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An efficient protocol for synthesizing dibenzodithiapentalenes

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ABSTRACT

Two new scalable methods for the synthesis of dibenzo[*bc*,*fg*]dithiapentalene (**2**) (DPP) are reported starting from either 1-bromo-3-fluoro-2-iodobenzene over four steps in 57% yield or from THP-protected 3-fluorothiophenol over three steps in 43% yield. Attempts to prepare dibenzodioxapentalene (**15**) using similar conditions were unsuccessful. Instead, we observed the formation of a macrocyclic dimeric product **16**. Fluorine–hydrogen bond interactions were observed by NMR in the F/SH- and F/OH-substituted dibenzothiophene and dibenzofuran intermediates.

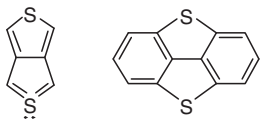
Conjugated scaffolds based on thienothiophenes are interesting targets for organic charge carrier transport materials.[1] Three of the four isomeric thienothiophenes are stable, isolable compounds, while the fourth isomer, thieno[3,4-*c*]thiophene (**1**, Fig. 1), is itself very unstable.[2] Stability is, however, enhanced by substitution,[2] and in 1992 Furukawa and co-workers[3] reported the first synthesis of the stable dibenzo-fused analog dibenzo[*bc*,*fg*][1,4]dithiapentalene (**2**, DDP) from the precursor **3** (Scheme 1) and showed, according to X-ray crystallography, that it has a completely planar structure. The synthesis suffers, however, from relatively modest yields and we became interested in developing an alternative route.[4]

Based on our recent work on substituted dibenzothiophenes,[5] we decided to try to expand the scope of the protocol to dibenzodithiapentalenes. In this Letter, we report a concise and efficient protocol for synthesizing functionalized DDPs under mild reaction conditions.

Scheme 2 summarizes our four-step DDP synthesis: (1) Ullmann-type coupling of a tris-halobenzene[6] at low temperature forming a 2,2′,6,6′-tetrahalobiphenyl, (2) Pd-catalyzed C–S coupling with ethyl 3-mercaptopropionate,[7] (3) deprotection to form the dithiol, and (4) tandem cyclization via intramolecular S_NAr-reactions[5] to give the desired DDP. Initially, we attempted to prepare the strained 2,2′,6,6′-tetrahalobiphenyl **6** by using modifications of the Suzuki–Miyaura coupling,[8] but no conversion of the starting material was observed. Therefore, we turned to Leroux's low temperature Ullmann-type coupling[6] using the trihalobenzene **7** as starting material.

Compound **7** was subjected to a metal–halogen exchange by treatment with butyllithium; the lithiated species was then transmetallated to the diarylcopper species, which furnished the sterically encumbered biphenyl **6** in good yield upon reductive elimination. In the second step we followed the previously reported sulfur-coupling reaction,[5,7] by means of which we obtained dithioether **5** in near-quantitative yield. The third step in the protocol was deprotection of thioether **5** with potassium *tert*-butoxide (2.5 M equiv) in THF at ambient temperature. Quenching with MeOH furnished dithiol **4**[9] in a yield of 91%. We note that formation of the six-membered tricyclic disulfide of **4** was not observed. The dithiol **4** was converted into the desired DDP (**2**) by nucleophilic aromatic substitution with cesium carbonate in DMSO. The formation of fluoro-mercaptodibenzothiophene **8**[10] as a result of the first ring-closure was rather easy since it was formed quantitatively at 50 °C after 1 h. Increasing the temperature to 150 °C for 5 h resulted in formation of **2** in 91% yield.[11] It should be noted that attempts at performing the deprotection of **5** and subsequent ring-closure in a one-pot reaction were not successful.

The difference in reactivity between the first and the second S_NAr reaction indicates that the formation of the last C–S bond is associated with a higher energy of activation owing to the flat



1 **2**

Figure 1. Structures of compounds **1** and **2**.

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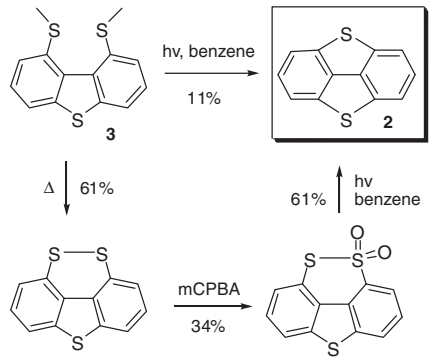
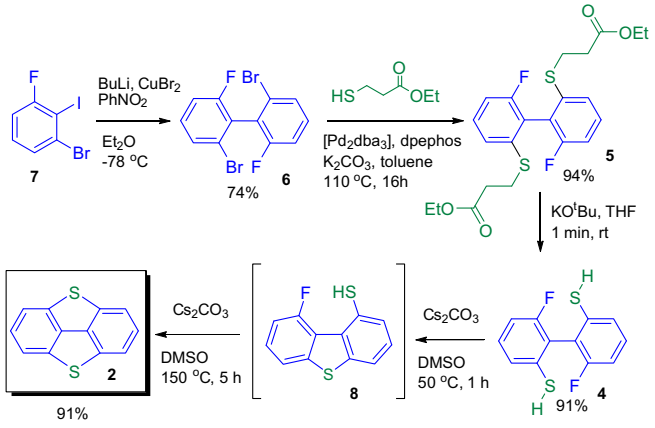
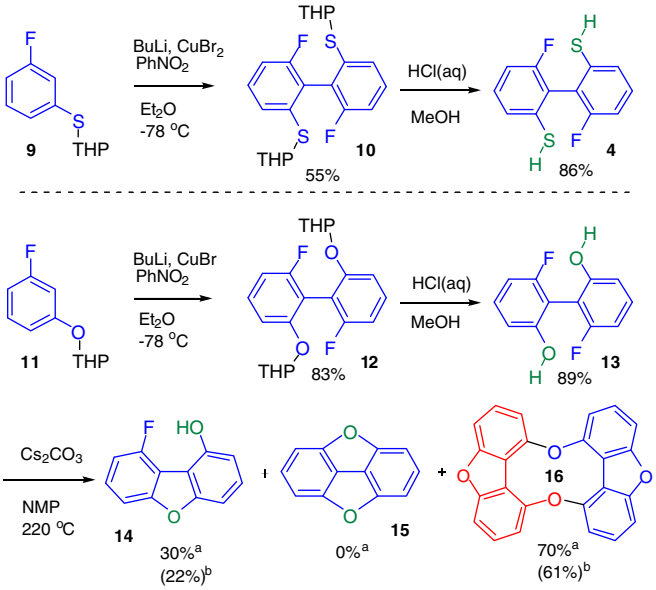


Scheme 1. Previous protocol for synthesizing DDP.[3]



Scheme 2. Four-step protocol for the synthesis of DDP.



Scheme 3. Modified protocol for synthesizing the DPP precursor **4** and the corresponding oxygen counterpart **13**. The product yields of the final S_NAr reaction are based on (a) GC/LC and (b) isolated products.

and strained structure of DDP[3] and the larger distance between the fluorine-bearing carbon and the sulfur in the intermediate dibenzothiophene **8**. As a testimony to the robustness of the protocol we managed to scale up the reactions without lowering the yields

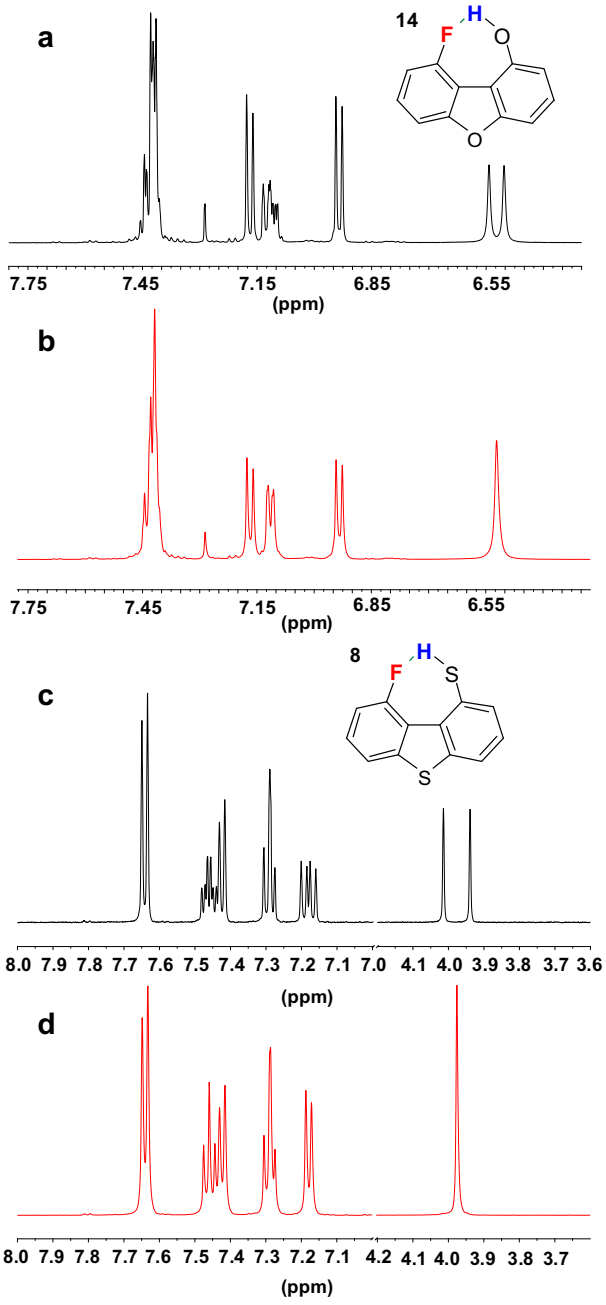


Figure 2. NMR spectral evidence of XH–F interactions in compounds **14** (X = O) and **8** (X = S). (a) ^{1}H NMR (500 MHz, $CDCl_3$) of **14** with OH-F resonance at δ_H 6.52 (d, J = 19.7 Hz); (b) ^{19}F-decoupled ^{1}H NMR (500 MHz, $CDCl_3$) of **14**; (c) ^{1}H NMR (500 MHz, $CDCl_3$) of **8** with SH-F resonance at δ_H 3.98 ppm (d, J = 37.5 Hz); (d) ^{19}F-decoupled ^{1}H NMR (500 MHz) of **8**.

and prepared the DDP on gram-scale (2.25 g) in an overall yield of 56% starting from **7**.

The mild conditions of our method should allow for the synthesis of substituted DPPs in the future and the incorporation of DPPs into larger conjugated scaffolds for materials science. Thus, a slight modification of our protocol by incorporating a non-symmetric biphenyl coupling via lithiation as described by Leroux,[12] or alternatively via the Molander modification[13] of the Suzuki-coupling, may allow access to asymmetrically functionalized DDPs. The scope of the protocol is currently being investigated.

The seleno derivative of DDP was prepared by Furukawa and coworkers[3b] in 1994, while the analogous preparation of the oxygen

derivative failed. To the best of our knowledge, dibenzodioxapentalene (**15**) has not been reported in the literature. Therefore, we decided to investigate this possibility by using our newly-developed protocol (Scheme 3). First, we enlarged the scope of Leroux's biphenyl synthesis by changing from metal–halogen exchange of the iodide to *ortho*-lithiation of the THP-protected 3-fluorothiophenol **9** and 3-fluorophenol **11**, whereby the heteroatom was already installed at the onset of the synthesis. This improved the synthesis of DDP by reducing the protocol from four to three steps, and completely avoided the use of palladium catalysis. We synthesized the THP-protected biphenyls **10** and **12** in moderate-to-good yields. The bis-phenol **13** and bis-thiophenol **4** were obtained by acid-mediated deprotection of **10** and **12**, respectively.

From this starting point we studied the ring-closure of the bisphenol **13** in an attempt to prepare dibenzodioxapentalene (**15**), and as expected it was much less reactive than the analogous bis-thiophenol **4**. We identified formation of the dibenzofuran product **14**[14] from reaction with cesium carbonate in DMSO at 150 °C overnight, but only 50% conversion of **13** and no trace of **15** was seen. Using harsher conditions with various bases such as potassium *tert*-butoxide and cesium carbonate in NMP at 220 °C, gave full conversion of **13** into **14** and the intermolecularly cyclized dimer of **14**, that is, the macrocyclic compound **16**.[14] However, still no trace of dibenzodioxapentalene (**15**) was observed. Based on the typical difficulty of performing intermolecular S_NAr reactions on unactivated substrates, the formation of the dimer **16** revealed the complexity of forming the desired, and thus far putative dibenzodioxapentalene (**15**). On the basis of these results, it seems unlikely that **15** can be prepared by the present protocol, reflecting the remarkably different properties of oxygen compared to sulfur, both with respect to bond angles, bond lengths, atom size, and nucleophilicity.

It was possible to isolate the intermediate mercaptofluorodibenzothiophene **8** (Scheme 2). We observed an interesting intramolecular F–H interaction in the ^{1}H NMR spectrum recorded in $CDCl_3$ of compound **8** as well as in that of compound **14**, which we assign to XH–F (X = S, O) hydrogen bonds. Indeed, unambiguous spectroscopic evidence of an interaction between F and H was obtained from the ^{19}F decoupled ^{1}H NMR spectra (Fig. 2). We reasoned that the F–H interaction was possible because of the rigidity of the tricyclic scaffold, since the hydrogen and the fluorine atoms are located in close proximity. We note that F–H bonding in *o*-fluorobenzanilides corresponding to a six-membered ring is known in the literature,[15] while to our knowledge, it has not been observed in seven-membered rings fused to a dibenzothiophene/furan scaffold.

In conclusion, we have developed efficient three- and four-step protocols for the synthesis of DDPs. The use of milder reaction conditions offers a significantly improved scalable protocol with the potential of preparing functionalized DDPs. We are currently in the process of exploring the scope of the protocol to facilitate future studies of the electronic and spectroscopic properties of DDP molecules.

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9. Compound **4**: Mp 107–108 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (td, J = 8.1, 5.5 Hz, 2H), 7.26–7.23 (m, 2H), 7.00 (td, J = 8.8, 1.1 Hz, 2H), 3.37 (s, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.3 (d, J = 248.8 Hz), 135.1, 130.7 (d, J = 9.4 Hz), 125.1, 120.5 (d, J = 19.9 Hz), 113.0 (d, J = 22.3 Hz); GC–MS: m/z = 254 [M$^+$], Anal. Calcd for $C_{12}H_8F_2S_2$: C, 56.67; H, 3.17. Found: C, 56.59; H, 3.26
10. Compound **8**: Mp 102–103 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 7.9 Hz, 2H), 7.45 (m, 2H), 7.29 (m, J = 7.9 Hz, 1H), 7.18 (dd, J = 12.6, 8.0 Hz, 1H), 3.98 (d, J = 37.5 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.3 (d, J = 246.3 Hz), 141.6, 141.1, 130.1, 130.0, 127.9, 126.9, 122.8, 119.5, 118.6, 111.8, 111.6; GC–MS: m/z = 234 [M$^+$], Anal. Calcd for $C_{12}H_7FS_2$: C, 61.51; H, 3.01. Found: C, 61.42; H, 3.13.
11. *Synthesis of **2***: Compound **4** (3.08 g, 12.1 mmol) and Cs_2CO_3 (9.87 g, 30.3 mmol) were dissolved in DMSO (35 mL). The mixture was stirred in a closed vial under an argon atmosphere for 5 h at 150 °C. Brine (150 mL) was added, and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were concentrated in vacuo onto Celite and purified by column flash chromatography on silica with heptane as eluent to give compound **2** as a white solid (2.25 g, 87%). The product was recrystallized from MeOH to afford **2** as a white cotton-like substance. Characterization data was in accordance with Ref. 3.
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14. *Synthesis of **14** and **16***: Compound **13** (50 mg, 0.2 mmol) and Cs_2CO_3 (183 mg, 0.56 mmol) were dissolved in NMP (3 mL). The mixture was stirred in a closed vial under an argon atmosphere for 5 h at 220 °C. Brine (30 mL) was added and the mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were concentrated in vacuo onto Celite and purified by column chromatography on silica with heptane as eluent to give compound **14** (10 mg, 22%) and **16** (25 mg, 61%) as white solids. Compound **14**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.40 (m, 3H), 7.19–7.08 (m, 2H), 6.94 (d, J = 8.1 Hz, 1H), 6.52 (d, J = 19.7 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.0, 155.8 (d, J = 240.6 Hz), 150.7, 129.5, 127.5 (d, J = 9.0 Hz), 111.47, 111.4 (d, J = 21.2 Hz), 109.6, 108.8, 108.7, 108.3, 103.7; GC–MS: m/z = 202 [M$^+$], Anal. Calcd for $C_{12}H_7FO_2$: C, 71.29; H, 3.49. Found: C, 71.27; H, 3.51.
Compound **16**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (dd, J = 8.2, 0.6 Hz, 4H), 7.51 (t, J = 8.2 Hz, 4H), 7.41 (dd, J = 8.2, 0.6 Hz, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.2, 152.9, 127.9, 116.5, 116.2, 108.3. GC–MS: m/z = 364 [M$^+$]. Anal. Calcd for $C_{24}H_{12}O_4$: C, 79.12; H, 3.32. Found: C, 79.07; H, 3.30. Calcd exact mass: m/z = 364.07301 [M$^+$], found: m/z = 364.07301 [M$^+$].
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