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Synthesis of annularly functionalized cyclophanes

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Abstract—Friedel–Crafts reaction of *m*- and *p*-benzenedicarboxylic acid chlorides with toluene gave diketones. The dicarbonyl dibromides, obtained by NBS bromination of diketones were coupled with various dithiols and dihydroxy benzenes to give cyclophanes incorporating two carbonyl groups. The dicarbonyl dibromide, derived from isophthalic acid chloride was converted into dithiol, which on coupling with the same dibromide afforded cyclophane incorporating four carbonyl groups. The $NaBH_4$ reduction of the tetraketone cyclophane in methanol gave the tetraalcohol derivative.

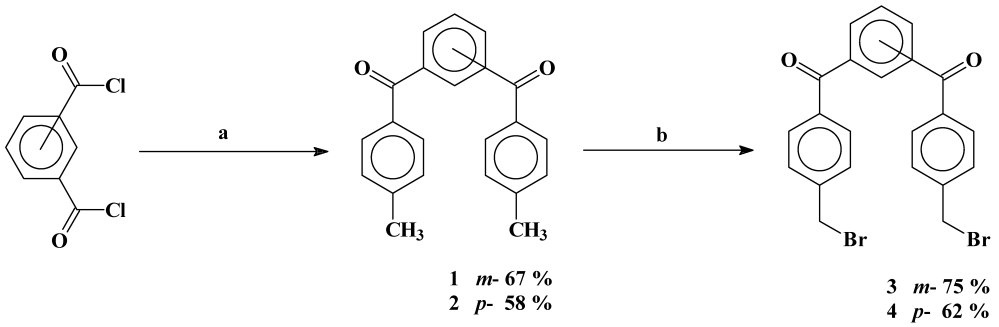
1. Introduction

Cyclophanes[1] are an important class of bridged aromatic compounds, which have received considerable attention in recent years due to their ability to form host–guest complex with neutral molecules as well as ionic species. Synthetic cyclophanes can mimic enzymes and biological systems.[2] Intra-annularly functionalized cyclophanes provide a hydrophilic cavity to the guest molecules.[3] Synthesis of cyclophanes with 1,1′-binaphthol[4] cationic pyridinophanes,[5] benzimidazolophanes[6] and benzotriazolophanes[7] were some of the earlier reports from our laboratory. Herein, we report the synthesis of cyclophanes possessing carbonyl units, which are particularly interesting because the carbonyl groups can be converted into many synthetically useful functional groups.

2. Results and discussion

Friedel–Crafts reaction of isophthalic and terephthalic acid chlorides with toluene in the presence of anhydrous $AlCl_3$ gave diketones **1**[4a] and **2**[8] in good yield. Two-fold radical bromination of diketones **1** and **2** with NBS in CCl_4 in the presence of benzoyl peroxide gave dicarbonyl dibromides **3**[4a] and **4** in 75 and 62%, respectively (Scheme 1).

In order to check the synthetic applicability of the dicarbonyl dibromides for the synthesis of cyclophanes, dibromide **3** was treated with *p*-xylenyl dithiol. Treatment of equimolar amounts of dibromide **3** and *p*-xylenyl dithiol in EtOH/benzene under high dilution conditions in nitrogen at rt for 18 h afforded the cyclophane **5a** in 63% yield. The IR spectrum of cyclophane **5a** showed a carbonyl stretching



1 *m*- 67 %
2 *p*- 58 %

3 *m*- 75 %
4 *p*- 62 %

Scheme 1. Preparation of dicarbonyl dibromides. *Reagents and conditions*: (a) $AlCl_3$, toluene, 0°C, 8 h; (b) 2.2 equiv. NBS, CCl_4, Bz_2O_2, 24 h.

Keywords: isophthalic acid; carbonyl cyclophanes; bromination.

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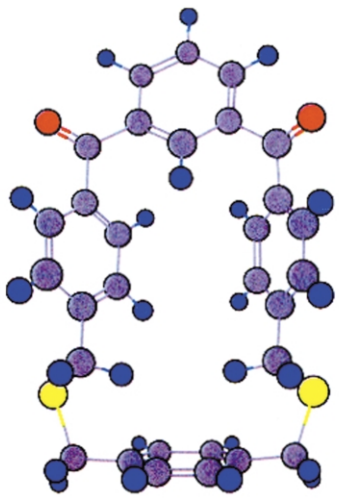


Figure 1. Energy minimized structure of cyclophane **5a**.

frequency at 1660 cm^{-1}. The ^1H NMR spectrum of cyclophane **5a** showed two singlets at δ 3.60 and 3.69 corresponding to two benzylic methylene groups. All four hydrogens of the *p*-xylene moiety resonate as a singlet at δ 6.95, which shows that all the xylenyl protons are equivalent. Two doublets were observed at δ 7.30 and 7.74 in the aromatic region along with a multiplet from δ 8.02 to 8.22, which corresponds to the protons of the isophthaloyl group. The ^{13}C NMR spectrum of cyclophane **5a** showed two signals at δ 35.18 and 35.70 for methylene carbons. The carbonyl carbon appeared at δ 194.84 along with ten aromatic carbons. In the mass spectrum, cyclophane **5a** showed M^+ at *m/z* 480, which confirmed the structure of the cyclophane **5a**.

Energy minimization calculation of the cyclophane **5a** by MOPAC method (Fig. 1) showed that the xylenyl benzene ring is planar and orthogonal with respect to the isophthalic acid group. The proof of the structure came from X-ray crystallographic data. XRD studies[9] on cyclophane **5a** also

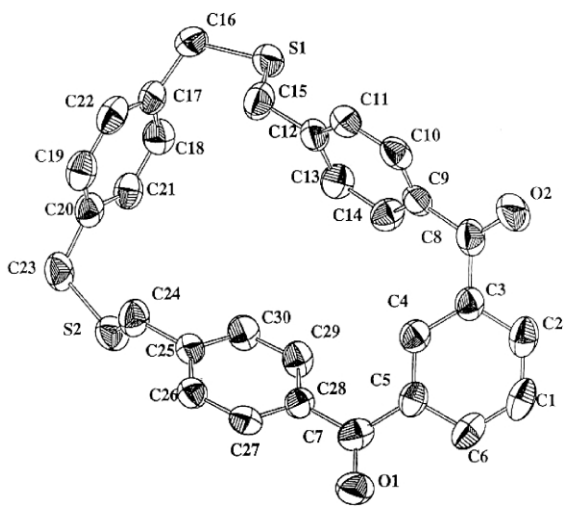


Figure 2. ORTEP diagram of cyclophane **5a**.

revealed that the benzene ring of xylenyl moiety is planar as shown in the ORTEP diagram (Figs. 2 and 3).

Using the same methodology, coupling of *m*- and *o*-xylenyl dithiols with dibromide **3** gave cyclophanes **5b** and **5c** in 52 and 55% yield, respectively. Cyclophanes **5b** and **5c** were characterized by spectroscopic and analytical data (Scheme 2).

Attention was then focused on the synthesis of cyclophanes with ethereal linkages by coupling of *m*-, *p*- and *o*-dihydroxy benzenes with dibromide **3**. Treatment of equimolar amounts of the dibromide **3** with resorcinol in acetone in the presence of K_2CO_3 at rt for 120 h gave cyclophane **6a** in excellent yield (82%). The IR spectrum of the cyclophane **6a** showed a band at 1659 cm^{-1} due to a carbonyl group. The proton NMR spectrum of the cyclophane **6a** showed a singlet at δ 5.20 corresponding to the benzylic protons. Two doublets were observed at δ 7.35 and 7.55. The protons of the isophthaloyl group appeared in the deshielded region. A doublet of doublets at δ 8.23, a triplet at δ 7.68 and a singlet at δ 7.51 were observed for the isophthaloyl group. The resorcinol protons appeared in the upfield region. A doublet of doublets at δ 6.55, a triplet at 7.05 and a triplet at 6.40 were observed. The ^{13}C NMR of the cyclophane **6a** showed signals at δ 69.64 for benzylic carbon and at 195.32 for carbonyl carbon in addition to eleven aromatic carbons. The cyclophane **6a** showed molecular ion peak at *m/z* 420 in mass spectrum, which further supports the proposed structure.

Similarly, equimolar amounts of catechol and hydroquinone, when treated individually with an equimolar amount of the dibromide **3**, in the presence of K_2CO_3 in acetone, gave cyclophanes **6b** and **6c** in 52 and 48% yield, respectively, which were characterized by spectroscopic and analytical data (Scheme 2).

Energy minimization calculations on cyclophane **8** (Fig. 4) and **9** (Fig. 5) by the MOPAC (PM3) method revealed that the cavity is large enough to accommodate molecules like durene (Fig. 6) and TCNE (Fig. 7) and hence it is of interest to synthesize cyclophane **8** and **9** by taking the advantage of the favorable angular nature of *m*-terphenyl. The angular nature and rigidity of the *m*-terphenyl provide larger non-collapsible cavity in cyclophane. Hence, coupling of *m*-terphenyl dithiol[10] with dicarbonyl dibromides might result in the formation of cyclophanes with a non-collapsible larger cavity. Reaction of equimolar amounts of *m*-terphenyl dithiol with dibromides **3** and **4** individually, under high dilution conditions gave the cyclophanes **8** and **9** in 48 and 43% yield, respectively (Scheme 3).

Encouraged by the facile synthesis of cyclophanes by coupling the dithiols with dibromides, focus was oriented in the direction of synthesis of cyclophanes with four carbonyl groups. The reduction of such tetracarbonyl cyclophanes should result in the formation of the corresponding tetraalcohol, which would be a potential hexadendate receptor. For example, cyclophane **12** has four OH groups and two S atoms and energy minimization calculations show that the molecule can fold up and create a suitable geometry for octahedral complexation. The dicarbonyl dithiol **10**,

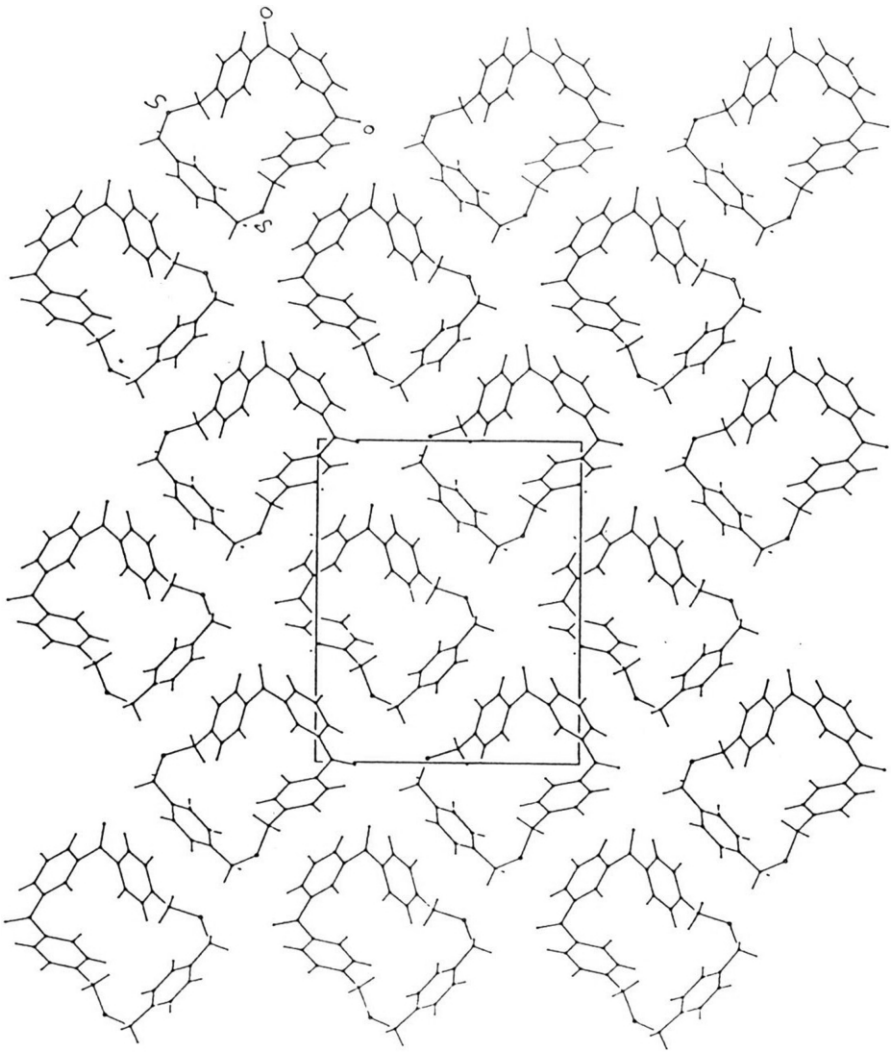
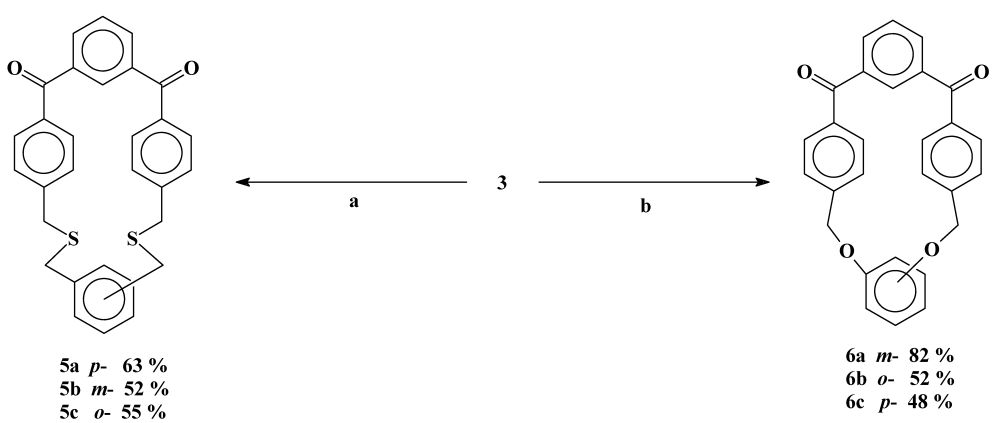


Figure 3. Unit cell packing of crystal structure of cyclophane **5a**.

required for the coupling reactions, was prepared from the dibromide **3**. The thiouronium salt, derived from **3** and thiourea, on hydrolysis with KOH in THF/H_2O gave dithiol **10**. Coupling of the dicarbonyl dithiol **10** with dibromide **3** under the usual conditions afforded the novel tetracarbonyl cyclophane **11** in 48% yield. Reduction of the cyclophane **11** with $NaBH_4$ in methanol at 0°C for 1 h gave the tetraalcohol **12** in 45% yield (Scheme 4).



Scheme 2. Synthesis of cyclophanes by coupling of dicarbonyl dibromides with various dithiols and dihydroxy benzenes. *Reagents and conditions*: (a) *p*-, *m*-, *o*-xylenyl dithiol, KOH, EtOH, benzene, rt, 18 h; (b) resorcinol/catacol and/hydroquinone, K_2CO_3, acetone, rt, 120 h.

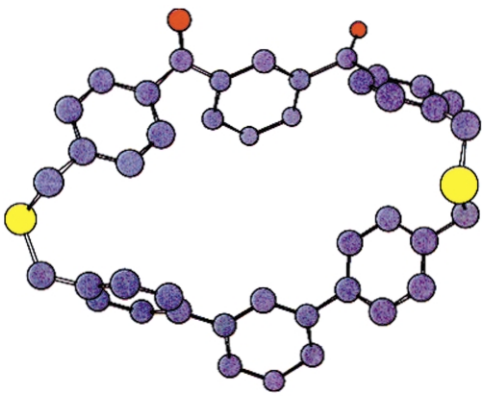


Figure 4. Energy minimized structure of cyclophane **8**.

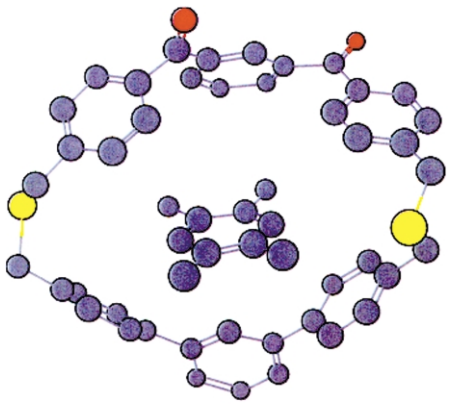


Figure 6. Structure of complex of cyclophane **8** with durene.

3. Energy minimization calculations and complexation studies

Energy minimization calculations based on PM3 by MOPAC were performed for cyclophanes **8** and **9**. The heat of formation of cyclophanes **8** and **9** are found to be 362.34 and 361.09 kJ, respectively. The cavity sizes of cyclophane **8** and **9** are approximately 7.5×13 and 8×13.5 Å, respectively and can easily form complexes with small molecules like TCNE, TCNQ, mesitylene and durene. Steric energies based on MM2 energy minimization for complexes of cyclophane **8** with TCNE, TCNQ, mesitylene and durene are 19.27, 2.46, −7.77 and −15.74 kJ which indicates that durene can form the strongest complex with cyclophane **8**.

The heat of formation of cyclophanes **11** and **12** are 212.66 and −50.13 kJ, respectively and energy minimization calculations by MOPAC (PM3) methods indicate that cyclophane **12** folds up and creates an favorable cavity for octahedral complexation.

Complexation studies were carried out in $CH_3CN/CHCl_3$ (1:4) for cyclophanes **6a–c** with TCNE. The UV–visible spectra of the CT complexes of cyclophanes **6a–c** with TCNE show two absorbance maxima at 416 and 398 nm. A plot of D_o/A against $1/A_o$ was linear. From slope and intercept, the K_a values were determined using Benesi–Hildebrand method.[11] The K_a was found to be 59, 44 and 47 M^{-1} for CT complexes of cyclophanes **6a-c** with TCNE, respectively.

4. Conclusion

In conclusion, we have developed a simple synthetic route for cyclophanes incorporating carbonyl units. The main advantage of carbonyl functionality is that it can be reduced to alcohol, hence, hydrophilic cavity could be generated and complexing ability of the cyclophane could be increased. In fact, we have reduced cyclophane **11** with $NaBH_4$ and the resulting tetraalcohol has been characterized. Complexation of cyclophane **11** with various metal ions and other guest molecules are under investigation.

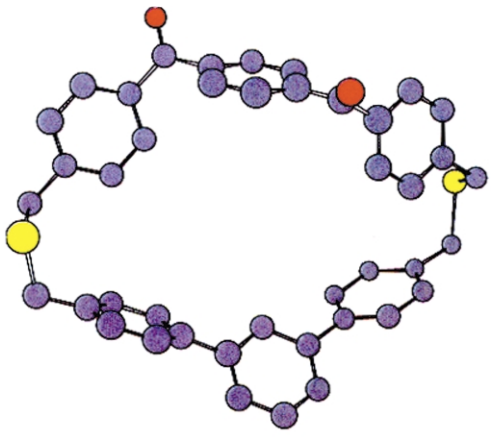


Figure 5. Energy minimized structure of cyclophane **9**.

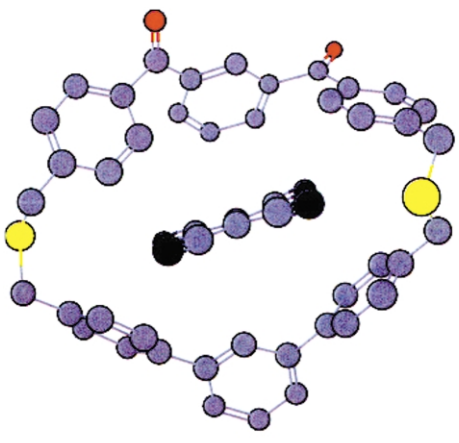
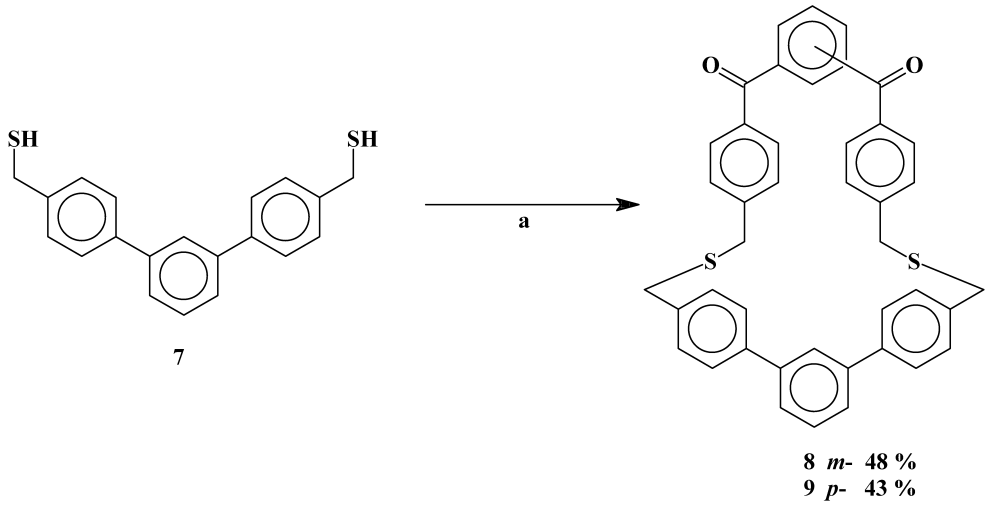
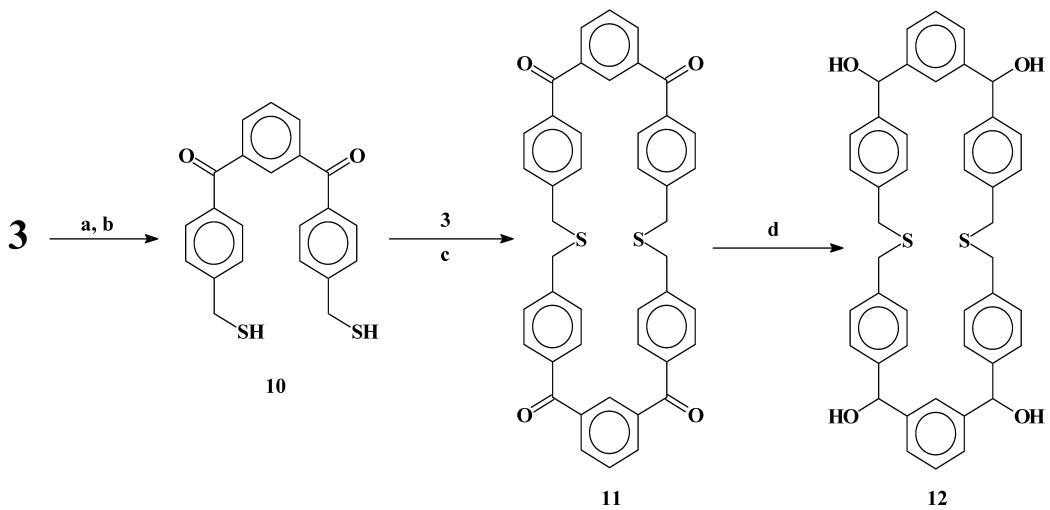


Figure 7. Structure of complex of cyclophane **8** with TCNE.



Scheme 3. Synthesis of cyclophanes with larger cavity. *Reagents and conditions*: (a) **3/4**, KOH, EtOH, benzene, rt, 18 h.



Scheme 4. Synthesis of tetracarbonyl cyclophane and its reduction to tetraalcohol cyclophane. *Reagents and conditions*: (a) thiourea, THF, 60°C, 12 h, 92%; (b) KOH, THF, H_2O, reflux, 12 h, 69%; (c) KOH, EtOH, benzene, rt, 24 h, 48%; (d) $NaBH_4$, MeOH, 0°C, 1 h, 45%.

5. Experimental

5.1. General

All melting points are uncorrected. The IR spectra were recorded using Shimadzu FT-IR 8300 Infrared Spectrometer. The ^1H and ^{13}C NMR spectra were recorded on Jeol GSX 400 NMR Spectrometer at 400 and 100.4 MHz, respectively or on a Varian EM 390 NMR spectrophotometer at 90 MHz with TMS as internal standard. The mass spectra were recorded using Jeol mass spectrometer (EI, 70 eV). THF was freshly distilled from Na/benzophenone ketyl before use. The xylenyl dithiols were prepared by the known literature procedure. The column chromatography was performed using silica gel (Acme, 100–200 mesh). The organic extracts were dried using anhydrous sodium sulfate. 1,3-Ditoluoylbenzene (**1**[4a]) and 1,4-Ditoluoylbenzene (**2**[8]) were prepared according to the literature procedure. 4,4″-Bis(bromomethyl)-1,3-dibenzoylbenzene (**3**[4a]) and 4,4″-Bis(bromomethyl)-1,4-dibenzoylbenzene (**4**) were prepared by two fold radical bromination of **1** and **2** using NBS.

5.1.1. Dibromide 4. Dibromide **4** was obtained by the radical bromination of **2** with 2 equiv. of NBS using similar procedures reported earlier.[4a] Yield 62%; mp 138–139°C (from $CHCl_3$+hexane); IR (cm^{-1}) 1657 (C=O); ^1H NMR ($CDCl_3$) 4.65 (S, 4H);7.52 (d, 4H, J=8.3 Hz); 7.80 (d, 4H, J=8.3 Hz); 8.10 (S, 4H); ^{13}C NMR ($CDCl_3$) 34.83, 125.56, 127.78, 137.87, 144.89, 197.37. Anal. calcd for $C_{22}H_{16}Br_2O_2$: C, 55; H, 3.42, found: 55.61; H, 3.25.

5.2. General procedure for assembling cyclophanes from the corresponding dibromides and dithiols

A solution containing equimolar amounts (1 mmol) of the appropriate dibromide and the dithiol in nitrogen degassed benzene (200 mL) was added dropwise over 8–10 h to a well stirred solution of KOH (0.2 g) in 95% ethanol (600 mL). After the addition, the reaction mixture was

stirred for an additional 8 h and evaporated to dryness. The crude product was purified over SiO_2 by column chromatography using $CHCl_3$/hexane (1:1).

5.2.1. Cyclophane 5a. Colourless solid; yield 63%; mp 214–215°C; IR (cm^{-1}) 1660 (C═O); ^1H NMR ($CDCl_3$) 3.60 (s, 4H); 3.69 (s, 4H); 6.95 (s, 4H), 7.30 (d, 4H, *J*=8.3 Hz); 7.74 (d, 4H, *J*=8.3 Hz); 8.20–8.22 (m, 4H); ^{13}C NMR ($CDCl_3$) 35.18, 35.70, 129.08, 130.10, 130.29, 132.16, 133.31, 135.29, 136.73, 137.09, 141.23, 143.86, 194.84; *m/z* 480 (89, M^+), 314 (62), 141 (55), 137 (57), 135 (66), 134 (70), 105 (70), 91 (80). Anal. calcd for $C_{30}H_{24}O_2S_2$: C, 74.97; H, 5.03. Found: C, 74.91, H, 5.01.

5.2.2. Cyclophane 5b. Colourless solid; yield 52%; mp 184–185°C; IR (cm^{-1}) 1653 (C═O); ^1H NMR ($CDCl_3$) 3.44 (s, 4H); 3.66 (s, 4H); 6.46 (s, 1H); 7.29 (d, 2H, *J*=4 Hz); 7.47 (d, 4H, *J*=8.3 Hz); 7.62 (s, 1H); 7.83 (d, 4H, *J*=8.3 Hz); 8.01 (s, 1H); 8.23 (d, 2H, *J*=4 Hz); 8.33 (s, 1H); ^{13}C NMR ($CDCl_3$) 35.28, 35.71, 128.21, 129.09, 130.21, 131.22, 132.46, 133.41, 135.29, 136.02, 136.37, 137.09, 141.31, 143.66, 195.38; *m/z* 480 (91, M^+), 314 (49), 136 (65), 134 (60), 104 (100), 91 (70), 90 (41). Anal. calcd for $C_{30}H_{24}O_2S_2$: C, 74.97; H, 5.03. Found: C, 74.87, 5.00.

5.2.3. Cyclophane 5c. Colourless solid; yield 55%; mp 202–205°C; IR (cm^{-1}) 1643 (C═O); ^1H NMR ($CDCl_3$) 3.56 (s, 4H); 3.77 (s, 4H); 7.38 (d, 4H, *J*=8.3 Hz); 7.72 (d, 4H, *J*=8.3 Hz); 8.23 (m, 8H); ^{13}C NMR ($CDCl_3$) 35.13, 35.67, 128.77, 129.23, 131.05, 131.29, 132.14, 133.54, 135.32, 136.73, 137.54, 141.04, 143.66, 195.34; *m/z* 480 (47, M^+), 136 (51), 135 (100), 90 (34), 69 (53). Anal. calcd for $C_{30}H_{24}O_2S_2$: C, 74.97; H, 5.03. Found: 74.92, 4.98.

5.3. General procedure for assembling of cyclophanes from the corresponding dibromide and dihydroxy benzenes

To a solution of the appropriate dibromide (1 mmol) and the respective dihydroxy benzene (1 mmol) in acetone (600 mL) was added anhydrous K_2CO_3 (7.0 g) and the mixture was stirred well at rt for 120 h. The reaction mixture was then filtered and evaporated to give a residue, which was extracted with CH_2Cl_2 (3×100 mL), washed with water (2×100 mL), then with NaOH (2×100 mL, 10%), again with water (2×100 mL), finally with brine (200 mL) and dried. Evaporation of the organic layer afforded the crude product, which was purified over SiO_2 by column chromatography using $CHCl_3$/hexane (1:1).

5.3.1. Cyclophane 6a. Colourless solid; yield 82%; mp 190–191°C; IR (cm^{-1}) 1659 (C═O); ^1H NMR ($CDCl_3$) 5.20 (s, 4H); 6.40 (t, 1H, *J*=4 Hz), 6.55 (dd, 2H, *J*=8.8, 1.95 Hz); 7.05 (t, 1H, *J*=7.8 Hz); 7.35 (d, 4H, *J*=8.3 Hz); 7.51 (s, 1H); 7.55 (d, 4H, *J*=8.3 Hz); 7.68 (t, 1H, *J*=7.8 Hz); 8.23 (dd, 2H, *J*=8.8, 1.95 Hz); ^{13}C NMR ($CDCl_3$) 69.64, 104.99, 110.41, 127.33, 129.60, 129.99, 130.25, 133.54, 135.11, 136.29, 136.87, 141.71, 158.66, 195.32; *m/z* 420 (100, M^+), 392 (24), 256 (9), 197 (20), 165 (14), 156 (23), 119 (25), 90 (30). Anal. calcd for $C_{28}H_{20}O_4$: C, 79.98; H, 4.79. Found: C, 79.85; 4.63.

5.3.2. Cyclophane 6b. Colourless solid; yield 52%; mp 191–193°C; IR (cm^{-1}) 1658 (C═O); ^1H NMR ($CDCl_3$) 5.22 (s, 4H); 6.82–6.96 (m, 4H); 7.15 (d, 4H, *J*=8.3 Hz); 7.58 (s, 1H); 7.76 (d, 4H, *J*=8.3 Hz); 8.26 (m, 3H); ^{13}C NMR ($CDCl_3$) 68.94, 105.19, 111.01, 127.43, 129.61, 129.92, 130.15, 133.55, 135.43, 136.69, 141.41, 158.74, 195.05; *m/z* 420 (60, M^+), 364 (74), 347 (41), 312 (47), 256 (32), 223 (31), 119 (100), 91 (53). Anal. calcd for $C_{28}H_{20}O_4$: C, 79.98; H, 4.79. Found: C, 79.90, H, 4.73.

5.3.3. Cyclophane 6c. Colourless solid; yield 48%; mp 194–195°C; IR (cm^{-1}) 1653 (C═O); ^1H NMR ($CDCl_3$) 5.16 (s, 4H); 6.67 (s, 4H); 7.19 (d, 4H, *J*=8.3 Hz); 7.55 (d, 4H, *J*=8.3 Hz); 7.80 (t, 1H, *J*=7.8 Hz), 7.92 (d, 1H, *J*=7.8 Hz); 8.27 (s, 1H); ^{13}C NMR ($CDCl_3$) 69.64, 105.19, 110.32, 128.36, 129.87, 131.24, 133.75, 135.41, 136.73, 141.72, 158.54, 195.43; *m/z* 420 (88, M^+), 327 (28), 312 (100), 284 (34), 256 (44), 156 (35), 131 (35), 119 (64), 90 (69). Anal. calcd for $C_{28}H_{20}O_4$: C, 79.98; H, 4.79. Found: C, 79.89; H, 4.66.

5.4. General procedure for assembling cyclophanes from *m*-terphenyl dithiol

A solution containing equimolar amounts (1 mmol) of the appropriate dibromide and *m*-terphenyl dithiol in nitrogen degassed benzene (200 mL) was added dropwise over 8–10 h to a well stirred solution of KOH (0.2 g) in 95% ethanol (600 mL). After the addition, the reaction mixture was stirred for an additional 8 h and evaporated to dryness. The crude product was purified over SiO_2 by column chromatography using $CHCl_3$/hexane (2:1).

5.4.1. Cyclophane 8. Colourless solid; yield 48%; mp 203–204°C; IR (cm^{-1}) 1656 (C═O); ^1H NMR ($CDCl_3$) 3.69 (s, 4H), 3.71 (s, 4H), 7.06–7.97 (m, 24H); ^{13}C NMR ($CDCl_3$) 35.42, 37.27, 119.54, 125.77, 126.03, 126.51, 126.73, 127.31, 128.77, 129.11, 129.45, 129.71, 130.43, 136.96, 137.91, 139.92, 141.22, 143.97, 195.24; *m/z* 632 (20, M^+), 376 (54), 312 (47), 256 (41), 223 (17), 119 (100), 91 (35). Anal. calcd for $C_{42}H_{32}O_2S_2$: C, 79.71; H, 5.10. Found: C, 79.84; 4.99.

5.4.2. Cyclophane 9. Colourless solid; yield 43%; mp 192–194°C; IR (cm^{-1}) 1660 (C═O); ^1H NMR ($CDCl_3$) 3.69 (s, 4H), 3.73 (s, 4H), 7.12–8.02 (m, 24H); ^{13}C NMR ($CDCl_3$) 36.75, 37.12, 119.48, 125.74, 126.31, 126.63, 127.37, 128.54, 129.51, 129.65, 129.71, 130.87, 136.72, 138.94, 139.07, 141.52, 143.79, 195.35; *m/z* 632 (17, M^+), 376 (45), 320 (23), 312 (56), 256 (63), 223 (27), 119 (100), 91 (54). Anal. calcd for $C_{42}H_{32}O_2S_2$: C, 79.71; H, 5.10. Found: C, 79.62; H, 5.22.

5.4.3. Synthesis of dithiol 10. A stirred solution of dibromide **3** (10 mmol) and thiourea (22 mmol) in THF (40 mL) was heated at reflux for 12 h. The mixture was cooled, and the precipitated thiouronium salt was filtered and dried. The salt was dissolved in H_2O/THF (120 mL) under nitrogen and KOH (1.0 g) was added. The reaction mixture was refluxed under nitrogen for 12 h, cooled and carefully quenched with a minimum amount of dil. HCl (4 M, 40 mL). The solvent was removed in vacuo and the crude product was purified over SiO_2 by column

chromatography using $CHCl_3$/hexane (1:2) to give dithiol **10** as a colourless solid; yield 69%; mp 140–142°C; IR (cm^{-1}) 1660 (C═O); ^1H NMR ($CDCl_3$) 1.72 (t, 2H, *J*=8.8 Hz); 3.68 (d, 4H, *J*=8.8 Hz); 7.31 (d, 4H, *J*=8.3 Hz); 7.48 (s, 1H); 7.65 (d, 4H, *J*=8.3 Hz); 7.84 (d, 2H, *J*=4 Hz); 8.06 (s, 1H). Anal. calcd for $C_{22}H_{18}O_2S_2$ (378.07): C, 69.81; 4.79. Found: C, 69.66; H, 4.82.

5.4.4. Cyclophane 11. Treatment of equimolar amounts of dibromide **3** (1 mmol) with dithiol **10** (1 mmol) as described above for assembling cyclophanes from dithiols, followed by column purification of the crude product over SiO_2 using $CHCl_3$/hexane (3:1) afforded tetraketone cyclophane **11** as colourless solid; yield 48%; mp 203–205°C; IR (cm^{-1}) 1656 (C═O); ^1H NMR ($CDCl_3$) 3.68 (s, 8H); 7.29 (d, 8H, *J*=8.3 Hz); 7.47 (d, 8H, *J*=8.3 Hz); 7.78–7.99 (m, 6H); 8.17 (s, 2H); ^{13}C NMR ($CDCl_3$): 35.44, 127.24, 128.94, 129.07, 130.44, 133.37, 136.02, 137.86, 144.03, 195.52; *m/z* 688 (12, M^+), 376 (29), 312 (37), 226 (14), 119 (100), 91 (45). Anal. calcd for $C_{44}H_{32}O_4S_2$: C, 76.72; H, 4.68. Found: C, 76.53; H, 4.54.

5.4.5. Reduction of cyclophane 11. A solution of cyclophane 11 (0.032 g, 0.5 mmol) in methanol (20 mL) was treated with $NaBH_4$ (0.040 g, 1 mmol) at 0°C for 1 h. The reaction mixture was stirred at rt for further 6 h, after which dil. HCl (4 M, 2 mL) was added. The precipitate formed was filtered off and the filtrate was evaporated to dryness in vacuo to give a residue, which was purified over SiO_2 using column chromatography using $CHCl_3$/hexane (3:1) to give cyclophane **12** as colourless solid; yield 45%; mp 224–226°C; IR (cm^{-1}) 3340 (OH); ^1H NMR ($CDCl_3$) 3.47 (s, 8H); 4.40 (bs, 4H, exchanged with D_2O); 7.17–7.78 (m, 24H); ^{13}C NMR ($CDCl_3$) 34.32, 68.02, 117.21, 123.58, 127.05, 129.74, 131.27, 133.25, 134.86, 136.08; *m/z* 696 (8, M^+), 378 (14), 315 (17), 271 (11) 208, (9), 118 (30), 105 (100), 89 (22), 77 (36). Anal. calcd for $C_{44}H_{40}O_4S_2$: C, 75.83; H, 5.79. Found: C, 75.68; H, 5.61.

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