Tetrathiafulvalenes in macrocyclic and supramolecular chemistry

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Abstract: We describe that use of a stepvise selective protection-deprotection of tetrathiafulvalene (TTF)-thiolates give rise to either two or three-dimensional macrobicyclic tetrathiafulvalenophanes in high yields by convergent syntheses. Configurationally selective self-assembly of cyclic or bicyclic tetrathiafulvalenes using the cyclic π-acceptor cyclo-bis(paraquat-*p*-phenylene) yields [2]- or [3]pseudocatenanes.
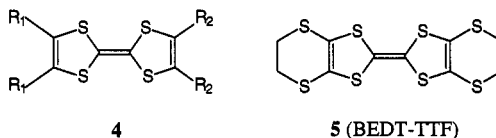
Tetrathiafulvalenes

Tetrathiafulvalenes (TTF's) and related heterocycles have been of high interest for more than two decades, due to their unique π-donor properties[1].

The unsubstituted TTF-molecule **1** is a planar non-aromatic 14-π system. Oxidation takes place sequentially in two discrete reversible steps with formation of ; *i*: a radical cation **2** and *ii*: the 2 x 6π dication **3**:

1	2	3
TTF	radical cation	dication
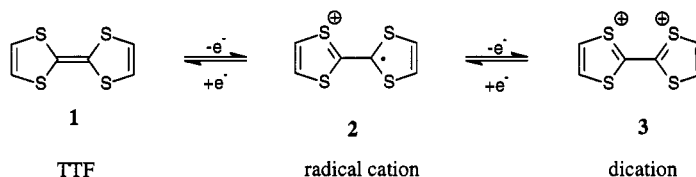
The redox potential for TTF is relatively low: $E^1_{1/2} = 0.35$ and $E^2_{1/2} = 0.71$V (sv Ag/AgCl, MeCN/TBAHFP). Change of substituents (R^1 or R^2) at the TTF system **4**, allows "fine tuning" of the redox properties. Among the large number of tetrathiafulvalenes which have been prepared, BEDT-TTF **5** is relative unique, it has given rise to more superconducting salts than any other TTF-derivative so far.


4	5 (BEDT-TTF)

Conducting materials

In order to develop new conducting charge transfer complexes and salts based on tetrathiafulvalenes it is necessary to control both the redox potential of the donor and the electron affinity of the acceptor simultaneously. However, it is still a fact that the control of the stoichiometry resulting in formation of partly ionized states between the donor and acceptor is serendipitous. Therefore control of the 2- and 3-dimensional molecular architecture of macrocyclic and oligo tetrathiafulvalenes is of great current interest, because it can be expected that their derived charge transfer salts may reveal new types of molecular interactions.

Macrocyclic and supramolecular chemistry

It is exactly the facile and reversible formation of a stable radical cation that makes the tetrathiafulvalene system such an interesting building block, not only for molecular conductors but also as a π-donor in macrocyclic and supramolecular chemistry[2]. From the beginning of our reseach on tetrathiafulvalene chemistry we were well aware that new TTF-building blocks might be useful in many areas of materials chemistry and supramolecular chemistry as well. Some examples where TTFs have been used are shown in the scheme.
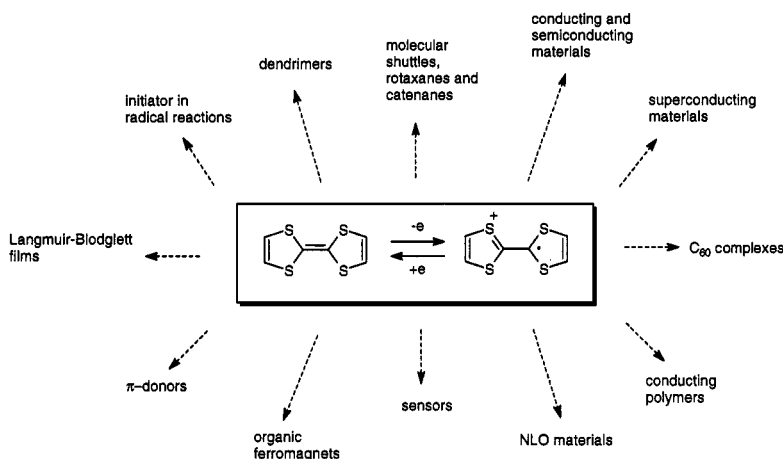
New TTF-building blocks

There are two standard routes to TTF-derivatives; *i*: coupling between two 1,3-dithiole derivatives and *ii*: functionalization of a preformed TTF-system according to the retrosynthetic scheme.
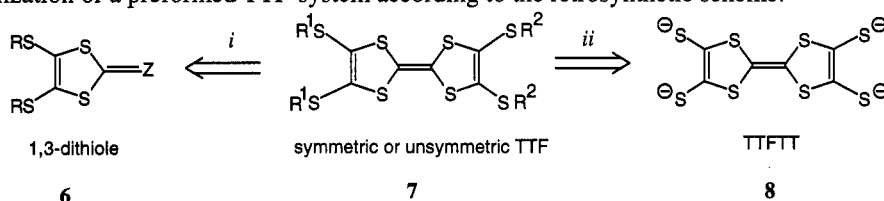

Coupling of 1,3-dithioles to tetrathiafulvalenes often gives rise to synthetic problems and furthermore bis-1,3-dithioles show a strong propensity to give intramolecular coupling reactions rather than bis-TTF macrocycles. We therefore realised, that the most useful route to macrocyclic and oligo-TTFs should be based on a preformed TTF-group *i.e.* route *ii* in the scheme above. This clearly would require a stable and versatile protecting group R.

Protection and deprotection of TTFTT

In a number of papers we have reported an effective protection/deprotection methodology for preparation of TTFTT derivatives using the cyanoethyl group as a versatile protecting group for TTF thiolate groups[3]. The cyanoethyl group almost univesally gives soluble and well crystalline products, both in the case of the 1,3-dithioles **6** as well as for the TTFs **7**. Not only can the tetrathiafulvalene tetrathiolate (TTFTT) **8** be prepared and subsequently realkylated in almost quantitative yield, but it is also possible to carry out stepvise protection/deprotection reactions using caesium hydroxide as base in the cleavage step. Although TTF-thiolates must be handled under inert atmosphere when for example sodium methoxide/methanol is used for dealkylation, the corresponding TTF-caesium thiolates are normally stable in the air and can be isolated. As noted above deprotection takes place stepwise and use of either 1-, 2- or in the case of TTFTT, 4 equivalents of caesium hydroxide (in dry DMF under N_2) followed by realkylation allows the preparation and subsequent construction of multible-TTF systems with both 2- and 3-dimensional structure, overall yields deprotection/realkylation being in the range 50 - 100%. The following schemes gives an overview of the various TTF-building blocks:

Unsymmetric TTFs

The unsymmetrical TTFs are prepared by cross coupling of a suitable 1,3-dithiole-2-thione with 4,5-bis(2'-cyanoethylthio)-1,3-dithiole-2-one.
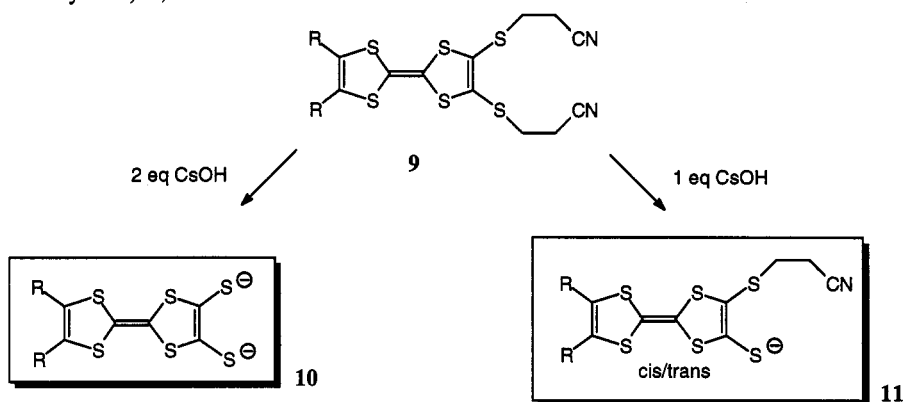
Mono- and bis-deprotection

Using the key starting material 2,3,5,7-tetrakis(2'-cyanoethylthio)tetrathiafulvalene and a suitable amount of caesium hydroxide gives access to either TTFTT as well as bis thiolate **13** and the monothiolate **14**.
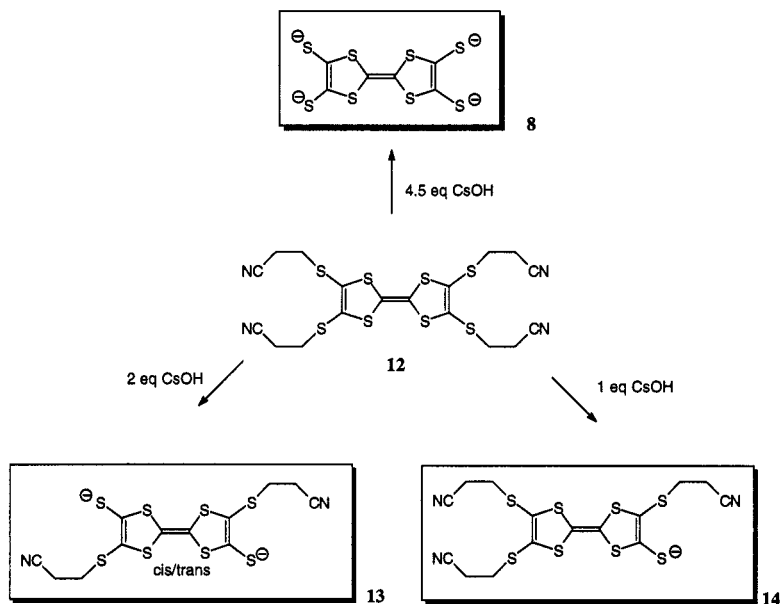

By suitable combination of these building blocks it has been possible to prepare a range of multible-TTF systems as described below.

Cyclic TTF-oligomers

The *charge-transfer* salt of multi-donor derivatives will be of great interest because of the possibility of obtaining materials with higher dimensionality as mentioned previously. CPK models of the cyclic TTF-tetramer **16** showed that one possible conformation had a calix-like geometry that perhaps would be appropriate for the interaction with a variety of acceptors. The synthetic strategy using the TTF-building blocks described above enabled us to prepare macrocycle **16** as well as a number of related oligomers. The yields are high in all steps as this synthetic strategy allows the sequential assembling of each synthon, ensuring an almost complete control of the oligo-purity. The methodology employed could be

extended to a variety of different spacer groups as well as different substituents. Exchange of the propylene units for example with small aromatic systems, methylene or acetylene units will give rise to more rigid macrocycles.
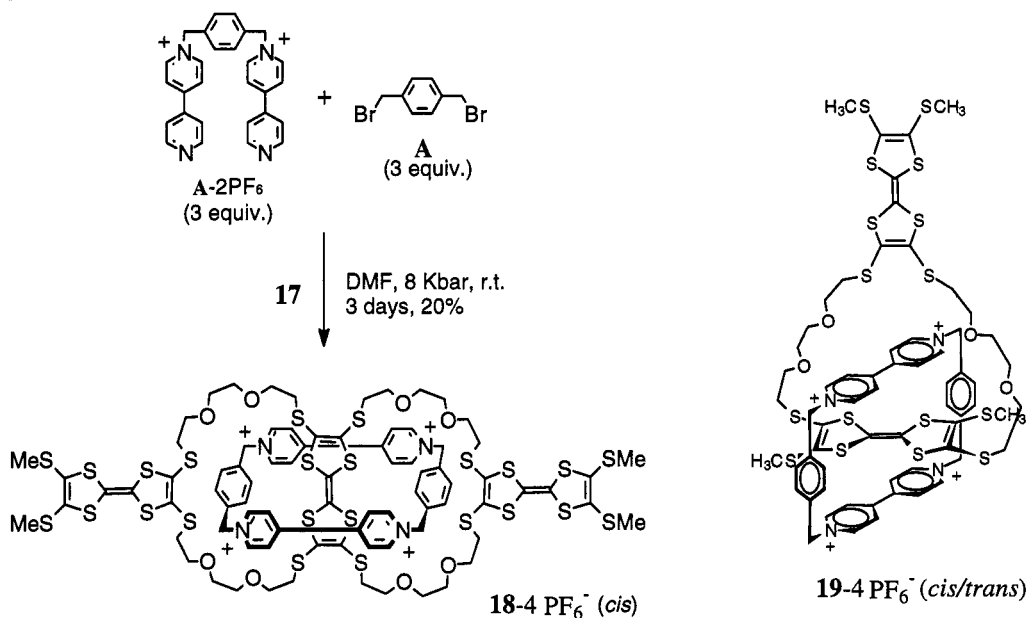

15

DMF
High Dilution
69%

1) 2 eq. CsOH·H₂O
2) 1 eq. ICH₂CH₂CH₂I

16
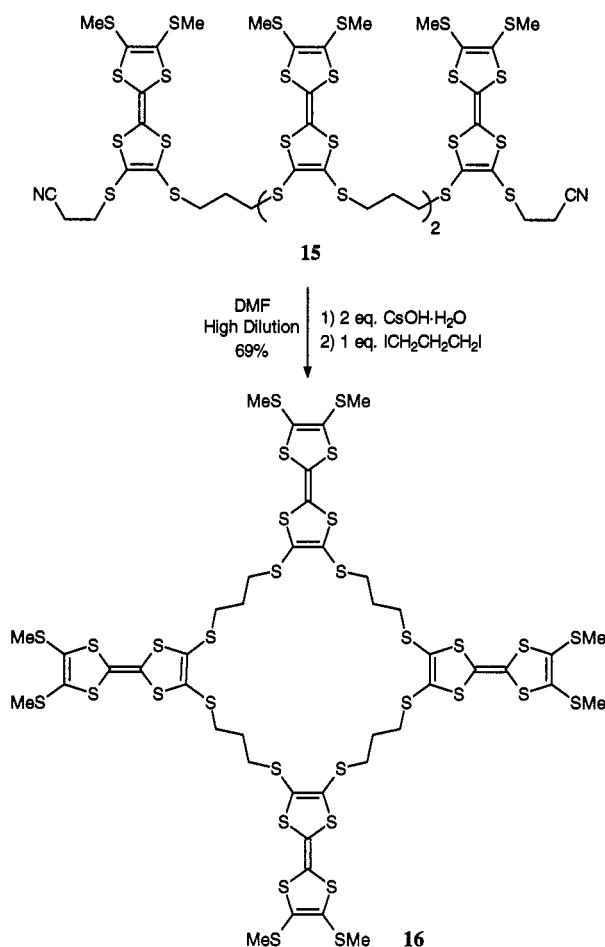
Catenanes

The formation of catenanes by self-assembling is controlled by the information stored in the "preprogramed" starting materials. The information, locked within the catenane molecules, also results in catenanes with properties quite different from those of their individual molecular components. Based on the donor-acceptor interactions, catenanes of different structures have been prepared from a variety of starting materials. By incorporating two dioxyphenylene units into a TTF-based dimacrocyclic system, we succeeded in obtaining both *cis* and *trans* [3]pseudocatenanes, whereas replacing the dioxyphenylenes with 9,10-dioxyanthrylenes resulted in the selective formation of the corresponding *trans* [3]pseudocatenane[4]. The example shown in the following scheme illustrate the selective self-assembling synthesis of a *cis* [3]pseudocatenane, using the dimacrocycle precursor **17**, in which the central TTF unit constitutes the bridge of the dimacrocycle while the peripheral TTF units control the configuration of the resulting catenane[5].

Preparation of compound **17** was chosen because investigation of a CPK model suggested that, only when the central TTF unit in [3]catenane **18** adopts a *cis* configuration, then the pheripheral TTF units will be able to form π-π donor-acceptor interactions with the two bipyridinium units. Such interaction are essential for the configurational control during the possible self-assembling process. The reaction scheme illustrate the sequential assembly of the macrocyclic TTFs.

17 (*cis/trans*)
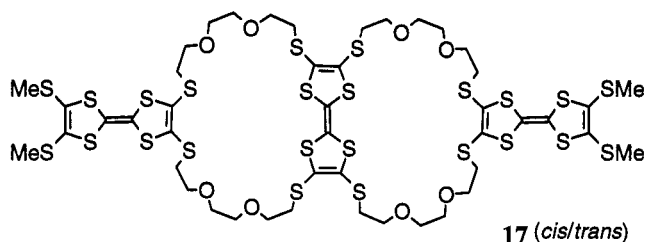
Tris-TTF **20** was prepared via two-step macrocyclizations using high dilution conditions (perfusor pump) in a 35% overall yield. No catenane products were detected after stirring the solution of **20** in DMF or acetonitrile in the presence of A-2PF$_6$ and **B** at room temperature for three weeks at atmospheric pressure. However under ultra-high pressure (8 Kbar), **18**-4PF$_6$ was obtained in 20% yield from the self-assembly of **17**, A-2PF$_6$, and **B** at room temperature in three days. Catenane **18**-4PF$_6$ was characterized by electrospray mass spectrometry, which exhibited ion peaks at m/z = 1160, 725, and 508, corresponding to [M-2PF$_6$]$^{2+}$, [M-3PF$_6$]$^{3+}$, and [M-4PF$_6$]$^{4+}$, respectively. CPK-models, as well as NMR studies indicate that tris-TTF catenane **18** adopt a structure in which the three TTF-groups effectively sandwich the cyclic acceptor around the central *cis*-TTF group. Two peripheral TTF are necessary for exclusive formation of the *cis*-isomer, thus the donor composed of only two TTF-groups gives rise to an inseparable mixture of the corresponding *cis/trans* isomers of the [2]catenane **19**.

A-2PF$_6$
(3 equiv.)

A
(3 equiv.)

17

DMF, 8 Kbar, r.t.
3 days, 20%

18-4 PF$_6^-$ (*cis*)

19-4 PF$_6^-$ (*cis/trans*)

TTF-macrocycles and cages

The construction of macrocycles containing tetrathiafulvalene (TTF) units has received a growing attention. Apart from the preparation of novel organic conducting materials, such molecules may act as hosts in host-guest chemistry. Moreover, since they contain one binding site close to an electroactive recognition site, host-guest interactions can be investigated electrochemically.

The properties of the TTF moiety as a reversible, stable two electron donor makes it a good candidate for the incorporation into macrocyclic systems that might act as receptors for electron poor compounds.

The molecular design of three dimensionally bridged macropolylic compounds is currently a challenge in synthetic chemistry and incorporation of redox active groups into such molecules is of interest for the preparation of macropolycyclic receptor molecules, such as the Cram cacerand synthesis. Our TTF-methodology is well suited to prepare macrobicyclic cyclotetrathiafulvalenophanes with three TTF-bridges, via tris-TTF intermediates as shown in the following scheme[6].
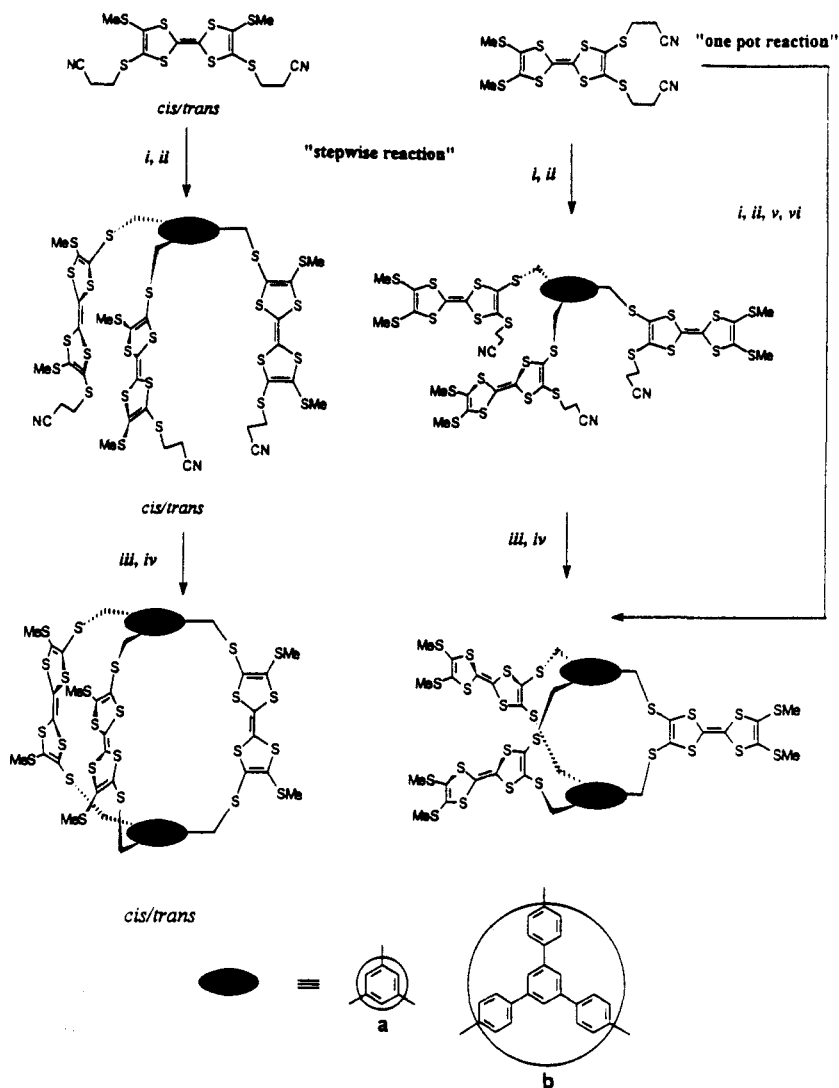
The reagents (under N_2 at room temp.) in this scheme are the following: *i*) CsOH, H_2O (1.05 eq), MeOH/DMF; *ii*) tribromide (0.33 eq), DMF; *iii*) CsOH,H_2O, DMF-high dilution; *iv*) tribromide (1 eq), MeOH/DMF; *v*) CsOH,H_2O (1.05 eq), MeOH/DMF; *vi*) tribromide (0.33 eq), DMF.

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