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Synthesis and Characterization of Naphtho[2,1-*b*:7,8-*b'*]bis[1]-benzothiophene

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Abstract: We describe a simple three-step synthesis of naphtho[2,1-*b*:7,8-*b'*]bis[1]benzothiophene, which is scalable to multi-hundred-gram. We report the subsequent functionalization of this compound into iodine, boronic ester and silane derivatives, which are useful intermediates for various applications. The core structure was analyzed by NMR and single-crystal X-ray diffraction, and the physical properties were investigated by cyclic voltammetry, UV/Vis- and fluorescence spectroscopy.

Introduction

Dibenzothiophene and its derivatives are of great interest as building blocks for organic semiconductor materials due to their stability,[1] high abundance[2] and good electron-conducting properties.[3] These have been explored in recent years for use in organic electronics such as organic field-effect transistors (OFETs),[4] organic photovoltaics (OPVs)[5] and organic light-emitting diodes (OLEDs).[6] New building blocks are essential to further increase the performance of these new technologies.
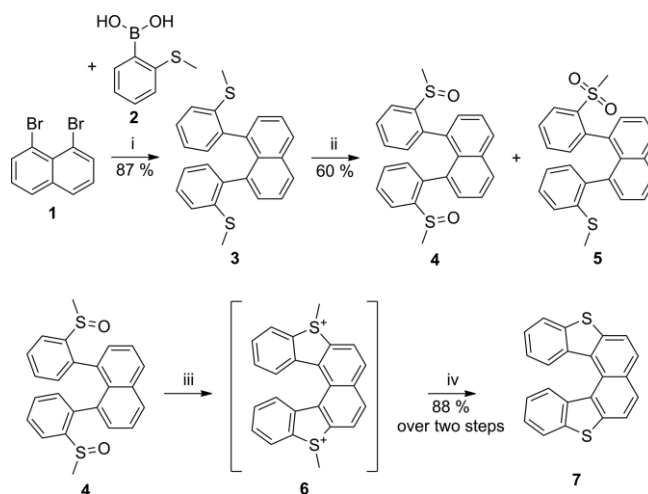
The naphtho[2,1-*b*:7,8-*b'*]bis[1]benzothiophene has received less attention for such applications than dibenzothiophene due to its poor accessibility. Since the first report in 1984 no other publications described the chemistry of the compound.[7] Kudo et al. reported the synthesis of various naphthobisbenzothiophenes via photochemical cyclization. However, the starting materials used for the synthesis are not commercially available in large quantities and the formation of isomers during the cyclization as well as their separation by column chromatography reduced the yield significantly. Therefore, we have developed an alternative approach based on commercially available materials to make this interesting building block available in larger quantities without the necessity of column chromatography. For this purpose, the intramolecular electrophilic cyclization of sulfoxides by means of strong acids, which was first reported in 1999 by Sirringhaus et al. was used.[8] Furthermore, we investi-

gated the compounds by X-ray crystal structure analysis, CV, UV/Vis, and IR and report further functionalizations.

Results and Discussion

Synthesis

The synthesis of compound **7** is shown in Scheme 1. We started the synthesis from commercially available 1,8-dibromonaphthalene (**1**). In the first step, the dibromine was coupled with methylsulfanylphenylboronic acid (**2**) in a Suzuki–Miyaura-reaction,[9] yielding 1,8-bis(2-methylsulfinylphenyl)-naphthalene (**3**). The catalyst system Pd$_2$(dba)$_3$/SPhos,[10] which was adopted from the synthesis of 1,8-bis(2-methoxyphenyl)-naphthalene,[11] promoted the reaction in excellent yields of 87 % after workup. In variation to the literature, we used the cheaper potassium

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Scheme 1. Synthesis of compound **7**: i: K$_2$CO$_3$, SPhos, Pd$_2$(dba)$_3$, DMF/water, 24 h, reflux; ii: H$_2$O$_2$, TMSCl, ACN, 5 h, r.t.; iii: H$_2$SO$_4$, 6 h, 0 °C; iv: NaOH, H$_2$O, 1 h, reflux.

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carbonate instead of cesium carbonate but kept the solvent system DMF/water.

In the second step of the synthesis, the sulfanyl-groups of compound **3** were oxidized, yielding 1,8-bis(2-methylsulfinyl-phenyl)-naphthalene (**4**). Optimizing the reaction conditions was crucial to avoid overoxidation and the formation of by-product **5** (Table 1). The best results were obtained with the method described by Bahrami et al., using hydrogen peroxide as oxidant and chlorotrimethylsilane as promoter.[12] Furthermore, dilution proved to be beneficial, since lower concentrations of the starting material suppressed the formation of the by-product. By-product **5** could be removed by washing the crude product with methanol. The desired compound **4** was isolated in a yield of 60 %.

Table 1. Overview of the screened reaction conditions for the synthesis of compound **4**.

Entry	Oxidant	Solvent	Temperature	Ratio **4/5**[a]
1	H_2O_2	AcOH	25 °C	61:21
2	H_2O_2 (2 equiv.)	AcOH/DCM	0 °C	54:46
3[13]	H_5IO_6 (2 equiv.), $FeCl_3$ (0.03 equiv.)	ACN	25 °C	53:47
4[12]	H_2O_2 (2 equiv.), TMSCl (3 equiv.)	ACN	25 °C	86:14

[a] Determined by ^{1}H-NMR in $CDCl_3$.

Common literature procedures for electrophilic ring closure reactions of sulfinyl-groups use concentrated sulfuric acid[14] as well as trifluoromethanesulfonic acid.[8] Both worked in our case, but concentrated sulfuric acid was used for economic reasons. The high polarity of the ionic intermediate (**6**) hampered the monitoring of the reaction by TLC. Therefore, samples were taken every hour and the reaction was monitored by ^{1}H-NMR (see supporting information). After complete conversion of the starting material to compound **6**, the reaction mixture was diluted and then carefully basified with sodium hydroxide solution in order to demethylate the ionic intermediate, isolating naphtho[2,1-*b*:7,8-*b'*] bis[1]benzothiophene (**7**) in a yield of 88 % over both steps. The overall yield for the three-step synthesis is 46 %.

It is well known, that dibenzothiophene and its derivatives can be *ortho*-lithiated and then quenched with different electrophiles to enable functionalization.[15] For the lithiation of compound **7**, *n*-butyllithium in THF at –45 °C gave the best results, since lower temperatures showed incomplete conversion. It is noteworthy that the directed lithiation occurs selectively at the 6-position of naphthalene and not at the *ortho*-position of the benzo-unit, as confirmed by ^{1}H-NMR of compound **8** with the appearance of a singlet resonance signal at 8.44 ppm, which can be assigned to the proton in 7-position (Figure 1). Iodide (**8**), boronic ester (**9**) and silane (**10**) could be prepared in this manner in excellent yields of 80 % to 89 %, respectively (Scheme 2). These intermediates give access to further functionalization using e.g. Suzuki–Miyaura[9] or Buchwald-Hartwig-coupling-reactions.[16] Furthermore, the silane can be used as a protecting group, for further functionalization, by lithiation and subsequent quenching with an electrophile.
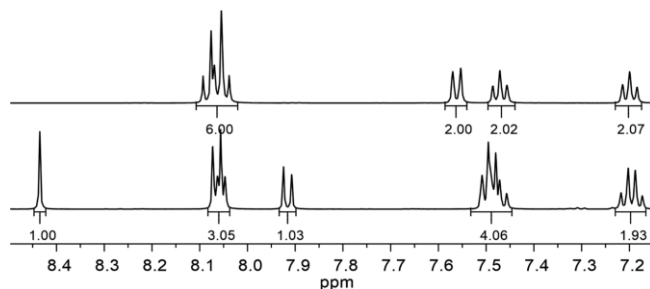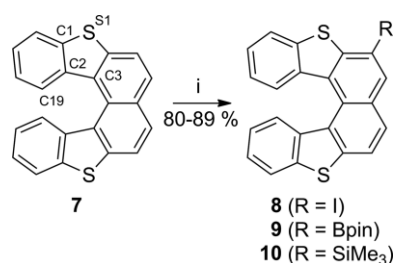

Figure 1. ^{1}H-NMR spectra (500 MHz, [D$_2$]TCE) of compound **7** (top) and compound **8** without purification (bottom).

Scheme 2. Functionalization of compound **7**. i: 1. *n*BuLi, THF, 5 h, –45 °C; 2. I$_2$ *or* TMSCl *or* isopropoxyboronic acid pinacol ester, –45 °C to r.t., 2 h.

X-ray Structure Analysis

Compound **7** was characterized by single-crystal X-ray diffraction studies. The molecular structure is shown in Figure 2. In the solid state, the substance shows atropisomerism[17] and is therefore chiral, since the two benzothiophene units are interlocked due to the steric demand of the hydrogen atoms in the bay region. The angle between the two benzothiophene units is 43°. The naphthalene unit is slightly bent. Furthermore, the bond length of C19–C2 (1.406 Å) is increased in comparison to dibenzothiophene, for which 1.391 Å are reported.[18] The same is valid for the bond length C2–C3 (1.456 Å), where 1.408 Å[18] are reported for dibenzothiophene. Also the carbon–sulfur bond C1–S1 (1.743 Å) is slightly elongated (1.734 Å for dibenzothiophene[18]). The elongation of the bonds in the bay-area clearly shows the strain of the molecular structure.
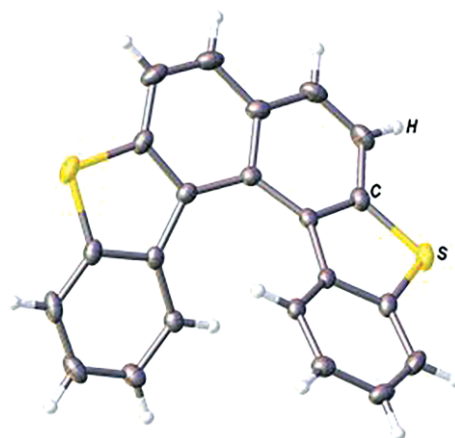

Figure 2. Crystal structure of compound **7**. CCDC: 1958749.

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Cyclic Voltammetry and Quantum Chemical Calculations

The redox potential of compound **7** was investigated by cyclic voltammetry measurement. HOMO and LUMO energy levels were determined, to be –5.85 eV and –2.17 eV respectively, by referencing against ferrocene (–4.8 eV), which was used as an internal standard. There is also no change in the redox behavior over ten oxidation and reduction cycles, proving the stability of the building block.

Furthermore, the HOMO and LUMO energy levels and distributions were calculated using TD-DFT calculations [B3-LYP/6-31G(d)], as shown in Figure 3. The HOMO, as well as the LUMO, is symmetrically distributed over the whole molecule.
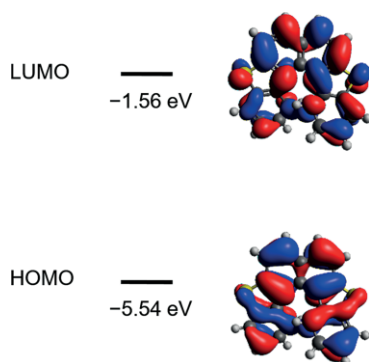

LUMO — –1.56 eV

HOMO — –5.54 eV

Figure 3. Geometry optimization, HOMO-LUMO-energies and -distributions of compound **7**.

Photophysical Properties

Since compound **7** shows strong fluorescence under UV-light its photophysical properties were investigated by UV/Vis and fluorescence spectroscopy in heptane and acetonitrile, respectively (see Figure 4.).
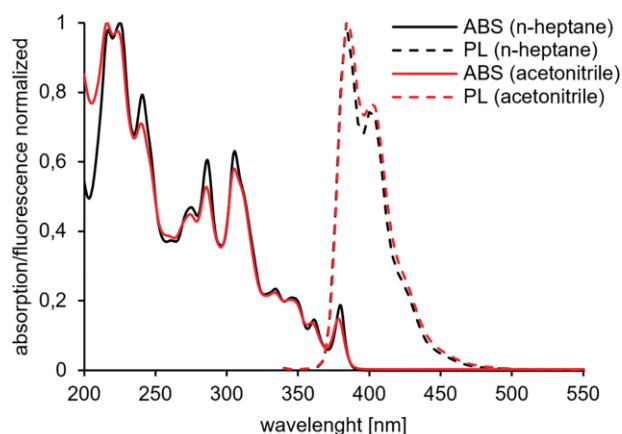

Figure 4. Normalized UV/Vis and fluorescence spectra of compound **7** in heptane (4 µg/mL); excited at 305 nm.

Compound **7** shows absorption in the area from 200 to 380 nm and emission at the wavelength of 384 nm with a narrow FWHM of 32 nm. There is no dependency of the emission wavelength on the polarity of the solvent and the emission λ_{max} remains unchanged in acetonitrile and heptane.

Conclusions

A fast and high yielding synthesis of naphtho[2,1-*b*:7,8-*b*′]bis-[1]benzothiophene was developed, which is suitable for a multi-hundred-gram scale. The crystal-structure, electrochemical and photochemical properties of this compound were determined. The subsequent monofunctionalization yields the corresponding iodine, boronic ester or silane derivatives, which may be used in subsequent C–C and C–N coupling reactions.

Experimental Section

General Information: All reagents and solvents were purchased from commercial suppliers (Sigma Aldrich, Merck, VWR). The starting materials were purchased from Combi-Blocks (1,8-dibromo-naphthalene) and ABCR (2-methylsulfanylphenylboronic acid). All reactions were carried out under a dry atmosphere of argon with dried solvents. Reactions were monitored by TLC (Merck Silica Gel 60 F$_{254}$). NMR-Spectra were recorded on a Bruker Avance III at 298 K.

1,8-Bis(2-methylsulfanylphenyl)-naphthalene (3): 1,8-Dibromo-naphthalene (437.1 mmol, 1.0 equiv., 125.0 g), 2-methylsulfanyl-phenylboronic acid (961.7 mmol, 2.2 equiv., 161.6 g) and potassium carbonate (2185.6 mmol 5.0 equiv., 302.1 g) were dissolved in DMF (1250 mL) and water (500 mL). Then, Pd$_2$(dba)$_3$ (21.9 mmol, 0.05 equiv., 21.1 g) and SPhos (21.9 mmol, 0.05 equiv., 9.0 g) were added subsequently and the mixture was heated to reflux for 24 h. The organic phase was separated, and the solvent removed in vacuo. The residue was dissolved in DCM (1000 mL), washed with water (1000 mL) and dried with magnesium sulfate. The filtered was concentrated in vacuo. The residue was purified by hot extraction over basic aluminium oxide using *n*-heptane to give the desired product as a white solid. Yield: 142 g; 87 %; m.p. 160 °C; ^{1}H NMR (500 MHz, [D$_2$]TCE) δ = 7.99 (dd, $^{3,4}J$ = 8.2, 1.4 Hz, 2H), 7.55 (dd, $^{3,3}J$ = 8.1, 7.0 Hz, 2H), 7.25 (ddd, $^{3,3,4}J$ = 12.4, 7.2, 1.4 Hz, 4H), 6.95 (td, $^{3,4}J$ = 7.7, 1.5 Hz, 2H), 6.79 (td, $^{3,4}J$ = 7.4, 1.1 Hz, 2H), 6.74 (dd, $^{3,4}J$ = 8.1, 1.1 Hz, 2H), 2.29 (s, 6H); ^{13}C NMR (126 MHz, [D$_2$]TCE) δ = 140.2, 137.9, 137.6, 134.9, 130.8, 129.6, 129.3, 129.0, 127.7, 125.2, 123.0, 122.8, 15.2; EI-MS (*m/z*): 372.101 [M].

1,8-Bis(2-methylsulfinylphenyl)-naphthalene (4): 1,8-Bis (2-methylsulfanylphenyl) naphthalene (378.5 mmol, 1.0 equiv., 141.0 g) was suspended in acetonitrile (5000 mL) and chlorotrimethylsilane (1135.4 mmol, 3.0 equiv., 124.6 g, 145.0 mL) was added. Hydrogen peroxide (30 %, 756.9 mmol, 2.0 equiv., 85.8 g, 77.3 mL) was then added dropwise over a period of three hours and the reaction mixture was stirred for another two hours. After the addition of saturated sodium sulfite solution (500 mL) the solvent was removed in vacuo and the residue taken up in water (2000 mL). The solid was filtered off and then washed with methanol (500 mL). After drying, the product was obtained as a white solid. Yield: 92 g; 60 %; ^{1}H NMR (500 MHz, [D]Chloroform) δ = 8.04 (dd, $^{3,4}J$ = 8.2, 1.4 Hz, 2H), 7.60 (dd, $^{3,3}J$ = 8.3, 7.0 Hz, 2H), 7.49 (dd, $^{3,4}J$ = 7.9, 1.4 Hz, 2H), 7.46 (dd, $^{3,4}J$ = 7.5, 1.3 Hz, 2H), 7.33 (td, $^{3,4}J$ = 7.4, 1.4 Hz, 2H), 7.27–7.21 (m, 8H), 1.98 (s, 6H); ^{13}C NMR (126 MHz, [D]Chloroform) δ = 144.3, 138.3, 135.1, 134.3, 131.9, 130.8, 130.3, 129.8, 128.6, 128.2, 125.7, 121.9, 41.3; EI-MS (*m/z*): 404.0904 [M].

Naphtho[2,1-*b*:7,8-*b*′]bis[1]benzothiophene (7): 1,8-bis (2-methylsulfinylphenyl) naphthalene (227.4 mmol, 1.00 equiv., 92.0 g) was added to concentrated sulfuric acid (300 mL) at 0 °C in such a way that the temperature did not exceed 10 °C. After the addition was completed the reaction mixture was stirred for six hours at room temperature. Then ice (2 kg) was added and the pH was basified

by slow addition of concentrated sodium hydroxide solution. The aqueous phase was extracted with toluene (1000 mL) and separated. The organic phase was dried with magnesium sulfate. The filtrate was concentrated in vacuo. The residue was washed with methanol (500 mL) and filtered. The product was obtained as a white solid. Yield: 68 g; 88 %; m.p. 207 °C, ^{1}H NMR (500 MHz, [D]Chloroform) δ = 8.00–7.89 (m, 6H), 7.45 (dd, [3,4]J = 8.2, 1.0 Hz, 2H), 7.33 (ddd, [3,3,4]J = 8.1, 7.1, 1.1 Hz, 2H), 7.05 (ddd, [3,3,4]J = 8.2, 7.1, 1.2 Hz, 2H); ^{13}C NMR (126 MHz, [D]Chloroform) δ = 140.6, 138.6, 136.3, 130.1, 128.9, 127.9, 127.5, 125.4, 124.6, 122.8, 122.4, 120.5; EI-MS (m/z): 340.038 [M].

6-Iodo-naphtho[2,1-b:7,8-b′]bis[1]benzothiophene (8): Naphtho[2,1-b:7,8-b′]bis[1]benzothiophene (102.8 mmol, 1.0 equiv., 35.0 g) was dissolved in dry THF (750 mL) and cooled to 45 °C (acetonitrile/dry ice). Then n-butyllithium (2.5 M in hexane, 154.2 mmol, 1.5 equiv., 61.7 mL) was added. After five hours, iodine (205.6 mmol, 2.0 equiv., 52.2 g) dissolved in dry THF (250 mL) was added. The reaction mixture was warmed to room temperature and then treated with saturated sodium sulfite solution (250 mL). The organic phase was separated, and the aqueous phase extracted with DCM (500 mL) until it showed no turbidity. The organic phases were combined and dried with magnesium sulfate. The filtrate was concentrated in vacuo. The product was obtained after recrystallization from heptane/toluene as a beige solid. Yield: 38 g; 80 %; m.p. 231 °C; ^{1}H NMR (500 MHz, [D8]THF) δ = 8.56 (s, 1H), 8.17–8.09 (m, 2H), 8.08 (d, [3]J = 8.0 Hz, 1H), 8.03 (d, [3]J = 8.5 Hz, 1H), 7.52–7.41 (m, 4H), 7.21–7.10 (m, 2H); ^{13}C NMR (126 MHz, [D8]THF) δ = 146.2, 141.1, 138.7, 137.8, 137.3, 136.5, 136.0, 131.7, 128.6, 128.5, 128.3, 127.6, 126.4, 125.8, 125.5, 123.7, 122.9, 122.8, 122.4, 122.2, 121.0, 84.9; EI-MS (m/z): 465.9346 [M].

6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-naphtho-[2,1-b:7,8-b′]bis[1]benzothiophene (9): Naphtho[2,1-b:7,8-b′]-bis[1]benzothiophene (293.7 μmol, 1.0 equiv., 100 mg) was dissolved in THF (5 mL) and cooled to 45 °C (acetonitrile/dry ice). Then n-butyllithium (2.5 M in hexane, 587.4 μmol, 2.0 equiv., 0.4 mL) was added. After five hours, isopropoxyboronic acid pinacol ester (587.4 μmol, 2.0 equiv., 0.1 g, 0.11 mL) was added. The reaction mixture was warmed to room temperature and the solvent removed in vacuo. The product was obtained after column chromatography (silica gel 60, heptane/DCM) as a white solid. Yield: 110 mg; 80 %; m.p. 166 °C; ^{1}H NMR (500 MHz, [D2]TCE) δ = 8.57 (s, 1H), 8.13–8.07 (m, 2H), 8.08–8.02 (m, 2H), 7.50 (t, [3]J = 8.5 Hz, 2H), 7.49–7.41 (m, 2H), 7.22–7.12 (m, 2H), 1.52 (d, [4]J = 1.9 Hz, 12H); ^{13}C NMR (126 MHz, [D2]TCE) δ = 145.8, 141.8, 139.5, 138.4, 136.4, 136.2, 135.8, 129.5, 128.8, 128.5, 128.1, 127.9, 127.6, 126.1, 125.7, 125.5, 123.1, 122.8, 122.6, 122.3, 120.7, 84.8, 25.4, 25.0; EI-MS (m/z): 466.123 [M].

6-(Trimethylsilyl)-naphtho[2,1-b:7,8-b′]bis[1]benzothiophene (10): Naphtho[2,1-b:7,8-b′]bis[1]benzothiophene (293.7 μmol, 1.0 equiv., 100 mg) was dissolved in THF (5 mL) and brought to 45 °C (acetonitrile/dry ice). Then n-butyllithium (2.5 M in hexane, 587.4 μmol, 2.0 equiv., 0.4 mL) was added. After five hours, chlorotrimethylsilane (587.4 μmol, 2.0 equiv., 64 mg, 0.07 mL) was added. The reaction mixture was warmed to room temperature and the solvent removed in vacuo. The product was obtained after column chromatography (silica gel 60, heptane/DCM) as a white solid. Yield: 110 mg; 89 %; ^{1}H NMR (500 MHz, [D2]TCE) δ = 8.32 (s, 1H), 8.24 (s, 2H), 8.25–8.17 (m, 2H), 7.70 (d, J = 8.2 Hz, 1H), 7.67 (d, J = 8.2 Hz, 1H), 7.65–7.58 (m, 2H), 7.37–7.30 (m, 2H), 0.80 (s, 9H); ^{13}C NMR (126 MHz, [D2]TCE) δ = 145.8, 141.0, 138.5, 138.4, 136.2, 135.8, 134.3, 131.9, 129.7, 128.7, 128.0, 127.9, 127.9, 127.8, 125.6, 125.5, 124.9, 123.1, 122.2, 122.6, 122.3, 120.6, 0.7; EI-MS (m/z): = 412.078 [M].

CCDC 1958749 (for **7**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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