ACCOUNTS

Tetrathiafulvalene Thiolates: Important Synthetic Building Blocks for Macrocyclic and Supramolecular Chemistry

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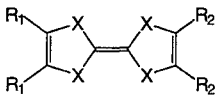
Received 20 November 1996

Abstract. The preparation of rather complex molecular assemblies can now be accomplished by using a complete set of tetrathiafulvalene (TTF) based building blocks. The facile deprotection of the 2-cyanoethyl group, a versatile protecting group for 1,3-dithiolium-2-thione-4,5-dithiolates and TTF-thiolates have proven to be a viable method for the incorporation of TTF units into macrocyclic and supramolecular compounds. Especially the stepwise protection-deprotection methodology have been used extensively by our group for the preparation of two and three dimensional macrocyclic (mono-, bis- and tricyclic) as well as TTF-based supramolecular systems. The generation, utilization and scope of the generated thiolates are illustrated by several examples: Dendrimeric and oligo-TTF's, three dimensional tetrathafulvalenophanes, TTF-containing catenanes and rotaxanes and donor acceptor systems based on TTF as the donating portion.

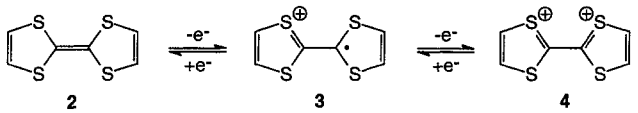
1. Introduction

Tetrachalcogenafulvalenes **1** and especially tetrathiafulvalene (**1**, X = S, TTF) and related heterocycles, have received much interest for more than two decades, due to their unique π-donor properties.[1]

Although the unsubstituted TTF-molecule **2** is a planar 14-π system, TTF is non-aromatic according to the Hückel definition because the 14-π electrons lack cyclic conjugation. TTF can be oxidized reversibly in two discrete steps with the formation of i) the radical cation **3** and ii) the dication **4**.



1 X = S, Se, Te



2 **3** **4**

Figure 1

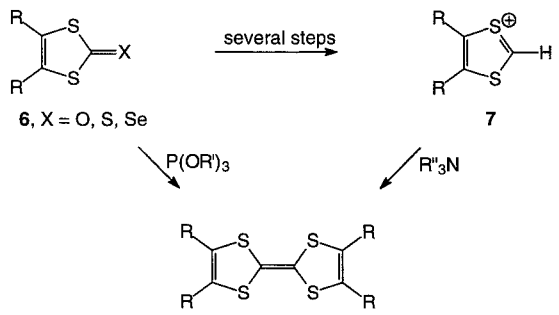
The redox potentials for TTF are relatively low: $E^1_{1/2}$ = 0.38 and $E^2_{1/2}$ = 0.70 V (vs. SCE). The ease of oxidation, and hence the ability to donate electrons, are explained by the gain of aromaticity in the two 1,3-dithiole rings during the first and second oxidation. Due to the effective resonance stabilization of the aromatic dithiolium system and to a minor extent the polarizable sulfur atoms, the radical cations **3** and dications **4** may be isolated as stable crystalline compounds.[2]

TTF form crystalline charge transfer (CT) complexes with a variety of acceptors; TCNQ (tetracyanoquinodimethane), TCNE (tetracyanoquinodimethane), chloranil and DDQ (dichlorodicyanoquinone). The CT complex between TTF and TCNQ exhibit a prominent conductivity (500 Siemes/cm) of metallic character.[3,4] Further a variety of "organic metals" based on TTF, both as CT complexes and radical cation salts (Bechgaard salts), e.g. $(TTF)_2X$ where X is a monocharged closed shell anion (vex. PF_6^- or ClO_4^-) have been prepared.[5]

The redox properties of a TTF derivative can be fine tuned by changing the substituents R_1 and R_2 in **1**. This is illustrated by the redox potentials of the electron rich tetramethyl-TTF (**1**, X = S, $R_1 = R_2 = CH_3$): $E^1_{1/2}$ = 0.25 and $E^2_{1/2}$ = 0.60 V (vs. SCE) compared to the relative electron deficient derivative tetramethoxycarbonyl-TTF (**1**, X = S, $R_1 = R_2 = COOCH_3$): $E^1_{1/2}$ = 0.80 and $E^2_{1/2}$ = 1.08 V (vs. SCE).[1]

The multitude of interesting properties of the TTF moiety, including superconductivity for some derivatives, have prompted much research and many excellent reviews have been reported.[1,6,7,8] The most important synthetic method commences with a 1,3-dithiole derivative which is converted into a TTF by different methods. Of these methods the phosphite mediated coupling of 1,3-dithiole-2-chalcogenones **6** and the coupling of 1,3-dithiolium salt **7** by deprotonation are dominant (Scheme 1). These two methods are complementary to each other, the first can only be used if the substituents are electron withdrawing while in the later case dithiolium bearing electron withdrawing group are very unstable and hence this methods only works for electron donating substituents.

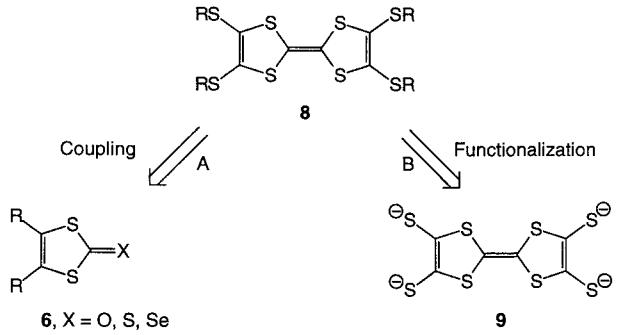
Prior to our work, a simple and practical method for incorporation of the TTF-group in larger structures was unknown. We therefore decided to



Scheme 1

improve this situation and in the last eight years we have been interested in the incorporation of TTF into macrocyclic and supramolecular compounds.[9]

There are two standard synthetic strategies for the preparation of structurally modified tetraalkylthio TTF's **8** (Scheme 2): disconnection A: the coupling method and disconnection B: functionalization of a preformed tetrathiafulvalene tetrathiolate (**9**, TTFTT).



Scheme 2

In many cases the known synthetic method (disconnection A) tends to give intramolecular products rather than larger oligomers. Further, a number of substituted 1,3-dithioles are unable to survive the reaction conditions, especially systems containing ester-, thioester-, urethane-, alcohol or carbonyl functionalities. Early on we therefore realized that the most successful route to macrocyclic and oligomeric TTF's should be based on a preformed tetrathia-TTF moiety and hence would require a stable and versatile protecting group for the thiolate function.

In this account we describe the utilization of the 2-cyanoethyl group as such a versatile protection group for 1,3-dithiole-4,5-dithiolate and TTF thiolates, and give some examples illustrating the ease in which these new building blocks can be converted stepwise to macro- and supramolecular assemblies by the effective protection/deprotection methodology, taking advantages of the high nucleophilicity of the thiolate sulfur.

2. Previous protecting groups

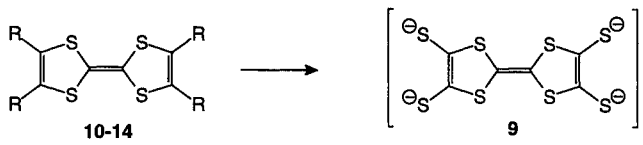
The quest for using TTF as a π-donor in supramolecular chemistry has stimulated the search for a suitable preformed TTF which could easily be functionalized.[10] Simultaneously a number of research groups realized that TTF-tetrathiolate **9** would be a useful synthon, and therefore disconnection B has been adopted by several groups for a more convergent route to functionalized TTF's. The precursors to TTFTT **9** are outlined in Scheme 3 together with the conditions for their conversion into **9**.[11–15]

Compounds **10**, **12** and **13** are converted into **9** by treatment with nucleophiles, while deprotection of **11** is achieved using tetrabutylammonium fluoride. Tetralithio-TTF **14** can be converted into alkylthio-TTF's (such as **8**, R = alkyl) by reaction with disulfides,[16] e.g. dimethyl disulfide or diphenyl disulfide, or by reaction with elemental

Biographical Sketches

Jan Becher was born at Frederiksberg, Denmark in 1939. He did graduate work and finished his thesis with professor Ole Buchardt, University of Copenhagen in 1966. Research associate at N. Clauson-Kaas A/S, 1966-68 and postdoctorate fellow at Synvar Research Institute, Fulbright fellowship, USA 1968-69.
Assistant professor 1969-89, awarded Dr. scient. 1986 and appointed docent (professor) in 1989 also at Odense University. Received the "Bjerrum Chemistry Award" and gold metal in 1992 for his work in organic synthesis and heterocyclic chemistry. Jan Becher is a member of the editorial board, Journal of Heterocyclic Chemistry, The Danish Natural Science Academy and his research interests covers heterocyclic chemistry, especially sulfur containing heterocycles, organic sulfur chemistry, tetrathiafulvalene chemistry, macrocyclic chemistry, macrocyclic ligands and supramolecular chemistry.

Klaus Bæk Simonsen was born in Odense, Denmark, in 1967. He received his B.Sc. degree in 1992 and M.Sc. degree in 1994 under the supervision of professor Jan Becher. He is presently a Ph.D. student with Professor Jan Becher working on the incorporation of the tetrathiafulvalene group into supramolecular assemblies together with other electroactive groups. From September 1995 he spent ten months as a visiting Ph.D. student in the laboratories of professor Michael P. Cava (University of Alabama).



10-14 9

entry	R	conditions	ref.
10	SC(O)S	nucleophiles	11
11	$SCH_2OCH_2CH_2SiMe_3$	Bu_4NF	12
12	SC(O)Ph	nucleophiles	13
13	$SCH_2C_6H_4OAc$-4	nucleophiles	14
14	Li	S_8	15

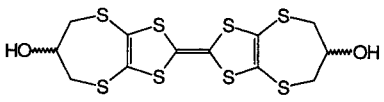
Scheme 3

sulfur.[15] However, all of these protection groups for TTF thiolates show various disadvantages: Synthetic problems, such as incomplete deprotection, difficulties to separate from protecting group by-products, low yields, and/or expensive starting materials. All these problems makes them inapplicable for the preparation of TTF-containing macromolecular assemblies in acceptable yields.

3. The development of new building blocks

3.1. Discovery of the cyanoethyl group

Because of the disadvantages summarized above, the search for an alternative preformed TTF was necessary if we wanted to continue our study of TTF as building-blocks in supramolecular and macromolecular chemistry. An alternative preformed TTF, the bishydroxy TTF **15** (Figure 2),[17] has been used successfully for the incorporation of TTF into rather complicated systems such as copper(I) [2]-catenates[18] and rotaxanes[19] by deprotonation of the hydroxyl groups followed by subsequent alkylation. This system **15**, did not meet our needs for a versatile TTF-based building block, because the two stereogenic carbon atoms, linking the seven-membered dithiolene rings to the remaining of the molecules, have two relative configurations (syn and anti). Furthermore, synthesis of compound **15** includes several steps.

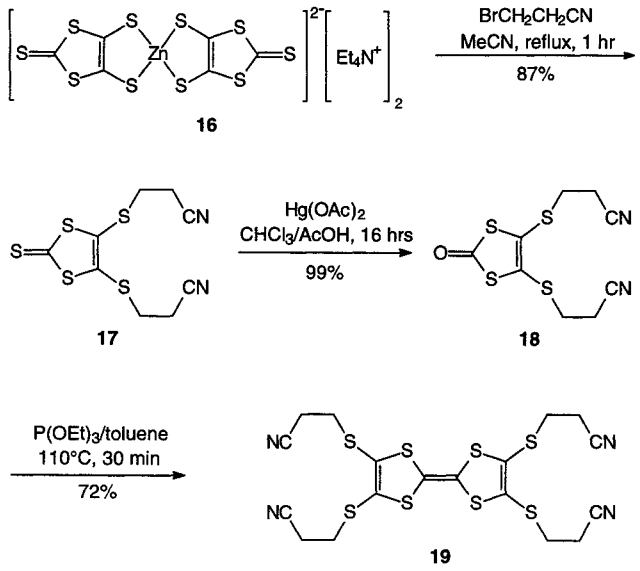


15

Figure 2

The annual meeting in the Danish Chemical Society in the summer of 1993 illustrated how a lecture in a totally different area can be fruitful for the alert student. During a seminar in oligonucleotide chemistry the 2-cyanoethyl group was mentioned as a protection group for the thiolate group in phosphorodithioates.[20] Further the cyanoethyl group has been used to protect heterocyclic thiolate functions.[21] This protecting group was easily removed with concentrated ammonium hydroxide, generating acrylonitrile and the free thiolate by a β-elimination. With this recently acquired knowledge, one group member went into the laboratory and during the course of two weeks 2,3,6,7-tetrakis(2-cyanoethylthio)tetrathiafulvalene **19** was prepared in three steps from the zincate salt **16** (Scheme 4) in excellent yields.[22]

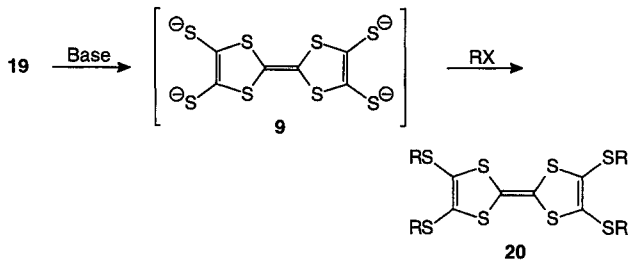
Hence **16** was alkylated with 3-propionitrile in refluxing acetonitrile and the resulting 4,5-bis(2-cyanoethylthio)-1,3-dithiole-2-thione **17** was converted to oxo derivative **18** by mercuric acetate trans-chalcogenation. The phosphite mediated self coupling was carried out in a mixture of toluene and triethyl phosphite affording **19** (62% overall).



16 **17** **18** **19**

Scheme 4

The first requirement for a new protecting group for TTFTT was accomplished, namely the ability of the cyanoethyl group to withstand the coupling reagents and the reaction conditions. Second the protecting group should be removed under conditions in which the redox active TTF unit would be unaffected and ideally in quantitatively yields. To our satisfaction 2,3,6,7-tetrakis(2-cyano-ethylthio)TTF **19** is an excellent precursor for TTFTT **9**. Generation of TTFTT is achieved in quantitative yield, as evidenced by the yields in the subsequent alkylation step (Scheme 5). Treatment with the appropriate electrophile gave the well known compounds bisethylenedithio tetrathiafulvalene (BEDT-TTF) and tetramethylthio tetrathiafulvalene (TMT-TTF) in almost quantitatively yields.[22]



9 **20**

R	X	yield	trivial name
CH_2CH_2	Br	98	BEDT-TTF
CH_3	I	95	TMT-TTF

Scheme 5

Several methods are effective for the deprotection of **19** (Table 1). Of these methods, the deprotection using a methanolic solution of caesium hydroxide in dimethylformamide is used exclusively in our laboratory. Because TTF-thiolates are very sensitive to oxidation (forming disulfides) all reactions must be carried out under an inert atmosphere.

Table 1

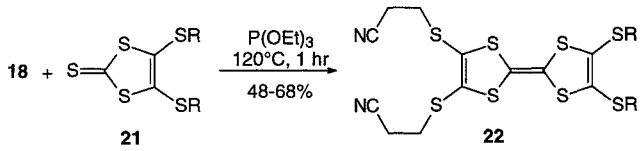
Base (8 equivalents)	solvent	time
NaOEt	EtOH	4 h
NaH	DMF	1 h
Bu_4NOH, MeLi or LDA	THF	5 min
CsOH in MeOH	THF or DMF	5 min

3.2. Cross coupling to unsymmetric TTF

Since the discovery of metallic conductivity and superconductivity in unsymmetrical TTF derivatives,[23] a variety of synthetic strategies have been employed for preparing such analogues; for example, the reaction of 1,3-dithiole-2-ylidene-λ^5-phosphoranes with 1,3-dithiolium salts[24] or 2-alkylseleno-1,3-dithiolium salts,[25] or dimerisation of two 1,3-dithiolium salts.[26]

The collaboration between synthetic groups working in the same area will often be fruitful and stimulating for the development and synthesis of new materials. Indeed, our collaboration with Prof. Gorgues group in France was especially useful as they reported that cross coupling of an equimolar amount of a 1,3-dithiole-2-thione and a 1,3-dithiole-2-one gave excellent yields of the unsymmetrical TTF.[27]

This methodology has been succesfully employed in the preparation of a range of the bis-cyanoethyl protected TTF's **22**. Thus reaction of an equimolar mixture of 4,5-bis(alkylthio)-1,3-dithiole-2-thiones **21** and 4,5-bis(2-cyanoethylthio)-1,3-dithiole-2-one **18** in neat triethyl phosphite at 120°C gave the unsymmetrical (cross coupled) TTF's in satisfying yields (48-68%, Scheme 6).[28]



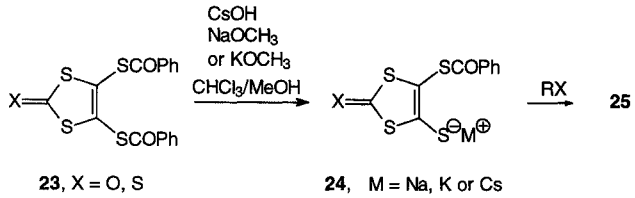
Scheme 6

Finally, the challenge to synthesize a disubstituted TTF in a selective fashion has been met, and the ease in which these divalent building block are prepared has several advantages compared to the lithiation route. Although the latter is a one step synthesis of a highly functionalized TTF, it is of limited preparative use due to the high price of TTF. Further, difunctionalization *via* lithiation gives rise to several isomers; namely 2,3; 2,6 or 2,7 disubstituted TTF's.[8]

So far we were able to synthesize these cyanoethyl protected bisthio- and tetrathio TTF's and convert them to corresponding bis- and tetra-alkylated TTF's by deprotection and subsequent alkylation with a variety of electrophiles. The derived TTF are all very soluble in standard solvents and hence easy to isolate by chromatography, furthermore, the compounds are stable and can be kept on the shelf without any precaution. Unfortunately the quest for the incorporation of TTF into larger assemblies by this preformed TTF's remained unsolved. But the solution to this challenge was already present in our compounds, although we just had to look harder.

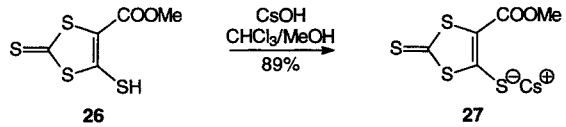
3.3. Selective Monodeprotection: key synthetic intermediates

Simultaneously with our work, Dr. Olk *et al.* reported the mono-deprotection of 4,5-bis(benzoylthio)-1,3-dithiole-2-chalcogenones **23** using one equivalent of base. The generation of the monoanionic derivatives **24** was achieved by ester cleavage using one equivalent of alkali metal hydroxide, preferably caesium hydroxide, in a mixture of chloroform and methanol.[29] These thiolate mono alkali metal salts (Na^+, K^+, Cs^+) are notably more stable, than the corresponding disodium or dipotassium salts of 1,3-dithiole-2-thione-4,5-dithiolate (DMIT). The application of these thiolates was illustrated by the reaction with several electrophilic reagents to the corresponding thioether compounds **25** (Scheme 7).



Scheme 7

One reasonable explanation for the relative stability of these mono alkali metal salts **24** is the ability of the carbonyl group on the neighboring sulfur atom to participate in the coordination of the alkali metal. This consideration was confirmed in our group. In another project, we used 4-methoxycarbonyl-1,3-dithiole-2-thione-5-thiol **26**.[25] Because the thione **26** is unstable for a longer period is was converted to stable caesium salt **27** by treatment with a methanolic caesium hydroxide solution in chloroform (Scheme 8).[30]



Scheme 8

The single crystal X-ray structure of the caesium thiolate **27** is shown in Figure 3. In the lattice each caesium ion (eight coordinated) is coordinated to four thiolates (S4, crystallographic numeration), two thione sulfur atoms (S1) and two carbonyl oxygen atoms (O6). Although the stability of this system to some extent is caused by π-electron delocalisation of the thiolate anion to the ester group, the evidence of the coordination of the carbonyl group confirms the stability of the related caesium thiolate **24**.

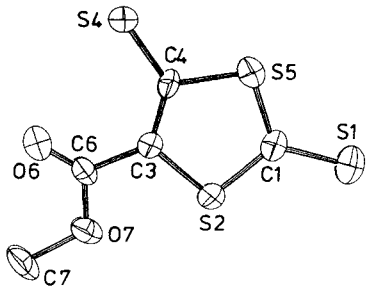
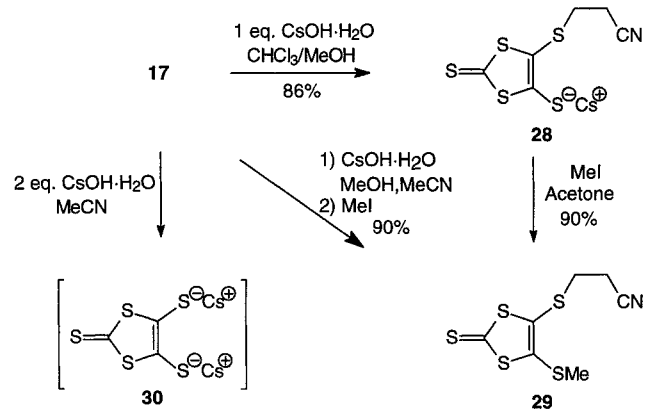


Figure 3

One of the main obstacles for progress of scientific research is sometimes simple natural skepticism, which has slowed down the research process for many a scientist.

Would it be possible to monodeprotect 4,5-(2-cyanoethylthio)-1,3-dithiole-2-thione **17** in a similar manner? This question was a logical extension to the work performed by Dr. Olk.

In the beginning we were skeptical and rejected this idea, due to the lack of a stabilizing effect by the cyanoethyl group in our system, as compared to the ester group. As a result this project was stalled for several months. But when the reaction was finally carried out it showed some very promising results. It was indeed possible to adopt the above strategy for the monodeprotection of compound **17**. Treatment of a chloroform solution of **17** with one equivalent caesium hydroxide monohydrate in methanol selectively generated the mono caesium salt **28**, which precipitated from the reaction mixture in excellent yield (Scheme 9).[28,31]

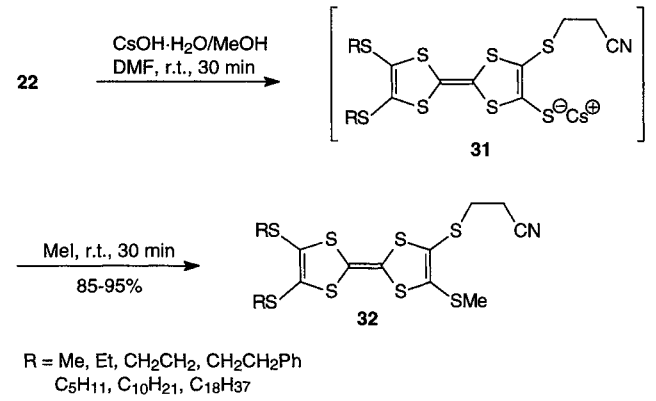


Scheme 9

We had already noted the enhanced stability of the DMIT caesium thiolates[32] compared to their sodium and potassium analogues. Since fortunately the caesium mono thiolate **28** is considerably more stable than the corresponding dicaesium salt **30** (prepared by using two eq. base in acetonitrile), it can be stored in the air for several months, and provides an excellent precursor to unsymmetrically substituted 1,3-dithiole-2-thiones.[33]

To our delight the caesium salt **4** underwent smooth alkylation in acetone with electrophiles, e.g. iodomethane to give **29**. Compound **29** could also be prepared by *in situ* mono deprotection (in acetonitrile) by slow addition of one equivalent of base, subsequent quenching with an electrophile (here iodomethane) gave **29**. Subsequently compound **29** could be converted to an unsymmetric bisalkylated 1,3-dithiole-2-thione by another deprotection/alkylation sequence.

This facile monodeprotection was then extended to the unsymmetrical TTF series **22**. Thus, when a dimethylformamide solution of the appropriate TTF **22** was treated dropwise with a methanol solution of caesium hydroxide monohydrate (one equivalent) over the course of one hour, the TTF-monothiolate **31** was generated selectively. Subsequent quenching of the thiolate with iodomethane (or another electrophile) gave the methylthio substituted TTF's **32** in near quantitative yields (Scheme 10).

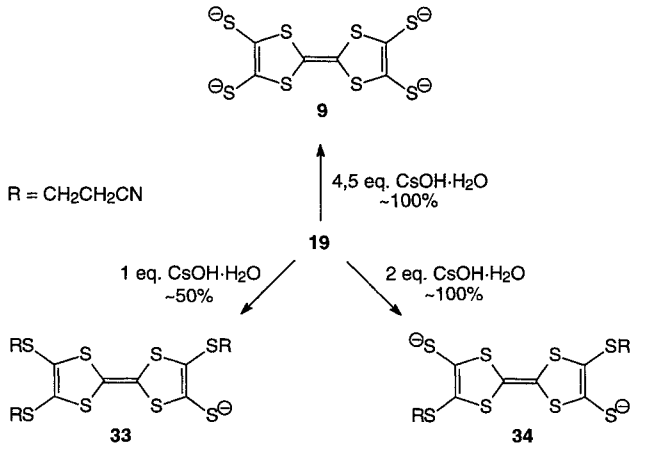


Scheme 10

The above monothiolates, 5-(2-cyanoethylthio)-1,3-dithiole-2-thione-4-thiolate **28** and 6,7-bis(alkylthio)-3-(2-cyanoethylthio)tetrathiafulvalene-2-thiolates **31**, are key synthetic intermediates, and this strategy enables us to control the selective stepwise incorporation of two different alkylthio substituents in the 4- and 5- positions of a 1,3-dithiole-2-thione and in the 2- and 3- positions of TTF in two subsequent high yielding reaction steps.

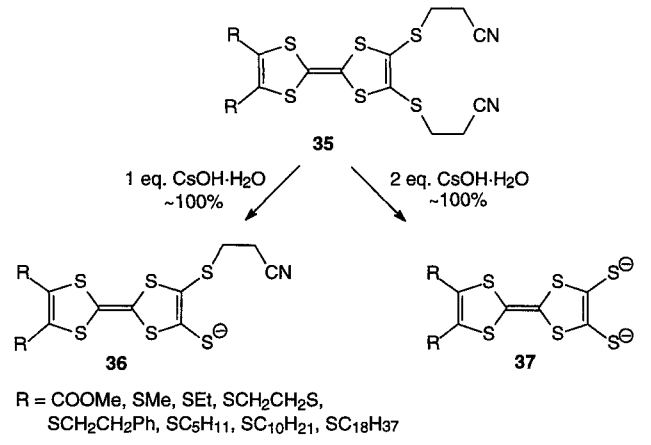
3.4. Complete set of TTF building blocks

The selective monodeprotection proved that it was indeed possible to carry out stepwise deprotection using caesium hydroxide in the cleavage step for TTF with several cyanoethylthio groups. From only three different TTF's it is possible to prepare a variety of TTF thiolates bearing from one to four thiolate moieties. Using the key starting material 2,3,6,7-tetrakis(2-cyanoethylthio)TTF **19** and the appropriate amount of caesium hydroxide gives access to TTFTT **9**, as well as the monothiolate **33** and bisthiolate **34** (Scheme 11).



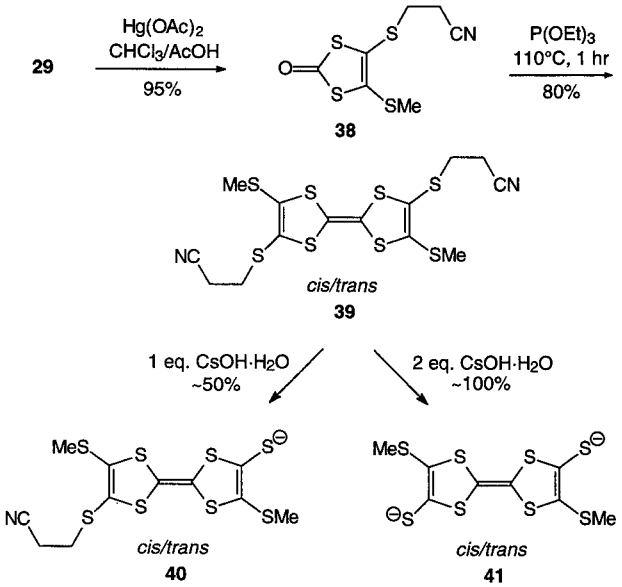
Scheme 11

Starting from the the unsymmetric TTF **35**, using either one or two equivalents of caesium hydroxide, generates the monothiolates **36** and the bisthiolate **37** in quantitatively yields (Scheme 12).



Scheme 12

Another possibility of a preformed TTF with two handles in the 2,6(7) position (recall compound **34**) can be prepared from the unsymmetric thione **29** in two standard reactions (Scheme 13).[31]



Scheme 13

The resulting TTF **39** was isolated as a mixture of *cis* and *trans* isomers. Again the amount of base gives access to either the monothiolate **40** or the bisthiolate **41**.

All the thiolates reported above are generated *in situ* in a degassed solution of dimethylformamide under inert atmosphere, by addition (slow addition for the monodeprotection) of a methanolic solution of caesium hydroxide monohydrate. The thiolates are stable in solution for at least 24 hours. Except for one TTF thiolate bearing three methoxycarbonyl substituents isolated as a stable caesium salt (see structure **43**, Scheme 14),[30] the other TTF thiolates are normally not isolated. Instead they are realkylated with electrophiles.

The thiolates **33**, **34**, **36** and **40** contain a latent thiolate function which can again be liberated in a later reaction-sequence by deprotection and realkylation.

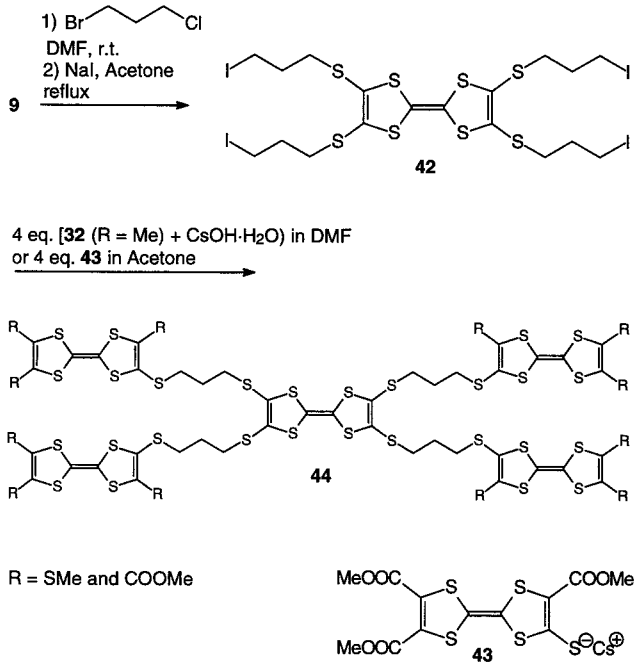
The above methodology allows the preparation and subsequent construction of multiple-TFF systems with two and three dimensional structures. In the last section we will focus on the versatility of these potential building blocks for the incorporation of TTF into macrocyclic and supramolecular assemblies.

4. The diversity and utility of the TTF thiolates

4.1. Dendrimeric and/or OligoTTF

The synthesis and investigation of dendrimeric molecules are presently an active research topic at the interface of supramolecular and polymer chemistry.[34] Molecules containing multidonor derivatives will be of great interest because of the possibility to form charge-transfer complexes of higher dimensionality.[24] Further the incorporation of electroactive components into macromolecular systems enables the exploration of inter- and intra-molecular interactions.[35] Although some examples have been reported by Bryce *et al.*,[36] the incorporation of TTF's into dendrimers has been restricted by the lack of suitable functionalized TTF's.

Stable pentakis TTF's were prepared in a convergent way, by the use of the above protection/deprotection strategy. Hence TTFTT **9** was generated *in situ* and realkylated with 3-chlorobromopropane, which was transformed to the tetrakis iodo TTF **42**. Compound **42** was then reacted with either the stable TTF caesium thiolate **43** in acetone or the thiolate generated from compound **32** (R = Me, Scheme 14) to give the pentamers **44**.[30]



Scheme 14

The cyclic voltammogram (CV) of the pentamers **44** showed four reversible well resolved redox couples, consistent with a multidonor system with no intramolecular interaction between the TTF units.

The pentamer of this type is soluble (purified by chromatography) in nonpolar solvents such as dichloromethane etc., confirming the expectation that oligo-TTF's having the right linkers will be soluble and therefore processable for the incorporation into polymeric materials in order to produce electroactive polymers.

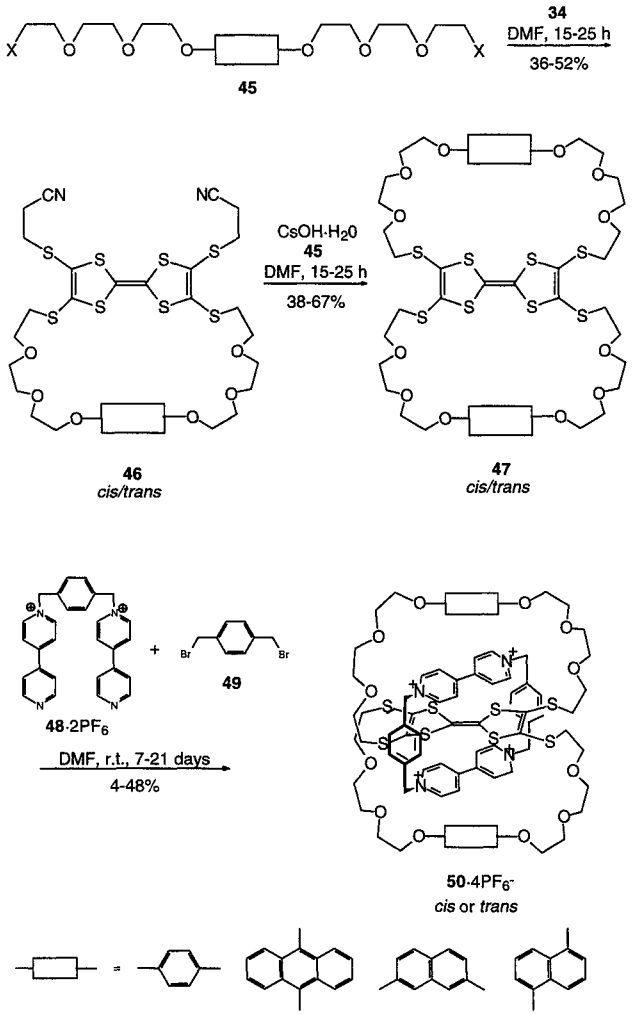
4.2. TTF-based Rotaxanes and Catenanes

The formation of interlocking molecular systems, such as rotaxanes and catenanes, has been a great challenge for the synthetic chemist during the last decade.[37] Especially self-assembly has stimulated the development of several new synthetic methods for the preparation of such topologically complex structures. The extensive research performed by Stoddart *et al.* using the ability of bis(benzyl)-4-4'-bipyridinium dication to self assemble with a variety of electron rich systems clearly illustrates the strong effect of noncovalent interaction in this type of synthesis.[38] In particular, the π–π interaction and the stacking between the donor and acceptor systems (donor-acceptor interactions) have made it possible to design and construct a variety of mechanically interlocked systems, such as catenanes and rotaxanes.[39] Although, some TTF-based catenanes and rotaxanes already have been synthesized the lack of a late common intermediate has prevented further exploration of such systems.[19]

The TTF-thiolates (**9**, **34**, **37** and **41**) reported above are excellent precursors for the incorporation of TTF into mono- and bis-macrocyclic systems and hence for the formation of TTF based catenanes.[40]

By a two step cyclisation reaction under high dilution conditions the dimacrocycles **47** were prepared from the bisalkylating reagents **45** and **34** *via* the monocycle **46** as intermediate (Scheme 15).

The new [3]catenanes **50**·4PF_6^- were obtained by reacting the bis-macrocycles **47** with the dication **48**·2PF_6^- and 1,4-bis(bromomethyl)-benzene **49** in dimethylformamide from three days to three weeks (Scheme 15).



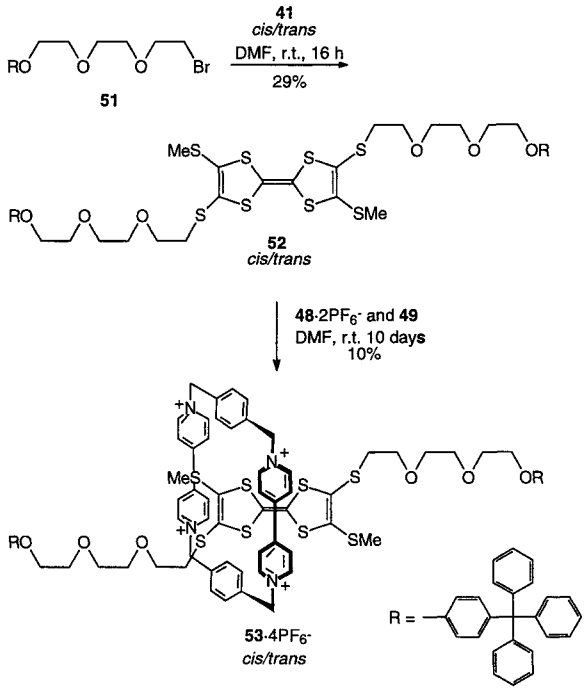
Scheme 15

Depending upon the nature of the linker these novel assemblies were isolated either as pure *cis* or *trans* isomers after chromatography and anion exchange, although the starting bismacrocycles were an inseparable mixture of *cis* and *trans* isomers.[40,42] Interestingly no *cis/trans* isomerisation[41] took place when a solution of [3]catenanes was treated with trifluoroacetic acid. Hence the fixation of the TTF by the tetracationic macrocycle prevent protonation of the fulvene bond.

Further the precursor to a TTF-based rotaxane, the linear TTF **52** was isolated as a mixture of *cis* and *trans* isomers by reacting the (triphenylmethyl)benzene derivative **51** with the bisthiolate **41**, (Scheme 16).[42]

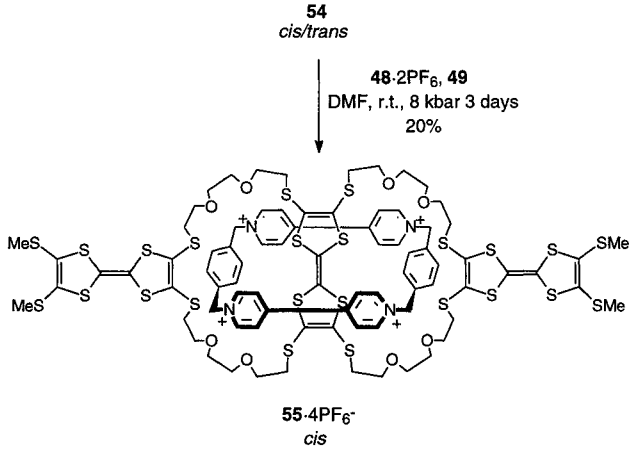
When compound **52** was reacted with the dication **48**·2PF_6^- and 1,4-bis(bromomethyl)benzene **49** in dimethylformamide for ten days the rotaxane **53**·4PF_6^- was obtained as a mixture of *cis* and *trans* isomers.

Starting from the bisprotected TTF **35** (R = SMe, Scheme 12) and the appropriate ethylene glycol linker followed by a two step macro cyclization on TTFTT **9** under high dilution condition afforded a bis macrocycle containing three TTF units **54**. When this bismacrocycle was treated with the dication **48** and 1,4-bis(bromomethyl)benzene **49** in dimethylformamide at ultra high pressure (8 kbar) the *cis*-catenane **55**·4PF_6^- was obtained as the *cis* isomer after three days (Scheme 17).



Scheme 16

As expected, **55** did not isomerize in solution in the presence of trifluoroacetic acid.



Scheme 17

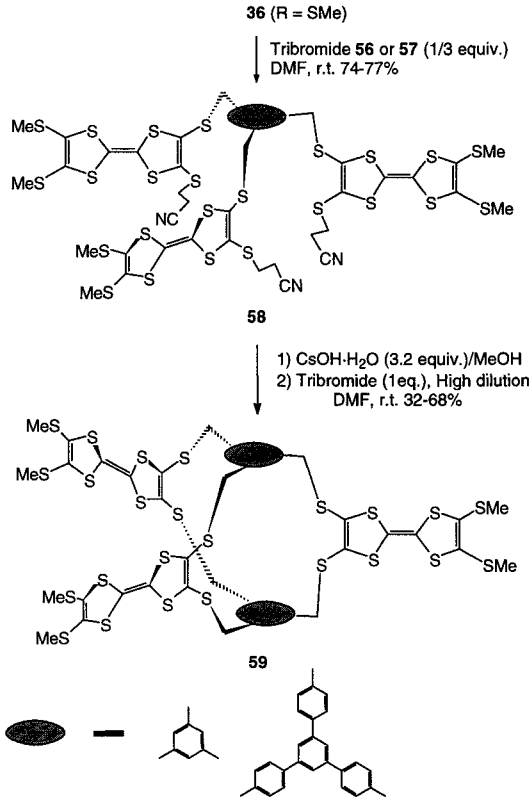
The catenanes were characterized by electrospray mass spectrometry (ESMS) and the various isomers were identified by their difference in the chemical shifts of the pyridinium protons. Variation of the linkers connecting the TTF units in these mono and bis-macrocycles, in order to change the geometry of these novel assemblies, are currently studied in our laboratory.

4.3. Macrobicyclic Tetrathiafulvalenophanes

The molecular design of three-dimensionally bridged macropolycyclic compounds is a challenge for the synthetic chemist[43] and incorporation of redox-active units into such molecules is of interest for the preparation of macropolycyclic receptor molecules.[44] Therefore the introduction of TTF into macrocycles could lead to interesting applications. Apart from the design of new three dimensional organic conducting materials, such topological complex molecules may act as receptor for electron poor compound (acceptors), and the resulting

electroactive recognition could easily be investigated and confirmed electrochemically.

The methodology described in the previous sections is well suited for the preparation of macrobicyclic cyclotetrathiafulvalenophanes containing three TTF-bridges, either by a stepwise method or in a one-pot synthesis (Scheme 18).[45]



Scheme 18

The thiolate **36** (R = SMe), generated *in situ*, was alkylated with 1/3 equiv. of either 1,3,5-tris(bromomethyl)benzene **56** or 1,3,5-tris[4-(bromomethyl)-phenyl]benzene **57** in DMF to give tris-TTF **58**. The tripod-tripod coupling for the construction of the cages **59** was achieved by simultaneous addition of a DMF solution of the deprotected tris TTF thiolates **58** and a DMF solution of the appropriate tribromide **56** or **57** under high dilution conditions. The macrocycles **59** were isolated in excellent yields (32-68%) after chromatographic separation.

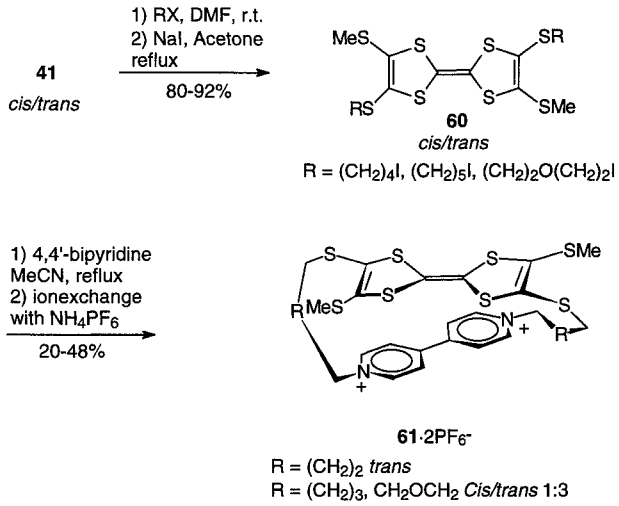
Interestingly it was also possible to prepare compound **59** by a one-pot reaction. Instead of isolating tris-TTF intermediate **58**, the solution containing compound **58** was treated *in situ* with caesium hydroxide (3 eq.) to cleave off the remaining protecting groups. The resulting trithiolate was realkylated with another 1/3 eq. of the tribromide **56** without high dilution conditions to give the macrocycle **59** as the sole product in 68% yield. The synthesis of **59** is an example of an assisted self-assembly reaction, since the individual components are pre-programmed due to their complementary geometry's.

4.4. Donor Acceptor Systems

Numerous bis- and oligo-TTF's have been prepared and investigated electrochemically,[25,30,36,46] due to the proposal by Wudl *et al.* [24] that molecules containing two electron donors might allow formation of charge transfer complexes of higher dimensionality. In these examples, the right geometry and connection of the donor portions are essential for intramolecular interactions. Cyclophanes containing two electron acceptors derived from a 4,4′-bipyridinium dication have been synthesized by Hünig *et al.*, and their intra- and inter-molecular interactions were extensively investigated.[47] The latter system was also used in the preparation of catenanes and rotaxanes (see 4.2).

With the exception of the prominent work performed by Staab *et al.* on donor and acceptor cyclophanes,[48] the literature is scarce on systems containing macrocyclic donor/acceptor units which are covalently attached.

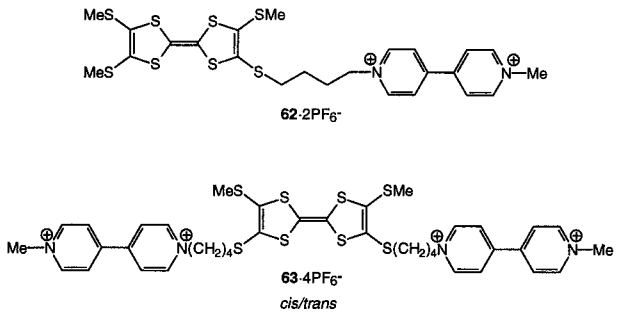
In order to obtain more insight into the structural conditions necessary for π-interactions between two different electroactive systems, we investigated systems in which the donor (TTF) and the acceptor (4,4′-bipyridinium unit) were connected *via* a chain either in a rigid conformation, *e.g.* a macrocycle, or in a open conformation where the two systems are linked together by a bridge. The direct synthesis to the donor acceptor systems was achieved by using the suitable TTF-thiolates. The alkylation of the bis-thiolate TTF **41**, generated *in situ* from **39**, with different α-bromo-ω-chloro reagents, followed by halogen exchange using sodium iodide in acetone gave the corresponding bis iodo TTF **60** in near quantitatively yields (Scheme 19).[49] The donor acceptor macrocycles were prepared by refluxing compound **60** with 4,4′-bipyridine for several days and purified by chromatography and anion exchange with ammonium hexafluorophosphate to give **61**·2PF_6^- as nice dark green crystals.



Scheme 19

The length and flexibility of the linker connecting the two redox active units have a great influence upon the conformation of the product. In the case of the short tetramethylene chain, the product was isolated in 48% yield only as the *trans* isomer (confirmed by X-ray). In the case of the pentamethylene and diethyl glycol linkers, the macrocycles were isolated as a mixture of *cis* and *trans* isomers. The macrocycles give rise to charge transfer band in the UV-VIS, situated around 650 nm. This indicates that an internal charge transfer interaction takes place between the TTF and the bipyridinium unit. We also synthesized a number of compounds in which the TTF and bipyridinium units were connected by one chain, hence allowing the systems to adopt an open conformation. Some representative examples are outlined below (Scheme 20).

Compounds **62**·2PF_6^- and **63**·2PF_6^- were prepared by refluxing the appropriate TTF iodo compound with an excess of 1-methyl-4-(4′-pyridyl)pyridinium iodide for several days in acetonitrile followed by chromatography and anion exchange. Interestingly these compounds give rise to much weaker CT interactions, suggesting that they adopt an open conformation in solution.



Scheme 20

We are currently trying to determine the scope and limitations of this type of reactions for the preparation of more complex donor acceptor systems. The surprisingly good yields observed in some cases, using the right linker, may be a result of self assembly during the formation of the donor-acceptor pair.

5. Conclusion and Outlook

We have shown that the cyanoethyl group is a versatile protecting group for TTF thiolates. The complete set of π-donor building blocks enables us to design and construct a variety of topological complex TTF assemblies by use of the simple deprotection-realkylation methodology. The fact that several research groups already have adopted these synthons clearly shows the viability of this strategy: for example Fabre *et al.* have synthesized the selenolate analogues using the cyanoethyl protecting group;[50] Underhill *et al.* have used the cross coupled TTF's **22** to prepare nickel complexes of TTF dithiolates which show relative high conductivity;[51] Bryce *et al.* have recently reported the synthesis of the 6,7 unsubstituted 2,3-bis(2-cyanoethylthio)TTF.[52]

As shown above, these new TTF thiolates serve as excellent building blocks for the incorporation of TTF into many different molecular structures and because the synthetic operations involved are very simple and give consistent high yields, we hope that chemists specialized outside the field of TTF chemistry will begin to explore the TTF moiety as a general electron donor.

Acknowledgment

We wish to thank all the enthusiastic members of the group who took part in the work described and whose names appear in the references.

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