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Improved synthesis of dithieno[3,2-*b*:2′,3′-*d*]thiophene (DTT) and derivatives for cross coupling†

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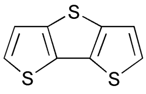
An improved synthesis of dithieno[3,2-*b*:2′,3′-*d*]thiophene (DTT) and its 2,6- and 3,5-dibromo derivatives has been devised; Stille cross coupling of 2,5-(bistrimethylstannyl)-DTT afforded the oligomer 12.

Dithieno[3,2-*b*:2′,3′-*d*]thiophene (DTT) **1** has emerged as an important building block in the synthesis of a wide variety of optoelectronic materials. Thus, bisdithienothiophene (BDT) has been used as a high mobility material in a field effect transistor,[1] and DTT derivatives have been used in photo- and electroluminescent devices,[2] two-photon absorption[3] and excited fluorescence,[4] non-linear optical chromophores,[5] and photochromic materials.[6] Polymers with DTT as repeat unit have been prepared by electrochemical[7] and photochemical oxidation[8] and recently DTT dioxide has been incorporated in thiophene oligomers.[9]

The use of DTT has been limited, however, by the lack of an efficient synthetic route amenable to upscaling and by the need for soluble derivatives, as DTT-derived molecules often suffer from severe solubility problems. We herein report a new synthesis of DTT **1** and the preparation of the two regioisomeric dibromo derivatives, 2,6-dibromo- **2** and 3,5-dibromo DTT **3**. These dibromides could serve as useful precursors for a spectrum of regioselective chemical modifications of the DTT core, as illustrated here by the Stille coupling of distannane **11**.



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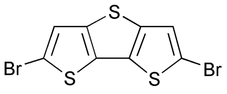

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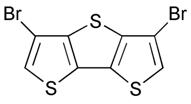

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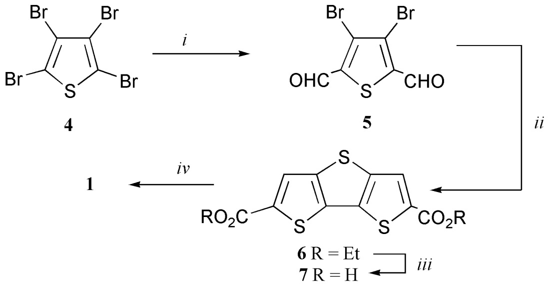
In the method employed previously for the preparation of **1**, based on the early work of De Jong and Janssen,[10] the central ring is assembled starting from the outer two thiophenes. The sulfur bridge is introduced first to give 3,3′-dithienyl sulfide, followed by a $CuCl_2$ mediated oxidative ring closure. This method afforded unsatisfactory yields, both in our and in others' hands.[11,12] Recently, Hellberg and coworkers introduced a modification to this route in which the order of the ring closure events was reversed.[12] Whereas their reported yields are higher, the scale up of the process remains a challenge.

We therefore decided to attempt a radically different approach in which the two outer thiophenes are built onto the central ring. Inspired by the extensive work of Iddon and coworkers on the synthesis of thienothiophenes[13] we elaborated the double annelation process shown in Scheme 1. 3,4-Dibromothiophene-2,6-dicarbaldehyde **5** is obtained in good yield from the dilithiation of tetrabromothiophene **4**, followed by quenching with 1-formylpiperidine. Reaction of dialdehyde **5** with ethylmercaptoacetate in the presence of excess base in DMF gave diethyl 2,6-DTT-dicarboxylate **6** which was easily saponified to form, upon acidification, the corresponding dicarboxylic acid **7**. Finally, decarboxylation of **7** with copper in quinoline afforded DTT **1** in an overall yield of 47% after filtration on a short silica column.



Scheme 1 *Reagents and conditions*: i, BuLi (2.1 equiv.), THF, −78 °C, 30 min, 1-formylpiperidine, 12 h, 25 °C (80%); ii, ethyl mercaptoacetate, K_2CO_3, DMF, 3 d, 25 °C (71%); iii, LiOH aq. (1 M), THF, reflux, 3 h (96%); iv, Cu, quinoline, 230 °C (87%).

This route has several advantages over those previously reported. First, all intermediates are readily purified by crystallisation, and only the final product requires a simple chromatographic purification step. Second, the process is easily scaled up to 30 g and more. Third, the two ester and acid functionalities in **6** and **7** can be used to introduce various substituents on the DTT skeleton.

Dibromination of DTT with NBS gave the 2,6-dibromide **2** in good yield.[14] Reductive debromination (Zn/AcOH) of tetrabromo-DTT or selective lithium halogen exchange followed by protonation are impractical approaches to the 3,5-dibromide **3**, in contrast to the analogous processes in thiophene, owing to the difficulty in preparing large quantities of the very insoluble DTT tetrabromide. Hence, the 3,5-dibromide **3** remains an elusive, yet important intermediate. Base-catalysed halogen dance is another useful method by which 3-bromothiophenes are prepared from their 2-bromo isomers.[15] Attempts to isomerise directly 2,6-dibromo DTT **2** by LDA-mediated halogen dance, however, did not yield **3** in any significant amount. When **2** was treated with 2 equivalents of LDA at −78 °C and the dianion was subsequently quenched with camphorsulfonic acid or methanol at this temperature, an inseparable mixture of **1**, monobromo and non symmetrical dibromo DTT derivatives was formed, as observed by ^{13}C NMR spectroscopy. Quenching the dianion with Me_3SiCl at −78 °C, gave the rearranged bis-TMS-DTT derivative **8**, (Scheme 2) which was spectroscopically different from **9**.‡

The dibromide **3** was finally obtained in good yield by protiodesilylation of **8** using hydroiodic acid in toluene.[16] This desilylation is unlikely to cause further rearrangement and the proposed regiochemistry is supported by ^{13}C NMR spectroscopy.‡ The signals of the halogen-substituted carbons in **2** [δ (C_α) 112.6 ppm] and **3** [(C_β) 104.0 ppm] are shifted upfield relative to their counterpart in **1** [δ (C_α) 120.9 and (C_β) 125.9 ppm][1] by 8.3 and 21.9 ppm, respectively. This is in accord with the trend of the substituent effect of bromine on the chemical shifts of C_α and C_β in 2-bromothiophene [$\Delta\delta$ (C_α) 13.6 ppm] and 3-bromothiophene [$\Delta\delta$ (C_β) 17.3 ppm].[17] Moreover, as in

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† Electronic supplementary information (ESI) available: spectral data for **2**, **3**, **6**, **8**, **9** and **12**, experimental data for **6**, displacement ellipsoid diagram for **9** and crystal packing diagram for **12**. See http://www.rsc.org/suppdata/cc/b2/b207403f/

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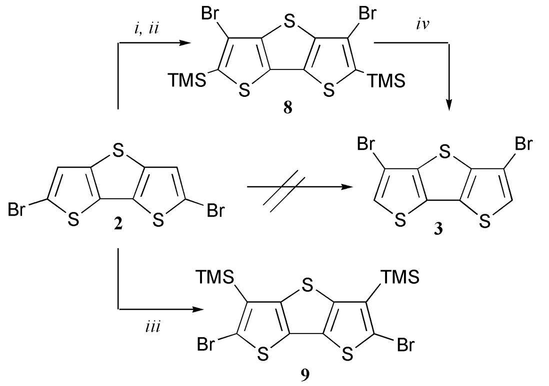
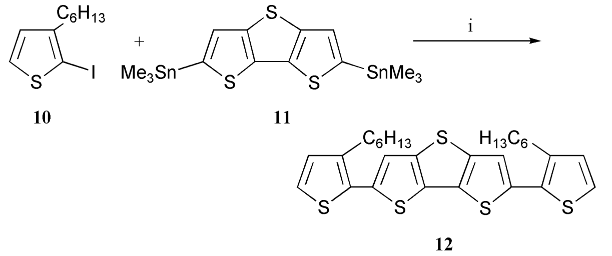


Scheme 2 *Reagents and conditions*: i, LDA, −78 °C, 1 h; ii, TMSCl, −78 °C → 25 °C, 30 min, (71%); iii, LDA/TMSCl, −78 °C, 1 h, → 25 °C (74%); iv, HI (55%), toluene, 25 °C (71%).

the bromothiophenes, but in a more pronounced way, the peaks of C_β are shifted upfield relative to that of C_α ($\Delta\delta$ 8.6 in the DTT systems *vs.* 2.0 ppm in the thiophene systems).

The unrearranged 2,6-dibromo-3,5-bis(trimethylsilyl)DTT **9** could be selectively prepared by an *in situ* deprotonation-silylation sequence in which **2** was treated with a preformed mixture of LDA and Me_3SiCl in THF at −78 °C.[18]‡ NMR based structure assignment in the related thiophene area has been controversial and the use of X-ray crystal structure determination is an essential component of such studies.[19] The structure of **9** was confirmed by single crystal X-ray diffraction.†§ The *in situ* regiospecific silylation method introduced here provides a novel approach to lithium based silylation reactions of thiophene derivatives.

Finally, we have prepared oligomer **12** in a Stille cross coupling (Scheme 3) of 2-iodo-3-hexylthiophene **12** and bis(trimethyl-stannyl)DTT **11** which was prepared by lithiation of dibromide **2** followed by stannylation.



Scheme 3 *Reagents and conditions*: i, $PdCl_2(PPh_3)_2$, DMF, 80 °C, 12 h (60%).

The X-ray crystal structure of **12** reveals an essentially planar molecular unit, with a *syn–anti* conformation around the thiophene-DTT bonds (Fig. 1).§ Molecules form planar centrosymmetric dimers, with intermolecular S···S contacts typical of those observed for nucleophilic approach to divalent S, *i.e.* in the plane of the C–S–C unit, along the direction of the (C–S)σ* orbitals.[20] Optimisation of these interactions may account for the *syn* conformation of S2, S4 and S5 in the solid state. Dimers are stacked in a face-to-face offset manner along the crystallographic *a* direction with an inter-plane separation of 3.5 Å. The hexyl substituents on the thiophene rings lie approximately in the plane of the dimers and interlock between dimer stacks.†

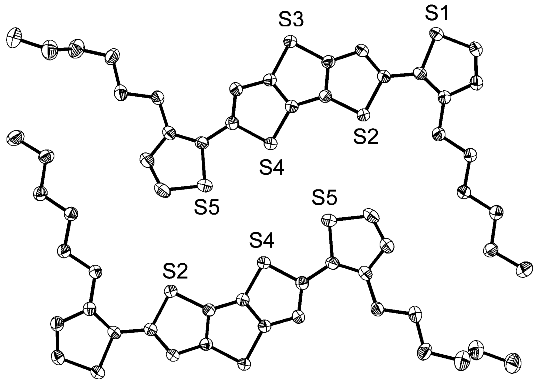


Fig. 1 Dimeric unit in the crystal structure of **12** (H atoms omitted). Displacement ellipsoids are shown at 50% probability.

In summary, DTT is now available on a large scale by an improved route. Orthogonally substituted DTT derivatives can be prepared. The halogen dance delivers bromines to positions 3 and 5 whereas a novel *in situ* silylation procedure provides a method for the introduction of silicon at these positions. A bishexylthienyl-DTT oligomer **12** was prepared by Stille cross coupling.

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Notes and references

‡ ^{13}C NMR for **2** (62.5 MHz, CS_2:$CDCl_3$) δ 112.61, 123.23, 130.93, 139.20 ppm; **3** (125 MHz, CS_2:$CDCl_3$) δ 103.95, 123.09, 130.70, 142.68 ppm; **8** (100 MHz, $CDCl_3$) δ −0.9, 109.9, 134.2, 136.2, 145.6 ppm; **9** (100 MHz, $CDCl_3$) δ −0.3, 118.4, 130.2, 133.8, 144.7 ppm.

§ *Crystal data for* **9**: $C_{14}H_{18}Br_2S_3Si_2$, M = 498.46, triclinic, space group $P\bar{1}$, a = 12.9980(10), b = 13.0198(9), c = 13.4649(10) Å, α = 75.266(4), β = 69.243(4), γ = 74.417(4)°, U = 2020.2(3) Å^3, Z = 4, D_c = 1.639 g cm^{-3}, μ(Mo-Kα) = 4.433 mm^{-1}. Of 15851 reflections measured, 7043 were unique (R_{int} = 0.1176) and were used in all calculations. The final $wR2$ = 0.1572 (all data), $R1$ [$F^2 > 2\sigma(F^2)$] = 0.0566, and goodness-of-fit on F^2, S = 1.02 (CCDC 190974). *Crystal data for* **12**: $C_{28}H_{32}S_5$, M = 528.84, triclinic, space group $P\bar{1}$, a = 7.8796(4), b = 11.3296(5), c = 15.8922(8) Å, α = 76.087(3), β = 83.466(3), γ = 71.136(3)°, U = 1302.2(1) Å^3, Z = 2, D_c = 1.349 g cm^{-3}, μ(Mo-Kα) = 0.461 mm^{-1}. Of 14683 reflections measured, 5930 were unique (R_{int} = 0.0371) and were used in all calculations. The final $wR2$ = 0.1192 (all data), $R1$ [$F^2 > 2\sigma(F^2)$] = 0.0482, and goodness-of-fit on F^2, S = 1.02. CCDC 190975. See http://www.rsc.org/suppdata/cc/b2/b207403f/ for crystallographic data in CIF or other electronic format.

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