Annelated Heptathiophene: A Fragment of a Carbon – Sulfur Helix**

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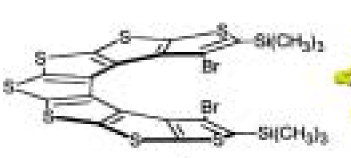
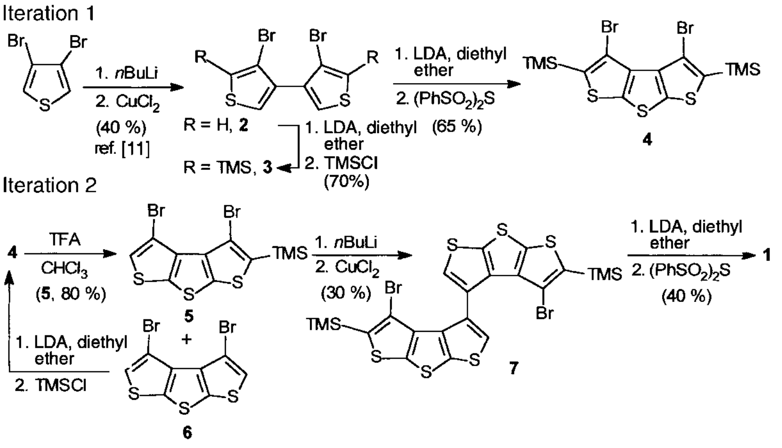
Herein we describe the iterative synthesis of a novel oligothiophene **1**, in which the thiophene rings are cross-conjugated and annelated into a helix.[1–3] Compound **1** may also be viewed as a fragment of the unprecedented carbon–sulfur (C$_2$S) helicene.[4–9]



1

C$_2$S-helix

The synthetic route to **1** consists of two iterations using 3,4-dibromothiophene and 4,4′-dibromo-5,5′-di(trimethylsilyl)dithieno[2,3-*b*:3′,2′-*d*]thiophene (**4**) as the tetrafunctionalized starting modules for the first and second iterations, respectively (Scheme 1). In each iteration, the modules are connected and then annelated. As the chirality is introduced only in the final annelation step, the stereochemical problems of racemic synthesis are avoided.[10]



Scheme 1. Synthesis of **1**. LDA = lithium diisopropylamide, TMS = trimethylsilyl, TFA = trifluoroacetic acid.

In the first iteration, 4,4′-dibromo-3,3′-bithienyl (**2**) is prepared from 3,4-dibromothiophene by a mono Li/Br exchange, as previously reported.[11] The two most acidic α-positions in **2** are TMS-protected to give **3**. Following the LDA-mediated lithiation of the unprotected α-positions in **3**, the reaction of the dilithiated **3** with bis(phenylsulfonyl) sulfide gives the annelated product **4**.[12]

In the second iteration, mono Li/Br exchange in **4** is not successful. Therefore, one of the TMS groups in **4** is removed to give **5** in which a modest selectivity for the mono Li/Br exchange can be attained. The incomplete conversion of **4** into a mixture of **5** and **6**, can be monitored by thin layer chromatography and NMR spectroscopy; after recycling (**6** to **4** and then to **5**), **5** is obtained in 80 % yield. Following the single Li/Br exchange on **5**, the resultant aryllithium species is oxidized with CuCl$_2$ to give **7**, which is subsequently annelated to give **1**.

^{1}H and ^{13}C NMR spectra indicate the expected twofold symmetry for **1**–**4**, **6**, and **7**. For **3**, and **5**–**7**, in which at least one α-position of thiophene is not silylated, the IR spectra show additional bands between 3094 and 3114 cm^{-1} in the C–H stretch region and the ^{1}H NMR spectra display one singlet in the aromatic region. In the EI mass spectra of **3**–**5**, isotopic clusters derived from M^+ and $[M-\mathrm{CH_3}]^+$ have comparable intensities; for **1** and **7**, the M^+ regions have dominant intensity. For **1**, the M^+, $[M+2]^+$, $[M+4]^+$ peaks have masses within less than 2.6 ppm of the calculated values and possess adequate relative amplitudes for $\mathrm{C_{22}H_{18}Si_2Br_2}$.

The structures of **4** and **1** were confirmed by single-crystal X-ray analysis (Figure 1).[13] In **4**, all the thiophene rings are approximately coplanar.[14] The C–Br bonds are nearly parallel, with the C2···C7 distance of 3.68 Å and the Br1-C2-C7-Br2 torsion angle is 13.3°; therefore, **4** may also be viewed as a 3.7 Å spacer molecule. The structure of **1** shows the molecule has approximate twofold symmetry and includes one chloroform molecule, which is statistically disordered over two positions. The Br···Br distance is 3.90 Å and the Br atoms are pointing away from each other. The repulsion of the facing terminal thiophene rings, and especially between the bromine atoms, causes a relatively large interplanar angle between the terminal thiophene rings, $180-125.9=54.1°$. This is similar to the 58.5° for the interplanar angle between the terminal benzene rings in [6]helicene.[5, 15] The individual thiophene rings are approximately planar with mean deviations of the least-square planes between 0.01 and 0.04 Å; the angles between the least-square planes of neighboring thiophene rings are between 7.9 and 11.2°. With the middle thiophene ring as a reference, the inner (C2, C3, C5, C7, C9, C11, C13, C15) helix climbs 2.92 Å and turns in-plane by 260°. Analogous values for [6]helicene are 3.12 Å and 317.7°, respectively.[16] In both **1** and [6]helicene, the helix climbs

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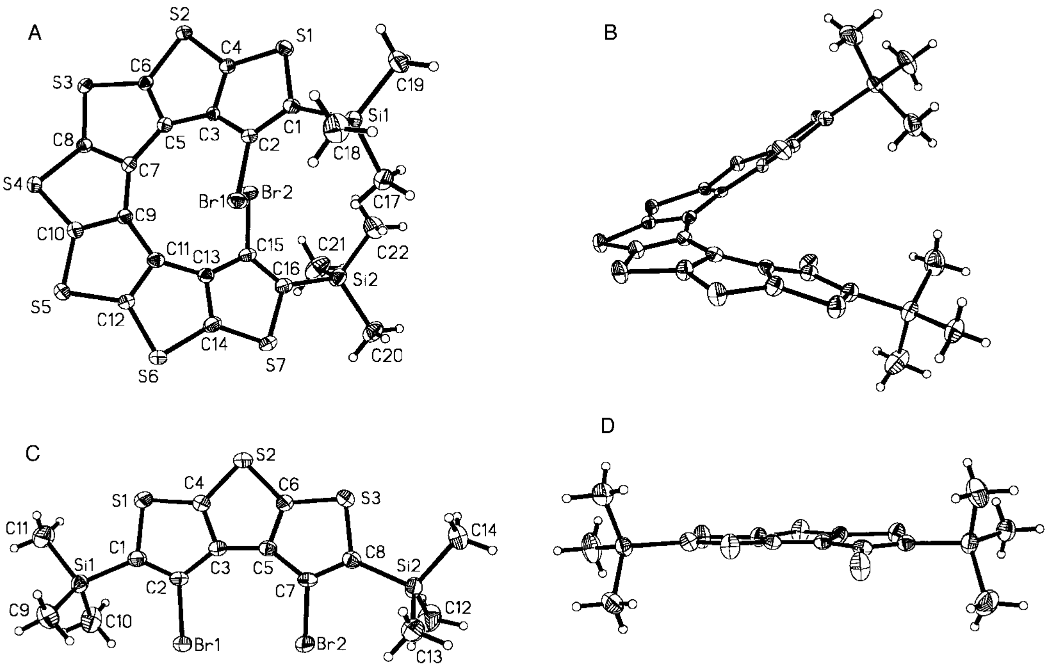

Figure 1. Molecular structure and conformation for helicene **1** and compound **4**. Carbon, bromine, silicon, and sulfur atoms are depicted with thermal ellipsoids set at the 50% probability level: A) top view for **1**, B) side view for **1**, C) top view for **4**, and D) side view for **4**.

for individual thiophene and benzene rings have similar patterns, with the smallest steps for the internal rings.[16]

UV/Vis spectra for **1** and **4** in methylene chloride are significantly different (Figure 2).[17] The integrated absorbance in **1** is approximately twice that of **4**. The bathochromic shift for **1** is rather substantial, considering that **1** and **4** possess

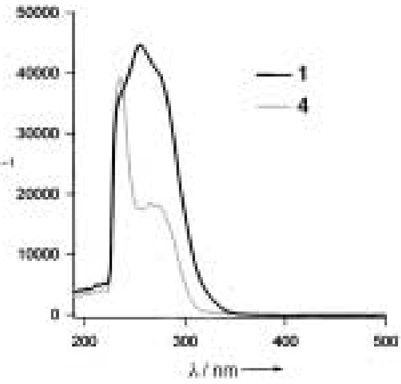

Figure 2. Electronic absorption spectra of **1** and **4** in methylene chloride at room temperature.

molecular connectivities of homologous cross-conjugated π systems.[18] Both the helical distortion in **1** and possible conjugation through the sulfur atoms may affect the increased π-electron delocalization in **1**.

In summary, the iterative synthesis of a racemic carbon–sulfur helicene **1** was developed. This synthetic route can be applied to the synthesis of the higher homologue(s) of **1**. However, as the tetrafunctionalized module **1** is chiral, it would be more efficient to use a single enantiomer of **1** (rather than its racemate) as the starting material.[10].

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[13] Crystal data for **1**, containing a disordered molecule of chloroform: colorless needle, $0.35 \times 0.06 \times 0.04$ mm, $C_{23}H_{19}Br_2Cl_3S_7Si_2$, $M = 842.15$, trigonal, $a = b = 36.319(2)$ Å, $c = 12.8012(8)$ Å, $V = 14623(2)$ Å^3, $T = 173(2)$ K, space group $R\bar{3}$, $Z = 18$, $\rho_{calcd} = 1.721$ Mg m^{-3}, $\mu = 3.281$ mm^{-1}, $2\theta_{max} = 55$, $Mo_{K\alpha}$ ($\lambda = 0.71073$). A total of 50542 reflections were measured, of which 7463 ($R_{int} = 0.073$) were unique. The included solvent molecule, chloroform, is statistically disordered over two positions. Final residuals were $R = 0.0370$ and $wR2 = 0.0857$ (for 5083 observed reflections with $I > 2\sigma(I)$, 352 parameters) with GOF 0.965 and largest residual peak 1.049 e Å^{-3} and hole -1.181 e Å^{-3}. Crystal data for **4**: colorless block, $0.35 \times 0.21 \times 0.20$ mm, $C_{14}H_{18}Br_2S_3Si_2$, $M = 498.46$, orthorhombic, $a = 10.0656(7)$, $b = 11.2301(8)$, $c = 35.400(3)$ Å, $V = 4001.5(5)$ Å^3, $T = 173(2)$ K, space group *Pbca*, $Z = 8$, $\rho_{calcd} = 1.655$ Mg m^{-3}, $\mu = 4.476$ mm^{-1}, $2\theta_{max} = 55.06$, $Mo_{K\alpha}$ ($\lambda = 0.71073$). A total of 39332 reflections were measured, of which 4596 ($R_{int} = 0.041$) were unique. Final residuals were $R = 0.0305$ and $wR2 = 0.0741$ (for 3701 observed reflections with $I > 2\sigma(I)$, 262 parameters) with GOF 1.068 and largest residual peak 0.628 e Å^{-3} and hole -0.468 e Å^{-3}. All data were collected on a SMART Platform CCD (Bruker) equipped with a low temperature device (Oxford cryostream). The intensity data were corrected for absorption (SADABS, R. Blessing, *Acta Crystallogr. Sect. A* **1995**, *51*, 33–38). Final cell constants were calculated from 8192 (for **1**) and 6423 (for **4**) strong reflections from the dataset (SAINT, Bruker Analytical Systems, Madison, WI, **1999**). The structures were solved using direct methods (SIR92, A. Altomare, G. Cascarno, C. Giacovazzo, A. Gualardi, *J. Appl. Cryst.* **1993**, *26*, 343–350) and refined by full-matrix least-square/difference Fourier cycles (SHELXTL V5.10, Bruker Analytical X-Ray Systems, Madison, WI). All non-hydrogen positions were refined anisotropically. All hydrogen atoms were refined isotropically as a riding model. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-149503 (**1**) and -149502 (**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[14] In **4**, the mean deviation from a calculated least-square plane including all the thiophene rings (S1–S3, C1–C8) is 0.0034 Å.

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[16] The inner helix climbs and in-plane turns for each thiophene (and benzene) ring are as follows: for **1**, 0.635 Å (36.6°), 0.501 Å (36.9°), 0.292 Å (38.2°), reference plane (38.1°), 0.286 Å (37.9°), 0.539 Å (37.4°), 0.668 Å (34.9°), and for [6]helicene, 0.696 Å (58.2°), 0.648 Å (49.5°), 0.201 Å (52.8°), 0.189 Å (53.0°), 0.622 Å (50.4°), 0.765 Å (54.0°). For [6]helicene, the reference plane includes the two carbons on the middle (approximate twofold) axis and the four nearest-neighbor carbons. Mean deviation from plane is 0.134 Å.

[17] UV/Vis (CH_2Cl_2): λ_{max}[nm] ($\lg(\varepsilon_{max}$[L mol^{-1}cm^{-1}])) = 235 (4.55, sh), 256 (4.65), 276 (4.60, sh) for **1**; 236 (4.59), 266 (4.27), 274 (4.25, sh) for **4**.

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Towards the DRED of Resin-Supported Combinatorial Libraries: A Non-Invasive Methodology Based on Bead Self-Encoding and Multispectral Imaging**

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Combinatorial synthetic methods allow for the preparation of large arrays of compounds as mixtures or individual entities. In the latter case, split synthesis has proven to be ideal in maximizing the number of compounds generated per synthetic step.[1] While the composition of chemical libraries produced using this method is predictable with a high level of confidence, the structural elucidation of potent member(s) after an activity assay remains a challenge. To unravel the chemical nature of the active members several tactics based on encoding methodologies[2] or deconvolutive strategies[3] have been developed. Herein we introduce the principles and describe preliminary studies towards the implementation of an alternative approach, termed *dual recursive deconvolution* (DRED), that draws its strengths from both chemical self-encoding techniques and deconvolution strategies. DRED operates through the iterative identification of the first and last randomized positions of the active members of combinatorial libraries generated through split synthesis. The last building block can be readily obtained from pool screening after the last coupling of the split synthesis, while the first position can be "encoded" by the unique vibrational "fingerprint" of the resin beads used. Once the first and last positions are identified, the second and second to last positions are subjected to the same deconvolution process. Remarkably, this exercise would dramatically simplify the synthetic *and* screening efforts (Supporting Information). For instance, the preparation and DRED of a 64-million hexapeptide library would barely double the number of chemical steps required for the split synthesis of the library (246 versus 120) and would involve only 20 spectroscopically distinguishable beads (DRED beads). Because the matrix is an encoding element of the DRED strategy, libraries can be evaluated while still attached to the bead or close to the beads from which they were released.

The suitability of a near-infrared Raman imaging (NIRIM) instrument[4] as a tool for the simultaneous identification of beads of various chemical composition was investigated. The NIRIM uses fiber-bundle image compression (FIC) technol-

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