz, 2H), 7.10 – 7.08 (m, 4H), 7.01 – 6.99 (m, 4H), 6.92 (d, J = 3.7 Hz, 2H), 6.59 (dd, J = 7.8 Hz, 2H), 6.49 (d, J = 1.9 Hz, 2H), 6.49 (d, J = 1.9 Hz, 2H), 6.41 (d, J = 7.8 Hz, 2H), 3.66 – 3.61 (m, 2H), 2.90 – 2.77 (m, 6H), 1.34 – 1.33 (m, 72H), 0.35 (s, 18H) ppm. 13C NMR (126 MHz, CDCl_{3}) δ = 151.61, 151.56, 142.16, 142.15, 141.59, 141.58, 141.31, 141.14, 140.67, 137.69, 137.22, 137.21, 136.25, 135.82, 135.74, 135.53, 135.52, 134.46, 132.32, 133.12, 133.60, 134.10, 130.19, 127.83, 127.71, 127.51, 124.79, 126.71, 125.80, 124.29, 124.28, 122.08, 122.23, 124.43, 34.73, 34.32, 31.80, 31.75, 0.10 ppm. HRMS (MALDI TOF, DCTB): m/z calcd for C_{16}H_{11}Se_{2}S_{2}: 2246.7069, found: 2246.7068.
1. M. M. supervised the work, I. Rios (d, 31a, H26a), 7.37 (d, 7.46 (t, 1J=3.7 Hz, 2H), 6.72 (d, 6.72 (m, 2H), 6.69 – 6.68 (m, 4H), 6.65 (d, 6.65 (d, J=3.7 Hz, 2H), 6.73 – 6.72 (m, 2H), 6.69 – 6.68 (m, 4H), 6.65 (d, J=3.7 Hz, 2H), 6.72 (d, 6.72 (m, 2H), 6.69 – 6.68 (m, 4H).)

2. The crude was diluted with toluene, and 2 m HCl was added. The organic layer was washed with 2 m HCl and brine, and the solvent was removed under reduced pressure. The crude was filtered through a plug of celite and purified by size exclusion chromatography (BioBeads SX-3, toluene) and column chromatography (pentane/CHCl3: 4:1).

3. Macrocyclic 23: Dyine 22 (60.0 mg, 32.8 µmol, 1.00 eq.) was dissolved in pyridine (60 mL) and degassed with argon. CuCl (48.7 mg, 490 µmol, 15.0 eq.) and Cu(OAc)2 (125 mg, 690 µmol, 21.0 eq.) were dissolved in pyridine (60 mL) and degassed with argon. The solution of dyine 22 was added dropwise via syringe pump over the course of 48 hours. After completed addition, the crude was diluted with toluene, and 2 m HCl was added. The organic layer was washed with 2 m HCl and brine, and the solvent was removed under reduced pressure. The crude was filtered through a plug of celite and purified by size exclusion chromatography (BioBeads SX-3, toluene) and column chromatography (pentane/CHCl3: 4:1). 23 was obtained as a red wax (19.8 mg, 10.8 µmol, 33%). 1H NMR (600 MHz, CDCl3) δ = 7.47 – 7.40 (m, 4H), 7.40 (d, J=1.8 Hz, 4H), 7.37 (d, J=1.8 Hz, 4H), 7.29 (s, 2H), 7.25 (d, J=3.8 Hz, 2H), 7.22 – 7.21 (m, 4H), 7.05 (d, J=3.8 Hz, 2H), 6.90 (d, J=3.7 Hz, 2H), 6.76 (d, J=3.7 Hz, 2H), 6.73 – 6.72 (m, 2H), 6.69 – 6.68 (m, 4H), 6.65 (d, J=3.9 Hz, 2H), 3.00 – 2.98 (m, 6H), 1.36 (s, 36H), 1.35 (s, 36H) ppm. 13C NMR (151 MHz, CDCl3) δ = 151.16, 150.51, 143.75, 141.07, 141.03, 140.82, 140.52, 136.89, 136.26, 135.68, 135.65, 135.48, 135.40, 134.78, 134.75, 134.16, 134.13, 133.05, 131.66, 131.14, 129.99, 129.98, 128.18, 126.91, 126.47, 126.27, 125.24, 123.87, 123.77, 123.69, 123.07, 122.16, 121.98, 121.01, 80.05, 78.62, 35.29, 35.28, 34.93, 34.85, 31.59, 31.58 ppm. HRMS (MALDI TOF, DCTB): m/z calcd for C14H16Cl2S1: [M+H]+ = 285.1022, found: 285.1019.

Supplementary Material

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/MS-number.

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Author Contribution Statement

K. J. W. performed the synthesis and characterization of all materials and co-wrote the manuscript. D. H., N. M., and W. G. performed NMR analyses of the macrocyclic compounds. M. M. supervised the work and wrote the manuscript. All authors commented on the manuscript.

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