Synthesis and Characterisation of Macrobicyclic Tetrathiafulvalene-Bridged Cage Molecules

Philippe Blanchard[a,b], Niels Svenstrup[a], Joëlle Rault-Berthelot[b], Amédée Riou[c], and Jan Becher*[a]

Department of Chemistry, Odense University[a],
Campusvej 55, DK-5230 Odense M, Denmark
Fax: (internat.) + 45-66/158780
E-mail: JBE@chem.ou.dk

IMMO, UMR CNRS 6501, Faculté des Sciences of Angers[b],
2 Bd Lavoisier, F-49045 Angers, France

Laboratoire d'Electrochimie Organique, UMR CNRS 6510, Université Rennes I[c],
Campus de Beaulieu, Av. Général Leclerc, F-35042 Rennes, France

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A series of new macrobicyclic tetrathiafulvalenophanes of type **1** and **2** with three tetrathiafulvalene bridges has been prepared under high-dilution conditions using a stepwise selective protection-deprotection of tetrathiafulvalenethiolates. All the macrobicyclic tetrathiafulvalenes, along with the intermediate compounds **5** and **6** and the unexpected tetrathiafulvalene pentamers **17**, were studied by cyclic voltammetry. An electrochemical investigation using the Bard-Anson equation and thin-layer cyclic voltammetry has been carried out, allowing an estimate of the number of electrons involved in each redox process of these multi-redox compounds. The X-ray crystal structure showing the unusual crystal packing of **2a** is also presented.

Introduction

The molecular design of three-dimensionally bridged macropolycyclic compounds is currently a challenge in synthetic chemistry[1] and incorporation of redox-active groups into such molecules is of interest for the preparation of macropolycyclic receptor molecules and "smart" catalytic systems.[2] With the proper design, systems of this type can in principle be designed to signal electrochemically the selective binding of any charged or neutral guest. Tetrathiafulvalene (TTF) is a well-known redox-active compound whose electrochemical properties have been extensively and principally used for the generation of conducting or even superconducting organic materials.[3] However, since the first tetrathiafulvalenocyclophane prepared by Staab et al. in 1980,[4] the focus of attention has gradually shifted towards the development of more complex tetrathiafulvalene systems. For example, various tetrathiafulvalene-like cyclophanes[5][6] such as double-bridged or even quadruple-bridged tetrathiafulvalenophanes ("belts")[7] with two tetrathiafulvalene units have been described recently. The recent combination of tetrathiafulvalene chemistry and supramolecular chemistry has led to the construction of new elaborated systems[8] such as crown ethers,[9] aza-[5c][9d] and thiacrowns,[10] a copper(I) [2]-catenate incorporating one tetrathiafulvalene unit,[11] a tetrathiafulvalene cryptand,[12] a tetrathiafulvalene rotaxane,[13] and cyclodextrin-TTF assemblies.[14] But until now, the preparation of highly symmetrical macrobicyclic molecules containing three or more tetrathiafulvalene units has not been reported. It would be interesting to study such molecular objects, and in addition to their potential use in conducting organic materials or in host-guest chemistry, these molecules can be seen as models for the study of electronic interactions between several redox-active centers.

Most of the tetrathiafulvalenes incorporated into macrocyclic compounds mentioned above have been prepared by a coupling reaction between two 1,3-dithiole moieties, generating the central fulvalene double bond of the tetrathiafulvalene in the final synthetic step, but a number of complications arise from the use of this strategy, most notably the lack of control over the macrocyclisation, the harsh reagents employed in the coupling reaction and the long synthetic routes involved in making analogous members of a series.[3a] Only few compounds of this type have previously been prepared using preformed mono- or bifunctionalised tetrathiafulvalenes. Thus, although a lot of complex molecules containing tetrathiafulvalene building blocks have been successfully prepared, further improvements in this research area requires new synthetic tools.

We have recently developed a strategy for the incorporation of preformed tetrathiafulvalenes into macrocyclic compounds.[15] This methodology is based on the facile protection-deprotection of tetrathiafulvalenethiolates and their subsequent in situ alkylation. We have earlier successfully applied this strategy for the synthesis of larger assemblies such as macrocyclic tetrathiafulvalenes,[15b][16] oligomeric tetrathiafulvalenes,[17] tetrathiafulvalene-based catenanes and rotaxanes,[18] and stable macrocyclic donor-acceptor

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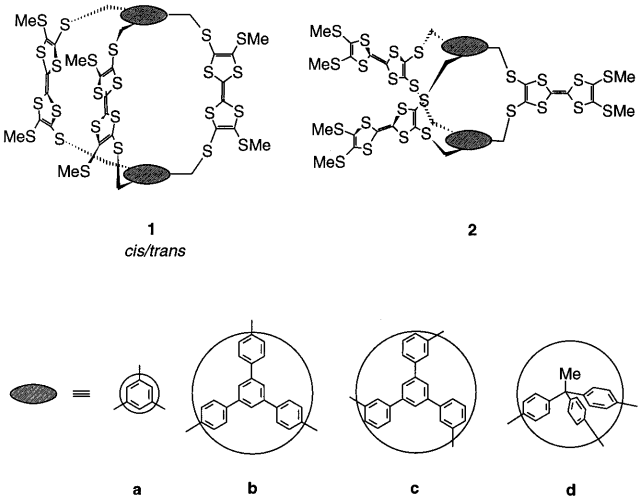
systems.[19] As an extension of this strategy, we have previously reported our preliminary findings on the synthesis of the first macrobicyclic tetrathiafulvalenophanes with three tetrathiafulvalene bridges grafted on aromatic spacers.[20] In this paper, we report the full experimental details on the synthesis of molecules **1** and **2**, including several new examples which have increased the range of molecules in this series, and report for the first time the crystal structure of **2a**, as well as cyclic voltammetry studies of the macrocycles.

Scheme 1



Results and Discussion

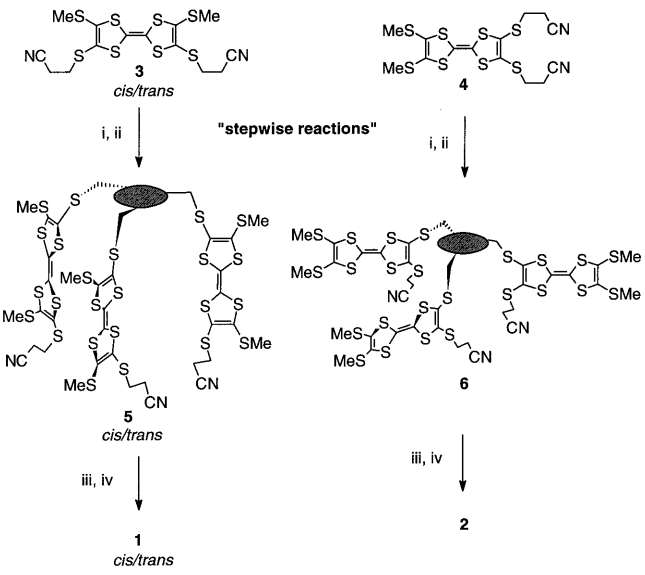
Synthesis

As mentioned in the previous section, our strategy is based on the facile deprotection of tetrathiafulvalenethiolates protected by cyanoethyl groups. The cyanoethyl groups are easily eliminated as acrylonitrile on treatment with caesium hydroxide monohydrate generating the thiolates which can subsequently be functionalised by reaction with a wide range of electrophiles. In a first attempt, the "simpler" and faster strategy of construction of the macrobicyclic compounds,[1] a synthetic strategy involving a six-fold bond formation under high-dilution conditions was tested, more specifically the reaction of three identical tetrathiafulvalenedithiolates with two identical tris-electrophiles.

The actual synthesis performed was the reaction between three tetrathiafulvalenebis(thiolates) and two aromatic spacers bearing three bromomethyl groups, in this case tris-(bromomethyl)benzene, in an attempt to prepare **1a**. Unfortunately, it results in the precipitation of an insoluble yellow powdery oligomeric or polymeric product which proved difficult to characterise, and the desired product **1a** was observed only in trace amounts along with significant amounts of other by-products in the mother liquor. Evidently, more control in the macrocyclisation step was needed to prevent the formation of linear oligomeric by-products, and consequently a stepwise strategy appeared to be necessary.

The synthesis of the macrobicyclic tetrathiafulvalenophanes of type **1** and **2** is outlined in Scheme 2. The first step of our reaction scheme involves the selective mono-deprotection of one of two different bis-protected tetrathiafulvalenethiolates recently described,[15a][b] namely 2,6(7)-bis(2′-cyanoethylthio)-3,7(6)-bis(methylthio)tetrathiafulvalene **3** (mixture of *cis* and *trans* isomers) and 2,3-bis(2′-cyanoethylthio)-6,7-bis(methylthio)tetrathiafulvalene **4**. One thiolate is generated and *S*-alkylated with the desired tris(bromomethyl) compound in the appropriate stoichiometry affording tris(tetrathiafulvalenes) of type **5** and **6**. Finally, the three latent thiolates of compounds **5** and **6** were generated using caesium hydroxide monohydrate, and the macrobicyclic triply bridged cyclophanes were synthesised by a tripod-tripod coupling with the corresponding tris(bromomethyl) compound under high-dilution conditions.

Scheme 2

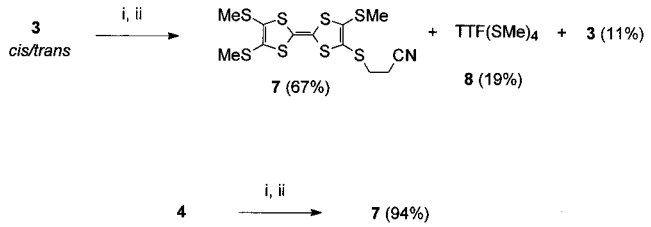


i) $CsOH{\cdot}H_2O$ (1.05 equiv.), MeOH, DMF, room temp., N_2; ii) tribromide (0.33 equiv.), DMF, room temp., N_2; iii) $CsOH \cdot H_2O$ (3.15−3.6 equiv.), MeOH, DMF, room temp., N_2; iv) tribromide (1 equiv.), DMF, high dilution, room temp., N_2.

The selectivity of the mono-deprotection of tetrathiafulvalenes of type **3** and **4** is different, however (Scheme 3), with the mono-deprotection of **4** being the cleanest by far. A simple experiment shows that slow addition at room temperature of $CsOH \cdot H_2O$ (1.05 eq.), dissolved in methanol, to an *N,N*-dimethylformamide solution of **3** (1 eq.), followed by methylation using an excess of iodomethane, gives a mixture of three products which can be separated by chromatography on silica gel. The desired 2-(2′-cyanoethylthio)-3,6,7-tris(methylthio)tetrathiafulvalene **7** is obtained in 67% yield along with tetrakis(methylthio)tetrathiafulvalene **8** resulting from a bis-deprotection, and unconverted starting

material **3**. On the contrary, by subjecting **4** to the same conditions, **7** is formed as essentially the only product in 94% isolated yield as shown by us earlier.[17] Thus, tris(tetrathiafulvalene) **5** will inherently be produced in lower yield and will involve a more elaborate purification step than does tris(tetrathiafulvalene) **6**.

Scheme 3



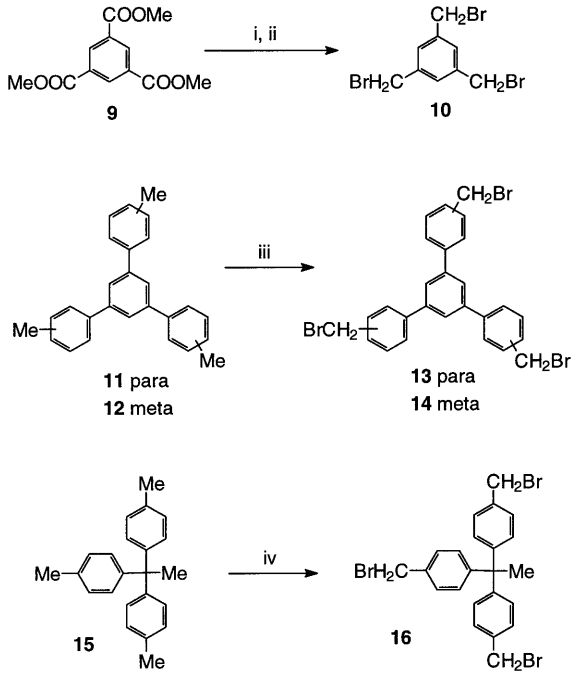
i) $CsOH \cdot H_2O$ (1.1 equiv.), MeOH, DMF, room temp., N_2; ii) MeI excess.

The preparation of tris(bromomethyl)aryl compounds has been described in the literature (Scheme 4). 1,3,5-Tris(bromomethyl)benzene (**10**) was readily obtained starting from trimethyl 1,3,5-benzenetricarboxylate (**9**) using the convenient one-pot synthesis of aralkyl bromides by reductive halogenation of aromatic carbonyl compounds described by Demerseman et al.[21] 1,3,5-Tris[4-(bromomethyl)phenyl]benzene[22] (**13**), 1,3,5-tris[3-(bromomethyl)phenyl]benzene[22] (**14**), and 1,1,1-tris[4-(bromomethyl)phenyl]-ethane[23] (**16**) were prepared by radical bromination of their corresponding methyl derivatives **11**, **12**, and **15** using *N*-bromosuccinimide (3 equiv.) following the procedure reported by Vögtle et al. The NBS bromination route is much less convenient than the Demerseman bromination protocol, as the tris(bromomethyl) compounds prepared by NBS bromination are always contaminated by products of asymmetric bromination and overbromination (detected by ^{1}H-NMR and electron-impact mass spectrometry) due to the unselective nature of the reagent. Purification of the reaction mixture employing the experimental procedure already reported, afforded compounds **13**, **14**, and **16** in 68%, 60%, 72% of purity respectively [HPLC analysis, reverse phase Nucleosil 5 C_{18}, CH_3CN/H_2O (9:1), 274 nm]. Further purification by column chromatography and recrystallisations (see Experimental Section) allowed us to isolate the desired compounds **13** and **14** in 93% and 69% purity respectively.

Cage Syntheses

For the synthesis of the tetrathiafulvalene cages we employed a strategy developed in our group, based on thiolate alkylation of an in situ generated thiolate function. Thiolate alkylations are highly efficient reactions, which have proven to be generally applicable for the synthesis of macropolycyclic compounds.[24] Thus, upon treatment of a DMF solution of a mixture of *cis*/*trans* isomers of the tetrathiafulvalene **3** (1 equiv.) with caesium hydroxide monohydrate (1.05 equiv.) in methanol and subsequent alkylation with **10**, **13**, **14**, and **16** (0.32 equiv.) in DMF, tris(tetrathiafulvalenes) **5a−d** were obtained in the range of 27−37% yields after purification by column chromatography on silica gel (see

Scheme 4



i) $LiAlH_4$, Et_2O, reflux 1 h, N_2; ii) HBr(g), −30°C to room temp.; iii) NBS, AIBN, CCl_4, reflux 3 h; iv) NBS, AIBN, hν, CCl_4, reflux 1.5 h.

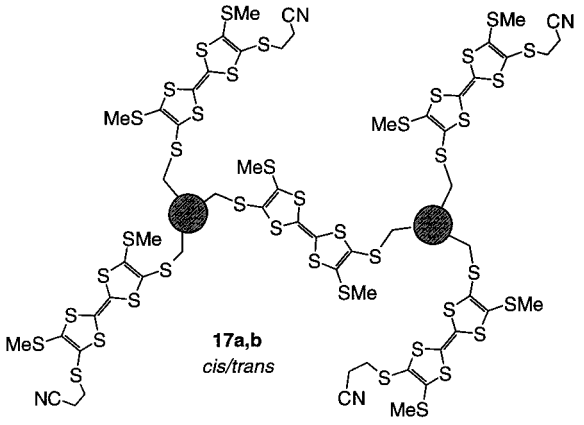
Table 1). Under the same conditions, but starting from tetrathiafulvalene **4**, tris(tetrathiafulvalenes) **6a−d** were prepared in significantly higher yields than the tris(tetrathiafulvalenes) **5**, for the reasons mentioned above. Note that compounds **5** were obtained as a mixture of four *cis*/*trans* isomers which could not be separated by column chromatography on silica gel. Whereas purification of tris(tetrathiafulvalene) **6** was easily achieved (essentially one spot in TLC), several by-products were observed during chromatographic separation of tris(tetrathiafulvalene) **5**. The most prominent by-product resulting from alkylation of a combination of one bis-deprotected and four mono-deprotected tetrathiafulvalenes by the tribromide compound afforded pentakis(tetrathiafulvalene) **17** as a mixture of isomers (Scheme 5). Although this reaction seems to be general during the preparation of compounds of type **5** as evidenced by TLC, we only isolated and characterised compounds **17a** and **17b** in 18% and 11−16% yield, respectively. These oligomeric tetrathiafulvalenes are fully characterised and stable under atmospheric conditions. Recently, Bryce et al. prepared and characterised a new air-stable dendritic molecule incorporating thirteen tetrathiafulvalene units[25a] while in a previous paper, a dodecakis(tetrathiafulvalene) derivative was unstable.[25b] The pentakis(tetrathiafulvalenes) **17**, having four protected thiolates, may be used as precursors to dendritic molecules containing multiple redox units.[26][27][28]

Construction of the macrobicyclic compounds **1** and **2** was achieved by the simultaneous addition of a DMF/MeOH solution of the fully deprotected tetrathiafulvalene-thiolate **5** or **6** (1 equiv.) and a DMF solution of the appro-

Table 1. Isolated yields after purification by chromatography for **1**, **2**, **5**, and **6**

Compound	Yield (%)			
	a	**b**	**c**	**d**
5	27−30	34−36	37	36
6	74−77	75	73	84
1	43	39	37	40
2	68	32	22	30

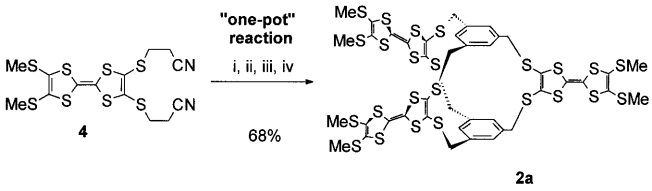
Scheme 5



priate tribromide **10**, **13**, **14**, or **16** (1 equiv.) to neat DMF under high dilution conditions using a perfusor pump. The new macrobicyclic tetrathiafulvalenes were isolated as yellow or orange amorphous powders after purification by column chromatography on silica gel using CH_2Cl_2/light petroleum ether (1:1) as eluent. The synthetic yields obtained for **1a−d** and **2a−d** are collected in Table 1. Except for **2a**, which was obtained in exceptionally high yield, the yields of **1** were only slightly better than those obtained for **2**.

Considering the high yield in the individual steps of the synthesis of the macrocycle **2a**, a one-pot reaction was envisaged (Scheme 6). Thus, using the same reaction conditions as before, the clean reaction mixture (as evidenced by TLC) containing the freshly generated tris(tetrathiafulvalene) **6a** was immediately treated with caesium hydroxide to cleave off the remaining protecting groups. The resulting trithiolate was realkylated by the dropwise addition 0.33 equiv. of 1,3,5-tris(bromomethyl)benzene (**10**) to give **2a** as the only product in 68% yield after the usual purification by column chromatography. This result demonstrates the efficiency of each individual step since a one-pot reaction of this type would be impossible if an incomplete synthetic step was involved. The synthesis of **2a** is an example of an assisted self-assembly reaction, since all the individual components of the macrocycle appear to be pre-programmed for cyclisation due to their complementary geometry. It is rare that a reaction, in which 6 new covalent bonds and 2 macrocyclic rings are formed, proceeds in such a high yield.

Scheme 6



i) $CsOH \cdot H_2O$ (1.05 equiv.), MeOH, DMF, room temp., N_2; ii) tribromide **10** (0.33 equiv.), DMF, room temp., N_2; iii) $CsOH \cdot H_2O$ (1.05 equiv.), MeOH, DMF, room temp., N_2; iv) tribromide **10** (0.33 equiv.), DMF, room temp., N_2.

Characterisation by Spectral Analyses

^{1}H-NMR spectra of compounds **5** (Table 2) show the presence of *cis*/*trans* isomers, demonstrated by two different signals for each methylene group of the cyanoethylthio group and two signals also for the methylthio groups in the β-position of the cyanoethylthio substituents. Compounds **6** displays much simpler ^{1}H- and ^{13}C-NMR spectra. One may note that the proton signals of the cyanoethylthio groups of **6** are slightly shifted upfield compared to those of **5** (on average 0.27 ppm for SCH_2 and 0.14 ppm for CH_2CN) indicating a stronger influence of the shielding effect by aromatic spacers in **6**. That is maybe why the triplets of **6b** and **6c** assigned to the SCH_2 moiety of the cyanoethylthio group are observed at lower chemical shifts than

Table 2. ^{1}H-NMR chemical shifts of tris(tetrathiafulvalenes) **5** and **6**

Compound	Chemical shifts (δ values relative to TMS)						
	CH_3 (s)	SCH_3 (s)	SCH_3 (s)[b]	SCH_2 (t)	CH_2CN (t)	$ArCH_2S$ (s)	Aromatic H
5a	−	2.32	2.47 and 2.48	2.71 and 2.72	3.03 and 3.04	3.97	7.18 (s)
5b	−	2.27 and 2.28	2.44 and 2.45	2.67 and 2.68	2.99 and 3.00	4.07	7.43 (d), 7.64 (d), 7.74 (s)
5c	−	2.27	2.42 and 2.43	2.65 and 2.66	2.97 and 2.99	4.12	7.35 (d), 7.45 (dd), 7.62 (d), 7.67 (s), 7.79 (s)
5d	2.11	2.26 and 2.27	2.45 and 2.46	2.68 and 2.69	3.03 and 3.15	3.98	7.02 (d), 7.21 (d)
6a	−	2.44	2.45	2.48	2.90	4.02	7.22 (s)
6b	−	2.42 (18 H)	2.34	2.84	4.09	7.42 (d), 7.67 (d), 7.77 (s)	
6c	−	2.38	2.41	2.36	2.82	4.14	7.34 (d), 7.45 (dd), 7.66 (d), 7.69 (s), 7.82 (s)
6d	2.14	2.41	2.43	2.48	2.89	4.03	7.04 (d), 7.23 (d)

[a] 250 MHz, $CDCl_3$ at 25°C. − [b] In β position of the cyanoethylthio group.

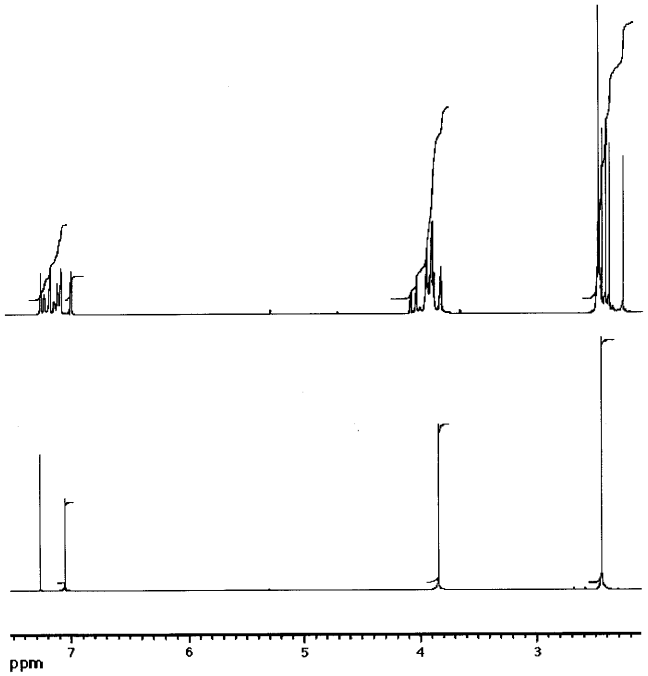
Table 3. ^{1}H-NMR chemical shifts of macrobicycles **1** and **2**

Compound	Chemical shifts (δ values relative to TMS)			
	CH_3	SCH_3	$ArCH_2S$	Aromatic H
1a	–	2.38−2.49 (m)	3.83-4.09 (m)	6.99−7.23 (m, 6 H)
1b	–	2.01−2.26 (m)	3.94-4.08 (m)	7.06−7.63 (m, 30 H)
1c	–	2.14−2.25 (m)	3.95-4.00 (m)	7.23−7.42 (m, 12 H), 7.53−7.58 (m, 12 H), 7.70−7.75 (m, 6 H)
1d	1.25−2.46 (m, 24 H)	3.75-3.96 (m)	6.61−7.23 (m, 24 H)	
2a	–	2.44 (s)	3.84 (s)	7.06 (s, 6 H)
2b	–	2.42 (s)	3.99 (s)	7.16 (d, 12 H), 7.28 (d, 12 H), 7.33 (s, 6 H)
2c	–	2.24 (s)	3.70 (s)	7.15−7.43 (m, 30 H)
2d ("out-out")	2.06 (br. s, 6 H)	2.42 (s)	3.85 (s)	6.91 (d), 7.06 (d)
2d ("in-out")	1.17 (br. s, 3 H "in") (m) 2.10 (br. s, 3 H "out")	2.40 and 2.42 (2s)	3.94 and 4.07 (s)	6.96−7.02 (m), 7.15−7.22 (m)

[a] 250 MHz, $CDCl_3$ at 25°C.

the primary methyl signal of the methylthio groups. Due to the *cis*/*trans* isomers, it is difficult to assign the ^{1}H-NMR spectra of the macrobicyclic systems **1** (Table 3). However, **1** displays three different main multiplets assigned to $-SCH_3$, $-SCH_2-$, and aromatic protons (Figure 1). CPK models show that protons of different *cis*/*trans* isomers can be subjected to a shielding or a deshielding effect due to the diamagnetic anisotropy of the aromatic spacers. Consequently, each of the three types of signal ($-SCH_3$, $-SCH_2-$, and aromatic H) give broad multiplets. In the case of the macrobicyclic compounds **2**, the aromatic protons are shielded compared to **6** and have relatively low chemical shifts compared to those of **1** (except for **2d**) indicating relatively stronger interactions between the aromatic spacers in **2** due to the small size of the cavity of **2**. The high symmetry of **2a** is clearly evident in its extremely simple ^{1}H-NMR spectrum, which displays three sharp singlets at δ = 7.06 (aromatic H), δ = 3.84 ($-SCH_2-$) and δ = 2.44 ($-SCH_3$) in the ratio of 1:2:3. This ^{1}H-NMR spectrum is only consistent with the macrobicyclic compound **2a** having an overall D_{3h} symmetry in $CDCl_3$ solution on the NMR time scale at room temperature. The ^{13}C-NMR spectrum of **2a** likewise reflects the high symmetry of the molecule: 8 lines in total (2 in the aliphatic and 6 in the aromatic region) is evident of the high symmetry of **2a**. On the contrary, compound **2d** exhibits a more complicated spectrum, as **2d** is an approximately 2:1 mixture of two different cage compounds (Scheme 7), namely one symmetrical cage (D_{3h} symmetry) with two methyl groups pointing out of the cavity ("out-out" isomer) and one unsymmetrical cage with one methyl group pointing into the cavity and one pointing out of the cavity ("in-out" isomer). The "in" methyl group is significantly shielded compared to the "out" methyl group as evidenced by its signal's upfield shift (δ_{in} = 1.17 and δ_{out} = 2.10). CPK models suggest that the construction of such an "in-out" isomer is sterically possible whereas the "in-in" isomer cannot be prepared, except in **1d**. Although not often observed, the in/out isomerism is a well-known feature of bridged bicyclic structures containing small or medium-sized rings[29] as reported by Vögtle et al,[30] who, using the same aromatic spacers, demonstrated differences in guest complexation selectivity between two isomeric "in-out" and "out-out" host molecules.[30a] In our case, separation by column chromatography of the two isomers was not possible.

Figure 1. ^{1}H-NMR (250 MHz) spectra in $CDCl_3$ at 25°C of **1a** (top) and **2a** (bottom)



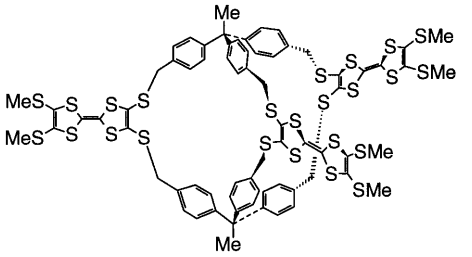
Mass-spectrometry studies confirmed the structure of our compounds.[*] Figure 2 shows the PDMS spectrum of **1d**.

X-ray Structure

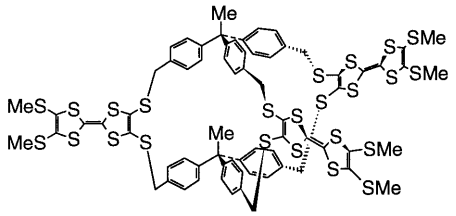
Attempts to grow single crystals of the compounds **1** and **2** were unsuccessful except in the case of **2a**, for which thin

[*] As commonly reported in the case of tetrathiafulvalene derivatives, small amounts of tetrathiafulvalene *S*-oxides ($M^{+\bullet}$ + 16) were detected in the case of macrobicycles **1** and **2** using Plasma Desorption Mass Spectrometry (PDMS).

Scheme 7



2d out-out



2d in-out

long orange needles were finally obtained after slow diffusion of ethanol into a CS_2 solution of **2a**. Nevertheless, after a few hours under N_2 or atmospheric conditions, approximately half of the needles became amorphous and twisted, while the other half seemed to keep their appearance, suggesting the presence of two different crystalline phases. X-ray structure determination performed on the stable needles revealed the structure of **2a** (Figure 3). The structure belongs to the $P2_1/n$ molecular point group (see Experimental Section). Several unusual aspects of this structure are noteworthy. Contrary to the ^{1}H-NMR study, where a D_{3h} symmetry was observed in $CDCl_3$ solution, it appears that the molecule **2a** adopts a different conformation in the solid state. Indeed, two tetrathiafulvalene units (**A** and **B**) are approximately parallel whereas the third one (**C**) is orientated almost perpendicularly to the parallel tetrathiafulvalene pair. Each tetrathiafulvalene framework adopts a different conformation. Tetrathiafulvalene unit **A** is the most planar; its external dithiole ring folds only by ca. 13° along the S···S vector. In the case of tetrathiafulvalene units **B** and **C**, the dithiole moieties close to the aromatic spacer exhibit an envelope conformation giving rise to an angle of ca. 25° for both of them between the central tetrathioethylene mean plane of the tetrathiafulvalene core and the dithioethylene mean plane of the dithiole moiety. Furthermore the benzene rings do not overlap face to face and hence, they tilt 33° away from each other. The shortest distance between two carbon atoms of two different benzene rings is 4.21 Å which is much more than in molecules with stacked benzene rings.[31] There is no interaction between the two tetrathiafulvalenes lying parallel since the shortest sulfur−sulfur distances are comprised between

Figure 2. Plasma desorption mass spectra of **1d**

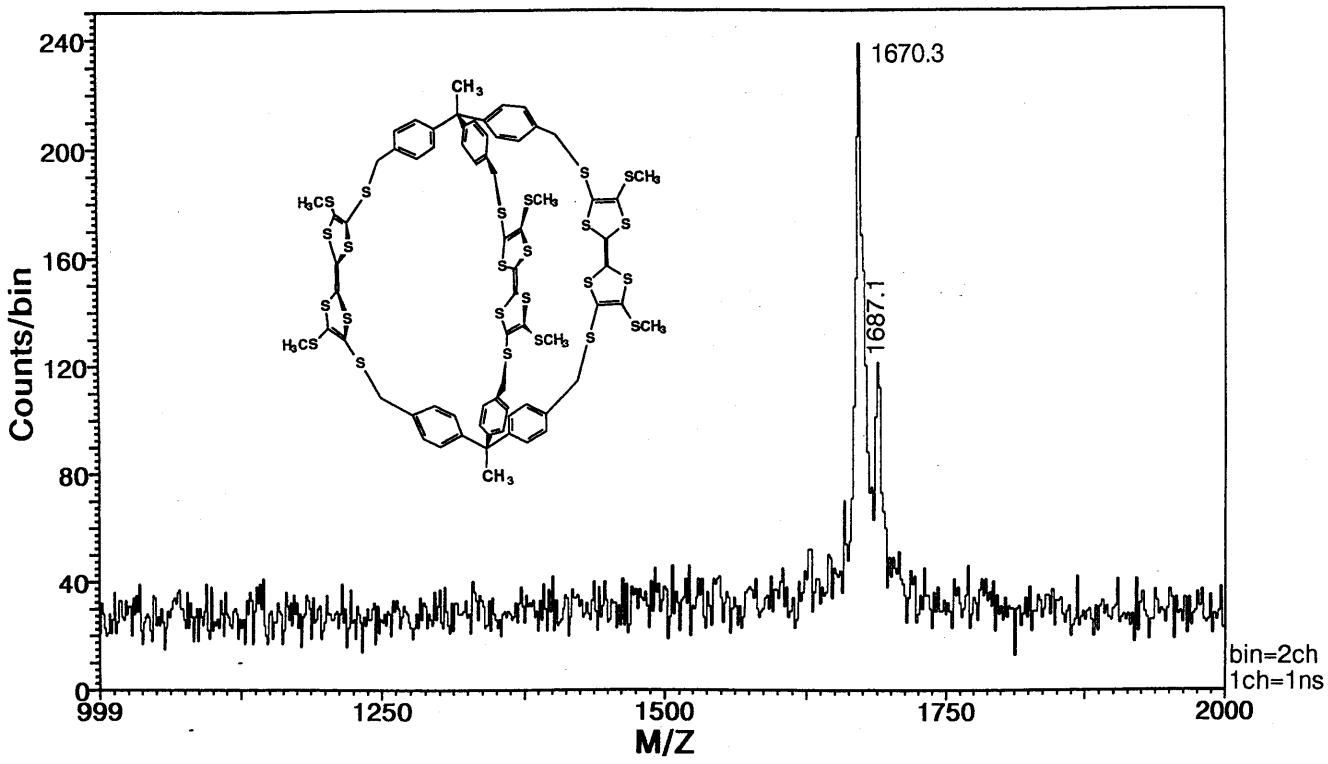
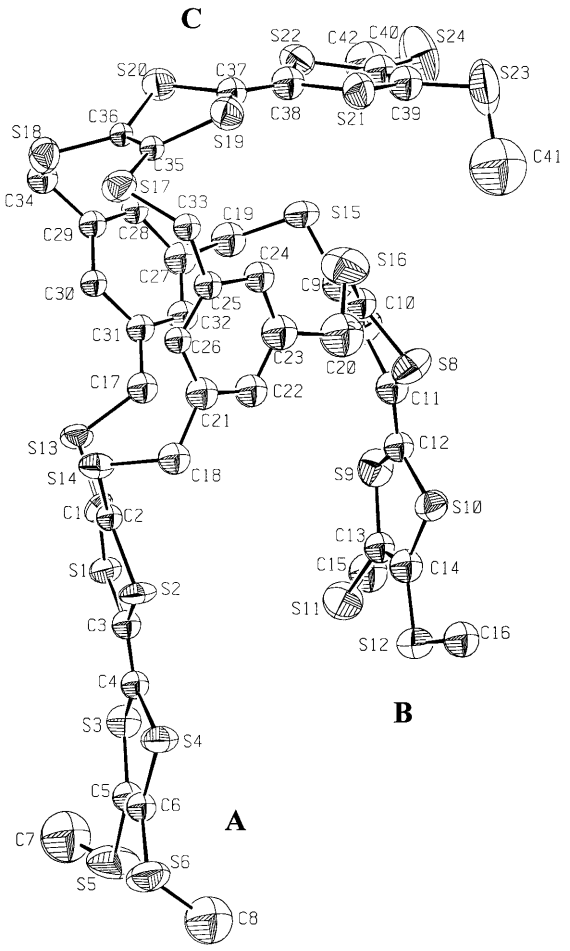
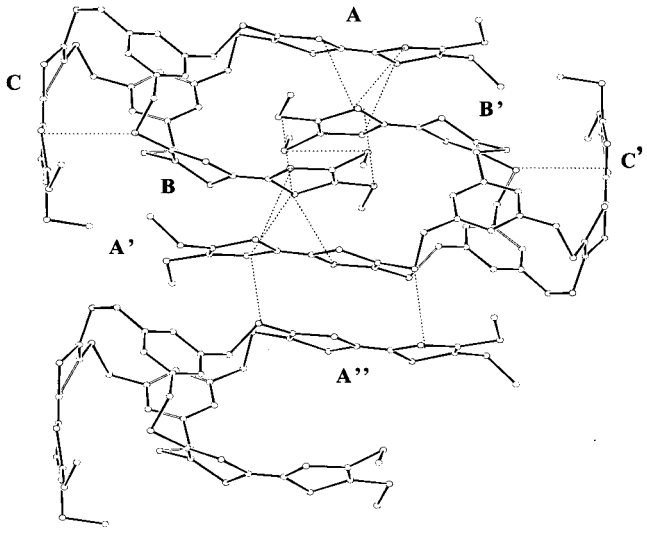


Figure 3. X-ray structure of macrobicycle **2a**



6.59 and 7.11 Å. On the other hand, there is one S···S intramolecular contact shorter than the sum of the van der Waals radii (3.70 Å) between two perpendicular tetrathiafulvalenes [d(S_{15}−S_{22}) = 3.54 Å]. This short distance cannot explain the loss of the C_3 symmetrical axis. A better explanation can be found in the peculiar mode of packing of compound **2a** in the crystal. As illustrated in Figure 4a, two

Figure 4a. Formation of tetrathiafulvalene columnar arrays along the *a* axis via bimolecular assemblies; dotted lines represent S···S distances shorter than the sum of the van der Waals radii (3.70 Å)

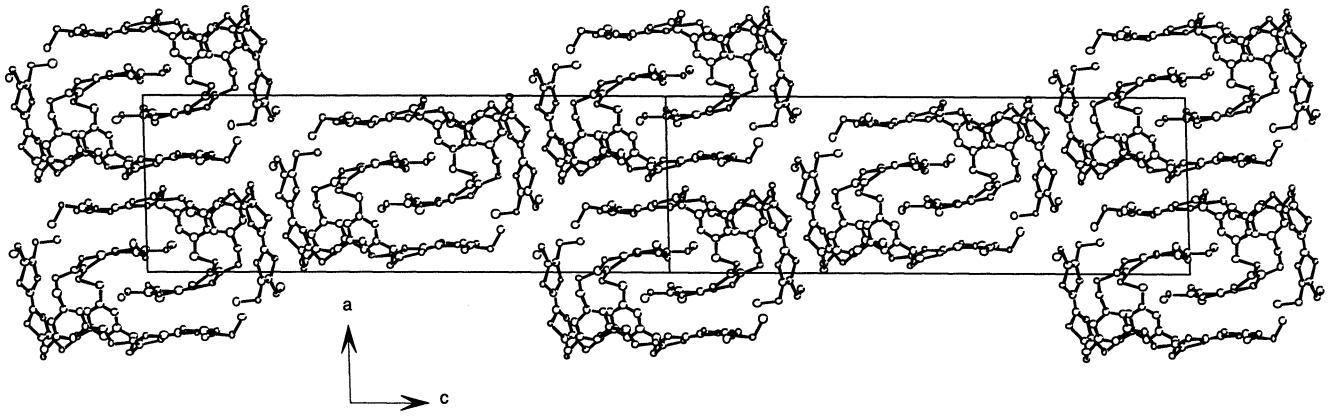


molecules fit together giving rise to a bimolecular assembly showing an inversion centre where four tetrathiafulvalene units lie roughly parallel. Inside the molecular unit, tetrathiafulvalenes **A** and **B′** as well as tetrathiafulvalenes **B** and **A′** show a ring-over-double bond overlap. This molecular arrangement is stabilised by interactions between parallel tetrathiafulvalenes as evidenced by the presence of numerous short S···S distances (Figure 4a). Figure 4b shows a view of the unit cell. The repetition of the bimolecular unit approximately along the *a* axis and the short S···S distances observed between tetrathiafulvalenes **A′** and **A′′**, lead to the existence of columnar arrays of tetrathiafulvalenes. Moreover, short S···S distances are observed between tetrathiafulvalenes of type **C** along the *c* axis [d(S_{22}−S'_{19}) = 3.68 Å, d(S_{19}−S'_{20}) = 3.61 Å] giving rise to the formation of tetrathiafulvalene dimers.

Electrochemistry

The redox behaviours of **1**, **2**, **5**, **6**, and **17** were investigated by cyclic voltammetry (Table 4) using a mixture of

Figure 4b. Packing of the molecules in the crystal



solvents CH_2Cl_2/CH_3CN (3:1).[*] The new macrobicycles **1b−d**, **2b−d**, and the new tris(tetrathiafulvalenes) **5b−d** and **6b−d** exhibit two reversible redox processes. As reported for the analogues of **5** and **6**[6a][32][33][34] and assuming the same peak area for each redox process, we can expect that the first and the second waves result from simultaneous formation of three radical cations followed by three dications at higher potentials. The fact that the two redox waves are well resolved, shows that the large and rigid aromatic spacers (**b**, **c**, **d**) prevent Coulombic through-space interaction between the three redox groups.

Table 4. Cyclic voltammetry data

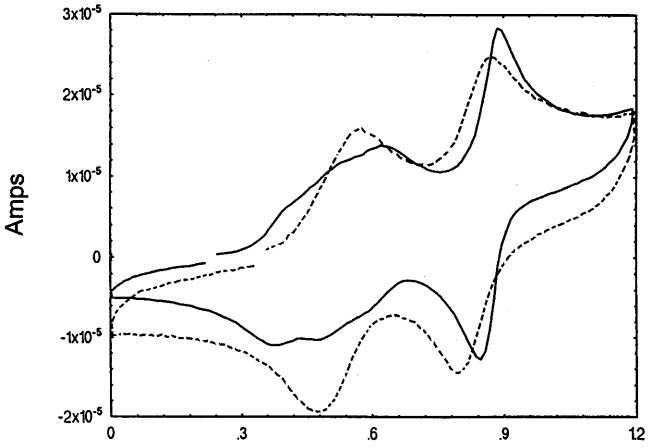
Compound	E_{ox} [V]/E_{red} [V]	
TTF[b]	0.37/0.28	0.775/0.69
TTF	0.41/0.32	0.88/0.79
1a	0.43/0.38, 0.53/0.47, 0.62/0.56	0.89/0.85
1b	0.53/0.49	0.86/0.80
1c	0.56/0.47	0.87/0.79
1d	0.57/0.48	0.88/0.80
2a	0.48/0.43, and 0.57/0.49	0.86/0.78
2b	0.54/0.47	0.86/0.79
2c	0.58/0.47	0.91/0.80
2d	0.58/0.48	0.89/0.82
3	0.59/0.52	0.91/0.84
4	0.595/0.525	0.91/0.83
5a	0.51 (sh) and 0.60/0.47 (br.)[c]	0.875/0.815
5b	0.56/0.495	0.87/0.81
5c	0.58/0.50	0.89/0.82
5d	0.575/0.495	0.89/0.82
6a	0.52 (sh) and 0.61/0.49 (br.)	0.88/0.82
6b	0.58/0.51	0. 88/0.81
6c	0.59/0.50	0.89/0.81
6d	0.59/0.51	0.91/0.82
7	0.555/0.49	0.87/0.795
17a	0.585 (br.)/0.42 (sh) and 0.51	0.88/0.82
17b	0.57/0.50	0.88/0.80

[a] Reference electrode: Ag/AgCl; working and counter electrodes: platinum; sweep rate: 100 mV s^{-1}; solvent: CH_2Cl_2/CH_3CN (3:1); supporting electrolyte: nBu_4NPF_6 (0.1 mol·l^{-1}). − [b] In CH_3CN. − [c] sh: shoulder, br.: broad.

On the contrary, in the case of **1a**, **2a**, **5a**, and **6a**, where the tetrathiafulvalenes are linked by the small 1,3,5-trimethylenebenzene spacer(s), cyclic voltammograms show broader waves, shoulders or additional waves for the generation of the radical cation state below 0.7 V (Table 4), similar to related oligomeric tetrathiafulvalenes.[6a][33] This electrochemical behaviour is a result of the flexibility in the molecule and a close proximity of the three redox moieties which allow Coulombic through-space interactions. However at higher potentials (E_{ox} > 0.7 V) a single sharp wave is observed with the same peak area than the sum of the previous ones. Assuming that the first processes involved three electrons, a simultaneous loss of three electrons occurs for the formation of a six-fold charged tris(dicationic) state; at this stage, the absence of interactions between electroactive centres is commonly observed.[33] In Figure 5, showing

[*] When CH_2Cl_2 only was used, in some cases the second oxidation waves (E_{ox} > 0.7 V) were distorted due to adsorption processes at the electrode, as commonly observed with large donor molecules.[32] The sufficient addition of CH_3CN allows a complete solubility of the adsorbed species giving a well-defined redox process.

Figure 5. Cyclic voltammograms of macrobicycles **1a** (−−) and **2a** (···) (CH_2Cl_2/CH_3CN, 3:1; nBu_4NPF_6, 0.1 mol·l^{-1}; Ag/AgCl; sweep rate 100 mV s^{-1})



the cyclic voltammograms of **1a** and **2a**, approximately three different redox waves are observed for the successive formation of a mono-, a bis-, and a tris(radical cation) species ($E_1^{1/2}$ = 0.405 V, $E_2^{1/2}$ = 0.50 V, $E_3^{1/2}$ = 0.59 V vs. Ag/AgCl) in the case of **1a**. Due to the architecture of macrocycle **1a** (CPK models), the three redox units are in close proximity and can interact easier and stronger than in the more strained macrobicycles **2a** where the electroactive groups are pointing out of the cavity. Consequently, the expected "first" redox waves of **1a** are broader than for **2a**, giving rise to almost three redox waves in the case of **1a** and only two for **2a**. The low values of the oxidation potentials of the first two waves of **1a** are consistent with a stabilisation by folding of one radical cation tetrathiafulvalene moiety and a close neutral tetrathiafulvalene to form a dimeric radical species $(TTF)_2^{\bullet+}$.[33] Whereas a folding of the three tetrathiafulvalene groups is possible in **1a**, this is not the case for **2a** where only two tetrathiafulvalene groups can come close (CPK models). In the last case, the broader wave observed results from the successive removal of electrons leading to the $\mathbf{2a}^{3\bullet+}$ species probably in two steps. The single well-defined wave obtained for the generation of the six-fold charged macrobicycles $\mathbf{1a}^{6+}$ supports the fact that tris(radical cation) species generated from **1a**, as is also the case for **1b−d**, **2a−d**, **5a−d**, and **6a−d**, all have perfect C_3 symmetry in solution.

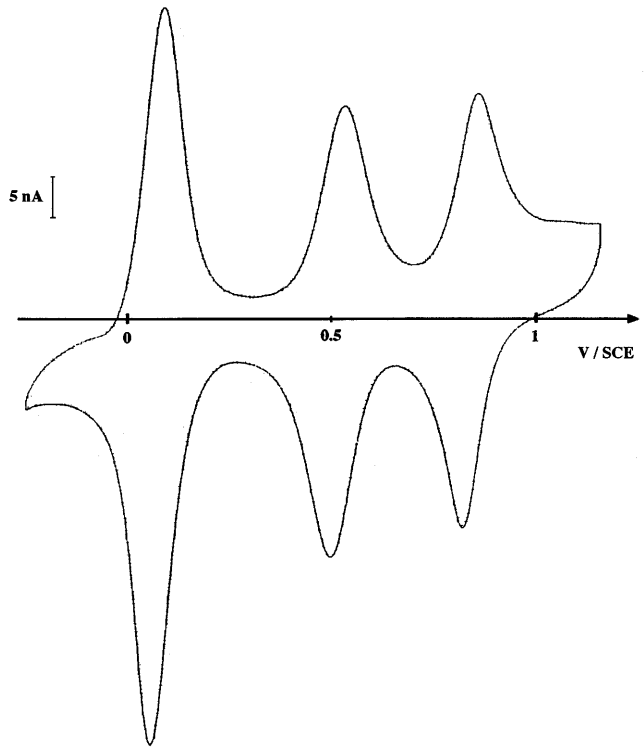
The pentakis(tetrathiafulvalene) **17b** contains five independent electroactive tetrathiafulvalene units as evidenced by its cyclic voltammogram, which exhibits two well-resolved reversible redox processes which can be assigned to the successive formation of a five-fold charged and a ten-fold charged species.[**]

TLCV[25a][35] studies in 1,1,2-trichloroethane solution in the presence of chloranil as an internal reference have been performed on compounds **2a** and **17b**. Since chloranil gives a one-electron reduction peak, the number of electrons ex-

[**] Using Thin Layer Cyclic Voltammetry (TLCV), Bryce et al. have recently shown that an analogous tetrathiafulvalene pentamer gave rise to two five-electron single waves upon electrooxidation.[25a]

changed per oxidation wave can be calculated by integrating the voltammetric waves if the concentrations of the sample and chloranil are known. The calculated value (4.8 ± 0.2 from different experiments) at the first oxidation potential of **17b** is close to the expected value. In the case of **2a**, experiments were complicated by interactions with the internal reference (chloranil, dichloronaphthoquinone). However, when studied alone, **2a** oxidation presents two waves, the first one exhibiting a shoulder. The area of each wave is identical. Furthermore, the use of ferrocene as internal reference solves the interaction problems observed before. The oxidation potential of ferrocene lies in the potential range of **2a** first oxidation wave. Calculations taking into account the integration of the second wave (belonging to **2a**) and the first wave (belonging both to ferrocene and **2a**) show that each wave is a 0.75 electron process. Consequently, three electrons are exchanged for two molecules of **2a**. This results suggest the occurrence of strong intermolecular interactions between tetrathiafulvalene units in the thin layer, which is not surprising when looking at the X-ray structure of **2a**. Figure 6 shows the TLCV of compound **17b**.

Figure 6. Thin layer cyclic voltammograms of compound **17b** ($7.5 \cdot 10^{-5}$ mol·l^{-1}) in the presence of chloranil ($6.90 \cdot 10^{-4}$ mol·l^{-1}) as internal reference (1,1,2-trichloroethane; nBu$_4$NPF$_6$, 1 mol·l^{-1}; reference vs. SCE; sweep rate 5 mV s^{-1})



In order to gain further insights into the determination of the number of electrons n_p exchanged in the redox processes of our new compounds, cyclic voltammetric measurements were made using Equation (1) of Bard and Anson which was originally applied for polymeric molecules containing identical non-interacting electroactive centers, [36] and where i, c, and M represent the intensity, concentration, and molar mass respectively. This equation was recently used for the determination of the number of electrons involved in the first reduction step of a multi-C_{60} derivative.[37]

$$n_p = \frac{i_p/c_p}{i_m/c_m} \times \left(\frac{M_p}{M_m}\right)^{0.275} \quad (1)$$

$$i = (i_{pa} + i_{pc}) - (i_a + i_c)_{solv./support.\ electr.} \quad (2)$$

The subscript p refers here to our compounds **1**, **2**, **5**, **6**, and **17**, and the subscript m corresponds to a reference compound chosen for similarity reasons to be either tetrakis(methylthio)tetrathiafulvalene (**8**) (in the case of **1** and **2**) or 2-(2′-cyanoethylthio)-3,6,7-tris(methylthio)tetrathiafulvalene (**7**) (in the case of **5**, **6** and **17**). For one redox process, i is defined by Equation (2) where i_{pa} is the peak anodic current at E_{pa} and i_{pc} the peak cathodic current at E_{pc}, and where i_a and i_c correspond to the anodic and cathodic currents of the couple solvent/supporting electrolyte determined with a solution free of electroactive compounds at E_{pa} and E_{pc}, respectively . When interactions between tetrathiafulvalenes occur at the first redox process, n_p has been calculated using the second redox process. In order to obtain more accurate concentrations, these experiments were achieved in a mixture of solvents CH_2Cl_2/CH_3CN (9:1), thus allowing a better solubilisation of our compounds. The experimental values i, c, and n_p are collected in Table 5. In the case of **5** and **6** these results confirm our previous interpretation, i.e. a three-electron transfer for the formation of a tris(radical cation) and then, another three-electron transfer for the formation of a six-fold charged species. Hence, this study shows that each of the two redox waves of **17** involves a five-electron transfer leading to a ten-fold charged compound. In the case of **17a**, the second redox wave showed the presence of adsorption at the electrode during the reduction process, giving rise to an overestimated n_p value (6.9). Thus, despite its slight broadening, the first redox wave of **17a** is more appropriate for the determination of n_p which is found to be close to five electrons. Consequently, these data reveal that, within an experimental error of ca. 10%, all the tetrathiafulvalene units present in each molecule can be oxidised.[38] On the other hand, while n_p is close to three exchanged electrons for **1b**, **2b**, and **2d**, the cases of **1a** and **2a**, where tetrathiafulvalenes can interact, remain ambiguous.

Charge-Transfer Complexation

Charge-transfer complexation experiments were investigated with the macrobicycles **1a**, **1b**, **2a**, **2b**, and also with the tris(tetrathiafulvalene) **6b** by UV/Vis spectroscopy. Thus, CH_2Cl_2 solutions of each compound rapidly became dark in the presence of iodine. The formation of charge-transfer complexes was confirmed by the emergence of a broad band in the UV/Vis spectra: λ_{max} = 826, 839, 862, 869, 827 nm, for **1a**, **1b**, **2a**, **2b**, and **6a**, respectively . Addition of equimolar amounts of either $AgClO_4$ or $CuCl_2 \cdot 2H_2O$, dissolved in CH_3CN, to a CH_2Cl_2 solution of **2a** led to the formation of black powders corresponding to charge-

Table 5. Determination of the number of electrons n_p involved in each redox process using the Bard-Anson equation

Compound	Amount taken [mg]	Mol. mass	c [mol·l^{-1}]	i [μA]	$E_{1/2}$ [V] vs. SCE	$n_p \pm \Delta n_p$[b]
8	0.82	388	$5.28 \cdot 10^{-4}$	2.36	0.50	1.00
	″	″	″	2.32	0.82	1.00
1a	0.50	1310	$4.24 \cdot 10^{-5}$	0.31	0.88[c]	2.3 ± 0.2
1b	0.67	1767	$4.74 \cdot 10^{-5}$	0.36	0.52	2.6 ± 0.3
2a	0.70	1310	$5.34 \cdot 10^{-5}$	0.34	0.86[c]	2 ± 0.2
2b	1.00	1767	$5.96 \cdot 10^{-5}$	0.46	0.52	2.6 ± 0.3
2d	0.89	1671	$6.66 \cdot 10^{-5}$	0.49	0.52	2.5 ± 0.3
7	1.65	427	$4.83 \cdot 10^{-4}$	1.73	0.535	1.00
	″	″	″	1.76	0.865	1.00
5a	0.80	1355	$1.102 \cdot 10^{-4}$	0.98	0.87[c]	3.3 ± 0.3
5b	0.73	1583.5	$7.68 \cdot 10^{-5}$	0.63	0.54	3.3 ± 0.3
5d	0.72	1535	$8.75 \cdot 10^{-5}$	0.69	0.55	3.1 ± 0.3
6a	0.91	1355	$1.36 \cdot 10^{-4}$	1.07	0.86[c]	3 ± 0.3
6b	1.45	1583.5	$1.22 \cdot 10^{-4}$	0.91	0.55	3 ± 0.3
17a	0.87	2244	$7.25 \cdot 10^{-5}$	0.82	0.55[d]	5 ± 0.5
	″	″	″	1.15	0.87[c][e]	6.9 ± 0.7
17b	1.13	2700	$5.23 \cdot 10^{-5}$	0.60	0.54	5.3 ± 0.5

[a] Reference electrode: SCE; working and counter electrodes: platinum; sweep rate: 100 mV s^{-1}; solvent: CH_2Cl_2/CH_3CN (9:1); supporting electrolyte: nBu$_4$NPF$_6$ (0.1 mol·l^{-1}). − [b] Δn_p takes into account all experimental errors and was estimated to be $\Delta n_p = 10\%$ n_p. − [c] $^n p$ was calculated using the second redox wave. − [d] Broad wave. − [e] Slight adsorption at the electrode during the reduction process.

transfer complexes. Electrocrystallisations of macrobicycles **2a** (9 mg) at 0°C under 1 μA using PF_6^- as anion and a CH_2Cl_2/EtOH (9:1) mixture as solvent, gave black plates in the bottom of the cell after nine days, however unsuitable for X-ray diffraction.

Conclusion

In this work, we have established an efficient methodology for the assembly of the first macrobicyclic cyclotetrathiafulvalenophanes **1a−d** and **2a−d**. They have been prepared using a two-step strategy based on the deprotection of protected thiolates and subsequent *S*-alkylation. It is worth noting that a relatively complicated molecule, such as **2a**, can be obtained in good yield in a one-pot reaction starting from the easily available tetrathiafulvalene derivative **4**. Isolation of the by-products, tetrathiafulvalene pentamers **17**, allowed a better understanding of the reaction leading to tris(tetrathiafulvalene) **5**. ^{1}H-NMR and cyclic voltammetry studies of these new compounds gave precise information on their conformational structures in solution. In the case of **2a**, where the crystal structure was established, a completely different conformation was observed in the solid state as a result of S···S intermolecular interactions. The reaction protocol described in this paper can be applied to the synthesis of a number of new macrobicycles either by introduction of new substituents (lipophilic or hydrophilic) instead of the methylthio group, or by incorporation of new spacers. Furthermore intermediate tris(tetrathiafulvalenes) **5a−d** and **6a−d** or pentakis(tetrathiafulvalenes) **17a**, **b** with potential thiolates can be seen as new building blocks for the preparation of new electron reseservoirs.[26][27] In addition, we have shown that the equation of Bard and Anson could be applied to multi(tetrathiafulvalene) oligomers for the determination of the number of electrons exchanged in a non-interacting electrochemical process. Preliminary host-guest chemistry with our macrobicyclic compounds gave poor results suggesting the synthesis of new molecules using alternative spacers and new functionalised tetrathiafulvalene derivatives.

Experimental Section

All solvents were purified/dried by standard methods prior to use. The petroleum ether used had a boiling range of 60−80°C. All reagents used were obtained from Aldrich or Fluka and used without purification. Microanalyses were performed at the Microanalytical Laboratory, University of Copenhagen. The silica gel used was Merck 60, 230−400 mesh. − NMR spectra were recorded with a Bruker AC 250; chemical shifts are given in ppm relative to TMS. − EI mass spectra were recorded with a Varian MAT 311A spectrometer. PDMS and FAB spectra were recorded with a BioIon 10K and a Kratos MS50TC, respectively. − IR spectra were recorded with a Perkin-Elmer 580 spectrophotometer and UV/Vis spectra with a Shimadzu 160A spectrophotometer. − Melting points were determined with a Büchi apparatus and are uncorrected. − CV measurements were carried out with nBu$_4$NPF$_6$ as supporting electrolyte, with a sweep rate of 100 mV/s. Counter and working electrodes were made of Pt, and the reference electrode was Ag/AgCl, unless otherwise stated. − The thin layer cyclic voltammetry cell used in this work was constructed as described previously.[35b]

X-ray Structural Analysis: Crystal data for **2a**: $C_{42}H_{36}S_{24}$, M_w = 1310.19 g·mol^{-1}, monoclinic, $P2_1/n$, Z = 4, a = 14.226(7), b = 8.964(2), c = 42.297(9) Å, β = 92.02(9)°, V = 5398(1) Å^3, $\rho_{calcd.}$ = 1.612 g·cm^{-3}, λ(Mo-K_α) = 0.71073 Å. − Data collection: Data collection was carried out by zig-zag ω scan technique (2° < θ < 25°) with an Enraf-Nonius Mach III diffractometer. Conditions of measurements were t_{max} = 40 s, range h, k, l (h 0 to10; k 0 to 16; l −50 to 50). Intensity-control reflections were measured every 2 h without appreciable decay (0.15%). 10597 independent reflections were collected from which 2701 correspond to $I > 3\sigma(I)$. − Structure refinement: After Lorentz and polarisation corrections, the structure was solved by direct methods (SIR) which reveal all the non-hydrogen atoms. After anisotropic refinement of all the C and S atoms, the coordinates of H atoms were determined from the HYDRO program. The whole structure was refined by full-matrix least-squares techniques {refinement on F, x, y, z, U_{ij} for S atoms, x, y, z and U for C atoms; 390 variables and 2701 observations, weighting scheme: non-Poisson contribution with $w = 1/\sigma(F_o)^2 = 4F_o^2/[\sigma(I)^2 + (0.04\ F_o^2)^2]$ with the resulting R = 0.099, R_w = 0.119}. All calculations were performed using the MolEN package.

2-(2′-Cyanoethylthio)-3,6,7-tris(methylthio)tetrathiafulvalene (**7**) *by Monodeprotection of the cis/trans Mixture of 2,6(7)-Bis(2′-cyanoethylthio)-3,7(6)-bis(methylthio)tetrathiafulvalene* (**3**): Compound **3** (0.466 g, 1.0 mmol) was dissolved in anhydrous degassed DMF (50 ml) under N_2 at room temp., and a solution of $CsOH \cdot H_2O$ (0.179 g, 1.05 mmol) in anhydrous degassed MeOH (10 ml) was added dropwise over a period of 1 h. After stirring for another 1 h, MeI (1.0 ml, excess) was added in one portion and the solution was stirred overnight. After concentration in vacuo, the residue was redissolved in CH_2Cl_2 (150 ml), the solution was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated. Compound **7** was isolated after column chromatography on silica gel using CH_2Cl_2 as eluent (0.287 g, 67%); R_f = 0.55 (CH_2Cl_2); m.p. 103−104°C (ref.[17] 102−104°C from toluene/cyclohexane). − ^{1}H NMR ($CDCl_3$): δ = 2.43 (s, 6 H, SCH_3), 2.47 (s, 3 H, SCH_3),

2.70 (t, 2 H, SCH_2, J = 7.2 Hz), 3.02 (t, 2 H, CH_2CN, J = 7.2 Hz). − ^{13}C NMR ($CDCl_3$): δ = 18.74, 19.13, 19.21, 31.23, 109.45, 112.57, 117.54, 120.13, 127.41, 135.13. − Two by-products were identified by ^1H-NMR spectroscopy and TLC as 2,3,6,7-tetrakis(-methylthio)tetrathiafulvalene (**8**) (0.073 g, 19%, R_f = 0.82 in CH_2Cl_2) and the starting material **3** (0.053 g, 11% recovered, R_f = 0.26 in CH_2Cl_2).

1,3,5-Tris(bromomethyl)benzene (**10**):[21] Starting material **9** was prepared by reaction of the corresponding acid chloride with methanol in the presence of trimethylamine in refluxing chloroform in 93% yield. White crystals. M.p. 144−144.5°C (Aldrich 145−147°C). Compound **10** was prepared according to a procedure described in the literature to give white crystals in 50% yield; m.p. 97−97.5°C (CH_2Cl_2/petroleum ether, 1:1; ref.[21] 96°C from petroleum ether). − ^1H NMR ($CDCl_3$): δ = 4.45 (s, 6 H, CH_2Br), 7.35 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 32.27, 129.68, 139.20. − MS (70 eV, EI); *m/z* (%): 360 (2), 358 (8), 356 (8), 354 (2), 279 (54), 277 (100), 275 (48), 198 (34), 196 (33), 115 (37).

1,3,5-Tris[4-(bromomethyl)phenyl]benzene (**13**):[22] A mixture of **11**[22] (5 g, 14.35 mmol), NBS (8.05 g, 45.23 mmol), and AIBN (ca. 0.010 g) in dry CCl_4 (57 ml) was refluxed for 3 h. The hot solution was filtered, and the filter was washed with hot CCl_4 (50 ml). The filtrate was concentrated in vacuo to give a white residue which was dissolved in $CHCl_3$ (120 ml). This solution was washed with a saturated aqueous solution of $NaHCO_3$ (3 × 50 ml), dried ($MgSO_4$), and concentrated. Recrystallisation from toluene/acetic acid (20 ml/15 ml) afforded, after 2 h at room temp., 4.87 g of white needles. HPLC analysis (reverse-phase Nucleosil 5 C_{18}; CH_3CN/H_2O, 9:1; 274 nm) exhibited a 68% purity. A sample of 1 g was purified by column chromatography on silica gel (d = 5 cm, h = 44 cm) using CH_2Cl_2/petroleum ether (1:2). As the crude product was not soluble in this solvent system, it was first adsorbed on silica gel and then deposited on the chromatography column: 1 g of product and 7 g of silica gel were mixed in 50 ml of CH_2Cl_2. This purification resulted in 0.61 g of a white powder which was recrystallised from CH_2Cl_2/petroleum ether to afford 0.56 g of white needles. Repeating these purification steps with the remaining 3.87 g of crude product, we finally obtained 2.73 g (32%) of white needles sufficienly pure for further reactions; m.p. 193−194°C. HPLC analysis showed a 90% purity of the final product. It was possible to increase the purity to 93% after another column chromatography on silica gel as described above; m.p. 200−200.5°C (ref.[22] 192−194°C). − ^1H NMR ($CDCl_3$): δ = 4.56 (s, 6 H, CH_2Br), 7.50 (d, 6 H, arom. H, J = 8.2 Hz), 7.65 (d, 6 H, arom. H, J = 8.2 Hz), 7.74 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 33.17, 125.30, 127.74, 129.63, 137.29, 141.05, 141.79. − MS (70 eV, EI); *m/z* (%): 588 (4), 587 (4), 586 (11), 585 (7), 584 (12), 583 (5), 582 (4), 507 (44), 505 (89), 503 (54), 426 (19), 424 (20), 345 (67), 213 (37), 212 (41), 173 (100).

1,3,5-Tris[3-(bromomethyl)phenyl]benzene (**14**):[22] A mixture of **12**[22] (5 g, 14.35 mmol), NBS (7.67 g, 43.09 mmol), and AIBN (ca. 0.010 g) in dry CCl_4 (250 ml) was refluxed for 3 h. The hot solution was filtered, and the filter was washed with hot CCl_4 (50 ml). The filtrate was left overnight at room temp. during which time a white product precipitated. After filtration with suction, the product was dissolved in CH_2Cl_2 (150 ml) and the solution was washed with a saturated aqueous solution of $NaHCO_3$ (2 × 50 ml), dried ($MgSO_4$), and concentrated in vacuo. The resulting residue was recrystallised from CCl_4 (180 ml) to give 3.43 g of white crystals after crystallisation overnight. The mother liquor was concentrated and the residue recrystallised twice affording an additional crop of 0.36 g of white crystals with the same purity (TLC; CH_2Cl_2/petroleum ether, 1:2); 3.79 g (45%), m.p. 185−187°C (ref.[22] m.p. 186−187°C). However, HPLC analysis showed a 60% purity of the desired product and the presence of two other products of mutibromination in 35% and 5%. A sample of higher purity was obtained by column chromatography on silica gel using a mixture CH_2Cl_2/petroleum ether (1:2) as eluent, followed by two successive recrystallisations from toluene/acetic acid (4:3) and one recrystallisation from CH_2Cl_2/petroleum ether. The final sample showed only a 69% purity in HPLC and a higher melting point; m.p. 191−194°C. − ^1H NMR ($CDCl_3$): δ = 4.58 (s, CH_2), 7.40−7.83 (m, arom. H).

1,1,1-Tris[4-(bromomethyl)phenyl]ethane (**16**):[23] A mixture of **15**[23] (10 g, 33.28 mmol), NBS (19.5 g, 109.56 mmol), and AIBN (0.016 g) in dry CCl_4 (125 ml) was allowed to reflux under UV light (200 W). When the reaction mixture began to boil strongly, refluxing and light were maintained for 90 min. The hot solution was filtered, and the isolated white precipitate was washed with hot CCl_4 (50 ml). The filtrate was concentrated in vacuo to give a white residue which was dissolved in $CHCl_3$ (200 ml). This solution was washed with a saturated aqueous solution of $NaHCO_3$ (3 × 50 ml), dried ($MgSO_4$), and concentrated. The resulting powder was purified by fractional recrystallisations from EtOAc to give 5.37 g (30%) of white crystalline powder; m.p. 192−195°C (ref.[23] 38−42% yield with m.p. 185−191°C; for an analytical sample: m.p. 199−200°C). HPLC analysis showed a 72% purity. − ^1H NMR ($CDCl_3$): δ = 2.13 (s, 3 H, CH_3), 4.48 (s, 6 H, CH_2Br), 7.05 (d, 6 H, arom. H, J = 8.4 Hz), 7.29 (d, 6 H, arom. H, J = 8.4 Hz). − ^{13}C NMR ($CDCl_3$): δ = 30.43, 33.24, 52.31, 128.80, 129.13, 135.77, 148.83. − MS (70 eV, EI); *m/z* (%): 537 [$M^{+\bullet}$] (20), 523 (49), 521 (64), 459 (40), 457 (100), 455 (48), 442 (11), 361 (32), 282 (68), 191 (47), 141 (67)

General Procedure for the Preparation of Tris(tetrathiafulvalene) **5**: To a solution of a mixture *cis*/*trans* isomers of **3** (0.44 g, 0.94 mmol) in anhydrous degassed DMF (40 ml) under N_2 was added dropwise a solution of $CsOH \cdot H_2O$ (0.168 g, 1 mmol) in dry and degassed MeOH (10 ml) over a period of 2 h at room temp. Then a solution of the tris(bromomethyl) compound (0.30 mmol) in anhydrous degassed DMF (30 ml) was added dropwise during 5 h at room temp. using a perfusor pump. After an additional 9 h of stirring at room temp., the reaction mixture was concentrated in vacuo. The resulting residue was dissolved in CH_2Cl_2 (150 ml) and the solution was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated to give a brown residue which was subjected to column chromatography on silica gel using CH_2Cl_2 as eluent. Several by-products were isolated and identified. The desired products were obtained as oils or as foamy solids.

1,3,5-Tris({[3′(4′)-cyanoethylthio-4,4′(3′)-bis(methylthio)-tetrathiafulvalen-3-yl]thio}methyl)benzene (**5a**): Starting from **10** (0.107 g, 0.30 mmol), 0.11−0.12 g (27−30% yield) of an orange foam was obtained. M.p. 53−55°C (CH_2Cl_2). R_f = 0.35 (CH_2Cl_2). − ^1H NMR ($CDCl_3$): δ = 2.32 (s, 9 H, SCH_3), 2.47 and 2.48 (2 s, 9 H, SCH_3), 2.71 and 2.72 (2 t, 6 H, SCH_2, J = 7.2 Hz), 3.03 and 3.04 (2 t, 6 H, CH_2CN, J = 7.2 Hz), 3.97 (s, 6 H, SCH_2Ar), 7.18 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 18.81, 19.11, 19.19, 19.29, 31.27, 40.21, 109.84, 111.99, 117.60, 120.12, 123.48, 123.75, 129.04, 132.92, 133.18, 135.05, 135.11, 137.42. − PDMS; *m/z*: 1355.4 [$M^{+\bullet}$]; calcd. for $C_{42}H_{39}N_3S_{24}$ 1355.23. − IR (KBr): $\tilde{\nu}$ = 2918, 2250 (CN), 1632, 1421, 889, 772 cm^{-1}. − $C_{42}H_{39}N_3S_{24}$: calcd C 37.22, H 2.90, N 3.10, S 56.78; found C 37.45, H 3.04, N 3.20, S 56.45.

Tetrathiafulvalene Pentamer **17a**: 0.06 g (18% yield) of an orange foam. M.p. 71−73°C (CH_2Cl_2). R_f = 0.21 (CH_2Cl_2). − ^1H NMR

($CDCl_3$): δ = 2.32 (br. s, 18 H, SCH_3), 2.47 and 2.48 (2 s, 12 H, SCH_3), 2.71 and 2.72 (2 t, 8 H, SCH_2, J = 7.1 Hz), 3.02 and 3.03 (2t, 8 H, CH_2CN, J = 7.1 Hz), 3.97 (br. s, 12 H, SCH_2Ar), 7.18 (br. s, 6 H, arom. H). − MS (FAB); *m/z*: 2243.3 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{70}H_{64}N_4S_{40}$ 2243. − IR (KBr): ṽ = 2918, 2250 (CN), 1631, 1421, 888, 772 cm^{-1}. − $C_{70}H_{64}N_4S_{40}$: calcd. C 37.47, H 2.88, N 2.50, S 57.16; found C 37.07, H 2.71, N 2.50, S 54.86.

1,3,5-Tris[4-({[3′(4′)-cyanoethylthio-4,4′(3′)-bis(methylthio)-tetrathiafulvalen-3-yl]thio}methyl)phenyl]benzene (**5b**): Starting from **13** (92.5% pure; 0.190 g, 0.30 mmol), 0.16−0.17 g (34−36% yield) of yellow foam was obtained. M.p. 81−83°C (CH_2Cl_2). R_f = 0.47 (CH_2Cl_2). − ^1H NMR ($CDCl_3$): δ = 2.27 and 2.28 (2 s, 9 H, SCH_3), 2.44 and 2.45 (2 s, 9 H, SCH_3), 2.67 and 2.68 (2 t, 6 H, SCH_2, J = 7.2 Hz), 2.99 and 3.00 (2 t, 6 H, CH_2CN, J = 7.2 Hz), 4.07 (s, 6 H, SCH_2Ar), 7.43 (d, 6 H, arom. H, J = 8.1 Hz), 7.64 (d, 6 H, arom. H, J = 8.1 Hz), 7.74 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 18.75, 18.77, 19.07, 19.17, 29.69, 31.21, 40.41, 109.16, 112.30, 117.53, 120.02, 120.20, 124.23, 124.55, 124.97, 127.51, 129.67, 132.68, 132.95, 135.03, 135.18, 136.27, 140.24, 141.93. − MS (FAB); *m/z*: 1583 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{60}H_{51}N_3S_{24}$ 1582.7. − IR (KBr): ṽ = 2917, 2249 (CN), 1596, 1510, 1418, 1394, 888, 830, 773 cm^{-1}.

Tetrathiafulvalene Pentamer **17b**: 0.045−0.065 g (11−16% yield) of orange foam. M.p. 104−107°C (CH_2Cl_2). R_f = 0.33 (CH_2Cl_2). − ^1H NMR ($CDCl_3$): δ = 2.23 (s, 6 H, SCH_3), 2.26−2.28 (m, 12 H, SCH_3), 2.43 and 2.45 (2 s, 12 H, SCH_3), 2.665 and 2.670 (2 t, 8 H, SCH_2, J = 7.1 Hz), 2.99 and 3.00 (2 t, 8 H, CH_2CN, J = 7.1 Hz), 4.06 (s, 12 H, SCH_2Ar), 7.40 (d, 12 H, arom. H, J = 8 Hz), 7.58−7.65 (m, 12 H, arom. H), 7.69 and 7.72 (2 s, 6 H, arom. H). − MS (FAB); *m/z*: 2700.4 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{106}H_{88}N_4S_{40}$ 2700. − IR (KBr): ṽ = 2920, 2853, 2249 (CN), 1598, 1510, 1419, 889, 828, 773 cm^{-1}. − $C_{106}H_{88}N_4S_{40}$: calcd. C 47.15, H 3.28, N 2.07, S 47.49; found C 47.51, H 3.14, N 2.16, S 46.05.

1,3,5-Tris[3-({[3′(4′)-cyanoethylthio-4,4′(3′)-bis(methylthio)-tetrathiafulvalen-3-yl]thio}methyl)phenyl]benzene (**5c**): Starting from **14** (69% pure; 0.255 g, 0.30 mmol), 0.175 g (37% yield) of yellow foam was obtained. M.p. 75−79°C (CH_2Cl_2). R_f = 0.41 (CH_2Cl_2). − ^1H NMR ($CDCl_3$): δ = 2.27 (s, 9 H, SCH_3), 2.42 and 2.43 (2 s, 9 H, SCH_3), 2.65 and 2.66 (2 t, 6 H, SCH_2, J = 7.1 and 7.2 Hz), 2.97 and 2.99 (2 t, 6 H, CH_2CN, J = 7.1 and 7.2 Hz), 4.12 (s, 6 H, SCH_2Ar), 7.35 (d, 3 H, arom. H, J = 7.6 Hz), 7.45 (dd, 3 H, arom. H, J = 7.6 and 7.6 Hz), 7.62 (d, 3 H, arom. H, J = 7.6 Hz), 7.67 (s, 3 H, arom. H), 7.79 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 18.73, 18.75, 19.09, 19.21, 31.22, 40.68, 109.36, 112.02, 117.55, 123.99, 124.30, 125.24, 126.69, 128.13, 128.37, 129.23, 132.79, 133.08, 135.02, 135.16, 137.39, 141.34, 142.02. − MS (FAB); *m/z*: 1582; isotope pattern calcd. for $C_{60}H_{51}N_3S_{24}$ 1582.7. − IR (KBr): ṽ = 2918, 2250 (CN), 1630, 1596, 1420, 889, 772, 706, 622 cm^{-1}.

1,1,1-Tris[4-({[3′(4′)-cyanoethylthio-4,4′(3′)-bis(methylthio)-tetrathiafulvalen-3-yl]thio}methyl)phenyl]ethane (**5d**): Starting from **16** (72% pure; 0.225 g, 0.30 mmol), 0.167 g (36% yield) of orange foam was obtained. M.p. 79−82°C (CH_2Cl_2). R_f = 0.38 (CH_2Cl_2). − ^1H NMR ($CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 2.26 and 2.27 (2 s, 9 H, SCH_3), 2.45 and 2.46 (2 s, 9 H, SCH_3), 2.68 and 2.69 (2 t, 6 H, SCH_2, J = 7.1 and 7.2 Hz), 3.005 and 3.015 (2 t, 6 H, CH_2CN, J = 7.2 and 7.1 Hz), 3.98 (s, 6 H, SCH_2Ar), 7.02 (d, 6 H, arom. H, J = 8.3 Hz), 7.21 (d, 6 H, arom. H, J = 8.3 Hz). − ^{13}C NMR ($CDCl_3$): δ = 18.77, 19.13, 19.29, 29.69, 31.26, 40.20, 52.06, 109.00, 117.54, 120.16, 124.35, 128.73, 128.92, 132.72, 132.94, 134.52, 135.13, 148.19, 124.63. − MS (FAB); *m/z*: 1536; isotope pattern calcd. for $C_{56}H_{51}N_3S_{24}$ 1535. − IR (KBr): ṽ = 2919, 2250 (CN), 1631, 1508, 1418, 1018, 890, 773 cm^{-1}.

General Procedure for the Preparation of Tetrathiafulvalene Macrobicycles **1**: Under N_2, a solution of $CsOH \cdot H_2O$ (3.6 equiv.) in anhydrous degassed MeOH (5 ml) was added to a solution of a *cis*/*trans* mixture of tris(tetrathiafulvalene) (1 equiv.) in anhydrous degassed DMF (25 ml) over a period of 10 min at room temp. This solution and a solution of the tribromide (1 equiv.) in anhydrous degassed DMF (30 ml) were added simultaneously, during 10 h at room temp. with stirring, to 50 ml of anhydrous degassed DMF under high-dilution conditions using a perfusor pump. Stirring was continued for additional 5 h and the reaction mixture was concentrated in vacuo. The residue was then dissolved in CH_2Cl_2 (200 ml). The solution was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated in vacuo. The resulting residue was firstly purified by filtration through a short column of silica gel using CH_2Cl_2 as eluent and then by column chromatography on silica gel using CH_2Cl_2/petroleum ether (1:1) as eluent to afford the tetrathiafulvalene macrobicycles as a mixture of four *cis*/*trans* isomers.

Macrobicycle **1a**: Starting from **5a** (0.31 g, 0.23 mmol), $CsOH \cdot H_2O$ (0.139 g, 0.83 mmol), and **10** (0.082 g, 0.23 mmol), 0.13 g (43% yield) of **1a** was obtained as yellow powder which slowly decomposed between 155−160°C without melting. − ^1H NMR ($CDCl_3$): δ = 2.38−2.49 (m, 18 H, SCH_3), 3.83−4.09 (m, 12 H, SCH_2Ar), 6.99-7.23 (m, 6 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 19.08, 19.15, 19.26, 19.33, 19.38, 39.74, 40.02, 40.08, 40.16, 40.30, 112.28, 112.39, 123.35, 129.22, 129.27, 129.48, 129.57, 136.79, 136.91, 137.39, 137.46, 138.04. − PDMS; *m/z*: 1309.1; calcd. for $C_{42}H_{36}S_{24}$ 1310.19. − IR (KBr): ṽ = 2917, 1603, 1455, 1425, 1227, 887, 772, 708 cm^{-1}. − $C_{42}H_{36}S_{24}$: calcd. C 38.54, H 2.77, S 58.68; found C 38.26, H 2.91, S 58.19.

Macrobicycle **1b**: Starting from **5b** (0.17 g, 0.11 mmol), $CsOH \cdot H_2O$ (0.065 g, 0.39 mmol) and **13** (90% pure; 0.070 g, 0.11 mmol), 0.074 g (39% yield) of **1b** was obtained as yellow powder which slowly decomposed above 185°C without melting. − ^1H NMR ($CDCl_3$): δ = 2.01−2.26 (m, 18 H, SCH_3), 3.94−4.08 (m, 12 H, SCH_2Ar), 7.06−7.63 (m, 30 H, arom. H). − PDMS; *m/z*: 1767.1 [$M^{+\bullet}$]; calcd. for $C_{78}H_{60}S_{24}$ 1766.77. − IR (KBr): ṽ = 2920, 1630, 1511, 1421, 831, 775 cm^{-1}.

Macrobicycle **1c**: Starting from **5c** (0.14 g, 0.09 mmol), $CsOH \cdot H_2O$ (0.053 g, 0.32 mmol) and **14** (69% pure; 0.075 g, 0.09 mmol), 0.058 g (37% yield) of **1c** was obtained as yellow powder; m.p. 175°C (dec.). − ^1H NMR ($CDCl_3$): δ = 2.14−2.25 (m, 18 H, SCH_3), 3.95−4.00 (m, 12 H, SCH_2Ar), 7.23−7.42 (m, 12 H, arom. H), 7.53−7.58 (m, 12 H, arom. H), 7.70−7.75 (m, 6 H, arom. H). − PDMS; *m/z*: 1766.0 [$M^{+\bullet}$]; calcd. for $C_{78}H_{60}S_{24}$ 1766.77. − IR (KBr): ṽ = 2918, 1595, 1582, 1489, 1421, 889, 876, 793, 772, 705 cm^{-1}. − $C_{78}H_{60}S_{24}$: calcd. C 53.07, H 3.43, S 43.50; found C 52.68, H 3.48, S 42.84.

Macrobicycle **1d**: Starting from **5d** (0.19 g, 0.12 mmol), $CsOH \cdot H_2O$ (0.075 g, 0.45 mmol) **16** (72% pure; 0.093 g, 0.12 mmol), 0.08 g (40% yield) of **1d** was obtained as yellow powder; m.p. 200−205°C (dec.). Statistically, this is a mixture of twelve isomers considering the *cis*/*trans* isomers and the out-out, in-out, and in-in isomers where the methyl groups of the benzylic positions can be outside or inside the cavity of the cage. − ^1H NMR ($CDCl_3$): δ = 1.25−2.46 (m, 24 H, CH_3 and SCH_3), 3.75−3.96 (m, 12 H, SCH_2Ar), 6.61−7.23 (m, 24 H, arom. H). − PDMS; *m/z*: 1670.3 [$M^{+\bullet}$]; calcd. for $C_{70}H_{60}S_{24}$ 1670.69. − IR (KBr): ṽ = 2918, 1630, 1508, 1419, 1018, 879, 773 cm^{-1}. − $C_{70}H_{60}S_{24}$: calcd. C 50.37, H 3.63, S 46.01; found C 50.59, H 3.52, S 45.17.

General Procedure for the Preparation of Tris(tetrathiafulvalene) **6**: To a solution of **4** (0.42 g, 0.90 mmol) in anhydrous degassed DMF (35 ml) under N_2, was added dropwise a solution of $CsOH \cdot H_2O$ (0.159 g, 0.95 mmol) in anhydrous degassed MeOH (10 ml) over a period of 45 min at room temp. After an additional 15 min of stirring, a solution of the tribromide (0.30 mmol) in anhydrous degassed DMF (25 ml) was added dropwise during 1 h at room temp. The reaction mixture was stirred overnight at room temp. and then concentrated in vacuo to afford a residue which was dissolved in CH_2Cl_2 (200 ml). This solution was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated in vacuo. The resulting oil was subjected to column chromatography on silica gel using CH_2Cl_2 as eluent to give the desired tris(tetrathiafulvalene) as an orange oil or foam.

1,3,5-Tris({[4-cyanoethylthio-3',4'-bis(methylthio)tetrathiafulvalen-3-yl]thio}methyl)benzene (**6a**): Using **10** (0.107 g, 0.3 mmol), we obtained 0.300−0.312 g (74−77% yield) of orange oil which becomes solid upon standing. M.p. 58−62°C (CH_2Cl_2). − ^{1}H NMR ($CDCl_3$): δ = 2.44 (s, 9 H, SCH_3), 2.45 (s, 9 H, SCH_3), 2.48 (t, 6 H, SCH_2, *J* = 7.2 Hz), 2.90 (t, 6 H, CH_2CN, *J* = 7.2 Hz), 4.02 (s, 6 H, SCH_2Ar), 7.22 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 18.54, 19.19, 19.26, 31.37, 40.25, 108.70, 113.51, 117.69, 126.56, 127.30, 127.53, 129.18, 131.25, 137.61. − MS (FAB); *m/z*: 1354.6 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{42}H_{39}N_3S_{24}$ 1355. − IR (KBr): $\tilde{\nu}$ = 2916, 2249 (CN), 1631, 1601, 1417, 887, 772, 728, 709 cm^{-1}. − $C_{42}H_{39}N_3S_{24}$: calcd. C 37.22, H 2.90, N 3.10, S 56.78; found C 36.84, H 2.69, N 2.97, S 55.92.

1,3,5-Tris[4-({[4-cyanoethylthio-3',4'-bis(methylthio)tetrathiafulvalen-3-yl]thio}methyl)phenyl]benzene (**6b**): Using **13** (93% pure; 0.190 g, 0.30 mmol), we obtained 0.355 g (75% yield) of orange foam. M.p. 87−89°C (CH_2Cl_2). − ^{1}H NMR ($CDCl_3$): δ = 2.34 (t, 6 H, SCH_2, *J* = 7.3 Hz), 2.42 (s, 18 H, SCH_3), 2.84 (t, 6 H, CH_2CN, *J* = 7.3 Hz), 4.09 (s, 6 H, SCH_2Ar), 7.42 (d, 6 H, arom. H, *J* = 8.2 Hz), 7.67 (d, 6 H, arom. H, *J* = 8.2 Hz), 7.77 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 18.21, 19.14, 31.29, 40.41, 108.86, 112.58, 117.58, 125.07, 126.05, 127.29, 127.62, 129.59, 131.88, 136.13, 140.38, 141.64. − MS (FAB); *m/z*: 1582.7 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{60}H_{51}N_3S_{24}$ 1582.7. − IR (KBr): $\tilde{\nu}$ = 2917, 2250 (CN), 1631, 1597, 1510, 1418, 888, 831, 773 cm^{-1}. − $C_{60}H_{51}N_3S_{24}$: calcd. C 45.51, H 3.25, N 2.65, S 48.59; found C 45.73, H 3.35, N 3.31, S 48.67.

1,3,5-Tris[3-({[4-cyanoethylthio-3',4'-bis(methylthio)tetrathiafulvalen-3-yl]thio}methyl)phenyl]benzene (**6c**): Using **14** (69% pure; 0.255 g, 0.30 mmol), we obtained 0.347 g (73% yield) of orange foam. M.p. 77−80°C (CH_2Cl_2). − ^{1}H NMR ($CDCl_3$): δ = 2.36 (t, 6 H, SCH_2, *J* = 7.4 Hz), 2.38 (s, 9 H, SCH_3), 2.41 (s, 9 H, SCH_3), 2.82 (t, 6 H, CH_2CN, *J* = 7.4 Hz), 4.14 (s, 6 H, SCH_2Ar), 7.34 (d, 3 H, arom. H, *J* = 7.6 Hz), 7.45 (dd, 3 H, arom. H, *J* = 7.6 and 7.6 Hz), 7.66 (d, 3 H, arom. H, *J* = 7.6 Hz), 7.69 (s, 3 H, arom. H), 7.82 (s, 3 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 18.24, 19.16, 31.26, 40.71, 108.76, 112.54, 117.60, 125.22, 126.28, 126.88, 127.28, 127.63, 128.08, 128.28, 129.33, 131.87, 137.38, 141.35, 141.86. − MS (FAB); *m/z*: 1582.6 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{60}H_{51}N_3S_{24}$ 1582.7. − IR (KBr): $\tilde{\nu}$ = 2919, 2250 (CN), 1595, 1582, 1419, 890, 772, 707 cm^{-1}. − $C_{60}H_{51}N_3S_{24}$: calcd. C 45.51, H 3.25, N 2.65, S 48.59; found C 45.56, H 3.09, N 2.56, S 45.61.

1,1,1-Tris[4-({[4-cyanoethylthio-3',4'-bis(methylthio)tetrathiafulvalen-3-yl]thio}methyl)phenyl]ethane (**6d**): Using **16** (72% pure; 0.225 g, 0.30 mmol), we obtained 0.385 g (84% yield) of orange foam. M.p. 74−77°C (CH_2Cl_2). − ^{1}H NMR ($CDCl_3$): δ = 2.14 (s, 3 H, CH_3), 2.41 (s, 9 H, SCH_3), 2.43 (s, 9 H, SCH_3), 2.48 (t, 6 H, SCH_2, *J* = 7.2 Hz), 2.89 (t, 6 H, CH_2CN, *J* = 7.2 Hz), 4.03 (s, 6 H, SCH_2Ar), 7.04 (d, 6 H, arom. H, *J* = 8.3 Hz), 7.23 (d, 6 H, arom. H, *J* = 8.3 Hz). − ^{13}C NMR ($CDCl_3$): δ = 18.54, 19.20, 19.22, 31.31, 40.32, 52.08, 109.18, 112.22, 117.57, 125.92, 127.37, 127.65, 128.79, 128.97, 131.98, 134.25, 148.34. − MS (FAB); *m/z*: 1534.5 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{56}H_{51}N_3S_{24}$ 1535. − IR (KBr): $\tilde{\nu}$ = 2917, 2249 (CN), 1630, 1507, 1416, 888, 772, 730 cm^{-1}. − $C_{56}H_{51}N_3S_{24}$: calcd. C 43.80, H 3.35, N 2.74, S 50.11; found C 43.42, H 2.57, N 2.83, S 49.64.

General Procedure for the Preparation of Tetrathiafulvalene Macrobicycles **2**: Under N_2, a solution of $CsOH \cdot H_2O$ (3.15 equiv.) in anhydrous degassed MeOH (10 ml) was added to a solution of **6** (1 equiv.) in anhydrous degassed DMF (40 ml) over a period of 10 min at room temp. This solution and a solution of the tribromide (1 equiv.) in anhydrous degassed DMF (50 ml) were added simultaneously, during 17 h at room temp. with stirring, to 50 ml of anhydrous degassed DMF under high-dilution conditions using a perfusor pump. Stirring was continued for an additional 1 h, and the reaction mixture was concentrated in vacuo. The residue was dissolved in $CHCl_3$ (200 ml). The solution was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated in vacuo affording a residue which was first purified by filtration through a short column of silica gel using CH_2Cl_2 as eluent and then by column chromatography on silica gel using a mixture of CH_2Cl_2/petroleum ether (1:1) as eluent.

Tetrathiafulvalene Macrobicycle **2a**: Starting from **6a** (0.29 g, 0.21 mmol), $CsOH \cdot H_2O$ (0.114 g, 0.68 mmol) and **10** (0.077 g, 0.21 mmol), 0.19 g (68% yield) of **2a** was obtained as orange powder; m.p. 240−243°C (dec.). − ^{1}H NMR ($CDCl_3$): δ = 2.44 (s, 18 H, SCH_3), 3.84 (s, 12 H, SCH_2Ar), 7.06 (s, 6 H, arom. H). − ^{13}C NMR 125.7 MHz ($CDCl_3$): δ = 19.24, 40.31, 110.05, 111.88, 127.64, 128.17, 128.95, 138.29. − MS (FAB); *m/z*: 1309; isotope pattern calcd. for $C_{42}H_{36}S_{24}$ 1309.6. − IR (KBr): $\tilde{\nu}$ = 2916, 1603, 1419, 969, 886, 772, 706 cm^{-1}. − $C_{42}H_{36}S_{24}$: calcd. C 38.54, H 2.77, S 58.68; found C 38.56, H 2.59, S 56.76.

Tetrathiafulvalene Macrobicycle **2b**: Starting from **6b** (0.34 g, 0.21 mmol), $CsOH \cdot H_2O$ (0.114 g, 0.68 mmol) and **13** (90% pure; 0.14 g, 0.21 mmol), 0.12 g (32% yield) of **2b** was obtained as yellow-orange powder; m.p. 202−207°C (dec.). − ^{1}H NMR ($CDCl_3$): δ = 2.42 (s, 18 H, SCH_3), 3.99 (s, 12 H, SCH_2Ar), 7.16 (d, 12 H, arom. H, *J* = 8.1 Hz), 7.28 (d, 12 H, arom. H, *J* = 8.1 Hz), 7.33 (s, 6 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 19.14, 39.78, 110.17, 110.73, 124.27, 127.18, 127.24, 127.52, 128.92, 136.77, 139.72, 141.12. − PDMS; *m/z*: 1765.8; calcd. for $C_{78}H_{60}S_{24}$ 1766.77. − IR (KBr): $\tilde{\nu}$ = 2918, 1631, 1599, 1511, 1419, 888, 833, 775 cm^{-1}. − $C_{78}H_{60}S_{24}$: calcd. C 53.07, H 3.43, S 43.50; found C 53.38, H 3.51, S 41.97.

Tetrathiafulvalene Macrobicycle **2c**: Starting from **6c** (0.30 g, 0.19 mmol), $CsOH \cdot H_2O$ (0.100 g, 0.60 mmol) and **14** (69% pure; 0.161 g, 0.19 mmol), 0.074 g (22% yield) of **2c** was obtained as yellow-orange powder; m.p. 174−178°C (dec.). − ^{1}H NMR ($CDCl_3$): δ = 2.24 (s, 18 H, SCH_3), 3.70 (s, 12 H, SCH_2Ar), 7.15−7.43 (m, 30 H, arom. H). − ^{13}C NMR ($CDCl_3$): δ = 19.08, 41.42, 109.31, 110.37, 124.61, 126.49, 127.48, 127.91, 128.04, 129.18, 131.34, 137.87, 140.74, 141.26. − MS (FAB); *m/z*: 1765.6 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{78}H_{60}S_{24}$ 1766. − IR (KBr): $\tilde{\nu}$ = 2918, 1596, 1582, 1420, 889, 874, 794, 772, 705 cm^{-1}. − $C_{78}H_{60}S_{24}$: calcd. C 53.07, H 3.43, S 43.50; found C 52.43, H 3.23, S 43.39.

Tetrathiafulvalene Macrobicycle **2d**: Starting from **6d** (0.29 g, 0.19 mmol), $CsOH \cdot H_2O$ (0.100 g, 0.60 mmol) and **16** (72% pure; 0.14 g, 0.19 mmol), 0.094 g (30% yield) of **2d** was obtained as yellow powder; m.p. 190−193°C (dec.). The ^{1}H-NMR spectra showed a ca. 2:1 mixture of two different macrobicycles, one symmetrical cage with two methyl groups outside the cavity ("out-out" or "o-

o") and one unsymmetrical cage with one methyl group inside and one outside the cavity ("in-out" or "i-o"). – ^{1}H NMR ($CDCl_3$): δ = 1.17 (br. s, in CH_3 of "i-o"), 2.06 (br. s, out-CH_3 of "o-o"), 2.10 (br. s, out-CH_3 of "i-o"), 2.40 (s, SCH_3 of "i-o"), 2.42 (s, SCH_3 of "o-o" and "i-o"), 3.85 (s, SCH_2Ar of "o-o"), 3.94 (s, SCH_2Ar of "i-o"), 4.07 (s, SCH_2Ar of "i-o"), 6.91 (d, arom. H of "o-o", J = 8.3 Hz), 6.96−7.02 (m, arom. H of "i-o"), 7.06 (d, arom. H of "o-o", J = 8.3 Hz), 7.15−7.22 (m, arom. H of "i-o"). – ^{13}C NMR ($CDCl_3$): δ = 19.18, 30.35, 30.52, 39.62, 40.50, 52.14, 52.39, 109.81, 110.23, 110.54, 110.61, 121.13, 126.94, 127.49, 127.90, 128.13, 128.54, 128.59, 128.94, 129.04, 120.20, 129.65, 133.10, 134.63, 134.90, 135.02, 147.76, 147.88, 148.08. – MS (FAB); *m/z*: 1669.5 [$M^{+\bullet}$]; isotope pattern calcd. for $C_{70}H_{60}S_{24}$ 1670. – IR (KBr): $\tilde{\nu}$ = 2919, 1631, 1508, 1418, 1018, 888, 773 cm^{-1}. – $C_{70}H_{60}S_{24}$: calcd. C 50.37, H 3.63, S 46.01; found C 50.32, H 3.40, S 44.94.

One-Pot Procedure for the Preparation of Tetrathiafulvalene Macrobicycle **2a**: To a solution of **4** (0.42 g, 0.90 mmol) in anhydrous degassed DMF (35 ml) under N_2, was added dropwise a solution of $CsOH \cdot H_2O$ (0.159 g, 0.95 mmol) in anhydrous degassed MeOH (10 ml) over a period of 45 min at room temp. After an additional 15 min of stirring, a solution of **10** (0.107 g, 0.30 mmol) in anhydrous degassed DMF (25 ml) was added dropwise during 1 h at room temp. The reaction mixture was stirred at room temp. for 2 h before addition of a solution of $CsOH \cdot H_2O$ (0.159 g, 0.95 mmol) in anhydrous degassed MeOH (10 ml). After 0.5 h of stirring, a solution of **10** (0.107 g, 0.30 mmol) in anhydrous degassed DMF (25 ml) was added over 30 min at room temp. After the work-up procedure described above, 0.267 g (68% yield) of macrocycle **2a** was obtained.

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