tinued for ~2 h. A conventional workup using diethyl ether gave a yellow oil after removal of all of the volatiles. A ^{1}H NMR spectrum and analysis by GC-MS indicated that the 1-methylbiphenylene was contaminated with some starting material and a small amount of dimethylbiphenylene(s). The biphenylene was removed by dissolving the oil in a small amount of ethanol and placing the solution in a freezer. The biphenylene precipitated out of solution and was filtered. This step was repeated until all the biphenylene was removed. The dimethylbiphenylenes could not be separated from the 1-methylbiphenylene by column chromatography, so the mixture was used in the reduction. ^{1}H NMR data for 1-methylbiphenylene: δ 2.07 (s) for CH_3, and multiplets for aromatic Hs at δ 6.5 and 7.2.

Preparation of Dianions. A weighed amount of hydrocarbon was placed within a flame-dried, degassed NMR tube (5-mm tube when THF-d_8 was solvent and 8-mm tube when 2-MeTHF was solvent, with external acetone-d_6 solvent in a 10-mm NMR tube for NMR lock purposes) along with about five small strips of lithium (~30 mg) cut from a flat piece of lithium under argon. A rubber septum was used to seal the tube, and then dry solvent was added via syringe. The tube was then placed inside a commercial ultrasound bath[38] and sonicated. Within a couple of minutes the solution was deep blue, indicating radical anion formation, and further sonication, usually about 10-20 min for the stable dianions, generated a deep red-brown color indicative of dianion formation. A color change to green-yellow indicated ring opening to the dilithiobiphenyl moiety.

Preparation of the Dication. Two-electron oxidation was achieved in a solution of 1.5 g of SbF_5 and 1.5 mL of SO_2ClF with 50 mg of OMBP in a 10-mm NMR tube.

Quenching of the Ions. Quenching of the methylated dilithiobiphenyls was achieved by cooling the sample within the NMR tube to 0 °C and slowly adding water via syringe. The quenching of the biphenylene dianions was achieved by bubbling pure oxygen via a long syringe needle through the red-brown solution until the intense color disappeared. All quench products were isolated by a conventional workup using dichloromethane.

The ^{13}C, ^{1}H, and ^{7}Li NMR spectroscopic studies were carried out on a Varian VXR-200 superconducting NMR spectrometer equipped with a 5-mm variable-temperature switchable probe or a 10-mm variable-temperature broad-band probe. Analysis of the methylated biphenyls was done by NMR and by using a Finnigan INCOS-50 GC-MS apparatus by comparison with standard samples of methylated biphenyls.

(38) Using a 200-W Mettler ME-11 ultrasound bath from American Brand Products.

Acknowledgment. We would like to thank Professors G. Fraenkel and T. E. Hogen-Esch for useful discussions. We also appreciate the critical comments of the reviewers. Support of our work at USC by the National Science Foundation is gratefully acknowledged.

Inversion Topologies of [*n*.8.8](2,1,4)Cyclophanes: Tethering Effects on Host-Cavity Stereodynamics

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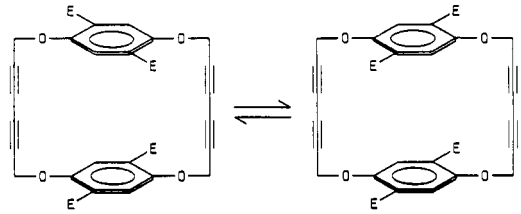
Received August 3, 1988

Abstract: The title compounds **4** (n = 3-11; formally, the diesters of diacid **11** with various α,ω-diols) have been prepared; their ring-inversion barriers were measured by dynamic NMR. Diesters of **11** with 6,6-dimethylundecane-1,11-diol and 2-[(*tert*-butyldimethylsilyl)oxy]propane-1,3-diol were similarly made and studied. Preparation of the siloxy phane entailed development of a new glyceride synthesis. Two inversion topologies are possible: the diester bridge can pass either through the paracyclophane cavity (donut-hole pathway) or around the outside (jump-rope pathway). The donut-hole pathway is followed for $n \leq 7$, while the jump-rope pathway is followed for $n \geq 9$. Two properties are characteristic of each inversion topology: (1) relative barriers of **4.*n*** and its hexadecahydro derivative **5.*n*** and (2) an effect on inversion barrier of formal *gem*-dimethylation in the middle of the diester chain.

There is considerable current interest in host-guest chemistry, particularly in connection with the quest for "artificial enzymes".[1] Cyclophane hosts are especially attractive for stereochemical studies of cavities: intermediate in stiffness between cyclodextrins and crown hosts, cyclophanes can be made in a wide variety of shapes and substitution patterns, yet the stiff arenes make it fairly simple to design cyclophane hosts with enforced or semienforced cavities.[2,3]

What is it to fit into a cavity? More precisely, how do the interrelations of host and guest size and flexibility translate into energetics? Earlier, we studied tetraesters **1**, which can exist as syn and anti isomers (one isomer of each shown); ring inversion must involve cavity passage of an ester substituted arene side.[4] Several points are noteworthy. First, sequential methylations in the middle of ester chains raise $\Delta G^{\ddagger}_{298}$ sharply (**1c**, 17.2 kcal/mol; **1d**, 23.3; **1e**, >35); *gem*-dimethylation (cf. **1e**) suppresses inversion altogether. This is a simple fit/borderline/no-fit sequence; the difference between **1c** and **1d** is essentially all entropic.[4a] Second, hexadecahydro derivatives **2a-c**, whose macrocycles are collapsed,[4,6a,7] have higher barriers than the corresponding **1**, presumably because phanes **1** have cavities enforced in the relevant



1: E = CO_2R a: R = Me f: R = CH_2Ph
b: R = Et g: R = CH_2CH_2Ph
c: R = n-Pr h: R = $(CH_2)_3$Ph
d: R = i-Bu i: R = $(CH_2)_4$Ph
e: R = CH_2(t-Bu) j: R = $(CH_2)_5$Ph

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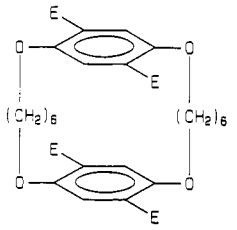
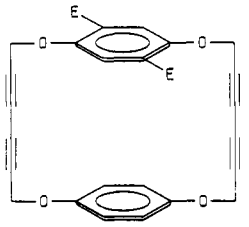


syn-2: a-c as 1

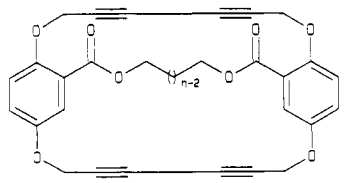
dimension, while phanes **2** do not.[4a] Third, barriers for **1c** and diester **3** are almost identical; barriers for series **1** thus reflect



3: E = CO_2(n-Pr)

independent arene motion.[4a,5] Finally, phanes **1a–c** show a barrier *increase* of ~2 kcal/mol per added methylene group;[4a] in phenyl-tipped **1f–j**, however, there is a smooth *decrease* of ~1.5 kcal/mol per added methylene group. All the ω-phenylalkyl esters invert more slowly than the *n*-alkyl esters; when an arene of **1f** rotates, it and the CO_2CH_2 connector push the pendant phenyl group into the nearest diyne bridge and/or the opposite arene. Chain lengthening relieves these interactions.[4b]

We have now prepared tribridged cyclophanes **4.*n***, and have studied their stereodynamics as a function of the length of the diester chain.[6] The plane of the page in structure **4** is a symmetry element under fast ring inversion, but not under slow inversion; inversion thus interconverts geminally related protons. Ring inversion can occur in two topologically distinct ways (Figure 1): the diester chain can pass either through the [8.8]paracyclophane cavity (pathway A: donut-hole pathway) or around the outside (pathway B: jump-rope pathway). Inversion of **4.*n*** by either



4.n

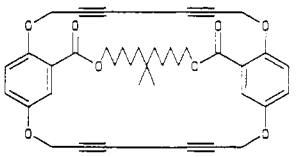
topology differs from that of **1** in that the arenes of **4** must disrotate, while those of **1** flip independently. The donut-hole pathway resembles the obligate ring-flip pathway of **1**.

Earlier results suggested some topological diagnostics. By analogy with **1** and **2**,[4a] donut-hole inversion should be easier for the diyne-bridged phanes than for their hexadecahydro counterparts. Under jump-rope inversion, however, the controlling interaction should presumably be the fit of the diester bridge around the paracyclophane "ball". The ball should be smaller, and jump-rope inversion easier, for the flexibly bridged hexadecahydro phanes than for the less-compact diyne-bridged phanes. Jump-rope processes in general are known to grow more facile as ring size increases;[8] jump-rope inversion thus may be favored at high *n*. The known suppression of donut-hole inversion by *gem*-dimethylation of an ester chain[4a] should provide another topological probe; *gem*-dimethylation should have little, if any, effect on jump-rope inversion.

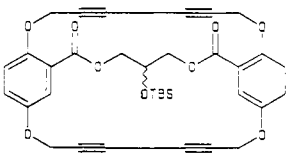
Macrocyclic compounds with the topological possibilities of **4** are rare;[9,10] we know of no previous stereodynamic studies of such systems. We find a striking topological dichotomy. Phanes **4.*n*** and **5.*n*** (*n* = 3–7) invert by the donut-hole pathway, and phanes **4.*n*** and **5.*n*** (*n* = 9–11) invert by the jump-rope pathway; the octamethylene pair is a borderline case.[6]

Synthesis: General Scheme

Ten tribridged cyclophatetraynes were made, viz., the straight-chain phanes **4.*n*** (*n* = 3, 6–11) and the branched-chain phanes **4.3os** and **4.11dm**; **4.3os** exists as epimers. Phanes **4.*n*** (*n*



4.11dm



4.3os

= 3, 6–11, 11dm) were made in four steps (Scheme I) from the corresponding α,ω-dibromides **6.*n***. Esterification[11] of **6.*n*** with the known[12] 2-hydroxy-5-(propargyloxy)benzoic acid (**7**) gave diesters **8.*n***. Oxidative cyclization,[13,14] propargylation of the phenols,[15] and a second oxidative cyclization then gave phanes **4.*n***, whose mass spectra lacked molecular ions; characterization of compounds **4.*n*** as cyclic monomers rests on hydrogenation[16] to derivatives **5.*n***.

Oxidative cyclizations in these series (i.e., **8.*n*** to **9.*n***, and **10.*n***

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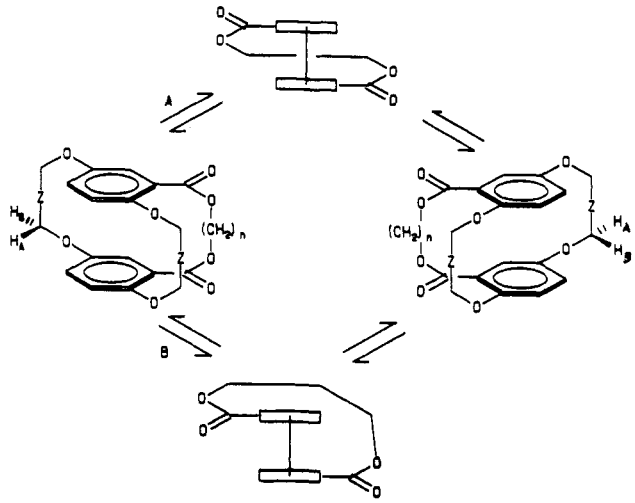
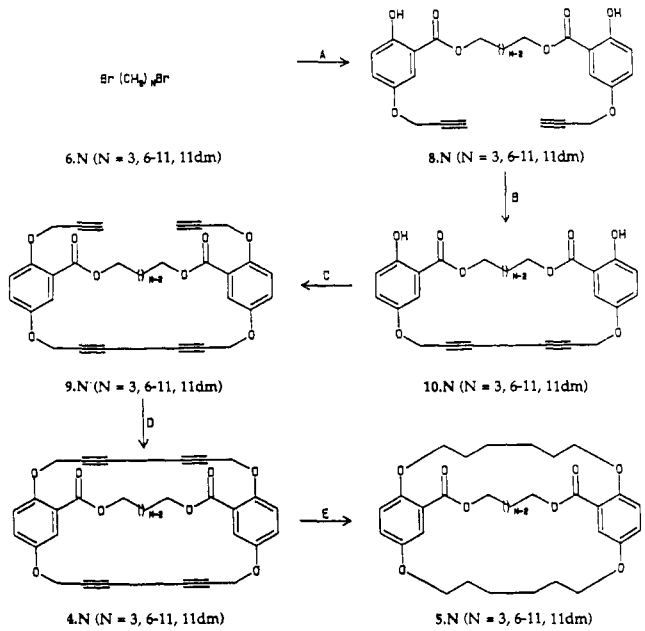


Figure 1. Inversion topologies of **4.*n*** and **5.*n***; A = donut hole, B = jump rope.

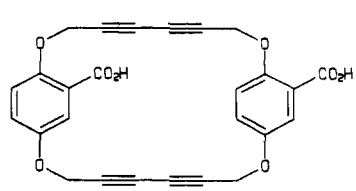
Scheme I[a]



[a] [N = 11dm: $(CH_2)_N = (CH_2)_5CMe_2(CH_2)_5$] A: **7**, Et_3N, DMF, 60 °C, 24–42 h; 69–94%. B: $Cu(OAc)_2 \cdot H_2O$, pyridine, 44 °C, 2–19 h; 52–64%. C: propargyl bromide, K_2CO_3, DMF, room temperature, 20–24 h; 88–94%. D: $Cu(OAc)_2 \cdot H_2O$, pyridine, 44 °C, 10 min–2 h, 18–35%. E: H_2 (1 atm), 5% Rh/Al_2O_3, EtOAc, room temperature; 60–90%.

to **4.*n***) slow as ring size increases, but there is little or no ring-size effect on yields. The largest ring made here is the 29-membered ring of **9.11**, which is isolated in 63% yield; these cyclizations do not require slow addition or high dilution (concentrations are ~10 mM). The tribridged targets **4.*n*** are all formed in ~35% yield. Only **4.3** is insoluble enough to make isolation at all difficult; phanes **4.*n*** ($n \geq 6$) are all soluble enough to recrystallize.

Attempts to shorten the synthesis by making both diynes at once or by bisesterification of the known[7a] diacid **11** led only to complex mixtures containing little **4.3** and were unsuccessful.



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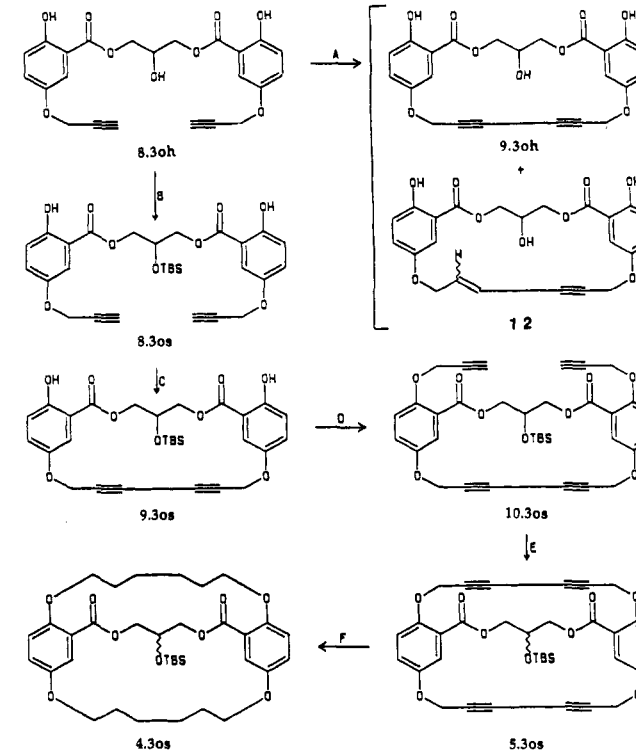
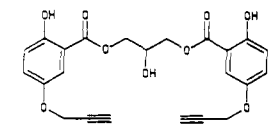
Scheme II[a]



[a] A: $Cu(OAc)_2 \cdot H_2O$, pyridine, 42 °C, 90 min; ~38% (**9.3oh**:**12** = ~1:2). B: TBSOTf, 2,6-lutidine, $CHCl_3$, room temperature, 20 min; 78%. C: $Cu(OAc)_2 \cdot H_2O$, pyridine, 45 °C, 2 h; 33%. D: propargyl bromide, K_2CO_3, DMF, room temperature, 28 h; 88%. E: $Cu(OAc)_2 \cdot H_2O$, pyridine, 41 °C, 25 min; 23% (4:3 mixture). F: H_2 (1 atm), 5% Rh/Al_2O_3, EtOAc, room temperature; quantitative (4:3 mixture).

Synthesis of Siloxy Cyclophanes

Synthesis of **4.3os** from the known[17] diglyceride **8.3oh**, along the lines of Scheme I, was then expected to proceed straightforwardly. Unfortunately, submission of **8.3oh** to cupric acetate



8.3oh

in pyridine (42 °C, 90 min)[13,14] gave (Scheme II) a 38% yield of a ~1:2 mixture, partly separable by medium-pressure liquid chromatography (MPLC), of products assigned by ^1H NMR as the desired **9.3oh** (*minor*) and Straus coupling[13] product **12** (major). The culprit must be the aliphatic OH group together with its enforced proximity to the reacting alkynes, since phanes **9.*n*** lacking this hydroxyl group form cleanly (see above), and since both ethynyl dimethyl carbinol and hex-5-yn-1-ol are known to undergo the desired Eglinton coupling efficiently.

A *tert*-butyldimethylsilyl (TBS) ether of the offending alcohol would have both appropriate protection characteristics, for possible future derivatization of **4.3oh**, and mutually geminal methyl groups, for the stereochemical point of immediate concern. Reaction of **8.3oh** with TBS chloride (TBSCl) and imidazole (DMF, 36 °C, 11 h)[18] gave a ~3:2:6:4 mixture of **8.3oh**, its 1,2-diglyceride isomer **13**, and silylated products identified (^1H NMR)[19] as **14** and either **15** or **16** (the silyl ethers were inseparable). No **8.3os** was obtained; imidazole apparently equilibrates **8.3oh** and **13** much

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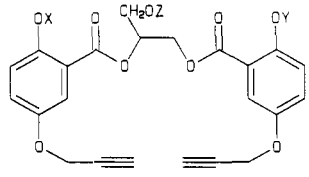

13: X = Y = Z = H
14: X = Y = H, Z = TBS
15: X = Z = TBS, Y = H
16: X = H, Y = Z = TBS

faster than **8.3oh** is silylated. Reaction of **8.3oh** with TBSCl and 1,2,4-triazole (DMF, room temperature, 48 h), conditions reported[20] to give silylation without acyl or silyl[21] migration, led to a 13:87 mixture of **8.3os** and **8.3oh**. A more reactive TBS source was needed, so **8.3oh** was treated with TBS triflate (TBSOTf) and 2,6-lutidine ($CHCl_3$, room temperature, 20 min)[22] to furnish the oily **8.3os** (78%). Oxidative cyclization of **8.3os** [$Cu(OAc)_2 \cdot H_2O$, pyridine, 45 °C, 2 h][13,14] gave Eglinton product **9.3os** (33%); Straus products were not detected. Propargylation of **9.3os** (propargyl bromide, K_2CO_3, DMF, room temperature, 16 h)[15] then provided **10.3os** (88%), which was cyclized [$Cu(OAc)_2 \cdot H_2O$, pyridine, 41 °C, 25 min][13,14] to give (23%) a 4:3 mixture of the **4.3os** epimers (we do not know which is which). The 4:3 mixture could be separated by chromatography into a 3:1 mixture (favoring the original major isomer) and a 1:1 mixture; two crystallizations of the former from hexane/$CHCl_3$ gave a 1% yield of the major compound. Samples of both mixtures in $CDCl_3$ and of the major epimer in benzene-d_6 showed no NMR-detectable interconversion after ~700 days (~2 years) at −30 °C. At least two of these three compositions must differ from the equilibrium one; assuming that a 5% composition change would have been detected, $k < 8 \times 10^{-10}$ s^{-1} and $\Delta G^{\ddagger}_{243} > 24$ kcal/mol.

The assignments of these materials as cyclic monomers **4.3os** rests on their quantitative hydrogenation (1 atm; 5% Rh/Al_2O_3)[16] to **5.3os**.

Conformation: Trimethylene Series

In earlier studies,[4,7] we have found diyne-bridged phanes (cf. ***4.n***) to show small ^{1}H NMR cyclization shifts[7a] (≤ 0.1 ppm) in either direction, presumably because the arenes are well-separated;[23] four crystal structures have also shown diynes to hold arenes apart.[7d-f] Flexibly bridged phanes (cf. ***5.n***), by contrast, show substantial (≥ 0.2 ppm) upfield cyclization shifts, indicating a collapsed conformation.[4,7a-d,f] As expected, cyclization shifts of **4.3** are small (~0.1 ppm), and those of **5.3** are much larger (~0.3 ppm) and negative (upfield). Thus, arenes of **4.3** are held apart, while **5.3** lies collapsed in solution, as it does in the crystal.[6a]

Comparison of the infrared C=O stretching frequency, ultraviolet (UV) absorbance, and carbonyl ^{13}C NMR shift of **4.3** to those of model **11.3** suggests that the carbonyl groups of **4.3** are twisted out of coplanarity with the attached arenes; the UV[24] and ^{13}C NMR[25] data yield a twist angle of 25 ± 12°.

The aliphatic ^{1}H NMR signals of **4.3** address both the diester-bridge conformation and the molecular stereodynamics. The CO_2CH_2 protons give an AA′BB′XY pattern and the $ArOCH_2$ protons give overlapping AB patterns, rather than a triplet and two singlets, respectively; furthermore, irradiation of the OCH_2CH_2 signals collapses the CO_2CH_2 signals to an AB pattern and vice versa. Therefore, ring inversion must be slow on the NMR time scale at room temperature.

The geminal chemical shift difference ($\Delta\delta_{gem}$) of the CO_2CH_2 signals (0.256 ppm) is much greater than that of the OCH_2CH_2 signals (0.087 ppm); i.e., $(\delta_B - \delta_A) > (\delta_X - \delta_Y)$. The $\Delta\delta_{gem}$ values presumably reflect the degree of through-space deshielding by the nearer diyne.[26] Thus, we assign the downfield signals B and X to the endo protons; the CO_2CH_2 protons must be closer than the OCH_2CH_2 protons to the diyne. The vicinal coupling constants are consistent[27] with an overall chairlike local conformation. The coupling constants of **4.3** and **5.3** (both geminal and vicinal) are similar; each phane probably exists as a rapidly equilibrating mixture of species each with C_1 symmetry (see below).

Table I. Auxiliary MM2 Parameters[a]

Torsional Parameters			
angle	V_1	V_2	V_3
C(sp)-C(sp^3)-O(sp^3)-C(alkene)	0.40	0.52	0.467
C(alkene)-C(alkene)-C(carbonyl)-O(sp^3)	0.15	0.0	0.0
C(alkene)-C(carbonyl)-O(sp^3)-C(sp^3)	−2.5	1.39	0.0
C(carbonyl-C(alkene)-C(alkene)-O(sp^3)	0.0	16.25	0.0
C(alkene)-C(sp^3)-O(sp^3)-C(carbonyl)	−2.03	1.21	−0.67
C(sp^3)-C(sp^3)-O(sp^3)-lone pair	0.0	0.0	0.0
C(alkene)-C(carbonyl)-O(sp^3)-lone pair	0.0	0.0	0.0

Bending Parameters		
angle	k_θ	θ_0
C(sp)-C(sp^3)-O(sp^3)	0.7	107.5
C(sp)-C(sp)-C(sp)	0.45	180.0
C(alkene)-C(carbonyl)-O(sp^3)	0.65	101.1

[a] Units: V_i, kcal/mol; k_θ, md Å rad^{-2}; θ_0, deg.

Table II. Energies (kcal/mol) of MM2 Conformations of **4.3** and Models, and Selected Arene–Carbonyl Dihedral Angles

molecule	E_s[a]	E_p[a]	θ_{dhd}, deg (conformation)
4.3	74.27[b]	57.60	12, 8.6 (p); 29, 24 ("s")[b]
11.3	47.0	56.34	8.1, 7.6 (s)
9.3	54.82	57.61	8.0, 7.4 (s)

[a] Conformations: p = pouched; s = sheet. [b] See the text and Figure 4 for "sheet" form of **4.3**.

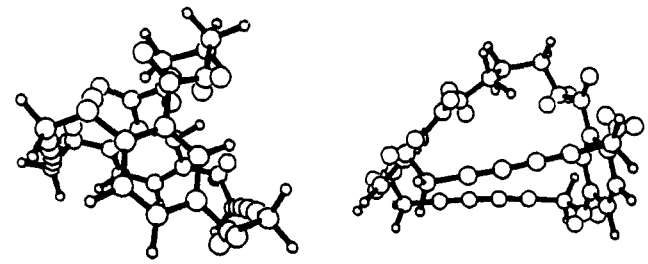

Figure 2. Less-symmetric MM2 structure of **4.3** (two views); strain energy: 55.75 kcal/mol.

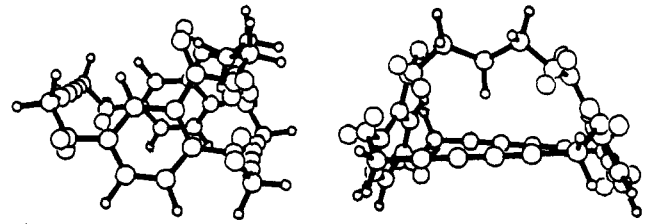

Figure 3. More-symmetric MM2 structure of **4.3** (two views); strain energy: 57.62 kcal/mol.

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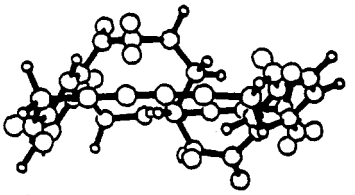

Figure 4. Anti,through MM2 form of **4.3**, derived by optimization of sheet structure; strain energy: 74.27 kcal/mol.

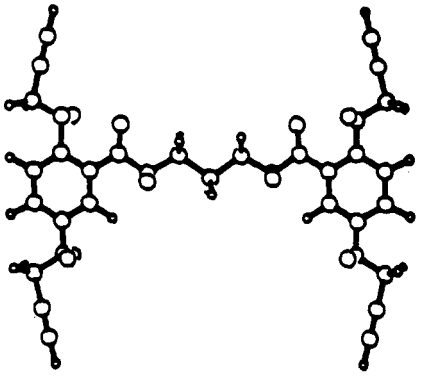

Figure 5. Sheet MM2 form of **11.3**.

The conformations of **4.3**, **9.3**, and **11.3** were also studied with MM2 calculations,[28,29] which employed some auxiliary parameters (Table I) as well as those supplied[28c] with the program. Each molecule was studied in two conformations: (1) a "sheet" form, with the arenes essentially coplanar in the initial structure, and (2) a "pouched" form, with the arenes initially 6–8 Å apart at a mutual angle of ~40°. Table II shows the energies of optimized conformations for each molecule, and selected arene–carbonyl dihedral angles. Since no two of these molecules are isomers, energies of different molecules in similar conformations are not comparable, but energies of *one* molecule in different conformations are.

Two pouched energy minima were found for **4.3** (Figures 2 and 3); that of lower energy is the less symmetric (Figure 2). In the more-symmetric structure (Figure 3), the trimethylene bridge assumes a pseudo-chair conformation reminiscent of those deduced from solution coupling constants (see above). Neither MM2 structure has the σ plane of solution NMR spectra; we propose that minimum-energy forms of C_1 symmetry (Figure 2) interconvert rapidly via a transition state of C_s symmetry. The more-symmetric MM2 form (Figure 3), which only just lacks the σ plane, is a reasonable intermediate; the crystal conformation of **5.3** also lacks a σ plane.[6a]

The sheet initial form of **4.3** did not optimize to another sheet form, but to an anti-through form (Figure 4), which was calculated to lie 15–17 kcal/mol higher in energy than the pouched forms. This anti-through form is similar to the presumed intermediate in donut-hole inversion. The experimental barrier (see below) is 23–24 kcal/mol; comparison suggests that an anti-through form may be an intermediate.

Apparently, **4.3** lacks a sheetlike energy minimum; by contrast, the sheet forms of **9.3** and **11.3** are favored over the pouched forms (Table II). This effect appears to arise because each diyne bridge holds the arene ends closer together than the diester bridge would alone.

In **11.3**, which lacks diyne bridges, the arenes are almost coplanar; the arenes' C(2)–C(5) axes are nearly parallel (Figure 5). The sheet form lies ~9 kcal/mol below the pouched form. Closure of one diyne bridge gives **9.3**, in whose sheet form (Figure 6) the arenes are again roughly coplanar; the arene *axes*, however, are nonparallel. The sheet form of **9.3** lies only 3 kcal/mol below the pouched form. Closure of the diyne with the arene axes parallel would require either very long bonds in the diyne bridge or rotation of the arenes out of coplanarity toward a pouched form; **9.3** restores its diyne bonds to normal length through mutual approach of the C(5) arene ends, which renders the arene axes nonparallel. In **4.3**, with *two* diyne bridges, the arene axes are *held* parallel, so that rotation in the sense shown by **9.3** is unavailable; **4.3** assumes the now-favored pouched form (Figure 2).

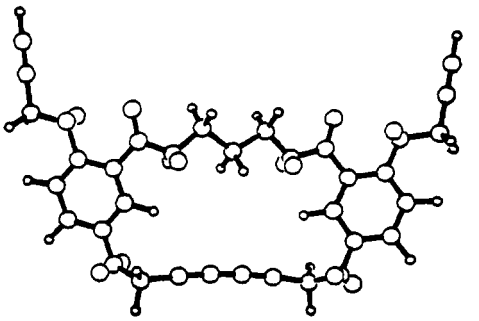

Figure 6. Sheet MM2 form of **9.3**.

Table III. UV Data and Calculated (MM2) Arene–Oxygen–Methylene Dihedral Angles for **4.3** and Models

molecule	$\lambda^{max DMSO}$, nm (ϵ)	θ_{dhd} (C-2), deg	θ_{dhd} (C-5), deg
4.3 (p)[a]	299 (4700)	53.58, 55.90	8.97, 1.78
11.3 (s)[a]	308 (6900)[b]	1.65, 2.33	5.35, 8.51
9.3 (s)	307 (8720)	8.64, 4.62	34.91, 34.16

[a] p = pouched, s = sheet. [b] This value of ϵ is ±400 (two data); others, one datum each.

MM2 predicts, then, a qualitative difference between the preferred conformations of **9.3** and **11.3** on one hand and that of **4.3** on the other. UV maxima are fully consistent with these predictions (Table III), but do not appear to follow arene–OCH_2 dihedral angles; we attribute the variation in λ_{max}, like that in ϵ (see above), to arene–carbonyl twisting.

Stereodynamics: Trimethylene Series

The ring-inversion rate of a phane **4.*n*** or **5.*n*** can in principle be extracted[30] from the mutual exchange of any geminal AB pair. The only such patterns in **4.3** or **5.3** well-separated enough for use are the CO_2CH_2 AB patterns produced by irradiating CO_2-CH_2CH_2. Neither phane showed any line broadening, even of the outer AB lines,[31] at any experimentally accessible temperature; **4.3** was studied up to 167 °C in DMSO-d_6 solution, and **5.3** up to 181 °C in bromobenzene-d_5 (C_6D_5) solution.

For estimation of maximum exchange rates, it was assumed that doubling of the line width (i.e., broadening by 3–5 Hz) would have been detected if present. Each system was simulated via Heidberg's expression[31a] for the intensity of an AB pattern versus observed frequency, coupling constant, chemical shift difference, no-exchange line width, and exchange rate constant (k); the simulation was carried out on an IBM PC-AT computer using the program DNMR (Bolin, W. N.). For **4.3** at 167 °C in DMSO-d_6, $t \geq 0.14$ s, $k \leq 7.1$ s^{-1}, and $\Delta G^{\ddagger}_{440} \geq 24$ kcal/mol; for **5.3** at 181 °C in C_6D_5, $t \geq 0.24$ s, $k \leq 4.2$ s^{-1}, and $\Delta G^{\ddagger}_{454} \geq 26$ kcal/mol. Here t is the site lifetime. The derived $\Delta G^{\ddagger}$ values are *minima*: the relative inversion barriers of **4.3** and **5.3** cannot be deduced therefrom.

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Table IV. Temperature Dependence of Kinetic Parameters for **4.3** in DMSO-d_6[a,e]

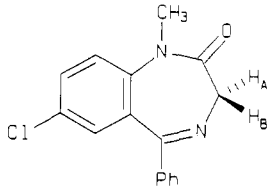
T	k	ln (k/T)[b]	σ	R_{1B}[c]	R_{1A}[c]	$\Delta G^{\ddagger}$[d]
111	0.35 (6)	−7.00	0.30 (5)	0.49 (7)	0.47 (5)	23.5 (1)
121	0.9 (2)	−6.1	0.34 (9)	0.3 (1)	0.5 (1)	23.4 (2)
129	0.8 (1)	−6.2	0.07 (5)	0.5 (1)	0.57 (7)	23.9 (2)
138	1.1 (2)	−5.92	0.08 (4)	0.40 (6)	0.46 (7)	24.2 (2)
147[f]	2.7 (11)	−5.05	0.05 (20)	0.5 (4)	0.2 (3)	24.0 (5)
152	2.5 (6)	−5.14	0.08 (4)	0.5 (2)	0.3 (2)	24.4 (2)

[a] Units: T, °C; k, σ, R_{1i}, s^{-1}; $\Delta G^{\ddagger}$, kcal/mol. [b] Kelvin temperatures were used for ln (k/T). [c] The upfield (exo) of the two CO_2CH_2 resonances is a perturbed (A) resonance. [d] Free energies of activation were estimated from the Eyring equation. [e] The figure in parentheses is the estimated error in the last digit. [f] At 147 °C, only one selective inversion-recovery experiment was performed (other temperatures: two).

Measurement of the inversion rates of **4.3** and **5.3** required the use of magnetization transfer, also known as spin-saturation transfer.[32] In this method, originally due to Forsén and Hoffman,[33] one site of an exchange network is perturbed selectively; the response of all exchanging sites is then observed versus time.

Published schemes for extracting rates from magnetization-transfer data cover the following cases: (1) two sites, perturbation fully selective, no mutual coupling, equilibrium constant K_{eq} = 1, relaxation times T_{1i} all roughly equal;[34] (2) same as case 1, but any K_{eq} or T_{1i};[33,35] (3) same as case 2, several sites;[36] (4) two sites, no mutual coupling, perturbation *not* necessarily fully selective, K_{eq} fairly close to unity;[37] (5) same as case 4, but any K_{eq};[38] (6) same as case 5, but several sites;[39] (7) fully selective perturbation, some mutual coupling;[40] and (8) nonselective perturbation, no mutual coupling, one component present in large excess.[41]

Many systems belong to one of these classes; **4.3** and **5.3** do not. The CO_2CH_2 geminal chemical shift differences are quite small: one cannot expect fully selective perturbation. Moreover, coupling is quite strong in both phanes. For **4.3**, $\Delta\nu/J$ = 2.2–4.6 between room temperature and 177 °C at 199.50 MHz; for **5.3**, $\Delta\nu/J$ = 0.7–2.3 under similar conditions. As far as we know, the most tightly coupled system previously studied by magnetization transfer is Valium (**17**),[40] for which $\Delta\nu/J$ = ~30.[42]



17

It can be shown (cf. ref 38) that the magnetizations of two mutually coupled, mutually exchanging sites A and B are given versus time by eq 1–10. Here $M_i(t)$ is the z magnetization of site i at time t, M_i^{∞} is M_i at equilibrium, M_i^0 is M_i at zero time, k_i is the rate constant for exchange out of site i, k_{1i} is the sum of k_i and the rate constant for spin-lattice relaxation of site i, σ is the rate constant for cross-relaxation, and α is the ratio of the A and B line widths (w_i).

$$M_A(t) = C_1e^{\lambda_+ t} + C_2e^{\lambda_- t} + M_A^{\infty} \quad (1)$$

$$M_B(t) = C_3e^{\lambda_+ t} + C_4e^{\lambda_- t} + M_B^{\infty} \quad (2)$$

$$C_1 = [(M_A^{\infty} - M_A^0)(k_{1A} + \lambda_-) - (1/\alpha)(k_B - \sigma)(M_B^{\infty} - M_B^0)]/(\lambda_+ - \lambda_-) \quad (3)$$

$$C_2 = [(1/\alpha)(k_B - \sigma)(M_B^{\infty} - M_B^0) - (M_A^{\infty} - M_A^0)(k_{1A} + \lambda_+)]/(\lambda_+ - \lambda_-) \quad (4)$$

$$C_3 = [-\alpha(k_A - \sigma)(M_A^{\infty} - M_A^0) - (\lambda_+ + k_{1A})(M_B^{\infty} - M_B^0)]/(\lambda_+ - \lambda_-) \quad (5)$$

$$C_4 = [\alpha(k_A - \sigma)(M_A^{\infty} - M_A^0) + (\lambda_- + k_{1A})(M_B^{\infty} - M_B^0)]/(\lambda_+ - \lambda_-) \quad (6)$$

$$\lambda_+ = \{-[k_{1A} + k_{1B}] + [(k_{1A} - k_{1B})^2 + 4(k_B - \sigma)(k_A - \sigma)]^{1/2}\}/2 \quad (7)$$

$$\lambda_- = \{-[k_{1A} + k_{1B}] - [(k_{1A} - k_{1B})^2 + 4(k_B - \sigma)(k_A - \sigma)]^{1/2}\}/2 \quad (8)$$

$$k_{1i} = R_{1i} + k_i \quad (9)$$

$$\alpha = w_A/w_B \quad (10)$$

When the chemical equilibrium constant is known, α can be evaluated from the ratio of equilibrium peak heights and eq 11,

$$\alpha = M_B^{\infty}[A]_{\infty}/M_A^{\infty}[B]_{\infty} \quad (11)$$

where $[I]_{\infty}$ is the equilibrium concentration of species I. This use of α lets the M_i be peak heights, which are much easier to measure accurately than intensities (areas).

Preliminary studies of **4.3** and **5.3** suggested that the relaxation and exchange rates might be similar; therefore, nonselective inversion-recovery experiments were done, to complement the selective experiments.[36b,39a] Typically, one nonselective and two selective inversion-recovery experiments were done per phane per temperature; the two selective experiments used different sets of mixing times.

The CO_2CH_2 signals of each phane appeared as two envelopes of six to eight lines each. The label pulse was placed slightly off-center on one of the envelopes, on the side away from the other envelope. The oscillator setting and pulse duration were chosen to give a bandwidth no greater than $(\delta\nu)_{gem}$.

The heights of the lines in the perturbed envelope were summed to give M_A, and those in the unperturbed envelope were summed to give M_B. The numbers of lines resolved in the two envelopes varied with the instrument tune, and in general were mutually unequal. Since exchange is chemically degenerate in the present cases, K_{eq} = 1 and intensities were normalized with α (eq 11 above); therefore, α lacks physical meaning here.

For quantitation, the summed peak heights for each envelope were expressed versus the height of the tallest $ArOCH_2$ line as internal standard, to correct for varying instrumental response. The data were fit to eq 1–8 (above) on a Harris/7 computer using a standard nonlinear least-squares routine. Relaxation-rate constants (R_{1i}) were fit first to the nonselective inversion-recovery data, then to all the data. Next, k and σ were fit, first individually, then together. The parameters were fit pairwise until all four were constant within error; finally, all four were fit at once. Separate fitting of the two R_{1i} gave slightly better fits than did fitting of one "R_1", but produced no large change in k.

The inversion barrier of **4.3** (Table IV) turned out to be just above the minimum estimated by line-shape analysis. This system is difficult; its least tractable properties are its small $(\delta\nu)_{gem}$, making selective perturbation difficult, and its relatively rapid T_1 relaxation (for **4.3** at 111 °C in DMSO-d_6, R_{1A}/k = ~1.4).

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Table V. Stereodynamics of **4.*n*** and **5.*n***

molecule	solvent	method[a]	T_c[b]	$\Delta G^{\ddagger}_{298}$[c]	$\Delta H^{\ddagger}$[c]	$\Delta S^{\ddagger}$[d]	n, ΔT, R[e]
4.3	DMSO-d_6	F-H	>>180	21.4 (2)[f]	14 (2)	−24 (5)	6, 41, 0.95
4.3os	[g]	K	>>180	>24	–	–	1,–,–
4.6	C_6D_5Br	LS	>179	~20–21	–	–	1,–,–
4.7	C_6D_5Br	LS	~160	19.2 (2)	16 (1)	−13 (3)	9,47,0.994
4.8	C_6D_5Br	LS	~115	~18	[h]	[h]	13,23,0.98
4.9	C_6D_5Br	LS	+72	16.5 (1)	14 (1)	−10 (3)	11,40,0.997
4.10	$CDCl_3$	LS	+12	13.8 (1)	15.0 (9)	+4 (3)	19,36,0.997
4.11	$CDCl_3$	LS	−43	10.5 (1)	14 (1)	+9 (5)	15,21,0.989
4.11dm	$CDCl_3$	LS	−35	10.7 (1)	13 (1)	+6 (2)	6,23,0.990
5.3	C_6D_5Br	F-H, LS	>>180	>26	–	–	–
5.7	C_6D_5Br	LS	>>160	>23.3	–	–	–
5.8	C_6D_5Br	LS	~110	17.8 (1)	13 (1)	−17 (3)	12,43,0.993
5.9	$CDCl_3$	LS	+17	15.1 (1)	[h]	[h]	13,28,0.95
5.10	$CDCl_3$	LS	−24[i]	12.8 (1)	9.4 (9)	−11 (4)	8,28,0.991
5.11	$CDCl_3$	LS	<<−50	<10	–	–	–

[a] F-H = Forsén–Hoffman (inversion-transfer); K = kinetics; LS = line shape. [b] Coalescence temperature (°C) at 270 MHz. [c] Units of $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$: kcal/mol. [d] Units of $\Delta S^{\ddagger}$: eu. [e] n = number of temperatures studied; ΔT = range of temperatures; R = correlation coefficient of Eyring plot. [f] The figure in parentheses is the stimated error in the last digit. [g] Phanes **4.3os** were studied in both $CDCl_3$ and benzene-d_6. [h] Activation parameters were not calculated: poor Eyring plots. [i] This temperature was measured at 500 MHz.

The acquisition time for a 2-KHz sweep is 2.0480 s, almost the same as the T_1; thus, relaxation during the scan is significant. Scanning could be speeded by use of very large sweep widths, but only at the cost of resolution, of which there is not much to spare here.

Attempts to study **5.3** in C_6D_5Br solution, by using the same methods, did not yield exchange-rate constants significantly different from zero. We can exclude neither insufficiently selective irradiation, and thus a too small $(\delta\nu)_{gem}$, nor exchange too slow to observe, as the cause of this failure. The minimum barrier for **5.3**, assigned by line-shape analysis (see above), is higher than the measured barrier for **4.3**, so the donut-hole topology is assigned.

Stereodynamics: Higher Cyclophanes

The inversion rates of the higher phanes (**4.6–4.11**, **4.11dm**, **5.7–5.11**, **5.11dm**), by contrast, could be measured by line-shape analysis. For each phane, only one NMR solvent combined an appropriate liquid range with substrate solubility and a substrate $(\delta\nu)_{gem}$ large enough for study; the solvent differed from phane to phane. We assume negligible solvent effect on the inversion stereodynamics; although untested, this assumption seems reasonable given that the transformations are unimolecular and the phanes nonpolar.

Experimental D NMR spectra were simulated with the program DNMR1 (Bolin, W. N.), a variant of DNMR. Fit criteria were peak separations, line widths, maximum:minimum ratio, and visual comparison; above coalescence, only line widths and visual comparison were usable.

Coupling constants were derived from slow-exchange spectra or by analogy with homologues where slow-exchange spectra were unavailable. No-exchange line widths were taken as approximately equal (±0.1 Hz) to values derived by addition to the slow exchange limit line width of changes in the width of a reference line,[43] usually one of the aromatic lines. The geminal chemical shift difference, $(\delta\nu)_{gem}$, was fit independently below coalescence and extrapolated above.[44]

Table V collects the stereodynamic data; parameter errors were estimated by using Sandström's method.[45] When $n \leq 7$, barriers were much *greater* for **5.*n*** than for **4.*n***, and for either than for the corresponding tetraesters **1**.[4] These results are consistent only with donut-hole inversion by these phanes. The activation parameters of series **1** and **4** differ in that activation entropies are much more negative for **4.3** and **4.7** than for **1a–c**; the activation parameters of **4.3** and tetrakis(ω-phenylpropyl) ester **1h** are virtually identical. We attribute this behavior to partly synchronous ring flipping imposed by the diester tether of **4.*n***; the degree of order is similar to that imposed by the ω-phenyl group of **1h**. The minimum barrier estimated for (*tert*-butyldimethylsilyl)oxy derivatives **4.3os** is appreciably higher than the barrier measured for **4.3**, which is also consistent only with donut-hole inversion. By interpolation, we presume that phanes **4.4–4.6** would also invert by the donut-hole pathway.

For $n \geq 9$, barriers were found to be *smaller* for **5.*n*** than for **4.*n***, and for either than for **1**. We assign the jump-rope topology on three grounds: (1) the *jumprope mechanism* predicts the observed relative barriers of **4.*n*** and **5.*n*** ($n \geq 9$), but the donut-hole mechanism predicts the opposite, as observed for $n \leq 7$; (2) the *donut-hole* barrier should be no less for **4.*n*** than for **1**, as indeed is observed for **4.*n*** ($n \leq 7$), but those for **4.*n*** ($n \geq 9$) are less than those for **1**; (3) formal *gem*-dimethylation of **4.11** to **4.11dm** does not raise the inversion barrier, which in fact stays essentially constant. As in other jump-rope systems,[8] activation entropies grow more positive with progressive homologation.

The inversion-barrier difference between **4.*n*** and **5.*n*** (same value of n) is typically large, whatever the topology. Donut-hole systems **5.3** and **5.7** invert much more slowly than **4.3** and **4.7**, respectively; jump-rope systems **5.*n*** (n = 9–11) undergo NMR coalescence at least 30 °C below the corresponding **4.*n***. Octamethylene phanes **4.8** and **5.8**, by contrast, undergo NMR coalescence within about 15 °C of each other, and their inversion rates at similar temperatures differ by a factor of only about 5. The simplest explanation is that **4.8** inverts by the donut-hole pathway, while **5.8** undergoes jump-rope inversion.

Stereodynamics: MM2 Calculations

The donut-hole inversion of **4.3** was modeled with MM2 calculations; the necessary turning of one arene about its C(2)–C(5) axis was accomplished by progressive shortening of a very strong pseudobond between one arene carbon and a pseudoatom (for which we use the name "bozonium" and the symbol Bz). Such pseudoatoms were used in pairs, with one Bz bonded to the arene and the second Bz bonded to the first (i.e., in the form of a perbozonide). The motion of four atoms was restricted, namely the C(2) and C(5) pivot atoms of each arene and the two Bz. If only one Bz was used, it would not stay still; the restricted-motion feature of MM2 seems not to work well for univalent atoms subject to strong forces.

Such a perbozonide manipulation of **4.3** (Figure 7) predicted an inversion barrier of 33 kcal/mol. This value agrees reasonably well with the observed barrier of 23–24 kcal/mol, given the molecule's large size and many degrees of conformational freedom; it also agrees about as well with observation as the barriers calculated for tetraesters **1** by using more conventional means of structural manipulation.[4,46,47]

(43) (a) Lidén, A.; Sandström, J. *Tetrahedron* **1971**, *27*, 2893–2901. (b) Liljefors, T. *Org. Magn. Reson.* **1974**, *6*, 144–150. (c) Carter, R. E.; Drakenberg, T.; Roussel, C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1690–1694.

(44) (a) Drakenberg, T.; Dahlqvist, K.-I.; Forsén, S. *Acta Chem. Scand.* **1970**, *24*, 694–702. (b) Shoup, R. R.; Becker, E. D.; McNeel, M. L. *J. Phys. Chem.* **1972**, *76*, 71–78.

(45) Berg, U.; Karlsson, S.; Sandström, J. *Org. Magn. Reson.* **1977**, *10*, 117–121.

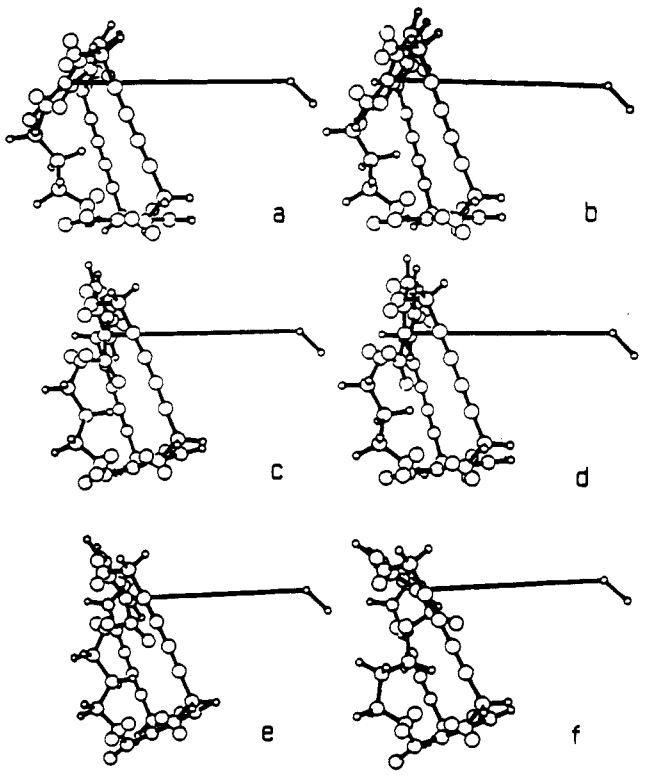

Figure 7. Selected structures from a perbozonide manipulation of **4.3**. The Bz atoms are the two at the extreme right of each structure; the long bond at the top center of each structure is the C–Bz pseudobond; C–Bz bond length (Å): (a) 10.0; (b) 9.7; (c) 9.3; (d) 9.0; (e) 8.6; (f) 8.3.

Conclusions

In summary, **4.*n*** and **5.*n*** (n = 3–7) invert by the donut-hole pathway, and **4.*n*** and **5.*n*** (n = 9–11) invert by the jump-rope pathway; **4.8** and **5.8** comprise a borderline pair. Imposition of a flexible third bridge impedes donut-hole inversion; if the third bridge is long enough, the competing jump-rope pathway becomes favored. Bridging thus offers a way to modulate a cavity's flexibility; the stereodynamic effects on the particular paracyclophatetrayne cavity studied are often similar to those of bulky ω-phenyl groups.

Experimental Section

Methods and Materials. Organic chemicals were reagent grade; inorganic chemicals were used as received. Thin-layer chromatography (TLC) was performed on plates precoated (EM Reagents) with a 0.25-mm layer of silica gel 60 F-254. The stationary phase for column chromatography was activated silica gel, 60–200 mesh.

Melting points (mp) were measured on a Fisher-Johns hot stage and are uncorrected. Infrared (IR) spectra were measured on a Beckman AccuLab 7 spectrophotometer; frequencies (ν_{max}) are in cm^{-1}. UV spectra were measured on a Cary Model 118 spectrophotometer; wavelengths (λ_{max}) are in nanometers. Proton (^1H) NMR spectra were obtained at 200 MHz on either a JEOL FX-200Q spectrometer or an IBM/Bruker WP200SY spectrometer, at 270 MHz on either a Bruker WH-270 spectrometer or an IBM/Bruker WP270 spectrometer, or at 500 MHz on a Bruker AM500 spectrometer. Shifts are in ppm (δ) versus internal tetramethylsilane (TMS); coupling constants are in hertz. Carbon-13 (^{13}C) NMR spectra were measured either at 15 MHz on a JEOL JNM-FX60 spectrometer or at 50 MHz on the FX200Q spectrometer. Carbon–proton connectivities were established by SFORD[48] or Ernst[49] experiments where so noted and otherwise by analogy. Mass spectra were obtained by electron impact, with MS-9 and MS-80 spectrometers. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN; results are expressed in percent.

For brevity's sake, the very cumbersome systematic names of cyclophanes have been omitted, as have routine NMR assignments.[50]

General Synthesis of Diesters 8. 1,3-Propanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.3). To a solution of 2-hydroxy-5-(2-propynyloxy)benzoic acid (**7**; 4.536 g, 23.60 mmol) in DMF (3.44 mL) at 60 °C were added Et_3N (3.47 mL, 2.52 g, 24.9 mmol) and 1,3-dibromopropane (**6.3**; 1.19 mL, 2.37 g, 11.7 mmol). The mixture was stirred at 60 °C for 24 h and then poured into water (70 mL) and allowed to settle. Filtration in vacuo gave crude **8.3** (4.6 g), which was crystallized (MeOH) to give **8.3** (4.0 g, 8.0 mmol, 69%): mp (MeOH) 92–93 °C; IR (KBr) 3270, 3250, 2120, 1695, 1625, 1495, 1295, 1220, 1190, 1040; UV (DMSO) 326 (ϵ = 9700); ^1H NMR (270 MHz, $CDCl_3$) 10.37 (s, 2 H), 7.42 (d, J = 3.0, 2 H), 7.16 (dd, J = 9.0, 3.0, 2 H), 6.94 (d, J = 8.8, 2 H), 4.64 (d, J = 2.4, 4 H), 4.54 (t, J = 6.1, 4 H), 2.55 (t, J = 2.4, 2 H), 2.30 (quin, J = 6.2, 2 H); ^{13}C NMR (15 MHz, $CDCl_3$) 169.5, 156.9, 150.0, 125.0, 118.6, 114.6, 111.9, 78.6, 75.7, 61.9, 57.0, 28.1; MS m/e 424 (30), 233 (100), 193 (29), 175 (89), 174 (82), 137 (3), 136 (18), 135 (78); m/e 424.1155 (calcd for $C_{23}H_{20}O_8$ 424.1152). Anal.: C, 65.35 (calcd: 65.09); H, 4.86 (4.75).

1,6-Hexanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.6): 91% yield; mp ($CHCl_3$) 153.5–154.5 °C; IR (KBr) 3250, 3110, 2980, 2940, 2870, 2120, 1675, 1620, 1495, 1420, 1370, 1355, 1295, 1275, 1230, 1095, 1040; ^1H NMR (270 MHz, $CDCl_3$) 10.48 (s, 2 H), 7.42 (d, J = 3.0, 2 H), 7.16 (dd, J = 9.0, 3.0, 2 H), 6.94 (d, J = 9.0, 2 H), 4.66 (d, J = 2.1, 4 H), 4.37 (t, J = 6.4, 4 H), 2.53 (t, J = 2.4, 2 H), 1.83 (m, 4 H), 1.55 (m, 4 H); ^{13}C NMR (50 MHz, DMSO-d_6, Ernst) 168.36 (C=O), 154.66 (C-2), 149.44 (C-5), 123.98 (C-4), 118.16 (C-3), 114.43 (C-6), 112.69 (C-1), 79.00 (HC≡*C*), 78.09 (HC≡C), 65.06 (CO_2CH_2), 56.20 (ArO-CH_2), 27.73 (OCH_2CH_2), 24.86 ($OCH_2CH_2CH_2$); MS m/e 466 (3), 465 (21), 464 (100), 175 (29), 174 (22), 137 (11), 136 (10), 135 (14); m/e 466.1629 (calcd for $C_{26}H_{26}O_8$ 466.1620). Anal.: C, 66.77 (calcd: 66.94); H, 5.76 (5.62).

1,7-Heptanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.7): 75% yield; mp (MeOH) 91–92 °C, IR (KBr) 3270, 3230, 2925, 2855, 2105, 1670, 1615, 1490, 1450, 1410, 1335, 1290, 1270, 1220, 1085, 1035; ^1H NMR (200 MHz, $CDCl_3$) 10.48 (s, 2 H), 7.42 (d, J = 3.1, 2 H), 7.15 (dd, J = 9.1, 3.1, 2 H), 6.93 (d, J = 9.0, 2 H), 4.65 (d, J = 2.4, 4 H), 4.46 (t, J = 6.6, 4 H), 2.52 (t, J = 2.4, 2 H), 1.81 (m, 4 H), 1.48 (m, 6 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.42, 154.80, 149.47, 124.01, 118.24, 114.40, 112.69, 79.00, 78.15, 65.18, 56.20, 28.11, 27.80, 25.17; MS m/e 481 (3), 480 (12), 306 (3), 175 (26), 174 (21), 136 (10), 135 (64); m/e 480.1779 (calcd for $C_{27}H_{28}O_8$ 480.1776). Anal.: C, 67.67 (calcd: 67.49); H, 6.06 (5.87).

1,8-Octanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.8): 60 °C, 29 h; purified by crystallization ($CHCl_3$); 79% yield; mp ($CHCl_3$) 131–132 °C; IR (KBr) 3205, 3110, 2900, 2845, 2090, 1660, 1595, 1470, 1395, 1330, 1270, 1210, 1070, 1005; ^1H NMR (270 MHz, $CDCl_3$) 10.49 (s, 2 H), 7.43 (d, J = 3.0, 2 H), 7.15 (dd, J = 9.0, 3.1, 2 H), 6.93 (d, J = 9.1, 2 H), 4.66 (d, J = 2.3, 4 H), 4.35 (t, J = 6.6, 4 H), 2.52 (t, J = 2.2, 2 H), 1.79 (m, 4 H), 1.42 (m, 8 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.36, 154.66, 149.44, 123.95, 118.16, 114.40, 112.69, 79.00, 78.12, 65.15, 56.20, 28.34, 27.80, 25.14; MS m/e 495.2007 (18), 494.1952 (57; calcd for $C_{28}H_{30}O_8$ 494.1932), 320.1615 (19), 176.0439 (10), 175.0426 (88), 174.0345 (52), 136.0141 (32), 135.0059 (74). Anal.: C, 67.61 (calcd: 68.00); H, 6.06 (6.11).

1,9-Nonanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.9): purified by crystallization ($CHCl_3$, then $ClCH_2CH_2Cl$); 73% yield; mp ($ClCH_2CH_2Cl$) 88–89.5 °C; IR (KBr) 3240, 3130, 3060, 2920, 2850, 2105, 1675, 1620, 1480, 1410, 1335, 1270, 1210, 1090, 1040; ^1H NMR (200 MHz, $CDCl_3$) 10.50 (s, 2 H), 7.43 (d, J = 3.1, 2 H), 7.15 (dd, J = 9.1, 3.1, 2 H), 6.93 (d, J = 9.1, 2 H), 4.66 (d, J = 2.3, 4 H), 4.35 (t, J = 6.6, 4 H), 2.52 (t, J = 2.3, 2 H), 1.79 (m, 4 H), 1.39 (b, 10 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.36, 154.69, 149.44, 123.95, 118.16, 114.43, 112.66, 78.94, 78.06, 65.15, 56.20, 28.59, 28.37, 27.80, 25.17; MS m/e 510 (2), 509 (13), 508 (42), 334 (15), 175 (65), 174 (100), 137 (10), 136 (20), 135 (7); m/e 510.2254 (calcd for $C_{29}H_{34}O_8$ = M + 2 H 510.2244), 508.2096 (calcd for $C_{29}H_{32}O_8$ 508.2097). Anal.: C, 68.06 (calcd: 68.22); H, 6.50 (6.71).

1,10-Decanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.10). The crude product was suspended three times in benzene and the solvent was evaporated in vacuo; the resulting residue was crystallized ($CHCl_3$) to give **8.10** (87% yield): mp ($CHCl_3$) 117–118 °C; IR (KBr) 3235,

(46) Structural manipulation in molecular mechanics is usually carried out by angle driving; see the following and references therein: (a) Jacob, E. J.; Thompson, H. B.; Bartell, L. S. *J. Chem. Phys.* **1967**, *47*, 3736–3753. (b) DeTar, D. F. *Comput. Chem.* **1977**, *1*, 141–144. (c) van de Graaf, B.; Baas, J. M. A. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 327–328.

(47) Critiques of angle driving: van de Graaf, B.; Baas, J. M. A. *J. Comput. Chem.* **1984**, *5*, 314–321 and references therein.

(48) See: Wehrli, F. W.; Wirthlin, T. *Interpretation of Carbon-13 NMR Spectra*; John Wiley & Sons: Chichester, 1978; pp 66–83.

(49) Burum, D. P.; Ernst, R. R. *J. Magn. Reson.* **1980**, *39*, 163–168.

(50) For full names and assignments, see: Brown, A. B. Ph.D. Thesis, University of Wisconsin—Madison, 1986 (*Diss. Abstr. Int., B* **1986**, *47*, 1057).

3130, 3055, 2950, 2930, 2920, 2895, 2875, 2855, 2835, 2105, 1680, 1615, 1490, 1410, 1345, 1290, 1270, 1220, 1100, 1035; ^{1}H NMR (270 MHz, $CDCl_3$) 10.50 (s, 2 H), 7.43 (d, J = 3.1, 2 H), 7.15 (dd, J = 9.0, 3.1, 2 H), 6.93 (d, J = 9.1, 2 H), 4.66 (d, J = 2.3, 4 H), 4.34 (t, J = 6.6, 4 H), 2.52 (t, J = 2.3, 2 H), 1.78 (m, 6 H), 1.39 (m, 10 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.45, 154.76, 149.57, 124.08, 118.29, 114.49, 112.78, 79.10, 78.21, 65.28, 56.26, 28.75, 28.49, 27.89, 25.30; MS m/e 522 (52), 192 (28), 175 (84), 174 (78), 137 (14), 136 (19), 135 (18); m/e 522.2255 (calcd for $C_{30}H_{34}O_8$ 522.2244). Anal.: C, 69.00 (calcd: 68.95); H, 6.52 (6.56).

1,11-Undecanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.11): 60 °C, 42 h; 97% yield; mp ($ClCH_2CH_2Cl$) 76.5–78 °C; IR (KBr) 3260, 3150, 3050, 2910, 2840, 2125, 1670, 1615, 1475, 1410, 1335, 1275, 1215, 1085, 1045; ^{1}H NMR (200 MHz, $CDCl_3$) 10.51 (s, 2 H), 7.43 (d, J = 3.1, 2 H), 7.15 (dd, J = 9.5, 3.6, 2 H), 6.93 (d, J = 9.1, 2 H), 4.66 (d, J = 2.3, 4 H), 4.34 (t, J = 6.6, 4 H), 2.52 (t, J = 2.3, 2 H), 1.79 ("quin", J = 7.3, 4 H), 1.32 (b, 14 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.45, 154.82, 149.54, 124.04, 118.23, 114.49, 112.69, 79.00, 78.09, 65.25, 56.30, 28.75, 28.49, 27.86, 25.27; MS m/e 537 (16), 536 (72), 362 (12), 175 (75), 174 (100), 137 (4), 136 (18), 135 (2); m/e 536.2409 (calcd for $C_{31}H_{36}O_8$ 536.2400). Anal.: C, 69.57 (calcd: 69.39); H, 6.78 (6.76).

6,6-Dimethylundecane-1,11-diyl Bis[2-hydroxy-5-(2-propynyloxy)-benzoate] (8.11dm). A solution of 1,11-dibromo-6,6-dimethylundecane (**6.11dm**; 3.672 g, 10.73 mmol),[51] **7** (4.4 g, 23 mmol), and Et_3N (3.5 mL, 2.5 g, 25 mmol) in DMF (3.5 mL) was stirred at 60 °C for 42 h. Water (70 mL) was added, and the mixture was extracted into $CHCl_3$ (0.10 L), followed by Et_2O (3 × 0.10 L). Drying (Na_2SO_4) and in vacuo evaporation of the combined extracts gave an oil, which was chromatographed rapidly ($CHCl_3$) to give **8.11dm** (4.3 g, 7.6 mmol, 71%) as a pale yellow oil: IR (neat) 3285, 3200, 2950, 2930, 2855, 2120, 1680, 1620, 1490, 1410, 1370, 1335, 1290, 1220, 1085, 1040; ^{1}H NMR (200 MHz, $CDCl_3$) 10.50 (s, 2 H), 7.44 (d, J = 3.1, 2 H), 7.15 (dd, J = 9.1, 3.1, 2 H), 6.93 (d, J = 9.0, 2 H), 4.66 (d, J = 2.4, 4 H), 4.35 (t, J = 6.6, 4 H), 2.52 (t, J = 2.4, 2 H), 1.80 ("quin", J = 7, 4 H), 1.40–1.17 (m, 12 H), 0.80 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) 169.74, 156.80, 149.84, 124.48, 118.47, 114.77, 112.36, 78.49, 75.58, 65.61, 56.92, 41.92, 32.59, 28.64, 27.19, 26.90, 23.70; MS m/e 566 (5), 565 (28), 546 (63), 390 (7), 175 (100), 174 (68), 137 (14), 136 (22), 135 (28); m/e 564.2713 (calcd for $C_{33}H_{40}O_8$ 564.2712).

General Synthesis of Metacyclophanediols 9. 1,8,16,20-Tetraoxa-15,21-dioxo[8.7]metacyclopha-3,5-diyne-12,23-diol (9.3). To a solution of $Cu(OAc)_2 \cdot H_2O$ (12.0 g, 60.1 mmol) in pyridine (1.30 L) at 44 °C was added **8.3** (4.766 g, 11.23 mmol). The solution was stirred at 44 °C for 2 h. After removal of solvent in vacuo, the residue was taken up in $CHCl_3$ (1.2 L); the solution was washed with 5% aqueous HCl (4 × 900 mL) and then dried (Na_2SO_4). Concentration in vacuo to a volume of ~250 mL, followed by chromatography ($CHCl_3$), gave **9.3** as a white solid (2.722 g, 6.444 mmol, 57%): mp ($ClCH_2CH_2Cl$) 238–241 °C dec; IR (KBr) 3220, 1675, 1620, 1495, 1295, 1280, ~1200, 1075, 1035; UV (DMSO) 328 (ϵ = 8960); ^{1}H NMR (270 MHz, $CDCl_3$) 10.41 (s, 2 H), 7.70 (d, J = 3.1, 2 H), 7.11 (dd, J = 9.0, 3.1, 2 H), 6.94 (d, J = 9.0, 2 H), 4.72 (s, 4 H), 4.58 (t, J = 6.0, 4 H), 2.33 (quin, J = 6.1, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) 169.61, 157.59, 150.44, 127.23, 119.08, 114.19, 111.71, 75.08, 71.58, 60.95, 58.34, 28.59; MS m/e 422 (7), 421 (4), 212 (7), 211 (8), 195 (17), 193 (19), 137 (24), 136 (53), 135 (21), 62 (100); m/e 422.0995 (calcd for $C_{23}H_{18}O_8$ 422.0996). Anal.: C, 65.37 (calcd: 65.40); H, 4.49 (4.29).

2,9,17,24-Tetraoxa-1,10-dioxo[10.8]metacyclopha-19,21-diyne-12,28-diol (9.6): 45 °C, 5 h; purified by chromatography (20% EtOAc/hexane), followed by crystallization ($ClCH_2CH_2Cl$); 52% yield; TLC R_f (20% EtOAc/hexane) 0.26; mp ($ClCH_2CH_2Cl$) 192.5–195.5 °C dec; IR (KBr) 3190, 3060, 2920, 2840, 1670, 1610, 1480, 1395, 1335, 1285, 1265, 1205, 1025; ^{1}H NMR (270 MHz, $CDCl_3$) 10.47 (s, 2 H), 7.47 (d, J = 3.0, 2 H), 7.08 (dd, J = 9.0, 3.4, 2 H), 6.92 (d, J = 9.0, 2 H), 4.74 (s, 4 H), 4.38 (t, J = 5.8, 4 H), 1.86 (m, 4 H), 1.69 (m, 4 H); ^{13}C NMR (50 MHz, DMSO-d_6, Ernst) 168.33 (C=O), 155.36 (C-2), 149.22 (C-5), 125.47 (C-4), 118.73 (C-3), 112.09 (C-1), 111.93 (C-6), 75.75 ($CH_2C{\equiv}C$), 69.90 ($CH_2C{\equiv}C$), 64.83 (CO_2CH_2), 56.11 ($ArOCH_2$), 27.39 (OCH_2CH_2), 24.82 ($OCH_2CH_2CH_2$); MS m/e 465 (14), 464 (54), 388 (18), 229 (22), 228 (37), 212 (16), 211 (11), 154 (26), 137 (38), 136 (100), 135 (10); m/e 464.1469 (calcd for $C_{26}H_{24}O_8$ 464.1464). Anal.: C, 67.07 (calcd: 67.24); H, 5.35 (5.21).

2,10,18,25-Tetraoxa-1,11-dioxo[11.8]metacyclopha-20,22-diyne-13,29-diol (9.7): 43 °C, 18 h; 59% yield; mp ($ClCH_2CH_2Cl$) 197–198.5 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 10.52 (s, 2 H), 7.42 (d, J = 3.1, 2 H), 7.07 (dd, J = 9.1, 3.1, 2 H), 6.92 (d, J = 9.1, 2 H), 4.74 (s, 4 H), 4.38 (t, J = 5.8, 4 H), 1.82 (m, 4 H), 1.55 (m, 6 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.42, 155.26, 148.94, 124.90, 118.51, 113.13, 112.12, 75.87, 69.93, 65.37, 56.07, 27.86, 25.90; MS m/e 479 (4), 478 (13), 403 (3), 402 (13), 229 (9), 228 (28), 212 (8), 211 (9), 154 (43), 137 (37), 136 (100), 135 (11); m/e 478.1637 (calcd for $C_{27}H_{26}O_8$ 478.1620). Anal.: C, 67.78 (calcd: 67.77); H, 5.68 (5.48).

2,11,19,26-Tetraoxa-1,12-dioxo[12.8]metacyclopha-21,23-diyne-14,30-diol (9.8): 45 °C, 20 h; purified by chromatography ($CHCl_3$), followed by rechromatography (20% EtOAc/hexane); 37% yield; mp ($CHCl_3$) 174–175.5 °C; IR (KBr) 3280, 3070, 3050, 2920, 2860, 1685, 1620, 1595, 1470, 1440, 1400–1150, 1080, 1040, the white sample turned orange on pressing into a pellet; ^{1}H NMR (200 MHz, $CDCl_3$) 10.46 (s, 2 H), 7.48 (d, J = 3.1, 2 H), 7.07 (dd, J = 9.0, 3.1, 2 H), 6.92 (d, J = 9.0, 2 H), 4.73 (s, 4 H), 4.38 (t, J = 5.8, 4 H), 1.82 ("tt", J = 6, 6, 4 H), 1.51 (m, 8 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.23, 155.07, 149.25, 124.90, 118.57, 113.32, 112.37, 76.00, 70.12, 64.87, 56.39, 28.37, 27.67, 25.39; MS m/e 493 (0.06), 492 (0.08), 419 (0.4), 418 (1), 283 (9), 282 (42), 155 (12), 154 (72), 137 (37), 136 (100); m/e 492.1779 (calcd for $C_{28}H_{28}O_8$ 492.1776). Anal.: C, 68.06 (calcd: 68.28); H, 5.77 (5.73).

2,12,20,27-Tetraoxa-1,13-dioxo[13.8]metacyclopha-22,24-diyne-15,31-diol (9.9): 44 °C, 18 h; 42% yield; mp (hexane/$CHCl_3$) 190.5–192 °C; IR (KBr) 3280, 3080, 2930, 2860, 1685, 1625, 1500, 1475, 1450, 1415, 1405, 1370, 1345, 1300, 1270, 1245, 1235, 1215, 1190, 1095, 1045; ^{1}H NMR (200 MHz, $CDCl_3$) 10.51 (s, 2 H), 7.45 (d, J = 3.1, 2 H), 7.08 (dd, J = 9.1, 3.1, 2 H), 6.92 (d, J = 9.0, 2 H), 4.72 (s, 4 H), 4.36 (t, J = 6.1, 4 H), 1.80 (m, 4 H), 1.44 (m, 10 H). MS m/e 508 (0.6), 507 (3), 506 (8), 505 (0.2), 434 (0.2), 433 (0.8), 432 (3), 431 (2), 430 (8), 297 (2), 296 (10), 155 (13), 154 (70); m/e 506.1957 (calcd for $C_{29}H_{30}O_8$ = M + 2 H 506.1941). The sample rapidly turns orange on standing; microanalysis was not attempted.

2,13,21,28-Tetraoxa-1,14-dioxo[14.8]metacyclopha-23,25-diyne-16,32-diol (9.10): 42 °C, 15 h; purified by chromatography (20% EtOAc/hexane); 59% yield; TLC R_f ($CHCl_3$) 0.5; mp ($ClCH_2CH_2Cl$) 164.5–165.5 °C; IR (KBr) 3200, 2910, 2840, 1685, 1615, 1590, 1490, 1465, 1450, 1405, 1375, 1365, 1330, 1285, 1270, 1205, 1080, 1070, 1040; ^{1}H NMR (270 MHz, $CDCl_3$) 10.51 (s, 2 H), 7.44 (d, J = 3.1, 2 H), 7.08 (dd, J = 9.0, 3.1, 2 H), 6.92 (d, J = 9.0, 2 H), 4.71 (s, 4 H), 4.37 (t, J = 5.8, 4 H), 1.80 (m, 4 H), 1.53–1.38 (m, 12 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.42, 155.20, 149.25, 124.84, 118.57, 113.51, 112.31, 75.87, 70.18, 65.37, 56.45, 28.75, 28.56, 27.61, 25.65. MS m/e 521 (19), 520 (73), 445 (12), 444 (69), 229 (8), 228 (47), 212 (12), 211 (20), 154 (100), 137 (25), 136 (87), 135 (1); m/e 520.2096 (calcd for $C_{30}H_{32}O_8$ 520.2088). Anal.: C, 68.93 (calcd: 69.22); H, 6.16 (6.20).

2,14,22,29-Tetraoxa-1,15-dioxo[15.8]metacyclopha-24,26-diyne-17,33-diol (9.11): 41 °C, 16 h; purified by chromatography (20% EtOAc/hexane); 63% yield; mp ($ClCH_2CH_2Cl$) 151.5–152.5 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 10.52 (s, 2 H), 7.42 (d, J = 3.1, 2 H), 7.08 (dd, J = 9.0, 3.1, 2 H), 6.92 (d, J = 9.1, 2 H), 4.71 (s, 4 H), 4.36 (t, J = 5.9, 4 H), 1.80 (m, 4 H), 1.55 (m, 4 H), 1.37 (m, 10 H). ^{13}C NMR (50 MHz, DMSO-d_6) 168.45, 155.23, 149.35, 124.68, 118.54, 113.35, 112.28, 75.75, 70.12, 65.28, 56.48, 28.27, 28.08, 27.39, 25.24; MS m/e 536 (4), 535 (31), 534 (100), 458 (36), 229 (34), 228 (67), 212 (21), 211 (16), 210 (13), 154 (79), 137 (23), 136 (85), 135 (4); m/e 534.2256 (calcd for $C_{31}H_{34}O_8$ 534.2244). Anal.: C, 69.49 (calcd: 69.65); H, 6.44 (6.41).

8,8-Dimethyl-2,14,22,29-tetraoxa-1,15-dioxo[15.8]metacyclopha-24,26-diyne-17,33-diol (9.11dm): 48 °C, 16 h; purified by chromatography (20% EtOAc/hexane); 41% yield; mp 105–115 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 10.51 (s, 2 H), 7.43 (d, J = 3.1, 2 H), 7.07 (dd, J = 9.0, 3.0, 2 H), 6.92 (d, J = 9.1, 2 H), 4.72 (s, 4 H), 4.35 (t, J = 6.3, 4 H), 1.81 (m, 4 H), 1.49–1.20 (m, 10 H), 0.86 (s, 6 H); ^{13}C NMR (50 MHz, DMSO-d_6) 168.33, 155.04, 149.16, 124.14, 118.29, 114.05, 112.37, 75.72, 70.02, 65.28, 56.42, 40.99, 32.10, 27.67, 27.13, 26.53, 23.09.

General Synthesis of Diethers 10. 1,8,16,20-Tetraoxa-15,21-dioxo-12,23-bis(2-propynyloxy)[8.7]metacyclopha-3,5-diyne (10.3). A mixture of **9.3** (0.750 g, 1.78 mmol), propargyl bromide (0.40 mL, 0.63 g, 5.3 mmol), and K_2CO_3 (1.798 g, 13.01 mmol) in DMF (75 mL) was stirred at room temperature for 20 h and then poured into ice/water (1.52 L) containing concentrated hydrochloric acid (2.2 mL, 26 mmol). The mixture was filtered in vacuo and the residue was air-dried to constant weight to give **10.3** (0.820 g, 1.65 mmol, 93%): mp (MeOH) 150–152 °C; IR (KBr) 3250, 2100, ~1715, 1605, 1585, 1490, 1315, 1280, ~1230, ~1075, ~1020; UV (DMSO) 307 (ϵ = 8720); ^{1}H NMR (270 MHz, $CDCl_3$) 7.450 (ABX, J = 3.2, 0.2, 2 H), 7.115 (ABX, J = 9.0, 0.2, 2 H), 7.076 (ABX, J = 9.0, 3.2, 2 H), 4.76 (d, J = 2.4, 4 H), 4.75 (s, 4 H), 4.46 (t, J = 6.1, 4 H), 2.53 (t, J = 2.5, 2 H), 2.26 (quin, J = 6.1, 2 H); ^{13}C NMR (15 MHz, $CDCl_3$) 165.3, 152.7, 152.2, 123.1, 122.2, 118.1, 116.2, 78.5, 75.8, 74.7, 71.6, 60.7, 58.2, 57.4, 28.0; MS m/e 499 (15), 498 (0.2), 460 (3), 249 (3), 233 (11), 193 (30), 175 (5), 135 (45), 45 (100); m/e 498.1305 (calcd for $C_{29}H_{22}O_8$ 498.1308). Anal.: C, 69.75 (calcd: 69.88); H, 4.48 (4.45).

(51) Friedman, P.; Allen, P., Jr. *J. Org. Chem.* **1965**, *30*, 780–784.

2,9,17,24-Tetraoxa-1,10-dioxo-12,28-bis(2-propynyloxy)[10.8]metacyclopha-19,21-diyne (10.6): purified by decolorization (Norit) of a $CHCl_3$ solution, followed by removal of solvent in vacuo; 96% yield; mp ($CHCl_3$) 179–180.5 °C; IR (KBr) 3265, 3230, 2925, 2855, 2120, 1720, 1590, 1500, 1465, 1455, 1290, 1245, 1225, 1200, 1075, 1040; ^{1}H NMR (270 MHz, $CDCl_3$) 7.524 (AB*X*, *J* = 3.2, −0.2, 2 H), 7.117 (*A*BX, *J* = 9.0, −0.2, 2 H), 7.053 (A*B*X, *J* = 9.0, 3.2, 2 H), 4.76 (d, *J* = 1.7, 4 H), 4.76 (s, 4 H), 4.32 (t, *J* = 6.0, 4 H), 2.51 (t, *J* = 2.4, 2 H), 1.81 (br, 4 H), 1.57 (br, 4 H); ^{13}C NMR (50 MHz, DMSO-d_6, Ernst) 164.18 (C=O), 151.12, 150.65 (C-2,5), 121.39 (C-1), 121.23 (C-4), 116.99 (C-6), 115.32 (C-3), 79.00 (HC≡*C*), 78.21 (H*C*≡C), 75.87 (C≡C-C≡*C*), 70.02 (C≡*C*C≡C), 64.11 (CO_2CH_2), 57.09 (2-ArOCH_2), 56.14 (5-ArOCH_2), 27.77 (OCH_2CH_2), 25.01 (O$CH_2CH_2CH_2$); MS *m/e* 540 (25), 249 (42), 211 (15), 210 (12), 175 (41), 137 (15), 136 (22), 135 (61), 83 (70), 55 (100); *m/e* 540.1776 (calcd for $C_{32}H_{28}O_8$ 540.1786). Anal.: C, 70.89 (calcd: 71.10); H, 5.31 (5.22).

2,10,18,25-Tetraoxa-1,11-dioxo-13,29-bis(2-propynyloxy)[11.8]metacyclopha-20,22-diyne (10.7): room temperature, 24 h; purified by crystallization ($CHCl_3$); 90% yield; mp ($CHCl_3$) 157.5–158 °C; IR (KBr) 3295, 3240, 2940, 2860, 2120, 1720, 1590, 1495, 1465, 1250, 1205, 1075, 1025; ^{1}H NMR (200 MHz, $CDCl_3$) 7.45 (d, *J* = 3.0, 2 H), 7.11 (d, *J* = 9.0, 2 H), 7.02 (dd, *J* = 9.1, 3.0, 2 H), 4.76 (s, 4 H), 4.75 (d, *J* = 2.6, 4 H), 4.31 (t, *J* = 5.8, 4 H), 2.51 (t, *J* = 2.4, 2 H), 1.76 (m, 4 H), 1.49 (m, 6 H); ^{13}C NMR (50 MHz, DMSO-d_6) 164.44, 150.90, 150.46, 121.77, 120.19, 116.68, 116.14, 78.97, 78.18, 75.97, 69.99, 64.55, 57.02, 56.01, 28.53, 27.96, 25.84; MS *m/e* 554 (46), 515 (11), 249 (71), 227 (23), 210 (36), 175 (40), 137 (15), 135 (100); *m/e* 554.1941 (calcd for $C_{33}H_{30}O_8$ 554.1932). Anal.: C, 71.17 (calcd: 71.47); H, 5.38 (5.45).

2,11,19,26-Tetraoxa-1,12-dioxo-14,30-bis(2-propynyloxy)[12.8]metacyclopha-21,23-diyne (10.8): room temperature, 25 h; purified by taking up crude material three times in toluene and removing solvent in vacuo; 91% yield; mp (hexane/$CHCl_3$) 142–142.5 °C; IR (KBr) 3260, 3040, 2915, 2850, 2120, 1725, 1610, 1590, 1500, 1470, 1460, 1440, 1420, 1385, 1365, 1315, 1300, 1285, 1245, 1205, 1090, 1070, 1045; ^{1}H NMR (200 MHz, $CDCl_3$) 7.48 (d, *J* = 3.0, 2 H), 7.11 (d, *J* = 9.0, 2 H), 7.02 (dd, *J* = 9.0, 3.0, 2 H), 4.754 (s, 4 H), 4.749 (d, *J* = 2.0, 4 H), 4.31 (t, *J* = 5.8, 4 H), 2.51 (t, *J* = 2.4, 2 H), 1.76 (m, 4 H), 1.01 (m, 8 H); ^{13}C NMR (50 MHz, DMSO-d_6) 164.40, 150.96, 150.61, 121.70, 120.41, 116.77, 115.63, 78.97, 78.18, 75.91, 70.12, 64.20, 57.05, 56.17, 28.34, 27.86, 25.36; MS *m/e* 568 (0.5), 529 (0.2), 175 (2), 137 (14), 136 (9), 135 (7); *m/e* 568.2097 (calcd for $C_{34}H_{32}O_8$ 568.2088). Anal.: C, 71.72 (calcd: 71.82); H, 5.65 (5.67).

2,12,20,27-Tetraoxa-1,13-dioxo-15,31-bis(2-propynyloxy)[13.8]metacyclopha-22,24-diyne (10.9): room temperature, 24 h; purified as for **10.8**, followed by trituration with MeOH/$CHCl_3$; 93% yield; mp (hexane/$CHCl_3$) 137.5–138 °C; IR (KBr) 3270, 3080, 3060, 2920, 2850, 2120, 1715, 1615, 1590, 1495, 1455, 1425, 1390, 1375, 1300–1180, 1080, 1030; ^{1}H NMR (270 MHz, $CDCl_3$) 7.45 (d, *J* = 3.1, 2 H), 7.11 (d, *J* = 9.0, 2 H), 7.02 (dd, *J* = 9.1, 3.1, 2 H), 4.750 (d, *J* = 1.8, 4 H), 4.746 (s, 4 H), 4.29 (t, *J* = 6.1, 4 H), 2.51 (t, *J* = 2.4, 2 H), 1.75 (m, 4 H), 1.34 (m, 10 H); ^{13}C NMR (50 MHz, DMSO-d_6) 164.31, 150.90, 150.61, 121.80, 119.96, 116.68, 116.20, 78.97, 78.18, 75.87, 70.05, 64.46, 57.02, 56.17, 28.65, 28.40, 27.83, 25.55; MS, no M^+. Anal.: C, 71.83 (calcd for $C_{35}H_{34}O_8$ 72.15); H, 5.91 (5.88).

2,13,21,28-Tetraoxa-1,14-dioxo-16,32-bis(2-propynyloxy)[14.8]metacyclopha-23,25-diyne (10.10): room temperature, 22 h; 95% yield; mp (MeOH) 123.5–124.5 °C; IR (KBr) 3270, 3240, 3050, 2910, 2850, 2120, 1715, 1585, 1490, 1460, 1280, 1200, 1075, 1025; ^{1}H NMR (200 MHz, $CDCl_3$) 7.45 (d, *J* = 3.0, 2 H), 7.11 (d, *J* = 9.2, 2 H), 7.03 (dd, *J* = 9.1, 2.7, 2 H), 4.75 (s, 4 H), 4.74 (d, *J* = 2.2, 4 H), 4.30 (t, *J* = 5.7, 4 H), 2.51 (t, *J* = 2.3, 2 H), 1.75 (m, 4 H), 1.60 (m, 2 H), 1.35 (m, 10 H); ^{13}C NMR (50 MHz, DMSO-d_6) 164.50, 150.99, 150.71, 121.89, 120.09, 116.77, 116.30, 79.00, 78.18, 75.84, 70.12, 64.42, 57.12, 56.26, 28.59, 28.43, 27.89, 25.43; MS, no M^+ or $(M - C_3H_3)^+$. Anal.: C, 72.19 (calcd for $C_{36}H_{36}O_8$ 72.47); H, 6.22 (6.08).

2,14,22,29-Tetraoxa-1,15-dioxo-17,33-bis(2-propynyloxy)[15.8]metacyclopha-24,26-diyne (10.11): room temperature, 22 h; purified by taking up crude product in toluene and removing solvent in vacuo; 98% yield; mp ($ClCH_2CH_2Cl$) 131.5–132.5 °C; IR (KBr) 3235, 2915, 2845, 2120, 1720, 1585, 1495, 1455, 1285, 1240, 1200, 1085, 1040; ^{1}H NMR (200 MHz, $CDCl_3$) 7.44 (d, *J* = 3.0, 2 H), 7.11 (d, *J* = 9.0, 2 H), 7.03 (dd, *J* = 9.1, 3.0, 2 H), 4.75 (d, *J* = 2.1, 4 H), 4.74 (s, 4 H), 4.30 (t, *J* = 6.1, 4 H), 2.51 (t, *J* = 2.4, 2 H), 1.75 ("quin", *J* = 6, 4 H), 1.33 (m, 14 H); ^{13}C NMR (50 MHz, DMSO-d_6) 164.37, 150.90, 150.74, 121.86, 119.87, 116.68, 116.20, 78.97, 78.21, 75.75, 70.02, 64.33, 57.05, 56.26, 28.40, 28.11, 27.70, 25.24; MS, no M^+. Anal.: C, 73.08 (calcd for $C_{37}H_{38}O_8$ 72.77); H, 6.30 (6.27).

8,8-Dimethyl-2,14,22,29-tetraoxa-1,15-dioxo-17,33-bis(2-propynyloxy)[15.8]metacyclopha-24,26-diyne (10.11dm): room temperature, 73 h; purified as for **10.8**, followed by chromatography ($CHCl_3$) to give **10.11dm** (54% yield) as a yellowish oil that solidified on standing; mp 90.5–97 °C; ^{1}H NMR (200 MHz, $CDCl_3$) 7.43 (d, *J* = 3.0, 2 H), 7.11 (d, *J* = 9.0, 2 H), 7.01 (dd, *J* = 9.0, 3.1, 2 H), 4.75 (s, 4 H), 4.74 (d, *J* = 2.6, 4 H), 4.29 (t, *J* = 6.4, 4 H), 2.52 (t, *J* = 2.4, 2 H), 1.75 (m, 4 H), 1.4–1.2 (m, 12 H), 0.84 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) 165.09, 152.21, 151.64, 122.80, 119.76, 117.61, 78.61, ~77.63 (partly obscured by solvent), 74.41, 71.21, 65.20, 58.29, 56.73, 41.74, 32.56, 28.70, 27.44, 27.10, 23.77.

1,8,15,22,30,34-Hexaoxa-29,35-dioxo[8.8.7](1,4,2)cyclopha-3,5,17,19-tetrayne (4.3). To a solution of $Cu(OAc)_2 \cdot H_2O$ (2.313 g, 11.59 mmol) in pyridine (0.20 L) at 42 °C was added over 5 min a solution of **10.3** (2.314 g, 4.642 mmol) in pyridine (0.20 L). The solution was stirred at 42 °C for 10 min longer and then concentrated in vacuo until solids appeared (at a volume of ~150 mL). The solution was diluted with $CHCl_3$ (0.57 L) and then washed with 6 N aqueous HCl (3 × 0.40 L) and dried (Na_2SO_4). Without prior concentration, the solution was chromatographed ($CHCl_3$); the cuts containing **4.3** as major component (TLC), which all also contained white precipitates, were combined and concentrated in vacuo to a volume of ~50 mL, chilled to −40 °C, and filtered to give the highly insoluble **4.3** (418 mg, 0.842 mmol, 18%): dec >140 °C without melting; IR (KBr) 1725, 1605, 1495, 1205, 1030; UV (DMSO) 299 (ε = 4700); ^{1}H NMR (270 MHz, DMSO-d_6) 7.30 (d, *J* = 9.0, 2 H), 7.22 (d, *J* = 3.0, 2 H), 7.09 (dd, *J* = 9.0, 3.0, 2 H), 5.03 (*AB*, *J* = 18, 4 H; 5-ArOCH_2), 4.98 (*A*B, *J* = 17.2, 2 H; 2-ArOCH_2), 4.95 (A*B*, *J* = 17.2, 2 H; 2-ArOCH_2), 4.537 (A_2B_2XY, *J* = −11.2, 7.0, 4.4, 2 H; *endo*-CO_2CH_2), 4.281 (A_2B_2XY, *J* = −11.2, 7.3, 4.2, 2 H; *exo*-CO_2CH_2), 2.193 (A_2B_2XY, *J* = −15.4, 7.3, 4.4, 1 H; *endo*-OCH_2CH_2), 2.106 (A_2B_2XY, *J* = −15.4, 7.0, 4.2, 1 H; *exo*-OCH_2CH_2); ^{13}C NMR (50 MHz, DMSO-d_6, SFORD) 165.50 (C=O), 151.47, 149.79 (C-2,5), 125.20 (C-1), 121.45 (C-4), 120.75 (C-6), 113.01 (C-3), 75.65, 75.45 (*C*≡CC≡*C*), 70.15, 69.88 (C≡*CC*≡C), 62.41 (CO_2CH_2), 59.47 (2-ArOCH_2), 55.41 (5-ArOCH_2), 27.41 (OCH_2CH_2); MS *m/e* 422 (15), 195 (11), 139 (19), 136 (17), 135 (17), 45 (100); *m/e* 496.1158 (calcd for $C_{29}H_{20}O_8$ 496.1152). Anal.: C, 69.97 (calcd: 70.16); H, 3.98 (4.06).

General Synthesis of Stiff-Bridged Cyclophanes 4.*n*. 2,9,17,24,31,38-Hexaoxa-1,10-dioxo[10.8.8](2,1,4)cyclopha-19,21,33,35-tetrayne (4.6). To a solution of $Cu(OAc)_2 \cdot H_2O$ (2.8 g, 14 mmol) in pyridine (0.49 L) at 44 °C was added **10.6** (3.015 g, 5.577 mmol); the solution was stirred at 44 °C for 55 min. The solvent was then removed in vacuo; the green, solid residue was taken up in $CHCl_3$ (0.49 L), washed with 5% aqueous HCl (3 × 0.49 L), and dried (Na_2SO_4). Removal of solvent in vacuo gave a solid (3.0 g), which was chromatographed (5% EtOAc/$CHCl_3$) to give **4.6** (860 mg, 1.60 mmol, 29%); TLC R_f (10% EtOAc/$CHCl_3$) 0.42; dec 195–200 °C without melting; IR (KBr) 3050, 2930, 2850, 2170, 2120, 1720, 1690, 1600, 1585, 1490, 1455, 1425, 1360, 1310, 1285, 1245, 1220, 1195, 1085, 1020; UV (MeOH) 302 (ε = 5100); ^{1}H NMR (270 MHz, $CDCl_3$) 7.309 (AB*X*, J = 3.4, −0.4, 2 H), 6.997 (*A*BX, *J* = 9.0, 3.4, 2 H), 6.954 (A*B*X, *J* = 9.0, −0.4, 2 H), 4.903 (*A*B, *J* = 16.5, 2 H; 2-ArOCH_2), 4.79 ("s", 4 H; 5-ArOCH_2), 4.713 (A*B*, *J* = 16.5, 2 H; 2-ArOCH_2), 4.359 (*A*BXY, *J* = −10.7, 5.9, 5.9, 2 H; *endo*-CO_2CH_2), 4.297 (A*B*XY, *J* = −10.7, 5.8, 5.8, 2 H; *exo*-CO_2CH_2), 1.77 (m, 4 H; OCH_2CH_2), 1.54 (m, 4 H); ^{13}C NMR (50 MHz, DMSO-d_6) 165.70, 150.61, 149.54, 124.33, 119.14, 117.81, 115.95, 75.87, 75.15, 69.61, 64.27, 57.37, 55.12, 27.64, 24.54; MS, no M^+. Anal.: C, 71.51 (calcd for $C_{32}H_{26}O_8$ 71.37); H, 5.01 (4.87).

2,10,18,25,32,39-Hexaoxa-1,11-dioxo[11.8.8](2,1,4)cyclopha-20,22,34,36-tetrayne (4.7): 45 °C, 2 h; 51% yield; dec 180–195 °C without melting; IR (KBr) 2920, 2870, 2150, 1710, 1630, 1605, 1460, 1385, 1275, 1200, 1095, 1010; ^{1}H NMR (270 MHz, $CDCl_3$) 7.29 (d, *J* = 2.9, 2 H), 7.00 (dd, *J* = 9.0, 3.0, 2 H), 6.94 (d, *J* = 9.0, 2 H), 4.90 (*A*B, *J* = 16.6, 2 H; 2-ArOCH_2), 4.78 ("s", 4 H; 5-ArOCH_2), 4.72 (A*B*, *J* = 16.6, 2 H; 2-ArOCH_2), 4.331 (*A*BXY, *J* = −10.4, 6.2, 6.2, 2 H; *endo*-CO_2CH_2), 4.237 (A*B*XY, *J* = −10.4, 6.2, 6.2, 2 H; *exo*-CO_2CH_2), 1.68 (br, 4 H; OCH_2CH_2), 1.41 (br, 6 H); ^{13}C NMR (50 MHz, DMSO-d_6) 165.80, 150.30, 149.22, 123.95, 117.78, 117.21, 115.92, 75.84, 74.86, 69.45, 69.26, 64.42, 56.17, 55.06, 27.64, 27.58, 25.14; MS, no M^+. Anal.: C, 69.70 (calcd for $C_{33}H_{28}O_8$ 71.73); H, 5.18 (5.11).

2,11,19,26,33,40-Hexaoxa-1,12-dioxo[12.8.8](2,1,4)cyclopha-21,23,35,37-tetrayne (4.8): 45 °C, 2.25 h; 32% yield; dec >160 °C without melting; IR (KBr) 3060, 3010, 2930, 2850, 2170, 1725, 1595, 1500, 1430, 1370, 1290, 1250, 1225, 1200, 1085, 1035; ^{1}H NMR (200 MHz, $CDCl_3$) 7.32 (d, *J* = 2.9, 2 H), 7.02 (dd, *J* = 9.1, 2.9, 2 H), 6.94 (d, *J* = 9.0, 2 H), 4.898 (*A*B, *J* = 16.5, 2 H; 2-ArOCH_2), 4.828 (*A*B, *J* = 17.0, 2 H; 5-ArOCH_2), 4.758 (A*B*, *J* = 16.5, 2 H; 2-ArOCH_2), 4.753 (A*B*, *J* = 17.0, 2 H, 5-ArOCH_2), 4.322 (*A*BXY, *J* = −10.5, 5.4, 5.4, 2 H; *endo*-CO_2CH_2), 4.242 (A*B*XY, *J* = −10.5, 7.1, 5.0, 2 H; *exo*-CO_2CH_2), 1.68 (m, 4 H; OCH_2CH_2), 1.38 (m, 8 H); ^{13}C NMR (50 MHz, DMSO-d_6) 165.92, 150.26, 149.35, 123.59, 117.75, 115.95, 75.78, 74.92, 69.45, 56.12, 55.19, 28.71, 27.99, 25.74; MS, no M^+. Anal.: C,

59.57 (calcd for $C_{34}H_{30}O_8$ 72.07); H, 4.81 (5.34).

2,12,20,27,34,41-Hexaoxa-1,13-dioxo[13.8.8](2,1,4)cyclopha-22,24,36,38-tetrayne (4.9): 43 °C, 2.5 h; in the workup, after the acid washes, the $CHCl_3$ phase was also washed with saturated aqueous $NaHCO_3$; 41% yield; mp ($CHCl_3$) 127.5–130.5 °C; ^1H NMR (200 MHz, $CDCl_3$) 7.36 (d, J = 2.9, 2 H), 7.03 (dd, J = 9.0, 3.0, 2 H), 6.96 (d, J = 9.0, 2 H), 4.920 (AB, J = 16.6, 2 H; 2-$ArOCH_2$), 4.81 ("s", 4 H; 5-$ArOCH_2$), 4.737 (AB, J = 16.6, 2 H; 2-$ArOCH_2$), 4.29 (t, J = 6.1, 4 H; CO_2CH_2), 1.69 (m, 4 H), 1.43 (m, 4 H), 1.32 (m, 10 H).

2,13,21,28,35,42-Hexaoxa-1,14-dioxo[14.8.8](2,1,4)cyclopha-23,25,37,39-tetrayne (4.10): 45 °C, 2 h; workup as for **4.9**; 35% yield; dec 175–180 °C without melting; IR (KBr) 2910, 2840, 1705, 1580, 1480, 1425, 1275, 1240, 1190, 1075, 1020; ^1H NMR (270 MHz, $CDCl_3$, room temperature) 7.33 (d, J = 2.9, 2 H), 7.04 (dd, J = 9.0, 3.0, 2 H), 6.96 (d, J = 9.1, 2 H), 4.84 (br, 4 H; $ArOCH_2$), 4.78 (br, 4 H; $ArOCH_2$), 4.28 (br, 4 H; CO_2CH_2), 1.68 (m, 4 H; OCH_2CH_2), 1.41 (br m, 4 H), 1.29 (br m, 8 H); ^{13}C NMR (50 MHz, DMSO-d_6) 165.76, 150.39, 149.47, 123.19, 118.67, 117.37, 115.32, 75.65, 75.24, 69.71, 69.61, 64.93, 56.01, 55.38, 28.75, 28.53, 28.21, 25.58; MS, no M^+. Anal.: C, 56.15 (calcd for $C_{36}H_{34}O_8$ 72.21); H, 4.46 (5.76).

2,14,22,29,36,43-Hexaoxa-1,15-dioxo[15.8.8](2,1,4)cyclopha-24,26,38,40-tetrayne (4.11): 45–46 °C, 2 h; workup as for **4.9**; 32% yield; dec >160 °C without melting; IR (KBr) 2920, 2850, 1725, 1590, 1500, 1295, 1250, 1205, 1035; ^1H NMR (200 MHz, $CDCl_3$) 7.38 (d, J = 3.0, 2 H), 7.06 (dd, J = 9.0, 3.1, 2 H), 6.97 (d, J = 9.0, 2 H), 4.85 (s, 4 H), 4.78 (s, 4 H), 4.28 (t, J = 5.9, 4 H), 1.68 (m, 4 H), 1.3 (m, 14 H); ^{13}C NMR (50 MHz, DMSO-d_6) 165.32, 150.36, 149.51, 122.97, 118.57, 117.56, 115.28, 75.56, 75.18, 69.61, 69.52, 64.30, 56.01, 55.38, 28.53, 28.02, 27.80, 25.14; MS m/e 154 (68), 136 (100), no M^+. Anal.: C, 61.38 (calcd for $C_{37}H_{36}O_8$ 73.01); H, 5.19 (5.96).

8,8-Dimethyl-2,14,22,29,36,43-hexaoxa-1,15-dioxo[15.8.8](2,1,4)-cyclopha-24,26,38,40-tetrayne (4.11dm): 44 °C, 2.5 h; further purified by crystallization ($CHCl_3$); 11% yield; mp 93–98.5 °C; ^1H NMR (200 MHz, $CDCl_3$) 7.35 (d, J = 2.8, 2 H), 7.04 (dd, J = 9.0, 3.1, 2 H), 6.97 (d, J = 9.1, 2 H), 4.84 (s, 4 H), 4.78 (s, 4 H), 4.28 (t, J = 5.9, 4 H), 1.69 (m, 4 H), 1.39 (m, 4 H), 1.19 (m, 10 H), 0.83 (s, 6 H); MS, no M^+.

General Synthesis of Floppy-Bridged Cyclophanes 5.*n*. 1,8,15,22,30,34-Hexaoxa-29,35-dioxo[8.8.7](1,4,2)cyclophane (5.3). To a suspension of 5% Rh/Al_2O_3 (17 mg) in EtOAc (10 mL) under H_2 (1 atm) was added a suspension of **4.3** (102 mg, 0.205 mmol) in EtOAc (10 mL); the mixture was stirred at room temperature under H_2 (1 atm). In 5.1 h, 38.8 mL of H_2 was taken up (96% of theory). Filtration through Celite and removal of solvent in vacuo gave crude **5.3** (92 mg), which was crystallized ($MeOH/CHCl_3$) to give **5.3** (85 mg, 0.17 mmol, 81%) as white crystals: mp ($MeOH/CHCl_3$) 157–160 °C; IR (KBr) 1725, 1580, 1500, 1280, 1215, 1075, 1040; ^1H NMR (270 MHz, $CDCl_3$) 7.08 (d, J = 3.0, 2 H), 6.72 (dd, J = 8.8, 3.2, 2 H), 6.62 (d, J = 9.0, 2 H), 4.574 (A_2B_2XY, J = −11.2, 8.1, 2.6, 2 H; CO_2CH_2), 4.528 (A_2B_2XY, J = −11.2, 6.9, 2.4, 2 H; CO_2CH_2), 3.92–3.81 (m, 8 H; $ArOCH_2$), 2.214 (A_2B_2XY, J = −15.9, 6.9, 2.6, 1 H; $CO_2CH_2CH_2$), 2.214 (A_2B_2XY, J = −15.9, 8.1, 2.4, 1 H; $CO_2CH_2CH_2$), 2.2–1.4 (m, 16 H); ^{13}C NMR (50 MHz, $CDCl_3$) 166.08, 152.53, 152.41, 121.61, 118.67, 116.41, 115.92, 70.04, 65.98, 64.33, 28.62, 28.11, 24.73, 22.39; MS m/e 512 (12), 430 (2), 136 (17), 44 (100); m/e 512.2412 (calcd for $C_{29}H_{36}O_8$ 512.2400). Anal.: C, 67.76 (calcd: 67.95); H, 7.16 (7.08).

2,9,17,24,31,38-Hexaoxa-1,10-dioxo[10.8.8](2,1,4)cyclophane (5.6): 71% yield; mp (hexane/$CHCl_3$) 110–111 °C; IR (KBr) 3040, 2920, 2860, 1720, 1585, 1500, 1475, 1425, 1280, 1235, 1215, 1090, 1030; ^1H NMR (200 MHz, $CDCl_3$) 7.05 (d, J = 3.2, 2 H), 6.75 (dd, J = 9.0, 3.2, 2 H), 6.53 (d, J = 9.0, 2 H), 4.29 (t, J = 5.4, 4 H; CO_2CH_2), 3.94 (m, 8 H; $ArOCH_2$), 1.74 (m, 16 H), 1.54 (m, 8 H) (Slow inversion is clear from the $ArOCH_2$ signals; the CO_2CH_2 triplet is apparently due to accidental isochrony.); ^{13}C NMR (50 MHz, $CDCl_3$) 166.92, 152.34, 151.93, 122.04, 119.22, 116.47, 115.14, 69.03, 67.01, 65.71, 28.51, 27.38, 23.99, 23.45; MS m/e 556 (8), 555 (36), 554 (100), 472 (12); m/e 554.2888 (calcd for $C_{32}H_{42}O_8$: 554.2868). Anal.: C, 68.55 (calcd: 69.29); H, 7.75 (7.63).

2,10,18,25,32,39-Hexaoxa-1,11-dioxo[11.8.8](2,1,4)cyclophane (5.7): 77% yield; mp (hexane/$CHCl_3$) 80–81.5 °C; IR (KBr) 2915, 2865, 1705, 1585, 1485, 1435, 1280, 1240, 1090, 1030; ^1H NMR (200 MHz, $CDCl_3$) 7.14 (d, J = 3.1, 2 H), 6.76 (dd, J = 9.0, 3.2, 2 H), 6.58 (d, J = 9.0, 2 H), 4.286 ($ABXY$, J = −10.7, 6.2, 6.2, 2 H; CO_2CH_2), 4.229 ($ABXY$, J = −10.7, 6.2, 6.2, 2 H; CO_2CH_2), 3.94 (m, 8 H; $ArOCH_2$), 1.68 (m, 12 H), 1.41 (m, 14 H); ^{13}C NMR (50 MHz, $CDCl_3$) 166.48, 152.40, 152.28, 122.23, 119.57, 117.26, 115.75, 69.50, 67.68, 64.29, 28.61, 28.29, 27.47, 26.71, 24.37, 24.18, 24.05; MS m/e 568 (0.3), 28 (100); m/e 568.3033 (calcd for $C_{33}H_{44}O_8$ 568.3024). Anal.: C, 69.34 (calcd: 69.70); H, 7.96 (7.80).

2,11,19,26,33,40-Hexaoxa-1,12-dioxo[12.8.8](2,1,4)cyclophane (5.8): 78% yield; mp (hexane/$CHCl_3$) 145–146 °C; IR (KBr) 3050, 2930, 2850, 1715, 1615, 1585, 1505, 1485, 1430, 1320, 1285, 1245, 1230, 1160, 1095, 1025; ^1H NMR (270 MHz, $CDCl_3$) 7.15 (d, J = 3.2, 2 H), 6.77 (dd, J = 9.0, 3.2, 2 H), 6.51 (d, J = 9.0, 2 H), 4.314 ($ABXY$, J = −10.9, 5.6, 5.6, 2 H; CO_2CH_2), 4.249 ($ABXY$, J = −10.9, 5.6, 5.6, 2 H; CO_2CH_2), 3.95 (m, 8 H; $ArOCH_2$), 1.74 (m, 8 H), 1.66 (m, 4 H), 1.36 (m, 8 H); MS m/e 583 (1), 582 (4), 500 (0.6), 69 (100); m/e 582.3190 (calcd for $C_{34}H_{46}O_8$: 582.3180). Anal.: C, 69.30 (calcd: 70.08); H, 8.06 (7.96).

2,12,20,27,34,41-Hexaoxa-1,13-dioxo[13.8.8](2,1,4)cyclophane (5.9): 84% yield; mp (hexane/$CHCl_3$) 110.5–112 °C; IR (KBr) 3030, 2910, 2850, 1710, 1585, 1495, 1475, 1420, 1305, 1275, 1240, 1215, 1145, 1080, 1025, 1015; ^1H NMR (200 MHz, $CDCl_3$) 7.29 (d, J = 3.1, 2 H), 6.74 (dd, J = 9.0, 3.1, 2 H), 6.59 (d, J = 9.0, 2 H), 4.23 (t, J = 6.0, 4 H; CO_2CH_2), 3.98 (br t, J = 5.8, 8 H; $ArOCH_2$), 1.75 (m, 14 H), 1.57 (m, 8 H), 1.31 (m, 8 H); ^{13}C NMR (50 MHz, $CDCl_3$) 166.67, 152.40, 152.31, 122.29, 119.86, 117.74, 115.68, 69.25, 68.18, 64.95, 28.48, 28.39, 28.17, 27.85, 27.72, 25.45, 24.28, 24.15; MS m/e 596 (100); m/e 596.3348 (calcd for $C_{35}H_{48}O_8$ 596.3336). Anal.: C, 70.28 (calcd: 70.44); H, 8.14 (8.11).

2,13,21,28,35,42-Hexaoxa-1,14-dioxo[14.8.8](2,1,4)cyclophane (5.10): 79% yield; mp (hexane/$CHCl_3$) 132.5–133; IR (KBr) 3050, 3010, 2920, 2850, 1710, 1585, 1505, 1475, 1430, 1305, 1275, 1245, 1225, 1090, 1030; ^1H NMR (500 MHz, $CDCl_3$) 7.23 (d, J = 3.2, 2 H), 6.73 (dd, J = 9.0, 3.2, 2 H), 6.58 (d, J = 9.0, 2 H), 4.28 (t, J = 5.8, 4 H), 4.00 (br t, J = 6, 4 H; 2-$ArOCH_2$), 3.98 (t, J = 5.9, 4 H; 5-$ArOCH_2$), 1.74 (m, 8 H; $ArOCH_2CH_2$), 1.64 (m, 4 H; $CO_2CH_2CH_2$), 1.57 (m, 8 H), 1.36 (m, 4 H), 1.27 (m, 4 H), 1.23 (m, 4 H); ^{13}C NMR (50 MHz, $CDCl_3$) 166.6, 152.50, 152.12, 122.45, 119.89, 117.61, 115.72, 69.09, 68.27, 65.17, 28.55, 28.26, 25.73, 24.40, 23.93; MS m/e 612 (7), 611 (32), 610 (32), 528 (4), 137 (7), 136 (12); m/e 610.3504 (calcd for $C_{36}H_{50}O_8$ 610.3492). Anal.: C, 70.70 (calcd: 70.79); H, 8.32 (8.25).

2,14,22,29,36,43-Hexaoxa-1,15-dioxo[15.8.8](2,1,4)cyclophane (5.11): 68% yield; mp (hexane/$CHCl_3$) 114.5–116 °C; ^1H NMR (500 MHz, $CDCl_3$) 7.27 (d, J = 3.2, 2 H), 6.72 (dd, J = 9.0, 3.2, 2 H), 6.62 (d, J = 9.0, 2 H), 4.28 (t, J = 5.8, 4 H), 4.08 (t, J = 6.2, 4 H), 3.98 (t, J = 5.9, 4 H), 1.74 ("tt", J = 6.1, 6.1, 8 H), 1.68 (tt, J = 6.6, 6.6, 4 H), 1.56 (m, 8 H), 1.36 (tt, J = 7, 7, 4 H), 1.26 (tt, J = 7, 7, 4 H), 1.20 (br, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) 166.89, 152.59, 152.31, 122.45, 120.11, 117.71, 116.00, 69.19, 68.40, 65.30, 28.83, 28.70, 28.32, 28.17, 26.21, 24.53, 23.93; MS m/e 625 (30), 624 (64), 524 (13), 154 (29), 137 (100), 136 (40); m/e 624.3680 (calcd for $C_{37}H_{52}O_8$ 624.3648). Anal.: C, 70.99 (calcd: 71.13); H, 8.53 (8.59).

8,8-Dimethyl-2,14,22,29,36,43-hexaoxa-1,15-dioxo[15.8.8](2,1,4)-cyclophane (5.11dm): not crystallizable; 81% yield as a thick syrup; ^1H NMR (270 MHz, $CDCl_3$) 7.24 (d, J = 2.8, 2 H), 6.69 (dd, J = 9.0, 2.98 2 H), 6.63 (d, J = 9.0, 2 H), 4.25 (t, J = 6.2, 4 H), 4.03 (t, J = 6.1, 4 H), 3.97 (t, J = 6.0, 4 H), 1.74 (m, 8 H), 1.67 ("t", J = 7, 4 H), 1.57 (m, 10 H), 1.35–1.07 (m, 10 H), 0.79 (s, 6 H); MS m/e 655.3879 (2), 654.3881 (12), 653.3940 (40), 652.3956 (99; calcd for $C_{39}H_{56}O_8$ 652.3960).

2-[(*tert*-Butyldimethylsilyl)oxy]-1,3-propanediyl Bis[2-hydroxy-5-(2-propynyloxy)benzoate] (8.3os). To a solution of 2-hydroxy-1,3-propanediyl bis[2-hydroxy-5-(2-propynyloxy)benzoate] (**8.3oh**; 877 mg, 1.99 mmol) in $CHCl_3$ (3.2 mL) at room temperature were added 2,6-lutidine (0.47 mL, 0.43 g, 4.0 mmol) and TBSOTf (0.7 mL, 0.8 g, 3 mmol); the solution was stirred at room temperature for 20 min and then poured into water (65 mL), extracted into Et_2O (3 × 65 mL), dried (Na_2SO_4), and evaporated in vacuo to give crude **8.3os** (1.11 g) as a yellow oil. Chromatography (10% EtOAc/hexane) gave **8.3os** (866 mg, 1.56 mmol, 78%) as a pale yellow oil: TLC R_f (20% EtOAc/hexane) 0.35; IR (neat) 3270, 3060, 3030, 2935, 2905, 2870, 2840, 2105, 1675, 1610, 1485, 1455, 1395, 1330, 1280, 1200, 1145, 1075, 1030, 1005; ^{H} NMR (270 MHz, $CDCl_3$) 10.33 (s, 2 H), 7.43 (d, J = 3.0, 2 H), 7.17 (dd, J = 9.0, 3.0, 2 H), 6.95 (d, J = 9.0, 2 H), 4.65 (d, J = 2.2, 4 H), 4.45 (A_2B_2X, J_{AB} = −11.4, J_{AX} = J_{BX} = 4.7, 4 H), 4.36 (A_2B_2X, J = 4.7, 4.7, 1 H), 2.53 (t, J = 2.4, 2 H), 0.89 (s, 9 H), 0.14 (s, 6 H); ^{13}C NMR (50 MHz, acetone-d_6, Ernst) 170.30, 157.55, 151.10, 125.86, 119.31, 115.36, 112.83, 79.58, 77.18, 69.24 (CHOSi), 67.00 (CO_2CH_2), 57.35 nArOCH$_2$), 26.07 (CMe_3), 18.51 (CMe_3), −4.48 ($SiMe_2$). MS m/e 554 (10), 249 (5), 175 (100); m/e 554.1971 (calcd for $C_{29}H_{34}O_9Si$: 554.1962).

18-[(*tert*-Butyldimethylsilyl)oxy]-1,8,16,20-tetraoxa-15,21-dioxo-[8.7]metacyclopha-3,5-diyne-12,23-diol (9.3os). To a solution of $Cu(OAc)_2·H_2O$ (25.5 g, 128 mmol) in pyridine (1.5 L) at 45 °C was added a solution of **8.3os** (13.6 g, 24.5 mmol) in pyridine (1.4 L); the solution was stirred at 45 °C for 2 h and then evaporated in vacuo. The residue was taken up in $CHCl_3$ (1.5 L), washed with 5% aqueous HCl (3 × 1.4 L), and dried (Na_2SO_4). Evaporation in vacuo gave a tan, solid foam (12.7 g), which was chromatographed (10% EtOAc/hexane) to give crude **9.3os** (7.1 g); crystallization (hexane/benzene) gave **9.3os** (4.47

g, 8.09 mmol, 33%): TLC R_f (2:1 hexane/EtOAc) 0.56; mp (hexane/benzene) 152–152.5 °C; ^{1}H NMR (270 MHz, $CDCl_3$) 10.38 (s, 2 H), 7.70 (d, J = 3.0, 2 H), 7.12 (dd, J = 9.2, 3.2, 2 H), 6.95 (d, J = 9.0, 2 H), 4.726 (AB, J = 17.7, 2 H), 4.693 (AB, J = 17.7, 2 H), 4.51 (A_2B_2X, $J_{AX} = J_{BX}$ = 5.2, 4 H), 4.32 (A_2B_2X, J = 5.2, 5.2, 1 H), 0.88 (s, 9 H), 0.14 (s, 6 H); ^{13}C NMR (50 MHz, DMSO-d_6, Ernst) 167.69, 155.53, 149.54, 126.58, 118.73, 114.30, 111.99, 75.94, 70.65, 68.03, 64.48, 57.53, 25.36, 17.49, −5.19; MS m/e 552 (1), 495 (100), 211 (8), 137 (23), 136 (15), 135 (3); m/e 552.1818 (calcd for $C_{29}H_{32}O_9Si$ 552.1806). Anal.: C, 63.12 (calcd: 63.03); H, 5.83 (5.84).

18-[(*tert*-Butyldimethylsilyl)oxy]-12,23-bis(2-propynyloxy)-1,8,16,20-tetraoxa-15,21-dioxo[8.7]metacyclopha-3,5-diyne (10.3os). To a solution of **9.3os** (219 mg, 396 μmol) in DMF (16 mL) at room temperature were added K_2CO_3 (400 mg, 2.89 mmol) and propargyl bromide (86 μL, 0.14 g, 1.1 mmol); the mixture was stirred at room temperature for 28 h and then poured into water (0.32 L) containing concentrated hydrochloric acid (0.49 mL, 5.9 mmol), extracted into Et_2O (4 × 0.25 L), and dried (Na_2SO_4). Evaporation in vacuo gave a reddish semisolid, which was chromatographed ($CHCl_3$) to give **10.3os** (218 mg, 347 μmol, 88%): TLC R_f ($CHCl_3$) 0.17; mp (hexane/benzene) 71.5–73 °C; IR (KBr) 3290, 2950, 2920, 2890, 2850, 2120, 1730, 1610, 1495, 1245, 1190, 1070, 1025; ^{1}H NMR (270 MHz, $CDCl_3$) 7.540 (ABX, J = 3.2, −0.4, 2 H), 7.119 (ABX, J = 9.1, 3.2, 2 H), 7.071 (ABX, J = 9.1, −0.4, 2 H), 4.767 (ABX, J = −13.8, 2.0, 2 H), 4.755 (AB, J = 17.1, 2 H), 4.743 (ABX, J = −13.8, 2.4, 2 H), 4.714 (AB, J = 17.1, 2 H), 4.45–4.32 (m, 5 H), 2.512 (ABX, J = 2.4, 2.0, 2 H), 0.91 (s, 9 H), 0.15 (s, 6 H); ^{13}C NMR (50 MHz, acetone-d_6) 165.58, 153.12, 152.74, 123.61, 123.01, 118.84, 116.97, 79.77, 77.31, 76.29, 71.71, 69.53, 65.67, 58.61, 57.95, 26.19, 18.64, −4.58; MS m/e 571 (12), 40 (100); m/e 571.1427 [calcd for $C_{31}H_{27}O_9Si$ = $(M - C_4H_9)^+$ 571.1416], no M^+. Anal.: C, 66.67 (calcd for $C_{35}H_{36}O_9Si$ 66.86); H, 5.83 (5.77).

***endo*- and *exo*-32-[(*tert*-Butyldimethylsilyl)oxy]-1,8,15,22,30,34-hexaoxa-29,35-dioxo[8.8.7](1,4,2)cyclopha-3,5,17,19-tetraynes (4.3osn and 4.3osx).** To a solution of $Cu(OAc)_2 \cdot H_2O$ (819 mg, 4.10 mmol) in pyridine (0.14 L) at 41 °C was added **10.3os** (1.000 g, 1.590 mmol); the solution was stirred at 41 °C for 25 min and then evaporated in vacuo. The green-black residue was taken up in $CHCl_3$ (0.14 L), washed with 5% aqueous HCl (3 × 0.14 L), and dried (Na_2SO_4); evaporation in vacuo gave a dark-brown, solid foam (1.1144 g), which was chromatographed (20% EtOAc/hexane) to give a 4:3 mixture of the **4.3os** isomers (225 mg). Chromatography ($CHCl_3$) of the 4:3 mixture gave a 1:1 mixture (159 mg), followed by a 3:1 mixture favoring the original major epimer (57 mg). Two crystallizations of the 3:1 mixture (hexane/$CHCl_3$) gave the major isomer (8 mg). The minor isomer was not obtained pure; its NMR spectrum below was obtained by computational subtraction of the spectrum of the major isomer from that of the 1:1 mixture. **Major isomer**: TLC R_f (20% EtOAc/hexane) 0.17, R_f ($CHCl_3$) 0.11; ^{1}H NMR (270 MHz, benzene-d_6) 7.74 (d, J = 3.0, 2 H), 6.80 (dd, J = 9.0, 2.9, 2 H), 6.42 (d, J = 9.1, 2 H), 4.92 (dd, J = 10.9, 4.9, 2 H; CO_2CH_2), 4.58 (m, 1 H; CHOSi), 4.400 (AB, J = 17.0, 2 H; 2-ArOCH_2), 4.34 (dd, J = 10.9, 5.8, 2 H; CO_2CH_2), 4.10 ("s", 4 H; 5-ArOCH_2), 3.918 (AB, J = 17.0, 2 H; 2-ArOCH_2), 0.98 (s, 9 H), 0.24 (s, 6 H). **Minor isomer**: TLC R_f (20% EtOAc/hexane) 0.17, R_f ($CHCl_3$) 0.18; ^{1}H NMR (270 MHz, benzene-d_6) 7.47 (d, J = 3.2, 2 H), 6.75 (dd, J = 9.0, 3.2, 2 H), 6.41 (d, J = 9.0, 2 H), 4.87 (dd, J = 10.9, 5.4, 2 H; CO_2CH_2), 4.72 (m, 1 H; CHOSi), 4.64 (dd, J = 11.0, 3.8, 2 H; CO_2CH_2), 4.35 (d, J = 17.7, 2 H; 2-ArOCH_2), 4.03 (AB, J = 17.0, 2 H; 5-ArOCH_2), 3.94 ("d", J = 17, 4 H; ArOCH_2), 0.97 (s, 9 H), 0.19 (s, 6 H). **4:3 Mixture**: MS, no M^+.

***endo*- and *exo*-32-[(*tert*-Butyldimethylsilyl)oxy]-1,8,15,22,30,34-hexaoxa-29,35-dioxo[8.8.7](1,4,2)cyclophanes (5.3osn and 5.3osx).** A suspension of **4.3os** (4:3 mixture; 7 mg, 11 μmol) and 5% Rh/Al_2O_3 (7 mg) in EtOAc (1 mL) was stirred under H_2 (1 atm) for 24 h; filtration through Celite and evaporation in vacuo gave a 4:3 mixture of the **5.3os** isomers as an oil (7.2 mg, 11 μmol, quant. within error). **Major isomer**: ^{1}H NMR (270 MHz, $CDCl_3$) 7.05 (d, J = 3.1, 2 H), 6.71 (dd, J = 9.0, 3.2, 2 H), 6.60 (d, J = 9.0, 2 H), 4.40 (m, 5 H), 3.86 (m, 8 H; ArOCH_2), 1.75 (m, 8 H), 1.56 (m, 6 H), 1.42 (m, 2 H), 0.94 (s, 9 H), 0.21 (s, 6 H). **Minor isomer**: ^{1}H NMR (270 MHz, $CDCl_3$) 7.10 (d, J = 3.1, 2 H), 6.71 (dd, J = 9.0, 3.2, 2 H), 6.60 (d, J = 9.1, 2 H), 4.40 (m, 5 H), 3.86 (m, 8 H; ArOCH_2), 1.75 (m, 8 H), 1.56 (m, 6 H), 1.42 (m, 2 H), 0.97 (s, 9 H), 0.20 (s, 6 H). **Mixture**: MS m/e 643.3241 (7), 642.3227 (10; calcd for $C_{35}H_{50}O_9Si$ 642.3224), 587.2627 (11), 586.2565 (13), 585.2571 (32), 438.1811 (5), 437.1623 (17).

Forsén–Hoffman Studies. Selective inversion-recovery experiments employed a variant of a pulse program first devised by Redfield and Gupta.[52] A selective 180° pulse was applied to one of the exchanging signals; after a "mixing time", a spectrum was taken normally (nonselective 90° pulse, then scan). The system was allowed to return to equilibrium during a relaxation delay of at least $5T_1$ (a 20-s delay sufficed); after a phase inversion,[53] the sequence was repeated. The time dependence of the signals was followed by varying the mixing time. The 180° pulse duration corresponding to each setting of the irradiation oscillator of the FX-200Q spectrometer was measured by the FID-null method.[54]

Nonselective inversion-recovery experiments employed a standard inversion-recovery sequence,[55] with the irradiation oscillator gated off throughout. This gating lets one stack selective and nonselective inversion-recovery experiments together.

Solutions of phanes in 5-mm NMR tubes were put through three freeze–pump–thaw cycles and then sealed under dry N_2 (slightly less than 1 atm). Probe temperature for Forsén–Hoffman studies was measured with a copper constantan thermocouple; this particular thermocouple is known (see below) to read ~2 °C higher than a standard Pt resistance wire.

Thermometers for Line-Shape Studies. Above room temperature, probe temperature was measured with an ethylene glycol sample.[56] The alkyl chemical shifts of simple alcohols (e.g., ethylene glycol and MeOH) are similar to the OCH_2 chemical shifts of **4.*n*** and **5.*n***; thus, such alcohols can be used only as *external* thermometers (i.e., by substitution) in studies of these phanes. For use in a capillary *within* the sample,[57] we devised a simplified version of Schneider's Yb(fod)$_3$-based low-temperature thermometer.[58]

Schneider's thermometer was first devised for ^{13}C studies; three of its components ($CFCl_3$, CS_2, TMS) are very volatile, and in our hands capillaries of the mixture were hard to seal. Thus, because $CFCl_3$ and CS_2 are not needed for ^{1}H studies, they were omitted. Acetone (6 μL, 0.08 mmol), TMS (16 μL, 0.12 mmol), and Yb(fod)$_3$ (74 mg, 70 μmol) were dissolved in acetone-d_6 (289 μL, 3.9 mmol); an aliquot of this solution was sealed in a chilled melting point capillary.

This lanthanide sample was calibrated versus methanol[56c] on the WP-270 spectrometer, and was found to obey eq 12. Here T is the Kelvin temperature, and $\delta\nu$ is the chemical shift difference (in hertz, at 270.13 MHz) between the TMS and acetone signals of the sample.

$$T = \{[(9.056 \times 10^5)/(\delta\nu)] - [(4.40 \times 10^8)/(\delta\nu)^2] - 174.0\} \pm 0.7 \quad (12)$$

The methanol and ethylene glycol samples, as well as the thermocouple used for Forsén–Hoffman experiments (see above) were calibrated versus a standard Pt resistance wire[59] as primary standard.

Acknowledgment. We thank Dr. R. A. Porter for illuminating discussions of the Forsén–Hoffman experiment, Dr. B. R. Adams for help with thermometer calibration, Dr. W. N. Bolin for the programs DNMR and DNMR1, Dr. B. J. Whitlock for helpful discussions, and D. Ridout for technical assistance. This work was supported in part, through grants to H.W.W., by the National Science Foundation.

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