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Keyword:	Cyclophanes, cyclophenes, ring contraction, sulfone pyrolysis, Ramberg-Bäcklund reaction

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**Synthesis, Structure, and First Reactions of a
New Class of Thiacyclophanes*.**

Dedicated to Professor Reginald H. Mitchell

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30 [‡] Cyclophanes, Part 75; for Part 74 see ref.¹

31

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33

34 **Key words:** Cyclophanes, cyclophenes, ring contraction, sulfone
35 pyrolysis, Ramberg-Bäcklund reaction, X-ray structural
36 analysis

37

38

39 **Abstract:** In our effort to prepare [m.n]cyclophanes carrying
40 functional groups in their molecular bridges, the
41 thiacyclophanes **14**, **19**, **20**, and **21** have been prepared by
42 simple routes from the pseudo-gem dibromide **10a** and the
43 corresponding bis-thiol **10b**. The triply-bridged bis-thia-
44 cyclophanes **14**, and **19-21** were characterized by their
45 spectroscopic data as well as by X-ray structural analyses.
46 The *meta*-isomer **20** was oxidized to the bis-sulfone **23**, which,
47 on flash vacuum pyrolysis (FVP) yielded a product mixture
48 presumably containing the hydrocarbon **26** with a cleaved
49 molecular bridge. Subjecting **23** to Ramberg-Bäcklund conditions
50 (CCl₄, NaOH, phase transfer catalysis) provided the chloride **24**
51 in poor yield (9%), a [2.2]paracyclophane in which the new
52 molecular bridge is fully conjugated.

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Draft

Introduction: Compared to the chemical behavior of the aromatic rings in cyclophanes, much less is known about the reactivity of the bridges that hold these aromatic moieties together. Even when studying the electronic interactions between the latter, most authors are interested in the intraannular, through-space interactions between the aromatic "decks", rather than the through-bond interactions by way of the bridges. Indeed, if one exchanges one of the saturated ethano bridges in [2.2]paracyclophane (**1**) for an olefinic double bond, as in [2.2]paracyclophene (**2**) one would not expect any π - π -interaction (conjugation) at all since, as indicated in formula **2'** (Scheme 1), the p-orbitals of the olefinic and the adjacent aromatic units are orthogonal.

Scheme 1 here please

Scheme 1: Electronic interactions between the aromatic rings of [2.2]paracyclophanes.

Increasing the length of the (unsaturated) bridge(s) should result in a greater flexibility of this structural element and hence, by allowing more non-orthogonal orientations of the

79 respective p-orbitals, lead to more conjugation between the
80 aromatic rings.

81 We have recently described the first [2.2]paracyclophane
82 derivatives possessing such lengthened unsaturated bridges:²

83 The pseudo-*geminally* substituted dienyne **3** and the enediyne **4**,
84 as well as its pseudo-*ortho* isomer **5** (Scheme 2), were prepared
85 and some of their chemical properties studied.

86

87

88

89 Scheme 2 here please

90

91 Scheme 2: A selection of [2.2]paracyclophane derivatives with
92 a lengthened unsaturated bridge.

93

94 Since the hydrocarbons **3–5** are not very stable,² a property
95 also assumed to be characteristic for the yet unknown **6**, we
96 decided to replace at least one of the double bonds by a

benzene ring. This could be achieved in two ways: Exchange of a terminal double bond of the bridge by a benzene ring results in the generation of benz-annelated hydrocarbon **7**, whereas the analogous substitution of the central double bond of **6** by a benzene ring produces **8a** (Scheme 2). Note that the double bonds in **7** and **8** cannot only be anchored in the *ortho*-position as in **8a**, but also in the *meta*- and *para*-orientation: **8b** and **8c**, respectively.

For the preparation of hydrocarbons of type **8** we decided to proceed as illustrated by the retrosynthetic Scheme 3 for the model system **8c**:

Scheme 3 here please

Scheme 3: Preparation of the hydrocarbons **8**: retrosynthetic analysis.

One of the most often employed strategies to prepare bridged aromatic systems involves the preparation of sulfides, which

are subsequently subjected to ring contraction. This could start from the sulfide and use the *S*-analogous Stevens-rearrangement³ or oxidize the sulfide first to a sulfone and then remove the SO₂-linker thermally ("sulfone pyrolysis")⁴. Access to **9** could be provided by either coupling the pseudo-*gem*-dibromide **10a** or the pseudo-*gem* bis-thiol **10b** with the *para*-xylylene dibromides **11a** or bis-thiols **11b**. To prepare various isomers of **9** and products derived therefrom, the appropriate isomers of **10** and **11** have to be used. For the time being we wish to keep the functional groups in the [2.2]paracyclophane derivative **10** in the pseudo-*gem* position, since this guarantees closest proximity of the bridging elements in this part of the molecules.

In our first coupling experiment (Scheme 4) we reacted the pseudo-*gem* dibromide **10a** with either the *ortho*- (**12**) or the *meta*-xylylenedithiol **13** in the presence of potassium hydroxide in benzene/ethanol under high dilution conditions (Scheme 4).

Scheme 4 here please

Scheme 4: Coupling of the pseudo-gem cyclophane **10a** with *ortho*-, **12**, and *meta*-xylylenedithiol, **13**.

To our surprise in neither case could the desired bis-sulfides be obtained. Instead in both experiments the triply bridged [3.2.2]thiacyclophane **14** was obtained in approximately the same yield.

The compound was characterized by its spectroscopic data (see Experimental section) and an X-ray structural study.

The molecular structure of **14** in the crystal is shown in Fig. 1.

Fig. 1 here please

Fig. 1. The molecular structure of compound **14** in the crystal.

Ellipsoids represent 50% probability levels. Selected molecular dimensions ($\text{\AA}$ and $^\circ$): C1-C2 1.576(3), C9-C10 1.591(3), C17-S1 1.813(3), C18-S1 1.815(3); C2-C1-C14 112.2(2), C1-C2-C3 113.0(2), C6-C9-C10 113.1(2), C9-C10-C11 112.8(2), S1-C17-C15 114.7(2), S1-C18-C4 116.0(2), C17-S1-C18 102.05(12); C15-C17-S1-C8 58.7(2), C4-C18-S1-C17 -61.9(2).

The molecule of **14** (Fig. 1) displays approximate mirror symmetry (r.m.s. deviation 0.29 $\text{\AA}$). The introduction of the extra bridge scarcely alters the distortions that are well-known for [2.2]paracyclophane^{1,5}, features of which include lengthened bridge bonds, widened bridge angles, narrow ring angles at the bridgehead atoms; see the figure caption and the Experimental section for individual values. The flattened boat form adopted by the rings, in which the bridgehead atoms lie

some 0.13-0.16 Å out of the plane of the other four ring atoms, is also retained, and the interplanar angle between the rings (excluding bridgehead atoms) is 2.9°. The bond angles in the CH₂-S-CH₂ bridge may be compared to values obtained from a search of the Cambridge Database⁶ for the moiety C-CH₂-S-CH₂-C with two-coordinate central sulfur: 113.4° for the angle at the methylene carbon and 101.4° for the angle at sulfur, averaged from 1758 individual values.

A reasonable mechanism for the formation of **14** is summarized in Scheme 5.

Scheme 5 here please

193 Scheme 5: Mechanism of formation of the triply-bridged
194 cyclophane **14** from **10a** and the dipotassium salts of various
195 xylylenedithiols, **15**.

196

197 We propose that in the first step the salt **15** attacks the
198 dibromide **10a** in an S_N2-substitution and yields the monobromide
199 **16**. This, in principle, could react similarly for a second
200 time, but in an intramolecular fashion, to yield the desired
201 disulfides, e.g. **9**. In fact, the required ring-closure takes
202 place, but with the sterically much closer sulfur atom of the
203 thioether function as shown in **16**. This results in the
204 generation of the sulfonium ion **17**, which in the final step is
205 cleaved by the potassium salt **15** to provide the isolated
206 thioether **14**. The tris-sulfur compound **18**, which is also
207 produced, could participate in the process again to finally
208 yield the polymeric material which is also observed. We had
209 previously noted that the yields of this type of coupling
210 reactions to prepare thiacyclophanes are influenced by the
211 binding of the respective functional groups: thus, taking a
212 thiol of one coupling partner and reacting it with the bromide
213 of the other can yield different results than the combination
214 in which these two functional groups are reversed.⁷

215 We hence decided to replace the pseudo-*geminal* dibromide **10a**
216 by the dithiol **10b**. This derivative was prepared by reacting
217 **10a** with thiourea and hydrolysis of the resulting bis-iso-

thiouronium salt in the presence of ethylenediamine in aqueous dioxane; **10b** was produced in 70% yield (Schema 6).

Scheme 6 here please

Scheme 6: Preparation of the three dithiacyclophanes **19–21** from **10b**.

When **10b** was reacted with the *ortho*-, *meta*- and *para*-isomer of **9a**, the anticipated bisthioethers **19–21** were all formed. In the first two cases the yields were good, in the third case rather low. We would assume that this isomer is the most strained and that the transition state for the final intramolecular coupling process is the least favorable.

236 All compounds were characterized by their spectroscopic and
237 analytical data (see Experimental section), and also by X-ray
238 structural analyses.

239 The molecular structure of **19** in the crystal is shown in Fig.
240 2.

242 Fig. 2 here please

244
245 Fig. 2. The molecular structure of compound **19** in the crystal.
246 Ellipsoids represent 30% probability levels. Selected
247 molecular dimensions (Å and °): C1-C2 1.589(5), C9-C10
248 1.572(5), C17-S1 1.824(3), C18-S1 1.823(3), C25-S2 1.832(3),
249 C26-S2 1.819(3); C2-C1-C14 112.1(3), C1-C2-C3 112.4(3), C6-C9-
250 C10 111.9(3), C9-C10-C11 114.0(3), S1-C17-C4 111.4(2), S1-C18-
251 C19 114.7(2), S2-C26-C15 113.8(2), S2-C25-C20 113.7(2), C17-
252 S1-C18 101.5(2), C25-S2-C26 101.05(15), C25-C20-C19 122.8(3),
253 C18-C19-C20 122.7(3); C4-C17-S1-C18 163.0(2), C17-S1-C18-C19 -
254 54.4(3), C15-C26-S2-C25 -146.3(2), C26-S2-C25-C20 -34.9(3),
255 C5-C4-C17-S1 33.9(4), C16-C15-C26-S2 50.8(4).

256

257 In the *ortho*-isomer **19** (Fig. 2), the [2.2]paracyclophane
258 framework retains its usual features (see above), although the
259 interplanar angle is slightly increased to 4.2° . The aromatic
260 ring C19-24 of the newly introduced bridge is to a good
261 approximation perpendicular to the two rings of the
262 paracyclophane unit (this is also the case for the other two
263 isomers, see below), and shows little sign of strain except
264 for the slightly widened angles C25-C20-C19 and C18-C19-C20 to
265 the sulfur-containing bridges. The conformation of these
266 bridges is completely different; the atom S1 is directed into
267 the space between the cyclophane rings [torsion angle C5-C4-
268 C17-S1 $33.9(4)^\circ$], whereas S2 points away from the cyclophane
269 [C16-C15-C26-S2 $50.8(4)^\circ$].

270 The molecular structure of **20** in the crystal is displayed in
271 Fig. 3.

272

Fig. 3 here please

273

274

Fig. 3. The molecular structure of compound **20** in the crystal. Ellipsoids represent 30% probability levels. Selected molecular dimensions ($\text{\AA}$ and $^\circ$): C1-C2 1.585(4), C9-C10 1.585(4), C17-S1 1.820(3), C18-S1 1.826(3), C25-S2 1.835(3), C26-S2 1.821(3); C2-C1-C14 113.4(2), C1-C2-C3 113.9(2), C6-C9-C10 113.3(2), C9-C10-C11 113.3(2), S1-C17-C4 114.2(2), S1-C18-C19 112.4(2), S2-C26-C15 113.7(2), S2-C25-C21 113.0(2), C17-S1-C18 98.75(15), C25-S2-C26 98.27(15); C4-C17-S1-C18 153.0(2), C17-S1-C18-C19 67.2(3), C15-C26-S2-C25 163.9(2), C26-S2-C25-C21 -58.7(3), C3-C4-C17-S1 58.1(3), C14-C15-C26-S2 -64.2(3).

The molecule of the *meta*-isomer **20** (Fig. 3) is much more regular than that of **19** and displays approximate mirror symmetry (r.m.s. deviation 0.15 $\text{\AA}$). Both sulfur atoms point away from the cyclophane core, which again retains its

customary structural features (see above), although the interplanar angles between the cyclophane decks is 5.5° . The additional aromatic ring C19-24 is not itself distorted, but incipient strain may be indicated by the fact that the substituent atoms C18 and C25 are displaced by 0.16 and 0.14 Å respectively out of the ring plane towards the cyclophane.

The molecular structure of the *para*-isomer **21** in the crystal is shown in Fig. 4.

Fig. 4 here please

Fig. 4. The molecular structure of compound **21** in the crystal (one of two independent molecules; solvent omitted). Ellipsoids represent 30% probability levels. Selected molecular dimensions (Å and $^\circ$) for this molecule: C1-C2 1.587(4), C9-C10 1.574(5), C17-S1 1.837(3), C18-S1 1.850(3),

312 C25-S2 1.829(4), C26-S2 1.831(3); C2-C1-C14 114.1(3), C1-C2-C3
313 113.9(2), C6-C9-C10 113.3(2), C9-C10-C11 113.3(2), S1-C17-C4
314 114.2(3), S1-C18-C19 110.9(2), S2-C26-C15 112.1(2), S2-C25-C22
315 111.7(2), C17-S1-C18 100.52(15), C25-S2-C26 100.7(2); C4-C17-
316 S1-C18 173.3(2), C17-S1-C18-C19 -34.7(3), C15-C26-S2-C25 -
317 166.8(2), C26-S2-C25-C22 48.5(3), C3-C4-C17-S1 -63.8(4), C14-
318 C15-C26-S2 55.2(4).

319

320 The *para*-isomer **21** (Fig. 4) crystallizes with two independent
321 but similar molecules in the asymmetric unit, together with a
322 cyclohexane molecule that is disordered across an inversion
323 centre. Both molecules display approximate mirror symmetry,
324 with r.m.s. deviations 0.14 and 0.10 Å respectively; the fit
325 of one molecule to the other gives an r.m.s. deviation of 0.11
326 Å. There are indications that this isomer is the most strained
327 of the three; the paracyclophane decks are tilted by 7.5°, and
328 the substituent atoms C18 and C25 are displaced by 0.39 and
329 0.35 Å respectively out of the plane of the ring C19-24
330 towards the cyclophane core.

331

332 In another coupling experiment we tried to combine the two
333 pseudo-*gem*-[2.2]paracyclophanes **10a** and **10b** with each other.
334 In the first experiment with potassium hydroxide as the base,
335 only the thiaphane **14** was obtained in good yield (Scheme 7)

336

Scheme 7 here please

Scheme 7: The direct coupling of two pseudo-*gem*-[2.2]para-cyclophane derivatives, **10a** and **10b**.

This was still the main product when we changed to cesium hydroxide as the base; but in this case we also isolated a small amount of a disulfide to which we assign the "dimeric" structure **22** according to its spectroscopic and analytical data (see Experimental section). Note that in principle two diastereomers of **22** could be formed, a *meso*- and a *d,l*-diastereomer. At the present time we cannot distinguish between these two possibilities. The experiment illustrates, however, that besides the functionality of the respective building blocks, the base employed in their coupling can also play a significant role.

Summarizing our work up to this point, we have been successful in synthesizing and characterizing new thiacyclophane systems, the disulfides **19–21**, by simple and effective routes, compounds which are now ready for further transformation.

To obtain a first impression concerning their reactivities, we studied the ring contraction of **20**, hoping to obtain a representative of the hydrocarbons **8** shown in Scheme 2 (the *meta*-isomer, **8b**).

Towards this end the *meta*-derivative **20** was first oxidized to the bis-sulfone **23** in excellent yield with *meta*-chloroperbenzoic acid (MCPBA) in dichloromethane in the presence of acetic acid (Scheme 8).

Scheme 8 here please

Scheme 8: First reactions with the *meta*-bis-sulfide **20**: ring-contractions. Letters a-m in formula **24** indicate protons assigned by NMR (see Experimental).

Neither the conventional Ramberg-Bäcklund reaction⁸ nor employing the modified version of Chan et al.⁹, mixing powdered KOH and aluminum oxide, lead to isolable products.

Therefore, the reaction was carried out under phase-transfer conditions, using carbon tetrachloride as the halogenating reagent in the first step (Scheme 8). In this case, a diene was produced indeed, although in low yield (9%). According to its spectral data (see Experimental section) it bore a chlorine substituent at one of its double bonds. There are reports in the literature¹⁰ that under these conditions polyhalhalogenation takes place in the first step of the Ramberg-Bäcklund process causing the formation of vinylhalides after the sulfur dioxide has been extruded.

The structure of **24** was derived from close inspection of the coupling patterns in its ¹H NMR spectrum and from useful long-range correlations in its H,H-COSY spectrum. The deshielded protons, H^a-H^d in formula **24**, of the *m*-disubstituted benzene ring were easily identified. Protons H^j and H^k with a mutual coupling of 11.0 Hz indicate a *cis*-C=C double bond. Olefinic proton H^j displayed long-range correlations with H^a and H^c, so these latter ones are situated *ortho* to H^j of the -CH^k=CH^j- bond. The slightly broadened singlet of olefinic proton H^e had long-range cross-peaks with H^a and H^d, thus determining the position of the second olefinic bridge, -C(Cl)=CH^e-. Proton H^k of the first bridge correlates with the isolated proton, H^m, of the "upper" [2.2]paracyclophane deck, while the isolated proton, H^l, of the "lower" deck shows no correlation with any olefinic proton because its *ortho*-benzylic position is

occupied by the chloro substituent, the presence of which is evident from the mass spectrum and the elemental analysis.

To prepare the parent system, from which **24** is formally derived, the hydrocarbon **25**, we subjected the bissulfone **23** to flash vacuum pyrolysis (FVP) at 500–540 °C. From the pyrolysate, a hydrocarbon mixture could be isolated by column chromatography in ca. 22% yield. According to its NMR spectroscopic data, this must contain components carrying methyl groups as in **26** (Scheme 8 and Experimental Section). A rationalization for these signals would involve cleavage of one ethano bridge of the presumed intermediate **25**. Similar cleavage products have been obtained by pyrolysis of paracyclophane hydrocarbons, including the parent system **1**. Their formation presumably takes place via diradicals formed by homolysis of an ethano bridge.¹¹

We hence assume that **25** is generated as a reaction intermediate, that does not survive the harsh pyrolysis conditions in this case.

Conclusions: We have shown that dithiacyclophanes can be prepared readily by well-established routes in high yield. Exploratory experiments demonstrate that these intermediates can be converted into novel cyclophanes containing unsaturated bridges, compounds which are of interest in the study of conjugation effects between the rings ("decks") of layered organic compounds.

430

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Graphical abstract:

Experimental:

General methods: **Chromatography:** TLC: Polygram Sil G/UV₂₅₄ (Macherey and Nagel) - Column chromatography: Merck silica gel 60 (70-230 mesh). - **NMR:** solvent: CDCl₃ (δ_c = 77.01 ppm) or CD₂Cl₂ (δ_c = 53.84 ppm), internal standard: TMS for ¹H, solvent for ¹³C; Bruker AM 300 (¹H: 300.1 MHz, ¹³C: 75.5 MHz; Bruker AM 400 (¹H: 400.1 MHz, ¹³C: 100.6 MHz); degree of carbon atom substitution by DEPT-135. - **IR:** in solution, as film (neat), and as KBr pellets on a Perkin-Elmer 1420 instrument. - **UV:** in

ethanol and/or acetonitrile, Beckman UV 5230. - **MS:** EI (70 eV), Finnigan MAT 8436.

The dibromide **10a** was prepared according to the method described in the literature:¹²

General procedure for assembling thiacyclophanes: A solution containing equimolar amounts (1 mmol each) of the appropriate dibromide and the dithiol in degassed benzene (100 mL) was added by a syringe pump to a well-stirred solution of potassium hydroxide (0.14 g, 2.5 mmol) in ethanol (95%, 800 mL) during 8-10 h. After the addition was complete, the mixture was stirred for an additional 8 h period. The solvent was removed in vacuo and the crude product as chromatographed on silica gel to give the corresponding cyclophane.

4,15-Bis(mercaptomethyl)[2.2]paracyclophane (10b): A solution of 4,15-bis(bromomethyl)[2.2]paracyclophane (**10a**, 2.44 g, 6.2 mmol) and thiourea (0.95 g, 12.4 mmol) in anhydrous THF (60 mL) was heated to reflux for 12 h. The mixture was cooled to room temp. and the precipitated isothiuronium salt was removed by filtration and dried. The salt was dissolved in water/dioxane (1:2, v/v, 180 mL) under nitrogen and to this solution was added ethylene diamine (0.57 g, 9.4 mmol). The mixture was heated to reflux under nitrogen for 12 h, cooled to room temp., and hydrochloric acid (2 N) was added for hydrolysis until a pH of 4 was reached. The solvent was

506 removed in vacuo, and the crude product was chromatographed
507 using dichloromethane/hexane (1:1, v/v) as the eluent: 1.30 g
508 (70%) of **10b** as a colorless powder, m. p. 85 °C. – ^1H NMR: δ =
509 1.46 (t, J = 7.0 Hz, 2 H), 2.95–3.08 (m, 6 H), 3.38 (m,
510 AA'XX', N = 9.9 Hz, 2 H), 3.45 (dd, J = 12.8, 6.9 Hz, 2 H),
511 3.85 (dd, J = 12.8, 6.9 Hz, 2 H), 6.32 (d, J = 1.7 Hz, 2 H),
512 6.45 (dd, J = 7.7, 1.7 Hz, 2 H), 6.48 ppm (d, J = 7.7 Hz, 2 H).
513 – ^{13}C NMR: δ = 27.4 (t), 31.7 (t), 34.9 (t), 132.4 (d), 132.5
514 (d), 135.3 (d), 136.0 (s), 140.01 (s), 140.02 (s). – MS: m/z
515 (%) = 300 (18, M^+), 267 (40), 266 (86), 147 (100). – HRMS:
516 $\text{C}_{18}\text{H}_{20}\text{S}_2$: calcd.: 300.100; found: 300.100.

517

518 **Attempted coupling of 10a with o-xylylene dithiol (12):**

519 According to the above general procedure it was attempted to
520 couple the dibromide **10a** (0.40 g, 1.0 mmol) with o-xylylene
521 dithiol (**12**, 0.17 g, 1.0 mmol). Purification of the obtained
522 crude reaction product by silica gel chromatography with
523 dichloromethane/hexane (3:7, v/v) afforded the thiacyclophane **14**
524 as colorless needles (0.21 g, 80%), m. p. 240 °C. The compound
525 has been described previously,¹³ but its spectroscopic data are
526 incomplete in the literature. – ^1H NMR: δ = 2.84–3.07 (m, 6 H),
527 3.29–3.41 (m, 4 H), 4.09 (d, J = 14.7 Hz, 2 H), 6.24 (dd, J =
528 7.9, 1.9 Hz, 2 H), 6.34 (d, J = 7.9 Hz, 2 H), 6.85 ppm (d, J =
529 1.9 Hz, 2 H). – ^{13}C NMR: δ = 32.3 (t), 32.5 (t), 35.3 (t),
530 131.7 (d), 134.2 (d), 134.6 (d), 135.0 (s), 138.3 (s), 140.3
531 (s) ppm.

Attempted coupling of 10a with *m*-xylylene dithiol (13): As above **10a** (0.40 g, 1.0 mmol) was attempted to be coupled with *m*-xylylene dithiol (0.17 g, 1 mmol). Again, only the intramolecularly generated **14** was obtained (0.19 g, 70%).

Dithiacyclophane 19: According to the above general procedure was coupled **10b** (0.60 g, 2 mmol) with *o*-xylylene dibromide (**11**, 0.53 g, 2 mmol). The crude product was purified by silica gel column chromatography with dichloromethane/hexane (3:7, v/v) to provide **19** as colorless needles (0.50 g, 62%), m. p. 211 °C. - ^1H NMR: δ = 2.74–3.07 (m, 8 H), 3.48, 3.53 (AB system, J = 15.1 Hz, 4 H), 3.78 (d, J = 13.9 Hz, 2 H), 4.33 (d, J = 13.9 Hz, 2 H), 6.37 (d, J = 7.7 Hz, 2 H), 6.42 (dd, J = 7.7, 1.8 Hz, 2 H), 6.63 (d, J = 1.8 Hz, 2 H), 7.35, 7.55 (AA'XX', N = 9.2 Hz, 4 H). - ^{13}C NMR: δ = 31.3 (t), 31.7 (t), 33.2 (t), 35.0 (t), 127.6 (d), 131.11 (d), 131.17 (d), 131.25 (d), 133.9 (d), 136.3 (s), 136.6 (s), 137.0 (s), 139.6 ppm (s). - HRMS: $\text{C}_{26}\text{H}_{26}\text{S}_2$: calcd.: 402.147; found: 402.147.

Dithiacyclophane 20: According to the above general procedure was coupled **10b** (0.60 g, 2 mmol) with *m*-xylylene dibromide (**11**, 0.53 g, 2 mmol). The crude product was purified by silica gel column chromatography with dichloromethane/hexane (2:3, v/v) to provide **20** as a colorless powder (0.64 g, 80%), m. p. 224 °C. - ^1H NMR: δ = 2.52–2.62 (AA'BB', 4 H), 2.84–3.04 (CC'DD', 4 H), 3.36 (d, J = 12.3 Hz, 2 H), 3.738, 3.774 (AB

system, $J = 13.3$ Hz, 4 H), 3.86 (d, $J = 12.3$ Hz, 2 H), 6.26 (br. s, 2 H), 6.36 (d, $J = 7.7$ Hz, 2 H), 6.41 (dd, $J = 7.7$, 1.8 Hz, 2 H), 7.11 (t, $J = 1.8$ Hz, 1 H), 7.45 (2 H), 7.55 ppm (1 H) (br. A₂B, $J = 7.5$ Hz). - ¹³C NMR: $\delta = 31.5$ (t, 2 C), 34.6 (t, 2 C), 34.9 (t, 2 C), 37.3 (t, 2 C), 128.4 (d, 2 C), 130.5 (d, 1 C), 132.54 (d, 2 C), 132.60 (d, 1 C), 132.72 (d, 2 C), 135.2 (d, 2 C), 135.4 (s, 2 C), 137.3 (s, 2 C), 138.6 (s, 2 C), 139.1 ppm (s, 2 C). - HRMS: C₂₆H₂₆S₂: calcd.: 402.147; found: 402.147.

Dithiacyclophane 21: According to the above general procedure was coupled **10b** (0.60 g, 2 mmol) with *p*-xylylene dibromide (*p*-**11a**, 0.53 g, 2 mmol). The crude product was purified by silica gel column chromatography with dichloromethane/hexane (2:3, v/v) to provide **21** as a colorless powder (0.25 g, 32%), m. p. 221 °C (decomp.). - ¹H NMR: $\delta = 2.61$ (d, $J = 11.7$ Hz, 2 H), 2.81-2.99 (m, 6 H), 2.84 (d, $J = 11.7$ Hz, 2 H), 3.23-3.35 (m, 2 H), 3.89, 3.95 (AB system, $J = 12.1$ Hz, 4 H), 6.18 (br s, 2 H), 6.39 (dd, $J = 7.7$, 1.8 Hz, 2 H), 6.45 (d, $J = 7.7$ Hz, 2 H), 7.23, 7.76 ppm (AA'XX', $N = 2.3$ Hz, 4 H). - ¹³C NMR: $\delta = 32.5$ (t), 34.2 (t), 34.8 (t), 36.6 (t), 130.3 (d), 130.4 (d), 132.6 (d), 132.9 (d), 135.0 (s), 135.4 (d), 136.9 (s), 138.8 (s), 139.0 (s) ppm. - HRMS: C₂₆H₂₆S₂: calcd.: 402.147; found: 402.147.

Coupling of 10b (0.30 g, 1.0 mmol) **and 10a** (0.40 g, 1.0 mmol): under the above conditions after chromatography with dichloromethane/hexane (3:7) the thiacyclophane **14** was obtained

(0.21 g, 80%, with respect to the thiol **10b**): spectroscopic data as above.

Repeating the experiment (same concentrations of coupling partners **10a** and **10b**) in the presence of **cesium hydroxide** (0.38 g, 2.5 mmol) yielded after work-up (column chromatography with dichloromethane/hexane = 2:1 (v/v) the thiacyclophane **14** (0.16 g, 60%) and the dimer **22** (26.0 mg, 5%) as colorless powder, m.p. 195 °C. - ^1H NMR: δ = 2.89–3.10 (m, 12 H), 3.50–3.53 (m, 4 H), 4.37 (d, J = 12.7 Hz, 4 H), 4.94 (d, J = 12.7 Hz, 4 H), 6.26 (dd, J = 7.8, 1.7 Hz, 4 H), 6.35 (d, J = 7.8 Hz, 4 H), 6.45 ppm (d, J = 1.7 Hz, 4 H). - ^{13}C NMR: δ = 137.6, 136.0, 134.6, 134.4, 134.3, 132.7, 37.4, 35.0, 34.6 ppm. - MS (EI, 70 eV): m/z (%) = 532 (6, M^+), 266 (20), 147 (50), 104 (100). - $\text{C}_{36}\text{H}_{36}\text{S}_2$ (532.80): calcd.: C 81.16, H 6.81, S 12.03; found: C 81.19, H 6.80, S 12.06.

Disulfone 23 from disulfide 20: To a solution of the cyclophane **20** (1.2 g, 3.0 mmol) in a 1:1-mixture of dichloromethane/glacial acetic acid (300 mL) was added at 0 °C under stirring a solution of *m*-chloroperbenzoic acid (MCPBA, 70% purity, 3.52 g, 14.3 mmol) in glacial acetic acid (100 mL). The reaction mixture was slowly warmed to room temp., and stirred for 3 d. The precipitated disulfone was removed by filtration, washed with trichloromethane, and dried: 1.26 g (90%) of colorless crystals, m. p. 282 °C. - IR (KBr): $\nu(\text{tilde})$ = 1320 and 1115 cm^{-1} (vs, SO_2). - ^1H NMR (DMSO-d_6): δ = 2.50–2.52 (m, 4 H), 2.96 (m, 4 H), 3.96–4.18 (m, 4 H), 4.64

(m, 4 H), 6.33 (br. s, 2 H), 6.50 (d, $J = 7.7$ Hz, 2 H), 6.57 (dd, $J = 7.7, 1.3$ Hz, 2 H), 7.62–7.67 (m, 3 H), 7.98 ppm (br. s, 1 H). – ^{13}C NMR: $\delta = 139.8, 139.3, 135.1, 133.8, 131.9, 131.0, 129.9, 124.7, 61.1, 54.0, 34.2, 31.0$ ppm. – MS (EI, 70 eV): m/z (%) = 466 (44, M^+), 402 (8), 338 (60), 337 (100), 219 (76), 104 (44). – $\text{C}_{26}\text{H}_{26}\text{O}_4\text{S}_2$ (466.61): calcd.: C 66.93, H 5.62, S 13.74; found: C 66.91, H 5.63, S 13.72.

Diene 24: To a suspension of the disulfone **23** (0.47 g, 1.0 mmol) in dichloromethane/trichloromethane (50 mL, 2:1, v/v) was added carbon tetrachloride (0.5 mL), aqueous sodium hydroxide solution (25 mL, 10%), and cetyltrimethylammonium chloride (0.18 g, 0.50 mmol). The mixture was heated at reflux with vigorous stirring for 3 d. After cooling to room temp., the organic phase was separated, dried, and the solvent was removed in vacuo. Column chromatography (silica gel; hexane/dichloromethane = 8:2) yielded **24** (30.0 mg, 9%) as colorless crystals, m. p. 120 °C (decomp.) – ^1H NMR (CD_2Cl_2 ; protons are labeled as in formula **24**): $\delta = 2.42\text{--}2.61$ (m, 2 H), 2.91–3.01 (m, 2 H), 3.09–3.35 (m, 4 H), 5.79 (br. s, 1 H; H^{m}), 5.90), 6.14 (d, $J = 11.0$ Hz, 1 H; H^{k}), 6.66 (d, $J = 11.0$ Hz, 1 H; H^{j}), 6.72 (dd, $J = 7.3, 1.4$ Hz, 1 H; H^{i}), 6.77 (d, $J = 7.3$ Hz, 1 H; H^{h}), 6.80 (br. d, $J = 7.3$ Hz, 1 H; H^{g}), 6.85 (dd, $J = 7.3, 1.6$, 1 H; H^{f}), 6.94 (br. s, 1 H; H^{e}), 7.10 (br. d, $J = 7.7$ Hz, 1 H; H^{d}), 7.17 (br. d, $J = 7.7$ Hz, 1 H; H^{c}) 7.32 (t, $J = 7.7$ Hz, 1 H; H^{b}), 7.51 ppm (td, $J = 1.8, 0.6$ Hz, 1 H; H^{a}). – ^{13}C NMR (CD_2Cl_2): $\delta = 34.7$ (t), 34.95 (t), 35.04 (t), 35.08 (t),

125.7 (d), 126.5 (d), 129.0 (d), 129.3 (d), 130.0 (d), 130.3 (d), 130.6 (d), 131.2 (d), 132.3 (d), 133.9 (d), 135.2 (d), 135.5 (s), 136.0 (s), 136.2 (d), 136.9 (s), 138.11 (s), 138.16 (s), 138.4 (d), 138.9 (s), 139.0 (s, 2 C), 139.3 (s) ppm. – MS (EI, 70 eV): m/z (%) = 370 (20, M^+), 368 (56, M^+), 333 (100), 205 (45). – HRMS: calcd. 368.133, found 368.133. – $C_{26}H_{21}Cl$ (368.90): calcd.: C 84.65, H 5.74, Cl 9.61; found: 84.69, H 5.74.

Flash vacuum pyrolysis of 23: In a flash vacuum pyrolysis apparatus disulfone **23** (0.47 g, 1.0 mmol) was pyrolyzed at 500–540 °C and 0.2 torr. The pyrolysate was frozen out on a cold finger and the product mixture dissolved in dichloromethane. Chromatography (silica gel; dichloromethane/hexane = 1:9) yielded ca. 80 mg (22%) of **26**. – NMR: Mixture displaying methyl signals at δ_H = 2.13 and 2.25 ppm and at δ_C = 18.9 and 21.0 ppm. – MS (EI, 70 eV): m/z (%) = 340 (100, M^+), 249 (8), 235 (22), 221 (56), 119 (50). – $C_{26}H_{28}$ (340.50): calcd.: C 91.71, H 8.29; found 91.74 H 8.30.

X-Ray structure determinations

Crystals were mounted in inert oil on glass fibres and transferred to the cold gas stream of the diffractometer (Siemens P4 for **21**, otherwise Stoe STADI-4). Intensity data were recorded using monochromated Mo $K\alpha$ radiation (λ = 0.71073 Å). Absorption corrections were not performed. The structures were refined anisotropically on F^2 using the

program SHELXL-97 [20]. Hydrogens were included using a riding model starting from calculated positions. *Special features:* Compound **14** crystallizes in the non-centrosymmetric space group $Pna2_1$. The structure was refined as an enantiomeric twin, with a volume ratio of 0.58/0.42(10) for the two components. Compound **21** crystallizes as a cyclohexane $\frac{1}{4}$ -solvate; the solvent molecule adopts two alternative positions around an inversion centre. Dimensions of disordered groups should be interpreted with caution. The crystallographic data of **14**, **19**, **20** and **21** are collected in Table. 1

Table 1 here please

Table 1. Crystallographic data.

Compound	14	19	20	21 · $\frac{1}{4}$ C ₆ H ₁₂
Formula	C ₁₈ H ₁₈ S	C ₂₆ H ₂₆ S ₂	C ₂₆ H ₂₆ S ₂	C _{27.5} H ₂₉ S ₂
<i>M_r</i>	266.38	402.59	402.59	423.63
Habit	colourless block	colourless block	colourless tablet	colourless needle
Crystal size (mm)	0.7 × 0.6 × 0.4	0.4 × 0.4 × 0.3	0.4 × 0.4 × 0.2	1.0 × 0.2 × 0.1
Crystal system	orthorhombic	monoclinic	monoclinic	monoclinic
Space group	$Pna2_1$	$P2_1/c$	$P2_1/c$	$P2_1/c$
Temperature (°C)	−130	−130	−130	−100
Cell constants:				
<i>a</i> (Å)	17.285(5)	8.790(2)	17.927(4)	8.663(2)

b (Å)	8.230(2)	13.179(3)	7.831(2)	32.081(6)
c (Å)	9.159(2)	17.554(4)	15.020(3)	15.827(3)
α (°)	90	90	90	90
β (°)	90	90.93(2)	106.10(3)	90.17(2)
γ (°)	90	90	90	90
V (Å ³)	1302.9	2033.2	2025.8	4398.7
Z	4	4	4	8
D_x (Mg m ⁻³)	1.358	1.315	1.320	1.279
μ (mm ⁻¹)	0.23	0.27	0.27	0.25
$F(000)$	568	856	856	1808
$2\theta_{\max}$	50	50	50	50
Refl. measured	2305	3715	3857	9761
Refl. indep.	2305	3588	3574	7724
R_{int}	—	0.033	0.023	0.035
Parameters	173	253	253	560
Restraints	1	0	0	9
$wR(F^2, \text{all refl.})$	0.094	0.128	0.111	0.109
$R(F, >4\sigma(F))$	0.035	0.052	0.051	0.050
S	1.06	1.03	1.03	0.85
max. $\Delta\rho$ (e Å ⁻³)	0.16	0.24	0.31	0.26

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682 Table 1: Crystallographic data of **14**, **19**, **20**, and **21**.

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685 Crystallographic data have been deposited with the Cambridge

686 Crystallographic Data Centre as supplementary publications no.

687 CCDC-1063540 (**14**), -1063541 (**19**), -1063537 (**20**), -1063536

688 (21). Copies of the data can be obtained free of charge from
689 www.ccdc.cam.ac.uk/data_request/cif.

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Draft