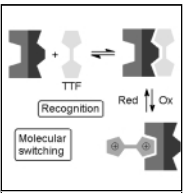
Tetrathiafulvalenes as building blocks in supramolecular chemistry II



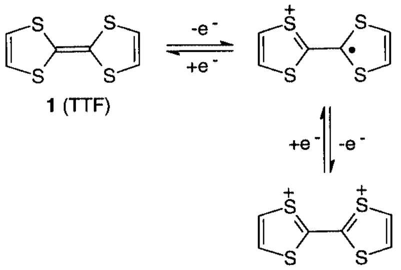
CSR

Mogens Brøndsted Nielsen, Christian Lomholt and Jan Becher*

Department of Chemistry, University of Southern Denmark, Odense University, Campusvej 55, DK-5230 Odense M, Denmark. E-mail: jbe@chem.sdu.dk

Received 10th December 1999
Published on the Web 4th April 2000

This account highlights developments in the field of supramolecular tetrathiafulvalene (TTF) chemistry. Progress in synthetic TTF chemistry during the past decade has allowed the preparation of a number of elaborate molecular systems based on host–guest interactions being able to act as either sensors, molecular switches or mediators for specific reactions. Among these systems interlocked architectures such as rotaxanes and catenanes make a significant contribution.



Scheme 1 Reversible oxidations of TTF.

1 Introduction

Tetrathiafulvalene (TTF, **1**) is a reversible, stable two-electron donor (Scheme 1) and has as such found widespread use in supramolecular chemistry. Since the discovery *ca.* 25 years ago of high electrical conductivity in a chloride salt of TTF[1] and metallic behaviour in the charge-transfer complex with 7,7,8,8-tetracyano-*p*-quinodimethane (TCNQ)[2] a huge number of TTF derivatives have been synthesized.[3] The developments in synthetic TTF chemistry have allowed the ready preparation of large quantities of derivatised TTF building blocks. It has thus become possible to incorporate TTF into macrocyclic and supramolecular structures, with the ultimate goal being to construct systems capable of acting as, for example, sensors, catalysts or switches at the molecular level.

Since our first review,[4] a break-through in synthetic TTF chemistry has occurred with the discovery of the cyanoethyl protection group for TTF-thiolates (Scheme 2).[5] Stepwise deprotection/alkylation protocols have been developed and used for the synthesis of a number of macrocyclic systems (Fig. 1), very often in high yields on account of the effective alkylation of TTF-thiolates.[6] However, the four attachment sites of TTF usually result in mixtures of two inseparable isomers, a *cis* and a *trans* isomer (Fig. 2). This isomeric problem is avoided

---

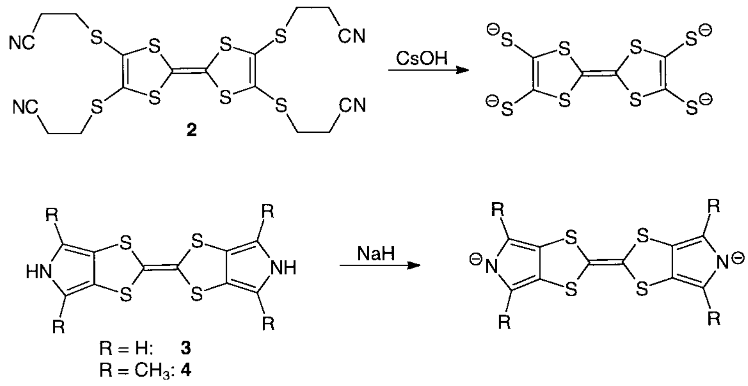
Jan Becher was born in Frederiksberg, Denmark, in 1939. Graduated from Professor Ole Buchardt's group, University of Copenhagen, 1966. Assistant professor at Odense University 1969–1989, awarded Dr. Scient. 1986 and appointed docent (professor) in 1989, also at Odense University. He was awarded 'The Bjerrum Chemistry Award' and Gold Medal 1992 as well as Docteur honoris causa *(Université d'Angers, France) 1998. His research interests cover heterocyclic chemistry, especially sulfur-containing heterocycles, macrocyclic chemistry, macrocyclic ligands and supramolecular chemistry.*

Mogens Brøndsted Nielsen was born in Grenå, Denmark, in 1972. He received his Cand. Scient. degree at Odense University in 1997 and his PhD degree in 1999 for work in tetrathiafulvalene chemistry under the supervision of Professor J. Becher. During his PhD studies he worked for one year in Professor J. Fraser Stoddart's group at the University of California, Los Angeles (UCLA).

Christian Lomholt was born in Kolding, Denmark, in 1970. He received his Cand. Scient. degree at Odense University in 1997 for his work in tetrathiafulvalene chemistry under the supervision of Professor J. Becher. He is currently working in J. Becher's group as a PhD student and is expected to receive his PhD in March 2000. During his PhD studies he worked for six months in Professor Michael P. Cava's group at the University of Alabama, Tuscaloosa.

Mogens Brøndsted Nielsen **Jan Becher** **Christian Lomholt**

DOI: 10.1039/a803992e



Scheme 2 Reactive TTF-nucleophiles.

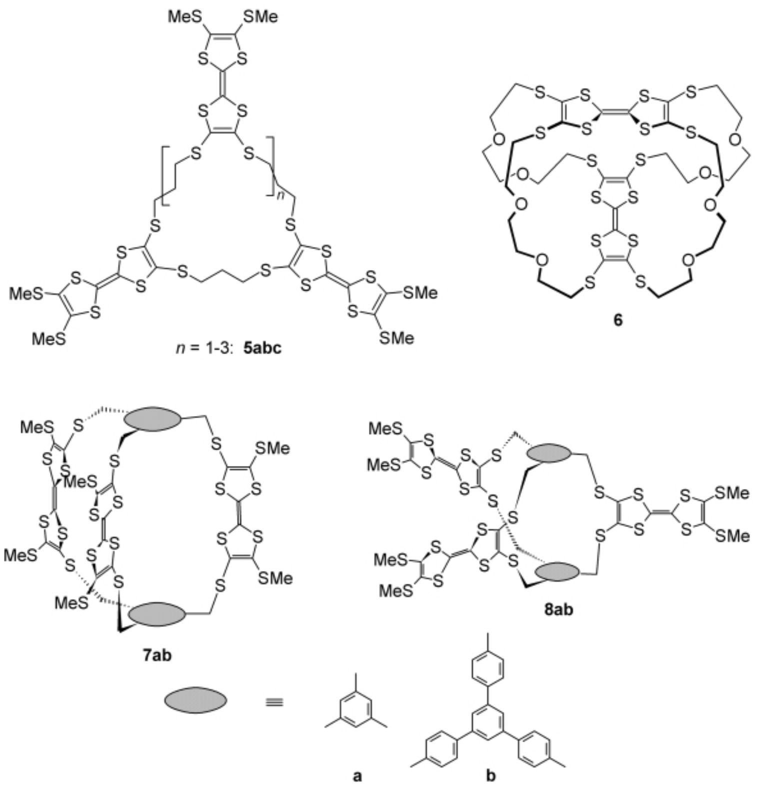


Fig. 1 TTF-macrocycles and cage molecules prepared by stepwise deprotection/alkylation of cyanoethyl-protected TTF-thiolates.[6]

when the pyrrolo-annelated TTFs **3** and **4** are used. Efficient syntheses of these strong π-donors have recently been developed.[7,8]

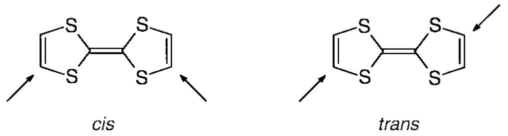
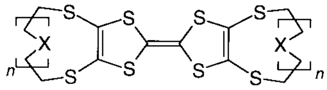


Fig. 2 Definition of *cis* and *trans* isomers for substituted TTFs.



X = O, *n* = 3-5 **9, 10, 11**
X = S, *n* = 2 **12**

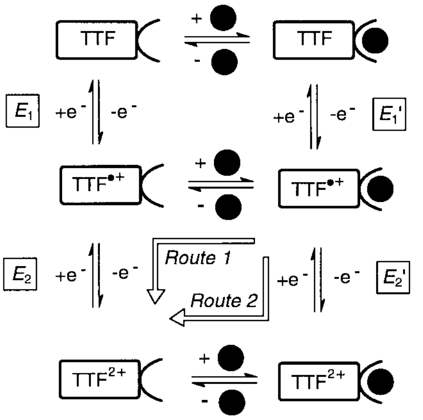
Fig. 3 Crown-ether annelated TTFs.

2 Crown-ether annelated TTFs as cation sensors

In previous reviews[4,6] we have described the ability of the crown-ether annelated TTFs **9–11** (Fig. 3) to host alkali metal cations (Li^+, Na^+ and K^+) with a concomitant increase of the first oxidation potential. The second potential remained unchanged, which was explained by expulsion of the cation after the first oxidation (Route 1 in Scheme 3). However, more than 250 equiv. of cations were necessary to observe any shifts for these ligands.

The cyclic voltammogram of the thiacrown **12** showed an anodic increase of both oxidation waves upon addition of Ag^+ ions (ΔE_{ox}^1 = +170 mV, and ΔE_{ox}^2 = 70 mV), whereas the reduction waves remained unchanged. This observation indicates that exchange is slow and Route 2 is operating for oxidation of the system.

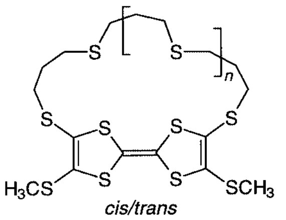
It was concluded that the relatively weak responses result from the weak coupling between the metal cation and the redox active fulvene center. However, two new developments in this area have recently been reported: (*i*) an enhanced sensitivity for cations exerted by TTF-thiacrowns cyclized in the 2,7(6)-positions; (*ii*) self-assembly of crown-ether annelated TTFs on gold surfaces.



Scheme 3 Schematic illustration of a TTF sensor. After the first oxidation, the guest may be expelled (Route 1) or kept hosted (Route 2). E_1, E_1', E_2, and E_2' denote the redox potentials for the shown processes.

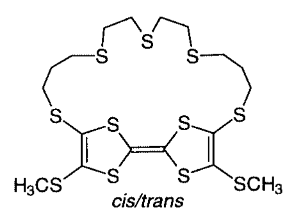
2.1 TTF-thiacrown sensor

The 2,7(6)-cyclized thiacrowns presented in Fig. 4 were synthesized and investigated by LSIMS (Liquid Secondary Ionisation Mass Spectrometry), ^{1}H NMR and cyclic voltammetry with respect to their inclusion of Ag^+ ions.[9] According to ^{1}H NMR titration studies only complexation of the terminal $SC{=}CSCH_3$ fragments in macrocycles **13** and **14** was observed. In contrast, for **15** the complexation preferentially involved the thiacrown cavity, which may be explained by a better orientation of the coordinating S atoms. The X-ray crystal structure of *cis*-**13** confirms that the propylene fragments cannot ensure a correct structural environment for complexation. The titration curves of the complex between **15** and Ag^+ show a plateau for 0.6 equiv. of added Ag^+. The ratio between *cis* and *trans* isomers is 60 : 40 suggesting that only the *cis* isomer binds Ag^+. A stability constant of $K_a = 10^{3.26}$ ($CDCl_3$–CD_3CN 1 : 1) for the *cis*-**15**•Ag^+ complex was determined from these data. Adding Ag^+ ions to **13** and **14** did not result in any changes of the cyclic voltammograms, whereas the first oxidation wave of **15** was significantly anodically shifted upon addition of up to 1 equiv. of Ag^+ (Route 1).



cis/trans

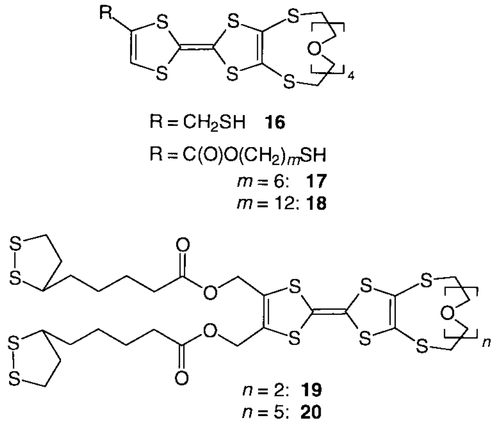
n = 1: **13**
n = 2: **14**



cis/trans

15

Fig. 4 TTF-thiacrowns.



R = CH₂SH **16**
R = C(O)O(CH₂)*ₘ*SH
m = 6: **17**
m = 12: **18**

n = 2: **19**
n = 5: **20**

Fig. 5 Crown-ether annelated TTFs used for assembly on electrode surfaces.

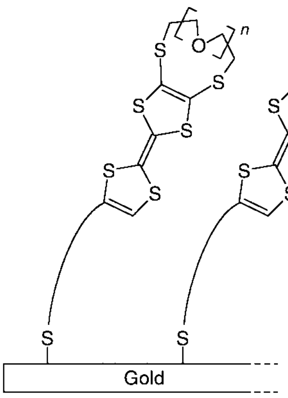


Fig. 6 Proposed orientation of a self-assembled monolayer of TTF crown-ethers.

2.2 Self-assembled crown-ether monolayers

Self-assembled monolayers (SAMs) of crown-ether annelated TTFs have been prepared on electrode surfaces. This was first exploited by Moore *et al.*[10] SAMs of the TTF thiols **16–18** presented in Fig. 5 were assembled from saturated acetonitrile or acetonitrile–benzene solutions onto gold or platinum surfaces (Fig. 6). The free compounds in acetonitrile solution showed a small, but reproducible, anodic response to Li^+ and K^+ (10–20 mV), a significant response to Na^+ and Ba^+ (45–55 mV) and a greater response to Ag^+ (60–90 mV). These same responses were obtained for the SAMs, showing for example a response to Ag^+ of 60–85 mV on platinum, being nondependent on the length of the thiol chain. However, these SAMs were not stable under various experimental conditions. Liu *et al.*[11] prepared the bis-thioctic ester TTF-derivatives **19** and **20**, which formed remarkably stable SAMs on gold with very clear and reversible surface-confined electrochemistry. According to cyclic voltammetry these layers are able to recognize alkali metal ions (M). Thus, in THF containing MPF_6 (5.0 mM) anodic shifts were observed for the first and second oxidation potentials of **20**; M = Na: $\Delta E_{\frac{1}{2}}^{1} = +60$ mV, $\Delta E_{\frac{1}{2}}^{2} = +55$ mV; M = K: $\Delta E_{\frac{1}{2}}^{1} = +20$ mV, $\Delta E_{\frac{1}{2}}^{2} = +30$ mV. However, the smaller crown **19** only showed a minor increase of +10 mV in the first oxidation potential in the presence of $NaPF_6$. The increase in both potentials for **20** contrasts with the observed solution state behaviour. It seems that the monolayer is able to complex the metal ion even after the second TTF oxidation according to a Route 2 mechanism, maybe as a result of either surface aggregation or cooperativity effects between neighbouring crown rings on the layers.

3 C_{60}–tetrathiafulvalene complexes

A high interest has emerged in incorporating buckminsterfullerene, C_{60}, in functional molecular assemblies and supramolecular arrays.[12] Numerous *charge-transfer* (CT) complexes of this weak electron acceptor have been obtained using planar donors of the tetrathiafulvalene, pyranylidene and dithiadiazafulvalene family.[13] Thus, Sugawara and coworkers[14] obtained black single crystals of a CT complex between C_{60} and 2 equivalents of bis(ethylenedithio)tetrathiafulvalene (BEDT-TTF, **21**) by co-crystallisation from a CS_2 solution (Fig. 7). X-Ray crystal analysis at 150 K showed the C_{60} to be sandwiched between a pair of largely concave BEDT-TTF molecules (Fig. 8) and that the rotational motion of C_{60} was quenched

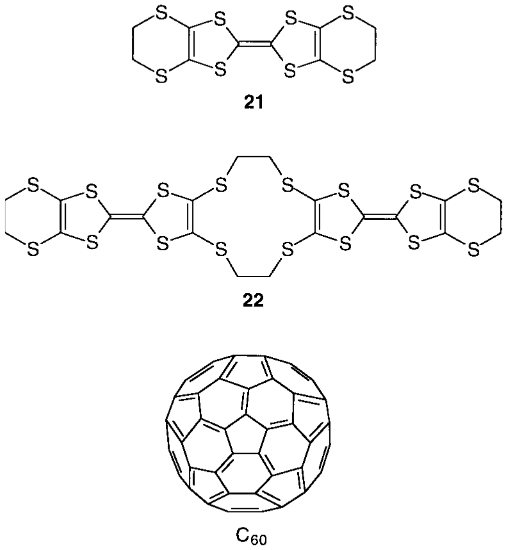


Fig. 7

completely. Co-crystallisation from an equimolar mixture in CS_2 of C_{60} with the twin donor **22** consisting of two covalently bridged TTFs afforded reddish-black single crystals.[15] The X-ray crystal structure (room temperature) revealed a 1:1 inclusion complex (Fig. 9). Free rotational motions of C_{60} in this complex are considerably suppressed, although large thermal ellipsoids are recognized in an equatorial region. UV–Vis spectroscopic measurements on both the $(\mathbf{21})_2$•C_{60} and **22**•C_{60} complexes (in KBr pellets) showed a distinct CT absorption at λ_{max} 750 nm. Most of the crystal structures reported in the literature describing complexes between TTF derivatives and C_{60} reveal stoichiometries between the TTF and C_{60} of 2:1, but other ratios[13] (such as 1:1) have been observed as well.

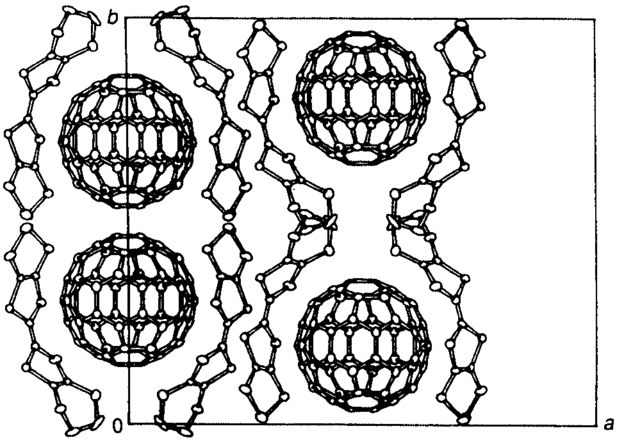


Fig. 8 Projection of the $[\mathbf{21}]_2$•C_{60} crystal structure along the *c* axis. Reproduced from ref. 14 by permission of The Royal Society of Chemistry.

A number of compounds in which TTF and C_{60} are covalently tethered have been reported in the literature.[16,17] By reacting C_{60} with the TTF diene precursor **23**, Rovira and coworkers[18] reported the first Diels–Alder adduct **24** of C_{60} with TTF, obtained as a dark brown solid (Scheme 4). Two other examples of TTF–σ-C_{60} diad species are presented in Fig. 10. **25** and **26** containing insulating σ-chains of different lengths were obtained by 1,3-dipolar cycloaddition of azomethine ylides to C_{60}.[19] The UV–Vis spectra of these three intramolecular donor–acceptor systems indicate no appreciable CT in the ground state. Photolysis of frozen toluene solutions of **25** and **26** at 77 K produced long-lived radicals, most likely the separately solvated pairs of radicals TTF$^{\bullet+}$–σ-C_{60} and TTF–σ-$C_{60}{}^{\bullet-}$, or possibly but less likely the zwitterionic biradical TTF$^{\bullet+}$–σ-$C_{60}{}^{\bullet-}$. The ability of TTF–σ-C_{60} compounds to form CT-complexes with the strong electron acceptor tetrafluorotetracyano-*p*-quinodimethane has been investigated by Martín *et al.*[20] Such complexes were shown to exhibit semiconducting properties and may be useful in the development of molecular materials with applications in molecular electronics.

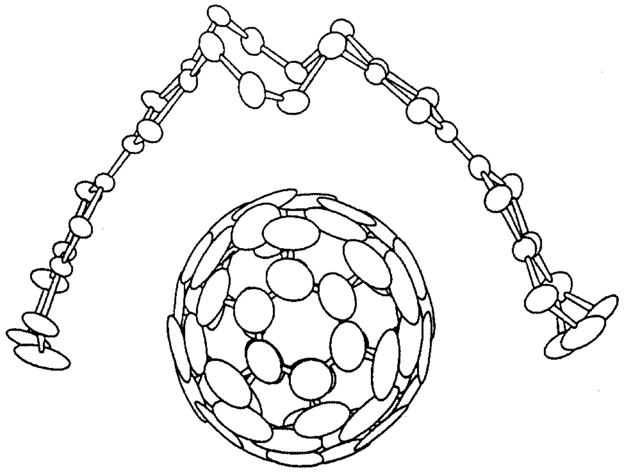
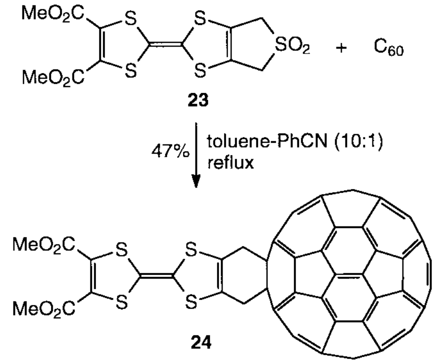


Fig. 9 Ortep drawing of C_{60} surrounded by the twin donor **22** viewed along the threefold axis of C_{60}. Reproduced from ref. 15 by permission of The Chemical Society of Japan.



Scheme 4 Formation of covalent linkage between TTF and C_{60} by a Diels–Alder cycloaddition.

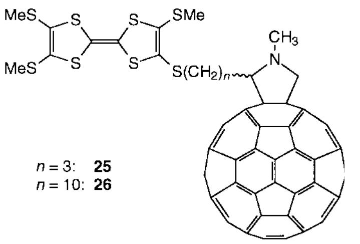


Fig. 10 TTF and C_{60} covalently linked.

4 Interlocked molecules

The developments in supramolecular chemistry in the past 20 years have demonstrated many elegant self-assembled interlocked compounds such as catenanes and rotaxanes (Fig. 11) in high yields.[21] Catenanes (from the Greek *catena* meaning chain) are molecules containing two or more interlocked rings, which cannot be separated without the breaking of a covalent bond. Rotaxanes (from the Latin *rota* meaning wheel, and *axis* meaning axle) contain a dumbbell-shaped component (a rod and

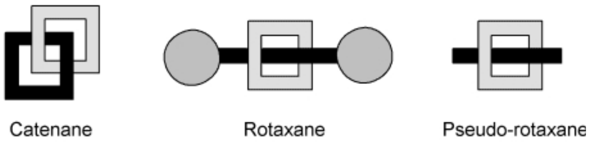


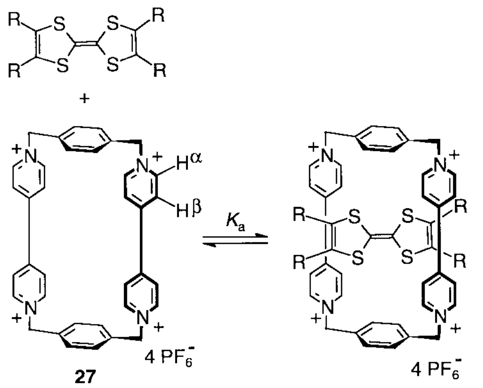
Fig. 11 Definitions of interlocked molecules.

two bulky stoppers), with a macrocyclic component encircled. The stoppers prevent the macrocycle unthreading from the rod. In the absence of these stoppers, the corresponding complex is called a pseudorotaxane.

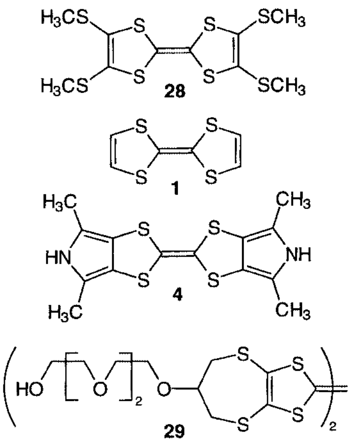
The synthesis of interlocked systems relies on the assistance of appropriate templates to keep the pre-catenane/rotaxane in the right arrangement before being mechanically locked, usually by a ring-closing of one component. Thus, one pioneer in the field, J. F. Stoddart, has developed a versatile template-assisted strategy based on electron donor–acceptor interactions, whereas a different strategy was developed by J. P. Sauvage employing complexation of two phenanthrolines around a Cu(I) center. Because of the specific redox properties of the chemically stable TTF group, a special interest has emerged in incorporating TTF into such systems in order to construct molecular systems such as switches, taking advantage of the three possible redox states of TTF and their reversible conversions.

4.1 Complexation studies

The ability of the cyclic acceptor cyclobis(paraquat-*p*-phenylene) (**27**) to act as a host for aromatic π-electron donors, such as hydroquinone and dioxynaphthalene, was exploited by Stoddart *et al.*[21] A similar strong complexation with TTF was observed. The X-ray crystal structure of the green 1:1 complex formed between TTF and **27** revealed a channel-type structure formed by the cyclic acceptor occupying TTF in its central cavity.[22] In acetonitrile solution a CT absorption band is observed at λ_{max} 855 nm. The association constant of the complex was determined to be K_a = 10 000 M^{-1} in acetonitrile[23] and 2600 M^{-1} in acetone[24] (Scheme 5, Fig. 12). However, functionalisation of the TTF nucleus results in different donor properties (measured by the first redox potential $E_{1/2}{}^1$) and has a profound influence on the inclusion ability.[25] Thus, the weak donor tetrakis(methylthio)tetrathiafulvalene (TMT-TTF, **28**) associates in a very weak complex. Association constants of K_a = 170 M^{-1} in acetonitrile and 40 M^{-1} in acetone have been determined from the ratio of complexed and uncomplexed cyclophane proton resonances (slow exchange on the 250 MHz NMR time-scale, Fig. 13). In contrast, the bis(pyrrolo)TTF **4** forms a strong complex (K_a = 7900 M^{-1} in acetone) due to a combination of its low redox potential and its extended π-surface. When a tetramercapto-TTF is substituted with polyether linkers (**29**), the association constant is increased dramatically as compared to TMT-TTF, since the formation of hydrogen bonds between the oxygens and the bipyridinium α-H's (relative to nitrogen) can add to the stability of the complex.[26] Recent calculations by Houk *et al.*[27] show that the ethyleneoxy groups are indeed very important in the complexation process.



Scheme 5 Equilibrium for the inclusion of a TTF derivative in the cavity of the cyclic acceptor **27**.



	Solvent	$E_{1/2}^1$/V	K_a/M^{-1}
28	MeCN	0.51	170
	Me_2CO		40
1	MeCN	0.34	10000
	Me_2CO		2600
4	Me_2CO	0.33	7900
29	MeCN		10000

Fig. 12 Association constants for the inclusion of TTF derivatives in the cyclic acceptor **27** correlated with the first redox potential of the free, uncomplexed TTFs.

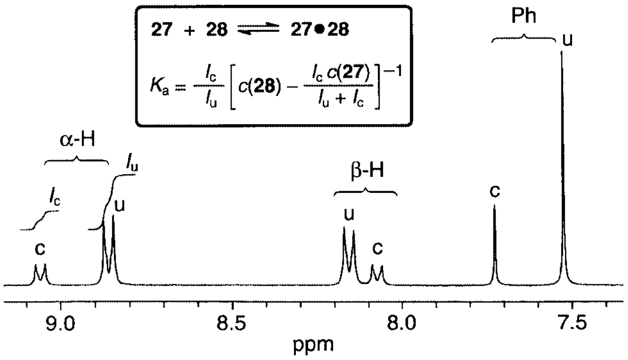
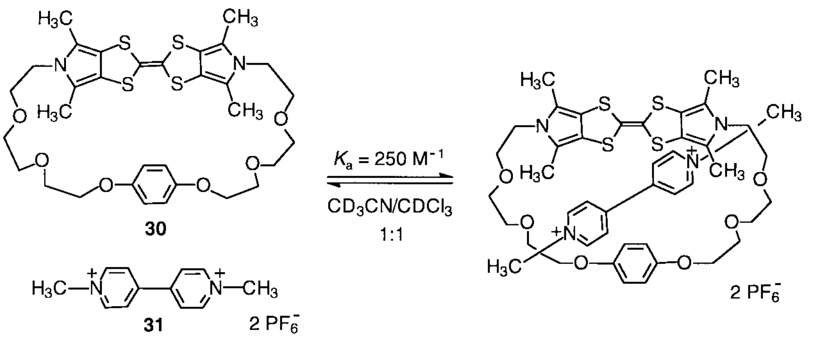


Fig. 13 Selected region of the ^1H NMR spectrum of the equilibrium solution between **27**, **28** (*ca.* 1:2) and the complex **27•28** at 303 K. Employing the exact initial concentrations c(**27**) and c(**28**) the association constant K_a can be calculated from the integrals I_c and I_u of complexed (c) and uncomplexed (u) cyclophane resonances.

Macrocycles containing two electron donors can act as host molecules for electron acceptors, such as paraquat (**31**). Such complex formation was studied for the macrocycle **30** in the solid and in the solution state (Scheme 6), by X-ray crystal structure analysis and ^1H NMR spectroscopy.[25] In solution ($CDCl_3$–CD_3CN 1:1) a complex with 1:1 stoichiometry was identified from a Job plot with an association constant of 250 M^{-1}. However, in the solid state a complex consisting of two molecules of **30** per one molecule of **31** was observed (Fig. 14). Each macrocycle adopts a conformation with an angle between the hydroquinone and the tetrathiafulvalene moiety of 70.1°. Two macrocycles dimerise to form a box-like structure encapsulating one completely planar paraquat molecule. The distance between the two tetrathiafulvalene moieties is 7.08 Å, which is optimal for CT and/or π–π interactions to stabilize inclusion of paraquat, although paraquat is tilted 15.9° away from co-planarity with the TTFs.

4.2 Donor–acceptor catenanes based on TTF

A number of catenanes between polyether-bridged tetramercapto-TTFs and the cyclic acceptor **27** have been reported.



Scheme 6 Inclusion of paraquat in a TTF-macrocycle.

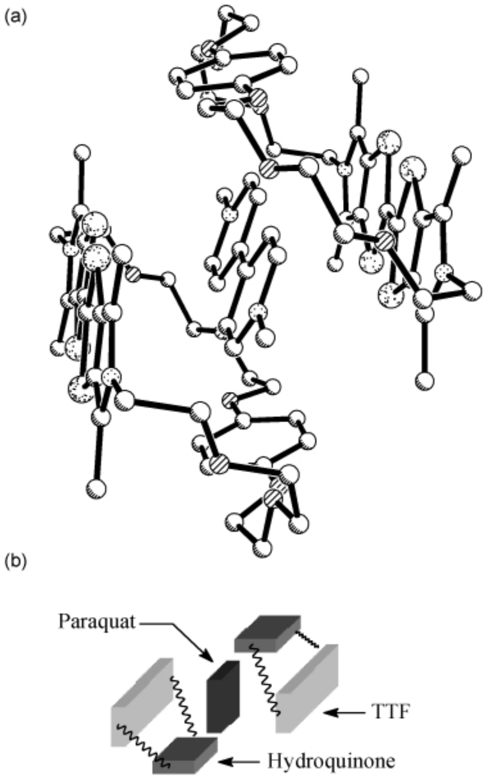
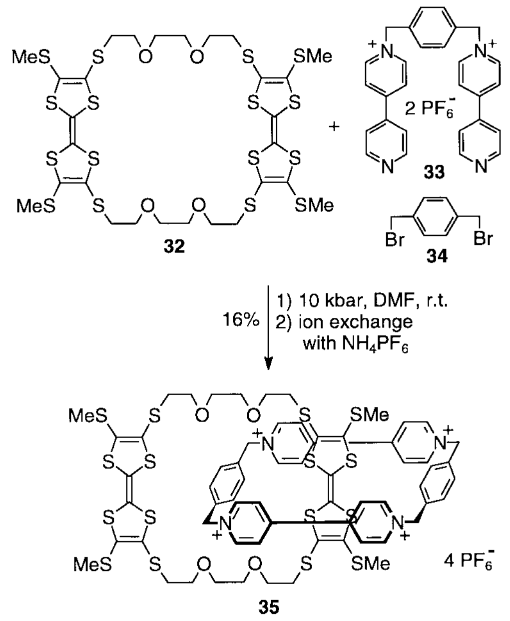
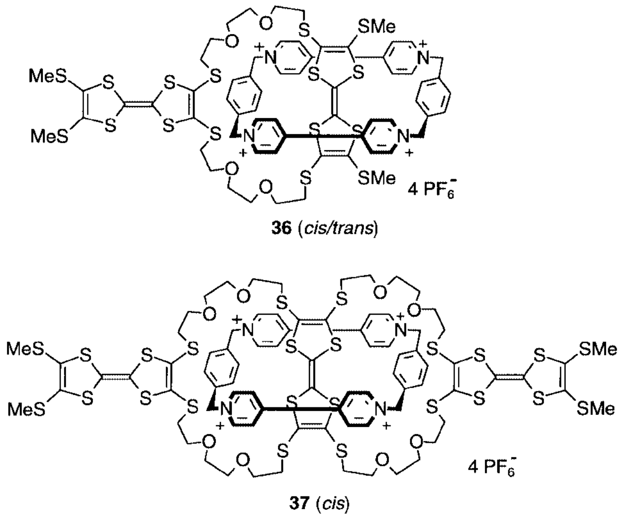


Fig. 14 (a) X-ray crystal structure (centrosymmetric) of the 2 : 1 complex between **30** and **31**. The solvent molecules and counter ions are omitted for clarity.(b) Schematic drawing of the solid state $(\mathbf{30})_2\bullet\mathbf{31}$ complex.



Scheme 7 Catenane formation.



36 (*cis/trans*)

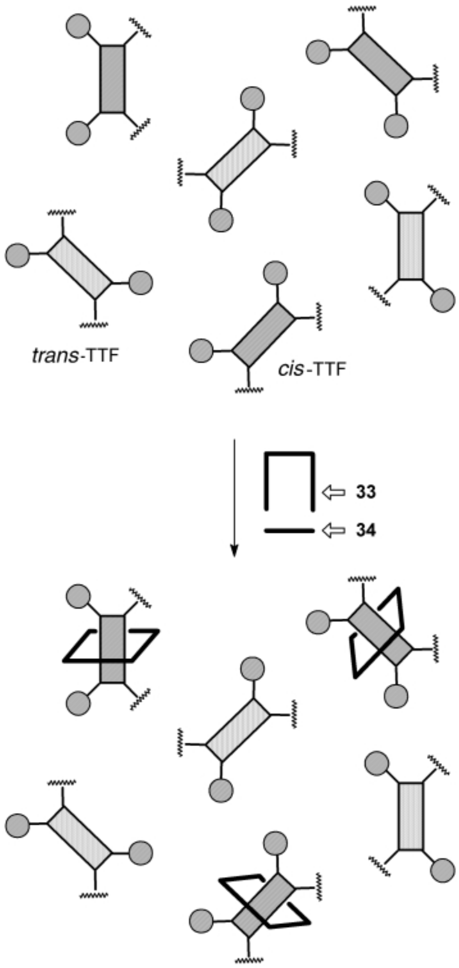
37 (*cis*)

Fig. 15 Catenane **36** was isolated as a mixture of *cis/trans* isomers, whereas only the *cis* catenane of **37** was obtained from catenation of an isomeric mixture of the corresponding macrocycle.

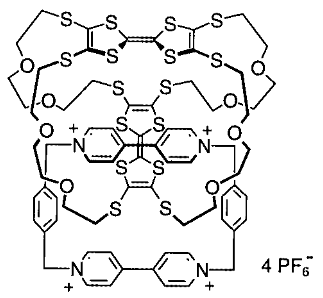
Treating the macrocycle **32** with the dication **33** and the dibromide **34** under ultra-high pressure resulted in formation of the catenane **35** (Scheme 7).[28]

Two similar catenanes (**36** and **37**) are shown in Fig. 15.[28,29] The catenanes **35** and **36** were both obtained as a mixture of *cis/trans* isomers starting from a *cis/trans* isomeric mixture of the free macrocycle. However, only the *cis* configuration of the central TTF in **37** was obtained from the *cis/trans* mixture of the macrocycle. In order to shed light on the factors responsible for this isomeric selectivity during the catenation process (Scheme 8), we designed a quadruple-bridged *criss-cross* overlapped cyclophane (**6**).[30] Only the arrangement in which both TTFs are in the *cis* configuration seemed able to generate a catenane according to a CPK model. Indeed, only the *cis, cis* catenane **38** was isolated as evidenced by ^{1}H NMR spectroscopy (Fig. 16).

Based on the complexation studies we hoped to be able to predict which donor unit is to be catenated, when two different donor entities are present in the same macrocycle. However, such a prediction turned out to be rather complicated. Thus, Stoddart and coworkers[26] isolated the catenanes **39ab** in which the benzyl unit is encircled both in solution and in the solid state, even though benzyl is a poorer donor than TTF (Fig. 17). A preference for the hydroquinone donor relative to the strong bis(pyrrolo)TTF donor in the catenanes **41** and **42** was observed by J. Lau *et al.*,[25] whereas the bis(pyrrolo)TTF exclusively was encircled in catenane **40** (Scheme 9). These findings reflect the complicated and subtle balance between all the individual noncovalent forces acting in cooperation. A major factor is the ability of the polyether oxygens to form hydrogen bonds to the bipyridinium hydrogen atoms positioned in the α-position with

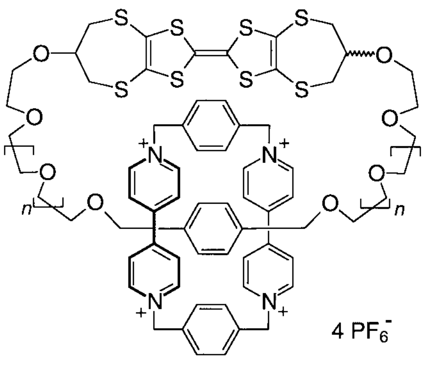


Scheme 8 Schematic illustration of the selection of a single isomer in the encirclement of TTF from a mixture of isomers; only the *cis*-isomer reacts.



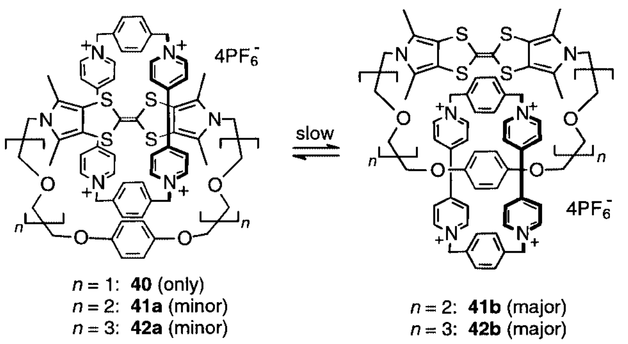
38 (*cis, cis*)

Fig. 16 Only the *cis, cis* catenane **38** is sterically allowed.



n = 1, 2: **39ab**

Fig. 17 The cyclic acceptor encircles the benzyl unit and not the TTF in these two catenanes.



Scheme 9 Translational isomerism in a catenane containing both a bis(pyrrolo)TTF and a hydroquinone donor.

respect to the nitrogen atoms. Occupation of the extended bis(pyrrolo)TTF moiety by **27** makes these interactions more difficult as compared to a situation where **27** occupies the smaller hydroquinone moiety.

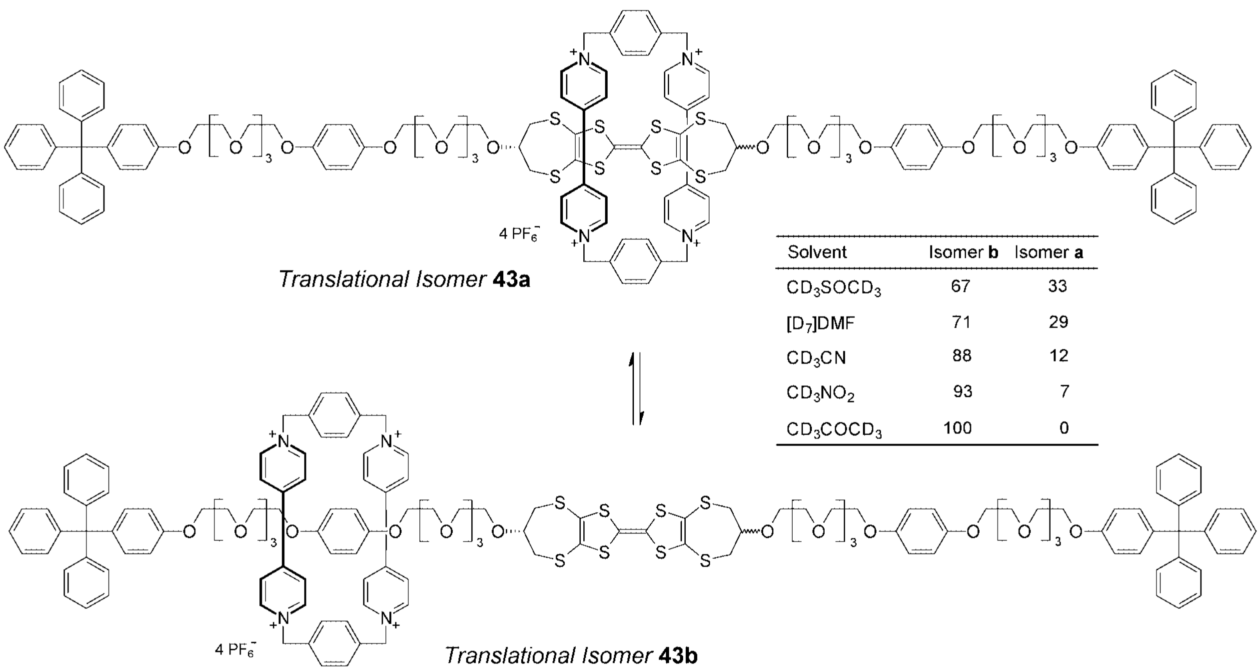
4.3 Molecular switches

Catenanes and rotaxanes are good candidates for the preparation of molecular switches, since the population of different translational isomers may be determined by external stimuli.[31] Stoddart and coworkers[32] prepared the two-station prototype shuttle **43ab** containing one TTF and two hydroquinone donor stations (Scheme 10). Depending on which donor is encircled by the cyclophane, two possible translational isomers exist. The ratio between the two translational isomers was observed to be very solvent dependent, with a preference however for the hydroquinones (**43b**). Electrochemical studies (cyclic voltammetry in acetonitrile) revealed an anodic increase of the first oxidation wave by +35 mV relative to the free dumbbell, whilst the second wave showed a shift of +5 mV. This observation is explained by a hampering of the shuttling movement of the cyclophane along the dumbbell by oxidation of the TTF nucleus. Hence, the first oxidation of TTF results in an increased energy barrier to the passage of the cyclophane along the thread causing the cyclophane to be effectively tethered at a hydroquinone site. Accordingly, the second oxidation of TTF is perturbed to a lesser extent than the first.

Taking advantage of TTF's reversible redox chemistry, the catenane **44a** was observed to act as a molecular switch (Scheme 11).[33] Thus, upon oxidation of the TTF unit (either chemically or electrochemically) the cyclic acceptor was moved from the TTF unit to the 1,5-dioxynaphthalene donor unit, affording the isomer **44b**. Subsequent reduction regenerates the original isomer **44a**.

The ability of the dication TTF^{2+} to act as an electron acceptor has been exploited in the construction of the three-pole switch presented in Scheme 12.[23] When the three components, TTF, the cyclic acceptor **27**, and the macrocycle 1,5-dinaphtho[38]crown-10 (**45**), are mixed together, the first redox potential of the TTF is increased by 70 mV according to cyclic voltammetry in acetonitrile. This observation indicates that the TTF is complexed inside the cyclic acceptor making the oxidation more difficult. However, the second oxidation now occurs more easily, by 14 mV, relative to a solution of TTF alone. This result indicates that the radical cation has left the cyclic acceptor, but enters the naphthocrown host when oxidised to the dication. These processes are reversible and the system can be characterised as a three-pole switch. The association constant for the **45**•TTF^{2+} complex was determined by absorption and emission spectral titrations in acetonitrile to be $K_a = 4.1 \times 10^3$ M^{-1} (298 K), confirming the strong association between the naphthocrown and the TTF dication.

A thermally controlled TTF-based molecular switch was obtained by tethering the cyclic acceptor and the TTF unit

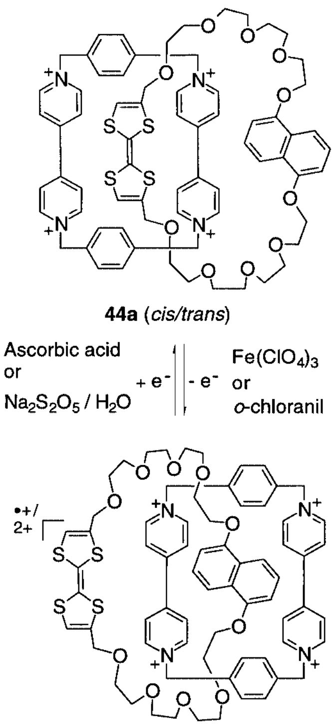


Translational Isomer **43a**

Solvent	Isomer **b**	Isomer **a**
CD_3SOCD_3	67	33
[D_7]DMF	71	29
CD_3CN	88	12
CD_3NO_2	93	7
CD_3COCD_3	100	0

Translational Isomer **43b**

Scheme 10 Translational isomerism in a rotaxane containing TTF and hydroquinone donor stations.



44a (*cis/trans*)

44b

Scheme 11 Chemically and electrochemically triggered redox-switching of a catenane.

together (Scheme 13),[34] affording the ‘self-complexing’ compound **46a**—we describe this intramolecular interaction as an anchimeric complexation. A solution of the open ‘uncomplexed’ form **46b** (obtained by fractional crystallisation) was according to UV–Vis observed to slowly equilibrate during about 19 h to a mixture of **46a** (CT band at λ_{max} 785 nm) and **46b** (Fig. 18). However, when this equilibrium solution was refluxed, almost total ‘decomplexation’ occurred as evidenced by the disappearance of the CT absorption band, but upon storage of the solution for one day at room temperature the equilibrium was reestablished—with a small decrease, however, in the equilibrium CT absorption.

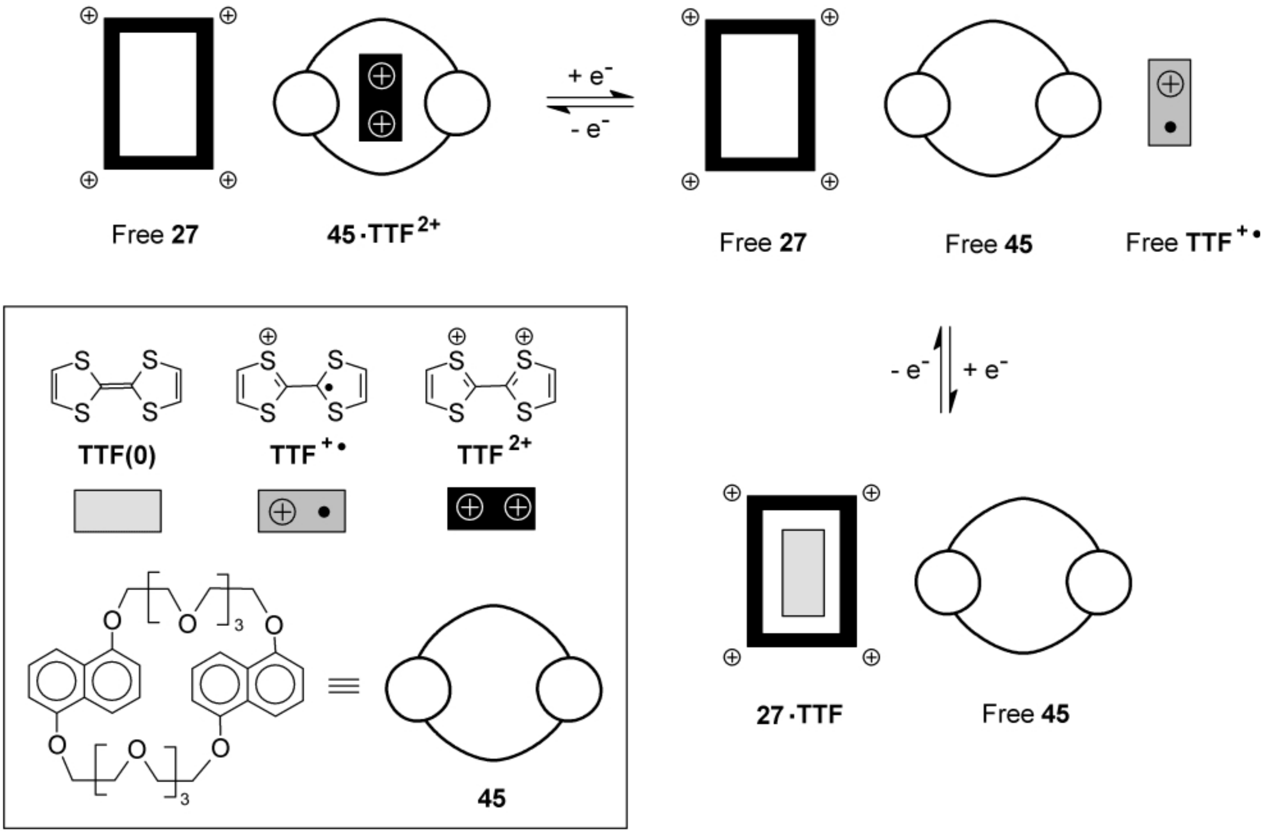
Another self-complexing system acting as a chromophoric receptor is presented in Scheme 14.[35] The macrobicycle **47** possesses complementary recognition sites, a donor part and an acceptor part allowing it to ‘self-complex’, which was observed both in solution and in the solid state. However, adding TTF to an acetonitrile solution of the compound results in a dramatic change of the colour of the solution from purple to green. Thus, the ‘self-complexation’ has been disrupted and instead the cyclic acceptor is including a molecule of TTF. The equilibrium constant for this process was determined to be K_a = 200 M^{-1}.

4.4 A TTF-containing catenate

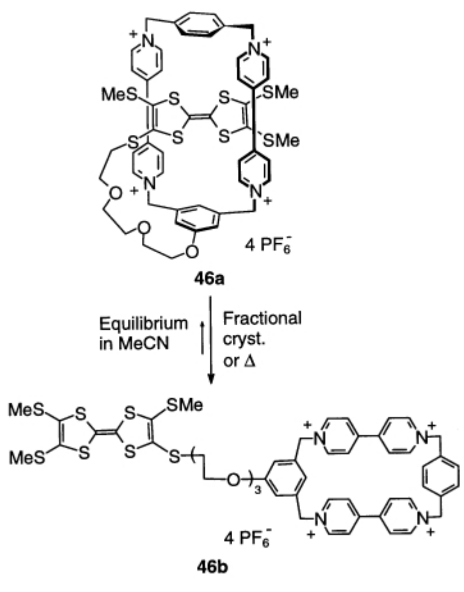
Employing the Cu(I)-template strategy developed by Sauvage *et al.*, a TTF-phenanthroline macrocycle was incorporated into the catenane **50** based on a central complex between Cu(I) and two 2,9-diphenyl-1,10-phenanthroline subunits, termed a catenate (Scheme 15).[36] Current work is focusing on the incorporation of an acceptor unit in the other macrocycle in order to achieve a system able to undergo light-induced charge-separation (Scheme 16), which is the first step of natural photosynthesis.

5 Donor–acceptor macrocycles

Intramolecular CT interactions were investigated for a number of donor–acceptor macrocycles, containing both a TTF and a bipyridinium unit (Fig. 19). Thus, the macrocycles **51a–c** show broad CT absorption bands with λ_{max} in the region 620–670 nm.[37] The conformational flexibility in the R group of **51b** and **51c** results in a smaller intensity of the CT-band compared to that of **51a**. According to both ^{1}H NMR and X-ray crystal structure analysis, only the *trans* configuration **51a** was isolated upon reacting a TTF-diiodide (*cis/trans* mixture) with bipyridine. In contrast, *cis/trans* mixtures were obtained of the less constrained **51b** and **51c**. Also, the bicycle **52** (*trans*) containing two bipyridinium units has been prepared.[38] Conformational restrictions prevent the TTF interacting with both acceptors at the same time, resulting in a similar CT-absorption as obtained for **51a**. However, the two bipyridinium units present in **52** induce very large anodic shifts in both TTF oxidation potentials (70–90 mV). These shifts can be ascribed to



Scheme 12 A three-pole supramolecular switch.



Scheme 13 'Self-complexing' macrocycle.

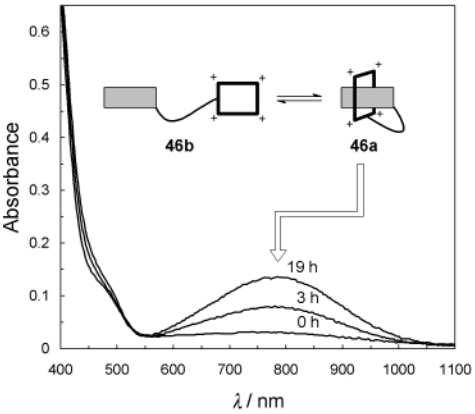


Fig. 18 The time variation of the maximum absorbance (λ_{max} ~ 785 nm) of initially 'decomplexed' **46b** (2.6×10^{-4} M in acetonitrile).

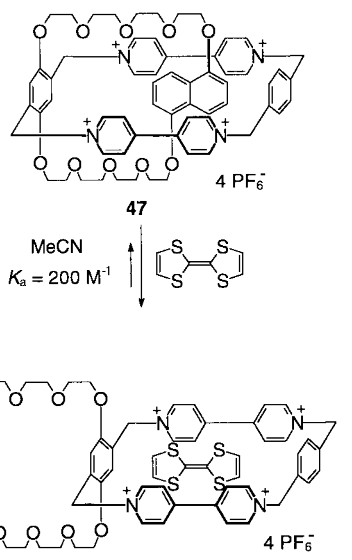
a combination of CT interactions and electrostatic repulsion between the four pyridinium cationic centers and the oxidized TTF system.

6 TTF as a mediator for chemical reactions

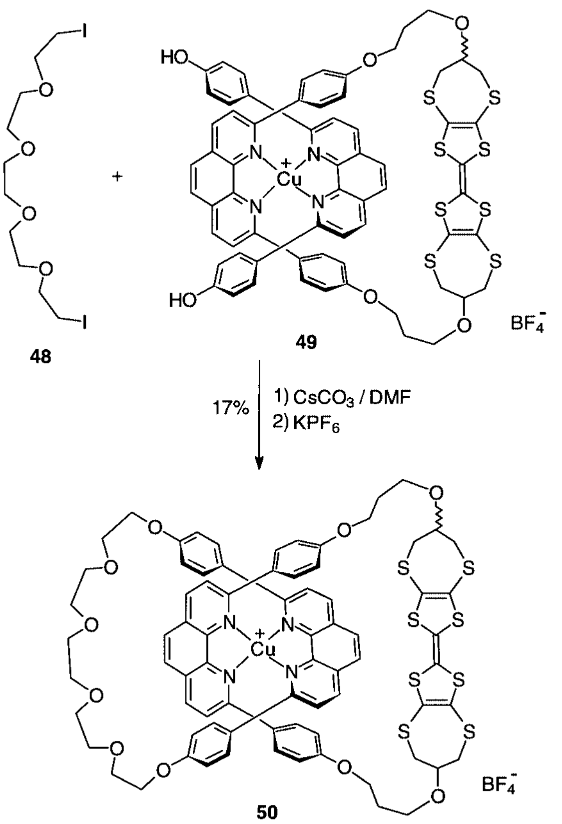
6.1 Enzyme reactions

The solubility of TTF in water, the medium of all physiological processes, is very low (0.20 mmol L^{-1}). Thus, in order to employ the donor properties of TTF in, for example, enzymatic processes it must be transferred to the water phase. Water-soluble cyclodextrins can include organic molecules of appropriate sizes in their cavities. Thus, 2-hydroxypropyl-β-cyclodextrin (hp-β-CD (**54**), Fig. 20) has a cavity size (*ca.* 7.8 Å in diameter and 7.8 Å in depth) appropriate for hosting one molecule of TTF (size *ca.* 6 Å).[39] Indeed, a 1 : 1 complex between **54** and TTF was identified in water with an association constant of 5.40×10^3 M^{-1}. This complex behaved as a homogeneous mediator at 100 mV for the enzyme-catalyzed electro-oxidation of glucose, hypoxanthine and lactate by shuttling electrons from the redox center of the enzyme to the surface of the indicator electrode (Fig. 21).

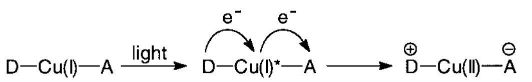
Another interesting example of using TTF for enzyme reactions has been reported by G. F. Khan *et al.*[40] The CT complex between TTF and TCNQ was grown at the surface of a shapeable electroconductive film affording a tree-shaped TTF–TCNQ crystal structure standing vertically on the surface. The enzyme glucose oxidase was adsorbed and cross-linked with glutaraldehyde at the surface of this electrode. The space between the tree-shaped crystals was filled with cross-linked gelatin ensuring the stability of the crystals as well as the stability of the enzyme. The close proximity and the favorable



Scheme 14 Formation of 1 : 1 complex between TTF and a 'self-complexing' macrobicycle.



Scheme 15 Cu(I)-templated synthesis of TTF-containing catenate.



Scheme 16 Light-induced electron transfer from a donor unit (D) to an acceptor unit (A).

orientation of the enzyme at the electrode surface lead to a glucose sensor with high performance.

6.2 Radical reactions

TTF has been exploited by J. A. Murphy and coworkers[41] as an electron donor in radical reactions. Electron transfer from TTF to the diazonium salts **55ab** results in liberation of N_2 followed by radical cyclisation and trapping of the TTF radical cation on sulfur. Nucleophilic displacement yields the final product and regenerates TTF, ready to start a new cycle (Scheme 17). The mildness of the conditions has encouraged the use of TTF in a

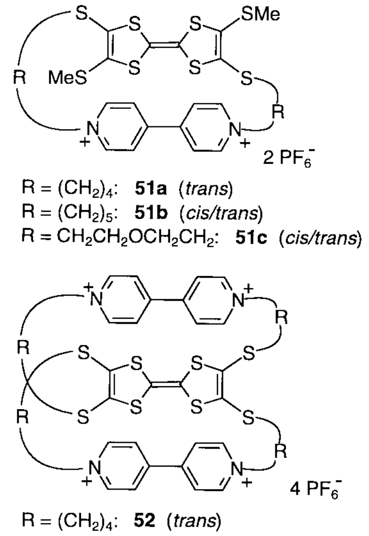


Fig. 19 Donor–acceptor mono- and bicycles.

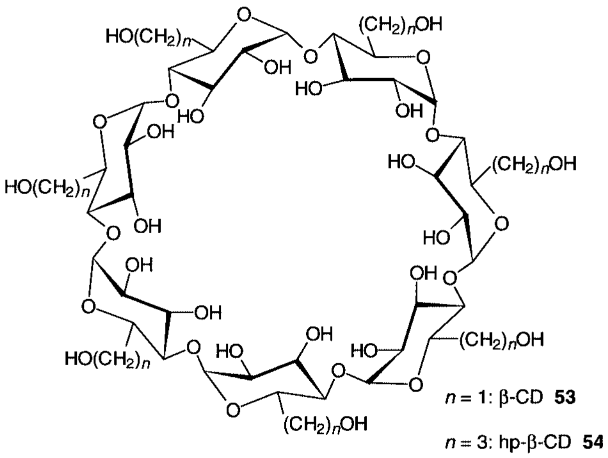


Fig. 20 Structure of β-cyclodextrin.

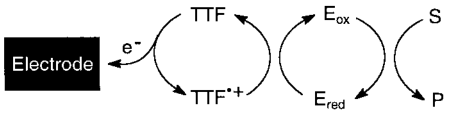
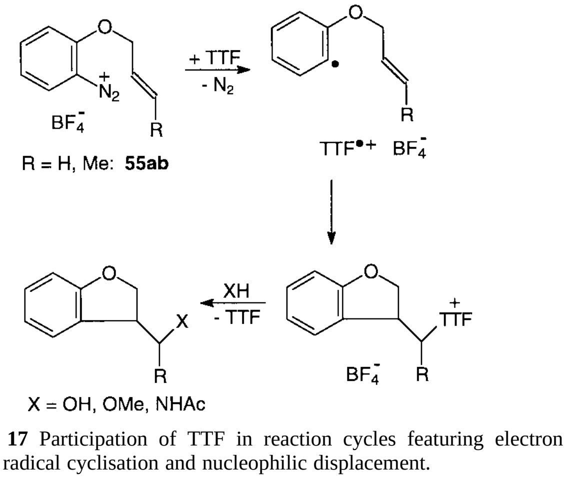
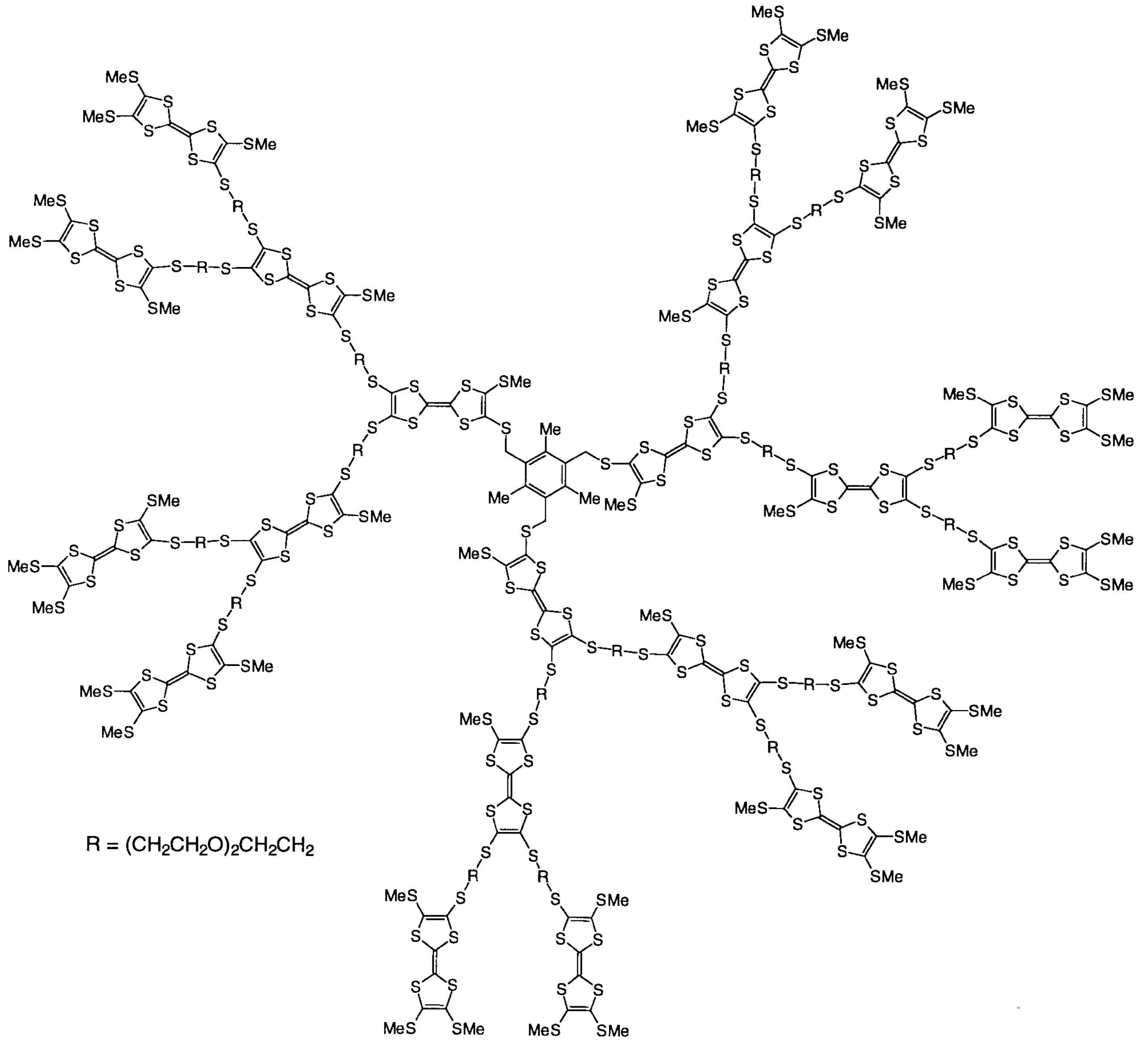


Fig. 21 Schematic diagram of a TTF-mediated oxidation of the substrate S to the product P carried out by the enzyme E.



Scheme 17 Participation of TTF in reaction cycles featuring electron transfer, radical cyclisation and nucleophilic displacement.



$R = (CH_2CH_2O)_2CH_2CH_2$

56

Fig. 22 Tetrathiafulvalene $[TTF]_{21}$-glycol dendrimer.

number of such radical reactions, recently in one of the steps in the total synthesis of (±)-aspidospermidine.[42] This field of chemistry may also benefit from supramolecular chemistry, since capture of TTF in appropriate host molecules may render it either active or inactive for participating in the radical reaction under study, thereby offering a way to control the progress of the reaction.

6.3 Dendritic macromolecules incorporating TTFs

M. R. Bryce and coworkers have reported a number of interesting dendritic macromolecules (also termed ‘starburst polymers’ or ‘cascade molecules’) based on TTF.[43] Such molecules comprise a polyfunctional core surrounded by covalently linked layers of monomers, with a branch occurring at each monomer unit. One such dendrimer (**56**) containing a total of 21 TTF units is shown in Fig. 22.[44] The close spatial contact between TTFs in the dendrimer resulted in intramolecular π-dimerisations of the generated radical cations upon electrochemical oxidation. As a result of the many redox active units present, a great challenge exists in employing macromolecules of this kind as catalysts or in molecular recognition processes.

7 Conclusions

The electron donating abilities of TTF have been exploited in a number of supramolecular host–guest systems in order for these to act as either sensors, molecular switches or catalysts for specific reactions. The developments in both synthetic TTF chemistry and supramolecular chemistry have made possible the construction of many elaborate systems, with applications in both the chemical, physical and biological world. Much synthetic TTF-work has been focusing on the TTF-tetrathiolate on account of its ready preparation and strong nucleophilicity. The recent access to pyrrolo-annelated TTFs possessing strong π-donor properties offers great opportunities in the design and construction of future redox active supramolecular systems.

8 References

1 F. Wudl, D. Wobschall and E. J. Hufnagel, *J. Am. Chem. Soc.*, 1972, **94**, 671.

2 J. Ferraris, D. O. Cowan, V. V. Walatka and J. H. Perlstein, *J. Am. Chem. Soc.*, 1973, **95**, 948.

3 Review on TTF: G. Schukat and E. Fanghänel, *Sulfur Rep.*, 1995, **18**, 1.

4 T. Jørgensen, T. K. Hansen and J. Becher, *Chem. Soc. Rev.*, 1994, **23**, 41.

5 K. B. Simonsen, N. Svenstrup, J. Lau, O. Simonsen, P. Mørk, G. J. Kristensen and J. Becher, *Synthesis*, 1996, **3**, 407.

6 Review on TTF macrocycles: M. B. Nielsen and J. Becher, *Liebigs Ann./Recueil*, 1997, 2177.

7 K. Zong, W. Chen, M. P. Cava and R. D. Rogers, *J. Org. Chem.*, 1996, **61**, 8117.

8 J. O. Jeppesen, K. Takimiya, F. Jensen and J. Becher, *Org. Lett.*, 1999, **1**, 1291.

9 F. Le Derf, M. Mazari, N. Mercier, E. Levillain, P. Richomme, J. Becher, J. Garín, J. Orduna, A. Gorgues and M. Sallé, *Chem. Commun.*, 1999, 1417.

10 A. J. Moore, L. Goldenberg, M. R. Bryce, M. C. Petty, A. P. Monkman and S. N. Port, *Adv. Mater.*, 1998, **10**, 395.

11 H. Liu, S. Liu and L. Echegoyen, *Chem. Commun.*, 1999, 1493.

12 Review on supramolecular fullerene chemistry: F. Diederich and M. Gómez-López, *Chem. Soc. Rev.*, 1999, **28**, 263.

13 D. N. Konarev, V. N. Semkin, A. Graja and R. N. Lyubovskaya, *J. Mol. Struct.*, 1998, **450**, 11; and references cited therein.

14 A. Izuoka, T. Tachikawa, T. Sugawara, Y. Suzuki, M. Konno, Y. Saito and H. Shinohara, *J. Chem. Soc., Chem. Commun.*, 1992, 1472.

15 A. Izuoka, T. Tachikawa, T. Sugawara, Y. Saito and H. Shinohara, *Chem. Lett.*, 1992, 1049.

16 Review on C_{60}-based electroactive organofullerenes: N. Martín, L. Sánchez, B. Illescas and I. Pérez, *Chem. Rev.*, 1998, **98**, 2527.

17 Review on TTFs involved in intramolecular CT-interactions: M. R. Bryce, *Adv. Mater.*, 1999, **11**, 11.

18 J. Llacay, M. Mas, E. Molins, J. Veciana, D. Powell and C. Rovira, *Chem. Commun.*, 1997, 659.

19 K. B. Simonsen, V. V. Konovalov, T. A. Konovalova, T. Kawai, M. P. Cava, L. D. Kispert, R. M. Metzger and J. Becher, *J. Chem. Soc., Perkin Trans. 2*, 1999, 657.

20 N. Martín, L. Sánchez, C. Seoane, R. Andreu, J. Garín and J. Orduna, *Tetrahedron Lett.*, 1996, **37**, 5979.

21 Review on interlocked and intertwined structures and superstructures: D. B. Amabilino and J. F. Stoddart, *Chem. Rev.*, 1995, **95**, 2725.

22 D. Philp, A. M. Z. Slawin, N. Spencer, J. F. Stoddart and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1991, 1584.

23 P. R. Ashton, V. Balzani, J. Becher, A. Credi, M. C. T. Fyfe, G. Mattersteig, S. Menzer, M. B. Nielsen, F. M. Raymo, J. F. Stoddart, M. Venturi and D. J. Williams, *J. Am. Chem. Soc.*, 1999, **121**, 3951.

24 W. Devonport, M. A. Blower, M. R. Bryce and L. M. Goldenberg, *J. Org. Chem.*, 1997, **62**, 885.

25 J. Lau, M. B. Nielsen, N. Thorup, M. P. Cava and J. Becher, *Eur. J. Org. Chem.*, 1999, 2807.

26 M. Asakawa, P. R. Ashton, V. Balzani, S. E. Boyd, A. Credi, G. Mattersteig, S. Menzer, M. Montalti, F. M. Raymo, C. Ruffilli, J. F. Stoddart, M. Venturi and D. J. Williams, *Eur. J. Org. Chem.*, 1999, 985.

27 K. N. Houk, S. Menzer, S. P. Newton, F. M. Raymo, J. F. Stoddart and D. J. Williams, *J. Am. Chem. Soc.*, 1999, **121**, 1479.

28 M. B. Nielsen, Z.-T. Li and J. Becher, *J. Mater. Chem.*, 1997, **7**, 1175.

29 Z.-T. Li and J. Becher, *Chem. Commun.*, 1996, 639.

30 M. B. Nielsen, N. Thorup and J. Becher, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1305.

31 Review on molecular machines: V. Balzani, M. Gómez-López and J. F. Stoddart, *Acc. Chem. Res.*, 1998, **31**, 405.

32 P.-L. Anelli, M. Asakawa, P. R. Ashton, R. A. Bissell, G. Clavier, R. Górski, A. E. Kaifer, S. J. Langford, G. Mattersteig, S. Menzer, D. Philp, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, M. S. Tolley and D. J. Williams, *Chem. Eur. J.*, 1997, **3**, 1113.

33 M. Asakawa, P. R. Ashton, V. Balzani, A. Credi, C. Hamers, G. Mattersteig, M. Montalti, A. N. Shipway, N. Spencer, J. F. Stoddart, M. S. Tolley, M. Venturi, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1998, **37**, 333.

34 M. B. Nielsen, S. B. Nielsen and J. Becher, *Chem. Commun.*, 1998, 475.

35 R. Wolf, M. Asakawa, P. R. Ashton, M. Gómez-López, C. Hamers, S. Menzer, I. W. Parsons, N. Spencer, J. F. Stoddart, M. S. Tolley and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1998, **37**, 975.

36 T. Jørgensen, J. Becher, J.-C. Chambron and J. P. Sauvage, *Tetrahedron Lett.*, 1994, **35**, 4339.

37 K. B. Simonsen, K. Zong, R. D. Rogers, M. P. Cava and J. Becher, *J. Org. Chem.*, 1997, **62**, 679.

38 K. B. Simonsen, N. Thorup, M. P. Cava and J. Becher, *Chem. Commun.*, 1998, 901.

39 J. H. T. Luong, R. S. Brown, K. B. Male, M. V. Cattaneo and S. Zhao, *Trends Biotechnol.*, 1995, **13**, 457; and references cited therein.

40 G. F. Khan, M. Ohwa and W. Wernet, *Anal. Chem.*, 1996, **68**, 2939.

41 C. Lampard, J. A. Murphy and N. Lewis, *J. Chem. Soc., Chem. Commun.*, 1993, 295.

42 O. Callaghan, C. Lampard, A. R. Kennedy and J. A. Murphy, *J. Chem. Soc., Perkin Trans. 1*, 1999, **1**, 995.

43 M. R. Bryce and W. Dewonport, *Adv. Dendritic Macromol.*, 1996, **3**, 115.

44 C. A. Christensen, L. M. Goldenberg, M. R. Bryce and J. Becher, *Chem. Commun.*, 1998, 509.