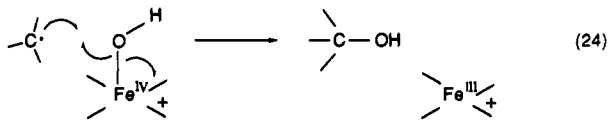
Mechanism of Oxygen Rebound. The detailed mechanism of hydroxylation of carbon-centered radicals (reaction 3) has generally been either ignored or considered to be a combination of the carbon-centered radical with a hydroxyl radical.[92] The latter mechanism implies that the iron–oxygen bond in the hydroxyferryl species must undergo thermal cleavage before hydroxylation can occur. This is, of course, improbable both on energetic grounds and because an enzyme which generated a free hydroxyl radical would not survive for long. Furthermore, the reaction of an alkyl radical with a free hydroxyl radical would be expected to yield disproportionation products, i.e., alkene and water as well as the alcohol combination product. In the case of hexamethylcyclopropane we have shown that olefin is not produced, and hence we rule out the production of a free hydroxyl radical.

The actual hydroxylation step most probably involves a bimolecular homolytic substitution[94] (S_H2) at oxygen of carbon for iron,[95] i.e., reaction 24. We cannot rule out, but see no reason



(24)

to invoke, a direct interaction between the carbon-centered radical and the iron atom to form an Fe^V species; i.e., we see no reason to invoke an intermediate with a carbon–iron bond, particularly in such a "crowded" local environment.

Finally, in all cases where there is no clear evidence for the intermediate formation of carbon-centered radicals, it must not be forgotten that an oxene insertion mechanism may be in operation.

Acknowledgment. We thank Dr. D. O. Foster for preparation of the P-450 microsomes, D. A. Lindsay for his valuable technical assistance, E. Lusztyk for a second, extremely careful examination of the products formed from the P-450-catalyzed oxidation of **1eH**, and the Association for International Cancer Research and the National Foundation for Cancer Research for partial support of this work. We also thank Prof. J. Warkentin for generously providing a sample of 3-methoxy-3,5,5-trimethyl-4-oxa-1-pyrazoline and two referees for some very useful suggestions.

Registry No. 1aH, 594-11-6; **1aOH**, 2516-33-8; **1a'**, 2154-76-9; **1bH**, 2402-06-4; **1bOH**, 21003-36-1; **1b'**, 62131-99-1; **1cH**, 930-18-7; **1cOH**, 21003-35-0; **1c'**, 62131-98-0; **1dH**, 1630-94-0; **1dOH**, 2746-14-7; **1d'**, 24389-71-7; **1eH**, 4127-47-3; **1eOH**, 133753-26-1; **1e'**, 133753-28-3; **1fH**, 2570-81-2; **1fOH**, 133753-27-2; **1f'**, 133753-29-4; **1kH**, 24518-94-3; **1lH**, 1667-00-1; **1lOH**, 1007-03-0; **1l'**, 126281-30-9; **2a'**, 2154-62-3; **2b'**, 51685-66-6; **2bOH**, 24389-75-1; **2eOH**, 19781-53-4; **2e'**, 50517-76-5; **2fOH**, 4819-92-5; **2f'**, 133753-31-8; **2lOH**, 937-58-6; **2l'**, 133753-32-9; **3bOH**, 4516-90-9; **3b'**, 52898-42-7; **3eOH**, 3329-43-9; **3e'**, 133753-30-7; **4H**, 185-94-4; **$d_2$4H**, 51794-28-6; **4OH**, 24461-57-2; **4'**, 84592-00-7; **5OH**, 14320-38-8; **5'**, 14461-09-7; cytochrome P-450, 9035-51-2; monooxygenase, 9038-14-6; 2-butyn-1-ol, 764-01-2; ethyl dimethylacetoacetate, 597-04-6; ethyl 2,2,3-trimethyl-3-butenoate, 35293-39-1; methyl 1,2,2-trimethylcyclopropanecarboxylate, 20459-94-3; 3-methoxy-3,5,5-trimethyl-4-oxa-1-pyrazoline, 77879-49-3; 4-phenyl-3-butenoic acid, 2243-53-0.

(92) For example,[93] "attack of this iron–oxo species on the substrate molecule through hydrogen abstraction followed by radical recombination to generate the alcohol product".

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Vases and Kites as Cavitands[1]

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Contribution from the Department of Chemistry and Biochemistry, University of California at Los Angeles, Los Angeles, California 90024. *Received December 3, 1990*

Abstract: The syntheses, characterizations, and substituent effects on the vase vs kite conformations of **1–17** are described. These compounds are assembled by two-step syntheses from resorcinol (or 2-substituted derivatives) and aldehydes to form octols **18–26** in high yields, followed by 4-fold bridging reactions with quinoxalines **27–29** or pyrazine **30**. In the crystal structure of **3**·2CH_2Cl_2, one CH_2Cl_2 is enclosed in the vase cavity, while a second CH_2Cl_2 is found surrounded by the four $(CH_2)_4Cl$ groups. When the 2-position of resorcinol is hydrogen, only the vase form of the cavitands exists at 25 °C or higher when quinoxaline bridged, as in **1–7**, and at all available temperatures when pyrazine bridged, as in **13**. The R and B groups of **1–7** can be varied to control solubility and cavity size without greatly affecting the vase–kite structures. When the 2-position of resorcinol is occupied by a methyl, an ethyl, or a bromine, as in **14–17**, only the kite conformation is observed at all available temperatures. When the 2-position is hydrogen and the system is quinoxaline, only the kite conformer is observed at temperatures below −50 °C. When the 2-position is CH_3, the kite conformer equilibrates with its dimer. When the 2-position is CH_3CH_2, as in **17**, the kite conformer does not form a dimer. The kite C_{2v} structures under pseudorotation and also dimerize when they contain 2-methylresorcinyl groups to give dimers of D_{2d} symmetry. In some systems, these processes could be differentiated by use of variable-temperature ^1H NMR spectra.

In an earlier paper,[2] we described the preparation and equilibration of the vase (four quinoxaline flaps axial, or aaaa conformation) and kite (four quinoxaline flaps equatorial, or eeee conformation) structures for **1**. Compound **1** was reported to form crystalline solvates that were stable to moderate heat and vacuum, which suggested the solvent molecules occupied the sizable cavity as guests of **1**. In a later paper, Vincenti, Dalcanale, Soncini, and Guglielmetti found that an analogue of **1** (R = C_6H_{13}) bound guest molecules strongly in the gas phase.[3] Our paper reports the following: (1) the syntheses of cavitands **1–17** and **31** and octols **21** and **25**; (2) the crystal structure of the vase form of **3**·2CH_2Cl_2; and (3) the results of an investigation of the effects of substituents

(1) (a) We warmly thank the National Science Foundation for Grant CHE 88-02800, which supported this work. (b) Host–Guest Complexation. 57.

(2) Moran, J. R.; Karbach, S.; Cram, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 5826–5828.

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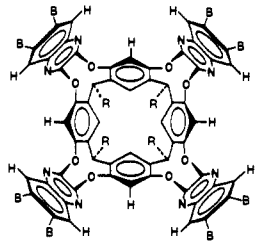
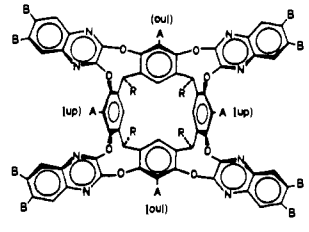
R, A, and B and of solvent on the vase vs kite vs dimer–kite structures.



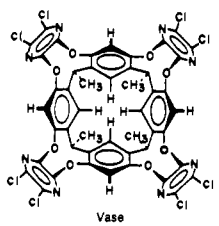
Vase, or *aaaa* conformer



Kite, or *eeee* conformer

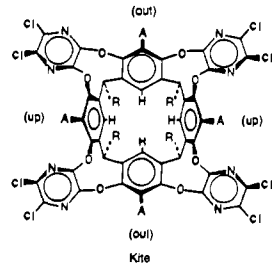
1, R = CH_3, B = H
2, R = $(CH_2)_4CH_3$, B = H
3, R = $(CH_2)_5Cl$, B = H
4, R = $(CH_2)_5I$, B = H
5, R = $CH_2CH(CH_3)_2$, B = H
6, R = $CH_2CH(CH_3)_2$, B = CH_3
7, R = CH_3, B = Br

8, R = A = CH_3, B = H
9, R = A = B = CH_3
10, R = $(CH_2)_4CH_3$, A = CH_3, B = H
11, R = $(CH_2)_5Cl$, A = CH_3, B = H
12, R = $(CH_2)_5I$, A = CH_3, B = H



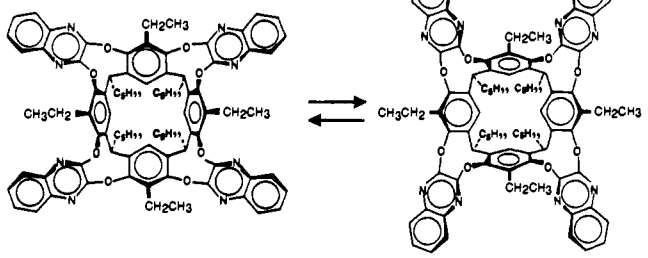
Vase

13

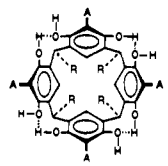


Kite

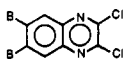
14, A = R = CH_3
15, A = Br, R = CH_3
16, A = CH_3, R = $(CH_2)_4CH_3$



17a 17b

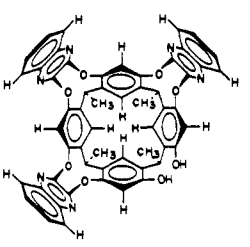


18, R = CH_3, A = H
19, R = $(CH_2)_4CH_3$, A = H
20, R = $(CH_2)_5Cl$, A = H
21, R = $(CH_2)_5Cl$, A = CH_3
22, R = $CH_2CH(CH_3)_2$, A = H
23, R = A = CH_3
24, R = CH_3, A = Br
25, R = $(CH_2)_4CH_3$, A = CH_2CH_3
26, R = $(CH_2)_4CH_3$, A = CH_3



27, B = H
28, B = CH_3
29, B = Br

30



31

Results and Discussion

Syntheses. In a previous paper, we reported the syntheses and characterizations of octols **18–20**, **22**, **23**, and **26**[4] by condensation of 4 mol of the appropriate aldehyde with 4 mol of resorcinol (or 2-methylresorcinol)[4] catalyzed by acid. Octol **18** was also brominated to give **24**.[2] Only the diastereomer drawn was isolated. The yields ranged from 60–95%, and the dominant conformer in each case is the one formulated.[4] In the present work, octol **21** was similarly prepared from 2-methylresorcinol and 6-chlorohexanal (65%) and **25** from 2-ethylresorcinol[5] and hexanal (87%).

The octols were converted to cavitands by treatment with 2,3-dichloro-1,4-diazines **27–30**, whose chlorines are good leaving groups for nucleophilic aromatic substitution reactions. Of these bridging aromatic reagents, only **27** was commercially available. Quinoxalines **28** and **29** were prepared as before,[6] and pyrazine **30**[7a] was prepared as well. In general, reactivity decreases for each chlorine displaced, while alkoxy and phenoxy groups substituted for Cl in **30** appear to direct substitution ortho.[7b,c] The strong fluorescence of the cavitands facilitated isolation of the desired products.

The bridging of the four sets of hydrogen-bonded hydroxyls by the reaction of octols with 4 mol of diazines produces four new nine-membered rings (eight bonds broken and made). The reactions were best conducted in dry, aprotic, dipolar solvents with K_2CO_3, $CsHCO_3$, or Cs_2CO_3 as bases. The highest yields were observed when $CsHCO_3$ or Cs_2CO_3 were used in $(CH_3)_2SO$ or $(CH_3)_2NCOCH_3$, which provides another example of Kellogg's "cesium effect".[8] For example, the reaction **18** + 4 **27** → **1** went in 34% yield with KOH–$(CH_3)_2NCHO$, but in 83% with Cs_2CO_3–$(CH_3)_2SO$. The synthesis of **1**, when conducted in dry ($CH_3)_2SO$–$CsHCO_3$ with 3 equiv of **27** for 2 days at 25 °C, gave a mixture of **1** (30%) and **31** (40%), which was easily separated. Thus, it appears that the first three bridges are formed faster than the fourth, probably for steric reasons. This observation provides an easy means of synthesizing cavitands with two different kinds of bridges[3] in the same molecule.

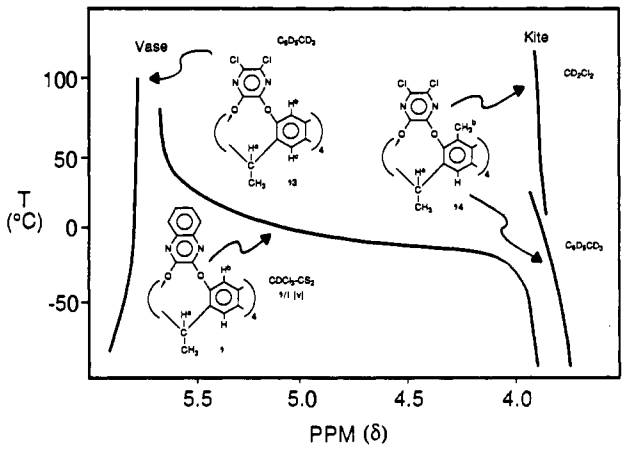


Figure 1. Effect of temperature changes in the chemical shifts of H^a protons (500-MHz ^1H NMR spectra) of **1**, **13**, and **14** in various solvents.

The cesium effect seems to apply generally to the other systems as well. In the syntheses of **2** (37%), **3** (40%), **10** (30%), **11** (30%), **16** (16%), and **17** (32%), K_2CO_3–$(CH_3)_2NCHO$ was employed, whereas in those of **8** (77%) and **9** (68%) ($CH_3)_2SO$–Cs_2CO_3) was used. In the preparation of **13** (75%), **14** (50%), and **15** (1%), $(CH_3)_2NCOCH_3$–Cs_2CO_3 served as solvent–base. The low yield in the last reaction is attributed to the steric effect of the bromines ortho to the hydroxyls. Tetraiodides **4** and **12** were obtained (85% each) by heating the respective chlorides **3** and **11** with NaI in refluxing 2-butanone.

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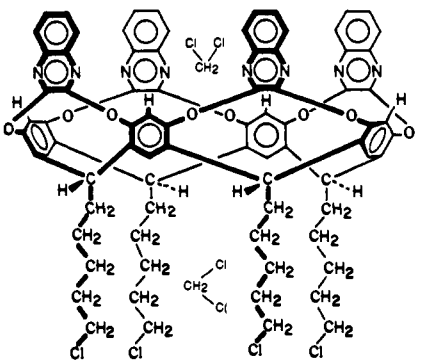
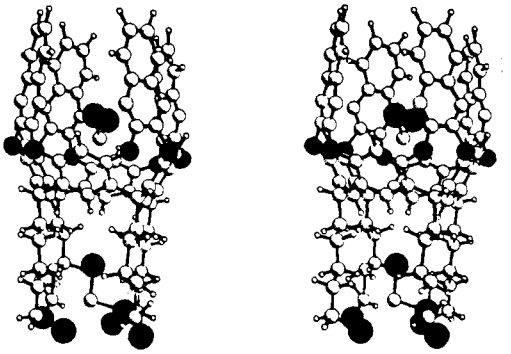
(8) Piepers, D.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1978**, 383–384.



$3{\cdot}2CH_2Cl_2$



Stereoview 32 of $3{\cdot}2CH_2Cl_2$, with O's and Cl's darkened.

Crystal Structure of $3{\cdot}2CH_2Cl_2$. The crystal structure of $3{\cdot}2CH_2Cl_2$ was determined and refined to give an *R* value of 0.13. Stereoview **32** shows that the compound is in a vase conformation whose upper and lower cavities each contain one molecule of CH_2Cl_2. The host possesses approximate C_{4v} symmetry, with the guests' CH_2 groups lying close to the C_4 axis. The bottom part of the upper cavity is lined with the four resorcinyl units sloping inward at the bottom. The middle and upper parts of the cavity are lined with the four quinoxaline units arranged as if their faces were the sides of a box. However, these planes are tilted an average of 6° inward at their tops so that their attached 6- and 9-hydrogen atoms essentially touch one another. The eight ether oxygens are arranged with their unshared electron pairs facing outward.

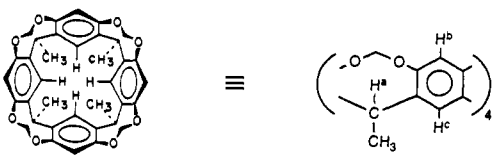
The crystal structure of the host corresponds closely to that observed in CPK molecular models of the host, the upper cavity of which is rigid and apparently strain-free. In models, the cavity is much larger than the CH_2Cl_2 guest. A molecular model of [2.2]paracyclophane (inner faces shaved) shows it just about occupies the interior of the cavity of a model of **1**.

The two cavities of crystal structure **32** closely resemble that of the analogue of **1**, in which A = $(CH_2)_5CH_3$ and B = H, which we will call **33** (Dalcanale et al.).[9] This compound, when crystallized from acetone, gave $33{\cdot}3(CH_3)_2CO$ (not formulated), whose upper cavity contained two acetone molecules (one fully enclosed, and one slightly enclosed) and whose lower cavity contained 1 mol of acetone fully enclosed by the four hexyl groups. The close similarities between $32{\cdot}2CH_2Cl_2$ and $33{\cdot}3(CH_3)_2CO$ on the one hand and CPK models of the two complexes on the other add to the growing number of examples in which predictions based on CPK models about the structures of highly preorganized hosts have been verified by crystal structure determination.[10]

Vase and Kite Forms of Cavitands 1, 5, 6, and 13. The ^1H NMR spectra of cavitands taken in different solvents and at different temperatures proved useful in identifying the structures of the vase vs the kite conformers, of the monomer vs dimer forms of the kite conformers, the degeneracy of the kite monomers, the substituent effects on the stabilities of all forms, and the activation free energies for their interconversions. Fortunately, the substituent effects, both steric and electronic, were large enough in certain cases to allow the spectra of single species to be taken and related to crystal structures and CPK models of the same species. Crystal structures have been determined for the vase form of $3{\cdot}2CH_2Cl_2$ and of $33{\cdot}3(CH_3)_2CO$,[9] the monomer form of kite **17**,[11] the dimer–kite form of **10**,[11a] and of the dimer–kite form of **16**.[11b]

Cavitand **1** in 1:1 $CDCl_3$–CS_2 (v/v) appears to exist only in the vase form at temperatures of 45 °C and above and only in the kite form at temperatures below −62 °C. In the 500-MHz ^1H NMR spectrum of **1** from 45–70 °C, all protons exhibit sharp signals consistent with C_{4v} symmetry. The H^a signal changed dramatically and continuously as the temperature was lowered from 45 to −62 °C, but changed little from −62 to −72 °C (Figure 1). The signals at intermediate temperatures are broad and show coalescence at about −5 °C. The well-defined methine quartet (H^a) moves from δ 5.67 at 45 °C to δ 3.92 at −62 °C ($\Delta\delta$ = 1.75) and broadens. The $\Delta G^{\ddagger}$ for the conformational changes involved is about 11.6 kcal mol^{-1}.[12] The two benzene proton singlets at 8.04 (H^b) and 7.27 (H^c) at 45 °C shift *much less* when the temperature is lowered to 62 °C, and each of these divides into two singlets found at δ 7.38 and 7.28 and at 7.21 and 6.41, respectively. The protons of the quinoxaline ring at 45 °C exhibit a symmetrical AA′BB′ splitting pattern, which at −62 °C divided into two doublets and two triplets interpreted as an ABCD spectrum. Thus, the spectrum from −50° to −62 °C is consistent with a structure of C_{2v} symmetry.[13]

These spectra, coupled with the crystal structure of **3** (see **32**) and CPK model examinations of the vase and kite forms of **1**, correlate to provide the following interpretations: (1) The 45–70 °C spectrum is explained by **1** assuming the vase (aaaa) conformation, which has C_{4v} symmetry. In this structure, the H^a methine protons are relatively distant from the faces of the quinoxaline ring and at δ 5.67 are at lower field than the methines of the rigid C_{4v} model compound **34** (4.96).[14] (2) The −62 to



34

−72 °C spectrum is explained by **1** having the kite (eeee) conformation (C_{2v} symmetry). The $\Delta\delta$ = 1.75 upfield shift of the methine H^a signal from δ 5.67 to 3.92 as the temperature is lowered correlates with the methine protons moving into the shielding cone of the quinoxaline rings as the latter occupy the e positions. (3) Although all protons exhibit shifts between 45 and −62 °C, their signals do not change above 45 and below −62 °C. The spectra above 45 °C show no detectable (<5%) C_{2v} conformer, and spectra below −62 °C show no detectable (<2%) C_{4v} conformer. Thus, the conversion of the aaaa vase to the eeee kite conformer is favored by >3 kcal mol^{-1} as the temperature is lowered.

Molecular model examinations provide a definite prediction that the vase conformers of **1**–**7** and **13** are less strained than the

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(12) (a) Sandström, J. *Dynamic NMR Spectroscopy*; Academic Press, London, 1982; p 96, eq 7.4b. (b) We reported in ref 2, $\Delta G^{\ddagger} \sim 10$ kcal mol^{-1}.
(13) We warmly thank Drs. Martin Feigel and Thorleif Anthonsen for helping us in this interpretation and Dr. Frank Anet for critical and useful discussions.
(14) Cram, D. J.; Karbach, S.; Kim, H.-E.; Knobler, C. B.; Maverick, E. F.; Ericson, J. L.; Helgeson, R. C. *J. Am. Chem. Soc.* **1988**, *110*, 2229–2237.

kite conformer. In the latter, the four H^a protons are so forced into the faces of the four aryl rings that the CPK models of the kite are difficult to make and preserve. Although both conformers possess equal molecular surfaces, the more *extended surfaces* of the kite form must contact and orient more solvent molecules than the more *confined* surfaces of the vase conformer. These contacts are expected to be enthalpy stabilizing but entropy destabilizing for both systems. In the conversion of vase to kite, more solvent molecules are collected and oriented. At low enough temperatures, the kite form is the more stable conformer in solution because its more favorable enthalpy of solvation overrides the sum of the unfavorable $T\Delta S$ of solvation and the greater strain energy of this conformer. As the temperature increases, the unfavorable $T\Delta S$ cancels more of the favorable enthalpy until the free energy of solvation no longer overrides the greater internal strain of the kite form. Above this temperature, the vase form dominates, since its stability in solution does not depend as much as that of the kite form on its free energy of solvation. To our knowledge, this synthetic system is unique in providing such very large surface conformations that present such widely differing opportunities for solvation.

Figure 1 also contains the ^1H NMR methine (H^a) signals of 5,6-dichloropyrazine **13** in $C_6D_5CD_3$, whose δ changes little with temperature from 90 to −65 °C. They remained between δ 5.8 and 5.9 over the 155° range. This signal for H^a is close to that for **1** at δ 5.67 at 45 °C in its vase form. We conclude that unlike quinoxaline **1**, pyrazine **13** remains in its vase form over the whole temperature range due to this conformation's intrinsically greater stability and the smaller solvating surface of the four pyrazines vs those of the four quinoxalines. The chemical shifts of protons H^b and H^c of **13** likewise undergo only small changes[15a] and do not split at low temperatures as do those systems that exhibit C_{2v} C_{2v}' behavior (see the following text).

Figure 1 likewise records the ^1H NMR methine H^a signals' δ changes with temperature from −90 to 115 °C of 5,6-dichloropyrazine system **14** containing four 2-methylresorcinyl moieties. To maintain solubility, $C_6D_5CD_3$ was used as solvent up to about +30 °C and CD_2Cl_2 from about 10 to 115 °C. The δ of H^a varied only from about 3.4–3.9 over the whole temperature–solvent range, with no splitting observed for H^a. However, in $C_6D_5CD_3$, the 2-$CH_3{}^b$ signal splits into two singlets at about 70 °C.[15b] The relatively invariant chemical shift of H^a and the splitting of H^b indicate that **14** exists in the C_{2v} kite structure, whose two identical forms are pseudorotating rapidly on the ^1H NMR time scale above 70 °C. The insensitivity of H^a to this pseudorotation is compatible with the fact that CPK models of the C_{2v} conformer indicate a similar immediate environment for all four of these methine protons.

Compound **5** differs from **1** only in the sense that **5** contains four $CH_2CH(CH_3)_2$ "feet" in place of the four methyl feet of **1**. As hoped, **5** proved more soluble than **1**. Spectral plots of the δ values of protons a–c in $CDCl_3/CS_2$ (1:1, v/v with changes in temperature from about 40 to −75 °C provided a $\Delta\delta$ value for H^a of ~1.8, which again provided an indicator system for the vase vs the kite structure.[15c] Above 5 °C, the vase is observed, and below −70 °C, the kite is stable with the coalescence point at about −30 °C. The conversion from vase to kite for **5** occurs at a lower temperature than for **1**. The $\Delta G^{\ddagger}$ for the conformational change in **5** is about 10.5 kcal mol^{-1}, close to that of 11.6 for **1**. The change in the feet from methyl in **1** to isobutyl in **5** has only the minor effect of lowering the temperatures above which the vase is stable and below which the kite is stable. The H^b and H^c as well as the CH_2 and CH_3 protons of the isobutyl feet are split in the kite form of **5** below ~−45 °C. In the C_{2v} form, these protons are diastereotopic.[15c] Similar patterns were observed in the spectrum of **6** in $CDCl_3$, which provided $\Delta\delta$ ~1.9 for H^a in passing from +30 to −40 °C, a $\Delta G^{\ddagger}$ of ~10.4 kcal mol^{-1} (T_c ~−30 °C), and splitting of H^b, H^c, and the other diastereotopic protons of the C_{2v} form of **6** below ~−50 °C.[15d] Thus, altering substituents B and R of these quinoxaline systems had only minor effects on the kite–vase equilibrium.

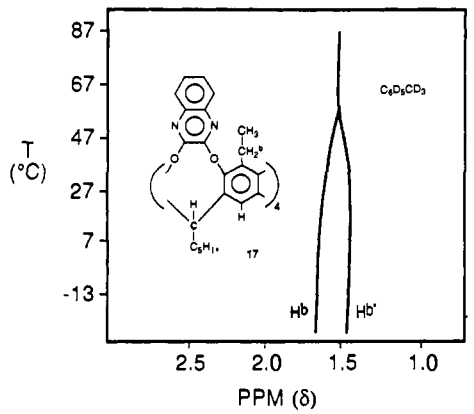

Figure 2. Effect of temperature changes on the chemical shifts in the 360-MHz ^1H NMR spectra of **17** in $C_6D_5CD_3$.

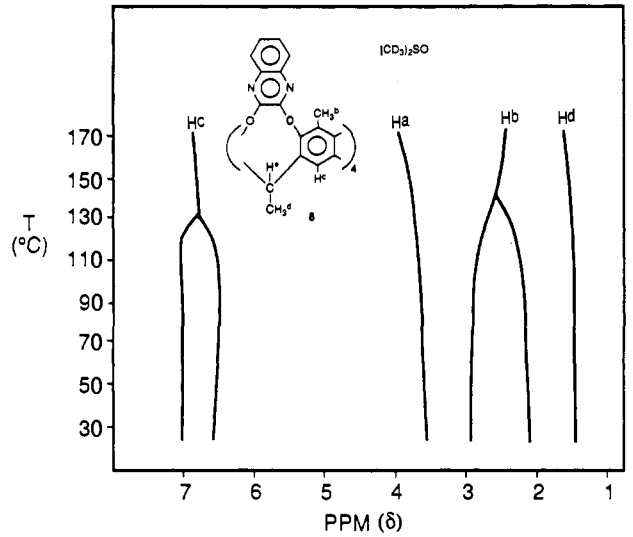

Figure 3. Effect of temperature changes on the chemical shifts in the 500-MHz ^1H NMR spectra of **8** in $(CD_3)_2SO$.

Effect of Alkyl Substituents in the 2-Resorcinyl Positions of the Cavitands. As indicated by the crystal structures of monomer **17** and the dimer **10**, substitution of a methyl or an ethyl in the 2-resorcinyl positions of the quinoxaline cavitands forced the molecule to avoid the vase and exist in only the kite conformation. An examination of CPK models of the vase form of **8–12** and **14–17** shows that such substituents protrude into the space occupied by the unshared electron pairs on the eight nitrogens of the four pyrazine or quinoxaline groups. These steric interactions are absent in models of the kite forms. The 500-MHz ^1H NMR spectra of **8–12** and **14–17** are consonant with these compounds existing only in their kite conformation. Their H^a proton signals moved little, and did not split with changes of pyrazine **14**[15b] to quinoxaline **8** in $C_6D_5CD_3$,[15e] with changes in temperature,[15b,e-g] changes in solvent,[15e,f] (Figure 3), changes in substituent X,[15g] or the change from 2-methylresorcinyl (**8**)[15f] to 2-ethylresorcinyl (**17**; Experimental Section). The maximum changes for the H^a signal with all the above structural and solvent changes is 3.8 ± 0.3, or $\Delta\delta$ = 0.6. This contrasts with the $\Delta\delta$ = 1.75–1.90 observed for H^a changes for **1**, **5**, and **6** with changes in temperature used as an indicator for vase vs kite conformation.

Compound **17** is particularly useful for observing the degenerate $C_{2v} \rightleftarrows C_{2v}'$ pseudorotation, since its 2-resorcinyl ethyl group inhibits both vase and dimer–kite formation.[11] Its $CH_3CH_2{}^b$ proton signal in its ^1H NMR spectrum provides the best indicator for this phenomenon. Figure 2 is a plot of δ for H^b of **17** in $C_6D_5CD_3$ (360 MHz spectrum). The T_c occurred at 42 °C with $\Delta\nu$ = 75.6 Hz to give a $\Delta G^{\ddagger}$ ~15.3 kcal mol^{-1} at 42 °C. A similar plot in

(15) See supplementary material: (a) Figure 1; (b) Figure 2; (c) Figure 3; (d) Figure 4; (e) Figure 5; (f) Figure 6; (g) Figure 7; (h) Figure 8; (i) Figure 9.

$CDCl_2CDCl_2$ gave a T_c at 100 °C with $\Delta\nu$ = 126 Hz to give $\Delta G^{\ddagger}$ ~17.8 kcal mol^{-1} at 100 °C.[15h] These C_{2v} equilibrations must occur by fast conformational reorganizations in which partial vaselike structures are involved whose formation requires desolvation. Apparently, desolvation is more costly in $CDCl_2CDCl_2$ than in $C_6D_5CD_3$.

Figure 3 is a plot of the chemical shifts in the 500-MHz spectra for the various protons of **8** as the temperature is changed, with $(CH_3)_2SO$ as solvent. Similar plots were made with $C_6D_5CD_3$[15e] and $CDCl_3$[15f] as solvents. In all three solvents, and at temperatures that ranged from −10 to 170 °C, the protons of the methyl feet (H^d) and the methine (H^a) did not change their multiplicity. In $CDCl_3$ from −10 to +97 °C,[15f] the arylmethyl protons (H^b) and the only resorcinyl aryl proton (H^c) produced two signals over the whole temperature range, which are probably associated with the two kinds of each proton in the C_{2v} structure, the equilibration $C_{2v} \rightleftarrows C_{2v}'$ (pseudorotation) being slow on the ^{1}H NMR time scale (as with **17** below 87 °C in $CDCl_2CDCl_2$ and below 40 °C in $C_6D_5CD_3$). In $C_6D_5CD_3$,[15e] **8** again produced two signals for H^b and H^c from 0 to 80 °C for the former and 0 to 100 °C for the latter. The coalescence temperature for H^c, which produces the more symmetrical fork-shaped plot, occurs at about 100 °C, which provides $\Delta\delta$ = 0.5 and $\Delta G^{\ddagger}$ ~17–18 kcal mol^{-1} for the activation free energy for interconversion of the two identical C_{2v} forms. In $(CD_3)_2SO$ (Figure 3), each of the two signals for H^b and H^c exist from 30 to about 120 °C, and both coalesce at about 130 °C to provide $\Delta\delta$ = 0.6 and $\Delta G^{\ddagger}$ ~18–19 kcal mol^{-1} for interconversion of the two identical C_{2v} forms. Desolvation of $(CD_3)_2SO$ appears a little more energy-rich than that of $C_6D_5CD_3$ in going from C_{2v} to C_{4v}-like transition states for the equilibrations.

In the temperature-dependent 500-MHz ^{1}H NMR spectrum of the octachloropyrazine **14** in $C_6D_5CD_3$, the $CH_3{}^b$ signal splits as the temperature is lowered, the coalescence temperature for the $C_{2v} \rightleftarrows C_{2v}'$ process being about 70 °C.[15b] At temperatures below 25 °C, the signal to noise ratio of **14** deteriorates. However, **16**, which differs from **14** only in the sense of possessing pentyl instead of methyl feet, possesses greater solubility. This property allowed lower temperatures to be reached. The coalescence temperature for H^b in the 360-MHz ^{1}H NMR spectrum of **16** in $C_6D_5CD_3$ also occurs at about 70 °C.[15i] A kite–monomer ⇄ kite–dimer equilibration was identified by changes in molecular weight and in the intensity of $CH_3{}^b$ signals with changes in concentration of **16** in $CDCl_3$.[16] At −18 °C, the monomer provided a δ 2.19 signal for the two "up methyls" and at δ 2.43 for the two "out methyls", whereas these respective signals moved to δ 1.69 and 2.63 in the dimer.[16] In $C_6D_5CD_3$ at −18 °C, the same four $CH_3{}^b$ signals form a similar pattern. The monomer gave a δ 2.44 signal for the two "up methyls" and δ 2.51 for the two "out methyls", whereas these respective signals moved to δ 2.22 and 2.95 in the dimer.[15i] The ^{1}H NMR spectrum of tetrabromide **15** clearly indicated it has the kite structure. The small supply of it and the absence of $CH_3{}^b$ protons limited its study. A thorough discussion of the effects of structure and solvent on the thermodynamic parameters associated with monomer–dimer equilibria in a large variety of systems is reserved for a later paper.

The thorough and critical discussion of the evolution and present state of the phenol-based calixarenes and cavitand fields is found in Gutsche's beautifully illustrated monograph.[17] The conformational equilibria discussed there provide interesting comparisons with our kite–vase equilibria. This publication also provides a broad context for the results and discussions of our paper.[17]

Correlation of Structure with Solubility. The low solubility encountered with the vases hampered their study. For example, for **13**, 0.2 mg dissolved in 1 mL of C_6H_6 and 0.3 mg in 1 mL of $C_6H_5CH_3$ were the best solvents for this compound. Cavitands that prefer the kite structure, such as **14** and **16**, were much more soluble. Generally, the chloropyrazines tend to be more soluble in organic media than the quinoxalines. The substitutions of alkyl groups for the methyl feet tend to increase solubility for both the vase and kite conformers. Substitution of two methyls or two bromines on the 6,7-positions of the quinoxaline decrease the solubility markedly.

(16) Bryant, J. A.; Ericson, J. L.; Cram, D. J. *J. Am. Chem. Soc.* **1990**, *112*, 1255.

(17) Gutsche, C. D. *Calixarenes, Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: London, 1989; pp 1–204.

Summary

These studies report simple two-step syntheses of 17 new cavitands of C_{4v} vase symmetry, of C_{2v} symmetry, of rapidly pseudorotating degenerate C_{2v} symmetry, or of dimerized cavitands of D_{2d} symmetry. These structures were differentiated by crystal structure determinations and by variable-temperature ^{1}H NMR studies. The cavitands made from resorcinol aldehydes and 2,3,5,6-tetrachloropyrazine existed only in their vase forms. Those made from resorcinol, aldehydes, and 2,3-dichloroquinoxaline existed in their vase forms at 5 °C or higher, and in their kite forms at low temperatures. Those made from 2-methylresorcinol and aldehydes and from either the pyrazine or quinoxalines existed only in their kite forms, which underwent pseudorotation ($C_{2v} \rightleftarrows C_{2v}'$) at variable temperatures and dimerized to give material of D_{2d} symmetry. The one made from 2-ethylresorcinol, hexanal, and 2,3-dichloroquinoxaline existed only in its kite monomeric form. Aldehydes such as hexanal or 3-methylbutanal gave much more soluble cavitands than those made from ethanal.

Experimental Section

General. Tetrahydrofuran (THF) and diethyl ether were distilled under N_2 from sodium benzophenone ketyl. Dichloromethane was distilled twice from CaH_2 if dryness was required or if used in size-exclusion chromatography. Benzene was distilled from lithium aluminum hydride (LAH). Dimethylformamide (DMF), dimethylacetamide (DMA), and vacuum-distilled dimethylsulfoxide (DMSO) were allowed to stand over 3-Å molecular sieves (activated at 360 °C for 5 h or more) for at least a week. Infrared spectra were taken on a Perkin-Elmer 297 spectrometer, and proton NMR spectra were taken on Bruker WP-200, AM-360, or AM-500 spectrometers referenced to $(CH_3)_4Si$ as an internal standard at 0.00 ppm. Gravity column chromatography employed E. Merck silica gel 60 (particle size 0.063–0.200 mm), and flash chromatography involved silica gel 60 (particle size 0.040–0.063 mm). Thin-layer and preparative thin-layer chromatography (TLC) involved precoated plates (E. Merck F_{254}, thickness 0.2 mm or 2 mm, respectively) or RP-18 plates (E. Merck F_{254}, thickness 0.025 mm or 2 mm, respectively). Melting points were measured on a Mel Temp melting point apparatus. The mass spectra were recorded on an AEI Model MS-9 double-focusing spectrometer interfaced by Kratos Co. to a Data General Nova 3 or by a ZAB SE for FAB spectra with *m*-nitrobenzyl alcohol (NOBA) as matrix. All glassware used under dry conditions was dried by heating it under vacuum, followed by flushing and cooling it under dry argon. All analyses were performed after drying under a diffusion pump (at least 100 °C (10^{-5} Torr) 24 h).

Pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13-(27),15,17,19(26),21,23-dodecaen-4,6,10,12,16,18,22,24-octol, 2,8,14,20-Tetrapentyl-5,11,17,23-tetraethyl-, Stereoisomer (25). To a solution of 2,6-dihydroxyacetophenone (2.3 g, 15 mmol) in 75 mL of CF_3CO_2H was added Et_3SiH (5.3 mL, 33 mmol) dropwise. The solution was stirred for 3 h. Water was added, and the product was extracted into ether. Crystallization from CH_2Cl_2/C_5H_{12} yielded 44% of 2-ethylresorcinol.[5] Hexanal (0.79 mL, 6.6 mmol) and 2-ethylresorcinol (0.91 g, 6.6 mmol) were dissolved in 10 mL of ethanol. Water (10 mL) and concentrated HCl (4 mL) were added, and the mixture was stirred for 48 h at 80 °C. A dark brown oil settled out after 1 h and persisted throughout the reaction. After being cooled to room temperature, the oil solidified into a dark brown glass. This material was recrystallized from CH_3CN/H_2O to provide **25** (87%): ^{1}H NMR (360 MHz, $(CD_3)_2SO$) δ 0.83–0.94 overlapping peaks (m, 24 H, CH_2CH_3 and pentyl CH_3), 1.19–1.34 overlapping peaks (m, 32 H, $-CH_2CH_2CH_2-$ and CH_2CH_3), 2.21 (m, 8 H, CH_2, α to methine), 4.20 (t, 4 H, methine), 7.25 (s, 4 H, ArH), 8.59 (s, 8 H, OH); MS (FABS, NOBA) *m/e* 880 (M^+, 4.3), 809 ($M^+ - C_5H_{11}$, 37.3). Anal. Calcd for $C_{56}H_{80}O_8$: C, 76.33; H, 9.15. Found: C, 75.97; H, 9.35.

Pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1-(25),3,5,7(28),9,11,13-(27),15,17,19(26),21,23-dodecaen-4,6,10,12,16,18,22,24-octol, 2,8,14,20-Tetrakis(5-chloropentyl)-5,11,17,23-tetramethyl-, Stereoisomer (21). The procedure for synthesizing octol **26**[4] was applied to 6-chlorohexanal (3.2 g, 23 mmol) and 2-methylresorcinol (2.9 g, 23 mmol) to provide **21** in 60% yield. A sample was recrystallized from CH_3CN/H_2O for elemental analysis: ^{1}H NMR (360 MHz, $(CD_3)_2SO$) δ 1.21 (m, 8 H, CH_2), 1.48 (m, 8 H, CH_2), 1.70 (m, 8 H, CH_2), 1.94 (s, 12 H, CH_3),

2.23 (m, 8 H, CH_2), 3.60 (t, 8 H, CH_2Cl), 4.20 (t, 4 H, methine), 7.26 (s, 4 H, ArH), 8.67 (s, 8 H, OH); MS (FABS, NOBA) Cl isotope pattern centered at m/e 963 ($M + H^+$, 43%), Cl isotope pattern centered at 857 ($M^+ - C_5H_{10}Cl$, 85%). Anal. Calcd (dried at 130 °C (10^{-5} Torr, 3 h) for $C_{52}H_{68}Cl_4O_8 \cdot H_2O$: C, 62.43; H, 6.85. Found: C, 62.25; H, 6.97.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino[6′5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 9,11,13,15-Tetramethyl-, Stereoisomer (1). To a solution, stirred under argon, of 0.68 g (1.25 mmol) of octol **18**,[4] 1.26 g (19.1 mmol) of 86% aqueous KOH, and 50 mL of DMF was added 1.0 g (5.0 mmol) of quinoxaline **27**. The suspension was stirred at 25 °C for 1.25 h and then at 80 °C for 2.75 h. It was then cooled and shaken gently (to avoid an emulsion) with 200 mL of 1 N NaOH and 100 mL of CH_2Cl_2. The organic layer was washed with brine and dried. Toluene (13 mL) was added, the solution was evaporated to 10 mL, and the product that precipitated was filtered to give 0.45 g (34%) of **1**, which was recrystallized from DMF and dried (110 °C, 7 days (0.1 mm), and then 200 °C, 6 h (5×10^{-5} Torr), to give **1**·$(CH_3)_2NCHO$ as a white powder: mp > 360 °C; m/e 1048 (M^+). Anal. Calcd for **1**·$(CH_3)_2NCHO$: C, 71.71; H, 4.22. Found: C, 71.68; H, 4.09. Recrystallization of **1**·$(CH_3)_2NCHO$ from $CHCl_3$ followed by drying (100 °C, 24 h (0.1 mm)) produced **1**·*n*-$CHCl_3$ as a white powder: mp > 360 °C; m/e 1048 (M^+). Anal. Calcd for **1**·1.4$CHCl_3$, $C_{65.4}H_{41.4}N_8O_8Cl_{4.2}$: C, 64.58; H, 3.43; N, 9.46; Cl, 12.24. Found: C, 64.49; H, 3.37; N, 9.38; Cl, 12.01.

The 500-MHz ^1H NMR spectra were determined in $CDCl_3/CS_2$ (1:1, v/v) at 45 °C, δ 1.84 (d, 12 H, J = 7.4 Hz, CH_3), 5.67 (q, 4 H, J = 7.4 Hz, C*H*), 7.27 (s, 4Ar*H*, H^c by NOE), 7.63 (center of AA′BB′ m, 16 H, quinoxalinyl-*H*), 8.04 (s, 4Ar*H*, H^b by NOE); at −62 °C, δ 1.64 (b s, 12 H, CH_3), 3.92 (b q, 4*H*, C*H*), 6.41 (s, 2Ar*H*, H^c), 7.21 (s, 2Ar*H*, H^c), 7.28 (s, 2Ar*H*, H^b), 7.38 (s, 2ArH, H^b), 7.63–7.74 (nonsymmetrical m, 8 H, quinoxalinyl-*H*), 7.87–7.94 (nonsymmetrical m, 8 H, quinoxalinyl-*H*).

Application of Method C (see the following text) to this synthesis of **1** increased the yield to 83%.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′10′][1,4]benzodioxonino[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 9,11,13,15-Tetrapentyl-, Stereoisomer (2). Method A. Octol **19**[4] (2 g, 2.6 mmol) and quinoxaline **27** (2.2 g, 11 mmol) were dissolved in 200 mL of dry DMF. Potassium carbonate (4.5 g, 33 mmol) was added, and the mixture was stirred at 25 °C for 12 h, at 40 °C for 24 h, at 60 °C for 24 h, and at 80 °C for 48 h. The mixture was cooled to 25 °C and poured into water, and the mixture was filtered. The residue was chromatographed on silica gel with CH_2Cl_2 as the mobile phase. The product was recrystallized from CH_2Cl_2/EtOAc to give **2** as a white crystalline solid (37%): ^1H NMR (200 MHz, $CDCl_3$) δ 0.95 (t, 12 H, alkyl CH_3), 1.35–1.44 (m, 24 H, $-CH_2CH_2CH_2-$), 2.26 (m, 8 H, CH_2, α to methine), 5.55 (t, 4 H, methine J = 8.2 Hz), 7.21 (s, 4 H, ArH); AA′BB′ pattern centered at δ 7.47 and 7.79 (16 H, quinoxalinyl-H)), 8.15 (s, 4 H, ArH); MS (FABS, NOBA) m/e 1273 ($M + H^+$, 100.0). Anal. Calcd (dried at 150 °C (10^{-5} Torr), 12 h) for $C_{80}H_{72}N_8O_8 \cdot 0.25CH_2Cl_2$: C, 74.96; H, 5.68. Found: C, 74.88; H, 5.83.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 9,11,13,15-Tetrakis(5-chloropentyl)-, Stereoisomer (3). Method A was applied to octol **20** (6 g, 6.6 mmol), 2,3-dichloroquinoxaline (**27**; 5.6 g, 28 mmol), 11 g of K_2CO_3 (80 mmol), and 600 mL of DMF to give after crystallization (CH_2Cl_2/EtOAc) 3.72 g (40%) of **3** as a white solid: ^1H NMR (360 MHz, $CDCl_3$) δ 1.46 (m, 8 H, CH_2), 1.65 (m, 8 H, CH_2), 1.85 (m, 8 H, CH_2), 2.30 (m, 8 H, CH_2), 3.60 (t, 8 H, CH_2Cl), 5.60 (t, 4 H, CH), 7.20 (s, 4 H, ArH), 7.47 and 7.80 (AA′BB′ pattern, 16 H, quinoxaline-ArH), 8.17 (s, 4 H, ArH); MS (FABS, NOBA) m/e 1411 ($M + H^+$, 100); R_f (silica gel, CH_2Cl_2) 0.15. Anal. Calcd (dried for 12 h at 150 °C (10^{-5} Torr)) for $C_{80}H_{68}Cl_4N_8O_8$: C, 68.09; H, 4.86. Found: C, 67.92; H, 4.98.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 9,11,13,15-Tetrakis(3-Iodopentyl)-, Stereoisomer (4). Method B. Tetrachloride **3** (0.12 g, 0.000 085 mmol) was dissolved in 10 mL of 2-butanone. Sodium iodide was added to saturation, and the mixture was refluxed for 12 h. After the mixture was cooled to 25 °C, water was added to the mixture and the layers were separated. This provided tetraiodide **4** as a white crystalline solid, 0.128 g (85%): ^1H NMR (200 MHz, $CDCl_3$) δ 1.48 (m, 8 H, CH_2), 1.60 (m, 8 H, CH_2), 1.90 (m, 8 H, CH_2), 2.31 (m, 8 H, CH_2), 3.26 (t, 8 H, CH_2I), 5.60 (t, 4 H, CH), 7.20 (s, 4 H, ArH), 7.47 and 7.79 (AA′BB′ pattern, 16 H, quinoxaline ArH), 8.17 (s, 4 H, ArH); MS (FABS, NOBA) m/e 1777 ($M + H^+$, 100). Anal. Calcd (dried at 140 °C (10^{-3} Torr) for 12 h) for $C_{80}H_{68}I_4N_8O_8$: C, 54.07; H, 3.86. Found: C, 54.31; H, 3.89.

7,18:8,16-Dimethyl-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]-benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6″,5″:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 9,11,13,15-Tetrakis(2-methylpropyl)-, Stereoisomer (5). Method C. To a dry solution stirred under argon of octol **22**[4] (0.556 g, 0.780 mmol) and 0.621 g (3.12 mmol) of 2,3-dichloroquinoxaline in 30 mL of dry DMSO was added 1.12 g (3.43 mmol) of Cs_2CO_3. The suspension was stirred for 3 days at 25 °C. The precipitate formed was filtered, washed to neutrality with water, and dried on a diffusion pump to give material that was crystallized from $CHCl_3$ to give 0.883 g (93%) of **5**: mp > 360 °C; MS (FABS, NOBA) m/e 1217 ($M^+ + H$, 100). Anal. Calcd for $C_{76}H_{64}N_8O_8 \cdot 1.4CHCl_3$: C, 67.14; H, 4.76; N, 8.09. Found: C, 66.74; H, 5.09; N, 7.91.

The ^1H NMR spectrum (500 MHz) of the C_{4v} form at 40 °C ($CDCl_3/CS_2$ (1:1, v/v)) δ 1.09 (d, 24 H, $(CH_3)_2CH$), 1.58 (m, 4 H, $(CH_3)_2CH$), 2.13 (t, 8 H, CH_2), 5.71 (*t*, 4 H, CH^a), 7.13 (s, 4 H, ArH^c), 7.41 (center of AA′BB′ m, 8 H, quinoxaline-6,7-ArH), 7.72 (center of AA′BB′ m, 8 H, quinoxaline-5,8-ArH), 8.07 (s, 4 H, ArH^b); of the C_{2v} form at −80 °C δ 0.74 (b s, 12 H, $(CH_3)_2CH$), 0.98 (b s, 12 H $(CH_3)_2CH$), 1.42 (b s, 4 H, $(CH_3)_2CH$), 1.62 (b t, 4 H, CH_2), 2.16 (b t, 4 H, CH_2), 3.78 (b t, 4 H, CH^a), 6.31 (b s, 2 H, ArH^c), 7.13 (b s, 2 H, ArH^c), 7.28 (s, 2 H, ArH^b, 7.39 (s, 2 H, ArH^b), 7.64 (t, 4 H, quinoxaline-6,7-ArH), 7.73 (t, 4 H, quinoxaline-6,7-ArH), 7.88 (d, 4 H, quinoxaline-5,8-ArH), 7.92 (d, 4 H, quinoxaline-5,8-ArH).

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 2,3,21,22,30,31,39,40-Octamethyl-9,11,13,15-tetrakis(2-methylpropyl)-, Stereoisomer (6). Application of Method C to 0.458 g (0.642 mmol) of octol **22**,[4] 0.583 g (2.57 mmol) of quinoxaline **28**, 35 mL of DMSO, and 0.920 g (2.82 mmol) of Cs_2CO_3 gave after 3 days at 50 °C 0.790 g (92%) of **6**, crystallized from $CHCl_3$: MS (FABS, NOBA) m/e 1329 ($M^+ + H$, 100); ^1H NMR (500 MHz, $CDCl_3$), C_{4v} form (47 °C) δ 1.06 (d, 24 H, $(CH_3)_2CH$), 1.60 (m, 4 H, $(CH_3)_2CH$), 2.15 (t, 8 H, CH_2), 2.32 (s, 24 H, $ArCH_3$), 5.77 (t, 4 H, H^a), 7.22 (s, 4 H, H^c), 7.55 (s, 8 H, quinoxaline-ArH), 8.13 (s, 4 H, H^b); ($CDCl_3/CS_2$ (1:1, v/v)), C_{2v} form (−91 °C) δ 0.69 (b s, 12 H, $(CH_3)_2CH$), 0.95 (b s, 12 H, $(CH_3)_2CH$), 1.36 (b s, 4 H, $(CH_3)_2CH$), 1.55 (b t, 4 H, CH_2), 2.12 (b t, 4 H, CH_2), 2.44 (d, 24 H, $ArCH_3$), 3.73 (t, 4 H, H^a), 6.25 (b s, 2 H, H^c), 7.08 (b s, 2 H, H^c), 7.21 (s, 2 H, H^b), 7.21 (s, 2 H, H^b), 7.34 (s, 2 H, H^b), 7.61 (d, 8 H, quinoxaline-ArH). Anal. Calcd for $C_{84}H_{80}N_8O_8 \cdot CHCl_3$: C, 70.46; H, 5.63; N, 7.73; Cl, 7.34. Found: C, 70.06; H, 5.67; N, 8.00; Cl, 7.35.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 2,3,21,22,30,31,39,40-Octabromo-9,11,13,15-tetramethyl-, Stereoisomer (7). Application of Method C to 0.175 g (0.322 mmol) of octol **18**,[4] 0.460 g (1.29 mmol) of dibromoquinoxaline (**29**), 14 mL of dry DMSO, and 0.462 g (1.41 mmol) of Cs_2CO_3 gave after 1 day at 30 °C 0.433 g (80%) of **7** crystallized from DMSO: mp > 360 °C; MS (FABS, NOBA), no molecular ion detected; ^1H NMR (500 MHz, $CDCl_3$ at 30 °C) δ 1.73 (d, 12 H, CH_3), 4.75 (q, 4 H, H^a), 7.01 (s, 4 H, H^c), 7.57 (s, 4 H, H^b), 8.17 (s, 8 H, quinoxaline-ArH). Anal. Calcd for $C_{64}H_{32}Br_8N_8O_8 \cdot (CH_3)_2SO$: C, 45.08: H, 2.18; N, 6.37; Br, 36.35. Found: C, 45.06; H, 2.15; N, 6.26; Br, 36.15.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 9,11,13,15,26,35,44,47-Octamethyl-, Stereoisomer (8). Application of Method C to 0.300 g (0.500 mmol) of octol **23**,[4] 0.398 g (2.00 mmol) of quinoxaline **27**, 32 mL of dry DMSO, and 0.684 g (2.1 mmol) of Cs_2CO_3 gave after 2 days at 30 °C 0.423 g (77%) of **8** crystallized from $CHCl_3$: mp > 360 °C; MS (FABS, NOBA) m/e 1105 ($M^+ + 1$, 100); ^1H NMR (500 MHz, $C_6D_5CD_3$) pseudorotating form, 110 °C δ 1.33 (d, 12 H, CH_3CH, J = 6.9 Hz), 2.74 (s, 12 H, $ArCH_3^b$), 4.03 (q, 4 H, H^a, J = 6.9 Hz), 6.55 (b s, 4 H, H^c), 7.24 (center of AA′BB′ m, 8H, quinoxaline-6.7-ArH), 7.76 (center of AA′BB′ m, 8 H, quinoxaline-5,8-ArH); C_{2v} form, 23 °C 1.11 (d, 12 H, CH_3CH), 2.68 (s, 6 H, $ArCH_3^b$), 3.43 (b s, 6 H, $ArCH_3^b$), 3.86 (b q, 4 H, CH_3CH^a), 6.21 (s, 2 H, H^c), 6.60 (b s, 2 H, H^c), 7.12 (t, 4 H, quinoxaline-6,7-ArH), 7.28 (t, 4 H, quinoxaline-6,7-ArH), 7.33 (b s, 4 H, quinoxaline-5,8-ArH), 7.94 (d, 4 H, quinoxaline-5,8-ArH);

($(CD_3)_2SO$) pseudorotating form, +170 °C δ 1.66 (d, 12 H, CH_3CH), 2.50 (b s, 12 H, $ArCH_3^b$), 4.02 (q, 4 H, CH_3CH^a), 6.90 (b s, 4 H, H^c), 7.70 (center of AA′BB′ m, 8 H, quinoxaline-6,7-ArH), 7.85 (center of AA′BB′ m, 8 H, quinoxaline-5,8-ArH): C_{2v} form, +23 °C δ 1.48 (d, 12 H, CH_3CH), 2.12 (s, 6 H, $ArCH_3^b$), 2.97 (s, 6 H, $ArCH_3^b$), 3.59 (q, 4 H, CH_3CH), 6.60 (s, 2 H, H^c), 7.03 (s, 2 H, H^c), 7.05 (d, 4 H, quinoxaline-5,8-ArH), 7.51 (t, 4 H, quinoxaline-6,7-ArH), 7.61 (d, 4 H, quinoxaline-5,8-ArH), 7.71 (t, 4 H, quinoxaline-6,7-ArH). Anal. Calcd for $C_{68}H_{48}N_8O_8$: C, 73.90; H, 4.38; N, 10.14. Found: C, 73.77; H, 4.52; N, 9.97.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 2,3,9,10,13,15,21,22,26,30,31,35,39,40,44,47-Hexadecylmethyl-, Stereoisomer (9). Application of Method C to 0.263 g (0.438 mmol) of octol **23**,[4] 0.398 g (1.75 mmol) of quinoxaline **28**, 35 mL of dry DMSO, and 0.599 g (1.84 mmol) of Cs_2CO_3 stirred at 30 °C for 3 days gave 0.361 g (68%) of **9** crystallized from $CHCl_3$: mp > 360 °C; MS (FABS, NOBA) *m/e* 1217 (M^+ + H, 100); ^1H NMR (500 MHz, $CDCl_3$) C_{2v} form at −60 °C: δ 1.37 (b s, 12 H, CH_3CH), 2.09 (s, 6 H, $ArCH_3^b$), 2.37 (s, 12 H quinoxaline-$ArCH_3$), 2.55 (s, 12 H, quinoxaline-$ArCH_3$), 3.05 (s, 6 H, $ArCH_3^b$), 3.72 (b q, 4 H, CH_3CH), 6.11 (s, 2 H, H^c), 6.71 (s, 4 H, quinoxaline-ArH), 6.85 (s, 2 H, H^c), 7.44 (s, 4 H, quinoxaline-ArH). Anal. Calcd for $C_{76}H_{64}N_8O_8$: C, 74.98; H, 5.30; N, 9.20. Found: C, 74.49; H, 5.15; N, 8.86.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 26,35,44,47-Tetramethyl-9,11,13,15-tetrapentyl-, Stereoisomer (10). Application of Method A to octol **26** (0.99 g, 1.2 mmol), quinoxaline **27** (0.98 g, 4.9 mmol), 100 mL of dry DMF, and 1.3 g of K_2CO_3 (7.6 mmol) gave after stirring for 12 h at 25 °C and at 40 °C (24 h) 0.48 g (30%) of **10** after recrystallization from hot acetone: MS (FABS, NOBA) *m/e* 1330 (M + H^+, 100); ^1H NMR (360 MHz, $CDCl_3$, 30 °C) δ 0.68 (t, 12 H, alkyl-CH_3), 1.08 (m, 24 H, $-CH_2CH_2CH_2-$), 1.78 and 1.89 (overlapping m, 8 H, CH_2, α to methine), 2.24 (s, 6 H, $ArCH_3^b$), 3.15 (s, 6 H, $ArCH_3^b$), 3.53 (m, 4 H, H^a), 6.18 (s, 2 H, H^c), 6.87 (s, 2 H, H^c), 7.15 (d, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.43 (t, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.64 (t, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.79 (d, 4 H, quinoxaline-ArH, *J* = 8 Hz); dimer (500 MHz, −13 °C, $CDCl_3$) δ 0.68 (t, 12 H, alkyl-CH_3), 1.06 (m, 24 H, $-CH_2CH_2CH_2-$), 1.91 (m, CH_2, α to methine), 2.23 (s, 6 H, $ArCH_3^b$), 3.16 (s, 6 H, $ArCH_3^b$), 3.52 (m, methine), 6.17 (s, 2 H, H^c), 6.87 (s, 2 H, H^c), 7.16 (d, 4 H, quinoxaline-ArH), 7.46 (t, 4 H, quinoxaline-ArH), 7.67 (t, 4 H, quinoxaline ArH), 7.80 (d, 4 H, quinoxaline-ArH); monomer (500 MHz, −13 °C, $CDCl_3$) δ 2.52 (s, 6 H, $ArCH_3^b$), 2.66 (s, 6 H, $ArCH_3^b$), 3.76 (m, 4 H, H^a). The other resonances of monomer and dimer overlap. Anal. Calcd (dried at 150 °C at 150 °C (10^{-5} Torr), 3 h) for $C_{84}H_{80}N_8O_8$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.77; H, 6.14; N, 8.25.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 26,35,44,47-Tetramethyl-9,11,13,15-tetrakis(5-chloropentyl)-, Stereoisomer (11). Application of Method A to octol **21** (0.68 g, 0.71 mmol), quinoxaline **27** (0.59 g, 2.98 mmol). K_2CO_3 (1.2 g, 8.6 mmol), and 100 mL of dry DMF after stirring at 25 °C for 12 h and at 40 °C for 24 h gave, after chromatography on alumina (30% C_5H_{12} in CH_2Cl_2 as mobile phase), 0.31 g (30%) of **11**: MS (FABS, NOBA) *m/e* 1468 (M^+ + H, 100); ^1H NMR (360 MHz, $CDCl_3$, 30 °C), 0.88 (t, 12 H, alkyl-CH_3), 1.12–1.95, overlapping peaks (m, 32 H, $-CH_2CH_2CH_2CH_2-$), 2.25 (s, 6 H, $ArCH_3^b$), 3.15 (s, 6 H, $ArCH_3^b$), 3.33 (m, 8 H, CH_2Cl), 3.55 (m, 4 H, H^a), 6.18 (s, 2 H, H^c), 6.85 (s, 2 H, H^c), 7.16 (d, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.45 (t, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.66 (t, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.78 (d, 4 H, quinoxaline-ArH, *J* = 8 Hz). Anal. Calcd (dried at 150 °C (10^{-5} Torr), 12 h) for $C_{84}H_{76}Cl_4N_8O_8$: C, 68.76; H, 5.22. Found: C. 68.85; H, 5.31.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′,3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 26,35,44,47-Tetramethyl-9,11,13,15-tetrakis(5-iodopentyl)-, Stereoisomer (12). Application of Method B to 0.20 g (0.12 mmol) of **11** and excess NaI (2-butanone at reflux) gave 0.19 g (85%) of **12** after crystallization from acetone/hexanes: MS (FABS, NOBA), isotope pattern centered at *m/e* 1834 (M + H, 100). ^1H NMR (360 MHz, $CDCl_3$, 30 °C) δ 1.14 (m, 24 H, $-CH_2CH_2CH_2-$), 1.81 and 1.95 (m, 8 H, CH_2, α to methine), 2.25 (s, 6 H, $ArCH_3^b$), 2.99 (m, 8 H, CH_2I), 3.15 (s, 6 H, $ArCH_3^b$), 3.55 (m, 4 H, H^a), 6.17 (s, 2 H, H^c), 6.85 (s, 2 H, H^c), 7.16 (d, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.45 (t, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.66 (t, 4 H, quinoxaline-ArH, *J* = 8 Hz), 7.78 (d, 4 H, quinoxaline-ArH, *J* = 8 Hz). Anal. Calcd (dried at 180 °C (10^{-5} Torr), 6 h) for $C_{84}H_{80}I_4N_8O_8 \cdot (CH_3)_2CO$: C, 55.25; H, 4.37. Found: C, 55.73; H, 4.27.

7,17:8,16-Dimetheno-9*H*,11*H*,13*H*,15*H*-quinoxalino[2″,3″:2′3′]-[1,4]benzodioxonino[10′,9′:5,6]quinoxalino[2″,3″:2′3′]quinoxalino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]quinoxaline, 26,35,44,47-Tetraethyl-9,11,13,15-tetrapentyl-, Stereoisomer (17). Octol **25** (0.461 g, 0.52 mmol) and quinoxaline **27** were dissolved in 50 mL of dry DMF. Potassium carbonate (0.5 g, 3.73 mmol) was added, and the mixture was stirred at 40 °C for 12 h, at 60 °C for 12 h, and at 80 °C for 6 h. The mixture was cooled to 30 °C, poured into 100 mL of water and filtered. The residue was chromatographed on silica gel with CH_2Cl_2 as the mobile phase. The product was recrystallized from CH_2Cl_2/EtOAc to give 0.115 g (16%) of **17**: MS (FABS, NOBA) *m/e* 1385 (M^+ + 1, 100). ^1H NMR (200 MHz, $CDCl_3$, 30 °C) δ 0.78 (t, 12 H, alkyl-CH_3), 1.27 (m, 36 H, $-CH_2CH_2CH_2-$ and CH_2CH_3), 1.99 (m, 8 H, CH_2 α to methine), 2.86 (q, 4 H, $CH_2^bCH_3$), 3.22 (q, 4 H, $CH_2^bCH_3$), 3.75 (t, 4 H, H^a), 6.26 (s, 2 H, H^c), 7.08 (s, 2 H, H^c), 7.63 (m, 8 H, quinoxaline-ArH), 7.96 (m, 8 H, quinoxaline-ArH). Anal. Calcd (dried at 150 °C (10^{-5} Torr), 12 h) for $C_{84}H_{80}N_8O_8$: C, 76.28; H, 6.40. Found: C, 75.90; H, 6.58.

27,37:28,36-Dimetheno-29*H*,31*H*,33*H*,35*H*-pyrazino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]pyrazino[2″,3″:2′,3′]pyrazino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6″,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]pyrazine, 2,3,9,10,16,17,23,24-Octachloro-29,31,33,35-tetramethyl-, Stereoisomer (13). Method D. To a stirred, dry mixture held at 56 °C of 0.166 g (0.762 mmol) of pyrazine **30**[7] in 100 mL of DMA and 0.439 g (1.35 mmol) of Cs_2CO_3 was added via syringe (30 min) a solution of 0.083 g (0.152 mmol) of octol **18**[4] in 5 mL of dry DMA. The mixture was stirred 14 h at 56 °C and cooled to 25 °C, and the solvent was evaporated in vacuo. The residue was collected and washed with water and CH_2Cl_2 to give 0.128 g (75%) of crude **1**. Recrystallization of the material once from toluene and once from benzene gave **1**, dried at 178 °C (2 × 1^{-6} Torr) for 14 h, R_f 0.35 (70% benzene, 30% CS_2, v) on TLC: mp > 275 °C; MS (70 eV, 330 °C) *m/e* 1124 ± 4 cluster (M^+ + 1, 100). Anal. Calcd. (after drying at 178 °C (10^{-6} Torr) for 14 h) for $C_{48}H_{24}N_8O_8Cl_8$: C, 51.29; H, 2.15; N, 9.97. Found: C, 51.32; H, 2.27; N, 9.91. For a sample obtained from $C_6D_5CD_3$ crystallization dried at 100 °C for 24 h (10^{-6} Torr): ^1H NMR (200 MHz, $C_6D_5CD_3$, 30 °C) δ 1.47 (d, 12 H, *J* = 7.6 Hz, CH_3CH), 5.78 (q, 4 H, *J* = 7.6 Hz, CH_3CH^a), 7.28 (s, 4 H, H^c), 7.84 (s, 4 H, H^b). Anal. Calcd for $C_{48}H_{24}N_8O_8Cl_8 \cdot C_6D_5CD_3$: C, 53.95; D, 3.24; N, 9.15. Found: C, 53.93; D, 3.24; N, 9.58.

27,37:28,36-Dimetheno-29*H*,31*H*,33*H*,35*H*-pyrazino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]pyrazino[2″,3″:2′,3′]pyrazino-[2‴,3‴:2‴,3‴[1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]pyrazine, 2,3,9,10,16,17,23,24-Octachloro-6,13,20,29,31,33,35,39-octamethyl-, Stereoisomer (14). Application of Method D to 0.122 g (0.203 mmol) of octol 23,[4] 0.199 g, (0.913 mmol) of pyrazine **30**,[7] a total of 15 mL of dry DMA, and 0.276 g (0.847 mmol) of Cs_2CO_3 gave (after 3 days at 30 °C and 50 °C for 1 day) 0.120 g (60%) of **15**: mp > 360 °C; R_f 0.35 (80% CH_2Cl_2/20% C_6H_{14}, v, silica gel); MS (70 eV, 330 °C) *m/e* 1180 ± 4 (M^+ cluster, 100). Anal. Calcd for $C_{48}H_{24}N_8O_8Cl_8$: C, 52.91; H, 2.73; N, 9.49. Found: C, 52.64; H, 2.88; N, 9.27.

27,37:28,36-Dimetheno-29*H*,31*H*,33*H*,35*H*-pyrazino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9:5,6]pyrazino[2″,3″:2′,3′]pyrazino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]pyrazine, 6,13,20,39-Tetrabromo-2,3,9,10,16,17,23,24-octachloro-29,31,33,35-tetramethyl-, Stereoisomer (15). Application of Method D to 0.492 g (0.572 mmol) of octol **24**,[2] 0.504 g (2.31 mmol) of pyrazine **30**, 0.382 g (1.17 mmol) of Cs_2CO_3, and 50 mL of dry DMA stirred 25–50 °C for 3 days, (then 0.408 g (1.25 mmol) of additional Cs_2CO_3 was added, and the mixture was stirred an additional 4 days at 50 °C) gave material that after chromatography (CH_2Cl_2 on alumina) and crystallization (CH_2Cl_2) gave 0.010 g (1.2%) of **15**: R_f 0.5 (CH_2Cl_2 silica gel), mp > 360 °C; MS (70 eV, > 350 °C) *m/e* 1437 ± 4 (M^+, 100); ^1H NMR (500 MHz, CD_2Cl_2) δ 1.68 (d, 12 H, *J* = 6.8 Hz, CH_3CH), 4.07 (q, 4 H, *J* = 6.8 Hz, CH_3CH), 6.29 (s, 2 H, H^c), 7.27 (s, 2 H, H^c). Anal. Calcd for $C_{48}H_{20}N_8O_8Br_4Cl_8$: C, 40.04; H, 1.40. Found: C, 39.75; H, 1.39.

27,37:28,36-Dimetheno-29*H*,31*H*,33*H*,35*H*-pyrazino[2″,3″:2′,3′]-[1,4]benzodioxonino[10′,9′:5,6]pyrazino[2″,3″:2′,3′]pyrazino-[2‴,3‴:2‴,3‴][1,4]dioxonino[6‴,5‴:9′,10′][1,4]benzodioxonino-[6′,5′:9,10][1,4]benzodioxonino[2,3-*b*]pyrazine, 2,3,9,10,16,17,23,24-Octachloro-6,13,20,39-tetramethyl-29,31,33,35-tetrapentyl-, Stereoisomer (16). Octol **26**, (1.9 g, 2.3 mmol) pyrazine **30** (2.1 g, 9.4 mmol), 150

mL of dry DMF, and 4.8 g (34.5 mmol) of K_2CO_3 were stirred under argon at 25 °C for 24 h. The solvent was evaporated in vacuo, and the residue was partitioned between CH_2Cl_2 and water. The CH_2Cl_2 phase was concentrated and filtered through a pad of silica gel. The product was recrystallized from hot acetone to give 1.03 g (32%) of **16**: MS (FABS, NOBA) *m/e* 1404 (M^+, 100). ^1H NMR (360 MHz, 22 °C, $CDCl_3$) δ 0.83 (t, 12 H, alkyl-CH_3), 1.22 (m, 24 H, $-CH_2CH_2CH_2-$), 1.95 (m, 14 H, $ArCH_3$ and CH_2, α to methine), 2.58 (s, 6 H, $ArCH_3^b$), 3.65 (m, 4 H, H^a), 6.04 (s, 2 H, H^c), 6.96 (s, 2 H, H^c); dimer (360 MHz, −18 °C, $CDCl_3$) δ 1.69 (s, 6 H, $ArCH_3^b$), 1.92 (m, 8 H, CH_2, α to methine), 2.62 (s, 6 H, $ArCH_3^b$), 3.60 (m, 4 H, H^a), 6.02 (s, 2 H, H^c), 6.93 (s, 2 H, H^c); monomer (360 MHz, −18 °C, $CDCl_3$) δ 2.01 (m, 8 H, CH_2, α to methine), 2.19 (s, 6 H, $ArCH_3^b$), 2.48 (s, 6 H, $ArCH_3^b$), 3.70 (m, 4 H, H^a), 6.05 (s, 2 H, H^c), 7.03 (s, 2 H, H^c). $-CH_2CH_2CH_2-$ resonances of monomer and dimer overlap. Anal. Calcd (dried at 150 °C (10^{-5} Torr), 12 h) for $C_{68}H_{64}Cl_8N_8O_8$: C, 58.13; H, 4.59. Found: C, 57.86; H, 4.71.

9,17-Methano-11*H*,13*H*,15*H*-bisbenzo[5′,6′]quinoxalino-[2″,3″:2′,3′][1,4]benzodioxonino[10′,9′:5,6:9″,10″:8,9][1,4]dioxonino[2,3-*b*]quinoxaline-8,18-diol, 11,13,15,40-Tetramethyl-, Stereoisomer (31). To a dry solution (stirred under argon) of octol **18**[4] (0.544 g, 1 mmol) and quinoxaline **27** (0.597 g, 3 mmol) in dry DMSO (30 mL) was added $CsHCO_3$ (1.166 g, 6 mmol). After 2 days of stirring at 25 °C, all the quinoxaline was consumed to produce a mixture of **31** and **1**. The precipitate that formed was filtered, and the filtrate was evaporated in vacuo to give a dark solid. Cavitand **1** was present only in the precipitate, whereas **31** was present in both phases, which were combined and chromatographed on silica gel with CH_2Cl_2/EtOAc (9:1, v/v) as the mobile phase to give 0.367 g (40%) of **31**: mp > 360 °C; MS (FAB, NOBA), 923 (M^+ + 1, 100). ^1H NMR (500 MHz $CDCl_3$) δ 1.74 (d, 3 H, $H^{d''}$), 1.80 (d, 6 H, H^d), 1.84 (d, 3 H, $H^{d'}$), 4.53 (q, 1 H, H_a''), 5.53 (m, 4 H, $H^c + H^{b'}$), 7.06 (s, 2 H, $H^{c'}$), 7.21 (s, 2 H, H^a), 7.35 (s, 2 H, $H^{b'}$), 7.37 (b s, 2 H, OH), 7.52 (m, 4 H, AA′BB′ m + t, $H^h + H^i$ or H^f), 7.59 (t or d, 2 H, H^i, or H^j), 7.74 (d of d, 2 H, H^f, or H^e), 7.84 (m center of AA′BB′, 2 H, H^g), 7.94 (d of d, 2 H, H^e or H^f), 8.11 (s, 2 H, H^b); (500 MHz, $(CD_3)_2SO$ δ 1.75 (d, 3 H, $H^{d''}$), 1.86 (d, 6 H, H^d), 1.94 (d, 3 H, $H^{d'}$), 4.46 (q, H, $H^{a''}$), 5.54 (q, 2 H, H^a), 5.68 (q, H, $H^{a'}$), 6.88 (s, 2 H, $H^{a''}$), 7.59 (t, 2 H, H^i or H^j), 7.69 (m, 6 H, H^e or $H^f + H^i$ or Hj + H^c), 7.75 (m center of AA′BB′ 2 H, H^h), 7.97 (d, 2 H, H^e or H^f), 7.98 (s, 2 H, $H^{b'}$), 8.04 (m center of AA′BB′, 2 H, H^g), 8.08 (s, 2 H, H^b), 9.86 (b s, 2 H, OH). Anal. Calcd for $C_{56}H_{38}N_6O_8 \cdot 2H_2O$: C, 70.14; H, 4.41. Found: C, 69.87; H, 4.68.

Crystal Structure Data on 3·2CH_2Cl_2. Compound 3·2CH_2Cl_2 crystallizes from CH_2Cl_2 as colorless, multifaceted crystals in the tetragonal system $P4_12_12$. Unit cell dimensions are as follows: a = 13.009 (2) Å, c = 47.221 (7) Å, V = 7991 Å^3, Z = 4 (the monomer has a 2-fold axis). The crystal was examined on a modified Syntex $P\bar{1}$ diffractometer, CuK_α radiation, at 295 K. The structure was determined by direct methods. Refinement of 238 parameters (2433 reflections with $I > 3_\sigma(I)$) has an agreement value, r, currently at 0.13. One solvent molecule is in the upper cavity and one is in the lower cavity. A possible third (unlocated) solvent is interstitial.

NMR Experiments. Analytical NMR samples were prepared in volumetric glassware. The purity of the NMR solvents were as follows: $CDCl_3$ minimum isotopic purity 99.96%; $C_6D_5CD_3$ minimum isotopic purity 99.96%; CD_2Cl_2 minimum isotopic purity 99.96%; $(CD_3)_2CO$ minimum isotopic purity 99.96%; CD_3OD minimum isotopic purity 99.96%; CD_3NO_2 99.1 atom%; THF-d_8 99.5 atom %; 1,1,2,2-$C_2D_4Cl_4$ 99.6 atom %. The temperature of the probe was calibrated using the difference in chemical shifts between the two peaks of MeOH as a standard. For spectra obtained at other than ambient temperature, the sample was equilibrated for at least 10 min at the temperature of the experiment before data were acquired. Typical relaxation delays were 1 s. NMR samples were immersed in an ice bath at the temperature of the experiment for 30 min prior to any data collection to ensure no precipitation occurred.

Supplementary Material Available: References 15a–i in the text apply to supplementary materials. Figures 1–9, which are plots of temperature against proton chemical shifts in the 500-MHz ^1H NMR spectra of compounds **13** (in $C_6D_5CD_3$), **14** (in $C_6D_5CD_3$), **5** (in $CDCl_3/CS_2$, 1/1 v/v), **6** (in $CDCl_3$), **8** (in $CD_3C_6D_5$), **8** (in $CDCl_3$), **9** (in $CDCl_3$), **17** (in $CDCl_2CDCl_2$), and **16** (in $C_6D_5CD_3$), respectively (9 pages). Ordering information is given on any current masthead page.

Endocyclic Cleavage in the Alkaline Hydrolysis of the Cyclic Phosphonate Methyl Propylphostonate: Dianionic Intermediates and Barriers to Pseudorotation

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Abstract: The hydrolysis of methyl propylphostonate in basic solutions leads exclusively to products resulting from cleavage of the internal ester linkage. On the basis of the mechanism of reaction deduced from the study of cyclic phosphate triesters, it is expected that the addition of hydroxide generates a five-coordinate phosphorus intermediate that reacts with a second hydroxide to give a dianion. Stereoelectronic properties of this dianionic intermediate prevent pseudorotation and lead to the exclusive formation of the endocyclic cleavage product, methyl (γ-hydroxypropyl)phosphonate. These results are consistent with a semiempirical formulation developed by Holmes. Ab initio calculations on related gas-phase systems, aimed at explaining the complex catalytic pathway of ribonuclease, do not suggest the consistent patterns observed in the present study and related experimental observations. Thus, the effects of solvation on reactivity patterns of cyclic phosphate esters are very significant.

The mechanisms of nucleophilic substitution reactions of phosphate esters and related derivatives have been developed in terms of early empirical and theoretical generalizations of Westheimer,[1] Muetterties,[2,3] and Berry.[4] The reactivity patterns of cyclic phosphates have been rationalized in terms of these generalizations,[5] and this information has been used to understand the mechanisms of reactions of complex systems, including the hydrolysis of ribonucleic acids.[6] Holmes extended the basis for

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