+ $a_6$)/2, respectively. Moreover, as expected, the hyperfine splitting for either system is always smallest at the position opposite the substituent containing the carbonyl group.

**Acknowledgment.** This research was supported by NIH Division of Research Resources Grant RR-01811, NIH Department of Health and Human Services Traineeship (5 T32 CA 09067) to M.J.N., and Lederle Laboratories.

**Registry No.** **1a**·HCl, 13614-98-7; **1a**, 10118-90-8; **1b**, 61650-68-8; **1b**·$^1/_4$HCl, 135513-29-0; **2a**, 135513-28-9; **2b**, 135535-66-9; $K_3Fe(CN)_6$, 127435-14-7.

# Synthesis of Self-Filled, Vaulted, and Intracavity-Functionalized Cappedophanes

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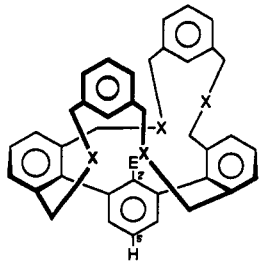
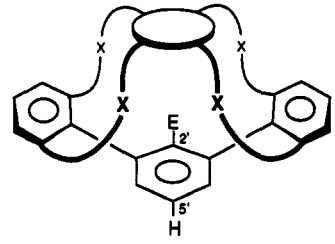
Two approaches to the synthesis of vaulted cappedophanes **3v** are described. In the first, the walls and ceiling were prefabricated as in tetrathiol **5** (**10a** and **10b**, Scheme II, are specific examples), which was then coupled with a *m*-terphenyl tetrabromide such as **4**. This route was most successful when the *m*-terphenyl base carried a large substituent (Ph, Br) in the 5′ position. Thus tetrathiol **10a** and tetrabromide **25** gave vaulted cappedophane **27v** in good yield (Scheme VIII). In the absence of a 5′ substituent, the major product was the self-filled conformer. For example, **10a** and **4** gave mainly **11sf** (62%) and only 2% of its vaulted conformer **11v** (Scheme III), and tetrathiol **10b** reacted with **4** to give (79%) only the self-filled conformer **15sf** (Scheme IV). In the second approach, a cuppedophane with suitably functionalized walls was first constructed, and the cap was attached in a second step. For example, bisphenol **29**, when coupled with *p*-xylylene dibromide, gave mainly vaulted conformer **11v** (51%) and only a trace of **11sf** (Scheme IX). Extension of this method to several other dihalides, however, gave mainly self-filled conformers (Schemes XI and XII) and even *p*-xylylene dibromide gave only self-filled product **33sf** when the bisphenol contained a substituent at $C_{2'}$ of the *m*-terphenyl base (Scheme XIII). The reasons for the predominant formation of self-filled vis-a-vis vaulted cappedophane conformers are discussed. These studies open the way for the synthesis of vaulted cappedophanes containing functionality within the molecular cavity.

We recently described efficient routes to two new classes of *m*-terphenyl-based cyclophanes **1** and **2**, called respectively *cuppedophanes* and *cappedophanes*.[1] The one-pot tandem aryne route[2] to the *m*-terphenyl moiety of **1** and **2** permits the direct introduction of substituents E at $C_{2'}$



1 (X=S, $SO_2$, NTs, NH, —)

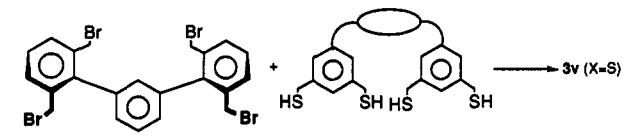


2 (X=S, $SO_2$, —)

and was used to prepare cuppedophanes with a substituent inside the "cup".[1b,3] In our first cappedophanes, however, the links between the *m*-terphenyl base and the cap were too short (only 2 or 3 atoms) to permit an E larger than a proton to be incorporated.

One goal of the present work was to enlarge the cavity in cappedophanes sufficiently to permit a functional group to be included at $C_{2'}$. This would permit a comparison of functional group chemistry within and outside a specifically designed microenvironment. To do this, the lengths

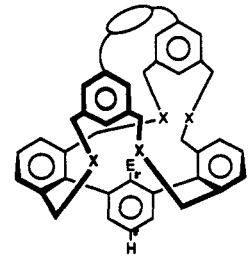
**Scheme I**



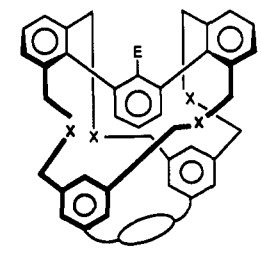
4 5

of the links would have to be increased. They would also have to be stiffened, because flexible links might allow collapsed conformations,[4] which would diminish the cavity volume.

The design we employed for this purpose is shown in **3v**, where a cap is added to the rigid walls of a cuppedophane to produce a vaulted cappedophane. We describe



**3v**



**3sf**

here several successful syntheses of this type. During this work, we also encountered a remarkably high propensity for the formation of **3sf**, a conformer of **3v** in which the central ring of the *m*-terphenyl moiety fills the molecular cavity. The relative energies of **3v** and **3sf** and factors that

(1) (a) Vinod, T. K.; Hart, H. *J. Am. Chem. Soc.* **1988**, *110*, 6574–6575. (b) Vinod, T.; Hart, H. *J. Org. Chem.* **1990**, *55*, 881–890. (c) Vinod, T. K.; Hart, H. *J. Org. Chem.* **1990**, *55*, 5461–5466.

(2) Du, C.-J. F.; Hart, H.; Ng, K.-K. D. *J. Org. Chem.* **1986**, *51*, 3162–3165. Du, C.-J. F.; Hart, H. *J. Org. Chem.* **1987**, *52*, 4311–4314.

(3) Our methodology was recently used by others for the same purpose, see: Lüning, U.; Wangnick, C.; Peters, K.; von Schnering, H. G. *Chem. Ber.* **1991**, *124*, 397–402.

(4) For examples, see: Jarvi, E. T.; Whitlock, H. W. *J. Am. Chem. Soc.* **1982**, *104*, 7196–7204.

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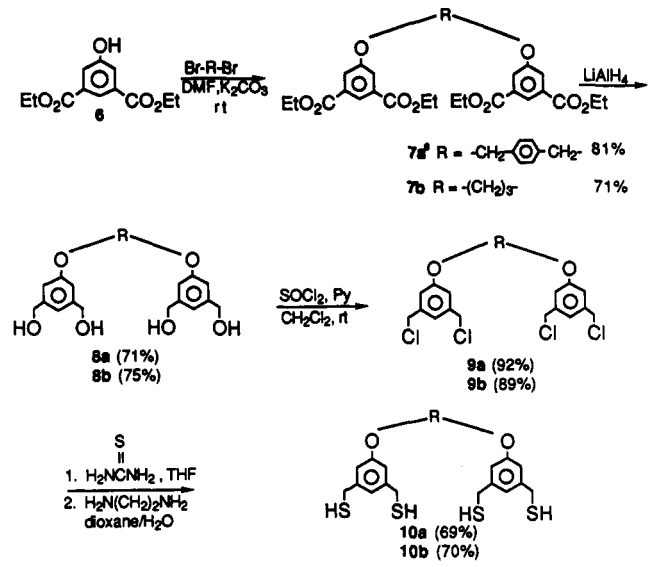
**Scheme II**




affect the formation of each are discussed.[5]

## Results and Discussion

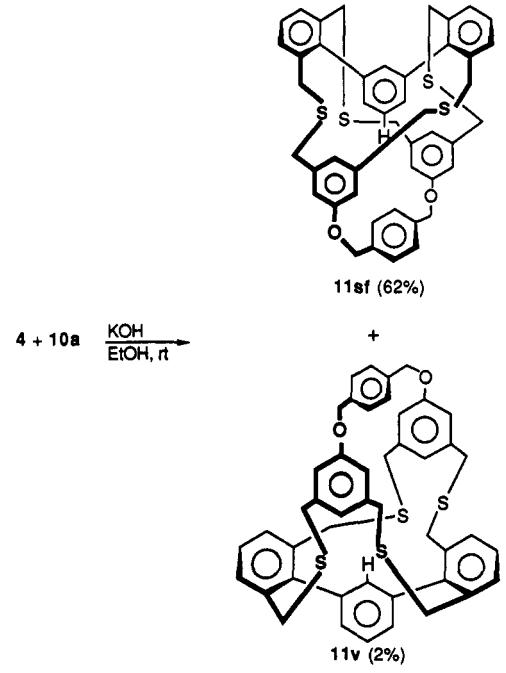
The two most direct routes to **3v** are (a) to prefabricate the walls and cap and then attach that unit to the base in one step and (b) to add to the base walls that contain suitable functionality for later attaching a cap. Each route was explored, the former first.

**Synthesis of Tetrathiols 10a and 10b.** *m*-Xylylene dithiols react with tetrabromide **4** across the outer rings to produce cuppedophanes **1** (X = S).[1] Consequently we expected that a linked tetrathiol such as **5** would react with **4**, via four-centered high dilution coupling, to give vaulted cappedophane **3v** (Scheme I).

Two tetrathiols of the type **5** were assembled as shown (Scheme II). Alkylation of diethyl 5-hydroxyisophthalate (**6**)[6] with either *p*-xylylene dibromide or 1,3-dibromopropane in anhydrous DMF gave tetraester **7a**[6] or **7b** in good yield. Reduction with lithium aluminum hydride gave the corresponding tetrols **8a** (mp 173 °C) and **8b** (mp 135–136 °C). Conversion to the corresponding tetrachlorides required an equivalent of pyridine with the thionyl chloride, to avoid acid-catalyzed cleavage of the ether linkages, a problem that was especially pronounced with benzylic ether **8a**. Chlorides **9a** (mp 118 °C) and **9b** (mp 110 °C) were then converted via their isothiouronium salts to the desired tetrathiols **10a** (mp 94 °C) and **10b** (mp 46–47 °C). All of the compounds in Scheme II had NMR spectra consistent with the assigned structures. The S*H* resonance of **10a** and **10b**, for example, appeared as triplets at $\delta$ 1.77 ($J$ = 7.6 Hz), coupled with the adjacent methylene protons (doublets at $\delta$ 3.69 and 3.68, respectively). In **10a** the benzylic methylenes appeared as a singlet at $\delta$ 5.07, whereas in **10b** the trimethylene protons appeared as a mutually coupled four-proton triplet at $\delta$ 4.17 and a two-proton quintet at $\delta$ 2.26.

**Coupling of Tetrathiols 10 with Tetrabromide 4. Molecules with Self-Filled Cavities.** The four-centered coupling of tetrabromide **4** with tetrathiol **10a** in KOH/EtOH proceeded in good overall yield (64%), but contrary to expectation the product was almost exclusively the

**Scheme III**




conformer with a self-filled cavity **11sf**, rather than the anticipated vaulted conformer **11v** (cf. **3sf** and **3v**). The yields were 62% and 2%, respectively (Scheme III). The major product **11sf** can arise through displacement of the four bromines of **4** by tetrathiol **10a** from *below*, thus encapsulating the central ring of the *m*-terphenyl moiety in a cavity, whereas vaulted cyclophane **11v** would arise by an analogous displacement from *above*.

Identification and characterization of the two conformers was accomplished by $^1$H NMR and was clear as a consequence of unique resonances in the two spectra. For example, the three vicinal aromatic protons on the central ring of the *m*-terphenyl unit in **11sf** were all shielded because they lie in a cavity lined by aromatic rings. The two magnetically equivalent protons of this set appeared as a doublet of doublets at $\delta$ 6.32 ($J$ = 7.7, 1.8 Hz, ortho- and meta-coupled, respectively). The central proton of this set, which points toward the center of the *p*-xylylene unit below it (see the structure), was highly shielded and appeared as a triplet at $\delta$ 4.31 ($J$ = 7.7 Hz). The spatial closeness of this proton to the *p*-xylylene ring, and hence the origin of its shielding, was confirmed by a strong signal enhancement (10.4%) of the *p*-xylylene singlet at $\delta$ 7.62 upon irradiation of the triplet at $\delta$ 4.31.

The most diagnostic signal in the $^1$H NMR spectrum of the vaulted conformer **11v** was a one-proton triplet at $\delta$ 5.70 with a small (meta) coupling constant ($J$ = 1.6 Hz). This signal is assigned to the isolated proton $H_{2'}$ on the central ring of the *m*-terphenyl unit. The upfield shift experienced by this proton is probably due to shielding by the flanking aryl rings (i.e., the 1,3,5-trisubstituted rings at the "front" and "back" of the cavity) and by the *p*-xylylene ring of the capping unit. For comparison, the corresponding proton in **11sf** appeared at lower field, as a broad singlet at $\delta$ 6.24. As expected, the three vicinal aryl protons on the central *m*-terphenyl ring in **11v** appeared in the normal aromatic region, as a set of doublet of doublets at $\delta$ 6.96 ($J$ = 7.7, 1.6 Hz, 2 H) and a triplet at $\delta$ 7.35 ($J$ = 7.7 Hz, 1 H).

The formation of **11sf** (and not **11v**) as the major coupling product of **4** and **10a** came as a surprise. It was unexpected because of previous synthesis of cuppedophanes **1** (X = S, NTs)[1] via analogous two-centered cou-

(5) A preliminary communication was published. Vinod, T. K.; Hart, H. *J. Am. Chem. Soc.* **1990**, *112*, 3250–3252.

(6) Collman, J. P.; Brauman, J. I.; Fitzgerald, J. P.; Hampton, P. D.; Naruta, Y.; Sparapany, J. W.; Ibers, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 3477–3486.

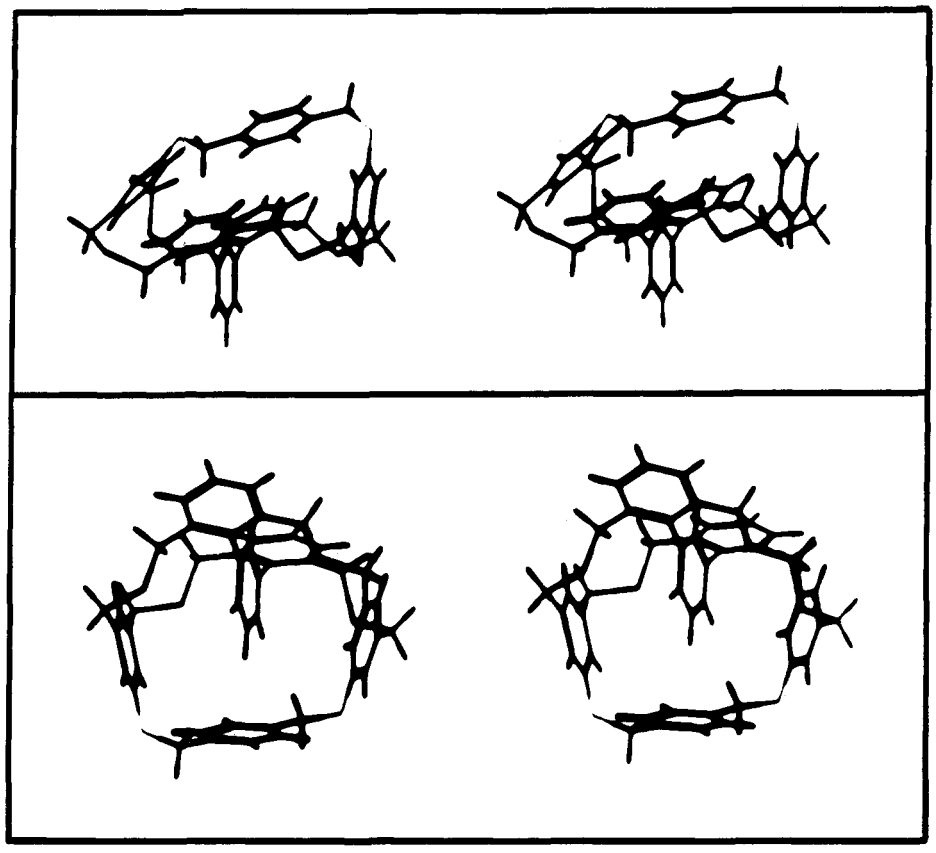
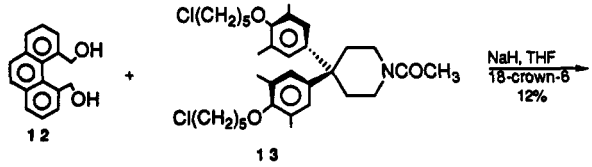
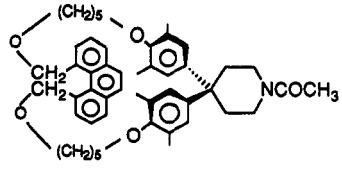


**Figure 1.** Stereoviews of energy-minimized conformations of **11v** (top) and **11sf** (bottom). The molecules are viewed end-on, looking through the molecular cavities.

plings gave products with the linking rings above the *m*-terphenyl unit in a roughly parallel and colinear arrangement, as shown, for example, by an X-ray structure of **1** (X = —).[1b]

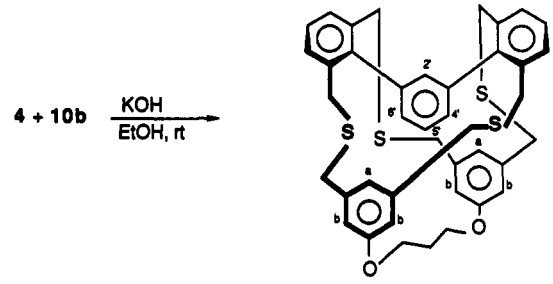
Compound **11sf**, with the central ring of the *m*-terphenyl unit embedded within a cavity lined by three aryl rings, may be described as a macrocycle filling its own cavity, that is, a self-filled molecular host. Similar formation of a self-filled macrocycle was reported by Diederich,[7] who observed that **14** was the exclusive coupling product of **12** and **13**. A detailed theoretical study[8] on the origin of the




self-filled cavity in **14** revealed that favorable van der Waals interactions of the phenanthrene moiety with the aryl rings that line the cavity lower the energy of the self-filled conformation by about 4–6 kcal mol$^{-1}$ relative to all other conformations, including the least sterically

**Scheme IV**




demanding one in which the phenanthrene unit lies outside the cavity.

A similar rationalization provides one explanation for the formation of **11sf**, i.e., favorable van der Waals interactions between the central *m*-terphenyl ring and the aryl rings that line the cavity. Figure 1 shows stereoviews of the energy-minimized structures of **11sf** and **11v** derived from molecular mechanics calculations with BIOGRAF using Dreiding force fields.[9] The van der Waals energy contributions toward the total energies of **11sf** and **11v** are 71.4 and 75.2 kcal mol$^{-1}$, respectively. The energy difference of 3.86 kcal mol$^{-1}$ favoring the self-filled conformation is similar to other reported values.[8,10] Presumably this energy stabilization is reflected in one or more of the $S_N2$ transition states in the coupling of **4** with **10a**.

A similar self-encapsulation result was obtained in the coupling of **4** with **10b**, despite (or possibly even because

(7) Rubin, Y.; Dick, K.; Diederich, F.; Georgiadis, T. M. *J. Org. Chem.* **1986**, *51*, 3270–3278.
(8) Loncharich, R. J.; Seward, E.; Ferguson, S. B.; Brown, F. K.; Diederich, F.; Houk, K. N. *J. Org. Chem.* **1988**, *53*, 3479–3491.

(9) We thank Professor Rawle Hollingsworth for help with the program and with the figure.
(10) Miller, S. P.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 1492–1494.

**Table I. Diagnostic Protons Used in Conformational Assignments**

| | | | | phenoxy rings | | |
|---|---|---|---|---|---|---|
| compd | $H_{2'}$ | $H_{4',6'}$ | $H_{5'}$ | 2 H | 4 H | $CH_2O$ |
| **11sf** | 6.24 | 6.32 | 4.31 | 6.24 | 6.63 | 5.19 |
| **15sf** | 6.13 | 6.89 | 6.23 | 6.16 | 6.74 | 4.37 |
| **26sf** | 6.41 | 6.61 | | 6.39 | 6.56 | 5.15 |
| **30sf** | 6.13 | 6.32 | 6.20 | 6.20 | 6.70 | 5.15 |
| **31sf** | 6.17 | 6.88 | 6.80 | 6.25 | 6.88 | 5.26 |
| **32sf** | 6.13 | 6.85 | 6.65 | 6.18 | 6.76 | 4.65 |
| **33sf** | | 6.38 | 4.34 | 6.25 | 6.68 | 5.17 |
| **11v** | 5.70 | 6.96 | 7.35 | 6.69 | 6.10 | 4.63 |
| **26v** | 5.65 | 7.17 | | 6.76 | 6.10 | 4.63 |
| **27v** | 5.66 | 7.21 | | 6.67 | 6.10 | 4.63 |
| **30v** | 5.74 | 6.92 | | 6.89 | 6.07 | 4.63 |

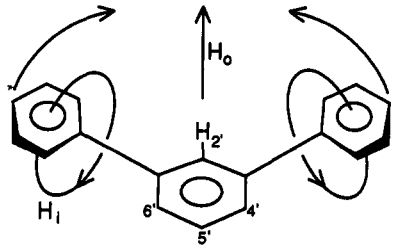


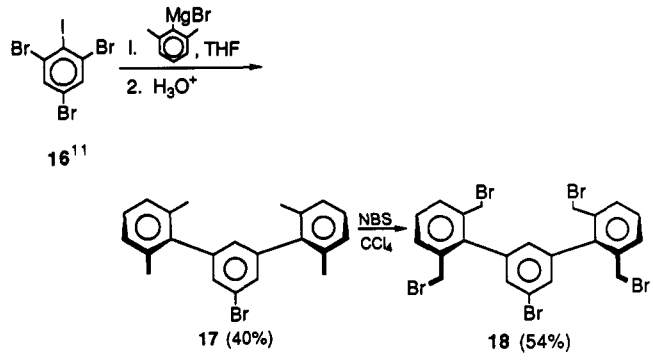

**Figure 2.** Shielding of $H_{2'}$ in self-filled conformations.

of) the shorter chain linking the two phenolic oxygens (Scheme IV). The sole product, formed in 79% yield, was assigned the self-filled structure **15sf** based on NMR data. The chemical shifts of the protons on the central *m*-terphenyl ring ($H_{2'}$, $H_{5'}$, and $H_{4'(6')}$) and the protons on the phenoxy rings ($H_a$, $H_b$) were particularly diagnostic (Table I). We cannot rely here (as with **11sf**) on the shielding of $H_5$, because the unit that links the phenolic oxygens is not aromatic. Several other spectral features, however, permit a clearcut decision. For example, protons $H_a$ on the phenoxy rings are shielded with respect to the other protons $H_b$ on these rings ($\delta$ 6.16 vis-a-vis $\delta$ 6.74). A similar result obtains for the corresponding protons in **11sf** and for all the other self-filled conformers described below (Table I). The converse is true for vaulted conformers (see **11v** and others in Table I). The reason for this difference is that in the self-filled conformers $H_a$ lies within the shielding region of the central *m*-terphenyl ring whereas $H_b$ is outside this zone. At the same time, the two outer *m*-terphenyl rings are pushed "upwards" in this conformation relative to their positions in the vaulted conformations. For this reason $H_{2'}$ moves into the shielding zone of these outer rings (Figure 2) and always appears at higher field than the remaining protons on that ring (Table I), except for the special cases of **11sf** and **33sf**, where $H_{5'}$ is shielded by the capping ring.

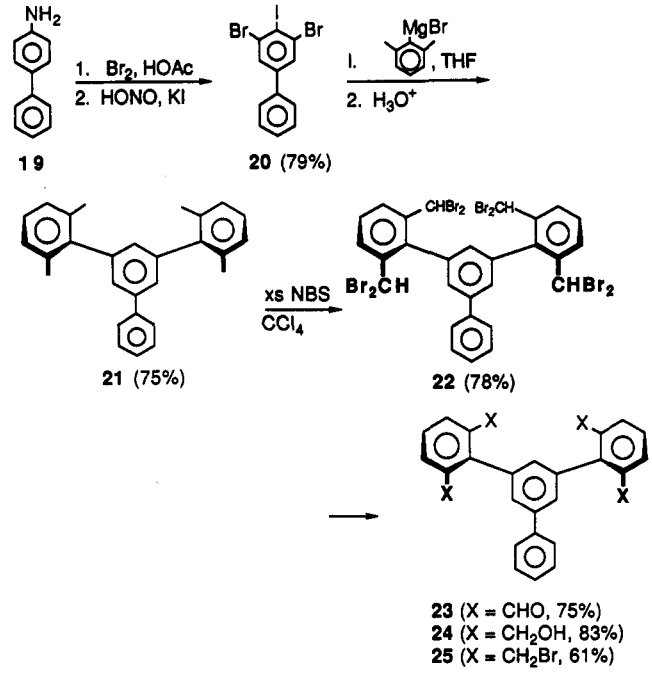
The protons of the trimethylene unit in **15sf** appeared as a triplet at $\delta$ 4.37 ($J$ = 4.7 Hz, 4 H) and a quintet at $\delta$ 2.41 ($J$ = 4.8 Hz, 2 H). The spatial proximity of $H_{5'}$ to this unit was confirmed by using NOE methods. Irradiation of the $H_{5'}$ triplet at $\delta$ 6.23 resulted in a 10.8% enhancement of the triplet at $\delta$ 4.37; the selective enhancement of this four-proton signal over the two proton signal ($\delta$ 2.41) shows that the trimethylene link is as drawn in structure **15sf**, with the central methylene group folded out and away from $H_{5'}$.

A CPK model of **15sf** can be constructed only with difficulty and only with the trimethylene link in the conformation described. Nevertheless the high yield of **15sf** from **4** and **10b**, and its exclusive formation relative to its vaulted conformer (whose CPK model is more easily constructed), again reflects the favorable van der Waals interaction between the three parallel aryl rings in the transition state(s) leading to **15sf**.

**Scheme V**




**Scheme VI**



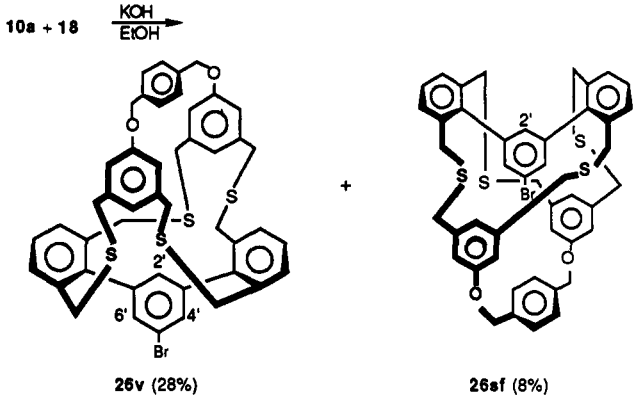

***m*-Terphenyls with Large Substituents at $C_{5'}$.** The failure of substantial amounts of vaulted cyclophanes to form in the coupling of **4** with **10a** or **10b** suggested that **4** be modified to include a large substituent at $C_{5'}$, since this should prohibit the formation of a self-filled host. Toward this end, the 5′-bromo and 5′-phenyl *m*-terphenyls **18** and **25** were prepared (Schemes V and VI).

Treatment of 2,4,6-tribromoiodobenzene[11] with (2,6-dimethylphenyl)magnesium bromide (3 equiv) gave 5′-bromo-*m*-terphenyl **17** in 40% yield via a tandem aryne sequence.[2] NBS bromination then afforded **18**, mp 160–162 °C, in 54% yield (Scheme V).

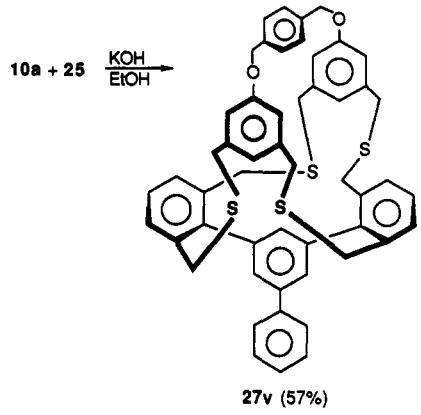
5′-Phenyl-*m*-terphenyl **21** was also obtained via the tandem aryne sequence[2] from 3,5-dibromo-4-iodobiphenyl (**20**), which in turn was prepared in two steps and 79% overall yield from commercially available 4-aminobiphenyl (Scheme VI). Attempted tetrabromination of **21** gave only impure **25**, contaminated with polybrominated compounds that were difficult to remove. With excess NBS, however, octabromide **22** (mp 265 °C) was readily obtained pure in good yield. The structure of **22** was clear from its $^1H$ NMR spectrum, which included a singlet at $\delta$ 6.42 for the four methine protons and a doublet at $\delta$ 8.13 ($J$ = 7.9 Hz) for

(11) Hodgson, H. H.; Mahadevan, A. P. *J. Chem. Soc.* **1947**, 173–174.

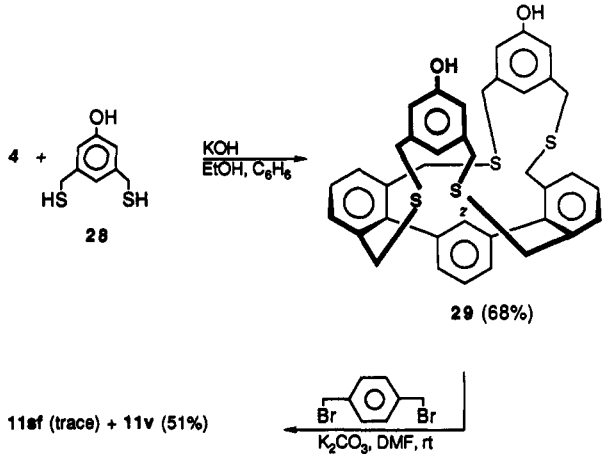
**Scheme VII**




**Scheme VIII**




**Scheme IX**




the four aryl protons adjacent to the $CHBr_2$ substituents.

Hydrolysis of **22** (sodium acetate, silver nitrate, THF/$H_2O$) gave tetraaldehyde **23**, mp 178 °C, $\nu_{C=O}$ 1690 $cm^{-1}$, -C*H*O, at $\delta$ 10.01. Sodium borohydride reduction gave tetrol **24**, mp 225 °C, which with $PBr_3$ in benzene afforded the required 5′-phenyl-2,2″,6,6″-tetrakis(bromomethyl)-*m*-terphenyl (**25**), mp 148 °C. Although this conversion of **21** to **25** required four steps and proceeded in only 30% overall yield, it gave pure **25** impossible to isolate from the direct bromination of **21**.

**Coupling of 5′-Substituted Bromides 18 and 25 with Tetrathiol 10a.** Base-catalyzed coupling of tetrathiol **10a** with **18** gave two products, **26v** and **26sf**, in 28% and 8% yields, respectively (Scheme VII). As expected, the yield of vaulted cyclophane increased compared with the coupling of **10a** with **4** (**26v**/**26sf** = 3.5 whereas **11v**/**11sf** = 0.03) but a surprising amount of the self-filled host **26sf** was formed despite the presence of the 5′-bromo substituent.

Conformers **26v** and **26sf** were characterized by their spectra and by chemical means. Both isomers produced an $MH^+$ ion at *m*/*e* 833 in their FAB mass spectra. The internal proton $H_{2'}$ in **26v** appeared as a narrow triplet at $\delta$ 5.65 ($J$ = 1.3 Hz, meta-coupled), almost identical with the corresponding proton in **11v** ($\delta$ 5.70). Chemical shifts of the $H_{4'(6')}$ protons and the phenoxy ring protons of **26v** and **11v** were also nearly identical (Table I).

The lack of a proton at $C_{5'}$ in **26sf** made its spectral characterization more difficult, although the relative chemical shifts of $H_{2'}$ vis-a-vis $H_{4'(6')}$ and of phenoxy protons $H_a$ vis-a-vis $H_b$ were similar for **26sf** and **11sf** (Table I) and supported the self-filled assignment. The structure was proved chemically. Treatment of **26sf** with *n*-BuLi (1 equiv) at −78 °C in THF, followed by an aqueous quench, afforded **11sf**. This result not only establishes the conformational relationship between **26sf** and **11sf** but it also demonstrates that encapsulated functionality in these structures is subject to chemical manipulation.

In contrast to **18**, coupling of **25** with **10a** gave only vaulted product (**27v**, Scheme VIII). The vaulted nature of this product was clear by comparing its $^1H$ NMR spectrum with that of **11v** and **26v**, critical portions of which are nearly identical (Table I).

From these experiments we concluded that if the substituent at $C_{5'}$ of the *m*-terphenyl moiety is sufficiently large, the cyclophane formed in these coupling reactions will be the vaulted conformer, but that in the absence of such substituents, there is a strong predilection for the self-filled conformer to be formed.

**Construction of Cappedophanes in a Stepwise Manner.** The vaulted and self-filled cappedophanes described so far were prepared by prefabricating the walls and cap and attaching that unit in one step to the *m*-terphenyl base (from the "top" or from the "bottom", respectively). In this section we describe results obtained by using the alternate strategy. That is, we first construct a cuppedophane with suitably functionalized walls and then attach the cap.

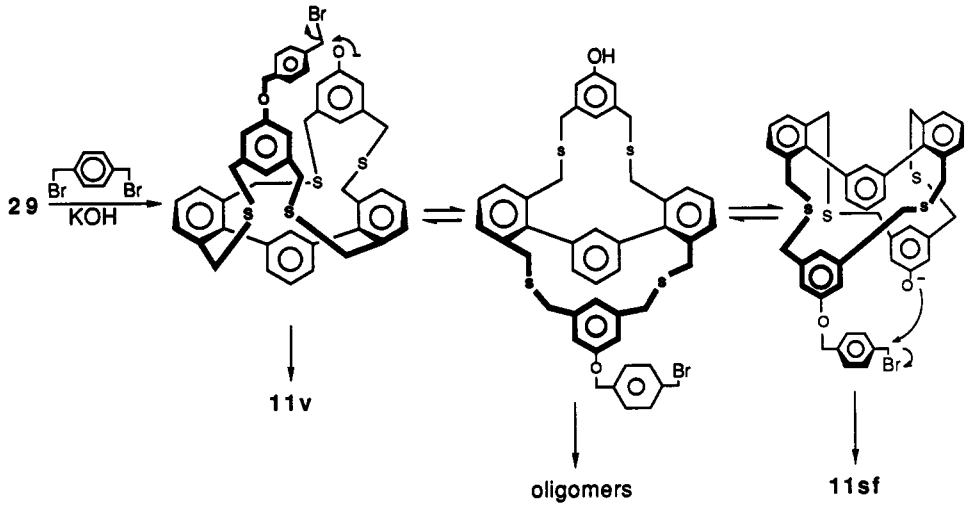
The cuppedophane first selected for this purpose was bisphenol **29**, readily prepared in 68% yield by coupling tetrabromide **4** with 2 equiv of dithiol **28** (Scheme IX), in turn obtained from 3,5-bis(bromomethyl)anisole[12] in three steps and 34% overall yield by conventional means (see Experimental Section). The internal aromatic proton (at $C_{2'}$) in **29** appeared as a triplet ($J$ = 1.2 Hz, meta-coupled) at $\delta$ 6.37, moderately shielded by the cofacial phenolic rings (the same proton appeared at $\delta$ 6.39 in the analogue of **29** that lacks the hydroxyl group[1b]).

Treatment of **29** with *p*-xylylene dibromide and base in DMF at room temperature gave mainly vaulted cyclophane **11v** and only traces of the self-filled conformer **11sf**. Thus with this example, the synthetic routes depicted in Schemes III and IX are complementary, giving mainly the self-filled or the vaulted conformer of **11**, respectively.

The results in Scheme IX were encouraging for the synthesis of vaulted cappedophanes, although the formation of traces of the self-filled conformer was somewhat disturbing and unexpected and requires some explanation. Thermal isomerization of the vaulted to the self-filled conformer, which would require a "flip" of the central *m*-terphenyl ring from outside to inside the cavity, was ruled out by the observation that traces of **11sf** were

(12) Boekelheide, V.; Griffin, R. W., Jr. *J. Org. Chem.* **1969**, *34*, 1960–1961.

**Scheme X**



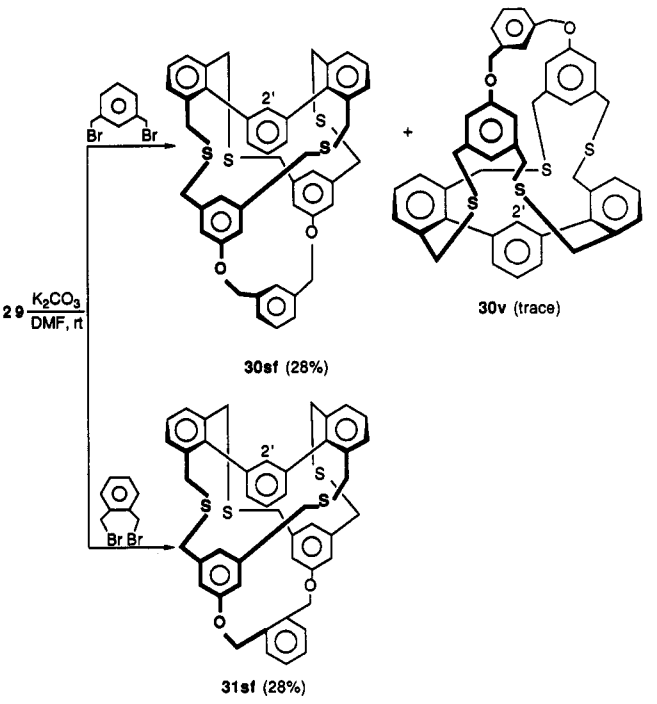

formed even when the entire reaction and workup were carried out at room temperature. Thermal isomerization of **11v** to **11sf** was observed, but occurred only very slowly even at the temperature of refluxing DMF.[13]

A more plausible explanation for the formation of **11sf** is that a conformational change occurs at some stage during the double alkylation of **29**. One possibility is shown in Scheme X. Monoalkylated intermediate may cyclize to give **11v**, or may undergo conformational change (perhaps for steric reasons) once or twice, to give, after the second displacement, oligomers or the self-filled conformer. The product ratio will then depend on a complex array of rate and equilibrium constants, and only if ring closure to **11v** is fast with respect to other possibilities will the vaulted conformer predominate. This rate may vary with the geometry of the capping unit, the nature of the leaving group, and so on. It is also possible that these conformational changes may occur in the mono- or dianions of **29**. In a sense, then, the predominant formation of vaulted conformer **11v** in this reaction, while fortunate from a synthetic viewpoint, could be fortuitous.

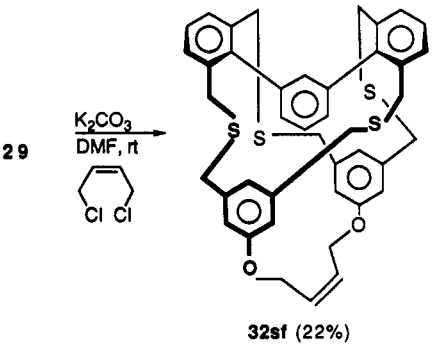
Indeed, this turned out to be the case! The seemingly minor change from *p*- to *m*-xylylene dibromide as coreactant with **29** gave only *traces* of vaulted conformer **30v**; the major product was the self-filled conformer **30sf** (Scheme XI). The two conformers were easily distinguished by their $^1$H NMR spectra (Table I). Conformer **30v** could only be obtained in about 90% purity, contaminated with **30sf**. Nevertheless the location of $H_{2'}$ at higher field ($\delta$ 5.74, t, $J$ = 1.2 Hz) in **30v** than in **30sf** ($\delta$ 6.13, br s), as well as other features of the spectra, is only consistent with the major product being the self-filled conformer. Analogous results were obtained with *o*-xylylene dibromide; only the self-filled product **31sf** was formed in 28% yield. Here, apparently, $H_{4',5',6'}$ come in the deshielding region of the *o*-xylylene ring, but otherwise all aspects of the $^1$H NMR spectrum are consistent only with the self-filled conformation (Table I).

Reaction of **29** with *cis*-1,4-dichloro-2-butene gave only the self-filled conformer **32sf** (Scheme XII). The same features of the aryl proton spectrum used all along support

**Scheme XI**




**Scheme XII**




this assignment (Table I), and NOE experiments confirm the spacial proximity of the three vicinal protons on the central *m*-terphenyl ring to the methylene protons of the butene unit. Thus irradiation of the methylene protons ($\delta$ 4.65) resulted in a 2.4% enhancement of the signal at $\delta$ 6.85 due to the $H_{4'(6')}$ protons on the central *m*-terphenyl ring and a 4% enhancement of the triplet at $\delta$ 6.65 due to the $H_{5'}$ proton on that ring.

(13) Heating a DMF solution of **11v** at reflux for about 1 h caused a 10–20% conversion to **11sf** (NMR). A detailed kinetic study of this interesting isomerization was not possible, however, due to accompanying decomposition at the high temperature required for the isomerization. The title of our preliminary communication on this subject described **11v** and **11sf** as "noninterconvertible" conformers; we now know that this is not quite accurate and that the unidirectional conversion of **11v** to **11sf** is possible, though with a high barrier.

**Scheme XIII**

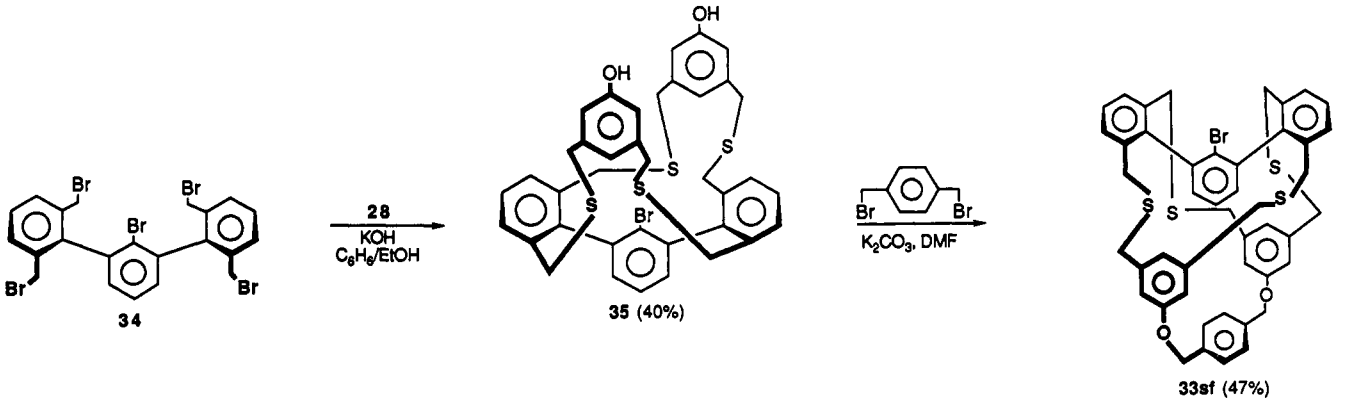



**Table II. NMR Comparison of 35 with 29 and 29-$(OMe)_2$**

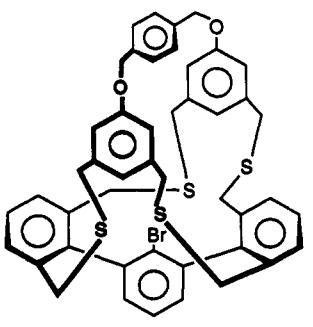
| protons | 35 | 29 | 29-$(OMe)_2$[1b] |
|---|---|---|---|
| $CH_2S$ (4 H) | 2.70 (d, $J$ = 10.5) | 2.96 (d, $J$ = 10.6) | 2.96 (d, $J$ = 11.0) |
| $CH_2S$ (8 H) | 3.37, 3.49 (AB q, $J$ = 14.4) | 3.43, 3.49 (AB q, $J$ = 14.1) | 3.48, 3.54 (AB q, $J$ = 14.3) |
| $CH_2S$ (4 H) | 3.51 (d, $J$ = 10.5) | 3.40 (d, $J$ = 10.6) | 3.37 (d, $J$ = 11.0) |
| phenoxy (2 H) | 6.21 (br s) | 6.29 (br s) | 6.33 (br s) |
| phenoxy (4 H) | 6.58 (d, $J$ = 1.5) | 6.55 (br s) | 6.60 (d, $J$ = 1.2) |
| $H_{4',5',6'}$ | 6.94 (m) | 6.96 (dd, $J$ = 8.1, 1.2, $H_{4',6'}$)<br>7.04 (t, $J$ = 8.1, $H_{5'}$) | 6.87–6.97 (m) |
| outer $m$-terphenyl rings | 7.26–7.35 (m, 6 H) | 7.26 (t, $J$ = 7.5, $H_{4,4''}$)<br>7.37 (d, $J$ = 7.5, $H_{3,5,3'',5''}$) | 7.23–7.42 (m, 6 H) |

In view of the similarity of $m$- and $o$-xylylene dibromides to the para isomer as alkylating agents, their differing reactions with **29** (Schemes IX and XI) is striking and suggests that shorter links favor the self-filled conformer. The exclusive formation of this conformer from *cis*-1,4-dichloro-2-butene (Scheme XII) may be due to a combination of factors, among which are a shorter link and a less reactive alkylating agent, allowing conformational changes in **29** or intermediates derived from it, prior to cyclization.

**Attempt To Prepare a Vaulted Cappedophane with Intracavity Functionality.** The successful preparation of **11v** from **29** (Scheme IX) prompted us to use this strategy to attempt the preparation of **33v**, a vaulted cappedophane with an intracavity bromine substituent, since such a substituent should be amenable to chemical transformations[1b] (as with **26sf**; vide supra).

Coupling of the known[1b] pentabromide **34** with dithiol **28** gave the bisphenolic cuppedophane **35**, mp 260 °C, in 40% yield (Scheme XIII). With the NMR-diagnostic $H_{2'}$ replaced by bromine, the cupped conformation of **35** could only be made by comparing other features of its $^1H$ NMR spectrum to those of the closely analogous **29** and its previously reported[1b] dimethoxy analogue **29**-$(OMe)_2$ (Table II).

Contrary to expectation, coupling of bisphenol **35** with $p$-xylylene dibromide gave only the self-filled conformer **33sf**, mp 268 °C, and none of the desired **33v**. The unmistakable resonance of $H_{5'}$ at $\delta$ 4.34 (t, $J$ = 7.5 Hz, ortho-coupling) establishes this assignment.




**33v**

The central bromine substituent in **35** may splay the phenolic rings somewhat, making the $p$-xylylene cap a less good fit than it is in coupling with **29**. Steric hindrance to encapsulating a bromine (**33v**) may also be a factor, as well as the strong predilection mentioned above for forming self-filled structures.

The results presented here suggest that in order to construct a vaulted cyclophane containing intracavity functionality, it also will be necessary to have a large group (i.e., phenyl, as in **27v**) at $C_{5'}$ of the $m$-terphenyl unit. Experiments along these lines are in progress. Experiments using acylation rather than alkylation to attach the cap may also affect the vaulted vis-a-vis self-filled product ratio.

## Experimental Section[14]

**1,3-Bis(3,5-dicarbethoxyphenoxy)propane (7b).** Under argon, a mixture of diethyl 5-hydroxyisophthalate[6] (15.0 g, 63 mmol), 1,3-dibromopropane (5.6 g, 27.7 mmol), and potassium carbonate (15 g) in 60 mL of anhydrous DMF was stirred for 60 h at rt. The mixture was poured into water (250 mL) and stirred vigorously. The resulting white precipitate was filtered, washed with water (3×), and dissolved in $CH_2Cl_2$ (350 mL). This solution was washed with 5% aqueous NaOH (3×), dried ($MgSO_4$), and evaporated to yield 10.2 g (71%) of **7b** as a white solid, mp 131 °C: $^1H$ NMR $\delta$ 1.41 (t, $J$ = 7.1 Hz, 12 H), 2.33 (quin, $J$ = 5.9 Hz, 2 H), 4.27 (t, $J$ = 5.9 Hz, 4 H), 4.40 (q, $J$ = 7.1 Hz, 8 H), 7.76 (d, $J$ = 1.4 Hz, 4 H), 8.27 (t, $J$ = 1.4 Hz, 2 H); mass spectrum, $m/e$ (relative intensity) 516 (6), 471 (10), 279 (6), 278 (14), 251 (13), 249 (14), 233 (13), 232 (24), 207 (25), 193 (21), 179 (31), 165 (24), 149 (69), 135 (58), 71 (45), 57 (87), 55 (60), 41 (100); IR ($CHCl_3$) $\nu_{C=O}$ 1721 $cm^{-1}$. Anal. Calcd for $C_{27}H_{32}O_{10}$: C, 62,78; H, 6.24. Found: C, 62.41; H, 6.23.

**$\alpha,\alpha'$-Bis[3,5-bis(hydroxymethyl)phenoxy]-$p$-xylene (8a).** To a solution of tetraester **7a**[6] (8 g, 13.8 mmol) in dry THF (300 mL) was added in portions 1.18 g (34.6 mmol) of $LiAlH_4$ at rt.

(14) For general procedures, see ref 1b, except that NMR spectra were recorded at 300 MHz and silica gel for chromatography was 230–400 mesh.

The mixture was stirred at reflux for 6 h, cooled, and quenched successively with $H_2O$ (1.2 mL), 15% NaOH (1.2 mL), and $H_2O$ (2.5 mL). The inorganic precipitate was removed by filtration, solvent was evaporated from the filtrate, and the resulting white solid was recrystallized from a minimum volume of THF/MeOH (3:1 v/v) to yield 4.03 g (71%) of **8a**, mp 173 °C: $^1$H NMR (DMSO-$d_6$) $\delta$ 4.44 (d, $J$ = 5.7 Hz, 8 H, $CH_2OH$), 5.08 (s, 4 H, benzylic $CH_2$), 5.15 (t, $J$ = 5.7 H, 4 H, $OH$), 6.82 (br s, 4 H), 6.85 (br s, 2 H), 7.45 (s, 4 H); mass spectrum, $m/e$ (relative intensity) 374 (1, $M^+ - 2H_2O$), 257 (3), 239 (49), 209 (45), 105 (82), 104 (100). Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C, 70.22; H, 6.44.

**1,3-Bis[3,5-bis(hydroxymethyl)phenoxy]propane (8b).** The procedure was similar to that described for **8a**. From 9.26 g (17.9 mmol) of **7b** and 1.53 g (44.9 mmol) of $LiAlH_4$ there was obtained 4.7 g (75%) of **8b** as a white solid, mp 135–136 °C: $^1$H NMR (DMSO-$d_6$) $\delta$ 2.13 (quin, $J$ = 6.4 Hz, 2 H), 4.10 (t, $J$ = 6.4 Hz, 4 H), 4.41 (d, $J$ = 5.5 Hz, 8 H, $CH_2OH$), 5.23 (t, $J$ = 5.5 Hz, 4 H, $OH$), 6.75 (s, 4 H), 6.81 (s, 2 H); mass spectrum, $m/e$ (relative intensity) 328 (2), 312 (27, $M^+ - 2H_2O$), 177 (22), 171 (21), 149 (68), 148 (14), 147 (100). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.61; H, 6.94. Found: C, 65.37; H, 7.23.

**$\alpha,\alpha'$-Bis[3,5-bis(chloromethyl)phenoxy]-$p$-xylene (9a).** To a stirred suspension of tetrol **8a** (4 g, 9.76 mmol) in 120 mL of $CH_2Cl_2$ containing 3.08 g (39 mmol) of pyridine was added a solution of thionyl chloride (4.6 g, 39 mmol) in 20 mL of $CH_2Cl_2$. The mixture was stirred at rt for 12 h and then washed with water (3 × 100 mL). The organic layer was dried ($MgSO_4$) and evaporated to yield 4.34 g (92%) of **9a** as an off-white solid, mp 118 °C: $^1$H NMR $\delta$ 4.42 (s, 8 H), 4.97 (s, 4 H), 6.85 (d, $J$ = 1.3 Hz, 4 H), 6.89 (br s, 2 H), 7.34 (s, 4 H); mass spectrum, $m/e$ (relative intensity) 484 (19), 482 (12), 332 (16), 330 (26), 328 (27), 310 (18), 308 (27), 295 (100), 294 (24), 293 (92). Anal. Calcd for $C_{24}H_{22}Cl_4O_2$: C, 59.53; H, 4.58. Found: C, 59.62; H, 4.47.

**1,3-Bis[3,5-bis(chloromethyl)phenoxy]propane (9b).** The procedure was analogous to that for **9a**. From 4.4 g (12.6 mmol) of tetrol **8b**, 4.0 g (50.4 mmol) of pyridine, and 6.1 g (51.0 mmol) of thionyl chloride there was obtained 4.74 g (89%) of **9b** as a white solid, mp 110 °C: $^1$H NMR $\delta$ 2.27 (quin, $J$ = 6.0 Hz, 2 H), 4.19 (t, $J$ = 6.0 Hz, 4 H), 4.54 (s, 8 H), 6.91 (d, $J$ = 1.3 Hz, 4 H), 6.99 (t, $J$ = 1.3 Hz, 2 H); mass spectrum, $m/e$ (relative intensity) 422 (0.1), 262 (9), 233 (11), 177 (22), 150 (13), 149 (100). Anal. Calcd for $C_{19}H_{20}Cl_4O_2$: C, 54.06; H, 4.77. Found: C, 54.29; H, 4.88.

**$\alpha,\alpha'$-Bis[3,5-bis(mercaptomethyl)phenoxy]-$p$-xylene (10a).** A stirred solution of tetrachloride **9a** (3.0 g. 6.2 mmol) and thiourea (1.89 g. 24.8 mmol) in THF (60 mL) was heated at reflux for 12 h. The mixture was cooled, and the precipitated isothiouronium salt was filtered and dried (6.15 g, 76%). This salt was dissolved in $H_2O$/dioxane (180 mL, 1:2 v/v) under argon, and to it was added 1.13 g (18.8 mmol) of ethylenediamine. The mixture was heated under argon at reflux for 12 h, cooled, and carefully quenched with a minimum amount of 2 N HCl. The solvent was removed under vacuum and the crude product was chromatographed (silica gel, $CH_2Cl_2$) to give 1.82 g (69%) of **10a** as a white solid, mp 94 °C: $^1$H NMR $\delta$ 1.77 (t, $J$ = 7.6 Hz, 4 H, $SH$), 3.69 (d, $J$ = 7.6 Hz, 8 H, $CH_2SH$), 5.07 (s, 4 H), 6.83 (d, $J$ = 1.6 Hz, 4 H), 6.88 (br s, 2 H), 7.45 (s, 4 H); mass spectrum, $m/e$ (relative intensity) 474 (1.8), 438 (1), 407 (1), 290 (13), 289 (42), 288 (43), 257 (12), 256 (17), 255 (72), 105 (100). Anal. Calcd for $C_{24}H_{26}O_2S_4$: C, 60.72; H, 5.52. Found: C, 60.84; H, 5.48.

**1,3-Bis[3,5-bis(mercaptomethyl)phenoxy]propane (10b).** The procedure was analogous to that for **10a**. From 5.3 g (12.6 mmol) of tetrachloride **9b** and 3.84 g (50.4 mmol) of thiourea there was obtained 8.5 g (93%) of isothiouronium salt. From 2.5 g (3.45 mmol) of this salt and 0.87 g (14.5 mmol) of ethylene diamine there was obtained 1.0 g (70.4%) of **10b** as a white solid, mp 46–47 °C: $^1$H NMR $\delta$ 1.77 (t, $J$ = 7.6 Hz, 4 H, $SH$), 2.26 (quin, $J$ = 6.0 Hz, 2 H), 3.68 (d, $J$ = 7.6 Hz, 8 H, $CH_2SH$), 4.17 (t, $J$ = 6.0 Hz, 4 H), 6.77 (d, $J$ = 1.0 Hz, 4 H), 6.86 (br s, 2 H): mass spectrum, $m/e$ (relative intensity) 412 (50), 279 (34), 193 (49), 121 (50), 91 (100), 77 (45). Anal. Calcd for $C_{19}H_{24}O_2S_4$: C, 55.30; H, 5.86. Found: C, 55.37; H, 5.83.

**5′-Bromo-2,6,2″,6″-tetramethyl-1,1′:3′,1″-terphenyl (17).** To a solution of (2,6-dimethylphenyl)magnesium bromide [prepared from 2,6-dimethylbromobenzene (10.2 g, 55 mmol) and magnesium (1.48 g, 63 mmol) in 180 mL of dry THF] heated at reflux under argon was added dropwise a solution of 2,4,6-tribromoiodobenzene (**16**)[11] (8.1 g, 18 mmol) in 40 mL of anhydrous THF. The solution was heated at reflux for an additional 3 h, cooled, quenched with 20 mL of cold 10% HCl, extracted with ether (2 × 100 mL), and dried ($MgSO_4$). The crude product obtained after removal of the ether was vacuum distilled to remove the byproduct 2,6-dimethyliodobenzene. The residue was chromatographed (silica gel, hexanes) to give 2.64 g (40%) of **17** as a white solid, mp 114 °C (hexanes): $^1$H NMR $\delta$ 2.09 (s, 12 H, $CH_3$), 6.89 (t, $J$ = 1.5 Hz, 1 H, $H_{2'}$), 7.11–7.31 (m, 8 H, remaining Ar H); mass spectrum, $m/e$ (relative intensity) 366 (98), 364 (100), 286 (20), 285 (83), 270 (70), 255 (31), 254 (14), 253 (19), 252 (17). Anal. Calcd for $C_{22}H_{21}Br$: C, 72.33; H, 5.79. Found: C, 72.61; H, 6.21.

**5′-Bromo-2,6,2″,6″-tetrakis(bromomethyl)-1,1′:3′,1″-terphenyl (18).** Freshly recrystallized NBS (4.1 g, 23 mmol) was added in two equal portions 12 h apart (total reaction time 24 h) to a solution of **17** (2.0 g, 5.46 mmol) in 125 mL of $CCl_4$ heated at reflux, each addition being followed by a few milligrams of benzoyl peroxide. The mixture was cooled and filtered to remove the succinimide. Solvent was evaporated from the filtrate and the residue was chromatographed (silica gel, $CH_2Cl_2$/hexanes, 1:4 v/v) to give 2.0 g (53.7%) of **18** as a white crystalline solid, mp 160–161 °C: $^1$H NMR $\delta$ 4.30 and 4.33 (AB q, $J$ = 10.2 Hz, 8 H, $CH_2$), 7.33 (t, $J$ = 1.6 Hz, 1 H, $H_{2'}$), 7.40–7.49 (m, 6 H, outer $m$-terphenyl ring protons), 7.63 (d, $J$ = 1.6 Hz, 2 H, $H_{4',6'}$); mass spectrum, $m/e$ (relative intensity) 680 (0.5), 679 (1), 678 (0.5), 441 (28), 440 (22), 439 (53), 438 (14), 437 (27), 280 (44), 279 (51), 265 (59), 139 (59), 132 (75), 106 (100). Anal. Calcd for $C_{22}H_{17}Br_5$: C, 38.81; H, 2.52. Found: C, 38.43; H, 2.51.

**3,5-Dibromo-4-iodobiphenyl (20).** A solution of bromine (9.45 g, 59.1 mmol) in 25 mL of glacial acetic acid was slowly added at rt to a well-stirred solution of 4-aminobiphenyl (**19**)[15] (OSHA carcinogen) (5.0 g, 29.5 mmol) in 80 mL of glacial acetic acid. After addition was complete, the mixture was stirred for 3 h and then poured into 200 mL of $H_2O$ with vigorous stirring. The resulting precipitate was filtered, dried, and recrystallized from heptane-/$CH_2Cl_2$ (4:1 v/v) to yield 8.4 g (87%) of 3,5-dibromo-4-aminobiphenyl as light brown needles, mp 114 °C: $^1$H NMR $\delta$ 4.59 (br s, 2 H, $NH_2$), 7.26–7.50 (m, 5 H, $H_{2'-6'}$), 7.64 (s, 2 H, $H_{2,6}$); mass spectrum, $m/e$ (relative intensity) 329 (45), 327 (100), 325 (45). Anal. Calcd for $C_{12}H_9Br_2N$: C, 44.07; H, 2.65. Found: C, 44.04; H, 2.65.

To a solution of this dibromoaminobiphenyl (8.4 g, 2.6 mmol) in 250 mL of 22% HCl maintained at 0–10 °C was slowly added an aqueous solution of sodium nitrite (2.65 g, 38.5 mmol). After being stirred at that temperature for 3 h, the diazonium solution was poured through a glass wool filter into a solution of KI (80 g) in 200 mL of $H_2O$. The mixture was stirred for 1 h and 300 mL of $CHCl_3$ and 30 mL of 1 N sodium sulfite was added. The aqueous layer was washed with $CHCl_3$ and the combined organic layers were dried. Solvent was evaporated and the crude product was chromatographed (silica gel, hexanes) to give 10.2 g (91%) of **20** as a white solid, mp 111 °C (hexanes): $^1$H NMR $\delta$ 7.41–7.54 (m, 5 H, $H_{2'-6'}$), 7.78 (s, 2 H, $H_{2,6}$); mass spectrum, $m/e$ (relative intensity ) 440 (45), 438 (100), 436 (48), 232 (45), 230 (45). Anal. Calcd for $C_{12}H_7Br_2I$: C, 32.91; H, 1.61. Found: C, 32.77; H, 1.60.

**5′-Phenyl-2,6,2″,6″-tetramethyl-1,1′:3′,1″-terphenyl (21).** The procedure was analogous to that described for **17**. From Grignard reagent prepared from 6.49 g (34.2 mmol) of 2,6-dimethylbromobenzene and 0.93 g (38 mmol) of Mg and 5.0 g (11.4 mmol) of **20** there was obtained 3.1 g (75%) of **21** as a white solid, mp 115 °C (hexanes): $^1$H NMR $\delta$ 2.18 (s, 12 H, $CH_3$), 6.97 (t, $J$ = 1.6 Hz, 1 H, $H_{2'}$), 7.18–7.25 (m, 6 H), 7.37–7.50 (m, 5 H, Ph), 7.71 (dd, $J$ = 7.2, 1.6 Hz, 2 H, $H_{4',6'}$); mass spectrum, $m/e$ (relative intensity) 362 (100), 347 (20), 332 (5), 257 (12). Anal. Calcd for $C_{28}H_{26}$: C, 92.77; H, 7.23. Found: C, 93.06; H, 7.42.

**5′-Phenyl-2,6,2″,6″-tetrakis(dibromomethyl)-1,1′:3′,1″-terphenyl (22).** NBS (12.7 g, 71.3 mmol) was added in two portions 6 h apart to a refluxing solution of **21** (2.15 g, 5.94 mmol) in 200 mL of $CCl_4$, each addition being followed by a few milligrams of benzoyl peroxide. After 48 h total reflux time, the hot mixture was filtered to remove the succinimide. The crude product ob-

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tained after evaporation of the solvent was recrystallized from benzene to yield 4.6 g (78%) of **22** as white needles, mp 265 °C: $^1$H NMR $\delta$ 6.42 (s, 4 H, C*H*Br$_2$), 7.26 (t, $J$ = 1.5 Hz, H$_{2'}$), 7.38–7.76 (m, 9 H), 8.13 (d, $J$ = 7.9 Hz, 4 H, Ar protons ortho to CHBr$_2$); mass spectrum, $m/e$ (relative intensity) 994 (1), 914 (0.5), 752 (20), 591 (19), 433 (14), 351 (67), 176 (100). Anal. Calcd for $C_{28}H_{18}Br_8$: C, 33.84; H, 1.83. Found: C, 33.93; H, 1.70.

**5′-Phenyl-2,6,2″,6″-tetraformyl-1,1′:3′,1″-terphenyl (23).** A mixture of octabromide **22** (4.0 g, 4.0 mmol), sodium acetate (2.8 g, 34.1 mmol), and silver nitrate (10.9 g, 64.4 mmol) in 240 mL of THF/H$_2$O (5:1 v/v) was heated at reflux for 24 h. The inorganic precipitate was filtered, the solvent was removed, and the crude product was chromatographed (silica gel, CHCl$_3$) to yield 1.26 g (75%) of **23** as a white solid, mp 178 °C: $^1$H NMR $\delta$ 7.27–7.78 (m, 10 H), 8.27 (d, $J$ = 7.7 Hz, 4 H, Ar protons ortho to CHO), 10.01 (s, 4 H, C*H*O); mass spectrum, $m/e$ (relative intensity) 418 (36), 372 (58), 343 (100), 315 (84); IR (CHCl$_3$) $\nu_{C=O}$ 1690 cm$^{-1}$. Anal. Calcd for $C_{28}H_{18}O_4$: C, 80.37; H, 4.34. Found: C, 80.41; H, 4.24.

**5′-Phenyl-2,6,2″,6″-tetrakis(hydroxymethyl)-1,1′:3′,1″-terphenyl (24).** A solution of tetraaldehyde **23** (1.0 g, 2.4 mmol) in 30 mL of 1:1 MeOH/THF was added dropwise to a slurry of NaBH$_4$ (0.12 g, 3.2 mmol) in 30 mL of THF at rt. The mixture was stirred at rt for 6 h and then quenched with a minimum amount of 10% HCl. The solvent was removed and the crude product was extracted (soxhlet) with 3% MeOH in CHCl$_3$ to yield 0.85 g (83%) of **24** as a pale yellow solid, mp 225 °C dec: $^1$H NMR (DMSO-$d_6$) $\delta$ 4.24 (d, $J$ = 4.6 Hz, 8 H, C*H*$_2$), 5.06 (t, $J$ = 4.6 Hz, 4 H, O*H*), 6.89 (br s, 1 H, H$_{2'}$), 7.34–7.44 (m, 9 H), 7.73 (d, $J$ = 7.2 Hz, 4 H, Ar protons adjacent to CH$_2$OH); mass spectrum, $m/e$ (relative intensity) 426 (20), 372 (32), 356 (20), 258 (20), 149 (100). The product was converted directly to **25** without analysis.

**5′-Phenyl-2,6,2″,6″-tetrakis(bromomethyl)-1,1′:3′,1″-terphenyl (25).** A solution of PBr$_3$ (0.76 g, 2.81 mmol) in 15 mL of dry benzene was slowly added at rt to a well-stirred suspension of tetrol **24** (0.6 g, 1.41 mmol) in 40 mL of dry benzene containing a few drops of pyridine. After addition was complete, the mixture was stirred for an additional 6 h, then washed successively with aqueous sodium bicarbonate and water, and dried. Evaporation of the solvent gave a yellowish gum, which was chromatographed [silica gel, CHCl$_3$/hexanes (1:5 v/v)] to yield 0.85 g (61%) of **25** as a white solid, mp 148 °C: $^1$H NMR $\delta$ 4.37 (s, 8 H, C*H*$_2$), 7.26–7.52 (m, 10 H), 7.71–7.77 (m, 4 H); mass spectrum, $m/e$ (relative intensity) 678 (16), 437 (100), 435 (75), 356 (80), 355 (82). Anal. Calcd for $C_{28}H_{22}Br_4$: C, 49.59; H, 3.27. Found: C, 49.55; H, 3.27.

**General Procedure for Assembling Cyclophanes 11, 15, 26, and 27 via Tetrabromide–Tetrathiol Coupling.** A solution containing equimolar amounts (0.83 mmol) of the appropriate tetrakis(bromomethyl) compound and tetrakis(mercaptomethyl) compound in 100 mL of argon-degassed benzene was added dropwise over 4–6 h to a well-stirred solution of KOH (0.28 g, 4.98 mmol) in 300 mL of 95% EtOH. After addition was complete, the mixture was stirred for an additional 2 h and then evaporated to dryness. The crude product was chromatographed (silica gel, CHCl$_3$). The yields, physical properties, and spectra are given below.

**11sf**: 62%, mp >300 °C dec; $^1$H NMR (CDCl$_3$) $\delta$ 3.00 (d, $J$ = 10.4 Hz, 4 H, C*H*$_2$S), 3.39 (d, $J$ = 10.4 Hz, 4 H, C*H*$_2$S), 3.41, 3.52 (AB q, $J$ = 14.5 Hz, 8 H, C*H*$_2$S), 4.31 (t, $J$ = 7.7 Hz, 1 H, H$_{5'}$), 5.19 (s, 4 H, C*H*$_2$O), 6.24 (br s, 3 H, 2 phenoxy ring + H$_{2'}$), 6.32 (dd, $J$ = 7.7, 1.8 Hz, 2 H, H$_{4',6'}$), 6.63 (d, $J$ = 1.1 Hz, 4 H, phenoxy ring), 7.14–7.34 (m, 6 H, outer $m$-terphenyl ring), 7.62 (s, 4 H, $p$-xylylene ring); $^1$H NMR (C$_6$D$_6$) $\delta$ 2.94 (d, $J$ = 10.8 Hz, 4 H, C*H*$_2$S), 3.19 (d, $J$ = 10.8 Hz, 4 H, C*H*$_2$S), 3.07 3.13 (AB q, $J$ = 13.8 Hz, C*H*$_2$S), 4.28 (t, $J$ = 7.5 Hz, 1 H, H$_{5'}$), 4.78 (s, 4 H, C*H*$_2$O), 5.88 (t, $J$ = 1.8 Hz, 1 H, H$_{2'}$), 6.08 (br s, 2 H, phenoxy ring), 6.37 (dd, $J$ = 7.5, 1.8 Hz, 2 H, H$_{4',6'}$), 6.53 (d, $J$ = 1.2 Hz, 4 H, phenoxy ring), 7.07 (t, $J$ = 7.5 Hz, 2 H, outer $m$-terphenyl ring), 7.25 (s, 4 H, $p$-xylylene ring), 7.36 (d, $J$ = 7.5 Hz, 4 H, outer $m$-terphenyl ring); $^{13}$C NMR $\delta$ 33.1 37.0 (*C*H$_2$S), 67.5 (*C*H$_2$O), 113.7, 121.1, 126.6, 127.6, 127.7, 128.0, 128.6, 128.9, 135.2, 135.8, 138.0, 139.3, 141.8, 158.1 (Ar); mass spectrum, $m/e$, 25 eV (relative intensity) 752 (11, M$^+$), 719 (2), 631 (2), 311 (5), 167 (14), 149 (28). Anal. Calcd for $C_{44}H_{36}O_2S_4$: C, 72.89; H, 5.00. Found: C, 72.76; H, 5.15.

11v: 2%, mp >300 °C dec; $^1$H NMR (CDCl$_3$) $\delta$ 2.58, 2.76 (AB q, $J$ = 14.6 Hz, 8 H, C*H*$_2$S), 3.52 (d, $J$ = 12.9 Hz, 4 H, C*H*$_2$S), 3.65 (d, $J$ = 12.9 Hz, 4 H, C*H*$_2$S), 4.63 (s, 4 H, C*H*$_2$O), 5.70 (t, $J$ = 1.6 Hz, 1 H, H$_{2'}$), 6.10 (d, $J$ = 1.6 Hz, 4 H, phenoxy ring), 6.69 (br s, 2 H, phenoxy ring), 6.96 (dd, $J$ = 7.7, 1.6 Hz, 2 H, H$_{4',6'}$), 7.10 (s, 4 H, $p$-xylylene ring), 7.35 (t, $J$ = 7.6 Hz, 1 H, H$_{5'}$), 7.48–7.61 (m, 6 H, outer $m$-terphenyl ring); $^1$H NMR (C$_6$D$_6$) $\delta$ 2.88 (s, 8 H, C*H*$_2$S), 3.46, 3.61 (AB q, $J$ = 13.2 Hz, 8 H, C*H*$_2$S), 4.56 (s, 4 H, C*H*$_2$O), 5.99 (t, $J$ = 1.6 Hz, 1 H, H$_{2'}$), 6.24 (br s, 4 H, phenoxy ring), 6.84 (br s, 2 H, phenoxy ring), 6.87 (dd, $J$ = 7.6, 1.6 Hz, 2 H, H$_{4',6'}$), 7.21 (t, $J$ = 7.6 Hz, 1 H, H$_{5'}$), 7.35 (s, 4 H, $p$-xylylene ring), 7.50 (t, $J$ = 7.7 Hz, 2 H, H$_{4,4''}$ of the $m$-terphenyl unit), 7.82 (d, $J$ = 7.7 Hz, 4 H, H$_{3,5,3'',5''}$ of the $m$-terphenyl unit); $^{13}$C NMR $\delta$ 32.4, 35.4 (*C*H$_2$S), 68.8 (*C*H$_2$O), 117.1, 121.9, 122.7, 126.6, 126.8, 128.1, 129.1, 135.3, 136.0, 138.4, 138.6, 141.0, 156.5 (Ar, one overlapped); mass spectrum, $m/e$, 25 eV (relative intensity) 752 (6, M$^+$). Anal. Calcd for $C_{44}H_{36}O_2S_4$: C, 72.89; H, 5.00. Found: C, 72.34; H, 4.94.

**15sf**: 79%, mp >260 °C dec; $^1$H NMR (CDCl$_3$) $\delta$ 2.41 (quin, $J$ = 4.8 Hz, 2 H, —CH$_2$C*H*$_2$CH$_2$—), 2.86 (d, $J$ = 9.9 Hz, 4 H, C*H*$_2$S), 3.34 (d, $J$ = 14.6 Hz, 4 H, C*H*$_2$S), 3.52 (d, $J$ = 14.6 Hz, 4 H, C*H*$_2$S), 3.58 (d, $J$ = 9.9 Hz, 4 H, C*H*$_2$S), 4.37 (t, $J$ = 4.7 Hz, 4 H, C*H*$_2$O), 6.13 (t, $J$ = 1.6 Hz, 1 H, H$_{2'}$), 6.16 (br s, 2 H, phenoxy ring), 6.23 (t, $J$ = 7.7 Hz, 1 H, H$_{5'}$), 6.74 (br s, 4 H, phenoxy ring), 6.81 (dd, $J$ = 7.7, 1.6 Hz, 2 H, H$_{4',6'}$), 7.15–7.26 (m, 6 H, outer $m$-terphenyl rings); $^1$H NMR (C$_6$D$_6$) $\delta$ 1.96 (quin, $J$ = 4.6 Hz, 2 H, —CH$_2$C*H*$_2$CH$_2$—), 3.10, 3.26 (AB q, $J$ = 14.6 Hz, 8 H, C*H*$_2$S), 3.38 (d, $J$ = 9.9 Hz, 4 H, C*H*$_2$S), 3.95 (br m, 4 H C*H*$_2$O), 5.86 (br s, 1 H, H$_{2'}$), 5.88 (br s, 2 H, phenoxy ring), 6.22 (t, $J$ = 7.6 Hz, 1 H, H$_{5'}$), 6.50 (br s, 4 H, phenoxy ring), 6.99 (dd, $J$ = 7.6, 1.8 Hz, 2 H, H$_{4',6'}$), 7.03 (t, $J$ = 7.6 Hz, 2 H, H$_{4,4''}$ of the $m$-terphenyl unit), 7.25 (d, $J$ = 7.6 Hz, 4 H, H$_{3,5,3'',5''}$ of the $m$-terphenyl unit); $^{13}$C NMR $\delta$ 30.0 (—CH$_2$CH$_2$CH$_2$—), 32.8, 37.1 (*C*H$_2$S), 62.2 (*C*H$_2$O), 121.7, 124.8, 126.9, 127.5, 128.0, 128.4, 135.2, 135.7, 139.2, 142.1, 160.3 (Ar, one overlapped); mass spectrum, $m/e$, 25 eV (relative intensity) 690 (8, M$^+$), 418 (4), 311 (11), 280 (9), 167 (13), 149 (100). Anal. Calcd for $C_{41}H_{38}O_2S_4 \cdot H_2O$: C, 69.45; H, 5.68. Found: C, 69.70; H, 5.37 ($^1$H NMR spectra in CDCl$_3$ and C$_6$D$_6$ showed peaks at $\delta$ ~1.50 for H$_2$O).

**26v**: 28%, mp >275 °C dec; $^1$H NMR (CDCl$_3$) $\delta$ 2.65 (s, 8 H, C*H*$_2$S), 3.54, 3.68 (AB q, $J$ = 13.1 Hz, 8 H, C*H*$_2$S), 4.63 (s, 4 H, C*H*$_2$O), 5.65 (t, $J$ = 1.3 Hz, 1 H, H$_{2'}$), 6.10 (br s, 4 H, phenoxy ring), 6.76 (br s, 2 H, phenoxy ring), 7.07 (s, 4 H, $p$-xylylene ring), 7.17 (d, $J$ = 1.3 Hz, 2 H, H$_{4',6'}$), 7.50–7.61 (m, 6 H, outer $m$-terphenyl rings); $^1$H NMR (C$_6$D$_6$) $\delta$ 2.73 (d, $J$ = 14.6 Hz, 4 H, C*H*$_2$S), 2.91 (d, $J$ = 14.6 Hz, 4 H, C*H*$_2$S), 3.56, 3.64 (AB q, $J$ = 13.1 Hz, 8 H, C*H*$_2$S), 4.60 (s, 4 H, C*H*$_2$O), 5.95 (t, $J$ = 1.5 Hz, 1 H, H$_{2'}$), 6.26 (d, $J$ = 1.4 Hz, 4 H, phenoxy rings), 6.97 (br s, 2 H, phenoxy rings), 7.15 (s, 4 H, $p$-xylylene ring), 7.25 (d, $J$ = 1.5 Hz, 2 H, H$_{4',6'}$), 7.54 (t, $J$ = 7.7 Hz, 2 H, H$_{4,4''}$ of $m$-terphenyl unit), 7.81 (d, $J$ = 7.7 Hz, 4 H, H$_{3,5,3'',5''}$ of $m$-terphenyl unit); $^{13}$C NMR (CDCl$_3$) $\delta$ 32.3, 35.4 (*C*H$_2$S), 68.7 (*C*H$_2$O), 116.9, 121.9, 122.3, 125.3, 126.4, 127.0, 128.5, 132.0, 135.3, 135.9, 138.6, 139.4, 140.0, 156.4 (14 Ar resonances for 36 Ar carbons, as required by symmetry; last peak is oxygen-bearing arom carbon); mass spectrum, FAB ($m$-nitrobenzyl alcohol matrix) 833 (MH$^+$). Anal. Calcd for $C_{46}H_{39}BrO_2S_4$: C, 66.41; H, 4.73. Found: C, 67.08; H, 4.84.

**26sf**: 8%, mp >300 °C dec; $^1$H NMR (CDCl$_3$) $\delta$ 3.41, 3.45 (AB q, $J$ = 15.0 Hz, 8 H, C*H*$_2$S), 3.36, 3.52 (AB q, $J$ = 10.9 Hz, 8 H, C*H*$_2$S), 5.15 (s, 4 H, C*H*$_2$O), 6.39 (br s, 2 H, phenoxy rings), 6.41 (t, $J$ = 1.4 Hz, H$_{2'}$), 6.56 (br s, 4 H, phenoxy rings), 6.61 (br s, 2 H, H$_{4',6'}$), 7.26–7.44 (m, 6 H, outer $m$-terphenyl rings), 7.52 (s, 4 H, $p$-xylylene ring); $^{13}$C NMR (CDCl$_3$) $\delta$ 33.0, 36.2 (*C*H$_2$S), 67.6 (*C*H$_2$O), 119.7, 128.2, 129.2, 131.0, 131.1, 131.12, 132.2, 135.2, 136.0, 138.4, 139.3, 141.2, 158.0 (13 Ar resonances, one overlapped); mass spectrum, FAB ($m$-nitrobenzyl alcohol matrix) 833 (MH$^+$); high resolution mass spectrum, calcd for $C_{46}H_{39}BrO_2S_4$ (M$^+$) 830.1016, found 830.1030.

Compound **26sf** was converted to **11sf** as follows. To a solution of **26sf** (50 mg, 0.06 mmol) in 5 mL of dry THF was added 7.5 $\mu$L of $n$-butyllithium (2.0 equiv, 1.6 M in THF) at −78 °C under Ar. The mixture was stirred under Ar at that temperature for 6 h, quenched with dilute HCl, extracted with CHCl$_3$ (2 × 10 mL), and dried. The $^1$H NMR spectrum of the crude product indicated a 60–65% conversion of **11sf** as deduced by its diagnostic triplet ($J$ = 7.7 Hz), due to H$_{5'}$ of **11sf**, which appeared at $\delta$ 4.31.

**27v**: 57%, mp >295 °C dec; $^1$H NMR (CDCl$_3$) $\delta$ 2.70 (s, 8 H, C*H*$_2$S), 3.46, 3.63 (AB q, $J$ = 12.9 Hz, 8 H, C*H*$_2$S), 4.63 (s, 4 H, C*H*$_2$O), 5.66 (t, $J$ = 1.6 Hz, 1 H, H$_{2'}$), 6.10 (br s, 4 H, phenoxy

rings), 6.67 (br s, 2 H, phenoxy rings), 7.07 (s, 4 H, *p*-xylylene ring), 7.21–7.41 (m, 7 H, $H_{4',6'}$ + phenyl ring), 7.48–7.60 (m, 6 H, outer *m*-terphenyl rings); $^1$H NMR ($C_6D_6$) δ 2.85, 2.99 (AB q, *J* = 14.5 Hz, 8 H, $CH_2S$), 3.45, 3.59 (AB q, *J* = 13.0 Hz, 8 H, $CH_2S$), 4.57 (s, 4 H, $CH_2O$), 5.98 (t, *J* = 1.6 Hz, $H_{2'}$), 6.26 (br s, 4 H, phenoxy rings), 6.88 (br s, 2 H, phenoxy rings), 7.13 (s, 4 H, *p*-xylylene ring), 7.30–7.40 (m, 5 H, $H_{4',6'}$ + three phenyl ring protons), 7.53 (t, *J* = 7.6 Hz, 2 H, $H_{4,4''}$ of *m*-terphenyl unit), 7.7 (dd, *J* = 7.2, 1.1 Hz, 2 H, ortho protons of phenyl ring), 7.84 (d, *J* = 7.6 Hz, 4 H, $H_{3,5,3'',5''}$ of *m*-terphenyl unit); $^{13}$C NMR δ 32.4 35.4 ($CH_2S$), 68.8 ($CH_2O$), 117.1, 121.9, 125.1, 126.5, 126.9, 127.0, 127.5, 127.8, 128.2, 128.8, 135.4, 136.0, 138.6, 138.7, 140.3, 140.7, 141.0, 156.5 (Ar); mass spectrum, FAB (*m*-nitrobenzyl alcohol matrix) 829 ($MH^+$); high resolution mass spectrum, calcd for $C_{52}H_{45}O_2S_4$ ($MH^+$) 829.23024, found 829.22809. Anal. Calcd for $C_{52}H_{44}O_2S_4$: C, 75.32; H, 5.35. Found: C, 75.20; H, 5.44.

**3,5-Bis(mercaptomethyl)phenol (28).** To a solution of 3,5-bis(bromomethyl)anisole[12] (2.5 g, 8.5 mmol) in 100 mL of $CH_2Cl_2$ was added 1.06 g (4.3 mmol) of $BBr_3$ as a 1.0 M solution in $CH_2Cl_2$. The mixture was heated at reflux for 10 h, cooled, and cautiously poured into cold water (100 mL). The organic layer was evaporated to yield 1.55 g (65%) of 3,5-bis(bromomethyl)phenol as a brown solid, mp 74 °C: $^1$H NMR δ 4.39 (s, 4 H, $CH_2$), 4.85 (br s, 1 H, O*H*), 6.79 (br s, 2 H, $H_{2,6}$), 6.97 (br s, 1 H, $H_4$); mass spectrum, FAB (*m*-nitrobenzyl alcohol matrix) 280 ($M^+$). Anal. Calcd for $C_8H_8Br_2O$: C, 34.32; H, 2.88. Found: C, 34.86; H, 3.25.

To a solution of this phenol in THF (100 mL) was added 0.88 g (11.6 mmol) of thiourea, and the mixture was stirred at gentle reflux for 6 h. On cooling, the isothiouronium salt that separated was filtered and dissolved in dioxane/water (100 mL, 1:1 v/v), and to it was added, under argon, 0.66 (11.1 mmol) of ethylenediamine. This mixture was stirred at reflux for 6 h. Solvent was removed at reduced pressure (rotavap) and the residue was dissolved in $CHCl_3$ (100 mL), washed with 10% HCl (2×60 mL), and dried. Evaporation of the solvent and chromatography of the residue (silica gel, $CHCl_3$) gave 0.54 g (52%) of **28** as a waxy white solid, mp 50–51 °C: $^1$H NMR δ 1.77 (t, *J* = 7.7 Hz, 2 H, S*H*), 3.67 (d, *J* = 7.7 Hz, 4 H, $CH_2$), 4.82 (br s, 1 H, O*H*), 6.70 (br s, 2 H, $H_{2,6}$), 6.84 (br s, 1 H, $H_4$); mass spectrum, FAB (*m*-nitrobenzyl alcohol matrix) 186 ($M^+$). Anal. Calcd for $C_8H_{10}OS_2$: C, 51.58; H, 5.41. Found: C, 51.53; H, 5.36.

**10,33-Dihydroxy-13*H*,15*H*-1,19-(methanothiomethano[1,3]benzenomethanothiomethano)-8,12:20,24-dimetheno-5*H*,7*H*-dibenzo[*k*,*r*][1,9]dithiacycloeicosin (29).** A solution of **4** (1.3 g, 2.2 mmol) and dithiol **28** (0.81 g, 4.4 mmol) in argon-degassed benzene (150 mL) was added dropwise over 6–8 h with vigorous stirring under argon to a solution of KOH (0.63 g, 11.3 mmol) in 300 mL of 95% EtOH. The mixture was stirred for an additional 2 h and then evaporated to dryness. The crude product was chromatographed (silica gel, 5% MeOH in $CHCl_3$) to give 0.95 g (68%) of **29** as a pale brown solid that softened at 130 °C and darkened at 220 °C: $^1$H NMR ($CDCl_3$/MeOD 12:1 v/v) δ 2.96 (d, *J* = 10.6 Hz, 4 H, $CH_2S$), 3.40 (d, *J* = 10.6 Hz, 4 H, $CH_2S$), 3.43, 3.49 (AB q, *J* = 14.1 Hz, 8 H, $CH_2S$), 6.29 (br s, 2 H, phenoxy rings), 6.37 (t, *J* = 1.2 Hz, 1 H, $H_{2'}$), 6.55 (br s, 4 H, phenoxy rings), 6.96 (dd, *J* = 8.1, 1.2 Hz, 2 H, $H_{4',6'}$), 7.04 (t, *J* = 8.1 Hz, 1 H, $H_{5'}$), 7.26 (t, *J* = 7.5 Hz, 2 H, $H_{4,4''}$ of *m*-terphenyl unit), 7.37 (d, *J* = 7.5 Hz, 4 H, $H_{3,5,3'',5''}$ of *m*-terphenyl unit); mass spectrum, FAB (*m*-nitrobenzyl alcohol matrix) 651 ($MH^+$). Anal. Calcd for $C_{38}H_{34}O_2S_4 \cdot 2H_2O$: C, 66.44; H, 5.58. Found: C, 67.04; H, 5.67.

**General Procedure for the Preparation of 11, 30, 31, and 32 from Bisphenol 29.** A solution of bisphenol **29** (0.325 g, 0.5 mmol) and the capping dihalide (0.5 mmol) in Ar-degassed DMF (80 mL) was added dropwise over 4–6 h to a well-stirred suspension of $K_2CO_3$ (4 g) in 100 mL of DMF at rt. The mixture was stirred for an additional hour after which the $K_2CO_3$ was removed by filtration. DMF was removed under reduced pressure to give the crude product, which was chromatographed (silica gel, $CHCl_3$) to give the pure cyclophanes with the following properties.

**11sf**: ~3%, identical properties as described above.

**11v**: 51%, identical properties as described above.

**30sf**: 28%, mp 300 °C dec; $^1$H NMR δ 2.85 (d, *J* = 9.9 Hz, 4 H, $CH_2S$), 3.42 (d, *J* = 9.9 Hz, 4 H, $CH_2S$), 3.22, 3.47 (AB q, *J* = 14.4 Hz, 8 H, $CH_2S$), 5.15 (s, 4 H, $CH_2O$), 6.13 (br s, 1 H, $H_{2'}$), 6.20 (br s, 2 H, phenoxy rings), 6.29–6.32 (m, 3 H, $H_{4',5',6'}$), 6.70 (br s, 4 H, phenoxy rings), 7.17–7.46 (m, 9 H, 3 vicinal *m*-xylylene ring protons + outer *m*-terphenyl rings), 8.02 (br s, 1 H, isolated proton on *m*-xylylene ring); $^{13}$C NMR δ 32.8, 37.0 ($CH_2S$), 69.5 ($CH_2O$), 113.9, 121.3, 127.3, 127.4, 127.5, 127.6, 128.1, 128.5, 128.7, 129.4, 135.1, 135.9, 138.2, 139.3, 141.9, 159.8 (16 Ar resonances as required by symmetry for 36 aromatic carbons); mass spectrum, FAB (*m*-nitrobenzyl alcohol matrix) 753 ($MH^+$); high resolution mass spectrum, calcd for $C_{46}H_{41}O_2S_4$ ($MH^+$) 753.19892, found 753.19703.

**30v** (trace): $^1$H NMR δ 2.87, 3.00 (AB q, *J* = 14.1 Hz, 8 H, $CH_2S$), 3.53, 3.61 (AB q, *J* = 13.4 Hz, 8 H, $CH_2S$), 4.65 (s, 4 H, $CH_2O$), 5.74 (t, *J* = 1.2 Hz, $H_{2'}$), 6.07 (br s, 4 H, phenoxy rings), 6.89 (br s, 2 H, phenoxy rings), 6.92 (dd, *J* = 7.2, 1.8 Hz, 2 H, $H_{4',6'}$), 7.26–7.60 (m, 10 H, outer *m*-terphenyl rings + 3 *m*-xylylene protons + $H_{5'}$). This compound was not characterized further due to lack of material.

**31sf**: 26%, mp 225–228 °C; $^1$H NMR δ 2.86 (d, *J* = 12.0 Hz, 4 H, $CH_2S$), 3.37, 3.53 (AB q, *J* = 15.0 Hz, 8 H, $CH_2S$), 3.57 (d, *J* = 12.0 Hz, 4 H, $CH_2S$), 5.26 (s, 4 H, $CH_2O$), 6.17 (t, *J* = 1.1 Hz, $H_{2'}$), 6.25 (br s, 2 H, phenoxy ring), 6.80 (m 1 H, $H_{5'}$), 6.88 (m, 6 H, phenoxy ring + $H_{4',6'}$), 7.22 (m, 6 H, outer *m*-terphenyl rings), 7.54 (m, 2 H, *o*-xylyl ring), 7.61 (m, 2 H, *o*-xylyl ring); $^{13}$C NMR δ 32.7, 37.1 ($CH_2S$), 67.2 ($CH_2O$), 114.4, 121.9, 125.9, 127.3, 127.5, 127.9, 128.5, 129.5, 132.6, 135.2, 135.3, 136.2, 139.4, 141.8, 160.0 (15 Ar carbons, as required by symmetry); high resolution mass spectrum, calcd for $C_{46}H_{41}O_2S_4$ ($MH^+$) 753.1989, found 753.1982.

**32sf**: 22%, mp 260 °C dec; $^1$H NMR δ 2.74 (d, *J* = 9.6, Hz, 4 H, $CH_2S$), 3.32, 3.48 (AB q, *J* = 14.4 Hz, 8 H, $CH_2S$), 3.50 (d, *J* = 9.6 Hz, 4 H, $CH_2S$), 4.65 (m, 4 H, $CH_2C{=}$), 6.13 (br s, 1 H, $H_{2'}$), 6.18 (br s, 2 H, phenoxy rings), 6.33 (t, *J* = 5.1 Hz, 2 H, vinyl), 6.65 (t, *J* = 7.5 Hz, 1 H, $H_{5'}$), 6.76 (s, 4 H, phenoxy rings), 6.85 (dd, *J* = 7.5, 1.2 Hz, 2 H, $H_{4',6'}$), 7.17–7.24 (m, 6 H, outer *m*-terphenyl rings); $^{13}$C NMR δ 29.6 ($CH_2C{=}$), 32.7, 37.2 ($CH_2S$), 61.7 ($CH_2O$), 114.2, 122.0, 126.6, 126.8, 127.4, 127.5, 128.6, 129.6, 135.0, 136.7, 139.3, 141.5, 159.7 (12 Ar and 1 vinyl carbon, as required by symmetry); mass spectrum, FAB (*m*-nitrobenzyl alcohol matrix) 703 ($MH^+$); high resolution mass spectrum, calcd for $C_{42}H_{39}O_2S_4$ ($MH^+$) 703.18327, found 703.18657. Anal. Calcd for $C_{42}H_{38}O_2S_4$: C, 71.75; H, 5.44. Found: C, 71.77; H, 5.60.

**10,33-Dihydroxy-25-bromo-13*H*,15*H*-1,19-(methanothiomethano[1,3]benzenomethanothiomethano)-8,12:20,24-dimetheno-5*H*,7*H*-dibenzo[*k*,*r*][1,9]dithiacycloeicosin (35).** A solution of **34**[1b] (0.7 g, 1.03 mmol) and dithiol **28** (0.38 g, 2.05 mmol) in Ar-degassed benzene (125 mL) was added dropwise over 6–8 h with vigorous stirring under argon to a solution of KOH (0.46 g, 8.24 mmol) in 250 mL of 95% EtOH. The mixture was stirred for an additional 2 h and then evaporated to dryness. The residue was chromatographed (silica gel, 2% MeOH in $CHCl_3$) to give 0.3 g (40%) of **35** as a white solid, mp 260 °C: $^1$H NMR ($CDCl_3$/MeOD 12:1 v/v) δ 2.70 (d, *J* = 10.5 Hz, 4 H, $CH_2S$), 3.37, 3.49 (AB q, *J* = 14.4 Hz, 8 H, $CH_2S$), 3.51 (d, *J* = 10.5 Hz, 4 H, $CH_2S$), 6.21 (br s, 2 H, phenoxy rings), 6.58 (d, *J* = 1.5 Hz, 4 H, phenoxy rings), 6.94 (m, 3 H, $H_{4',5',6'}$), 7.26–7.35 (m, 6 H, outer *m*-terphenyl rings); $^{13}$C NMR δ 32.6, 36.9 ($CH_2S$), 114.7, 120.8, 126.1, 127.9, 128.7, 129.8, 134.9, 135.1, 137.7, 139.3, 140.4, 157.3 (12 Ar carbons); high resolution mass spectrum, calcd for $C_{38}H_{34}BrO_2S_4$ ($MH^+$) 729.06254, found 729.06078. Anal. Calcd for $C_{38}H_{33}BrO_2S_4 \cdot H_2O$: C, 61.02; H, 4.72. Found: C, 60.64; H, 4.85.

**Cyclophane 33sf.** A solution of bisphenol **35** (0.15, 0.21 mmol) and *p*-xylylene dibromide (54 mg, 9.21 mmol) in Ar-gassed DMF (30 mL) was added dropwise over 2–3 h to a well-stirred suspension of $K_2CO_3$ (2 g) in 50 mL of dry DMF. The mixture was stirred for an additional hour and the $K_2CO_3$ was removed by filtration. Removal of the DMF under reduced pressure gave crude product, which was chromatographed (silica gel, $CHCl_3$) to give 81 mg (47%) of **33sf** as a white solid, mp 268 °C dec: $^1$H NMR δ 2.79 (d, *J* = 10.8 Hz, 4 H, $CH_2S$), 3.48 (d, *J* = 10.8 Hz, 4 H, $CH_2S$), 3.37, 3.49 (AB q, *J* = 14.4 Hz, 8 H, $CH_2S$), 4.34 (t, *J* = 7.5 Hz, $H_{5'}$), 5.17 (s, 4 H, $CH_2O$), 6.25 (br s, 2 H, phenoxy rings), 6.38 (d, *J* = 7.5 Hz, 2 H, $H_{4',6'}$), 6.68 (br s, 4 H, phenoxy rings), 7.28–7.38 (m, 6 H, outer *m*-terphenyl rings), 7.60 (s, 4 H, *p*-xylylene ring); $^{13}$C NMR δ 33.0, 36.9 ($CH_2S$), 67.5 ($CH_2O$), 113.7, 121.1, 124.3, 125.4, 128.1, 128.5, 128.9, 129.6, 135.0, 136.9, 137.9, 139.5, 140.7, 158.3 (14 Ar carbons); high resolution mass spectrum, calcd for $C_{46}H_{40}BrO_2S_4$ ($MH^+$) 831.10948, found 831.11004.

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**Supplementary Material Available:** $^1H$ and/or $^{13}C$ NMR spectra of **24**, **26sf**, **30sf**, **31st**, and **33sf** (16 pages). Ordering information is given on any current masthead page.

# Relative Homolytic Strengths of C–H Bonds in Meldrum's Acid and Dimethyl Malonate

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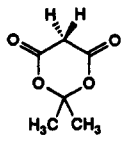
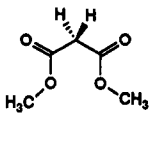
With the aid of a thermochemical cycle comprised of acidity and redox data in dimethyl sulfoxide and aqueous solution, relative homolytic bond dissociation energies (ΔBDE values) have been determined for 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid), dimethyl malonate, 5,5-dimethylcyclohexane-1,3-dione (dimedone), 2,4-pentanedione, acetone, 3-pentanone, and cyclopentanone. The ΔBDE data suggest that (a) secondary C–H bonds present in 3-pentanone are ca. 4 kcal/mol weaker (in a homolytic sense) than analogous primary C–H bonds in acetone; (b) C–H bonds located on carbon atoms adjacent to the carbonyl carbons in 3-pentanone and cyclopentanone are of equal homolytic strength, thus indicating a negligible effect due to cyclization; (c) homolytic BDEs for dimedone and 2,4-pentanedione are nearly equal, also indicative of no bond weakening due to cyclization; and (d) the C–H BDE for Meldrum's acid is ca. 3 kcal/mol less than that of the analogous C–H bond present in dimethyl malonate, indicative of a small cyclization effect on homolytic bond strengths. The Meldrum's acid/dimethyl malonate ΔBDE data are therefore in sharp contrast to published dimethyl sulfoxide solution $pK_a$'s for Meldrum's acid and dimethyl malonate (7.3 and 15.9, respectively: Arnett et al. *J. Am. Chem. Soc.* 1987, *109*, 809–812). The difference in the $pK_a$'s for Meldrum's acid and dimethyl malonate is thought to provide additional experimental support for the effects of rotational barriers on neutral closed-shell ester stabilities. The ΔBDE data in this article suggest that rotational barriers have substantial effects on the relative stabilities of the radicals derived from Meldrum's acid and dimethyl malonate as well.

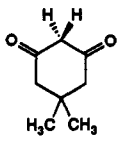
In dimethyl sulfoxide (DMSO) solution, at 25 °C, 2,2-dimethyl-1,3-dioxane-4,6-dione, (Meldrum's acid, **1**, $pK_a$ = 7.3) is 11.8 kcal/mol more acidic than dimethyl malonate (**2**, $pK_a$ = 15.9).[1] Under identical conditions, dimedone



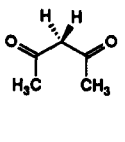
**1**



**2**



**3**



**4**

(**3**, $pK_a$ = 11.2) is only 2.9 kcal/mol more acidic than 2,4-pentanedione (**4**, $pK_a$ = 13.3).[1] The facile dimethyl sulfoxide solution ionization of Meldrum's acid has been attributed to two factors: (a) a 6–8 kcal/mol destabilization of Meldrum's acid (relative to dimethyl malonate) that results from its enforced *E* configuration and (b) a 3 kcal/mol stabilization of the conjugate based derived from Meldrum's acid (relative to the conjugate base derived from dimethyl malonate) that results from the enforced planarity of the cyclic enolate anion.[1] These data and the resulting interpretations are unique in that they enable analyses of structural and electronic factors that affect the relative stbilities of both partners in the respective acid–base equilibrium. In this article, we report our investigations of the cyclic voltammetric (CV) and, in some cases, second harmonic alternating current voltammetric (SHACV) oxidative reactions of the enolate anions derived from seven different organic acids. Redox data obtained in this fashion, when combined with the aforementioned acidity constants, enable comparisons of the free energy changes associated with the removal of hydrogen atoms from a given set of substrates. The resulting ΔBDE values

**Table I. DMSO Solution $pK_a$'s (25 °C) and Relative Acidity Constants ($\Delta pK_a$) for Substrates 1–7, Oxidation Potentials ($E_{ox(n-H^+)}$) and Relative Oxidation Potentials ($\Delta E_{ox}$) for the Conjugate Bases Derived from Substrates 1–7, and Relative Homolytic Bond Dissociation Energies (ΔBDE) for 1–7**

| substrate (n) | $pK_a$[4] | $\Delta pK_a$[5] (kcal/mol) | $E_{ox(n-H^+)}$[6,7] (V) | $\Delta E_{ox}$[8] (kcal/mol) | ΔBDE[9] (kcal/mol) |
|---|---|---|---|---|---|
| Meldrum's acid (1) | 7.3[1] | (0.0) | 1.16 | (0.0) | (0.0) |
| dimethyl malonate (2) | 15.9[1] | 11.8 | 0.77 | −9.0 | +3 |
| dimedone (3) | 11.2 | 5.3 | 0.93 (0.88) | −5.3 | 0 |
| 2,4-pentanedione (4) | 13.3 | 8.2 | 0.78 (0.73) | −8.8 | −1 |
| acetone (5) | 26.5 | 26.3 | 0.10 (0.08) | −24.4 | +2 |
| 3-pentanone (6) | 27.1 | 27.1 | −0.11 | −29.3 | −2 |
| cyclopentanone (7) | 25.8 | 25.3 | −0.03 | −27.4 | −2 |

(1) Arnett, E. M.; Maroldo, S. G.; Schilling, S. L.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 6759–6767. Arnett, E. M.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1987**, *109*, 809–812.

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