

# The First Electrochemically Active Cuppedophanes: Bis(tetrathiafulvalene)cuppedophanes

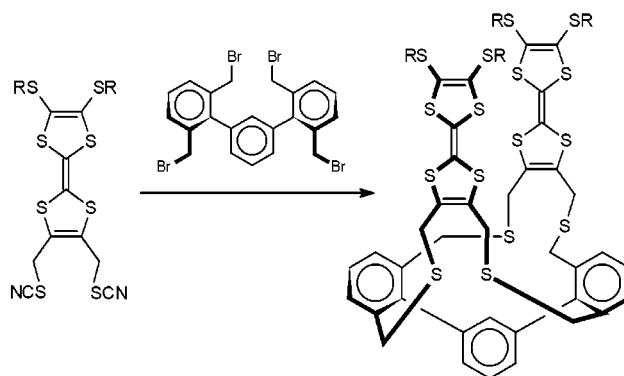
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## ABSTRACT



The synthesis of the first tetrathiafulvalene-containing cuppedophanes is reported, together with conformational study of the structures by <sup>1</sup>H NMR spectroscopy. The bis(TTF)cuppedophane **6** represents a novel type of cuppedophane.

Cyclophanes are fundamentally important compounds in many aspects of macrocyclic and supramolecular chemistry, and research in this field has expanded rapidly in recent years.<sup>1,2</sup> Tetrathiafulvalene (TTF, **1**) and its derivatives have been intensively studied during the past two decades, due to their unique  $\pi$ -electron donor properties, and have been incorporated into a number of electrochemically active macrocyclic systems with specific physical and chemical properties.<sup>3</sup> Bis(tetrathiafulvaleno)phanes (TTF-phanes) are of particular interest because the two TTF units can adopt a sandwich structure, which enables intramolecular interactions between the two redox units and increases the possibility of strong noncovalent inter- and intramolecular interactions.<sup>4</sup>

Cup-shaped cyclophanes based on the *m*-terphenyl framework, “cuppedophanes”, have been prepared by Hart and co-workers.<sup>5</sup> Links between the 2,2''- and 6,6''-positions in 2,6,2'',6''-tetrakis(bromomethyl)-1,1':3,1''-terphenyl (**2**) (Figure 1) create a molecular bowl or cup whose depth and host capacity depend on the nature of the linking units. The TTF

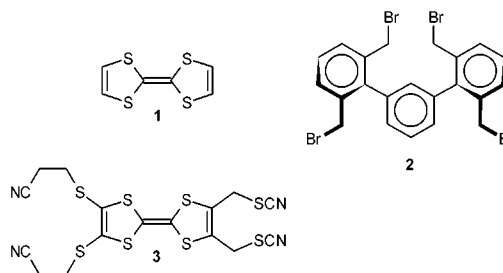


Figure 1.

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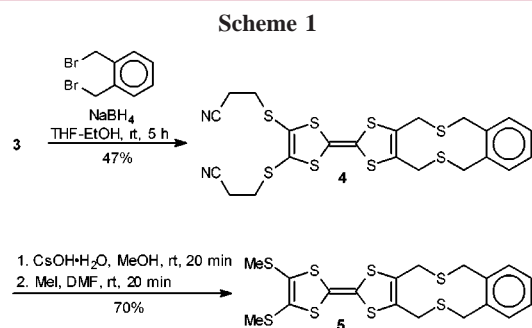
(1) (a) Vögtle, F., Ed. *Cyclophanes I, Topics in Current Chemistry*; Springer: Berlin, 1983; Vol. 113. (b) Vögtle, F., Ed. *Cyclophanes II, Topics in Current Chemistry*; Springer: Berlin, 1983; Vol. 115. (c) Vögtle, F. *Cyclophane Chemistry*; Wiley: Chichester, 1993.

moiety can, due to its interesting electrochemical properties and its sulfur atoms, potentially take part in molecular recognition events, e.g., as part of a molecular cavity. Thus, incorporation of TTF moieties into cuppedophanes seems to be an interesting approach to a new type of bis-(tetrathiafulvaleno)phanes, having the two TTF units connected by only one rigid linker.<sup>6</sup>

Recently we described the synthesis of 2,3-bis(2-cyanoethylthio)-6,7-bis(thiocyanatomethyl)tetrathiafulvalene (**3**) (Figure 1) as a potential versatile TTF building block possessing two orthogonal sets of thiolate protecting groups.<sup>7</sup> Although we have demonstrated that the thiocyanatomethyl groups in **3** can be smoothly deprotected with sodium borohydride and realkylated with "simple" alkylating reagents, the potential of **3** in cyclization/macrocyclization reactions has not been explored.

In this Letter we describe a general method for preparation of cyclophanes from **3**, and particularly the synthesis and characterization of the first TTF-containing cuppedophanes is presented.

To study the potential of **3** as a building block for cyclophane-type compounds, the following regioselective reaction with a bifunctional alkylating reagent was carried out. A 1:1 mixture of **3** and  $\alpha,\alpha'$ -dibromo *o*-xylene in THF–EtOH was added dropwise over a period of 5 h to a suspension of excess sodium borohydride in THF–EtOH. After usual workup, the desired [3.3]orthocyclophane **4** possessing the two intact cyanoethyl thiolate protecting groups was isolated in 47% yield (Scheme 1).



To test the stability of the [3.3]orthocyclophane moiety during the deprotection–realkylation protocol of the two cyanoethyl thiolate protecting groups, **4** was treated with 2.2

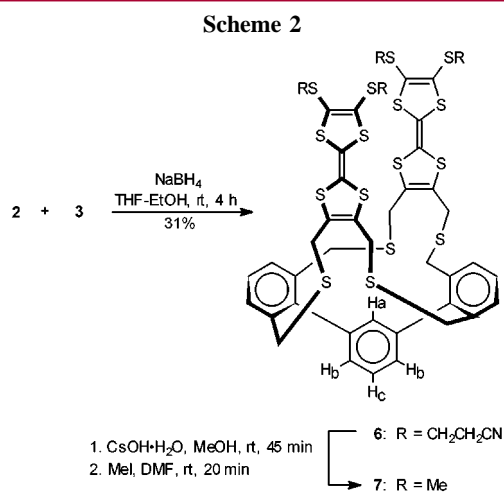
(2) Diederich, F. *Cyclophanes. Monographs in Supramolecular Chemistry*; Stoddart, F. J., Ed.; The Royal Society of Chemistry: London, 1991.

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equiv of cesium hydroxide monohydrate followed by addition of iodomethane,<sup>8</sup> affording the corresponding bis(methylthio)-[3.3]orthocyclophane **5** in 70% yield (Scheme 1). These results imply that **3** is a suitable building block for the synthesis of cyclophane-type TTF compounds with the additional bridgehead for further functionalization via deprotection–realkylation sequence.

Thus, we have employed **3** for the synthesis of a rather complicated cuppedophane system. Using similar high dilution conditions, coupling of 2,6,2'',6''-tetrakis(bromomethyl)-1,1':3',1''-terphenyl (**2**) with 2 equiv of **3** gave the tetrafunctionalized bis(TTF)cuppedophane **6** in 31% yield as an orange crystalline solid (Scheme 2).<sup>9</sup> Subsequently, the four



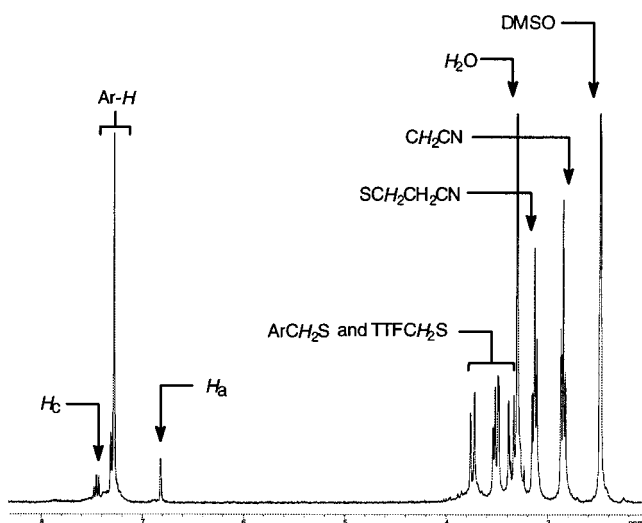
cyanoethyl thiolate protecting groups in **6** were deprotected using 4.5 equiv of cesium hydroxide monohydrate followed by addition of iodomethane, affording the corresponding tetrakis(methylthio)-bis(TTF)cuppedophane **7** in 57% yield after column chromatography (Scheme 2).

Figure 2 shows the <sup>1</sup>H NMR spectrum of the bis(TTF)-cuppedophane **6** recorded in CD<sub>3</sub>SOCD<sub>3</sub> at room temperature. The aromatic protons in **6** that can be unambiguously assigned were H<sub>a</sub> and H<sub>c</sub> on the central ring of the *m*-terphenyl moiety. The most diagnostic signal in the <sup>1</sup>H NMR spectrum of **6** is a one-proton triplet at  $\delta$  6.84 ppm with a small meta coupling constant ( $J = 1$  Hz). This signal

(6) A number of so-called double-bridged bis(tetrathiafulvaleno)phanes, connected in a 2,3-2',3' fashion by two linkers have been reported, see: (a) Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1343–1344. (b) Izuoka, A.; Tachikawa, T.; Sugawara, T.; Saito, Y.; Shinohara, H. *Chem. Lett.* **1992**, 1049–1052. (c) Tachikawa, T.; Izuoka, A.; Sugawara, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1227–1229. (d) Wang, C.; Ellern, A.; Khodorkovsky, V.; Becker, J. Y.; Bernstein, J. *J. Chem. Soc., Chem. Commun.* **1994**, 2115–2116. (e) Aqad, E.; Becker, J. Y.; Bernstein, J.; Ellern, A.; Khodorkovsky, V.; Shapiro, L. *J. Chem. Soc., Chem. Commun.* **1994**, 2775–2776. (f) Simonsen, K. B.; Thorup, N.; Becher, J. *Synthesis* **1997**, 1399–1404. (g) Fujiwara, H.; Arai, E.; Kobayashi, H. *J. Mater. Chem.* **1998**, 829–832. (h) Simonsen, K. B.; Svenstrup, N.; Lau, J.; Thorup, J.; Becher, J. *Angew. Chem., Int. Ed.* **1999**, *38*, 1417–1420.

(7) Jeppesen, J. O.; Takimiya, K.; Thorup, N.; Becher, J. *Synthesis* **1999**, 803–810.

(8) For the deprotection–realkylation protocol using the cyanoethyl thiolate protecting group, see: Simonsen, K. B.; Becher, J. *Synlett* **1997**, 1211–1220, and references therein.



**Figure 2.**  $^1\text{H}$  NMR (300 MHz,  $\text{CD}_3\text{SOCD}_3$ ) spectrum of **6**.

is assigned to the isolated proton  $\text{H}_a$  on the central ring of the *m*-terphenyl moiety.<sup>5</sup> The upfield shift of this proton is probably due to the weakly shielding effect by the two flanking TTF moieties and/or the outer *m*-terphenyl rings.<sup>5</sup> The proton  $\text{H}_c$  appears as a one-proton triplet at  $\delta$  7.48 ppm with an ortho coupling ( $J = 7.6$  Hz). The remaining eight aromatic protons appear as a complex multiplet. The bridging methylene protons in **6** (i.e.,  $\text{TTFCH}_2\text{S}$  and  $\text{ArCH}_2\text{S}$ ) are not singlets but two overlapping AB quartets at  $\delta$  3.37 and  $\delta$  3.53 ppm ( $J = 14.6$  Hz) and  $\delta$  3.52 and  $\delta$  3.76 ppm ( $J = 11.4$  Hz), respectively. Heating the solution of **6** up to 80

(9) **Sample Procedure for the Preparation of Compound 6.** A mixture of compound **3**<sup>7</sup> (0.37 g, 0.72 mmol) and compound **2**<sup>5b</sup> (0.22 g, 0.37 mmol) in anhydrous THF–EtOH (60 mL, 2:1) was added dropwise over a period of 4 h to a suspension of excess sodium borohydride (0.35 g, 9.3 mmol) in anhydrous THF–EtOH (300 mL, 19:1) under bubbling  $\text{N}_2$  with vigorous stirring at rt. After addition was finished the orange reaction mixture was stirred for further 30 min, whereupon it was concentrated in vacuo to approximately 100 mL. Ice containing a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (80 mL) was added to precipitate the product as an orange yellow solid, which was collected by filtration, washed with  $\text{H}_2\text{O}$  ( $3 \times 20$  mL), and dried in vacuo. The crude product was purified by column chromatography (150 mL of silica gel, 4 cm  $\varnothing$ , eluent  $\text{CH}_2\text{Cl}_2/\text{EtOAc}$  24:1). The orange band ( $R_f = 0.15$ ) was collected and concentrated to give an orange solid, which was repeatedly dissolved in  $\text{CH}_2\text{Cl}_2$  ( $2 \times 20$  mL) and concentrated to give 0.13 g (31%) of analytically pure **6** as an orange solid. Recrystallization from  $\text{CHCl}_3/\text{MeOH}$  gave **6** as fine orange needles: mp 134–135 °C;  $^1\text{H}$  NMR (300 MHz,  $\text{CD}_3\text{SOCD}_3$ )  $\delta$  2.87 (t,  $J = 6.7$  Hz, 8H), 3.15 (t,  $J = 6.7$  Hz, 8H), 3.37 and 3.53 (AB q,  $J = 14.6$  Hz, 8H), 3.52 and 3.76 (AB q,  $J = 11.4$  Hz, 8H), 6.84 (t,  $J = 1.0$  Hz, 1H), 7.2–7.4 (m, 8H), 7.48 (t,  $J = 7.6$  Hz, 1H); MS (PD)  $m/z$  1212.4 ( $\text{M}^+$ ), calcd for  $\text{C}_{50}\text{H}_{42}\text{N}_4\text{S}_{16}$ , 1211.9; IR (KBr)  $\nu$  2250 (CN)  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{50}\text{H}_{42}\text{N}_4\text{S}_{16}$  (1211.9): C, 49.56; H, 3.49; N, 4.62; S, 42.33. Found: C, 49.38; H, 3.49; N, 4.57; S, 42.17.

°C in  $\text{CD}_3\text{SOCD}_3$  caused no change in the methylene parts. Furthermore, any significant change in the  $^1\text{H}$  NMR spectrum of **6** down to  $-70$  °C (in  $\text{CDCl}_3$ ) was not observed. Hence, it is likely that **6** adopts a rigid structure in which all four bridging sulfurs are equivalent.<sup>5</sup>

Solution oxidation potentials obtained from cyclic voltammograms (CVs) of new TTF cyclophanes are summarized in Table 1. CVs of compound **4** and **5** showed two reversible

**Table 1.** Oxidation Potentials  $E_{1/2}^1$  and  $E_{1/2}^2$  of TTF Cyclophanes **4**–**7** Determined by Cyclic Voltammetry<sup>a</sup>

compound	$E_{1/2}^1$ [V]	$E_{1/2}^2$ [V]	$\Delta E_p$ [V]
<b>4</b>	0.59	1.01	0.42
<b>5</b>	0.49	0.91	0.42
<b>6</b>	0.56	0.89 <sup>b</sup>	0.33
<b>7</b>	0.47	0.85	0.38

<sup>a</sup> Conditions: Ag/AgCl electrode, Pt electrode, 20 °C,  $\text{Bu}_4\text{NPF}_6$  (0.1 M in  $\text{CH}_2\text{Cl}_2$ ), scan rate 0.1  $\text{V s}^{-1}$ , [compound]  $10^{-3}$  M. <sup>b</sup> Quasi-reversible.

one-electron redox waves as expected. The bis(TTF)-cuppedophane **7** showed two reversible two-electron redox waves, whereas bis(TTF)cuppedophane **6** showed one reversible two-electron redox wave and one quasi-reversible two-electron redox wave.

In conclusion, we have demonstrated a general method for the preparation of TTF–cyclophanes from 2,3-bis-(2-cyanoethylthio)-6,7-bis(thiocyanatomethyl)tetrathiafulvalene (**3**). As a practical application, the first TTF-containing cuppedophanes, which are appealing systems for the preparation of charge-transfer inclusion complexes,<sup>6b,c</sup> were successfully prepared. Compound **6** represent a novel type of cuppedophane. The presence of four cyanoethyl thiolate protected functional groups in **6** opens up the possibility for the preparation of more sophisticated systems. Work is currently in progress to unleash this potential, together with mixing the donors **6** and **7** with  $\pi$ -electron acceptors such as tetracyanoquinodimethane (TCNQ), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), and  $\text{C}_{60}$ .

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**Supporting Information Available:** Detailed experimental procedures and complete characterization data for compounds **4**–**7**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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