

Two New Cyclophanes with Face-to-Face Arene Rings

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The electronic interactions between aryl rings held in a face-to-face arrangement have interested chemists for many years.¹ We describe here short syntheses of two new cyclophanes of this type, 4 and 10.

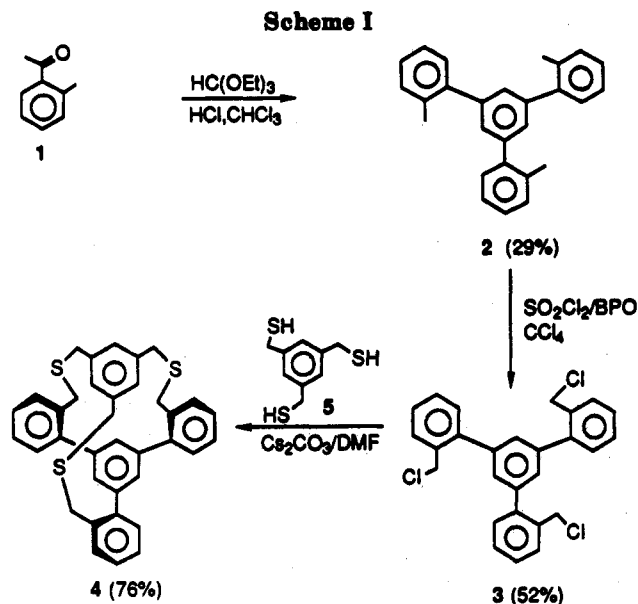
The route to 4 is outlined in Scheme I. Trimerization of 2-methylacetophenone (1)² with ethyl orthoformate and HCl in chloroform³ afforded the previously unknown 1,3,5-tris(2'-methylphenyl)benzene (2), mp 129–130 °C, in modest yield. The structure of 2 was clear from its NMR spectra, particularly the ¹³C spectrum which showed one aliphatic and eight aryl carbons as required. Side-chain chlorination of 2 with 3 equiv of sulfuryl chloride and benzoyl peroxide (BPO) gave tris(chloromethyl) derivative 3, mp 154 °C, in good yield. The ¹H NMR spectrum of 3 showed a singlet (δ 4.67) for the methylene protons, and the ¹³C spectrum again showed one aliphatic and eight aryl carbons as required. Coupling of 3 with 1,3,5-tris(mercaptomethyl)benzene (5) under high dilution, using Cs₂CO₃/DMF as the base, gave the desired 4, mp 221–222 °C, in remarkably high yield. Once the first displacement occurs, the remaining functionalities are ideally located to complete the triple ring closure; no polymer is formed.

The structure of 4 was clear from its NMR spectra. The ¹H spectrum showed singlets for the two sets of methylene protons (δ 3.56, 3.65, 6 H each) and for the two sets of protons on the face-to-face aryl rings (δ 6.998, 7.015, 3 H each), and the rigidity of the structure was indicated by the ABCD pattern of the remaining aryl ring protons (doublet, triplet, doublet, each peak split into a doublet as a consequence of meta coupling). The ¹³C spectrum showed two aliphatic and 10 aromatic carbons, as required by symmetry.

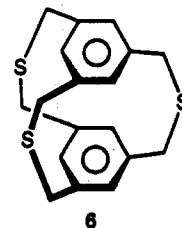
An X-ray determination confirmed the structure (Figure 1).¹² As anticipated, the capping aryl ring (C₁, C₂, C₃, C₂₇, C₂₀, C₁₉) and the central ring (C₉, C₁₀, C₁₁, C₁₂, C₁₃, C₂₈) of the triphenylbenzene moiety lie in nearly parallel planes (the interplanar angle is 18.7°) with a mean interplane distance of only 4.12 Å. When one allows for the π cloud associated with each ring, the rings are essentially "touching". The aryl rings in the linking arms are not twisted at all in the same sense; one ring (C_{14,15,28-31} in the figure) is twisted in the opposite sense of the other two. The dihedral angles between these rings and the central aryl ring range from 46 to 72°.

* To whom inquiry regarding the X-ray structure of 4 should be directed.
(1) Cram, D. J.; Steinberg, H. *J. Am. Chem. Soc.* 1951, 73, 5691–5704.
Cristol, S. J.; Lewis, D. C. *Ibid.* 1967, 89, 1476–1483. For pertinent reviews, see: Hopf, H. In *Cyclophanes*; Keehn, P. M., Rosenfeld, S. M., Eds.; Academic Press: New York, 1983; Vol. II, pp 521–572; Misumi, S. *Ibid.* pp 573–628. Knops, P.; Sendhoff, N.; Mekelburger, H.-B.; Vögtle, F. *Top. Curr. Chem.* 1992, 161, 1–36; Ostrowicki, A.; Koepf, E.; Vögtle, F. 37–67; Dohm, J.; Vögtle, F. 69–106. For two recent examples, see: Danks, I. P.; Lane, T. G.; Sutherland, I. O.; Yap, M. *Tetrahedron* 1992, 48, 7679–7688. Takeuchi, M.; Nishimura, J. *Tetrahedron Lett.* 1992, 33, 5563–5566.

(2) Purchased from Aldrich Chemical Company (Cat. No. M2659-3).
(3) Cf.: Hohner, G.; Vögtle, F. *Chem. Ber.* 1977, 110, 3052–3077.



The UV spectrum of 4 is shown in Figure 2, where it is compared with the spectrum of 6.⁴ Clearly there is more interaction between the rings in 6, where they are closer than in 4. The λ_{max} in both compounds are at 218–219 and 240 nm, but the absorptions are more intense with 6.^{5,6}



The synthesis of 10 is outlined in Scheme II. The first step, preparation of tetramethyl-*p*-terphenyl (8) from dibromodiodobenzene (7), employs the tandem aryne technology that we developed earlier.⁷ Side-chain bromination of 8 gave the tetrakis(bromomethyl)-*p*-terphenyl (9) which, with *p*-xylylenedithiol and base, gave the desired 10, mp 313–314 °C. The structural assignment of 10 is based on its spectral properties. The ¹H NMR spectrum showed two singlets for the methylene protons (δ 3.11, 3.55, 8 H each) and singlets for the aryl protons of the 1,4-disubstituted benzene rings (δ 6.99, 7.07, 4 H and 8 H, respectively). The remaining aryl protons (outer rings of the *p*-terphenyl moiety) appeared as a mutually coupled triplet and doublet (δ 7.41, 7.70, 2 H and 4 H, respectively, *J* = 7.5 Hz). The ¹³C spectrum also supported the proposed structure, with two aliphatic carbons and only eight aromatic carbons as required by the molecule's symmetry. Unfortunately the extreme insolubility of 10 made it impossible for us to obtain a single crystal suitable for X-ray study.

(4) Boekelheide, V.; Hollins, R. A. *J. Am. Chem. Soc.* 1970, 92, 3512–3513; 1973, 95, 3201–3208.

(5) It would be desirable to shorten the –CH₂SCH₂– arms to –CH₂CH₂– or –CH=CH– in 4 and 10. Unfortunately, due to retirement (H.H.) we are unable to continue these studies. We encourage others to do so.

(6) Adaptation of Scheme I to 2,6-dimethylacetophenone, to prepare the triply-stacked analog of 4, would also be worthwhile.

(7) Hart, H.; Harada, K.; Du, C.-J. *F. J. Org. Chem.* 1985, 50, 3104–3110.

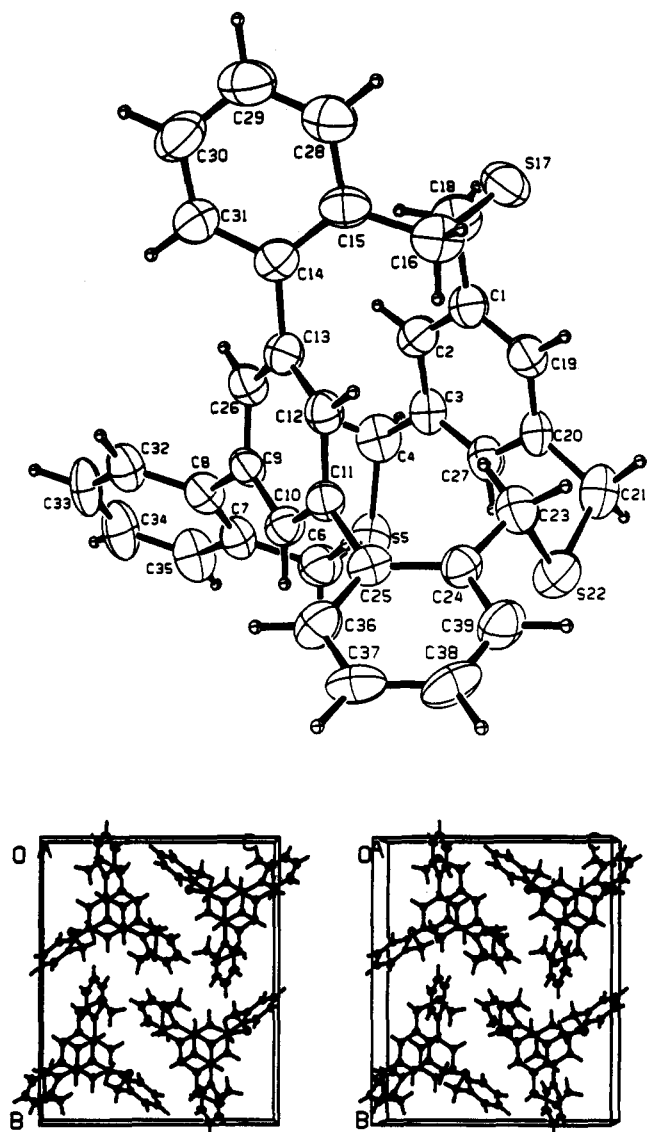
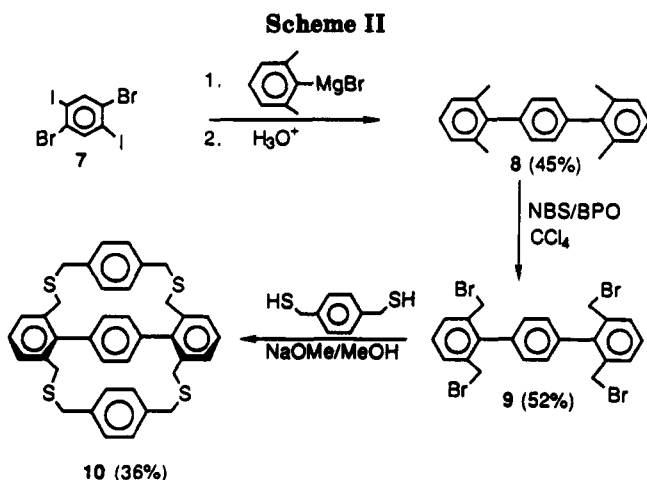
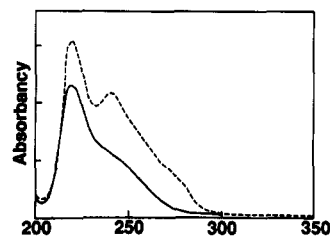
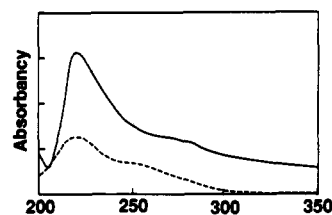


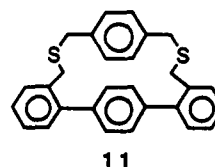
Figure 1. Ortep (top) and stereoview of 4.



For comparison with 10, its known analogue 11⁸ with only one link across the outer *p*-terphenyl rings was synthesized.⁹ Cyclophane 11 is known to have a flexible structure⁸ (partial rotation of the two "outer" terphenyl

Figure 2. UV spectra of 4 (—) and 6 (---) in CH₃CN.Figure 3. UV spectra of 10 (—) and 11 (---) in CH₃CN.

rings), whereas the second linking arm in 10 rigidifies the structure. The methylene singlets in 11 appear at δ 3.55



and 3.64 (cf. 3.11, 3.55) in 10, and the aromatic singlets also appear at lower field (δ 7.16, 7.20) in 11 than in 10 (6.99, 7.07). These shielding effects in 10 can be attributed to the impossibility of rotation about the outer terphenyl rings.

The UV spectra of 10 and 11 are compared in Figure 3. Although the effects are small, the longer wavelength absorption of 10 vis-a-vis 11 is apparent (λ_{\max} 280 and 262 nm, respectively).⁵

In summary, short syntheses of the novel cyclophanes 4 and 10, each with face-to-face arene rings, are described. These syntheses should direct attention to other fascinating possibilities using similar technologies.

Experimental Section¹⁰

1,3,5-Tris(2'-methylphenyl)benzene (2). Hydrogen chloride gas was passed into a vigorously stirred solution of 2-methylacetophenone (25 g, 0.181 mol) and triethyl orthoformate (33.2 g, 0.223 mol) in 80 mL of chloroform at rt. The solution, which was stirred at rt overnight, became dark red. The reaction was quenched with ice, and the mixture was extracted with chloroform. The organic layer was evaporated under reduced pressure, and the solid yellow residue was chromatographed over silica gel using *n*-hexane/chloroform (2:1) as eluent to give 6.05 g (28.8%) of 2 as a white solid: mp 129–130 °C; ¹H NMR δ 2.39 (s, 9 H, CH₃), 7.25–7.36 (m, 15 H, arom); ¹³C NMR δ 20.2, 125.4, 126.9, 128.1, 129.5, 130.0, 135.0, 141.0, 141.2; mass spectrum, *m/e* 348 (M⁺). Anal. Calcd for C₂₇H₂₄: C, 93.06; H, 6.94. Found: C, 93.23; H, 6.92.

1,3,5-Tris(2'-(chloromethyl)phenyl)benzene (3). A solution of 2 (2.42 g, 6.94 mmol), sulfuryl chloride (2.81 g, 10.8 mmol), and benzoyl peroxide (1.2 mg) in CCl₄ (80 mL) was heated at

(9) Instead of the literature⁸ procedure, we used our tandem aryne synthesis⁷ to prepare the required intermediate 2,2'-dimethyl-1,1':4',1''-terphenyl (one step and 46% yield⁷ vis-a-vis two steps and 39% yield⁸).

(10) For general procedures, see: Chiu, J.-J.; Grewal, R. S.; Hart, H.; Ward, D. L. *J. Org. Chem.*, manuscript submitted.

reflux for 8 h. The cooled mixture was washed with water, dried, and evaporated under reduced pressure. The solid residue was chromatographed over silica gel using *n*-hexane/chloroform (2.5:1) as eluent to give 1.62 g (51.6%) of **3** as a white solid: mp 154 °C; ¹H NMR δ 4.67 (s, 6 H, CH₂), 7.39–7.59 (m, 15 H, arom); ¹³C NMR δ 44.1, 127.8, 128.3, 128.5, 130.0, 130.1, 134.5, 139.9, 141.0; mass spectrum, *m/e* (relative intensity) 450.52 (16.4), 451.56 (2.2), 452.50 (14.9), 453.58 (0.9), 454.56 (1.6). Anal. Calcd for C₂₇H₂₁Cl₃: C, 71.78; H, 4.68. Found: C, 71.88; H, 4.62.

Coupling of 3 with 1,3,5-Tris(mercaptopethyl)benzene: Synthesis of 7,8:14,15:24,25-Tribenzo-5,17,22-trithiatetracyclo[9.7.7.1^{3,20}.1^{9,13}]heptacos-1,3(27),7,9,11,13(26),14,19,24-nonaene (4). To a well-stirred suspension of cesium carbonate (1.09 g, 3.33 mmol) in DMF (500 mL) held at 45–50 °C in an argon atmosphere was added simultaneously over 15 h from separate addition funnels solutions of **3** (1.0 g, 2.22 mmol) and 5¹¹ (0.48 g, 2.22 mmol), each in 100 mL of DMF. The mixture was then heated at reflux for 8 h, concentrated under vacuum, and extracted with CH₂Cl₂. The organic layer was washed with water, dried (MgSO₄), and evaporated to a solid residue which was chromatographed over silica gel using CH₂Cl₂/hexanes (2:1) as eluent to give 0.94 g (76%) of **4**: mp 221–222 °C; ¹H NMR δ 3.56 (s, 6 H), 3.65 (s, 6 H), 6.998 (s, 3 H), 7.015 (s, 3 H), 7.19 (dd, *J* = 5.1, 0.75 Hz, 3 H), 7.26 (td, *J* = 6.9, 0.6 Hz, 3 H), 7.37 (td, *J* = 7.2, 0.75 Hz, 3 H), 7.68 (dd, *J* = 7.5, 0.6 Hz, 3 H); ¹³C NMR δ 31.4, 35.7, 126.4, 126.8, 127.4, 128.4, 129.6, 129.9, 134.3, 138.0, 139.6, 141.1; mass spectrum, *m/e* (relative intensity) 558 (45), 559 (16.5), 560 (8.7), 561 (2.5); UV (CH₃CN) λ_{max} (ε) 219 nm (4300), 240 (2000); for **6**, 218 (6000), 240 (4000). A colorless rod-shaped crystal for X-ray determination was prepared by crystallization from CH₂Cl₂ with a little hexanes.

2,6,2',6''-Tetramethyl-1,1':4',1''-terphenyl (8). A solution of 1,4-dibromo-2,5-diiodobenzene (**7**)⁷ (15 g, 30.8 mmol) in 130 mL of anhydrous THF was added over 30 min to a solution of (2,6-dimethylphenyl)magnesium bromide [prepared from 2-bromo-*m*-xylene (24.5 g, 132.4 mmol) and magnesium (3.29 g, 135.4 mmol) in 450 mL of anhydrous THF], and the mixture was stirred for an additional 8 h at rt. The reaction was quenched with ice and dilute HCl, and the mixture was extracted with CHCl₃. The organic layer was dried (MgSO₄), and the solvent was evaporated under reduced pressure to leave a residue of a solid and an oil. This mixture was washed with hexane and filtered to give 3.97 g (45%) of **8**: mp 204 °C (recrystallized from hexanes); ¹H NMR δ 2.13 (s, 12 H), 7.17–7.23 (m, 10 H); ¹³C NMR δ 20.3, 126.6, 126.8,

128.6, 135.8, 138.9, 141.4; mass spectrum, *m/e* (relative intensity) 285 (2.8), 286 (M⁺, 100), 287 (20.5), 288 (2.4).

2,6,2',6''-Tetrakis(bromomethyl)-1,1':4',1''-terphenyl (9). A solution of tetramethylterphenyl (**8**) (1.5 g, 5.24 mmol), NBS (3.73 g, 21 mmol), and a few milligrams of BPO in CCl₄ (150 mL) was heated at reflux for 8 h. The mixture was cooled, and the precipitated succinimide was removed by filtration. The solvent was removed (rotavap), and the residue was chromatographed on silica gel using *n*-hexane/CH₂Cl₂ (3:1) as eluent to give 1.64 g (52%) of **9**: mp 242–243 °C; ¹H NMR δ 4.32 (s, 8 H), 7.38–7.54 (m, 10 H); ¹³C NMR δ 31.2, 128.2, 129.0, 130.2, 135.9, 136.4 (one aryl peak missing); mass spectrum, *m/e* (relative intensity) 600 (2.1), 602 (3.0), 604 (1.9).

Coupling of *p*-Xylylenedithiol with 9. Synthesis of 10. To a well-stirred solution of NaOMe (0.9 g, 16.7 mmol) in 500 mL of MeOH were added at rt under argon over 15 h simultaneously from separate addition funnels solutions of *p*-xylylenedithiol (1.19 g, 6.99 mmol) and (bromomethyl)terphenyl **9** (2 g, 3.32 mmol), each in 200 mL of MeOH. After addition was complete, the mixture was heated at reflux for 8 h and then concentrated under vacuum. The residue was extracted with CH₂Cl₂, and the organic layer was washed with water and dried (MgSO₄). Removal of the solvent gave a solid that was chromatographed over silica gel using hexanes/CH₂Cl₂ (2:1) as eluent to give 0.74 g (36%) of **10**: mp 313–314 °C; ¹H NMR δ 3.11 (s, 8 H), 3.55 (s, 8 H), 6.99 (s, 4 H), 7.07 (s, 8 H), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.70 (d, *J* = 7.5 Hz, 4 H); ¹³C NMR δ 32.2, 35.2, 127.4, 128.1, 128.3, 128.4, 129.7, 134.5, 136.0, 136.7; mass spectrum, *m/e* (relative intensity) 618 (M⁺, 48.6), 619 (19.3), 620 (11.9), 621 (4.0), 622 (1.3); UV (CH₃CN) λ_{max} (ε) 220 nm (2900), 280 (1100); for **11**, 220 (1600), 262 (800). Anal. Calcd for C₃₈H₃₄S₄: C, 73.74; H, 5.54. Found: C, 73.86; H, 5.59.

5,7,12,14-Tetrahydro-8,11:19,22-diethenodibenzo[*J*,*P*][1,8]-dithiacyclooctadecin (11). Although **11**, mp 266–267 °C (lit.⁸ mp 263–271 °C), was previously reported, its spectra were not: ¹H NMR δ 3.55 (s, 4 H), 3.64 (s, 4 H), 7.16 (s, 4 H), 7.20 (s, 4 H), 7.26–7.40 (m, 6 H), 7.69 (dd, *J* = 7.4, 1.6 Hz, 2 H); ¹³C NMR δ 32.0, 36.0, 126.7, 127.2, 128.3, 128.4, 129.6, 130.1, 133.7, 136.5, 138.8, 141.1; mass spectrum, *m/e* (relative intensity) 424 (M⁺, 100), 425 (32.6), 426 (12.5), 427 (2.9).

Acknowledgment. We are indebted to the National Science Foundation (CHE-90-08503) for financial support of this research.

Supplementary Material Available: ¹H and ¹³C NMR spectra of compounds **4**, **8**, and **9** (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(11) Houk, J.; Whitesides, G. M. *J. Am. Chem. Soc.* 1987, 109, 6825–6836.

(12) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.