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Stereoselective Synthesis of Dithia[3.3]cyclophane *S*,*S*′-Dioxides with Planar and Central Chirality

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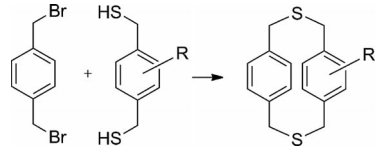
5,8-Dimethyl-1,12-dimethylene-2,11-dithia[3.3]cyclophane 2,11-dioxides with planar and central chirality were synthesized in high yields, starting from 2,5-dimethyl-1,4-benzenedimethanethiol, through the formation of suitable transient sulfenic functions that add to the triple bonds of disubstituted benzenes. Experimental observations allowed mechanistic and stereochemical insights into the key step of the synthetic pathway, and NMR experiments were diagnostic for the structure assignments of the cage-like compounds. The stereochemical characteristics of the new dithiacyclophane *S*,*S*′-dioxides synthesized may be applicable in the field of organocatalysis.

Introduction

Planar chirality plays a main role in determining the properties and behavior of cyclophanes (CPs) as chiral reagents, backbones of organocatalysts, and a source of functional materials.[1] Therefore, an increasing number of investigations have been conducted on the relationship between structure and chemical properties of these molecules, as examples of compounds without stereogenic centers but comprising well-defined stereoelectronic characteristics.[2] A planar and centrally chiral bicyclic 1,2,4-triazolium salt, synthesized from [2.2]paracyclophanes, has been shown to be an efficient catalyst for the asymmetric β-borylation of acyclic enones, producing β-boryl ketones in high yields and enantioselectivities.[3] A planar chiral bis(thiourea) catalyst, based on the pseudo-*ortho*-substituted [2.2]paracyclophane skeleton, has been synthesized and found to catalyze a highly enantioselective Henry reaction, as a result of its asymmetric environment.[4] Worthy of note is the work conducted on planar chiral ansa-bridge cyclophanes used to mimic the stereospecificity of hydrogen transfer in biological asymmetric reduction with NADH.[5]

A number of synthetic strategies have been developed to obtain planar chiral cyclophanes and heteracyclophanes. In particular, a general, well-assessed route to thiacyclophanes is represented by the use, under dilution conditions, of suitably functionalized cyclization partners, for instance bis(bromomethyl)benzene and variously substituted benzenedimethanethiols, as illustrated in Scheme 1.[2] The planar chirality is generated by the introduction of at least one substituent on one of the aromatic rings, so enhancing the conformational barrier related to complete rotation of the substituted ring.[2d]



Scheme 1. Synthetic approach to dithia[3.3]paracyclophanes with planar chirality.

Recently, Tanaka and co-workers[6] reported an interesting example of rhodium-catalyzed enantioselective synthesis of planar chiral dithiacyclophanes with up to 50% yield. Among the limited number of approaches achieved by intramolecular cyclization of functionalized disubstituted aromatics, the synthesis of a series of ansa-bridge [*n*]paracyclophanediols (n = 8–12) has been reported by samarium-catalyzed pinacol coupling, with yields ranging from 14 to 64%.[7] Previously, we disclosed a new synthetic route to a series of dithiacyclophane *S*,*S*′-dioxides and their tris-bridged analogues, through the generation of suitable transient sulfenic acids in situ and their completely regioselec-

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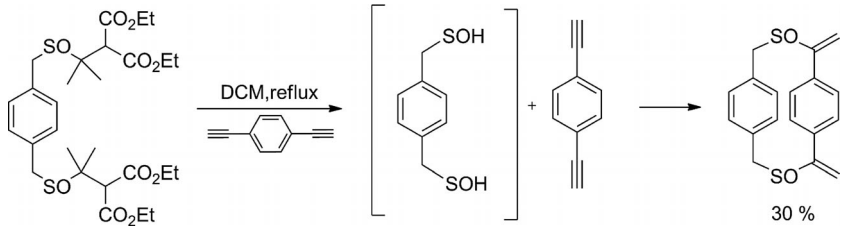
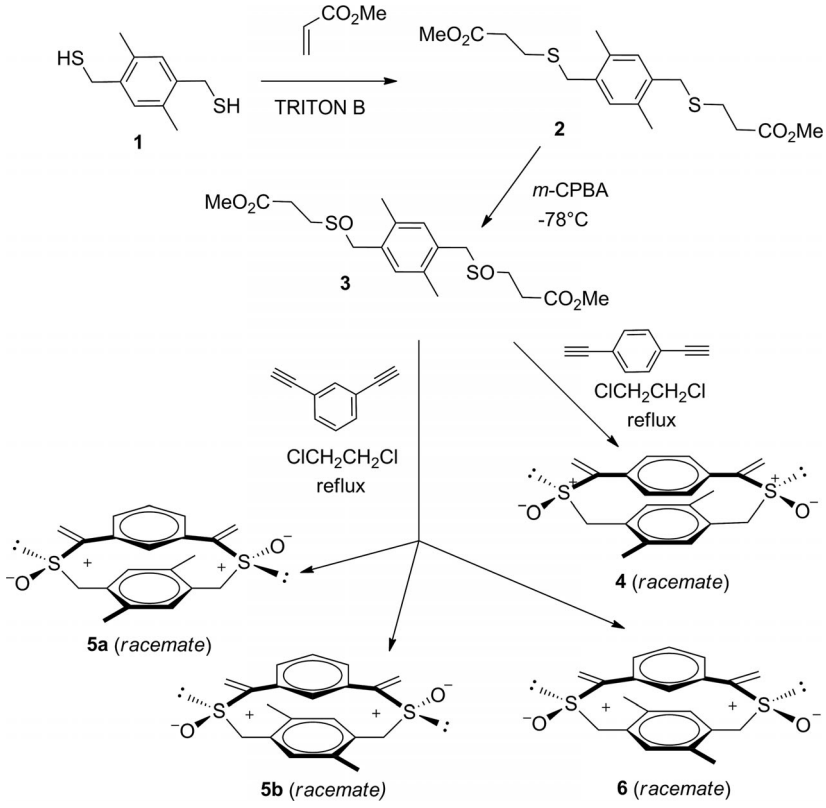


Scheme 2. A typical synthetic approach to dithia[3.3]paracyclophane *S*,*S*′-dioxides via transient sulfenic acids.



Scheme 3. Synthetic procedure to dithiacyclophane *S*,*S*′-dioxides **4**–**6** with planar and central chirality.

tive and stereocontrolled addition onto the triple bonds of di- and tri-ethynylbenzenes (Scheme 2).[8]

Herein, we describe a consistent approach to new dithiacyclophane *S*,*S*′-dioxides showing both planar and central chirality. The cage skeleton of dithiacyclophanes **4**–**6** (Scheme 3) with the coexistence of two different sources of chirality – chiral sulfinyl groups and planar chirality – obtained through the introduction of two methyl groups on both sides of one of the rings, to provide an equal steric bias, represents a model system to enhance the structure/chirality relationship of these molecules. The synthetic methodology adopted for their preparation employs a new sulfenic acid precursor **3** and guarantees higher yields with respect to published procedures,[2,6–8] allowing mechanistic insights into the sulfenic acid chemistry that can offer stimulating stereochemical applications.

Results and Discussion

Our synthetic approach to dithiacyclophane *S*,*S*′-dioxides **4**–**6**, with planar and central chirality, is reported in Scheme 3.

2,5-Dimethyl-1,4-benzenedimethanethiol (**1**), already possessing the elements required for induction of planar chirality in the cage-like compounds, was applied in the nucleophilic addition of the two sulfur functions onto the terminal electrophilic carbon atom of methyl acrylate, to obtain disulfide **2**, which, in turn, underwent controlled oxidation to disulfoxide **3**. Thermolysis of the latter generates transient sulfenic acid functionalities that can add to the triple bonds of *meta*- and *para*-diethynylbenzene[9] in a completely regio- and stereocontrolled process. The electronic nature of the substituents, located β to the sulfur

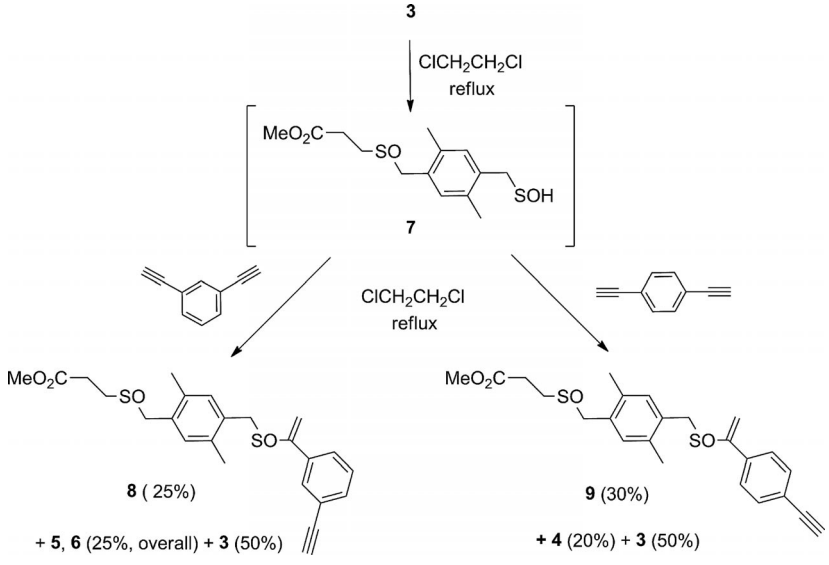
atoms, is crucial for the generation of the bis-sulfenic acid from disulfoxide **3**. Methyl acrylate was recognized as the best partner[10] of the nucleophilic disulfide addition in the presence of Triton B (benzyltrimethylammonium hydroxide).[11] Disulfoxide **3** generates the sulfenic functions at 83 °C in 1,2-dichloroethane (DCE), has a good shelf-life, and can be easily handled. Furthermore, yields of the new dithiacyclophane *S*,*S*′-dioxides **4**–**6** range from 70 to 82%, thus representing a significant improvement with respect to previously reported analogues[8] (see for example Scheme 2) and is an example of a generally applicable synthetic approach to this class of molecule. Dithiacyclophane *S*,*S*′-dioxides **4**–**6** were obtained under dilution conditions, with a 1:1 ratio between the sulfenic acid precursor **3** and diethynylbenzene, and could be easily purified and separated by column chromatography as racemic mixtures. It should be noted that no traces of sulfenic acid self-condensation products were isolated.[12]

The appearance and disappearance of spots on the TLC plates before completion (almost four days) of the reactions of disulfoxide **3** with *meta*- or *para*-diethynylbenzene suggested to us the possible stepwise formation of the transient sulfenic functions and, therefore, a parallel or alternative synthetic pathway compared to that outlined in Scheme 2 for which the generation of 1,4-benzenedimethanesulfenic acid is shown.[8] To confirm this, the final step of the synthetic procedure was stopped after 24 h; the results are shown in Scheme 4.

Compounds **8** and **9**, still possessing a 2-(methoxycarbonyl)ethylsulfinyl function on one of the two arms, were isolated in similar yields as diastereomeric mixtures, together with the corresponding dithiacyclophane *S*,*S*′-dioxides **5**, **6** or **4** and unreacted disulfoxide **3**. Furthermore, the two open-chain intermediates **8** and **9** were subjected, separately, to a new thermolysis in DCE, under the dilution conditions used before; in this case, within 4 h dithiacyclophane *S*,*S*′-dioxides **4**–**6** were obtained with the same stereochemical outcomes observed above. Compounds **4**–**6** were obtained with long reaction times but without decomposition products. We suggest that, under these conditions, the slow formation of one sulfenic function from disulfoxide **3** is accomplished when sulfenic acid precursor and unsaturated acceptor are near in space. It is immediately followed by sulfenic acid **7**/triple bond addition, which appears to be the fastest process. This pathway gives rise to the formation of intermediates **8** and **9**, without appreciable amounts of sulfenic acid self-condensation byproducts. The generation of a second sulfenic function and its intramolecular *syn*-addition to the remaining triple bond could be governed by the favorable geometrical contiguity of the two reactive centers due to the interactions between the two aromatic rings. This would be consistent with the short reaction time observed when compounds **8** or **9** were separately thermolyzed, compared to the long reaction time recorded for the overall thermolysis step of the synthetic pathway towards cyclophane derivatives **4**–**6** (Scheme 3).

Complete stereoselectivity was observed when disulfoxide **3** was thermolyzed in the presence of *para*-diethynylbenzene, providing, as a unique product of the reaction, dithiacyclophane *S*,*S*′-dioxide **4** in high yield (71%). With *meta*-diethynylbenzene, the reaction (84% overall yield) appeared to be more complex and less stereoselective; in this case, dithiacyclophane *S*,*S*′-dioxides **5a** and **5b**, differing in the configuration of the chiral plane, were obtained in a 1:1:3 ratio with respect to dithiacyclophane *S*,*S*′-dioxide **6**, analogous to **4** and was the dominant product formed in the process. Suitable computational studies could clarify this significant aspect of the formation of the dithiacyclophane *S*,*S*′-dioxides.

The ^{1}H NMR spectra with NOESY experiments were diagnostic for the structure assignment of dithiacyclophane *S*,*S*′-dioxides **4**–**6**. In the ^{1}H NMR spectra of **5a** and **5b** (Table 1) the methyl groups linked to the (1,4)-bridged aromatic ring appear as one sharp singlet, and one singlet is



Scheme 4. Isolation of the intermediates in the synthesis of dithiacyclophane *S*,*S*′-dioxides **4**–**6**.

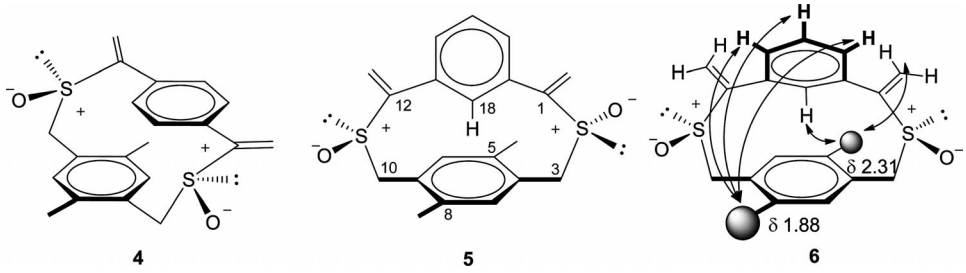


Figure 1. Graphical description of the proposed benzene ring disposition for **4**–**6** and diagnostic NOESY experiments conducted on the methyl groups in **6** (the two shaded spheres).

recorded for the two aryl protons (6,9-H) of the same aromatic ring. Moreover one AB system is observed for the two methylene protons (3,10-H_2) adjacent to the (1,4)-bridged ring, one multiplet pertains to three of the four protons of the (1,3)-bridged aromatic ring, and a tiny triplet is observed for the highfield shifted aromatic inner proton (18-H). The simplicity of such spectra allows the assumption that molecules **5a** and **5b** adopt, as preferred, an almost orthogonal edge-to-face (EtF) disposition (Figure 1),[2d] with the presence of a symmetry C_2-axis perpendicular to the (1,4)-bridged aromatic ring and bisecting protons in the 15- and 18-positions of the *meta*-disubstituted benzene. Variable-temperature NMR (VTNMR) experiments, performed on a sample of **5a** (see the Supporting Information) support this assumption, but the possibility of flipping of the (1,3)-bridged aromatic ring from one side to the other of the (1,4)-bridged aromatic ring on the NMR time-scale, cannot be ruled out.[2e]

Table 1. Chemical shifts (δ) in ^{1}H NMR spectra of dithiacyclophane *S*,*S*′-dioxides **5a** and **5b**.

	5,8-Me_2	3,10-H_2[a]	C=CH_2[b]	18-H	6,9-H	14–16-H
5a	1.99	4.02, 4.53	5.98; 6.17	6.15	6.64	7.15–7.26
5b	2.13	3.61, 4.82	5.99; 6.10	5.97	6.46	7.22–7.26

[a] AB system. [b] Two singlets.

On the other hand, the complexity of the ^{1}H NMR spectrum of dithiacyclophane *S*,*S*′-dioxide **6**, showing signal doubling for all the resonances (Table 2), allows the assignment of *rel*-R_S,S_S configuration and suggests that the molecule does not adopt a symmetric conformation, but instead, the two aromatic rings adopt a tilted EtF disposition with the two oxygen atoms analogously pointing outside. The attribution of the structure of compound **6** was confirmed by NOESY experiments. As an example, the methyl protons linked to the (1,4)-bridged aromatic ring in **6** resonate as two distinct singlets, one (δ = 2.31 ppm) close in space to the olefin protons of one of the two ethenyl moieties and to the inner proton 18-H of the (1,3)-bridged aromatic ring (δ = 6.11 ppm), whereas the second (δ = 1.88 ppm) is close in space to the three protons of the *meta*-disubstituted benzene and located in its shielding cone.

Table 2. Most significant chemical shifts (δ) in ^{1}H NMR spectra of dithiacyclophane *S*,*S*′-dioxides **4** and **6**.

	5,8-Me_2	3-H_2 and 10-H_2[a]
4	1.96; 2.47	3.63 and 4.59; 4.02 and 4.33
6	1.88; 2.31	3.34 and 4.94; 3.86 and 4.64

[a] Two AB systems.

The dithiaparacyclophane *S*,*S*′-dioxide **4** shows a pattern of signals similar those of **6** (Table 2), suggesting in this case a parallel offset disposition[2d] of the two *para*-disubstituted aromatic rings, with the sulfinyl functions analogously pointing outside.

Conclusions

We have described a significant improvement, in terms of yields, of a three-step synthesis of dithiacyclophane *S*,*S*′-dioxides, that can now be regarded as an efficient route to this kind of molecule. The isolation of an intermediate in the process, which had previously[8] been considered an almost synchronous concerted *syn*-addition of the two sulfurated functions of a bis-sulfenic acid onto the two triple bonds of a diethynylbenzene, provides mechanistic insights into the generation and reactivity of sulfenic acids. The most relevant characteristic of reported 5,8-dimethyl-1,12-dimethylene-2,11-dithia[3.3]cyclophane 2,11-dioxides is the coexistence in the same structure of different elements of chirality (plane and centers) that appear to be a promising feature for their use as organocatalysts. For this reason, it would clearly be desirable to obtain these dithiacyclophane *S*,*S*′-dioxides in enantiomerically pure form.

Experimental Section

General Methods and Materials: All commercial reagents and solvents (AR, LabScan Ltd., SpS, Romil Ltd.) were used without further purification. All syntheses were carried out under open atmospheric conditions unless otherwise noted. Analytical TLC was performed on Aldrich silica gel 60 F 254 plates. Products were visualized by UV or vanillin [1 g dissolved in MeOH (60 mL) and conc. H_2SO_4 (0.6 mL)]. Column chromatography was performed on Aldrich 60 silica gel (40–63 mm). ^{1}H and ^{13}C NMR measurements

were performed in $CDCl_3$ solutions at 300.1 and 75.5 MHz or at 500.1 and 125.7 MHz, respectively. All chemical shifts are reported in parts per million (δ, ppm), downfield to tetramethylsilane (Me_4Si) as an internal standard (δ = 0.00 ppm), or referenced to residual solvent $CHCl_3$ (^{1}H NMR 7.27 ppm and ^{13}C NMR 77.0 ppm); coupling constants *J* are given in Hertz. Multiplicities are reported as: s = singlet, br. s = broad singlet, t = triplet, m = multiplet. NMR peak assignments were based on homonuclear (COSY, COrrelationSpectroscopY) and heteronuclear correlation (^{1}H-^{13}C) spectra. Phase sensitive ^{1}H 2D-NOESY (Nuclear Overhauser Effect SpectroscopY) experiments were acquired by using a standard pulse sequence with mixing times of 350 ms. ^{1}H-^{13}C HSQC (Heteronuclear Single Quantum Coherence) correlation experiments were also performed for several compounds, and were recorded in a gradient-selected phase-sensitive mode. Melting points were determined with a Kofler hot-stage apparatus and are uncorrected.

Dimethyl 3,3′-[(2,5-Dimethyl-1,4-phenylene)bis(methylenethio)]dipropanoate (2): To a solution of **1** (0.50 g, 2.5 mmol) in anhydrous THF (6 mL), under an argon atmosphere at –78 °C, Triton B solution (40 wt.-% in MeOH, 0.68 mL, 1.5 mmol) was added. After 5 min stirring at –78 °C, methyl acrylate (0.57 mL, 6.3 mmol) was added and the reaction (monitored by TLC every 5 min) was allowed to proceed until completion (ca. 30 min). The reaction mixture was concentrated in vacuo and the crude residue was purified by flash column chromatography (ethyl acetate/hexane, 2:8) to provide disulfide **2** (0.75 g, 80%) as a transparent oil; R_f = 0.60 (ethyl acetate/hexane, 4:6). ^{1}H NMR: δ = 6.99 (s, 2 H, ArH), 3.69 (s, 6 H, 2× OCH_3), 3.68 (s, 4 H, 2× ArCH_2), 2.74 and 2.58 (2× t, $^3J_{vic}$ = 7.0 Hz, 8 H, 2× CH_2CH_2), 2.32 (s, 6 H, 2× ArCH_3) ppm. ^{13}C NMR: δ = 172.3 (2× CO), 134.6 and 134.0 (C-1,2,4,5), 132.0 (C-3,6), 51.8 (2× OCH_3), 34.5 (2× $CH_2CH_2CO_2CH_3$), 34.1 (2× ArCH_2), 26.8 (2× $CH_2CO_2CH_3$), 18.5 (2× ArCH_3) ppm. $C_{18}H_{26}O_4S_2$ (370.52): calcd. C 58.35, H 7.07; found C 58.42, H 7.05.

Dimethyl 3,3′-[(2,5-Dimethyl-1,4-phenylene)bis(methylenesulfinyl)]dipropanoate (3): A solution of **2** (0.33 g, 0.89 mmol) in CH_2Cl_2 (9 mL) was stirred at –78 °C and a solution of *m*-CPBA (< 77%, 0.40 g, 1.8 mmol) in CH_2Cl_2 (13 mL) was slowly added. The reaction was monitored by TLC and appeared to be complete by the end of the oxidant addition. The mixture was quenched by adding aqueous $Na_2S_2O_3$ (10 wt.-%) and the combined organics were washed twice with a satd. $NaHCO_3$ solution and twice with brine, dried (Na_2SO_4), filtered, and concentrated to give **3** (0.36 g) in almost quantitative yield as a white solid diastereomeric racemate mixture; R_f = 0.10 (acetone/hexane, 7:3); m.p. 120–122 °C. ^{1}H NMR: δ = 7.09 (s, 2 H, ArH), 4.01 (AB m, 4 H, 2× ArCH_2), 3.71 (s, 6 H, 2× OCH_3), 3.08–2.82 (m, 8 H, 2× CH_2CH_2), 2.35 (s, 6 H, 2× ArCH_3) ppm. ^{13}C NMR: δ = 171.7 (2× CO), 135.5 (C-2,5), 133.7 (C-3,6), 129.7 (C-1,4), 57.0 (2× ArCH_2), 52.2 (2× OCH_3), 46.3 (2× $CH_2CH_2CO_2CH_3$), 26.6 (2× $CH_2CO_2CH_3$), 19.4 (2× ArCH_3) ppm. $C_{18}H_{26}O_6S_2$ (402.52): calcd. C 53.71, H 6.51; found C 53.85, H 6.53.

Thermolysis of Disulfoxide 3 in the Presence of Diethynylbenzene. General Procedure: A solution of disulfoxide **3** (0.40 g, 0.99 mmol) and commercial diethynyl acceptor (0.13 g, 1.0 mmol) in DCE (100 mL) was heated at reflux temp. (83 °C) until the reaction appeared to be complete (TLC; disappearance of starting sulfoxide and intermediate products **8/9**), the solvent was removed under reduced pressure and the crude material was purified by column chromatography on silica gel to give dithiacyclophane S,S′-dioxides **4**–**6**.

(*rel*-R_S,S_S,R_p)-5,8-Dimethyl-1,12-dimethylene-2,11-dithia[3.3]paracyclophane 2,11-Dioxide (4): Following the general procedure, compound **4** was prepared from 1,4-diethynylbenzene and disulfoxide **3**, and isolated, after chromatography purification (acetone/hexane, 2:8), as a white solid (0.25 g, 0.70 mmol, 71%) that decomposed before melting (> 170 °C); R_f = 0.54 (acetone/hexane, 5:5). ^{1}H NMR: δ = 7.40 and 7.24, and 6.88 and 6.79 (two split AB systems, $^3J_{ortho}$ = 8.1 Hz, $^4J_{meta}$ = 1.8 Hz, 4 H, 14,15-H and 17,18-H), 6.86, 6.19, 6.16, 6.13, and 6.12 (5× s, 6 H, 6,9-H and 2× =CH_2), 4.59 and 3.63, and 4.33 and 4.02 (two AB systems, $^2J_{gem}$ = 11.8 Hz, 4 H, 3,10-H_2), 2.47 and 1.96 (2× s, 6 H, 2× CH_3) ppm. ^{13}C NMR: δ = 152.5 and 152.1 (C-1,12), 136.1, 135.2, 135.1, 134.2, 129.0, 128.6 (C-4,5,7,8,13,16), 135.9 and 131.6 (C-6,9), 127.5, 126.1, 125.3, 124.5 (C-14,15,17,18), 115.3 and 115.2 (2× =CH_2), 64.0 and 60.3 (C-3,10), 19.8 and 19.0 (2× CH_3) ppm. $C_{20}H_{20}O_2S_2$ (356.50): calcd. C 67.38, H 5.65; found C 67.30, H 5.66.

(*rel*-R_S,R_S,R_p)- or (*rel*-R_S,R_S,S_p)-5,8-Dimethyl-1,12-dimethylene-2,11-dithia[3.3]parametacyclophane 2,11-Dioxide (5a) (more mobile by chromatography): Racemate **5a** was prepared, together with its diastereoisomer **5b** and compound **6**, from 1,3-diethynylbenzene and disulfoxide **3** by following the general procedure. Compound **5a** was isolated after chromatographic purification (ethyl acetate/hexane, 2:8) as a white solid (0.06 g, 17%); R_f = 0.47 (ethyl acetate/hexane, 8:2) that decomposed before melting (> 170 °C). ^{1}H NMR: δ = 7.26–7.15 (m, 3 H, 14–16-H), 6.64 (s, 2 H, 6,9-H), 6.17 and 5.98 (2× s, 4 H, 2× =CH_2), 6.15 (t, $^4J_{meta}$ = 1.5 Hz, 1 H, 18-H), 4.53 and 4.02 (AB system, $^2J_{gem}$ = 12.3 Hz, 4 H, 3,10-H_2), 1.99 (s, 6 H, 2× CH_3) ppm. ^{13}C NMR: δ = 152.1 (C-1,12), 134.9, 134.6, and 129.3 (C-4,5,7,8,13,17), 132.7 (C-6,9), 127.7 and 127.0 (C-14,15,16), 122.9 (C-18), 117.9 (2× =CH_2), 60.7 (C-3,10), 19.8 (2× CH_3) ppm. $C_{20}H_{20}O_2S_2$ (356.50): calcd. C 67.38, H 5.65; found C 67.40, H 5.67.

(*rel*-R_S,R_S,R_p)- or (*rel*-R_S,R_S,S_p)-5,8-Dimethyl-1,12-dimethylene-2,11-dithia[3.3]parametacyclophane-2,11-dioxide (5b) (less mobile by chromatography): Racemate **5b** was prepared, together with its diastereoisomer **5a** and compound **6**, from 1,3-diethynylbenzene and disulfoxide **3** by following the general procedure. Compound **5b** was isolated after chromatographic purification (ethyl acetate/hexane, 2:8) as a white solid (0.06 g, 17%) that decomposed before melting (> 170 °C); R_f = 0.45 (ethyl acetate/hexane, 8:2). ^{1}H NMR: δ = 7.26–7.22 (m, 3 H, 14–16-H), 6.46 (s, 2 H, 6,9-H), 6.10 and 5.99 (2× s, 4 H, 2× =CH_2), 5.97 (br. s, 1 H, 18-H), 4.82 and 3.61 (AB system, $^2J_{gem}$ = 12.3 Hz, 4 H, 3,10-H_2), 2.13 (s, 6 H, 2× CH_3) ppm. ^{13}C NMR: δ = 152.2 (C-1,12), 134.8, 134.6 and 129.3 (C-4,5,7,8,13,17), 132.1 (C-6,9), 127.8 and 127.4 (C-14,15,16), 122.6 (C-18), 117.7 (2× =CH_2), 63.4 (C-3,10), 19.1 (2× CH_3) ppm. $C_{20}H_{20}O_2S_2$ (356.50): calcd. C 67.38, H 5.65; found C 67.45, H 5.65.

(*rel*-R_S,S_S,R_p)-5,8-Dimethyl-1,12-dimethylene-2,11-dithia[3.3]parametacyclophane 2,11-Dioxide (6): Compound **6** was prepared, together with compounds **5a** and **5b**, from 1,3-diethynylbenzene and disulfoxide **3** by following the general procedure. Compound **6** was isolated after chromatographic purification (ethyl acetate/hexane, 2:8) as a white solid (0.18 g, 0.50 mmol, 50%) that decomposed before melting (> 170 °C); R_f = 0.44 (ethyl acetate/hexane, 8:2). ^{1}H NMR δ = 7.20 (t, $^3J_{ortho}$ = 7.6 Hz, 1 H, 15-H), 6.99 (m, 2 H, 14,16-H), 6.82 and 6.26 (2× s, 2 H, 6,9-H), 6.24, 6.19, 5.98 and 5.92 (4× s, 4 H, 2× =CH_2), 6.11 (t, $^4J_{meta}$ = 1.8 Hz, 1 H, 18-H), 4.94 and 3.34, and 4.64 and 3.86 (two AB systems, $^2J_{gem}$ = 12.0 Hz, 4 H, 3,10-H_2), 2.31 and 1.88 (2× s, 6 H, 2× CH_3) ppm. ^{13}C NMR: δ = 153.5 and 152.2 (C-1,12), 136.4, 135.0, 134.5, 134.1, 130.6, 129.5

(C-4,5,7,8,13,17), 133.0 and 131.0 (C-6,9), 128.1, 128.0, 127.3 and 127.0 (C-14–16,18), 117.6 and 117.3 (2× $=CH_2$), 65.6 and 61.6 (C-3,10), 19.9 and 18.9 (2× CH_3) ppm. $C_{20}H_{20}O_2S_2$ (356.50): calcd. C 67.38, H 5.65; found C 67.26, H 5.66.

Methyl (*rel*-R_S,R_S)- and (*rel*-R_S,S_S)-3-{(2,5-Dimethyl-1,4-phenylene)-1-(methylenesulfinyl)-4-([1-(3-ethynylphenyl)ethenyl]sulfinylmethylene)}propanoate (8): A solution of disulfoxide **3** (0.40 g, 0.99 mmol) and 1,3-diethynylbenzene (0.13 g, 1.0 mmol) in DCE (100 mL) was heated to reflux temp. (83 °C). After 24 h, the solvent was removed under reduced pressure and the crude material was purified by flash column chromatography on silica gel (acetone/hexane, 2:8), giving, together with the expected dithiacyclophane *S*,*S*′-dioxides **5** and **6** (31% overall yield) and the starting disulfoxide **3** (60% yield), compound **8** (0.04 g, 0.09 mmol, 9%), as a low-melting solid; R_f = 0.43 (acetone/hexane, 5:5). ^{1}H NMR: δ = 7.51–7.35 (m, 4 H, 2′,4′,5′,6′-H), 7.00 and 6.92 (2× s, 2 H, 3,6-H), 6.09 and 6.06 (2× s, 2 H, $=CH_2$), 4.11–3.68 (m, 4 H, 2× ArCH_2), 3.72 and 3.71 (2× s, 3 H, OCH_3), 3.14 (s, 1 H, ≡CH), 3.05–2.84 (m, 4 H, CH_2CH_2), 2.30, 2.18 and 2.17 (3× s, 6 H, 2× ArCH_3) ppm. ^{13}C NMR: δ = 171.4 (CO), 152.2 (C=CH_2), 135.2–126.8 (C-1,1′,2,2′,3,4,4′,5,5′,6,6′), 123.2 (C-3′), 118.1 (=CH_2), 82.5 (C≡CH), 78.5 (≡CH), 58.2 and 56.9 (2× ArCH_2), 52.2 (OCH_3), 46.0 and 26.9 (CH_2CH_2), 19.2 and 19.1 (2× ArCH_3) ppm. $C_{24}H_{26}O_4S_2$ (442.59): calcd. C 65.13, H 5.92; found C 65.23, H 5.93.

Methyl (*rel*-R_S,R_S)- and (*rel*-R_S,S_S)-3-{(2,5-Dimethyl-1,4-phenylene)-1-(methylenesulfinyl)-4-([1-(4-ethynylphenyl)ethenyl]sulfinylmethylene)}propanoate (9): A solution of disulfoxide **3** (0.40 g, 0.99 mmol) and 1,4-diethynylbenzene (0.13 g, 1.0 mmol) in DCE (100 mL) was heated at reflux temp. (83 °C). After 24 h, the solvent was removed under reduced pressure and the crude material was purified by flash column chromatography on silica gel (ethyl acetate/hexane, 3:7), giving, together with the expected dithiacyclophane *S*,*S*′-dioxide **4** (28% yield) and the starting disulfoxide **3** (64% yield), compound **9** (0.03 g, 0.08 mmol, 8%) as a low-melting solid; R_f = 0.38 (ethyl acetate/hexane, 8:2). ^{1}H NMR: δ = 7.50 and 7.37 (AB system, $^3J_{ortho}$ = 8.3 Hz, 4 H, 2′,3′,5′,6′-H), 7.01 and 6.89 (2× s, 2 H, 3,6-H), 6.09 and 6.06 (2× s, 2 H, $=CH_2$), 4.05–3.69 (m, 4 H, ArCH_2), 3.71 (s, 3 H, OCH_3), 3.18 (s, 1 H, ≡CH), 3.03–2.82 (m, 4 H, CH_2CH_2), 2.29, 2.28 and 2.19 (3× s, 6 H, 2× ArCH_3) ppm. ^{13}C NMR: δ = 171.7 (CO), 152.5 (C=CH_2), 135.1 and 134.4 (C-2,5), 133.8 and 133.1 (C-3,6), 132.8 (C-3′,5′), 129.5 and 128.7 (C-1,1′,4), 126.4 (C-2′,6′), 123.3 (C-4′), 118.1 (=CH_2), 82.7 (C≡CH), 79.0 (≡CH), 58.3 and 56.9 (2× ArCH_2), 52.2 (OCH_3), 46.0 and 26.9 (CH_2CH_2), 19.2 (2× ArCH_3) ppm. $C_{24}H_{26}O_4S_2$ (442.59): calcd. C 65.13, H 5.92; found C 65.05, H 5.94.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra for all key intermediates and final products and NOESY spectra for compound **6**.

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[12] Thermolysis of disulfoxide **3** with *para*-diethynylbenzene was performed in 1,4-dioxane (100 °C) and in benzene (80 °C). In the first case, we obtained only sulfenic acid self-condensation products, in the second case, results similar to those of the reaction performed in DCE were obtained. Thus, the thermolysis temperature appears to be crucial for the formation of dithiacyclophane *S*,*S*′-dioxides.

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