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Tetrathiafulvalene and π -extended tetrathiafulvalene pillar[5]arene conjugates: synthesis, electrochemistry and host-guest properties

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Pillar[5]arene derivatives decorated with ten peripheral TTF subunits have been efficiently prepared from a decabrominated pillar[5]arene building block and appropriate TTF-thiolate nucleophiles. While the preparation of related systems with peripheral exTTF subunits could not be achieved under the same conditions, a fully substituted pillar[5]arene exTTTF conjugate has been prepared from a clickable pillar[5]arene derivative and an exTTF derivative bearing a terminal alkyne function. Electrochemistry investigations have revealed substantial electronic interactions between the TTF subunits in the conjugates. The peripheral TTF moieties are indeed confined in a restricted space and thus forced to interact. In contrast, no electronic interactions could be detected for the exTTF-containing system. Finally, binding studies have shown all the conjugates are capable of forming host-guest complexes with 1,6-dicyanohexane and a methanofullerene bearing a cyanoalkane moiety.

Introduction

With their ten peripheral substituents, pillar[5]arene derivatives are attractive compact nanoscaffolds for the construction of multifunctional compounds with specific properties.¹ The copper-catalysed alkyne-azide cycloaddition (CuAAC) reaction² has been particularly useful for the ten-fold post-functionalization of pillar[5]arene building blocks bearing ten peripheral azide or terminal alkyne functions.³ Alternatively, nucleophilic substitutions of the ten peripheral alkyl bromide functions of pillar[5]arene derivatives have been also useful reactions to decorate the macrocyclic scaffold.⁴ A wide range of advanced materials and bioactive compounds build on a pillar[5]arene scaffold have been thus prepared in recent years.⁵⁻¹¹ Examples include efficient hole transporting materials for perovskite solar cells,⁵ redox-driven molecular machines,⁶ photoactive molecular devices,⁷ and multivalent glycoclusters targeting bacterial lectines.⁸ On the other hand, the pillar[5]arene moiety is also a supramolecular receptor offering additional opportunities to modify the properties of these multifunctional materials.⁹ This has been for example

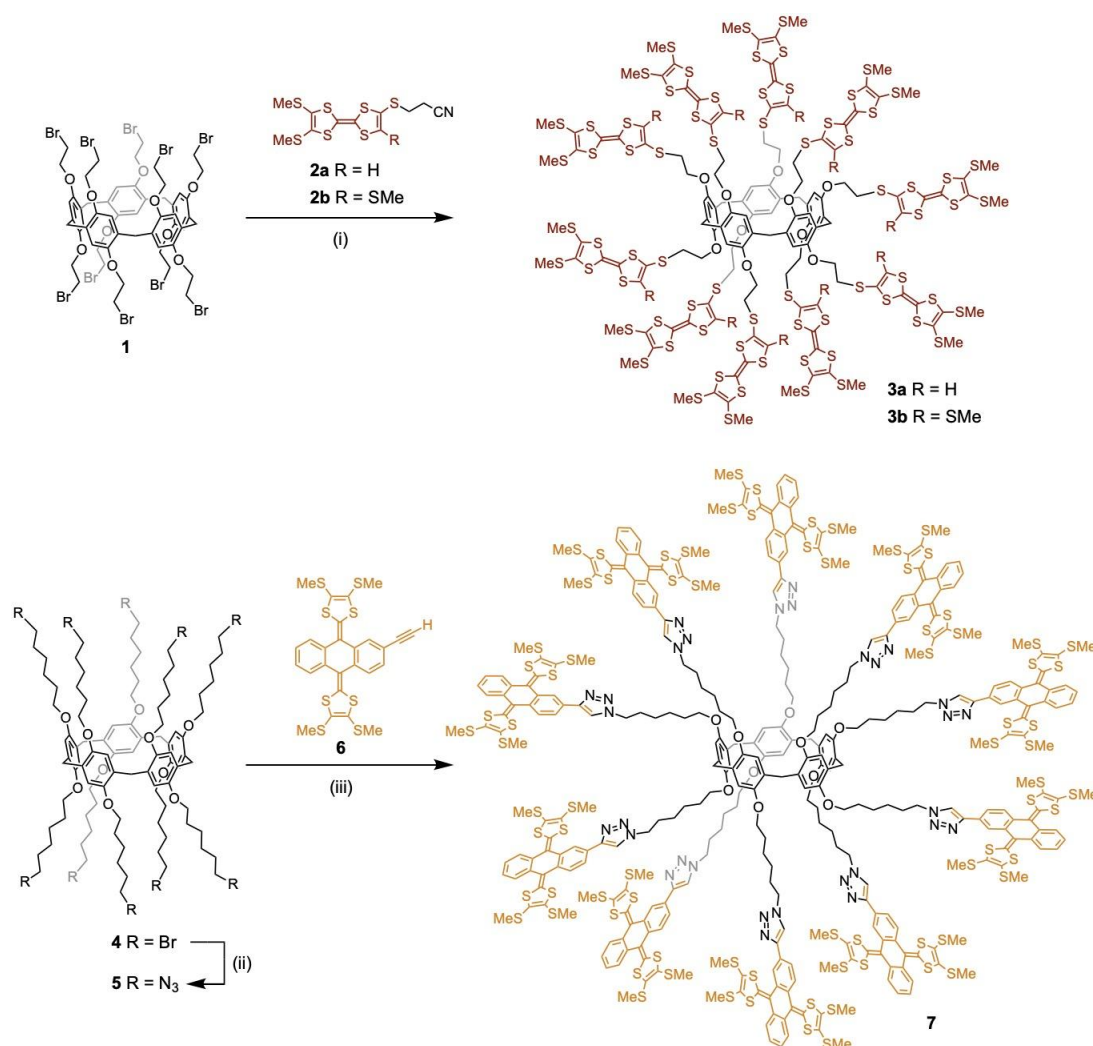
used to modulate the liquid crystalline properties of pillar[5]arene columnar assemblies¹⁰ and to develop targeted drug delivery systems.¹¹ As part of this research, we became interested in the preparation of redox-active materials constructed on a pillar[5]arene core and in evaluating their host-guest properties. For this purpose, tetrathiafulvalene (TTF) and π -extended tetrathiafulvalene (exTTF; 2-[9-(1,3-dithiol-2-ylidene)anthracen-10(9H)-ylidene]-1,3-dithiole) have been selected as the electroactive moieties. TTF is a well-known π -electron donor which has been the subject of intensive interest for the development of conducting organic materials.¹²⁻¹⁴ Besides this historical use, the combination of a strong π -donor ability and a remarkable chemical stability over three stable redox states (i.e. TTF, TTF^{•+}, TTF²⁺), have propelled this unit as a key building block for the construction of redox-responsive architectures.¹⁵⁻¹⁹ In particular, TTF and derivatives have been extensively used in redox-active macrocyclic and supramolecular systems designed for guest recognition.²⁰⁻²¹ Unlike TTF, the so-called π -extended tetrathiafulvalene (exTTF), in which the two dithiole moieties are attached to a central dihydroanthracenyl platform, undergoes a

single two-electron oxidation to yield the corresponding aromatic dication exTTF^{2+} .²²⁻²³ Strong internal S...H steric repulsions, leads to the 'saddle-type' conformation of exTTF in the neutral state. The oxidation process is accompanied by dramatic structural changes to reach a fully aromatic species in which both dithiolium rings are mostly perpendicular to the central anthracene scaffold. These singular features were successfully explored in curved host compounds designed to bind fullerene derivatives,²⁵ or for the controlled delivery of guests.²⁶⁻²⁷ On the other hand, macrocyclic cores such as calixarene,^{15,18,28-32} calixpyrrole,¹⁷⁻¹⁸ resorcinarene,^{18,33-34} and cyclotriveratrylene³⁵ decorated with TTF or exTTF substituents have been previously reported. However, to the best of our knowledge, no example of TTF or exTTF-pillararene conjugate has been described so far. Such appealing macrocyclic electron-rich systems are expected to be suitable supramolecular receptors for guests to construct non-covalent acceptor-donor ensembles. This has been demonstrated by the association of the new TTF- and exTTF-pillar[5]arene derivatives with a fullerene-containing guest.

Results and discussion

Synthesis. The synthesis of the TTF- and exTTF-substituted pillar[5]arene derivatives is depicted in Scheme 1. TTF-based compounds 3a-b were synthesized starting from pillar[5]arene 136 and the cyanoethylthio-protected TTF derivatives 2a-b. The thiolate intermediates derived from 2a³⁷ and 2b³⁸

were generated in situ by treatment with caesium hydroxide in MeOH/N,N-dimethylformamide (DMF). Subsequent reaction with decabromide 1 at 45°C then afforded compounds 3a and 3b with excellent yields (91%), having in mind that ten covalent bonds are created in a single step. The synthesis of an analogous pillar[5]arene derivative bearing ten peripheral exTTF moieties was also attempted under nucleophilic substitution conditions. However, the treatment of 1 with an exTTF derivative bearing a hydroxymethyl function (compound 15) in the presence of NaH in DMF afforded only defected products (Scheme S1). As evidenced by MALDI-TOF MS analysis, a maximum of six exTTF units could be effectively grafted onto the pillar[5]arene core (Figure S1). In order to overcome the negative steric effects preventing the complete functionalization of building block 1 with exTTF residues, it was decided to use pillar[5]arene 4 bearing longer alkyl chains as the starting material. However, treatment of 4 with an excess of exTTF-based nucleophile gave again defective products. This prompted us to change our synthetic approach. Specifically, the CuAAC reaction was selected for the functionalization of the pillar[5]arene scaffold with exTTF moieties as these conditions are by far less sensitive to steric effects.⁵⁻⁸ For this purpose, clickable building block 5 was prepared by reaction of 4 with sodium azide in DMF. The functionalization of 5 with terminal alkyne 6 was then achieved under the classical CuAAC conditions developed by Sharpless (CuSO₄·5H₂O, sodium ascorbate, CH₂Cl₂/H₂O).² Clicked derivative 7 was thus obtained in 85% yield.



Scheme 1. Synthesis of the TTF and exTTF-based pillar[5]arene derivatives. Reagents and conditions: (i) CsOH·H₂O, MeOH, DMF, 45°C (3a: 91% and 3b: 91%); (ii) NaN₃, DMF, rt (85%); (iii) CuSO₄·5H₂O, sodium ascorbate, CH₂Cl₂/H₂O, rt (85%).

The structures of 3a-b and 7 were confirmed by mass spectrometry. Their MALDI-TOF mass spectra revealed the expected signals for [3a + H]⁺, [3b + H]⁺ and [7 + H]⁺ at *m/z* = 4157.1, 4616.9 and 7751.5 respectively (Figures S4d, S5d and S7d). Importantly, no signals of defective by-products could be detected. In the particular case of 7, additional peaks corresponding to the successive loss of [(CH₃)₂C₃S₂] fragments were also detected. This characteristic fragmentation pattern of exTTF derivative³⁹ further confirmed the structure

of 7 as these fragments can only arise from a fully clicked compound. The ¹H and ¹³C NMR spectra of 3a-b and 7 were also fully consistent with their D₅-symmetrical structures. As typical examples, the ¹H NMR spectra recorded for 3a-b are depicted in Figure 1. In both cases, the spectra revealed a single set of signals for the ten equivalent peripheral TTF groups. The two characteristic singlets of the pillar[5]arene central core are observed at δ = 6.88 and 3.76 ppm for 3a, and at δ = 7.01 and 3.80 for 3b. Owing to their D₅

symmetry, compounds 3a and 3b are chiral and the protons of the ethylene groups are therefore diastereotopic. As a result, they appear as an AA'XX' in the ¹H NMR spectra of 3a-b.

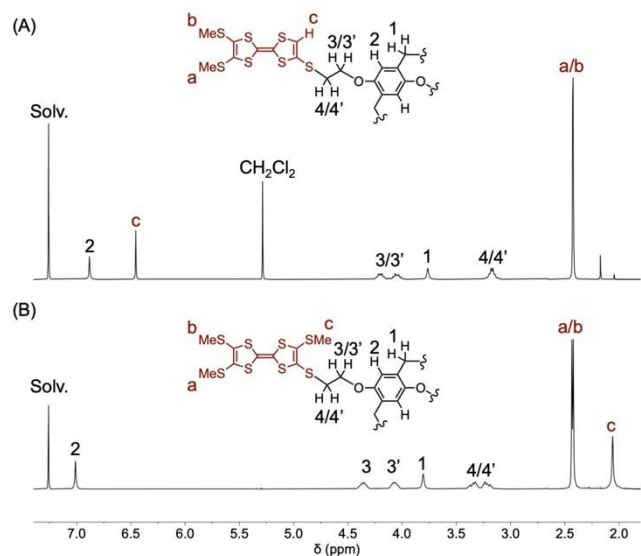


Figure 1. ¹H NMR spectra (300 MHz) of compounds 3a (A) and 3b (B) recorded in CDCl₃ at 298 K.

Electrochemical properties. The redox properties of compounds 3a, 3b and 7 were studied by cyclic voltammetry (Figure 2). In solution, both TTF-based pillar[5]arene compounds 3a and 3b (Figure 2a) undergo two reversible oxidation processes at $E_{1ox} = 0.077$ V and $E_{2ox} = 0.381$ V vs Fc/Fc⁺ for 3a, and $E_{1ox} = 0.110$ V and $E_{2ox} = 0.392$ V vs Fc/Fc⁺ for 3b. These processes are assigned to the successive oxidations of the TTF frameworks to radical-cation and dication states, respectively. One should note that an adsorption process occurs during the formation of TTF₂⁺ moieties, which results in a sharp but reversible oxidation peak probably due to a lack of solubility of the accumulated dicationic TTF₂⁺ moieties in the electrolyte medium.⁴⁰ A slightly lower π -donor ability is observed for compound 3b compared to 3a. This behavior is ascribed to the presence of an additional thiomethyl group in 3b. In both cases the first redox process appears moderately broadened, suggesting intramolecular electronic interactions between

proximal TTF units. These interactions produce mixed valence and π -dimer species once the cation-radical state has been reached. Such a behavior is commonly encountered with poly-TTF derivatives.^{15,32,41-42} To determine whether these interactions occur intra- or intermolecularly, a concentration study was conducted (Figure 2c). Even at concentration as low as 2.5×10^{-6} M, the first oxidation wave remains broad, which confirms the occurrence of intramolecular interactions between TTF units.

In order to assess the number of electrons exchanged in both redox processes, 10 equiv. of an internal coulometric reference was introduced in the electrolytic solution. We selected the 2,3-dichloro-1,4-naphthoquinone (Dichlon), an electron acceptor with a first well-defined reversible one-electron reduction peak which occurs at $E_{red} = -0.922$ V vs Fc/Fc⁺, i.e. at a potential sufficiently different from the TTF oxidation ones. The mixture was studied in finite diffusion conditions (thin layer cyclic voltammetry (TLCV)) at $v = 10$ mV.s⁻¹ (Figure 2b and S11). In this method, all the electroactive species confined in the thin layer (<25 μ m) are oxidized (or respectively reduced), which allows to access to the coulometry of the redox process.⁴³ This is done by comparing the charge exchanged (integration of the redox-wave areas) to the reference compound one (Dichlon in our case). It is worth noting that under those conditions, the area of both oxidation waves of TTF in 3a and 3b (2.5×10^{-4} M) are remarkably similar to the reduction wave of Dichlon (2.5×10^{-3} M) in both experiments (Figure S13). This result confirms nicely that 10 electrons per molecule are exchanged for each redox process and that all TTF units are successively oxidized to the radical-cation and dication states, meaning a reversible generation of twenty positive charges on the periphery of the molecule.

For solubility reason, the electrochemical properties of the exTTF-based pillar[5]arene 7 were studied in pure dichloromethane. The latter exhibits a voltammogram which is typical for exTTF derivatives. A single two electrons oxidation is observed at $E_{1ox} = 0.172$ V vs Fc/Fc⁺ with a poor electrochemical reversibility, which is assigned to the geometrical reorganization occurring

upon the reduction of the planar

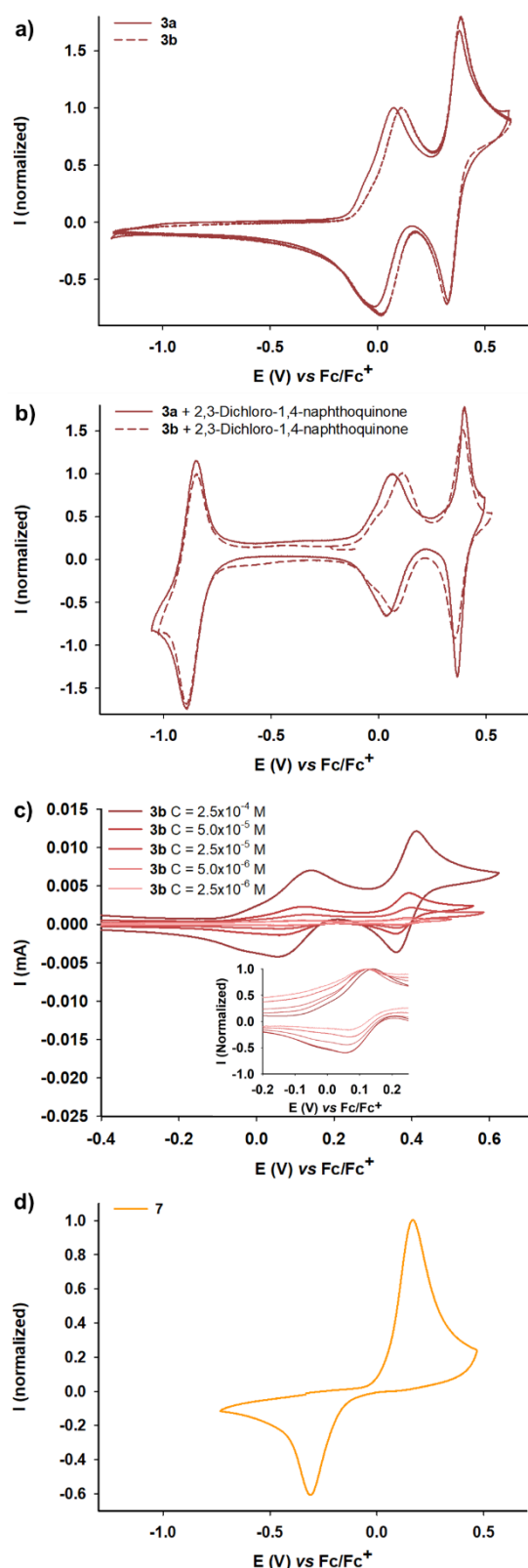


Figure 2. Cyclic voltammograms (0.1 M nBu₄NPF₆, Pt, E vs Fc/Fc⁺) of compounds 3a and 3b (C = 2.5×10⁻⁴ M, CH₂Cl₂:CH₃CN, 90:10 for 3a, 75:25 for 3b): a) semi-

infinite diffusion conditions, $\nu = 100 \text{ mV}\cdot\text{s}^{-1}$, b) thin layer conditions (<25 μm), in presence of 10 equiv. of 2,3-dichloro-1,4-naphthoquinone, $\nu = 10 \text{ mV}\cdot\text{s}^{-1}$; c) compound 3b ($2.5\times 10^{-4} \text{ M} < C < 2.5\times 10^{-6} \text{ M}$, CH₂Cl₂:CH₃CN 75:25), diffusion regime, $\nu = 100 \text{ mV}\cdot\text{s}^{-1}$ (for full voltammogram see Figure S13); d) compound 7 (0.1 M nBu₄NPF₆, Pt, E vs Fc/Fc⁺, C = 2.5×10⁻⁴ M, (CH₂Cl₂), semi-infinite diffusion conditions, $\nu = 100 \text{ mV}\cdot\text{s}^{-1}$.

aromatic anthracene species (exTTF²⁺) to the neutral folded dihydroanthracene derivative (Figure 2d).⁴⁴ As expected from this two-electrons process, no electrochemical signature of interacting exTTF units can be observed. Unfortunately, due a lack of solubility of the oxidized exTTF²⁺ pillar[5]arene derivative, the charge exchanged during the oxidation process appears different from the reduction one (Figure S12) which precludes evaluating the number of exchanged electrons by TLCV experiments.

Host-guest properties. The host-guest properties of 3b and 7 were also investigated. For comparison purposes, 1,4-diethoxypillar[5]arene (8, Chart 1) was used as a model host compound in the present study. 1,6-Dicyanohexane (9) and methanofullerene 14 were selected as guests. Indeed, given their donor - acceptor electronic complementarity, host-guest complexes between TTF or exTTF derivatives on one hand, and fullerene compounds on the other hand, have already been described.^{22,25} While compound 9 is commercially available, fullerene derivative 14 was prepared from 11-bromo-1-undecanol (10) as depicted in Scheme 2.

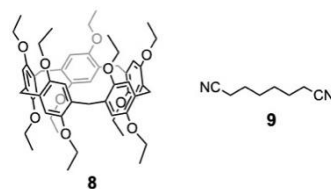
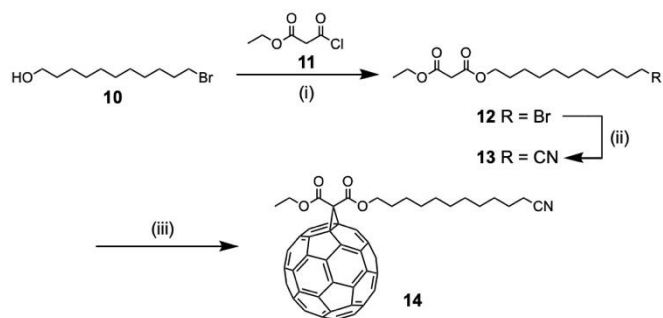


Chart 1. Compounds 8 and 9.



Scheme 2. Synthesis of fullerene guest 14. Reagents and conditions: (i) pyridine, CH₂Cl₂, rt (91%); (ii) Et₄N.CN, DMF, rt (94%); (iii) C₆₀, I₂, DBU, PhMe, rt (40%).

The synthetic approach to prepare methanofullerene 14 relies upon Bingel-type chemistry.⁴⁵ To this end, malonate 13 was prepared by esterification of alcohol 10 with ethyl malonyl chloride (11) followed by treatment of the resulting 12 with tetraethylammonium cyanide in DMF. The functionalization of C₆₀ with malonate 13 was then achieved under modified Bingel conditions.⁴⁶ The α -iodomalonate intermediate derived from 13 was generated in situ from the reaction of iodine with the malonate in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). Addition of the corresponding stabilized α -iodocarbanion to C₆₀ was then followed by an intramolecular nucleophilic displacement of iodide by the anionic centre generated on the fullerene core to form the cyclopropane ring. Methanofullerene 14 was thus obtained in 40% yield.

The formation of inclusion complexes from α,α -dicyanoalkanes with 1,4-dialkoxypillar[5]arene has been investigated in DMSO-d₆/CDCl₃ by C. Li and co-workers.⁴⁷ Under these conditions, an association constant (K_A) of 6.5 x 10² M⁻¹ has been derived from the NMR binding studies of 1,4-diethoxypillar[5]arene 8 with 1,6-dicyanohexane (9). For solubility reasons, the experimental conditions used by C. Li and co-workers were not applicable to investigate the binding of 1,6-dicyanohexane and nitrile 14 with pillar[5]arene derivatives 3b and 7. We therefore performed all the NMR binding studies in pure CDCl₃. By adding increasing amount of the appropriate guest to a CDCl₃

solution of the host, continuous chemical shift changes were observed in all the cases (Figures S14-S19). The K_a values for the 1:1 complexes were then calculated based on the complexation-induced changes in chemical shifts by using curve-fitting analysis.⁴⁸ The binding constants derived from the titrations are reported in Table 1.

Table 1. Values of the association constants (logK_a) calculated for the 1:1 host-guest complexes of compounds 9 and 14 with pillar[5]arene hosts 3b, 7 and 8 in CDCl₃ at 298 K.

	Guest	Host		
		3b	7	8
	9	1.5(1)	3.35(9)	2.9(1)
	14	0.7(2)	2.2(1)	1.62(5)

When compared to model compound 8, the K_A values obtained for compound 3b and both guests are significantly decreased. In contrast, the same comparison reveals increased K_A values for compound 7 despite the increased size of the peripheral groups. These observations show that the difference in stability of the inclusion complexes obtained from hosts 3b, 7 and 8 with guests 9 and 14 are not simply resulting from steric effects. Indeed, electronic interactions between the encapsulated guest and the peripheral units of the host must also play an important role. Specifically, the TTF subunits grafted onto the macrocyclic core of [9 \subset 3b] and [14 \subset 3b] potentially destabilize the inclusion complexes owing to repulsive interactions between the nitrile functions of the guest and the sulfur-rich substituents. Molecular modeling studies revealed a close proximity of the CN groups of 9 with some thioether functions of 3b in the inclusion complex (Figure S20). In the case of [14 \subset 3b], the nitrile group of 14 is also located in the proximity of the TTF substituents of pillar[5]arene 3b. In contrast, such negative electronic interactions are totally vanished for the inclusion complexes obtained from compound 7. Owing to the presence of the long alkyl spacers, the

nitrile moieties of guests 9 and 14 remain always located far from the exTTF moieties in inclusion complexes [9⊂7] and [14⊂7]. Furthermore, the increased stability observed for [9⊂7] and [14⊂7] when compared to the analogous systems obtained from model pillar[5]arene 8 suggests the establishment of favorable secondary interactions. These are tentatively ascribed to the presence of the 1,2,3-triazole subunits in 7. Effectively, a similar increased stability has been already reported for the inclusion complexes obtained from 9 and clicked pillar[5]arene liquid crystalline receptors.¹⁰

Conclusions

Pillar[5]arene derivatives 3a-b decorated with ten peripheral TTF subunits have been efficiently prepared from pillar[5]arene building block 1 and appropriate TTF-thiolate nucleophiles. The preparation of related systems with peripheral exTTF subunits could not be achieved under the same conditions because of steric congestion and only defective products have been obtained in this case. However, fully substituted pillar[5]arene exTTF conjugate 7 has been successfully prepared from a clickable pillar[5]arene derivative. Detailed investigations of their electrochemical properties have revealed some electronic interactions between the TTF subunits in 3a-b. Due to their compact molecular structures, the peripheral TTF moieties are confined in a restricted space and thus forced to be in close contact. In contrast, no electronic interactions could be detected for deca-exTTF derivative 7. In this case, the extended molecular structure does not generate particular contacts between the peripheral subunits. Finally, NMR binding studies have shown that pillar[5]arene derivatives 3b and 7 are capable of forming host-guest complexes with 1,6-dicyanohexane (9) and methanofullerene 14. These macrocycles are therefore suitable building blocks for the construction of complex redox and/or photo-active rotaxanes. Work in this direction is currently under way.

Experimental section

General

Reagents were purchased as reagent grade and used without further purification. Compounds 1,36 449 and 650 were prepared according to previously reported procedures. All reactions were performed in standard glassware under an inert Ar atmosphere. Evaporation and concentration were done at water aspirator pressure and drying in vacuo at 10-2 Torr. Column chromatography: silica gel 60 (230-400 mesh, 0.040-0.063 mm) was purchased from E. Merck. Thin Layer Chromatography (TLC) was performed on aluminum sheets coated with silica gel 60 F254 purchased from E. Merck. NMR spectra were recorded with a Bruker Avance III 300, AC 300 or AC 400 spectrometer with solvent peaks as reference. IR spectra (cm⁻¹) were recorded with a Perkin-Elmer Spectrum One or a Bruker VERTEX 70 spectrophotometer. Absorption spectral measurements were carried out with a PerkinElmer Lambda 365 spectrophotometer equipped with PCB 1500 water Peltier system or with Shimadzu UV-1800 spectrophotometer. MALDI-TOF mass spectra were recorded on a Bruker ULTRAFLEXTM matrix-assisted laser desorption ionization time-of-flight mass spectrometer by the analytical service of the School of Chemistry (Strasbourg, France) or on a JEOL JMS3000 by the ASTRAL platform from the SFR MATRIX (Angers, France). Elemental analyses were performed by the analytical service of the Fédération de Chimie Le Bel FR (Strasbourg, France) or the ASTRAL platform from the SFR MATRIX (Angers, France).

Electrochemistry

Cyclic voltammetry experiments were carried out in a glovebox with a BioLogic SP-150 potentiostat driven by the EC-Lab software; a silver wire was used as a quasi-reference electrode and a platinum wire counter electrode, and the set-up was calibrated using internal ferrocene. Experiments were recorded in dry HPLC-grade acetonitrile and dichloromethane with tetrabutylammonium hexafluorophosphate (electrochemical grade, Aldrich) as supporting electrolyte. Thin layer cyclic voltammetry experiments were carried out in similar conditions with a home-made setup.⁵¹

Titration experiments

All the ¹H NMR titration experiments were performed on a Bruker AC 300 at 25(1)°C, in CDCl₃ purchased from Sigma Aldrich Chemical Company. The appropriate amount of guest (9 or 14) stock solution (CDCl₃) was added to the solution of hosts (3b, 7 and 8) in CDCl₃. The association constants (K_a) for the 1:1 host-guest complexes were determined based on the complexation-induced changes in chemical shifts of the signals from hosts. The calculations were done using the nonlinear least-square regression analysis program HypNMR.⁴⁸ In the particular case of [14 ⊂ 3b], the K_a value was estimated by manual fitting using HypNMR.

Synthesis

Compound 2a

A solution of 4-(2-cyanoethylthio)-1,3-dithiole-2-one (0.2 g, 0.98 mmol) and 4,5-bis(methylthio)-1,3-dithiole-2-thione (0.668 g, 2.95 mmol) in freshly distilled triethyl phosphite (10 mL) was heated at 120°C under argon. After 3h, the reaction mixture was cooled to rt and the solvent was removed under reduced pressure. Purification by column chromatography (SiO₂, CH₂Cl₂/petroleum ether: 1/1 v/v) afforded 2a as a red-orange solid (258 mg, 69%). ¹H NMR (300 MHz, CDCl₃): δ = 6.57 (s, 1H), 2.96 (t, J = 7.1 Hz, 2H), 2.69 (t, J = 7.0 Hz, 2H), 2.43 (d, J = 1.7 Hz, 6H) ppm. Analytical data is identical to the one previously reported in the literature.³⁷

Compound 2b

A solution of cesium hydroxide monohydrate (262 mg, 1.56 mmol) in absolute methanol (3.5 mL) was added to a solution of 2,3-bis(2-cyanoethylsulfanyl)-6,7-bis(methylsulfanyl)tetrathiafulvalene (694.5 mg, 1.488 mmol) in DMF (20 mL). After 15 minutes of stirring at rt and bubbling with Ar, iodomethane (0.925 mL, 2.1092 g, 14.86 mmol, 10 equiv) was added. After 1h of

additional stirring and bubbling with Ar, the solvents were evaporated under reduced pressure (60 °C, 10 mBar). Purification by column chromatography (SiO₂, CH₂Cl₂) gave 2b as a red solid (580 mg, 91 %). ¹H NMR (300 MHz, CDCl₃): δ = 3.02 (t, J = 7.3 Hz, 2H), 2.70 (t, J = 7.3 Hz, 2H), 2.47 (s, 3H), 2.43 (s, 6H) ppm. Analytical data is identical to the one previously reported in the literature.³⁸

Compound 3a

A solution of cesium hydroxide monohydrate (90 mg, 0.535 mmol) in absolute methanol (3.5 mL) was added via a cannula to a solution of 2a (205 mg, 0.535 mmol) in DMF (15 mL) at rt. After 30 minutes of stirring and bubbling with Ar, a solution of 1 (60 mg, 0.036 mmol) in anhydrous THF (30 mL) was added. The reaction mixture was stirred at 45 °C under Ar for 3h. Then, the reaction was cooled to rt, the solvents were evaporated under vacuum and the residue was dissolved in a minimum amount of dichloromethane, precipitated with diethyl ether and filtered to give compound 3a (135 mg, 91%) as a yellow-brown solid. IR (neat): 2914, 2856 cm⁻¹ (Csp³-H). ¹H NMR (300 MHz, CDCl₃): δ = 6.88 (s, 10H), 6.45 (s, 10H), 4.25–4.13 (m, 10H), 4.12–4.00 (m, 10H), 3.76 (s, 10H), 3.25–3.08 (m, 20H), 2.43 (s, 30H), 2.42 (s, 30H). ¹³C NMR (75 MHz, CDCl₃): δ = 149.8, 130.9, 128.8, 127.6, 127.5, 126.4, 123.3, 115.8, 67.4, 36.0, 29.3, 19.3, 19.3 ppm. MALDI-HRMS: m/z = 4149.0 ([M]⁺, calc. for C₁₃₅H₁₃₀O₁₀S₇₀: 4149.0). Anal. (%) calc. for C₁₃₅H₁₃₀O₁₀S₇₀·CH₂Cl₂: (4241.94): C, 38.51; H, 3.14; S, 52.91; Found: C, 38.38; H, 3.03; S, 53.01.

Compound 3b

To a solution of 2b (229 mg, 0.535 mmol) in DMF (15 mL) at rt, cesium hydroxide monohydrate (90 mg, 0.535 mmol) dissolved in absolute methanol (3.5 mL) was added via a cannula. After 30 minutes of stirring and argon bubbling, 1 (60 mg, 0.036 mmol) dissolved in anhydrous THF (30 mL) was added. The reaction mixture was stirred and heated at 45 °C under Ar for

3h. Then, the solvents were evaporated under vacuum and the residue was dissolved in a minimum amount of ethyl acetate, precipitated with diethyl ether and filtered to give 3b (150 mg, 91%) as a yellow-brown solid. IR (neat): 2914, 2854 cm⁻¹ (Csp³-H). ¹H NMR (300 MHz, CDCl₃): δ = 7.01 (s, 10H), 4.42–4.30 (m, 10H), 4.13–4.01 (m, 10H), 3.80 (s, 10H), 3.41–3.29 (m, 10H), 3.28–3.16 (m, 10H), 2.44 (s, 30H), 2.42 (s, 30H), 2.06 (s, 30H) ppm. ¹³C NMR (75 MHz, CDCl₃): δ = 149.4, 131.8, 129.0, 127.9, 127.0, 123.8, 115.1, 67.3, 36.5, 29.2, 19.4, 18.9. MALDI-HRMS: m/z = 4608.9 ([M]⁺, calc. for C₁₄₅H₁₅₀O₁₀S₈₀: 4608.9). Anal. (%) calc. for C₁₄₅H₁₅₀O₁₀S₈₀ (4617.92): C, 37.71; H, 3.27; S, 55.55; Found: C, 37.70; H, 3.22; S, 56.04.

Compound 5

A mixture of 4 (229 mg, 0.10 mmol) and NaN₃ (86 mg, 1.33 mmol) in DMF (3 ml) was stirred for 48h at rt, then H₂O was added. The aqueous layer was extracted with Et₂O (3 x). The combined organic layers were washed with H₂O (3 x), dried (MgSO₄), filtered and concentrated. Purification by column chromatography (SiO₂, CH₂Cl₂/cyclohexane: 8/2) gave compound 5 (162 mg, 85%) as a colorless glassy product. Caution: owing to its high number of azide residues, this compound must be handled with special care.⁵² Upon evaporation, compound 5 has never been dried under high vacuum and the use of a metallic spatula was avoided. Furthermore, this compound has been always prepared on a small scale. IR (neat): 2085 (N₃) cm⁻¹. ¹H NMR (300 MHz, CDCl₃): δ = 6.84 (s, 10H), 3.88 (broad s, 20H), 3.75 (s, 10H), 3.10 (m, 20H), 1.80 (m, 20H), 1.47 (m, 40H), 1.32 (m, 20H) ppm.

Compound 7

A solution of 5 (25 mg, 13.4 μmol) in CH₂Cl₂ (5 ml) was added to a Schlenk flask containing 6 (87 mg, 147.6 μmol) and H₂O (3.5 ml). The mixture was purged with Ar for 30 min. Then CuSO₄·5H₂O (3.3 mg, 13.4 μmol) and sodium ascorbate (10.6 mg, 54 μmol) were added and the resulting mixture was stirred vigorously at rt

overnight. Next, the organic layer was washed with H₂O (2 × 20 ml), dried over MgSO₄, filtered and concentrated under vacuum. Purification by column chromatography (SiO₂, CH₂Cl₂) gave 7 (90 mg, 85 %) as a yellow solid. IR (neat): 2918, 2858 cm⁻¹ (Csp³-H). ¹H NMR (500 MHz, CDCl₃) δ = 8.05–7.93 (m, 10H), 7.82–7.73 (m, 10H), 7.62 (s, 10H), 7.57–7.39 (m, 30H), 7.28 (s, 20H), 6.74 (s, 10H), 4.25 (s, 20H), 3.86 (s, 10H), 3.68 (s, 20H), 2.38–2.16 (m, 120H), 1.87 (s, 20H), 1.70 (s, 20H), 1.49 (s, 20H), 1.34 (s, 20H) ppm. ¹³C NMR (125 MHz, CDCl₃) δ = 149.8, 147.0, 135.1, 134.4, 134.0, 131.8, 131.6, 128.7, 128.2, 126.8, 126.46, 126.1, 125.9, 125.5, 123.4, 123.3, 122.3, 120.2, 114.9, 77.3, 77.3, 77.2, 77.1, 76.8, 68.3, 53.5, 50.4, 32.0, 30.4, 29.7, 29.4, 26.6, 26.0, 22.7, 19.3, 19.3, 19.2, 19.1 ppm. MALDI-MS: m/z = 7751.6 ([M]⁺, calc. for C₃₅₅H₃₄₀N₃₀₀O₁₀S₈₀: 7751.9). Anal. (%) calc. for C₃₅₅H₃₄₀N₃₀₀O₁₀S₈₀ (7751.89): C, 55.00; H, 4.42; S, 33.09; Found: C, 54.87; H, 4.36; S, 33.02.

Compound 12

Ethyl malonyl chloride 11 (0.5 mL, 3.91 mmol) was added to a solution of 10 (1.18 g, 4.69 mmol) and pyridine (0.4 mL, 4.69 mmol) in CH₂Cl₂ (8 ml) at 0°C. After 1h, the mixture was warmed up to rt, stirred for 16 h, filtered through SiO₂ (CH₂Cl₂) and concentrated. Purification by column chromatography (CH₂Cl₂/cyclohexane 7:3) gave compound 12 (1.30 g, 91%) as a pale yellow oil. IR (neat): 1732 (C=O) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 4.22 (q, J = 7 Hz, 2H), 4.15 (t, J = 7 Hz, 2H), 3.42 (t, J = 7 Hz, 2H), 3.38 (s, 2H), 1.87 (m, 2H), 1.66 (m, 2H), 1.44 (m, 2H), 1.36–1.27 (m, 15H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 166.7, 166.6, 65.7, 61.5, 41.7, 34.0, 32.8, 29.43, 29.42, 29.3, 29.2, 28.7, 28.5, 28.2, 25.8, 14.1 ppm. Anal. (%) calc. for C₁₆H₂₉BrO₄ (365.31): C, 52.61; H, 8.00; Found: C, 52.28; H, 8.06.

Compound 13

A mixture of 12 (0.70 g, 1.92 mmol) and Et₄NCN (0.90 g, 5.75 mmol) in DMF (24 ml) was stirred overnight at

rt. Then the solvent was evaporated and the residue was diluted with H₂O. The product was extracted with CH₂Cl₂ (3 x) and the combined organic layers were washed with H₂O (2 x), dried (MgSO₄), filtered and concentrated. Purification by column chromatography (SiO₂, CH₂Cl₂ containing 0.6% of CH₃OH) gave compound 13 (0.56 g, 94%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃): δ = 4.21 (q, J = 7 Hz, 2H), 4.15 (t, J = 7 Hz, 2H), 3.37 (s, 2H), 2.34 (t, J = 7 Hz, 2H), 1.66 (m, 4H), 1.45 (m, 2H), 1.36-1.27 (m, 15H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 166.7, 166.6, 119.9, 65.6, 61.5, 41.7, 29.4, 29.3, 29.2, 29.1, 28.7, 28.6, 28.5, 25.8, 25.4, 17.1, 14.1 ppm.

Compound 14

DBU (0.26 mL, 1.73 mmol) was added under Ar to a stirred solution of C60 (0.50 g, 0.69 mmol), I2 (264 mg, 1.04 mmol) and 13 (187 mg, 0.60 mmol) in toluene (550 ml) at room temperature. After 18 h, the reaction mixture was filtered through a plug of silica (toluene then CH₂Cl₂) and concentrated. Purification by column chromatography (SiO₂, CH₂Cl₂/cyclohexane 7:3) gave compound 14 (0.285 g, 40 %) as a brown glassy product. UV/vis: λ_{max} (CH₂Cl₂)/nm (ε/dm³ mol⁻¹ cm⁻¹ 142 300) 326 (40650), 413 (2 700), 425 (2 830), 488 (1 650), 687 (245). IR (neat): 2245 (CN), 1743 (C=O) cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ = 4.58 (q, J = 7 Hz, 2H), 4.52 (t, J = 7 Hz, 2H), 2.35 (t, J = 7 Hz, 2H), 1.86 (m, 2H), 1.67 (m, 2H), 1.51 (t, J = 7 Hz, 3H), 1.47 (m, 4H), 1.36-1.27 (m, 10H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ = 163.7, 163.6, 145.4, 145.32, 145.28, 145.21, 145.19, 144.9, 144.7, 144.69, 144.67, 144.6, 143.9, 143.89, 143.1, 143.04, 143.02, 142.9, 142.23, 142.22, 141.94, 141.93, 140.9, 139.1, 138.9, 119.9, 71.7, 67.5, 63.5, 52.4, 29.5, 29.4, 29.3, 29.2, 28.8, 28.7, 28.6, 26.0, 25.4, 17.2, 14.3 ppm. MALDI-TOF-MS: m/z = 1052.00 (7%, [M+Na]⁺ calc. for C₇₇H₂₇NO₄Na: 1052.18), 1029.19 (100%, [M]⁺, calc. for C₇₇H₂₇NO₄: 1029.19), 720.03 (9%, [C₆₀]⁺, calc. for C₆₀: 720.00). Anal. (%) calc. for C₇₇H₂₇NO₄ (1030.05): C, 89.79; H, 2.64; N, 1.36; Found: C, 89.22; H, 2.43; N, 1.38.

Conflicts of interest

There are no conflicts to declare

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