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Simon Guélen,[a] Max Blazejak, [a] Lise-Marie Chamoreau, [a] Arnaud Huguet,[b] Sylvie Derenne,[b] François Volatron,[c] Virginie Mouriès-Mansuy*[a] and Louis Fensterbank*[a]

This study focusses on the [2+2]-photocycloaddition of symmetric polyenic system tethered by an aryl bis-sulfide or sulfone platform. Using direct irradiation or photosensibilization, no expected ladderane product was isolated. In most cases, only tricyclic products including a single cyclobutane moeity were formed. Irradiation of bis-acrylic precursors in water with encapsulation by a host (cyclodextrin or cucurbituril) provided a stereoselective access to valuable cyclobutyl adducts.

Introduction

Context

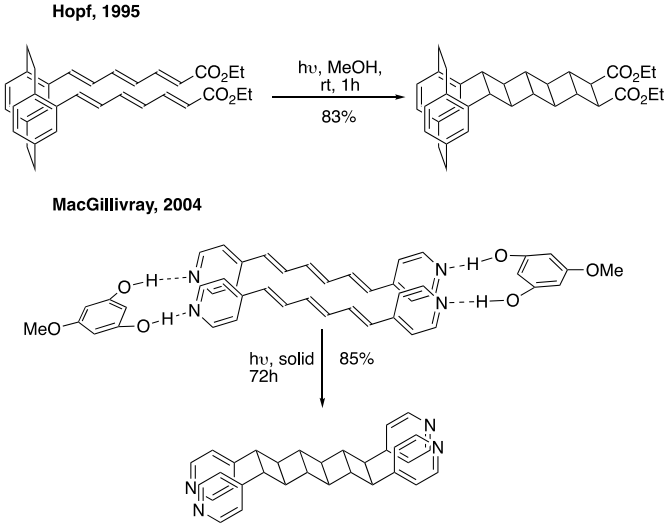
Ladderanes are fascinating molecules. By exhibiting two or more linearly fused cyclobutanes, they draw the attention of the organic chemist who is not used to encounter this type of molecular structures.[1] The high ring strain of these edifices gives them potentially interesting electronic and optical properties which are of interest for physical chemists and theoreticians.[2] Interestingly, ladderane lipids are present in nature. They have been identified in anammox bacteria performing *an*aerobic *amm*onium *ox*idation (anammox), where they form impermeable intracytoplasmic membranes, the anammoxosome.[3] The anammoxosome protects the bacteria from the formation of highly toxic species like hydrazine and hydroxylamine generated as intermediates during the anammox process. This process was discovered two decades ago and it seems to be an important component of the nitrogen biogeochemical cycle.[4]

Because of their intriguing architecture and properties, ladderanes have elicited synthetic developments. The latter have culminated in the total syntheses by Corey of the naturally occuring ladderane pentacycloanammoxic acid in 2004[5] and 2006[6] which was isolated in 2002 by Sinninghe Damsté and coworkers.[7] These total syntheses are outstanding tour de force and it is only very recently that the group of Burns came up with a second similarly elegant and efficient total synthesis of natural 3- and 5-ladderanes.[8] Both approaches rely on the [2+2] photochemical cycloaddition which is the obvious methodology to make 4-membered rings[9] but they also involve cyclobutene building blocks which are not straightforward to prepare.[10]

Ladderanes via multiple [2+2] cycloaddition

Assembling the ladderane framework in a single synthetic operation has constituted a highly stimulating challenge for a lot of groups and some important findings have been made in polycyclization strategies via [2+2] photocycloaddition. Prototype systems have in fact already been devised and are based on the Schmidt topochemical principle[11] transposed to solutions, which consists in fixing two polyenic chains in a coplanar configuration and separated by a 350 to at most 420 pm distance.[12] An early and illustrative example was given by Hopf in 1995[13] who used a cyclophane anchor to ensure the adequate arrangement of the polyenic systems. A high yield (83%) of a five fused cyclobutane unit corresponding to a [5]-ladderane framework was obtained after irradiation (450W Hg high pressure lamp) at room temperature in methanol (Scheme 1). MacGillivray proposed a supramolecular approach, relying on the cocrystallization of a resorcinol derivative with pyridine ended polyene systems.[14] Upon irridiation (broadband Hg lamp) in the solid state, the obtained crystals undergo quantitative [2+2] cycloaddition on gram amounts (Scheme 1).

Other reports of multiple [2+2] cycloadditions have confirmed the viability of such an approach.[15]



Scheme 1. Polycyclizations leading to ladderanes

Our objective

Recently, we have initiated a research program dealing with the development of alternative platforms which would promote the polycyclization process and provide more readily functionalizable anchors for further elaboration. Sulfur based linkers which should be easily disposable after the ladderane framework formation drew our attention. We initiated this study by first modeling the proposed substrates.

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† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

Results and discussions

Calculations

While only few theoretical studies have been published on ladderane frameworks focusing on their heats of formation as well as putative mechanisms of formation,[16] we have recently engaged into a theoretical analysis of ladderane at high computational level. Our findings on an unsubstituted hydrocarbon species as well as on new phenyl bis-sulfone and bis-sulfide tethered substrates are discussed below.

Unsusbtituted ladderane

First, we focused on polyunsaturated systems of formula $C_{12}H_{16}$. Acyclic (**I-Acyc**), monocyclic (**I-Mono**, three isomers), tricyclic (**I-Tric**) and pentacyclic (**I-Pent**) isomers (Figure 1) were optimized and characterized at two levels of calculation. The B3LYP level with the 6-31G(d,p) basis set was first used. The structures were reoptimized at the more sophisticated PW1PW91 level with the pVT basis set. Then, single point calculations were performed at the CCSD(T) level on both sets of optimized structures. The results are given in Table 1.

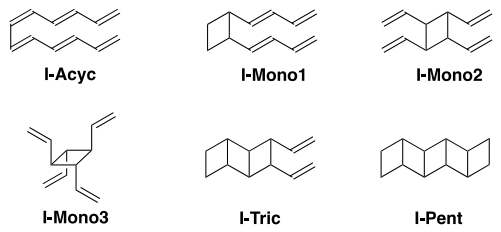


Figure 1. Unsubstituted isomers under study

The values at the PW1PW91 level differ noticeably from those at the B3LYP level (Table 1) and are always lower. However, the two sets of results become almost identical when CCSD(T) calculations are performed on the geometries obtained at the two DFT (B3LYP or PW1PW91) levels. In most cases, the CCSD(T) relative energies are also lower than the DFT ones.[17]
As a consequence, calculations in the following series will be undertaken at the CCSD(T) level with the geometries optimized at the B3LYP level.

Aryl bis-sulfone and aryl bis-sulfide platform study

The theoretical study of the ladderane formation from the cyclization of **II-Acyc** was also carried out. Seven isomers were studied with zero (**II-Acyc**), one (**III-Mono**), three (**II-Tric**), or five (**II-Pent**) cyclobutane rings in the structure. Similar treatment was achieved from aryl bis-sulfide **III-Acyc**. Their structures and relative energies are given in Figure 2 and Tables 2 and 3.

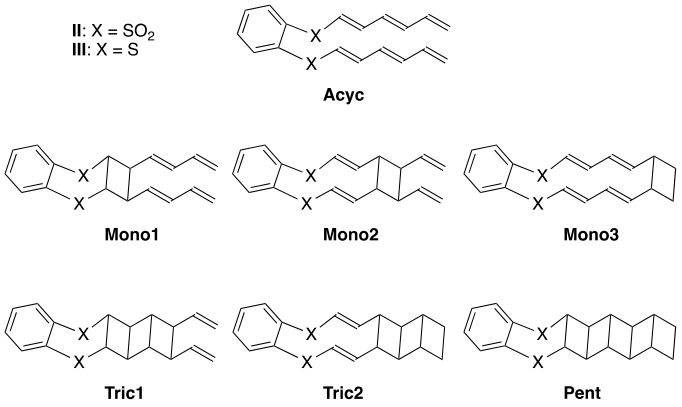


Figure 2. Structures of the computed isomers of the bis-sulfone (**II**) and bis-sulfide (**III**) platforms

Table 1a. Relative energies (in kcal/mol) of the computed isomers of the unsubstituted system at the B3LYP and CCSD(T) levels

	I-Acyc	**I-Mono 1**	**I-Mono 2**	**I-Mono 3**	**II-Tric**	**II-Pent**
ΔE B3LYP	0.0	-6.8	3.5	7.8	16.7	21.2
ΔE CCSD(T)	**0.0**	**-15.3**	**-9.6**	**-6.1**	**1.9**	**4.2**
ΔE mPW1PW91	0.0	-11.8	-2.6	-16.8	6.1	5.7
ΔE CCSD(T)	**0.0**	**-14.2**	**-9.4**	**-6.2**	**3.4**	**7.9**

Table 2. Relative energies (in kcal/mol) of the computed isomers of the arylbissulfone system at the B3LYP and CCSD(T) levels

	II-Acyc	**II-Mono1**	**II-Mono2**	**II-Mono3**	**II-Tric1**	**II-Tric2**	**II-Pent**
ΔE B3LYP	0.0	-4.8	21.7	5.0	17.8	29.3	21.7
ΔE CCSD(T)	**0.0**	**-15.3**	**6.8**	**-4.8**	**1.8**	**13.8**	**3.7**

Table 3. Relative energies (in kcal/mol) of the computed isomers of the arylbissulfide system at the B3LYP and CCSD(T) levels

	III-Acyc	**III-Mono1**	**III-Mono2**	**III-Mono3**	**III-Tric1**	**III-Tric2**	**III-Pent**
ΔE B3LYP	0.0	-1.8	24.4	9.2	20.9	31.4	28.7
ΔE CCSD(T)	**0.0**	**-15.0**	**7.0**	**-3.7**	**1.3**	**12.7**	**3.5**

As in the previous case, the relative energies are much lower at the CCSD(T) level in the bis-sulfone and bis-sulfide series compared to those obtained at the B3LYP level. Among the three monocyclic structures, **II-Mono2** and **III-Mono2** are the less stable ones, probably because of the loss of any conjugation between the C-C double bonds. Interestingly also, 10-membered ring isomers **II-Tric2** and **III-Tric3** are the less stable of the series. Finally, in both series, the pentacyclic structure **II-Pent** or **III-Pent** are rather close in energy to the corresponding **Acyc** precursors **I** (ΔE ≈ 3.5 kcal/mol, Tables 2 and 3).

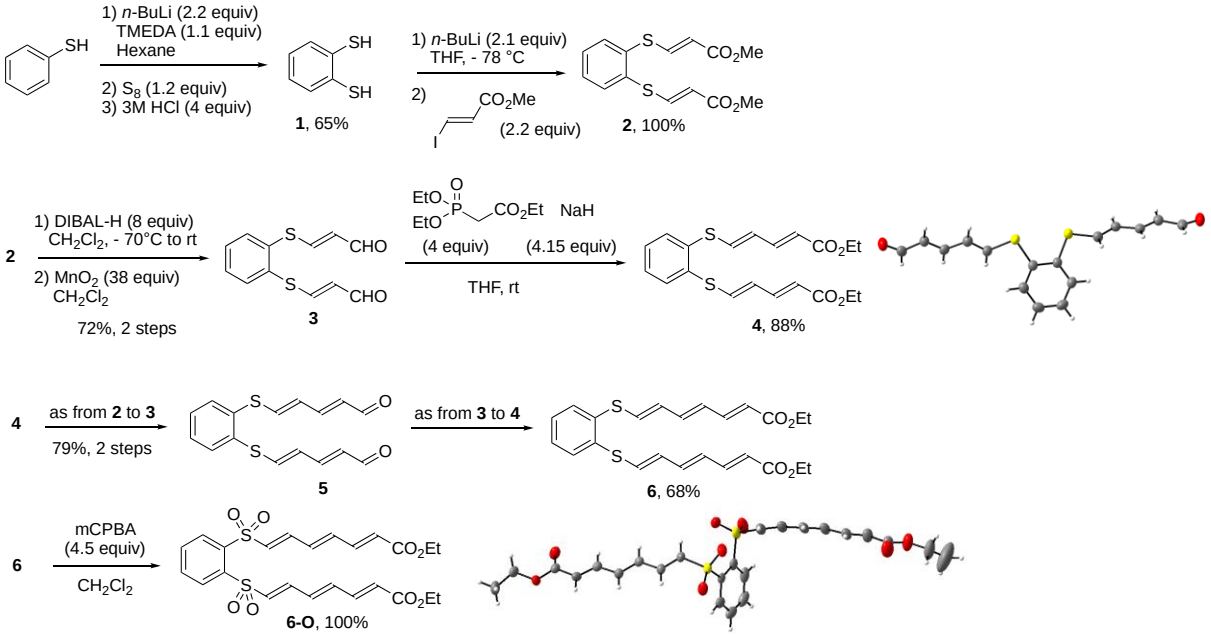
These findings suggest that **II-Acyc** or **III-Acyc** and congeners could therefore be good candidates to access to pentacyclic ladderanes.

Preparation of precursors

We devised a straightforward preparation of the photocyclo-addition precursors. Starting from 1,2-benzenedithiol 1 which is commercially available or can be made on large scale, deprotonation with n-BuLi and controlled addition on β-iodoacrylate provided a quantitative yield of bis-acrylate **2**. The competitive intramolecular addition of a thiolate anion on a branched acrylate unit could be suppressed by working in cold (-78°C) and concentrated conditions (see Experimental). Homologation of the acrylate was achieved by a sequence of DIBAL reduction, allylic oxidation (to give bis-aldehyde **3** in 72% yield) and Horner Wadsworth Emmons (HWE) olefination which delivered bis-diene **4** in 63% overall yield. Similarly, bis-triene **6** was obtained in 54% overall yield. The latter could be oxidized to the bis-sulfone precursor 6-O in quantitative yield using 4.5 equiv of MCPBA. Worthy of note, all these polyene substrates proved to be quite stable, notably upon silica gel chromatography. Some of them crystallized fairly easily by pentane diffusion in a dichloromethane solution of the polyene substrate and a X-ray diffraction (XRD) analysis was obtained for **4**, **5**, **6** and **6-O**.‡

X-ray diffraction analyses of precursors

All the XRD structures share common features and, contrary to the previous calculations, show no overlap of the ortho ene units whatever the number of ene units (from the acrylate to the triene acrylate). Instead, unsaturated arms lie in opposite directions as illustrated by the structures of **4** and **6-O** on Scheme 2. In some cases (**4**, **6**, **6-O**), the chains of two different precusors are almost coplanar and parallel. Some weak interactions C-H…O interactions[18] also take place between the hydrogen atoms of the enes and the O atom of the ester function, leading to a distance between polyene arms of more than 5 Å. Despite these findings, we attempted the photocycloaddition of the precursors in solution assuming that some conformations of cyclization could be reached.

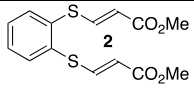
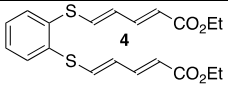
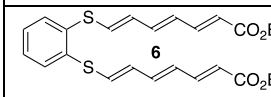
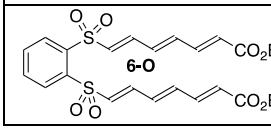


Scheme 2. Synthesis of substrates

UV absorbance

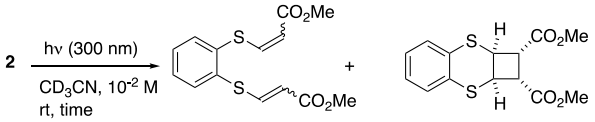
We measured the UV spectra of the polyene substrates **2**, **4**, **6** and **6-O** and values are given in Table 4. Logically, a bathochrom effect was observed by adding C=C units, from λ_{max} = 281 nm for **2** to 356 nm for **6** which was accompanied by a hyperchrome effect. Interestingly, also the replacement of the sulfide linker by a sulfone one led to a hypsochrome effect: a diminution of 50 nm is observed between from the sulfide to the corresponding sulfone, suggesting that the sulfone function attenuates the conjugation.

Table 3. UV data of of polyenic precursors

substrate	λ_{max} (nm)	ε (l/mol.cm)
 **2**	281	23859
 **4**	330	33484
 **6**	356	60872
 **6-O**	309 (327)	62719

Preliminary Irradiation results

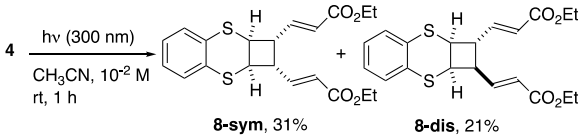
We first irradiated a CD_3CN solution of precursor **2** in a Rayonet reactor. The latter converted very slowly to the [2+2] cycloaddition product **7** and in an incomplete fashion since the main competitive pathway was the isomerization of **2** to provide the *E,Z* and *Z,Z* isomers (Scheme 3).[#] The proposed relative configuration of **7** is based on our subsequent findings (see below).



	2-mix	7
45 min	97%	2%
	(*E*/*E*: 22% ; *E*/*Z*: 48% ; *Z*/*Z*: 29%)	
93 h	67%	33%
	(*E*/*E*: 13% ; *E*/*Z*: 32% ; *Z*/*Z*: 22%)	

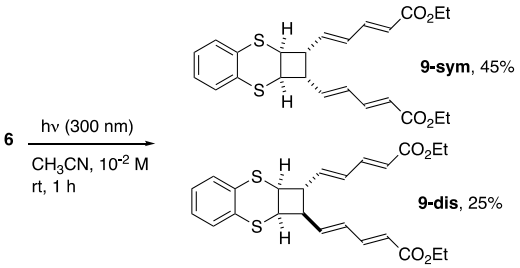
Scheme 3. Direct irradiation of bis-monoene **2**

We looked at the photocycloaddition of bis-diene **4** which proved to be more reactive since a total conversion was observed in 1h (Scheme 4). Two stereoisomeric cyclobutyl products products were isolated. The major one (**8-sym**, 31%) displayed half of the expected signals by ^{1}H and ^{13}C NMR patterns which suggested a symmetric structure contrary to the second dissymmetric product one (**8-dis**, 21%) for which all resonances were distinct. While the relative configuration of **8-sym** was deduced from findings detailed below, NOESY experiments on **8-dis** allowed us to propose a *syn-trans-anti* configuration.[19]



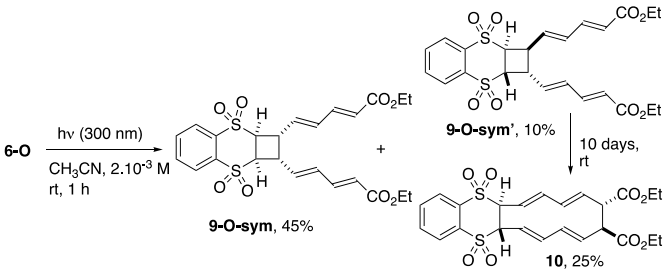
Scheme 4. Direct irradiation of bis-diene **4**

We also wished to examine the corresponding triene precursor **6**. Similar behaviour as for **4** was observed under irradiation (Scheme 5). In less than one hour, two stereoisomeric cyclobutane derivatives, **9-sym** (45%) and **9-dis** (25%), were formed displaying analogous ^{1}H NMR patterns as before. No polycyclobutane product was isolated from these reactions.



Scheme 5. Direct irradiation of bis-triene **6**

It was interesting to compare these results with the corresponding **6-O** precursor (Scheme 6). In that case, irradiation at 300 nm led to a new mixture of compounds, namely **9-O-sym** as major component and two unpreviously observed type of products, such as symmetric **9-O-sym'** and macrocycle **10**. The structure of **10** was unambiguously determined thanks to XRD analysis (see Figure 3).‡ Also, we observed that upon standing at rt for 10 days, **9-O-sym'** smoothly isomerized into **10** presumably via multiple Cope rearrangement.[2d,20] This observation allowed to safely attribute the *anti-cis-anti* configuration to C_2-symmetric **9-O-sym'** derivative.



Scheme 6. Direct irradiation of bis-triene sulfones **6-O**

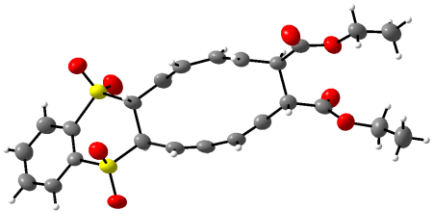


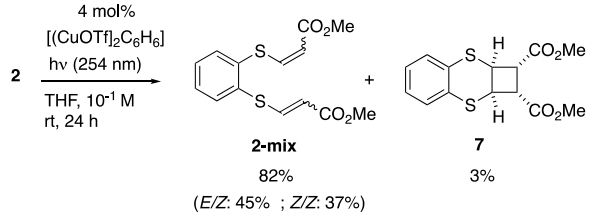
Figure 3. XRD structure of **10**

Confronted to these rather frustrating though interesting findings, we questioned several aspects of our methodology. First, was our irradiation system adequate? To check this, we resynthesized Hopf's precursor of Scheme 1. Upon irradiation in the Rayonet reactor in conditions similar to Hopf, we obtained the same result consisting of the formation of the [5]-ladderane in 85% yield. This confirmed the validity of our preliminary experiments.

Exploring other substrates and conditions

Copper(I) catalysis

We tested the use of the copper(I) $[(CuOTf)_2C_6H_6]$ complex first reported by Kochi, which is known to catalyse [2+2] photocycloadditions[21] thanks to the formation of a very stable photoexcitable complex with the alkene partners. Upon these catalytic conditions, precursor **2** led almost exclusively to the mixture of alkene isomerization products **2-mix** (Scheme 7).



Scheme 7. Copper(I) photocatalysis on **2**

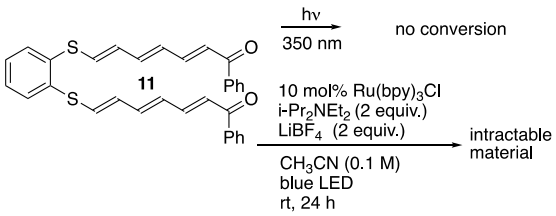
With bis-triene **6** and 8 mol % of $[(CuOTf)_2C_6H_6]$, a complex mixture was obtained which precluded further investigation with this catalytic system.

Photosensitizing

Although our lighting source seemed appropriate, we still wondered if milder conditions would not be more productive. We turned our attention to the use of photosensitizers which could transfer energy and promote the [2+2] photocycloaddition process. Some examples have been reported with the use of Ru(II) [22] and Ir(III)[23] upon visible light (28 W fluorescent bulb) irradiation. At their excited triplet state, these metal complexes are prone to single electron transfer (SET) but also to energy transfer.[22a] We focused on precursor **6** and aimed at the latter phenomenon anticipating no obvious

SET could take place between this substrate and the excited photocatalyst in the absence of sacrificial electron donor or acceptor. Upon visible light irradiation in DMF in the presence of 5 mol% of $Ru(bpy)_3Cl_2.6H_2O$, a mixture of **9-sym** and **9-dis** (44%, 25%) was smoothly obtained. Interestingly, by using blue LEDS, with or without photocatalyst, we also obtained the same mixture. In all cases, no ladderane was observed.

We also considered the possibility to have an internal photosensitizing function on the substrate[24] so we prepared bis-phenylketone **11** from bis-aldehyde **5** using a HWE olefination (54% yield). UV spectrum of **11** showed two big bands at 288 and 388 nm. Its irradiation at 350 nm in acetonitrile and methanol for 15 h did not show any conversion (Scheme 8). Based on the very elegant chemistry developed by Yoon,[25] we also considered using photoredox catalysis to assemble the ladderane framework. Using $Ru(bpy)_3^{2+}$ as photocatalyst and Hunig's base as a reductive quench, a mixture of polyunsaturated adducts suggesting oligomerization processes was observed.

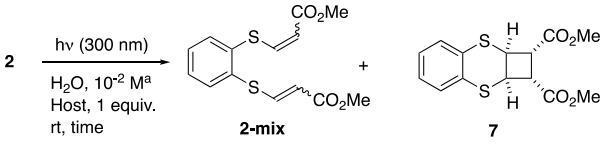


Scheme 8. Irradiation of bis-phenylketone **6**

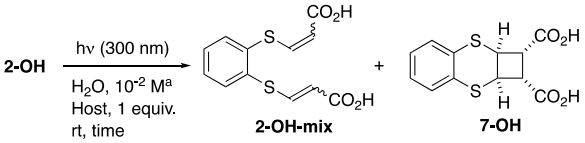
Encapsulation

A number of reports have shown that [2+2] photocycloadditions can be accomplished by using a cyclodextrin or a curcubituryl guest.[26] Using water as solvent, the polyene substrate interacts with the inner hydrophobic wall of the guest. In this confined space, the substrate has restricted motion which favors the ring closure process.

We initially concentrated on the monoene substrate **2** and the corresponding diacid **2-OH** obtained in 93% yield by saponification with LiOH in THF/H_2O. With substrate **2**, a host effect was observed with α-, β- and γ-CDs since higher proportions of products were obtained compared to reactions operated in pure water (Scheme 9). We also found that the β-CD provided the most favorable environment for the [2+2] cycloaddition. After 24 h, product **7** was present as 58% of the reaction mixture; after extended reaction time (93 h), only **7** was observed. The use of the cucurbit[8]uril (CB[8]) host did not bring any improvement and showed that the medium concentration was a key factor since by diluting, the proportion of product **7** could become major. Nevertheless, encapsulation brought significant improvement compared to our initial conditions (see Scheme 3).



none	93 h	**81%** (*E*/*E*: 35%; *E*/*Z*: 30%; *Z*/*Z*: 15%)	**20%**
γ-CD	24 h	65% (*E*/*E*: 17%; *E*/*Z*: 39%; *Z*/*Z*: 9%)	35%
β-CD	24 h	42% (*E*/*E*: 11%; *E*/*Z*: 19%; *Z*/*Z*: 12%)	58%
β-CD	93 h	**0%**	**100%**
α-CD	93 h	69% (*E*/*E*: 21%; *E*/*Z*: 31%; *Z*/*Z*: 17%)	31%
CB[8]	3 h	81% (*E*/*E*: 18%; *E*/*Z*: 31%; *Z*/*Z*: 17%)	19%
CB[8][b]	3 h	18% (*E*/*E*: 8%; *E*/*Z*: 10%)	82%

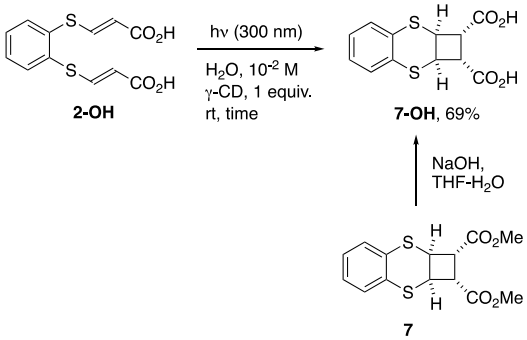


none	24 h	**88%** (*E*/*E*: 35%; *E*/*Z*: 53%)	**12%**
β-CD	24 h	**0%**	**100%**
γ-CD	24 h	**0%**	**100%**
CB[8][b]	24 h	**0%**	**100%**

[a] All reactions run on a (0.08-0.16 mmol) scale. Ratios determined by ^1H NMR after extraction (see SI).
[b] Reaction run at 1.6 10^{-4} M.

Scheme 9. Irradiation of bis-monoenes **2** and **2-OH** in water in the presence of a host

Better results were also obtained from diacid precursor **2-OH**. While, in pure water, very little cyclobutyl **7-OH** was formed, the use of a guest (cyclodextrin or cucurbituril) allowed the exclusive formation of **7-OH**. A preparative experiment was run and led to a 69% yield of isolated product **7-OH**. Diacid **7-OH** was also obtained from the saponification of **7** with NaOH in a mixture of THF and water (Scheme 10). Suitable crystals of **7-OH** for a XRD analysis‡ were obtained which allowed to cross-check the *syn-trans-syn* relative configuration of cyclobutyl derivatives **7-OH** and **7** obtained in all the photochemical experiments (see Schemes 3 and 9).



Scheme 10. Irradiation of **2-OH** and configuration cross-check

Encouraged by these findings, and also because the intermolecular formation of some ladderanes was reported on using CB[8],[27] we examined the longer systems such as bis-diene and bis-triene ester or acid substrates. In most cases, no conversion was observed and suspected that encapsulation was only partial (only one arm of the substrate) or could also involve two hosts.

Conclusions

This study has aimed at defining a new easily introduced and disposable tether between two symmetrical polyenic chains which could lead to ladderanes afer multiple [2+2] cycloadditions. Sulfur based platforms were explored. The corresponding polyenic precursors were readily synthesized and proved to be very stable. Although, their solid state structures did not exhibit a favourable spatial arrangement for intramolecular [2+2] cycloaddition, CCSD(T) calculations suggested a moderate enthalpic cost for the ladderane formation which conducted us to photochemical experiments in various conditions (direct irradiation, photosensitization, encapsulation). No ladderane could be isolated from all these attempts. Instead, all precursors generally provided monocycobutyl photo adducts. Thanks to the use of a host like a cyclodextrin or a cucurbituril in water, encapsulation led to a selective photocycloaddition process yielding a cyclobutyl product as a single diastereomer. The latter could serve after scale-up as a valuable building block for further elaboration on the ladderane route.

Experimental

Computational procedure

The Gaussian set of programs has been used throughout.[28] Geometry optimization and frequencies calculations were done at the B3LYP/6-31G** and mPW1/PW91 levels.[29] In order to get more reliable results, the correlation energies of the extrema were taken into account at the more sophisticated CCSD(T) level.[30]

Experimental: generalities

Unless otherwise noted, reactions were carried out under argon atmosphere. Methanol was dried overnight over freshly activated molecular sieves (4 Å), THF and diethyl ether were distillated from sodium/benzophenone. Other reagents and chemicals were purchased from commercial sources and used as received. Infrared (IR) spectra were recorded on a Bruker Tensor 27 (ATR diamond) spectrophotometer. Melting points were determined on a melting point apparatus SMP3 (Stuart scientific) and are uncorrected. NMR spectra were recorded at room temperature on Bruker AVANCE 600, 400 or 300 spectrometers. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in Hertz (Hz). ^{1}H and ^{13}C NMR assignments were based on COSY, HSQC and HMBC experiments. Abbreviations used for peak multiplicity are: s (singlet); bs (broad singlet); d (doublet); t (triplet); q (quartet); p (quintuplet), m (multiplet) and for assignments: cp (cyclopropyl); cb (cyclobutyl); cpe (cyclopentyl); ch (cyclohexyl). High resolution mass spectrometry was performed on a microTOF (ESI). Thin layer chromatography (TLC) was performed on Merck silica gel 60 F 254 and detected with a UV lamp (λ = 254 nm) and $KMnO_4$ or *p*-anisaldehyde staining. Flash column chromatography was performed on silica Geduran® Si 60 Å (40 – 63 µm).

General procedures

GP1: Diester DIBAL-H reduction and diol MnO_2 oxidation

To a stirred solution of diester (1 equiv) in DCM (0.1 M) at - 78 °C was added DIBAL-H (1 M in DCM, 8 equiv) dropwise and the reaction mixture was stirred at 0 °C for 2 h. The reaction was quenched with saturated Rochelle's salt solution and extracted with DCM. The combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the corresponding diol. To a stirred solution of this diol (1 equiv) in DCM (0.05 M) at rt was added MnO_2 (38 equiv) portionwise and the mixture was stirred at rt for 12 h. The reaction mixture was filtered on a Celite® pad, washed with DCM and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/Et_2O as eluent (60/40) afforded the corresponding dialdehyde.

GP2: Horner-Wadsworth-Emmons reaction

To a stirred solution of NaH (60 % in oil, 4.15 equiv) in THF (0.25 M) at 0 °C was added triethyl phosphonoacetate (4 equiv) dropwise and the mixture was stirred at rt for 45 min. The dialdehyde (1 equiv) in THF (0.2 M) was then added dropwise at 0 °C. The reaction mixture was stirred at rt for 12 h then quenched with saturated NH_4Cl solution and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel using petroleum ether/EtOAc (90/10) as eluent afforded the corresponding diester.

Dimethyl 3,3'-(1,2-phenylenebis(sulfanediyl))(2E,2'E)-diacrylate (2).

To a stirred solution of **1** (1.5 g, 10.5 mmol, 1 equiv) in THF (90 mL) at - 78 °C under argon was added *n*BuLi (11.4 mL, 1.95 M in hexanes, 2.1 equiv) dropwise. The yellow solution was stirred at - 78 °C for 30 min before being added dropwise to a solution of Methyl (E)-3-iodoacrylate (4.92 g, 23.2 mmol, 2.2 equiv) in THF (30 mL). The reaction mixture was stirred at - 78 °C for 2 h then quenched with water (30 mL), extracted with EtOAc, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the desired product (3.36 g, quant) as a brown oil. R_f 0.30 (PE-EtOAc = 90/10); (ATR) ν 2994, 1710, 1582, 1432, 1299, 1260, 1235, 1156, 1038, 944, 828, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 15.1 Hz, 2H), 7.58 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.44 (dd, *J* = 5.8, 3.4 Hz, 2H), 5.68 (d, *J* = 15.1 Hz, 2H), 3.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4 (2C), 144.9 (2CH), 134.5 (2C), 134.2 (2CH), 130.4 (2CH), 116.9 (2CH), 51.7 ($2CH_3$); HRMS (ESI) calcd for $C_{14}H_{14}O_4S_2Na$ ([M+Na]$^+$) 333.0226 found 333.0221.

(2E,2'E)-3,3'-(1,2-phenylenebis(sulfanediyl))diacrylic acid (2-OH)

To a stirred solution of **2** (0.11 g, 0.36 mmol, 1 equiv) in a mixture of THF/H_2O 3:1 (6.7 mL) under argon was added LiOH (0.043 g, 1.79 mmol, 5 equiv) at rt. The reaction mixture was

stirred at 50 °C for 12 h without light. The reaction mixture was diluted in water and extracted with DCM. Aqueous layer was acidified to pH 2 and cooled to 0 °C. Precipitate was filtered to afford the desired product **2-OH** (0.094 g, 93% yield) as white solid. Mp 212 °C; (ATR) ν 3017, 2822, 1667, 1579, 1416, 1305, 1264, 1190, 929, 847, 745, 685; ^{1}H NMR (400 MHz, MeOD) δ 7.77 (d, *J* = 15.1 Hz, 2H), 7.69 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.56 (dd, *J* = 5.8, 3.4 Hz, 2H), 5.59 (d, *J* = 15.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1 (2C), 146.6 (2CH), 135.6 (2C), 135.5 (2CH), 131.8 (2CH), 118.1 (2CH); HRMS (ESI) calcd for $C_{12}H_9O_4S_2$ ([M-H]$^-$) 280.9948 found 280.9948.

(2*E*,2'*E*)-3,3'-(benzene-1,2-diyldisulfanediyl)bisprop-2-enal (3)

Prepared according to GP1. Scale **2** (2.4 g, 7.73 mmol); Yield 1.39 g (72%); Orange solid; Mp 106 °C; R_f 0.15 (pentane-Et_2O = 60/40); (ATR) ν 3020, 2845, 1650, 1545, 1443, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (d, *J* = 7.6 Hz, 2H), 7.67 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.60 (d, *J* = 15.0 Hz , 2H), 7.54 (dd, *J* = 5.8, 3.4 Hz, 2H), 5.93 (dd, *J* = 15.1, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.5 (2CH), 154.1 (2CH), 134.7 (2CH), 133.6 (2C), 131.0 (2CH), 127.7 (2CH); HRMS (ESI) calcd for $C_{12}H_{10}O_2S_2Na$ ([M+Na]$^+$) 273.0014 found 273.0017.

Diethyl (2*E*,4*E*,2'*E*,4'*E*)-5,5'-(benzene-1,2-diyldisulfanediyl) bispenta-2,4-dienoate (4)

Prepared according to GP2. Scale **3** (0.62 g, 2.46 mmol); Yield 0.84 g (88%); Yellow solid; Mp 97 °C; R_f 0.18 (PE-EtOAc = 90/10); (ATR) ν 2980, 2359, 1700, 1618, 1557, 1464, 1364, 1265, 1225, 1135, 984, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.35 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.28 (dd, *J* = 15.3, 11.3 Hz, 2H), 6.78 (d, *J* = 14.8 Hz, 2H), 6.29 (dd, *J* = 14.8, 11.2 Hz, 2H), 5.76 (d, *J* = 15.3 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 4H), 1.28 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7 (2C), 142.3 (2CH), 135.9 (2CH), 134.9 (2C), 131.9 (2CH), 128.9 (2CH), 127.9 (2CH), 119.4 (2CH), 60.1 ($2CH_2$), 14.2 ($2CH_3$); HRMS (ESI) calcd for $C_{20}H_{22}O_4S_2Na$ ([M+Na]$^+$) 413.0852 found 413.0862.

(2*E*,4*E*,2'*E*,4'*E*)-5,5'-(benzene-1,2-diyldisulfanediyl)bispenta-2,4-dienal (5)

Prepared according to GP1. Scale **4** (1.12 g, 2.91 mmol); Yield 0.69 g (79%); Yellow/orange solid; Mp 139 °C; R_f 0.26 (PE-EtOAc = 60/40); (ATR) ν 2956, 1663, 1608, 1447, 1112, 981, 759; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, *J* = 7.9 Hz, 2H), 7.55 (dd, *J* = 5.8, 3.5 Hz, 2H), 7.43 (dd, *J* = 5.9, 3.4 Hz, 2H), 7.09 (ddd, *J* = 15.2, 11.1, 0.7 Hz, 2H), 6.97 (dt, *J* = 14.8, 0.7 Hz, 2H), 6.35 (ddd, *J* = 14.8, 11.1, 0.7 Hz, 2H), 6.02 (ddt, *J* = 15.2, 7.9, 0.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4 (2CH), 149.7 (2CH), 139.3 (2CH), 134.8 (2C), 133.1 (2CH), 129.8 (2CH), 129.7 (2CH), 126.9 (2CH); HRMS (ESI) calcd for $C_{16}H_{14}O_2S_2Na$ ([M+Na]$^+$) 325.0327 found 325.0331.

Diethyl 7,7'-(1,2phenylenebis(sulfanediyl)) (2E,2'E,4E,4'E,6E,6'E)-bis(hepta-2,4,6-trienoate) (6)

Prepared according to GP2. Scale **5** (0.36 g, 1.20 mmol); Yield 0.36 g (68%); Bright yellow solid; Purification by recrystallization in EtOH; Mp 124 °C; R_f 0.25 (PE-EtOAc = 90/10); (ATR) ν 2976, 1737, 1621, 1597, 1547, 1444, 1363, 1331, 1249, 1207, 1171, 1133, 1037, 1005, 967, 891, 835, 740; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.31 (dd, *J* = 5.8, 3.4 Hz, 2H), 7.27 (dd, *J* = 15.6, 11.2 Hz, 2H), 6.56 (dd, *J* = 14.7, 10.8 Hz, 2H), 6.56 (d, *J* = 14.8 Hz, 2H) 6.32 (dd, *J* = 14.9, 10.9 Hz, 2H), 6.22 (dd, *J* = 14.8, 11.4 Hz, 2H), 5.86 (d, *J* = 15.2 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 4H), 1.29 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (2C), 144.2 (2CH), 138.6 (2CH), 135.6 (2C), 131.8 (2CH), 131.3 (2CH), 130.6 (2CH), 129.1 (2CH), 128.7 (2CH), 121.3 (2CH), 60.4 ($2CH_2$), 14.5 ($2CH_3$); HRMS (ESI) calcd for $C_{24}H_{26}O_4S_2Na$ ([M+Na]$^+$) 465.1165 found 465.1181.

Diethyl 7,7'-(1,2-phenylenedisulfonyl)(2E,2'E,4E,4'E,6E,6'E)-bis(hepta-2,4,6-trienoate) (6-O)

To a stirred solution of sulfide **6** (1 equiv, 0.10 g, 0.22 mmol) in DCM (0.03 M) at 0 °C was added *m*CPBA (70%, 4.5 equiv) portion wise and the mixture was stirred at rt for 12 h. The reaction mixture was quenched at 0 °C by saturated $Na_2S_2O_3$ and Na_2CO_3 solutions, and extracted with DCM. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the corresponding sulfone **6-O** 0.11 g (quant.); White solid; Mp 149 °C; R_f 0.66 (PE-EtOAc = 50/50); (ATR) ν 2920, 2851, 2361, 2341, 1712, 1624, 1607, 1330, 1313, 1249, 1202, 1148, 1129, 1001, 848, 666, 598; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 5.9, 3.4 Hz, 2H), 7.74 (dd, *J* = 5.9, 3.4 Hz, 2H), 7.33-7.19 (m, 6H), 6.67 (dd, *J* = 14.9, 11.0 Hz, 2H), 6.56 (dd, *J* = 15.1, 9.1 Hz, 2H), 6.01 (d, *J* = 15.3 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 4H), 1.23 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (2C), 142.6 (2CH), 141.8 (2CH), 140.4 (2C), 139.8 (2CH), 134.3 (2CH), 134.2 (2CH), 133.2 (2CH), 132.0 (2CH), 126.3 (2CH), 60.7 ($2CH_2$), 14.3 ($2CH_3$); HRMS (ESI) calcd for $C_{24}H_{26}O_8S_2Na$ ([M+Na]$^+$) 529.0961 found 529.0982.

(2E,2'E,4E,4'E,6E,6'E)-7,7'-(1,2-phenylenebis(sulfanediyl))bis (1-phenylhepta-2,4,6-trien-1-one) (6-COPh)

Prepared according to GP3 using diethyl (2-oxo-2-phenylethyl)phosphonate. Purification by recrystallization in EtOH. Scale: **5** (0.10 g, 0.33 mmol); Yield: 0.042 g (54%); Orange solid; Mp 164 °C; (ATR) ν 1660, 1586, 1571, 1545, 1444, 1342, 1259, 1185, 1145, 1016, 994, 842, 767, 743, 699, 664**;** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.92 (m, 4H), 7.57-7.53 (m, 2H), 7.49-7.48 (m, 2H), 7.47-7.46 (m, 4H), 7.45-7.44 (m, 2H), 7.34 (dd, *J* = 5.8, 3.4 Hz, 2H), 6.98 (d, *J* = 14.8 Hz, 2H), 6.70 (dd, *J* = 14.4, 6.9 Hz, 2H), 6.64 (d, *J* = 14.8 Hz, 2H), 6.42-6.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4 (2C), 144.6 (2CH), 140.2 (2CH), 138.4 (2C), 135.6 (2C), 132.8 (2CH), 132.2 (2CH), 132.0 (2CH), 130.6 (2CH), 129.8 (2CH), 128.9 (2CH), 128.7 (4CH), 128.5 (4CH), 125.3 (2CH); HRMS (ESI) calcd for $C_{32}H_{26}NaO_2S_2$ ([M+Na]$^+$) 529.1266 found 529.1274

[2+2] photocycloaddition of 2

2 (1 equiv) was dissolved in MeCN (10^{-2} M). The bright yellow solution was degassed for 1 h then irradiated at rt under argon in the photoreactor Rayonet (λ = 300 nm, 16 light bulbs) for 1 h and concentrated under reduced pressure to afford a mixture of compounds **2-mix** and **7**. Ratio was determined by ^{1}H NMR on the crude.

^{1}H NMR (300 MHz, $CDCl_3$) δ Characteristic peaks

2-E/E 7.70 (d, *J* = 15.1 Hz, 2H), 5.67 (d, *J* = 15.1 Hz, 2H)

2-Z/Z 7.11 (d, *J* = 10.0 Hz, 2H), 5.96 (d, *J* = 10.0 Hz, 2H)

2-E/Z 7.72 (d, *J* = 15.0 Hz, 1H), 7.12 (d, *J* = 10.1 Hz, 1H), 5.97 (d, *J* = 10.1 Hz, 2H), 5.61 (d, *J* = 15.0 Hz, 1H)

7 4.54-4.52 (app-d, *J* = 5.1 Hz, 2H), 3.07-3.05 (app-d, *J* = 5.1 Hz, 2H)

[2+2] photocycloaddition in cyclodextrine cavity

A stirred solution of acyclic compound (1 equiv) and CD (1 equiv) in distilled water (10^{-2} M) was degassed under argon for 30 min. The suspension was irradiated while stirring in a photoreactor Rayonet (λ = 300 or 350 nm, 16 light bulbs) for a reaction time at rt under argon. The suspension was then extracted with DCM and EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the corresponding cyclobutane compound.

Dimethyl (1R,2S,2aS,8aR)-1,2,2a,8a-tetrahydrobenzo[b]cyclobuta[e][1,4]dithiine-1,2-dicarboxylate (7)

Prepared using β-CD. Yellow paste. R_f 0.22 (PE-EtOAc: 90/10); (ATR) ν 2950, 2851, 1731, 1434, 1330, 1161, 1083, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.28 (dd, *J* = 5.7, 3.4 Hz, 2H), 4.55-4.52 (app-d, *J* = 5.1 Hz, 2H), 3.68 (s, 6H), 3.07-3.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (2C), 135.6 (2C), 133.1 (2CH), 128.2 (2CH), 52.5 ($2CH_3$), 47.9 (2CH), 46.9 (2CH); HRMS (ESI) calcd for $C_{14}H_{14}O_4S_2Na$ ($[M+Na]^+$) 333.0226 found 333.0241.

(1R,2S,2aS,8aR)-1,2,2a,8a-tetrahydrobenzo[b]cyclobuta[e][1,4]dithiine-1,2-dicarboxylic acid (7-OH)

Prepared using γ-CD. Reaction time: 24 h. Scale: **2-OH** (0.016 g, 0.057 mmol); Yield: 0.011 g (69%); White solid; Mp 205 °C; (ATR) ν 3105, 2924, 1694, 1422, 1246, 1229, 758; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.32 (dd, *J* = 5.8, 3.4 Hz, 2H), 4.49-4.447 (m, 2H), 2.97-2.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1 (2C), 137.1 (2C), 133.8 (2CH), 129.1 (2CH), 49.0 (2CH), 48.5 (2CH); HRMS (ESI) calcd for $C_{12}H_{10}O_4S_2Na$ ($[M+Na]^+$) 304.9913 found 304.9918.

[2+2] photocycloaddition of 4

4 (0.27 g, 0.69 mmol, 1 equiv) was dissolved in MeCN (69 mL, 10^{-2} M). The yellow solution was degassed for 1 h then irradiated at rt under argon in the photoreactor Rayonet (λ = 300 nm, 16 light bulbs) for 1 h and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/EtOAc (94/6 to 50/50) as eluent afforded the symmetrical isomer product **8-sym** (0.084 g, 31% yield) as a yellow oil and the non-symmetrical isomer **8-dis** (0.057 g, 21% yield) as a colorless oil.

Diethyl 3,3'-(1,2,2a,8a-tetrahydrobenzo[b]cyclobuta[e][1,4]dithiine-1,2-diyl)(2E,2'E)-diacrylate (8-sym)

R_f 0.18 (pentane-EtOAc = 95/5); (ATR) ν 2980, 1713, 1649, 1446, 1367, 1266, 1157, 1095, 1033, 981, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.27 (dd, *J* = 5.6, 3.6 Hz, 2H), 6.86 (ddd, *J* = 15.6, 5.7, 2.5 Hz, 2H), 5.79 (d, *J* = 15.4, 0.8 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 4H), 4.14-4.12 (app-d, *J* = 5.0 Hz, 2H), 3.08-3.04 (m, 2H) 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (2C), 144.2 (2CH), 135.7 (2C), 132.8 (2CH), 128.0 (2CH), 123.6 (2CH), 60.7 ($2CH_2$), 49.8 (2CH), 47.6 (2CH), 14.4 ($2CH_3$); HRMS (ESI) calcd for $C_{20}H_{22}O_4S_2Na$ ($[M+Na]^+$) 413.0852 found 413.0853.

Diethyl 3,3'-((1R,2R)-1,2,2a,8a-tetrahydrobenzo[b]cyclobuta[e][1,4]dithiine-1,2-diyl)(2E,2'E)-diacrylate (8-dis)

R_f 0.09 (pentane-EtOAc = 95/5); (ATR) ν 2980, 1711, 1650, 1447, 1367, 1267, 1156, 1036, 977, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 5.9, 3.3 Hz, 1H), 7.45 (dd, *J* = 5.9, 3.2 Hz, 1H), 7.25 (dd, *J* = 5.8, 3.4 Hz, 2H), 6.90 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.88 (dd, *J* = 15.7, 9.8 Hz, 1H), 5.72 (dd, *J* = 15.6, 1.5 Hz, 1H), 5.59 (dd, *J* = 15.7, 1.3 Hz, 1H), 4.35 (ddd, *J* = 9.8, 8.4, 1.2 Hz, 1H), 4.21-4.14 (m, 4H), 4.08 (dd, *J* = 9.8, 8.9 Hz, 1H), 3.33 (tdd, *J* = 8.7, 7.5, 1.3 Hz, 1H), 2.68 (tdt, *J* = 9.2, 6.8, 1.4 Hz, 1H), 1.30-1.25 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1 (1C), 165.9 (1C), 145.7 (1CH), 144.8 (1CH), 136.1 (1C), 135.7 (1C), 133.1 (1CH), 132.1 (1CH), 128.3 (1CH), 127.9 (1CH), 123.0 (1CH), 122.3 (1CH), 60.7 ($1CH_2$), 60.6 ($1CH_2$), 51.5 (1CH), 48.0 (1CH), 47.6 (1CH), 45.6 (1CH), 14.4 ($1CH_3$), 14.2 ($1CH_3$); HRMS (ESI) calcd for $C_{20}H_{22}O_4S_2Na$ ($[M+Na]^+$) 413.0852 found 413.0852.

[2+2] photocycloaddition of 6

6 (0.22 g, 0.51 mmol, 1 equiv) was dissolved in MeCN (337 mL, $1{,}5.10^{-3}$ M). The yellow solution was degassed for 1 h then irradiated at rt under argon in the photoreactor Rayonet (λ = 350 nm, 16 light bulbs) for 1 h and concentrated under reduced pressure. Purification by column chromatography on silica gel using pentane/EtOAc (93/7 to 50/50) as eluent afforded the symmetrical isomer product **9-sym** (0.10 g, 45% yield) as a yellow oil and the non-symmetrical isomer **9-dis** (0.056 g, 25% yield) as a colorless oil.

Diethyl 5,5'-(1,2,2a,8a-tetrahydrobenzo[b]cyclobuta[e][1,4]dithiine-1,2-diyl)(2E,2'E,4E,4'E)-bis(penta-2,4-dienoate) (9-sym)

R_f 0.30 (pentane-EtOAc = 90/10); (ATR) ν 2955, 2870, 1702, 1639, 1445, 1367, 1301, 1238, 1129, 1031, 996, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 5.7, 3.4 Hz, 2H), 7.28 (dd, *J* = 5.8, 3.5 Hz, 2H), 7.19 (dd, *J* = 15.4, 10.5 Hz, 2H), 6.13 (dd, *J* = 15.1, 10.6 Hz, 2H), 6.06-6.00 (m, 2H) 5.83 (d, *J* = 15.3 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 4H), 4.09-4.08 (app-d, *J* = 4.9 Hz, 2H), 3.05-3.00 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9 (2C), 143.5 (2CH), 139.7 (2CH), 136.0 (2C), 132.8 (2CH), 130.3 (2CH), 127.9 (2CH), 121.7 (2CH), 60.5 ($2CH_2$), 50.2 (2CH), 48.9 (2CH), 14.4 ($2CH_3$); HRMS (ESI) calcd for $C_{24}H_{26}O_4S_2Na$ ($[M+Na]^+$) 465.1165 found 465.1182.

Diethyl 5,5'-((1R,2R)-1,2,2a,8a-tetrahydrobenzo[b]cyclobuta[e][1,4]dithiine-1,2-diyl)(2E,2'E,4E,4'E)-bis(penta-2,4-dienoate) (9-dis)

R_f 0.24 (pentane-EtOAc = 90/10); (ATR) ν 2928, 1703, 1637, 1615, 1446, 1366, 1300, 1236, 1130, 1033, 995, 749; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.50 (m, 1H), 7.46-7.44 (m, 1H), 7.26-7.23 (m, 2H), 7.21 -7.18 (m, 1H), 7.17-7.14 (m, 1H), 6.09-6.04 (m, 3H), 5.95 (dd, *J* = 15.3, 10.6 Hz, 1H), 5.81 (d, *J* = 15.2 Hz, 1H), 5.76 (d, *J* = 15.4 Hz, 1H), 4.30 (ddd, *J* = 9.7, 8.4, 1.2 Hz, 1H), 4.22-4.16 (m, 4H), 4.01 (dd, *J* = 9.7, 8.9 Hz, 1H), 3.23 (q, *J* = 8.3 Hz, 1H), 2.62 (td, *J* = 9.1, 4.6 Hz, 1H), 1.31-1.25 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (1C), 166.9 (1C), 143.8 (1CH), 143.6 (1CH), 141.1 (1CH), 139.9 (1CH), 136.4 (1C), 135.9 (1C), 133.0 (1CH), 131.8 (1CH), 130.0 (1CH), 129.2 (1CH), 128.0 (1CH), 127.7 (1CH), 121.6 (1CH), 121.4 (1CH), 60.5 ($1CH_2$), 60.5 ($1CH_2$), 52.0 (1CH), 49.1 (1CH), 48.1 (1CH), 47.1 (1CH), 14.4 ($1CH_3$), 14.4 ($1CH_3$); HRMS (ESI) calcd for $C_{24}H_{26}O_4S_2Na$ ($[M+Na]^+$) 465.1165 found 465.1156.

[2+2] photocycloaddition of 6-O

6-O (0.10 g, 0.20 mmol, 1 equiv) was dissolved in MeCN (50 mL, 4.10^{-3} M). The white solution was degassed for 1 h then irradiated at rt under argon in the photoreactor Rayonet (λ = 300 nm, 16 light bulbs) for 1 h and concentrated under reduced

pressure. Purification by column chromatography on silica gel using pentane/EtOAc (75/25 to 50/50) as eluent afforded the classical symmetrical isomer product **9-O-sym** (0.045 g, 45% yield) as a white paste, the other symmetrical isomer **9-O-sym'** (0.010g, 10% yield) as a white paste and the macrocycle **10** (0.025 g, 25% yield) as a bright yellow solid.

Diethyl 5,5'-(3,3,8,8-tetraoxido-1,2,2a,8a-tetrahydrobenzo [b]cyclobuta[e][1,4]dithiine-1,2-diyl)(2E,2'E,4E,4'E)-bis(penta-2,4-dienoate) (9-O-sym)

R_f 0.13 (pentane-EtOAc = 70/30); (ATR) ν 2920, 2359, 1716, 1701, 1334, 1263, 1146, 1125, 1028, 772; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 5.8, 3.3 Hz, 2H), 7.93 (dd, *J* = 5.8, 3.3 Hz, 2H), 7.19 (dd, *J* = 15.4, 10.9 Hz, 2H), 6.33 (dd, *J* = 15.3, 10.9 Hz, 2H), 6.03-5.97 (m, 2H), 5.91 (d, *J* = 15.4 Hz, 2H), 4.50-4.48 (app-d, *J* = 5.4 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 4H), 3.79-3.73 (m, 2H) 1.29 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6 (2C), 142.2 (2CH), 137.3 (2C), 135.0 (2CH), 134.7 (2CH), 132.7 (2CH), 127.7 (2CH), 123.6 (2CH), 61.4 (2CH), 60.7 ($2CH_2$), 41.5 (2CH), 14.4 ($2CH_3$); HRMS (ESI) calcd for $C_{24}H_{26}O_8S_2Na$ ([M+Na]$^+$) 529.0961 found 529.0982.

Diethyl 5,5'-((1R,2R)-3,3,8,8-tetraoxido-1,2,2a,8a-tetrahydro benzo[b]cyclobuta[e][1,4]dithiine-1,2-diyl)(2E,2'E,4E,4'E)-bis (penta-2,4-dienoate) (9-O-sym')

Fully characterized as the paranitrophenyl ester derivative

(2E,2'E,4E,4'E)-(3,3,8,8-tetraoxido-1,2,2a,8a-tetrahydro benzo[b]cyclobuta[e][1,4]dithiine-1,2-diyl)bis(penta-2,4-diene-5,1-diyl) bis(4-nitrobenzoate) (9-O-sym'-nitroester)

Mp 140-145 °C (dec); R_f 0.55 (pentane-EtOAc = 65/35); (ATR) ν 2924, 2854, 1721, 1607, 1525, 1347, 1320, 1269, 1148, 1103, 1014, 991, 873, 719; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-8.27 (m, 4H), 8.23-8.19 (m, 4H), 8.02 (dd, *J* = 6.0, 3.3 Hz, 2H), 7.83 (dd, *J* = 5.9, 3.3 Hz, 2H), 6.41-6.31 (m, 4H), 5.97 (dt, *J* = 14.3, 6.3 Hz, 2H), 5.90-5.84 (m, 2H), 4.91 (dd, *J* = 6.3, 1.2 Hz, 4H), 4.32-4.30 (app-d, *J* = 9.1 Hz, 2H), 3.72-3.67 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5 (2C), 150.8 (2C), 138.6 (2C), 135.5 (2C), 134.2 (2CH), 133.2 (2CH), 133.0 (2CH), 130.9 (4CH), 129.7 (2CH), 128.6 (2CH), 125.4 (2CH), 123.7 (4C), 65.7 ($2CH_2$), 59.0 (2CH), 45.8 (2CH); HRMS (ESI) calcd for $C_{34}H_{28}N_2O_{12}S_2$ ([M+Na]$^+$) 743.0976 found 743.0973.

Diethyl (5aR,6E,8E,10R,11R,12E,14E,15aR)-5a,10,11,15a-tetra hydrobenzo[b]cyclododeca[e][1,4]dithiine-10,11-dicarboxyla te 5,5,16,16-tetraoxide (10)

Mp 97 °C; R_f 0.35 (pentane-EtOAc = 70/30); (ATR) ν 2922, 2360, 1714, 1644, 1317, 1147, 1133, 1108, 1028, 994, 688, 620; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 5.9, 3.3 Hz, 2H), 7.86 (dd, *J* = 6.0, 3.3 Hz, 2H), 6.21 (dd, *J* = 15.7, 10.4 Hz, 2H), 5.92 (dd, *J* = 15.7, 10.4 Hz, 2H), 5.45-5.39 (m, 2H), 5.38-5.32 (m, 2H), 4.69 (dd, *J* = 7.1, 2.8 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 4H), 3.46 (dd, *J* = 7.5, 2.9 Hz, 2H), 1.31-1.27 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5 (2C), 143.5 (2CH), 137.2 (2CH), 137.2 (2C), 134.4 (2CH), 132.3 (2CH), 125.3 (2CH), 117.9 (2CH), 68.6 (2CH), 61.7 ($2CH_2$), 53.8 (2CH), 14.3 ($2CH_3$); HRMS (ESI) calcd for $C_{24}H_{26}O_8S_2Na$ ([M+Na]$^+$) 529.0961 found 529.0975.

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Notes and references

‡ CCDC **4**: 1535549, CCDC **5**: 1535551, CCDC **6**: 1535552, CCDC **6-O**: 1535553, **7-OH**: 1535554, **10**: 1535555.

[#]The quantum yield of the reaction of **2** was determined by chemical actinometry and was found to be 0.3%, much lower than for the corresponding diene and triene systems **4** and **6** which showed quantum yields above 50%. The actinometer used was Hopf's monoene derivative **2** from: H. Greiving, H. Hopf, P. G. Jones, P. Bubenitschek, J.-P. Desvergne, H. Bouas-Laurent, Liebigs Ann. 1995, 1949.

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