ORGANIC LETTERS

2000
Vol. 2, No. 23
3547−3550

Self-Assembly of an Amphiphilic [2]Rotaxane Incorporating a Tetrathiafulvalene Unit

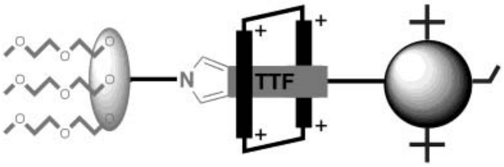
Jan Oskar Jeppesen,[†,‡] Julie Perkins,[†] Jan Becher,[‡] and J. Fraser Stoddart*,[†]

Department of Chemistry and Biochemistry, University of California, Los Angeles,
405 Hilgard Avenue, Los Angeles, California 90095-1569, and Department of
Chemistry, Odense University (University of Southern Denmark), Campusvej 55,
DK-5230, Odense M, Denmark

stoddart@chem.ucla.edu

Received July 27, 2000

ABSTRACT



The template-directed synthesis of a [2]rotaxane, in which a π-electron deficient ring component—cyclobis(paraquat-*p*-phenylene)—is assembled around a π-electron rich asymmetric monopyrrolotetrathiafulvalene unit on the rod section of an amphiphilic dumbbell component that is terminated by a hydrophilic dendritic stopper at one end and a hydrophobic tetraarylmethane stopper at the other end, is reported.

Catenanes and rotaxanes[1] are multicomponent functional assemblies comprising—in addition to covalent bonds—mechanical and noncovalent bonds that can become key elements in the operation of molecular devices.[2,3] In the case of rotaxanes, where a dumbbell component is encircled by a ring component, amphiphilic character, together with the presence of redox-active units in the two components, are desirable features that allows single-molecule-thick electrochemical junctions to be fabricated.[3] On account of their unique π-electron donating properties, tetrathiafulvalene (TTF) and their derivatives have found widespread use in materials chemistry.[4] Although a considerable range of catenanes and pseudorotaxanes,[1] incorporating a TTF unit in conjunction with the π-electron accepting tetracationic cyclophane,[5] cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}), have been reported,[6] a very few rotaxanes employing these particular components have been described to date in the literature.[6a,e,n] In addition, to the best of our knowledge, rotaxanes incorporating TTF units in dumbbell components

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[†] University of California, Los Angeles.

[‡] Odense University (University of Southern Denmark).

(1) (a) Fyfe, M. C. T.; Stoddart, J. F. *Acc. Chem. Res.* **1997**, *30*, 393−401. (b) Jäger, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930−944. (c) *Molecular Catenanes, Rotaxanes and Knots*; Sauvage, J.-P., Dietrich-Buchecker, C. O., Eds.; VCH−Wiley: Weinheim, 1999. (d) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643−1663.

(2) For a [2]catenane-based solid-state electronically reconfigurable switch, see: (a) Asakawa, M.; Higuchi, M.; Mattersteig, G.; Nakamura, T.; Pease, A. R.; Raymo, F. M.; Shimizu, T.; Stoddart, J. F. *Adv. Mater.* **2000**, *12*, 1099−1102. (b) Collier, C. P.; Mattersteig, G.; Wong, E. W.; Luo, Y.; Beverly, K.; Sampaio, J.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. *Science* **2000**, *289*, 1172−1175.

(3) For electronically configurable molecular-based logic gates, see: (a) Collier, C. P.; Wong, E. W.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F.; Kuekes, P. J.; Williams, R. S.; Heath, J. R. *Science* **1999**, *285*, 391−394. (b) Wong, E. W.; Collier, C. P.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F.; Heath, J. R. *J. Am. Chem. Soc.* **2000**, *122*, 5831−5840.

(4) For TTF reviews, see: (a) Adam, M.; Müllen, K. *Adv. Mater.* **1994**, *6*, 439−459. (b) Jørgensen, T.; Hansen, T. K.; Becher, J. *Chem. Soc. Rev.* **1994**, *23*, 41−51. (c) Bryce, M. R. *J. Mater. Chem.* **1995**, *5*, 1481−1496. (d) Garin, J. *Adv. Heterocycl. Chem.* **1995**, *62*, 249−304. (e) Schukat, G.; Fanghänel, E. *Sulfur Rep.* **1996**, *18*, 1−294. (f) Bryce, M. R. *J. Mater. Chem.* **2000**, *10*, 589−598. (g) Nielsen, M. B.; Lomholdt, C.; Becher, J. *Chem. Soc. Rev.* **2000**, *29*, 153−164.

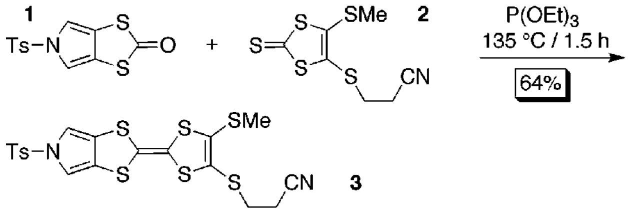
(5) (a) Philp, D.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 1584−1586. (b) Asakawa, M.; Dehaen, W.; L′abbé, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart J. F.; Williams, D. J. *J. Org. Chem.* **1996**, *51*, 9591−9595.

10.1021/ol006387s CCC: $19.00

comprising two *different* stoppers have been unknown hitherto, most likely because of the lack of an appropriate TTF building block. Now that such a building block in the shape of the pyrrolo[3,4-*d*]tetrathiafulvalene ring system[7] is available, we have self-assembled an asymmetric [2]rotaxane with a dumbbell component incorporating this asymmetric TTF unit situated in the rod section between a hydrophilic and hydrophobic stopper and encircled by CBPQT^{4+}. Here, we report this accomplishment.

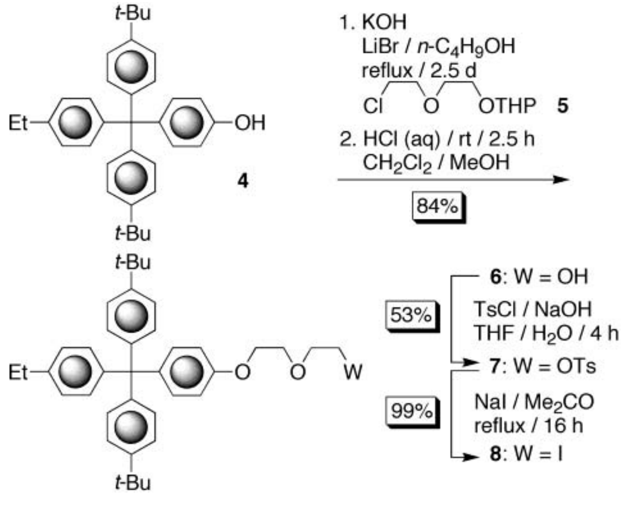
The asymmetric TTF building block **3** was synthesized as outlined in Scheme 1. Cross-coupling of (1,3)-dithiolo[4,5-*c*]pyrrole-2-one[7] (**1**) with 2 equiv of 4-(2-cyanoethylthio)-5-methylthio-1,3-dithiole-2-thione[8] (**2**) in neat P(OEt)$_3$ gave **3** (64%) in gram quantities after column chromatography.[9]

Scheme 1. Synthesis of the Asymmetric TTF Building Block



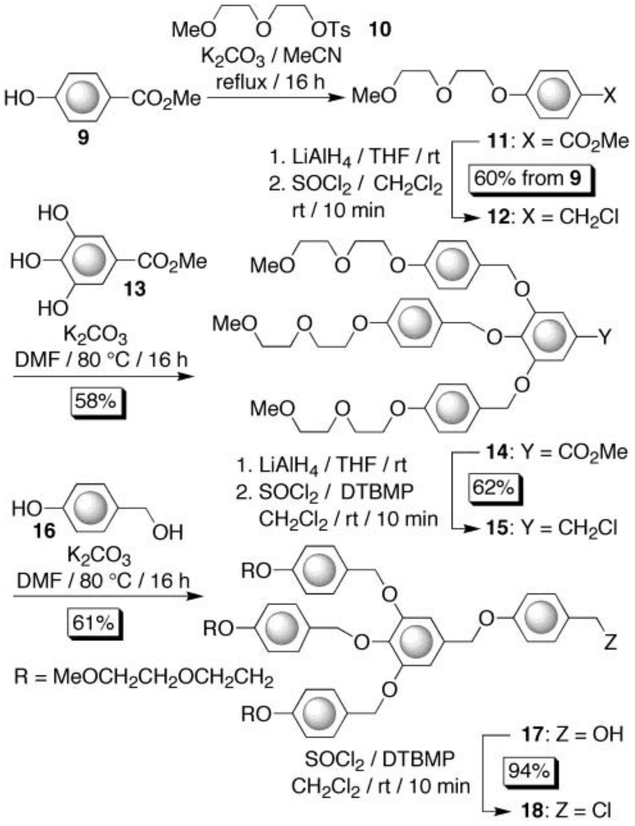
The hydrophobic stopper **6** was obtained (Scheme 2) in 84% yield by a modification of the procedure already reported in the literature.[10] 4-[Bis(4-*tert*-butylphenyl)(4-ethylphenyl)methyl]phenol[11] (**4**) was alkylated with [2-(2-chloroethoxy)ethoxy]tetrahydropyran[12] (**5**) in *n*-butanol, followed by removal of the THP protecting group with aqueous HCl. Tosylation (53%) of **6**, and subsequent treatment of **7** with NaI, gave (99%) the hydrophobic stopper **8**.

Scheme 2. Synthesis of the Hydrophobic Stopper



The synthesis of the hydrophilic stopper which is outlined in Scheme 3 follows a synthetic methodology first described by Percec and co-workers.[13] Methyl 4-hydroxybenzoate (**9**) was alkylated with toluene-4-sulfonic acid 2-(2-methoxyethoxy)ethyl ester[14] (**10**) in MeCN in the presence of K$_2$CO$_3$. The ester **11** was reduced with LiAlH$_4$ in THF, and the resulting benzyl alcohol was chlorinated with SOCl$_2$ in dry CH$_2$Cl$_2$, affording **12** in 60% overall yield for the three steps. Etherification of methyl 3,4,5-trihydroxybenzoate (**13**) with the benzyl chloride **12** was carried out in DMF in the

Scheme 3. Synthesis of the Hydrophilic Stopper



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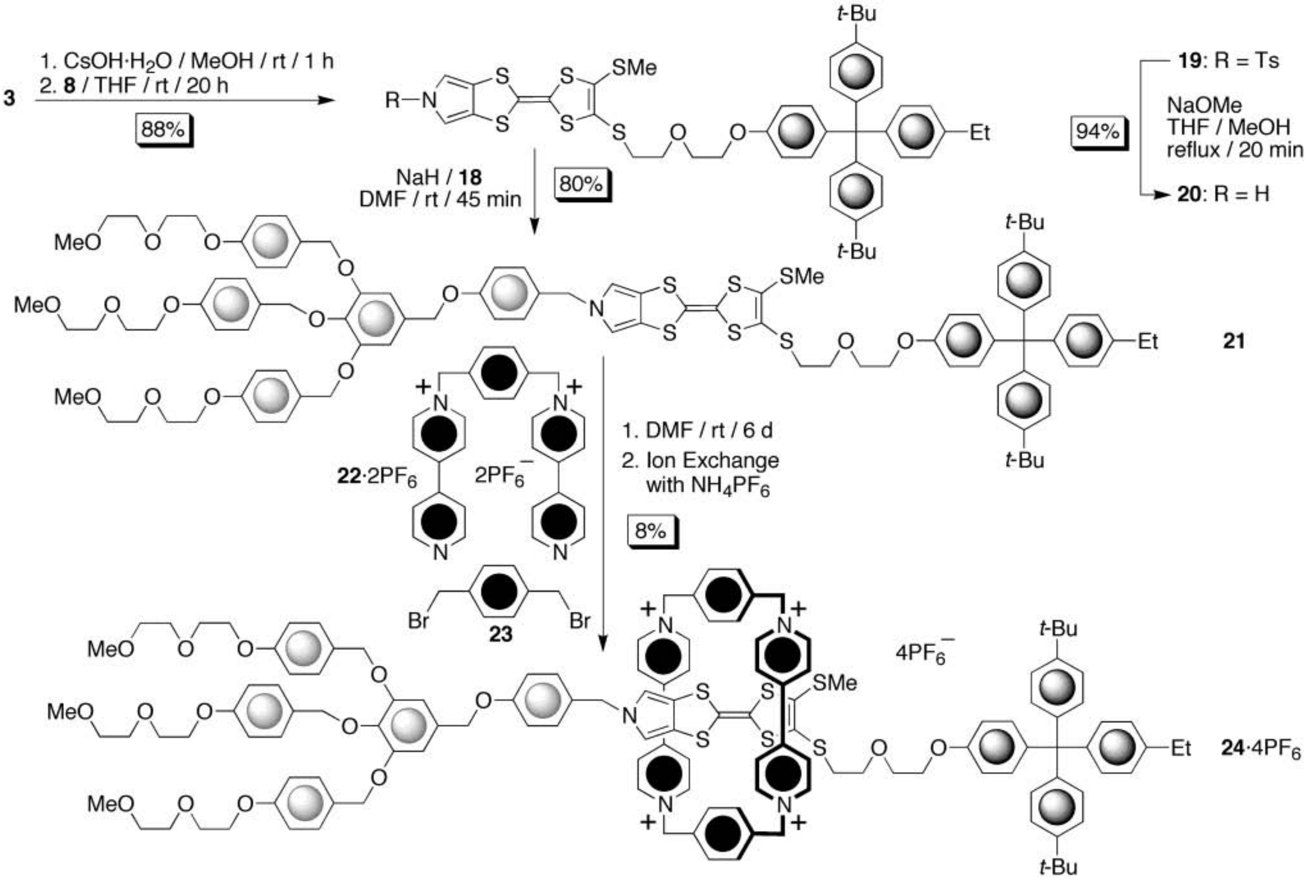
(6) For examples of catenanes, rotaxanes and pseudorotaxanes containing TTF, see: (a) Ashton, P. R.; Bissell, R. A.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 923−926. (b) Jørgensen, T.; Becher, J.; Chambron, J.-C.; Sauvage, J.-P. *Tetrahedron Lett.* **1994**, *35*, 4339−4342. (c) Li, Z.-T.; Stein, P. C.; Svenstrup, N.; Lund, K. H.; Becher, J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2524−2528. (d) Li, Z.-T.; Becher, J. *Chem. Commun.* **1996**, 639−640. (e) Li, Z.-T.; Stein, P. C.; Becher, J.; Jensen, D.; Mørk, P.; Svenstrup, N. *Chem. Eur. J.* **1996**, *2*, 624−633. (f) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Mattersteig, G.; Matthews, O. A.; Montalti, N.; Spencer, N.; Stoddart, J. F.; Venturi, M. *Chem. Eur. J.* **1997**, *3*, 1992−1996. (f) Li, Z.-T.; Becher, J. *Synlett* **1997**, 557−560. (g) Nielsen, M. B.; Li, Z.-T.; Becher. J. *J. Mater. Chem.* **1997**, *7*, 1175−1187. (h) Asakawa, M.; Ashton, P. R.; Balzani, V.; Credi, A.; Hamers, C.; Mattersteig, G.; Montalti, N.; Shipway, A. N.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 333−337. (i) Nielsen, M. B.; Thorup, N.; Becher, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1305−1308. (j) Credi, A.; Montalti, M.; Balzani, V.; Langford, S. J.; Raymo, F. M.; Stoddart, J. F. *New J. Chem.* **1998**, *22*, 1061−1065. (k) Asakawa, M.; Ashton, P. R.; Balzani, V.; Boyd, S. E.; Credi, A.; Mattersteig, G.; Menzer, S.; Montalti, M.; Raymo, F. M.; Ruffilli, C.; Stoddart, J. F.; Venturi, M.; Williams, D. J. *Eur. J. Org. Chem.* **1999**, 985−994. (l) Lau, J.; Nielsen, M. B.; Thorup, N.; Cava, M. P.; Becher, J. *Eur. J. Org. Chem.* **1999**, 3335−3341. (m) Balzani, V.; Credi, A.; Mattersteig, G.; Matthews, O. A.; Raymo, F. M.; Stoddart, J. F.; Venturi, M.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **2000**, *65*, 1924−1936. (n) Damgaard, D.; Nielsen, M. B.; Lau, J.; Jensen, K, B.; Zubarev, R.; Levillian, E.; Becher, J. *J. Mater. Chem.* **2000**, *10*, 2249−2258.

Scheme 4. Synthesis of the Dumbbell **21** and Self-Assembly of the [2]Rotaxane $\mathbf{24}\cdot 4PF_6$



presence of K_2CO_3, giving **14** in 58% yield. Compound **15** was prepared in 62% overall yield from (i) reduction of **14** with $LiAlH_4$, followed by (ii) chlorination of the benzyl alcohol by $SOCl_2$ in dry CH_2Cl_2 with 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) as proton trap. Compound **17** was obtained in 61% yield by the reaction of 4-hydroxybenzyl alcohol (**16**) with **15** in DMF in the presence of K_2CO_3. Finally, **17** was chlorinated, using conditions similar to those used for the preparation of **15**, in 94% yield.

The synthesis of the dumbbell **21** was achieved as outlined in Scheme 4. A solution of **3** in THF was treated with 1 equiv of $CsOH\cdot H_2O$. This procedure generated the TTF-monothiolate, which was subsequently alkylated with 1 equiv of the hydrophobic stopper **8**, affording the TTF derivative **19** in 88% yield. Removal of the tosyl protecting group was carried out in near quantitative yield by refluxing **19** in a 1:1 mixture of THF−MeOH in the presence of an excess of NaOMe. An 80% yield of the dumbbell[15] **21** was obtained following *N*-alkylation of the pyrrole unit in **20** with the hydrophilic stopper **18** in DMF containing NaH. Finally, the [2]rotaxane[16] $\mathbf{24}\cdot 4PF_6$ was self-assembled in 8% yield[17] using the dumbbell **21** as the template for the formation of interlocked cyclobis(paraquat-*p*-phenylene) tetracation from the dicationic precursor[18] $\mathbf{22}\cdot 2PF_6$ and 1,4-bis(bromomethyl)-benzene (**23**) (Scheme 4).

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(7) Recently, two of us developed an efficient synthesis of the pyrrolo-[3,4-*d*]tetrathiafulvalene ring system using a simple and nonclassical pyrrole synthesis. See: (a) Jeppesen, J. O.; Takimiya, K.; Jensen, F.; Becher, J. *Org. Lett.* **1999**, *1*, 1291−1294. (b) Jeppesen, J. O.; Takimiya, K.; Jensen, F.; Brimert K.; Nielsen, K.; Thorup, N.; Becher J. *J. Org. Chem.* **2000**, *65*, 5794−5805.

(8) Simonsen, K. B.; Svenstrup, N.; Lau, J.; Simonsen, O.; Mørk, P.; Kristensen, G. J.; Becher, J. *Synthesis* **1996**, 407−418.

(9) Although the synthesis of **3** has been described before in the literature (see ref 7b), it was prepared by a different route and only on a very small scale.

(10) Ashton, P. R.; Ballardini, R.; Balzani, V.; Belohradsky, M.; Gandolfi, M. T.; Philp, D.; Prodi, L.; Raymo, F. M.; Reddington, M. V.; Spencer, N.; Stoddart, J. F.; Venturi, M.; Williams, D. J.*J. Am. Chem. Soc.* **1996**, *118*, 4931−4951.

(11) Although we have previously used (see ref 10) compound **4** as its potassium salt in alkylations, we now prefer to isolate it directly as the phenol after an acid-catalyzed reaction between bis(4-*tert*-butylphenyl)-4-ethylphenylmethanol and phenol, followed by silica gel column chromatography and recrystallization from hexane.

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(13) Percec, V.; Cho. W.-D.; Mosier, P. E.; Ungar, G.; Yeardley, D. J. P. *J. Am. Chem. Soc.* **1998**, *120*, 11061−11070 and references therein.

(14) Satoru, I.; Hideo, M.; Kiyoshi, T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1357−1360.

(15) **Data for dumbbell 21:** ^1H NMR (400 MHz, CD_3COCD_3, 298 K) δ 1.17 (t, $J = 7.6$ Hz, 3H), 1.26 (s, 18H), 2.39 (s, 3H), 2.57 (q, $J = 7.6$ Hz, 2H), 3.02 (t, $J = 6.3$ Hz, 2H), 3.26 (s, 9H), 3.44−3.49 (m, 6H), 3.59−3.64 (m, 6H), 3.72 (t, $J = 6.3$ Hz, 2H), 3.76−3.81 (m, 8H), 4.05−4.13 (m, 8H), 4.88 (s, 2H), 4.97 (s, 2H), 5.00 (s, 2H), 5.01 (s, 4H), 6.70 and 6.72 (AB q, $J = 2.1$ Hz, 2H), 6.79 (d, $J = 8.7$ Hz, 4H), 6.84 (s, 2H), 6.89−6.94 (m, 6H), 7.03−7.16 (m, 12H), 7.25−7.33 (m, 6H), 7.37 (d, $J = 8.8$ Hz, 4H); MS(FAB) m/z 1736 (M^+). Anal. Calcd for $C_{98}H_{113}NO_{15}S_6$ (1737.3): C, 67.75; H, 6.56; N, 0.81. Found: C, 67.61; H, 6.46; N, 0.80.

The fast atom bombardment mass spectrum (FAB-MS) of the [2]rotaxane **24**·4PF$_6$ is illustrated in Figure 1 and shows peaks corresponding to the [M − PF$_6$]$^+$, [M − 2PF$_6$]$^+$, and [M − 3PF$_6$]$^+$ as well as for [M − 2PF$_6$]$^{2+}$, [M − 3PF$_6$]$^{2+}$, and [M − 4PF$_6$]$^{2+}$ ions. A comparison of the ^{1}H NMR spectra (CD$_3$COCD$_3$, 298 K) of the dumbbell **21** and the [2]rotaxane **24**·4PF$_6$ revealed (Table 1) significant changes in the chemical shift of the signals associated with the protons located close to the TTF unit. Furthermore, the UV−vis spectrum of the [2]rotaxane **24**·4PF$_6$ recorded in Me$_2$CO shows a broad charge transfer (CT) absorption band centered on 810 nm, which is characteristic of structures containing a TTF unit located “inside” the tetracationic cyclophane[19] CBPQT^{4+}. These observations clearly suggest, that, in solution at least, the tetracationic cyclophane encircles the TTF unit in the [2]rotaxane **24**·4PF$_6$.

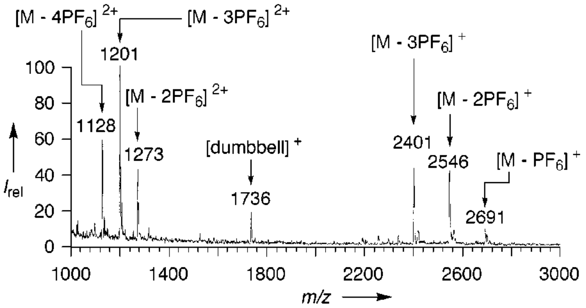

Figure 1. FAB-MS spectrum of the [2]rotaxane **24**·4PF$_6$.

Table 1. Selected ^{1}H NMR Spectroscopic Data (δ and $\Delta\delta$ Values in ppm) for the Dumbbell **21** and the [2]Rotaxane **24**·4PF$_6$ in CD$_3$COCD$_3$ at 298 K

compd	SC*H*$_3$	SC*H*$_2$CH$_2$O	SCH$_2$C*H*$_2$O	NC*H*$_2$Ar	Pyr-H
21	2.39	3.02	3.72	4.88	6.71
24·4PF$_6$	2.64	3.29	3.95	5.18	6.44
	+0.25	+0.27	+0.23	+0.30	−0.27

In summary, we have devised and completed the synthesis of a dumbbell-shaped component employing the recently developed[7] asymmetric monopyrrolo-TTF unit in its rod section to direct the attachment in a stepwise manner of first a hydrophobic and then second a hydrophilic stopper. This dumbbell was used subsequently as a template in self-assembling a [2]rotaxane. While these new amphiphilic redox-active components are being assessed for their abilities to self-organize into monolayers—as a prelude to their introduction into devices[3]—with single-molecule-thick electrochemical junctions, we are extending the synthetic methodology disclosed in this Letter to the construction of more elaborate amphiphilic [2]rotaxanes containing additional recognition sites in their rod components so that ring components can be induced to shuttle mechanically between two states, thereby functioning as an array of electronic switches.

Acknowledgment. We thank DARPA and Hewlett-Packard for generous financial support and the University of Odense for a Ph.D. Scholarship to J.O.J.

Supporting Information Available: Experimental procedures for **21** and **24**·4PF$_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) **Data for [2]rotaxane 24•4PF$_6$:** ^{1}H NMR (400 MHz, CD$_3$COCD$_3$, 298 K) δ 1.19 (t, J = 7.6 Hz, 3H), 1.28 (s, 18H), 2.60 (q, J = 7.6 Hz, 2H), 2.64 (s, 3H), 3.28 (s, 6H), 3.29 (s, 3H), 3.29 (t, J = 6.4 Hz, 2H), 3.47−3.50 (m, 6H), 3.61−3.65 (m, 6H), 3.77−3.81 (m, 6H), 3.95 (t, J = 6.4 Hz, 2H), 3.98−4.01 (m, 2H), 4.08−4.14 (m, 6H), 4.23−4.25 (m, 2H), 4.69 (s, 2H), 4.80 (s, 4H), 4.97 (s, 2H), 5.18 (s, 2H), 5.98−6.08 (m, 8H), 6.43 and 6.45 (AB q, J = 2.1 Hz, 2H), 6.78 (s, 2H), 6.83−6.85 (m, 4H), 6.94 (d, J = 8.7 Hz, 4H), 7.07−7.12 (m, 10H), 7.18 (d, J = 8.6 Hz, 2H), 7.26−7.31 (m, 10H), 7.38 (bs, 4H), 7.69 (d, J = 8.7 Hz, 2H), 7.94−8.06 (m, 8H), 8.45 (bs, 4H), 9.16 (bs, 4H), 9.48 (bs, 4H); MS(FAB) *m/z* 2691 (M − PF$_6$)$^+$, 2546 (M − 2PF$_6$)$^+$, 2401 (M − 3PF$_6$)$^+$, 1736 (dumbbell)$^+$, 1273 (M − 2PF$_6$)$^{2+}$, 1200.5 (M − 3PF$_6$)$^{2+}$, 1128 (M − 4PF$_6$)$^{2+}$; UV−vis (Me$_2$CO) λ_{max} 810 nm, (ϵ 1400 L mol^{-1} cm^{-1}). Anal. Calcd for $C_{134}H_{145}F_{24}N_5O_{15}P_4S_6\cdot 2H_2O$ (2837.6): C, 56.00; H, 5.23; N, 2.44. Found: C, 56.07; H, 5.06; N, 2.28.

(17) Unreacted dumbbell can be recovered and reused.

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(19) Devonport, W.; Blower, M. A.; Bruce, M. R.; Goldenberg, L. M. *J. Org. Chem.* **1997**, *62*, 885−887.