Host–Guest Complexation. 48. Octol Building Blocks for Cavitands and Carcerands

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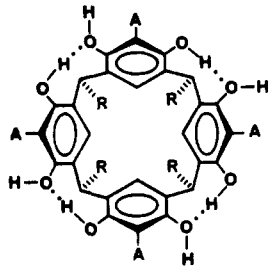
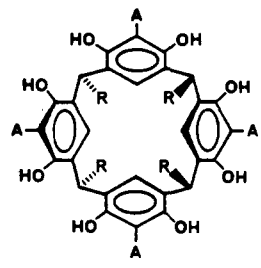
The scope of limitations of the syntheses of octols 1 by the fourfold condensations of various aldehydes with resorcinol and 2-substituted resorcinols are reported. At most, two stereoisomers of 1 were detected, one with C_{4v} and the other with C_{2v} symmetry (^{1}H NMR). With aliphatic aldehydes, only 1 (C_{4v}) product was isolated in yields ranging from 45 to 92%. With 4-substituted benzaldehydes (R = (4-XC_6H_4)), the yields and isomer ratios varied with the character of the X substituent. With X = CH_3 and CH_3CH_2, the C_{4v}/C_{2v} ratios were >32 and the yields were 73–96%. With X = H or Br, C_{4v}/C_{2v} values ranged from 1.0 to >30 as a function of reaction time. With X = OCH_3 or X = C_6H_5, the C_{4v}/C_{2v} ratio was 1.5 and the yields were 93 and 99%, respectively. When X = NC, $(CH_3)_3C$, HO_2C, and AcNH, the C_{4v}/C_{2v} ratios (yields) were <0.03 (52%), 0.03 (28%), 0.4 (79%), and 0.5 (52%), respectively. With X = O_2N, OHC, or $CH_3(CH_2)_3C{\equiv}C$, no cyclic tetramer was detected. Condensation of 2-methylresorcinol with CH_3CHO gave 79% of the C_{4v} isomer, but with C_6H_5CHO, C_{4v}/C_{2v} = <0.03 (78%). No cyclic tetramer was obtained with either aldehyde and 2-nitroresorcinol or 2-bromoresorcinol. An indeterminate mixture of isomers was produced with CH_3CHO and 2-carboxyresorcinol. Crystal structures of two octols 1 (C_{4v}) were determined (A = H, R = CH_3 and A = H, R = $CH_3(CH_2)_3$) as solvates, and these octols exhibited bowl-shaped conformations. These compounds serve as important starting materials for the syntheses of cavitands and carcerands.

Previous work in this series demonstrated that the four proximate oxygen atom pairs of the C_{4v} isomer of 1[2] could be bridged with four methylene, dimethylene, or trimethylene groups,[3] four dialkylsilylidene groups,[4] or four 2,3-disubstituted-1,4-diazanaphthalene groups.[5] These



1 (C_{4v})



1 (C_{2v})

bridges constrained the conformational mobility of the aryl groups originally present in 1 to produce bowl-shaped cavitands whose width and depth were partially determined by the molecular dimensions of the bridges. The low solubility of many of these cavitands limited their usefulness as starting materials for making organic catalysts or carcerands.[6]

The current study was initiated for the following reasons. (1) The limited solubility of the cavitands and carcerands appears to be associated with their rigidity. It seemed probable that conformationally mobile hydrocarbon chains as R in 1 would increase the solubility of the derived cavitands and carcerands. (2) Examination of molecular models (CPK) in which four phenyls are R in 1 leads to "duplex" cavitands in which a box-like cavity defined by the four phenyls is fused to a bowl-like cavity defined by the four resorcinol units. A crystal structure of a simple cavitand prepared from 1 (C_{4v}) in which R = C_6H_5 and A = H confirmed this expectation, a benzene molecular guest being partially embraced by each kind of cavity. The compound possessed very poor solubility properties, a limitation potentially modifiable by conformationally mobile groups substituted in the 4-positions of the phenyls.[7] (3) The ease of syntheses of the octols by the fourfold condensation of aldehydes and resorcinols[2] provides a potential source of molecular frameworks for preparation of polyfunctional compounds whose convergent heteroatoms can act cooperatively to bind and catalyze.

In the current work, we addressed the question of which groups substituted on the resorcinol and aldehyde moieties tolerate the fourfold oligomeric cyclization reactions leading to the C_{4v} isomers of 1. We also wished to prepare octols whose crystals were suitable for crystal structure determination.

Results

Syntheses. Some of the octols reported here have been prepared previously, but were thought to possess other structures until the work of A. G. S. Högberg,[2] who determined the configurations of several of them through ^{1}H NMR spectra and crystal structures of derivatives,[8] and who summarized and rationalized the earlier literature.[2] Our standard procedure[2] for the cyclooligomerization involving the aliphatic aldehydes was carried out at 25 °C with equal molar quantities of aldehyde and resorcinol in solutions of 2:2:1 respective volumes of EtOH, H_2O, and

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(2) (a) Högberg, A. G. S. *J. Org. Chem.* **1980**, *45*, 4498–4500. (b) Högberg, A. G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6046–6050, and references therein.

(3) 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.

(4) Cram, D. J.; Stewart, K. D.; Goldberg, I.; Trueblood, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2574–2575.

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

(6) Cram, D. J.; Karbach, S.; Kim, Y. H.; Baczynskyj, L.; Marti, K.; Sampson, R. M.; Kalleymeyn, G. W. *J. Am. Chem. Soc.* **1988**, *110*, 2554–2560.

(7) Tucker, J. A.; Knobler, C. B.; Cram, D. J. Unpublished work.

(8) (a) Erdtman, H.; Högberg, A. G. S.; Abrahamsson, S.; Nilsson, B. *Tetrahedron Lett.* **1968**, 1679–1682. (b) Nilsson, B. *Acta Chem. Scand.* **1968**, *22*, 732–747. (c) Palmer, K. J.; Wong, R. Y.; Jurd, L.; Stevens, K. *Acta Cryst. Chem.* **1976**, *B32*, 847–852.

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Table I. Yields and Melting Points of Octol 1 Produced from Aliphatic Aldehydes and Resorcinol or 2-Substituted Resorcinols

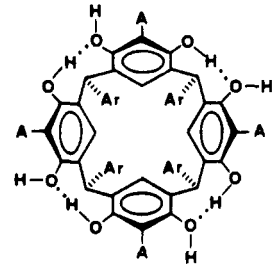
run no.	compd. no.	R of 1	A	% yld	mp, °C
1	2	CH_3	H	60	>360
2	3	CH_3CH_2	H	88	>360
3	4	$CH_3(CH_2)_2$	H	92	>360
4	5	$CH_3(CH_2)_3$	H	89	344–345
5	6	$CH_3(CH_2)_4$	H	77	329–330
6	7	$CH_3(CH_2)_{10}$	H	68	285
7	8	$(CH_3)_2CHCH_2$	H	95	340–342
8[a]	9	$HO(CH_2)_4$	H	80	280–284
9	10	$Cl(CH_2)_5$	H	67	170–175 dec
10	11	$C_6H_5CH_2$	H	70	>300
11	12	$C_6H_5CH_2CH_2$	H	69	>280
12	13	4-$O_2NC_6H_4$-CH_2CH_2	H	64	285–290
13	14	4-BrC_6H_4-CH_2CH_2	H	56	>280
14	15	CH_3	CH_3	79	>360
15	16	$CH_3(CH_2)_4$	CH_3	80	260 dec
16	17	CH_3	CO_2H	UM[b]	
17	18	CH_3	Br	Olig[c]	
18	19	CH_3	NO_2	OP[d]	

[a] Failed to obtain satisfactory elemental analysis. [b] Unseparated mixture of cyclic oligomers. [c] Unseparated mixture of oligomers. [d] Other product (21).

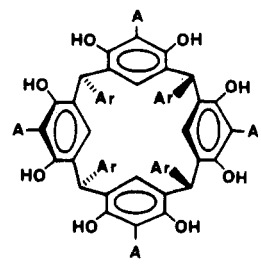
concentrated aqueous HCl with reaction times of 1 day or longer. Generally, the product crystallized from solution and was recrystallized and characterized. With aliphatic aldehydes only the C_{4v} isomers were isolated, although small amounts of other isomers were undoubtedly present in the filtrates. Table I reports the structures and yields (not maximized) of 1 produced from the aliphatic aldehydes. As expected, as the R groups became longer, the octols became more soluble in hexane, benzene, and chloroform.

The yields of the C_{4v} isomeric products varied from 56 to 95% when the A group of 1 was H and the R groups were CH_3, CH_3CH_2, $CH_3(CH_2)_2$, $CH_3(CH_2)_3$, $CH_3(CH_2)_4$, $CH_3(CH_2)_{10}$,[9] $(CH_3)_2CHCH_2$, $HO(CH_2)_4$, $Cl(CH_2)_5$, $C_6H_5CH_2$, $C_6H_5CH_2CH_2$, 4-$O_2NC_6H_4CH_2CH_2$, and 4-$BrC_6H_4CH_2CH_2$ (runs 1–13). The reaction also went well with A = CH_3 and R = CH_3 or $CH_3(CH_2)_4$ (runs 14 and 15). However, it failed to give readily isolable amounts of the desired C_{4v} isomeric product when R = CH_3 and A = CO_2H, Br, or NO_2 (runs 16–18). No cyclic oligomer was detected when resorcinol and $ClCH_2CHO$ or glucose were condensed under our standard conditions. With R = CH_3 and A = CO_2H, an unresolved mixture of cyclic oligomers was produced (run 16, ^1H NMR spectra only).

The condensation of equal molar amounts of benzaldehyde or 4-substituted benzaldehydes with resorcinol or 2-substituted resorcinols has also been studied in 95% ethanol-concentrated hydrochloric acid at 80 °C[2] (runs 19–34). Table II records the results. When A = H and Ar = C_6H_5, 4-$CH_3C_6H_4$, or 4-$C_2H_5C_6H_4$, of the products characterized (runs 19–21), only **20** of C_{4v} configuration was detected (^1H NMR) in the solid that separated from the reaction mixture. When A = H and Ar = C_6H_5, the C_{2v} isomer of **23** was isolated (10%) and fully characterized from a run of shorter duration than run 19. The ^1H NMR spectra of the fully characterized C_{4v} and C_{2v} isomers of **23** served as spectral models for the estimated ratios of isomers in runs 19–23 of Table II. When A = H and Ar = BrC_6H_4, the C_{2v} isomer of **26** (characterized only by ^1H NMR) was obtained by trituration of the crude precipitate from run 22 with hot ethanol, filtration of the mixture, and evaporation of the solvent. The C_{4v} isomer remained undissolved. In the syntheses of both **23** and **26**, the C_{4v}/C_{2v} ratio increased with longer reaction times. When A = H and Ar = 4-NCC_6H_4 or 4-$(CH_3)_3CC_6H_4$, or when A = CH_3 and Ar = C_6H_5, only **20** of C_{2v} configuration was detected by ^1H NMR of the crude precipitate (runs 27–29). When A = H and Ar = 4-$CH_3OC_6H_4$, 4-$AcNHC_6H_4$, 4-$C_6H_5C_6H_4$, or $HO_2CC_6H_4$, 3:2, 1:2, 3:2, and 2:5 respective mixtures of **20** of C_{4v} and of C_{2v} configurations were detected by ^1H NMR in the carefully washed and dried precipitates that separated from the reaction mixtures. The chemical shift differences in the resorcinol protons for the two isomers were used in these estimates (runs 23–26). The ^1H NMR spectra of the characterized C_{4v} and C_{2v} isomers of **23** served as spectral models. When A = H and Ar = 4-$O_2NC_6H_4$ or 4-$CH_3(CH_2)_3C{\equiv}C$, or when A = Br and Ar = C_6H_5, no crystalline solids precipitated from the reaction medium (runs 30–34). The products from runs 23–29 were not isolated in a pure state.



20·(C_{4v})



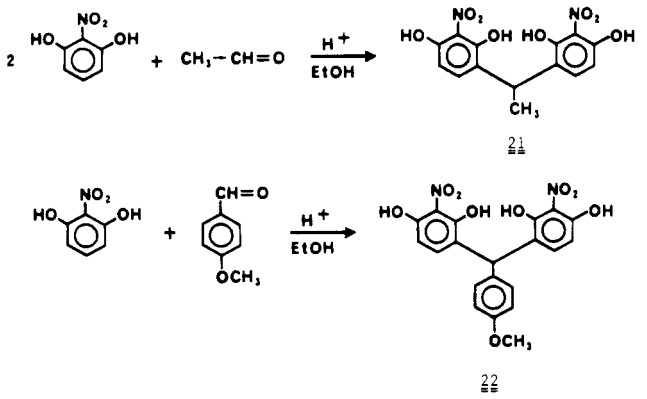
20·(C_{2v})

Högberg[8] has shown that in the reactions of resorcinol with benzaldehyde or 4-bromobenzaldehyde, the ratio of C_{4v} to C_{2v} isomeric products varies with reaction time, longer reaction times favoring the C_{4v} product. In our hands, increasing the scale of the 4-bromobenzaldehyde reaction from 1 g to 64 g of starting aldehyde increased the time necessary for complete conversion to the C_{4v} isomer from less than 1 day to greater than 28 days. Differences in mixing efficiency may be responsible. In contrast, the reaction of resorcinol with 4-methoxybenzaldehyde gave increasing amounts of the C_{2v} isomer as the reaction progressed. The time dependence of the C_{4v}/C_{2v} ratio of other entries in Table II was not investigated by us. The values listed refer to reaction times of 48 h and are believed to closely approximate terminal (equilibrium) values.

In runs 18 of Table I and 34 of Table II, 2-nitroresorcinol was condensed with acetaldehyde and 4-$CH_3OC_6H_4CHO$, respectively. The products were examined to see if the nitro group completely deactivated the resorcinol nucleus as a nucleophile. From run 18, the partially condensed product, **21**, was isolated (30% yield), and **22** was isolated (30% yield) from run 34. Apparently partial condensation occurs slowly.

Crystal Structures. Crystal structures of **2**·2.5CH_3CN·3H_2O and **5**·EtOH·$(CH_3)_2CO$·H_2O were determined and refined to R values of 0.083 and 0.066, respectively. Table I provides the distances and angles that define the shapes of the cavities. Chart I gives both side and face views of the structures. The crystal structure of caviplex **39**·CH_2Cl_2 is included in both the table and chart for comparison purposes. In **39**, the bowl conformation is enforced by replacing the four OH···OH groups of **2** with four OCH_2O bridging groups.[3] The structural parameters that are compared are defined in Scheme I.

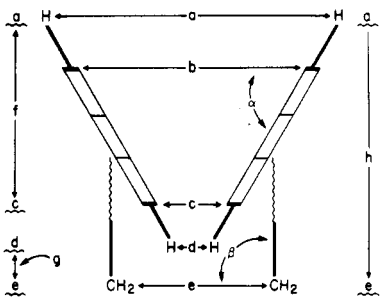
(9) After 7 had been prepared and characterized, the compound was reported: Aoyama, Y.; Tanaka, Y.; Toi, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1988**, *110*, 634–635.



21

22

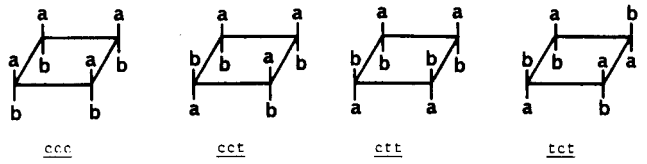
Scheme I



I

Discussion

Correlation of Configurations and Conformations. The cyclotetrameric oligomers derived from condensations of resorcinol with aldehydes can in principle exist in the four possible configurations formulated, cis-cis-cis (ccc), cis-cis-trans (cct), cis-trans-trans (ctt), and trans-cis-trans (tct). In these formulations, the "a" is the methine H and



ccc cct ctt tct

the "b" group is the R of the original aldehyde (RCHO). This discussion presumes that the diastereomers are conformationally mobile enough to preclude the isolation of isomers due solely to inhibition of ring inversion. Examination of CPK models of the isomers indicates that barriers to ring inversion are low enough to allow conformational equilibrations to occur rapidly on the human time scale at ordinary working temperatures. Thus in configurational assignments, conformations can formally be ignored.

The configurations of the ester derivatives of the two diastereomers of **26** (produced in the condensation of resorcinol and 4-bromobenzaldehyde) were established by crystal structure determinations[8b,c] to have ccc and ctt configurations. Högberg[2] through the use of dynamic ^{1}H NMR spectral correlations and analogies found that the ccc isomers of **2** and **23** possessed a bowl conformation with effective C_{4v} symmetry and that the ctt isomer of **23** existed in a chair conformation providing effective C_{2v} symmetry. Our crystal structures of octols **2** and **5** indicate that the dominant isomers produced possess the ccc configuration and the bowl conformation in the crystalline state. Their ^{1}H NMR spectra indicate that they possess effective C_{4v} symmetry in solution, as well. Crystal structures of several fully bridged cavitands (each near oxygen pairs are linked) derived from **23–25** (e.g., **39**) indicate that the dominant octols isolated from runs 19–21 also possess the ccc configuration.[7] The combined body of results leaves little doubt that the isomers whose ^{1}H NMR spectra indicate C_{4v} symmetry possess the ccc configuration and those isomers whose ^{1}H NMR spectra exhibit C_{2v} symmetry possess the ctt configuration. This generalization, we assume, applies to runs 1–15 of Table I and runs 19–29 of Table II.

Origins of the Stereoselectivity in the Cyclooligomerizations. Högberg[2b] has given a convincing argument for the virtual absence of the cct and tct isomers when benzaldehyde is condensed with resorcinol to give **23**. He also demonstrated that under the conditions of cyclooligomerization, the ctt isomer was formed faster than the ccc isomer but that the ctt isomer isomerized to the more stable ccc isomer through reversible protoalkylation–protodealkylation reactions under the conditions of their formations. In runs 1–7, 9–15, and 19–29 in our work, product precipitated from the reactions, and we believe that in many cases the insolubility of the ccc isomers relative to their diastereomeric cousins provided an important source of the stereoselectivity.

In runs involving alkyl and substituted alkyl groups attached to the aldehyde function and with resorcinol or 2-methylresorcinol as starting materials, the ccc isomer dominated (Table I, runs 1–15). Substitution of electron-withdrawing groups such as CO_2H, Br, or NO_2 in the 2-position of the resorcinol starting material did not lead to a single dominant product but to either no detectable cyclic oligomers (e.g., runs 17 and 18) or to mixtures of many isomeric products (run 16). These three substituents all deactivate the resorcinol nucleus toward electrophilic substitution, both with respect to forming cyclic oligomers and equilibrating them once formed. The isolation of a 30% yield of intermediate **21** from run 18 indicates the cyclooligomerization reaction to be slow.

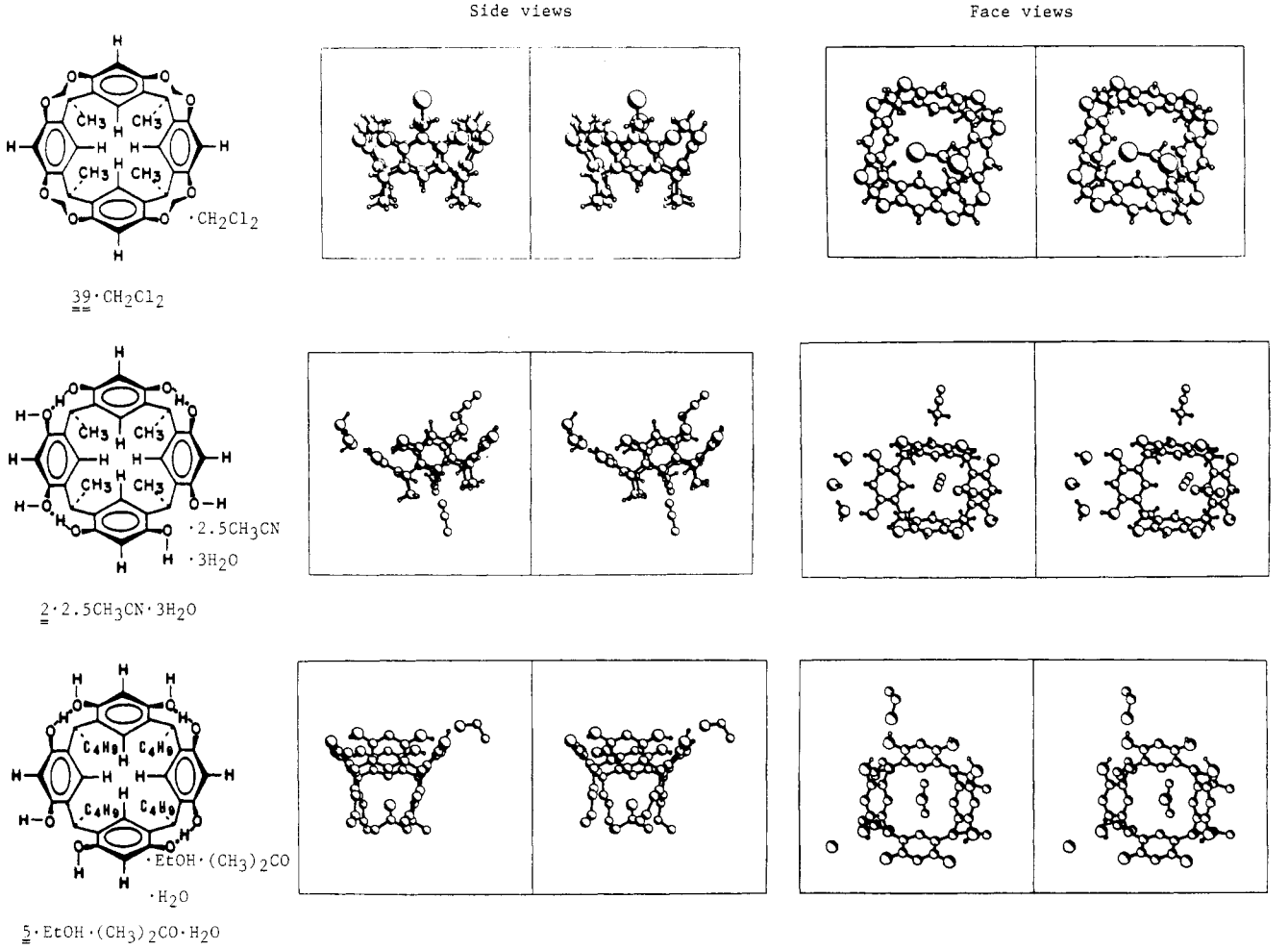
We interpret the stereoselectivity shown in runs 1–15 as being due to a combination of higher intrinsic stability associated with the ccc isomers, coupled with the reversibility of the condensation reactions and the relatively high insolubility of the ccc isomers in the reaction medium. The crystal structures of *ccc*-**1** and *ccc*-**5** show the presence of intramolecular hydrogen bonds between the phenolic hydroxyls, which is the most extensive with a bowl conformation. Since CPK molecular models of bowl conformations can be readily constructed from isomers of any of the four configurations, the intrinsic stability of the ccc isomers must be mainly associated with the tendency of the R groups of the aldehyde to be more stable in the axial than in the equatorial positions of the bowl conformations. As these R substituents become longer, they can intramolecularly associate with one another only when in axial conformations. The ccc isomers are unique in the sense that they alone provide the conformation that maximizes the proximity of like groups on the hydrophilicity–lipophilicity scale. For example, *ccc*-**5** in its bowl conformation maximally concentrates its eight hydroxyl groups in proximity to one another and its four butyl groups in proximity to one another and as distant as possible from the hydroxyl groups. The eight hydroxyls in the ccc-bowl structure fit best into the water structure (the major component of the reaction medium), and hydrophobic effects drive the four butyl groups as close together as possible to minimize the surface they expose to the ethanol–water medium. This hypothesis also explains why in run 8 with R of **1** equal to $HO(CH_2)_4$, *ccc*-**9** still dominated in the reaction mixture in spite of the fact that precipitate did not form during the reaction. The ccc-bowl structure

Table II. Yields and Configurations of the Dominant Products of Octols 20 Produced from Aromatic Aldehydes and Resorcinol or 2-Substituted Resorcinols

run no.	compd. no.	Ar of **20**	A	% yld of isom mixt	composite C_{4v}/C_{2v}	mp, °C
19	**23**[a]	C_6H_5	H	83	>97/3	285–300 dec
20	**24**	4-$CH_3C_6H_4$	H	96	>97/3	>305
21	**25**	4-$CH_3CH_2C_6H_4$	H	73	>97/3	>360
22	**26**[b]	4-BrC_6H_4	H	43	>97/3	>390
23	**27**	4-$CH_3OC_6H_4$	H	93	3/2[c]	
24	**28**	4-$AcNHC_6H_4$	H	52	1/2	
25	**29**	4-$C_6H_5C_6H_4$	H	99	3/2	
26	**30**	4-$HO_2CC_6H_4$	N	79	2/5	
27	**31**	4-NCC_6H_4	H	52	<3/97	
28	**32**	4-$(CH_3)_3CC_6H_4$	H	28	<3/97	
29	**33**	C_6H_5	CH_3	78	<3/97	
30	**34**	4-$O_2NC_6H_4$	H	0	no ppt	
31	**35**[d]	4-$OCHC_6H_4$	H	0	no ppt	
32	**36**	C_6H_5	Br	0	no ppt	
33	**37**	$CH_3(CH_2)_3C{\equiv}C$	H	0	no ppt	
34	**38**	4-$CH_3OC_6H_4$	NO_2	0	no ppt	

[a] Previously characterized, ref 2. In another run similar to 19, after 1 h at 75 °C, the mixture while hot was filtered from the precipitated C_{4v} isomer. Addition of water to the filtrate precipitated the C_{2v} isomer, which was recrystallized to give a 10% yield of characterized material, mp 240 °C dec. [b] Previously characterized as octabutyrate, ref 7b, and octaacetates (both C_{4v} and C_{2v} isomers), ref 7c. [c] Reaction run at 25 °C. When run at 80 °C, only the C_{2v} isomer could be detected in the product. [d] Two moles of resorcinol were used for each mole of dialdehyde.

Chart I



provides the highest ability of identical groups to (in effect) solvate one another and thus minimally disturb the liquid structure of the ethanol–water medium.

The same explanation applies to the results of runs 19–21 of Table II in which essentially only ccc-C_{4v} product was produced. These runs involved the condensation of benzaldehyde or 4-alkylated benzaldehydes with resorcinol. When the 4-substituent of the benzaldehyde used was Br, CH_3O, ArNH, C_6H_5, or HO_2C, mixtures of ccc and ctt isomers were in the precipitated product even after long reaction times. With the strong electron-withdrawing N≡C group (run 27), only ctt product was detected. We attribute this to the high energy cost of aligning four cyanobenzenes in essentially parallel axes, with their dipoles all pointing in the same direction. Such a geometry is required in the C_{4v}-ccc-bowl structure. Operation of this

same effect at a lower level, mixed with the hydrophobic effect discussed earlier, is possibly responsible for the ccc–ctt mixtures obtained in runs 22–24 and 26. In run 25 involving 4-phenylbenzaldehyde, the insolubility of both diastereomeric products probably inhibited their equilibration after their precipitation.

Molecular model examination of *ccc-bowl*-**32**, a potential product of the reaction of 4-*tert*-butylbenzaldehyde and resorcinol, suggests this structure to be much destabilized by steric compressions of the four *tert*-butyl groups. Models of *ctt-chair*-**32** appear to be relatively noncompressed. Thus steric effects appear to drive the condensation to give essentially only *ctt*-**32**. Possibly in run 29 involving benzaldehyde and 2-methylresorcinol, the insolubility of the initially formed *ctt*-**33** may have inhibited its equilibration to give the ccc isomer. Runs 30–34 failed to give cyclic oligomer for reasons that are not clear. From run 34 involving 4-methoxybenzaldehyde and 2-nitroresorcinol as starting materials, only intermediate **22** was isolated (30%).

This survey demonstrates that with a large number of aliphatic aldehydes and resorcinol or 2-methylresorcinol, good yields of ccc-bowl product can be obtained. With benzaldehyde and 4-substituted benzaldehydes and resorcinol or 2-methylresorcinol, either ccc-bowl product, ctt-chair product, or mixtures are produced. The stereoselectivities appear to involve an interplay of a variety of effects that often oppose one another. The remarkable thing about the results is that given the large numbers of effects, the stereoselectivities are high enough to provide practical yields of highly desirable starting materials for cavitand and carcerand syntheses.

Crystal Structures. The stereoviews of Chart I show the bowl-like shapes of hosts **2** and **5**, which resemble the shapes of the cavitands in which the close pairs of oxygens are bridged not with hydrogen bonds but with $(CH_2)_n$ (n = 1–3 groups).[3] The stereoview of caviplex **39**·CH_2Cl_2 included in Chart I illustrates the similarity. In all three structures, the bowls "rest" on four nearly coplanar "feet" consisting of CH_3 groups in **2** and **39**, and of $CH_3(CH_2)_3$ groups in **5**. The bowl of **39** is filled with a CH_2Cl_2 molecule. One of the water molecules of **2** is located 0.3 Å above plane *a* (5.0 Å from plane *e*). The host in **5** differs from the other two hosts in the sense that the roughly parallel butyl "feet" create a cavity in **5** that is filled with the carbonyl group of an acetone molecule. The oxygen atom is nearly equidistant from the carbon atoms of plane *c* (3.56, 3.66, 3.73, and 3.80 Å) and is also nearly equidistant from the hydrogen atoms of plane *d*. This oxygen lies 0.98 Å below plane *e*.

Unlike the structure of **39**·CH_2Cl_2, that of **2**·2.5CH_3CN·3H_2O involves hydrogen bonds to three water molecules, and that of **5** to one water and one ethanol molecule. In **2**·2.5CH_3CN·3H_2O, only three of the four sets of oxygen pairs are hydrogen bonded to one another, the other two oxygens (at about 4 o'clock in the face view) donating their hydrogens to water and to the oxygen of a second octol molecule. The hydrogen bonds connecting the three resorcinol units range in length from 1.6 to 2.0 Å. In **5**·EtOH·$(CH_3)_2CO$·H_2O, all four resorcinol moieties are hydrogen bonded to one another to produce a more symmetrical bowl that is strikingly similar to that of **39**·CH_2Cl_2. This contrasts with **2**, which is elongated in the horizontal and narrowed in the vertical dimension of the face view.

Table III provides the distances and angles relevant to the shapes of the three hosts, generally pictured in Scheme I. The H···H diagonals of plane *a* in **39** and **5** range from 8.96 to 10.12 Å in length, whereas those of **2** are 7.54 and 10.62 Å. The distance the H's are out of plane *a* in **39**, **2**, and **5** are (±)–0.01, and ±0.54 and ±0.15 Å, respectively. Similarly, the C···C diagonals in the best plane *b* in **39** and **5** range only between 7.89 to 8.80 Å, whereas in **2** the distances are 6.94 and 9.55 Å. The plane *c* diagonals in all three hosts are pretty close together, ranging from 5.18 to 5.28 Å. Likewise, the H···H diagonals for plane *d* range in the three hosts only between 3.56 and 4.47 Å, but these extremes are both found in **2**. The C···C diagonals of plane *e* for the three hosts range only from 7.03 to 7.70 Å to provide averages for diagonals of 7.21 Å for **39**, 7.24 Å for **2**, and 7.14 Å for **5**. The respective C-out-of-plane-*e* distances are only ±0.03 Å for **39**, ±0.01 Å for **2**, and ±0.04 Å for **5**. The plane *a* to plane *c* distances (*f*) in **39**, **2**, and **5** are 3.34 Å, 3.09 Å, and 3.10 Å, respectively. These distances are rather close together. They provide a measure of the average depth of the bowls. The near $(O\cdots O)_{av}$ distances are also reasonably close together at 2.38 Å for **39**, 2.76 Å for **2**, and 2.70 Å for **5**.

Planes *a* through *e* are close to being parallel to one another, *d* and *e* being maximally out of parallel by 3.6° in **2**. The angles of intersection of the aryl planes and plane *b* only range from 59.2 to 61.6° ($(\alpha)_{av}$ = 60.85°) for

Table III. Distances and Angles Relevant to Shapes of Cavities[a]

	compd/solvate		
	39/CH_2Cl_2	**2**/2.5CH_3CN·3H_2O	**5**/EtOH, $(CH_3)_2CO$, H_2O
distances (Å) between			
H···H diagonal of plane *a* (*a*)	9.11, 8.96	10.62, 7.54	10.12, 9.29
$(H\cdots H)_{av}$ for *a*	9.04	9.08	9.71
H out of plane *a*	(±)0.01	(±)0.54	(±)0.15
C···C diagonal of plane *b* (*b*)	8.03, 7.89	9.55, 6.94	8.80, 8.21
$(C\cdots C)_{av}$ for *b*	7.96	8.25	8.51
C out of plane *b*	(±)0.01	(±)0.44	(±)0.12
C···C diagonal of *c* (*c*)	5.25, 5.27	5.28, 5.22	5.26, 5.18
$(C\cdots C)_{av}$ for *c*	5.26	5.25	5.22
C out of plane *c*	(±)0.00	(±)0.00	(±)0.03
H···H diagonal of plane *d* (*d*)	4.18, 4.20	4.47, 3.56	4.13, 3.88
$(H\cdots H)_{av}$ for *d*	4.19	4.01	4.00
H out of plane *d*	(±)0.01	(±)0.18	(±)0.05
$CH_2\cdots CH_2$ diagonal of plane *e* (*e*)	7.70, 7.32	7.28, 7.20	7.25, 7.03
$(CH_2\cdots CH_2)_{av}$ for *e*	7.21	7.24	7.14
C out of plane *e*	(±)0.03	(±)0.01	(±)0.04
plane *a* to *c* (*f*)	3.34	3.09	3.10
plane *d* to *e* (*g*)	0.64	0.79	0.84
plane *a* to *e* (*h*)	4.95	4.68	4.72
near O···O	2.39, 2.36	2.78, 2.72	2.69, 2.74
	2.38, 2.38	2.73, 2.80	2.67, 2.70
near $(O\cdots O)_{av}$	2.38	2.76	2.70
angles (deg) between			
planes *a* and *c*	0.4	1.7	1.1
planes *d* and *e*	0.6	3.6	1.9
planes *a* and *e*	0.5	1.4	0.6
planes benzene and *b* (α)	61.6, 61.2	38.3, 71.4	51.6, 56.4
	61.4, 59.2	40.7, 72.3	48.7, 56.9
$(\alpha)_{av}$	60.85	55.7	53.4
planes *e* to $CH_2CH(\beta)$	88.6, 89.5	86.9, 86.0	86.2, 89.0
	88.7, 88.5	85.9, 85.7	86.1, 88.3
$(\beta)_{av}$	88.8	86.1	87.4

[a] Planes *a*–*e* are defined as the best planes in Scheme I. Distances *a*–*e* (Å) refer to atoms in best planes most distant from one another. Distances *f*–*h* are those between best planes. Structure I in text explicitly defines the distances and angles.

39, from 38.3 to 72.3° ($(\alpha)_{av}$ = 55.7°) for **2**, and from 48.7 to 56.9° ($(\alpha)_{av}$ = 53.4°) for **5**. These average angles provide an overall measure of the tilt of the bowls' sides, and the variations give a measure of how much the hosts deviate from having a C_4 axis. Thus the bowls' sides rise most steeply in **39**, and the molecule is close to having a C_4 axis. The sides of bowl **2** rise less steeply, and the bowl comes closer to having a C_2 than a C_4 axis, while the sides of bowl **5** on average rise less steeply than those of the other two, but the bowl comes reasonably close to having a C_4 axis.

The symbol β measures the angles between planes *e* and the axes of the CH_2–CH bonds. For all three hosts, the total range is from 85.7° to 89.5°, and $(\beta)_{av}$ for **39**, **2**, and **5** are 88.8°, 86.1° and 87.4°, respectively. Thus, the "feet supporting the bowls" for all three hosts are very close to being maximally centered (β = 90°) beneath the bowls. The longer (C_4H_9) feet of **5** do not seem to much perturb the support structure for the bowl.

In summary, rigid host **39** and somewhat flexible host **5** greatly resemble each other in their bowl structures, whereas host **2** is less symmetrical. However, in their bowl-support structures, all three hosts are very similar except for the much longer feet in **5** than in **39** or **2**. The organization of the bowls in **2** and **5** appear to be associated with the hydrogen bonds between the hydroxyl groups of the resorcinol units, and possibly in **5** by van der Waals attractions between the four C_4H_9 feet.

Experimental Section

General. Melting points below 240 °C were measured on a Thomas-Hoover and those above 240 °C on a Mel-Temp apparatus, neither being corrected. Electron impact mass spectra were recorded on an AE1 Model MS-902 spectrometer at 16 or 70 eV at the temperatures indicated, whereas FAB-MS were recorded by using xenon ionization techniques with a *m*-nitrobenzyl alcohol (NOBA) as matrix on an AE1 Model MS-9 spectrometer. Proton NMR spectra were taken in $CDCl_3$ at 200.1 MHz on a Bruker WP-200 spectrometer unless otherwise specified. All δ values are reported in ppm with $(CH_3)_4Si$ at 0.00 ppm or $CHCl_3$ at 7.24 ppm as references.

2,8,14,20-Tetrakis(2-phenylethyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (12) (Procedure I, Run 11). Resorcinol (55 g, 0.5 mol) was dissolved in 400 mL of 95% ethanol and 100 mL of 37% HCl in H_2O was added under argon. To this mixture stirred at 0 °C was added dropwise over a 30-min period 67 g (0.5 mol) of dihydrocinnamaldehyde. The clear reaction was allowed to warm to room temperature. After 24 h at 25 °C, it was slowly heated to reflux temperature and held there for 3 days. After about 1 day, the clear solution turned cloudy and a precipitate separated over time. After the third day at reflux, 150 mL of H_2O was added to the mixture, which was cooled to 0 °C and filtered, and the solid was washed with cold 50% ethanol–water. This product was recrystallized from 1 L of methanol to produce 78 g (69%) of **12** as white needles, which when air dried lost their shape, mp >280 °C. Before any reactions were run on **12**, it was dried at 80–100 °C at 0.1 mm pressure to remove solvent of crystallization ^{1}H NMR ($(CD_3)_2SO$) δ 2.35–2.60 (m, 28 H, CH_2-CH_2Ar and $(CH_3)_2SO$ impurity), 3.35 (s, 24 H, H_2O), 4.20–4.32 (br s, 4 H, C*H* (methine), 6.20 (s, 4 H, Ar*H*, ortho to OH), 7.05–7.28 (m, 20 H, C_6H_5), 7.41 (s, 4 H, meta to OH), 9.04 (s, 8 H, O*H*); FAB-MS (16 eV) *m/e* 904 (M^+, 29), 799 ($M^+ - C_6H_5CH_2CH_2$). Anal. Calcd for $C_{60}H_{56}O_8 \cdot {}^1/_2H_2O$: C, 78.83; H, 6.29. Found (100 °C at 10^{-3} mm): C, 79.04; H, 6.13.

2,8,14,20-Tetrapentylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (6) (Procedure II, Run 5). To a solution of 110 g (1 mol) of resorcinol in 500 mL of 95% ethanol were added 500 mL of water and 250 mL of concentrated hydrochloric acid under argon. The stirred solution under argon was cooled to 15 °C, and 100 g (1 mol) of hexanal was added dropwise over a 30-min period. The mixture was then stirred at 50 °C for 1 h and then allowed to cool to 25 °C. Product started to precipitate after several hours. The mixture was stirred for 6 days under argon and filtered. The solid as triturated with water (twice), filtered, and recrystallized from ethanol–water to give 147 g (77%) of **6**, mp 330 °C dec: ^{1}H NMR ($(CD_3)_2CO$) δ 0.91 (t, *J* = 6.59 Hz, 12 H, CH_3), 1.30 (bs, 24 H, $CH_2(CH_2)_3CH_3$), 2.28 (m, 8 H, $CH_2(CH_2)_3CH_3$), 4.30 (t, *J* = 7.95 Hz, 4 H, C*H* (methine)), 6.23 (s, 4 H, Ar*H*, ortho to OH), 7.54 (s, 4 H, meta to OH), 8.50 (s, 8 H, OH); FAB-MS (16 eV) *m/e* 768 (M^+, 13), 697 ($M - C_5H_{11}$, 100). Anal. Calcd for $C_{48}H_{64}O_8$: C, 74.97; H, 8.39. Found (dried at 150 °C, 10^{-5} Torr, 12 h): 75.04; H, 8.48.

2,8,14,20-Tetraundecylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (7) (Run 6). A solution of 19.8 g (0.18 mol) of resorcinol in a solution of 75 mL of 95% ethanol and 25 mL of concentrated hydrochloric acid was cooled to 2 °C. Dodecanal (33.2 g, 0.18 mol) in 50 mL of 95% ethanol was added dropwise to the solution stirred under argon over a period of 2 h. The resulting solution was allowed to *slowly* warm to 25 °C and then heated to 75 °C for 21 h. The precipitate that separated was washed repeatedly with cold methanol and dried. The material was twice recrystallized from methanol to give after drying 34.2 g (68%) of octol **7**, mp 285 °C dec: ^{1}H NMR ($(CD_3)_2CO$) δ 0.89 (t, *J* = 6.45 Hz, 12 H, CH_3), 1.30 (bs, 72 H, $-CH_2(CH_2)_9CH_3$), 2.30 (m, 8 H, $CH_2(CH_2)_9$), 4.31 (t, *J* = 7.82 Hz, 4 H, methine), 6.24 (s, 4 H, Ar*H*, ortho to OH), 7.54 (s, 4 H Ar*H*, meta to OH), 8.44 (s, 8 H, OH); FAB-MS (16 eV) *m/e* 1104 (M^+, 3), 950 ($M^+ + 1 - C_{11}H_{23}$, 100). Anal. Calcd for $C_{72}H_{112}O_8$: C, 78.21; H, 10.21. Found (dried at 100 °C at 10^{-5} Torr, 12 h): C, 78.01; H, 10.31. The compound was soluble in hexane, benzene, and $CDCl_3$, but the ^{1}H NMR spectrum in $CDCl_3$ gave very broad peaks.[8]

2,8,14,20-Tetramethylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (2) (Run 1). From 55.05 g (0.5 mol) of resorcinol and 22.01 g (0.5 mol) of ethanal and 250 mL of reaction solvent (procedure II) after 4 days at 25 °C was produced a precipitate, which was recrystallized from ethanol–water to give 41 g (60%) of **2**,[2] mp >360 °C. This material was recrystallized from acetonitrile to give single crystals of X-ray quality.

2,8,14,20-Tetraethylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (3) (Run 2). Procedure II applied to resorcinol and propanal gave **3**; mp 360 °C dec: ^{1}H NMR ($(CD_3)_2CO$) δ 0.91 (t, *J* = 7.31 Hz, 12 H, CH_3), 2.13 (m, 8 H, CH_2), 4.18 (t, *J* = 7.7, 4 H, methine), 6.24 (s, 4 H, Ar*H*, ortho to OH), 7.53 (s, 4 H, Ar*H*, meta to OH), 8.59 (s, 8 H, O*H*); FAB-MS (16 eV) *m/e* 600 (M^+, 49), 571 ($M^+ - CH_3CH_2$, 100). Anal. Calcd for $C_{36}H_{40}O_8 \cdot 0.25H_2O$: C, 71.45; H, 6.66. Found: C, 71.41; H, 6.55.

2,8,14,20-Tetrapropylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (4) (Run 3). Procedure II applied to resorcinol and butanal gave **4** ^{1}H NMR ($(CD_3)_2CO$) δ 0.94 (t, *J* = 7.3, 12 H, CH_3), 1.30 (m, 8 H, CH_2CH_3), 2.28 (m, 8 H, $CH_2CH_2CH_3$), 4.33 (t, *J* = 8.0 Hz, 4 H, methine), 6.24 (s, 4 H, Ar *H*, ortho to OH), 7.58 (s, 4 H, Ar H, meta to OH), 8.44 (s, 8 H, O*H*); FAB-MS (16 eV) *m/e* 656 (M^+, 22), 613 ($M^+ - CH_3CH_2CH_2$, 100). Anal. Calcd for $C_{40}H_{48}O_8 \cdot H_2O$: C, 71.19; H, 7.47. Found: C, 71.26; H, 7.45.

2,8,14,20-Tetrabutylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (5) (Run 4). Procedure II applied to resorcinol and pentanal gave **5**: ^{1}H NMR ($(CD_3)_2CO$) δ 0.88 (t, *J* = 6.9 Hz, 12 H, CH_3), 1.33 (m, 16 H, $CH_2CH_2CH_2CH_3$), 2.28 (m, 8 H, $ArCHCH_2$), 4.29 (t, *J* = 7.78 Hz, 4 H, methine), 6.22 (s, 4 H, ArH, ortho to OH), 7.54 (s, 4 H, ArH, meta to OH), 8.46 (s, 8 H, O*H*); MS (70 eV, 300 °C) *m/e* 712 (M^+, 6), 655 ($M^+ - C_4H_9$, 55). Anal. Calcd for $C_{44}H_{56}O_8 \cdot H_2O$: C, 72.50; H, 7.74. Found: C, 72.69; H, 7.82. For production of single crystals of X-ray quality material, **5** was recrystallized from acetone and ethanol.

2,8,14,20-Tetraisobutylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (8) (Run 7).

Procedure II applied to resorcinol and 3-methylbutanal gave **8**: ^{1}H NMR ($(CD_3)_2CO$) δ 0.95 (d, J = 6.58, 24 H, CH_3), 1.47 (m, 4 H, $(CH_3)_2CH$), 2.17 (dd, J = 7.3 Hz, 8 H, CH_2), 4.46 (t, J = 7.1 Hz, 4 H, ArC*H*), 6.25 (s, 4 H, Ar*H*, ortho to OH), 7.55 (s, 4 H, Ar*H*, meta to OH), 8.49 (s, 8 H, O*H*); MS (70 eV, 250 °C) m/e 712 (M^+, 13), 655 ($M^+ - (CH_3)_2CHCH_2$, 100). Anal. Calcd for $C_{44}H_{56}O_8 \cdot {}^3/_2H_2O$: C, 71.42; H, 8.04. Found: C, 71.11; H, 8.11. Anal. Calcd for $C_{44}H_{56}O_8$ (after drying the sample at 100 °C and 10^{-5} Torr): C, 74.13; H, 7.92. Found: C, 73.92; H, 7.88.

2,8,14,20-Tetrakis(4-hydroxybutyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (9) (Run 8). Procedure II (reaction run for 4 days at 25 °C and then poured into water to precipitate product) applied to 5-hydroxypentanal gave crude **9**. This material was recrystallized from CH_3OH/Et_2O (1/1 v/v), mp 280–284 °C dec, which contained water of crystallization even after drying at 120 °C at 10^{-5} Torr for 48 h. Repeated attempts at elemental analyses failed to provide rational data: ^{1}H NMR ($(CD_3)_2SO$) δ 0.94 (m, 8 H, $ArCHCH_2CH_2$), 1.24 (m, 8 H, $ArCHCH_2CH_2CH_2$), 1.58 (m, 8 H, $ArCHCH_2$) 3.18 (m, 8 H, CH_2OH), 4.13 (t, 4 H, ArC*H*), 4.33 (t, 4 H, CH_2OH), 6.12 (s, 4 H, Ar*H*, ortho to OH), 6.76 (s, 4 H, ArH, meta to OH), 8.36 (s, 8 H, O*H*); FAB-MS (16 eV) m/e 776 (M^+, 66), 703 ($M^+ - (CH_2)_4OH$, 94).

2,8,14,20-Tetrakis(4-chlorobutyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (10) (Run 9). Procedure II applied to resorcinol and 6-chlorohexanal (reaction run 3 days at 80–85 °C) gave **10**: ^{1}H NMR ($(CD_3)_2SO$) δ 1.22 (m, 8 H, CH_2), 1.42 (m, 8 H, CH_2), 1.68 (m, 8 H, CH_2), 2.04 (m, 8 H, CH_2) 3.57 (t, 8 H, CH_2Cl), 4.22 (t, 4 H, ArC*H*), 6.15 (s, 4 H, Ar*H*, ortho to OH), 7.15 (s, 4 H, Ar*H*, meta to OH), 8.87 (s, 8 H, O*H*); FAB-MS (16 eV) m/e 906 (M^+, 16), 801 ($M^+ - C_5H_{10}Cl$, 100). Anal. Calcd for $C_{48}H_{60}Cl_4O_8$: C, 63.58; H, 6.67. Found (dried 12 h at 180 °C, 10^{-5} Torr): C, 63.62; H, 6.74.

2,8,14,20-Tetrakis(2-phenylethyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (11) (Run 10). Procedure II applied to resorcinol and phenylethanal (finally 2 days at reflux) gave no precipitate. The reaction mixture was cooled to 25 °C and added to a tenfold amount of water. The voluminous precipitate was collected, water washed, dried, and recrystallized from ethanol to give **11**; mp >300 °C: ^{1}H NMR ($(CD_3)_2CO$) δ 3.82 (d, J = 7.3 Hz, 8 H, CH_2Ar), 4.77 (t, J = 7.3 Hz, 4 H, ArC*H*), 6.19 (s, 4 H, Ar*H*, ortho to OH), 7.10–7.29 (m, 20 H, C_6H_5), 8.02 (s, 4 H, Ar*H*, meta to OH), 8.42 (s, 8 H, O*H*); FAB-MS (16 eV) m/e 849 (M^+, 10), 758 ($M^+ - CH_2C_6H_5$, 100). Anal. Calcd for $C_{56}H_{48}O_8 \cdot 2H_2O$: C, 75.99; H, 5.92. Found: C, 75.63; H, 6.06.

2,8,14,20-Tetrakis[2-(4-nitrophenyl)ethyl]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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (13) (Run 12). Procedure I applied to 4-nitrodihydrocinnamaldehyde[10] (11.4 of this aldehyde was liquified by mixing with 2 mL of CH_2Cl_2) and resorcinol gave **13**, which was recrystallized from hot $(CH_3)_2SO$: ^{1}H NMR ($(CD_3)_2SO$) δ 2.30–2.50 (m, 20 H, $ArCH_2CH_2$ and $(CH_3)_2SO$), 2.55–2.70 (m, 8 H, $ArCH_2CH_2$), 4.30 (t, J = 7 Hz, 4 H, ArC*H*), 6.21 (s, 4 H, ortho to OH), 7.30 (s, 4 H, meta to OH), 7.35 (d, $J \sim 8$ Hz, 8 H, ortho to nitro), 7.98 (d, J = 8 Hz, 8 H, meta to nitro), 9.00 (s, 8 H, O*H*); FAB-MS (16 eV) m/e 1084 (M^+, 1), 934 (3, $M^+ - 4\text{-}O_2NC_6H_4CH_2CH_2$). Anal. Calcd for $C_{60}H_{52}N_4O_{16} \cdot 2.5H_2O$: C, 63.73; H, 5.00; N, 4.98. Found: C, 63.63; H, 4.70; N, 4.81.

2,8,14,20-Tetrakis[2-(4-bromophenyl)ethyl]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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (14) (Run 13). Procedure I applied to 4-bromodihydrocinnamaldehyde[11] and resorcinol gave **14**, which was recrystallized from a mixture of methanol and acetone: ^{1}H NMR ($(CD_3)_2SO$) δ 2.30–2.60 (m, >16, CH_2, $(CH_3)_2SO$), 4.25 (m, 4 H, ArC*H*), 6.18 (s, 4 H, Ar*H*, ortho to OH), 7.04 (d, $J \sim 8$ Hz, Ar*H*, meta to Br), 7.34 (d, $J \sim 8$ Hz, 8 H, Ar*H*, ortho to Br), 7.37 (s, 4 H, Ar*H*, meta to OH), 9.01 (s, 8 H, O*H*); FAB-MS (16 eV) m/e 1220 (M^+, 45), 1034 ($M^+ - 4\text{-}BrC_6H_4CH_2CH_2$, 40). Anal. Calcd for $C_{60}H_{52}Br_4O_8$: C, 59.04; H, 4.29; Br, 26.18. Found: C, 58.92; H, 4.23; Br, 26.22.

2,5,8,11,14,17,20,23-Octamethylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (15) (Run 14). Procedure II applied to 2-methylresorcinol and acetaldehyde (3 days at 25 °C, reaction conditions) gave **15**: ^{1}H NMR ($(CD_3)_2SO$) δ 1.69 (d, 12 H, $CHCH_3$), 1.94 (s, 12 H, $ArCH_3$), 4.43 (q, 4 H, ArC*H*), 7.38 (s, 4 H, Ar*H*, meta to OH), 8.65 (s, 8 H, O*H*); FAB-MS (16 eV) m/e 600 (M^+, 92). Anal. Calcd for $C_{36}H_{40}O_8$: C, 71.98; H, 6.71. Found: C, 71.92; H, 6.74.

2,8,14,16-Tetrapentyl-5,11,17,23-tetramethylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (16) (Run 15). Procedure II applied to hexanal and 2-methylresorcinol gave **16**, which was recrystallized from acetonitrile: ^{1}H NMR ($(CD_3)_2SO$) δ 0.87 (t, 12 H, CH_3), 1.31 (m, 24 H, $(CH_2)_3$, 1.96 (s, 12 H, CH_3), 2.18 (m, 8 H, CH_2), 4.21 (t, 4 H, ArC*H*), 7.19 (s, 4 H, Ar*H*), 8.62 (s, 8 H, OH); FAB-MS (16 eV) m/e 825 ($M + H^+$, 33), 754 ($M^+ - C_5H_{11}$, 100). Anal. Calcd for $C_{52}H_{72}O_8 \cdot 0.5H_2O$: C, 74.88; H, 8.70. Found (after drying at 100 °C, 10^{-5} Torr, 6 h): C, 74.94; H, 8.68.

1,1-Bis(2,4-dihydroxy-3-nitrophenyl)ethane (21). A solution of 200 mL of 95% ethanol, 50 mL of concentration hydrochloric acid, and 5.5 g of 2-nitroresorcinol (35 mmol) was cooled to 0 °C. To this stirred mixture was added dropwise 2.0 mL of ethanal. The solution was allowed to warm to 25 °C. Crystals formed after a day. After 3 days, the solid was collected, washed with ethanol–water, and dried to give 2.0 g (33%) of **21**, mp 174–175 °C: ^{1}H NMR ($CDCl_3$) δ 1.55 (d, J = 7.3 Hz, 3 H, CH_3), 4.70 (q, J = 7.3 Hz, 1 H, $CHCH_3$), 6.60 (d, J = 8.8 Hz, 2 H, Ar*H*, para to OH), 7.40 (d, J = 8.8 Hz, 2 H, ArH, para to NO_2), 10.54 (s, 2 H, O*H*); MS (70 eV, 230 °C) m/e 336 (M^+, 70), 321 ($M^+ - CH_3$, 100). Anal. Calcd for $C_{14}H_{12}N_2O_8$: C, 50.01; H, 3.59; N, 8.33. Found: C, 49.89; H, 3.39; N, 8.19.

Bis(2,4-dihydroxy-3-nitrophenyl)(4-methoxyphenyl)methane (22) (Run 30). A solution of 80 mL of 95% ethanol, 1.0 g of 2-nitroresorcinol (6.45 mmol), 0.80 mL of *p*-anisaldehyde (6.45 mmol), and 20 mL of concentrated hydrochloric acid was heated to 75 °C for 5 days. When cooled to 25 °C, the precipitate that separated was collected and washed with ethanol–water to give after drying, 0.50 g (30%) of **22**, mp 186–192 °C: ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 3 H, OCH_3), 6.00 (s, 1 H, Ar_3CH), 6.55 (d, J = 8 Hz, 2 H, Ar*H*, ortho to OH), 6.85 (d, J = 8 Hz, 2 H, Ar*H*, ortho to OCH_3), 7.01 (d, J = 8 Hz, 2 H, Ar*H*, ortho to CH_3O), 7.08 (d, J = 8 Hz, 2 H, Ar*H*, ortho to OH), 10.58 (s, 2 H, O*H*), 11.13 (s, 2 H, O*H*); MS (70 eV, 180 °C) m/e 428 (M^+, 100). Anal. Calcd for $C_{20}H_{16}N_2O_9$: C, 56.08; H, 3.76; N, 6.54. Found: C, 56.19; H, 3.62; N, 6.45.

2,8,14,20-Tetrakis(4-ethylphenyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (25) (Run 21, Procedure III). To a solution of 80.2 g (0.729 mol) of resorcinol and 97.7 g (0.729 mol) of 4-ethylbenzaldehyde in 580 mL of 95% ethanol was added 146 mL of concentrated hydrochloric acid. The solution was heated at 80 °C under argon for 11 days. The product that separated was filtered. The solid was suspended in 95% ethanol, vortexed 20 min, and filtered. This process was repeated three more times to free the product from hydrochloric acid. The product was dried to give 120.6 g (73%) of **25**, mp >360 °C: ^{1}H NMR ($(CD_3)_2SO$) δ 1.18 (t, J = 7.5 Hz, 12 H, CH_3), 2.3 (m, CH_2 and $(CH_3)_2SO$ impurity), 5.61 (s, 4 H, Ar_3CH), 6.11 (s, 4 H, Ar*H*, ortho to OH), 6.37 (bs, 4 H, Ar*H*, meta to OH), 6.66 (d, J = 8.1 Hz, 8 H, Ar*H*, meta to Et), 6.81 (d, J = 8.1 Hz, 8 H, Ar*H*, ortho to Et), 8.47 (bs, 8 H, O*H*); MS (16 eV) m/e 904 (M^+, 100). Anal. Calcd for $C_{60}H_{56}O_8 \cdot 1.5H_2O$: C, 77.31; H, 6.24. Found (after drying 48 h at 180 °C, 10^{-5} Torr): C, 77.31; H, 6.38.

2,8,14,20-Tetraphenylpentacyclo[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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (23) (Run 19). Procedure III applied to resorcinol and benzaldehyde gave **23** (reaction time 4 days), 1 g of which dissolved in 20 mL of

(10) Ingold, C. K.; Piggott, H. A. *J. Chem. Soc.* **1923**, *123*, 1469–1509.
(11) (a) Gabriel, S.; Zimmermann, J. *Ber.* **1880**, *13*, 1680–1684. (b) Glaser, C. *Liebigs Ann.* **1864**, *143*, 325–346.

$(CH_3)_2NCHO$: ^1H NMR ($(CD_3)_2SO$) δ 5.65 (s, 4 H, Ar_3CH) 6.17 (s, 4 H, ArH, ortho to OH), 6.32 (bs, 4 H, ArH, meta to OH), 6.72–6.80 (m, 8 H, ArH), 6.92–7.02 (m, 12 H, ArH), 8.58 (bs, 18 H, OH); MS (70 eV) m/e 792 (M^+, 100). Anal. Calcd for $C_{52}H_{40}O_8 \cdot 1.5H_2O$: C, 76.18; H, 5.29. Found (after drying 24 h at 150 °C and 10^{-5} Torr): C, 76.38; H, 4.92.

A sample C_{2v} isomer was needed whose ^1H NMR could serve as a reference for the estimations of C_{4v}/C_{2v} values found in Table I. The C_{2v} (ctt) isomer of **23** was prepared and characterized as follows. Benzaldehyde (12.6 mL, 0.25 mol) and resorcinol (13.8 g, 0.25 mol) were dissolved in 1 L of 95% ethanol, and 250 mL of concentrated hydrochloric acid was added. The mixture was heated for 1 h at 75 °C and vacuum filtered while hot to remove precipitated C_{4v}-**23**. Water (600 mL) was added to the filtrate to precipitate the C_{2v} isomer. The solid was filtered and washed several times with water. This C_{2v} isomer was recrystallized from hot EtOH to provide 4.8 g (10%) of *ctt*-**23**, mp 240 °C dec: ^1H NMR (200 MHz, $(CD_3)_2SO$) δ 5.53 (s, 4 H, Ar_3CH), 5.55 (s, 2 H, ArH, ortho to OH), 6.12 (s, 2 H, ArH, ortho to OH), 6.34 (overlapping s, 4 H, ArH, meta to OH), 6.59–6.62 (m, 8 H, ArH), 6.83–6.88 (m, 12 H, ArH), 8.44 (s, 4 H, ArOH), 8.55 (s, 4 H, ArOH); MS-FAB (NOBA) m/e 792 (M^+, 100), 715 ($M^+ - C_6H_5$, 18). Anal. (dried at 110 °C, 10^{-5} Torr, 6 h). Calcd for $C_{52}H_{40}O_8 \cdot 2H_2O$: C, 75.35; H, 5.35. Found: C, 75.39; H, 5.36.

2,8,14,20-Tetrakis(4-methylphenyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (24) (Run 20). Procedure III applied to resorcinol and 4-methylbenzaldehyde gave **24** (96%, reaction time, 68 h), 1 g of which dissolved in 150 mL of $(CH_3)_2NCHO$: ^1H NMR ($(CD_3)_2SO$) δ 2.24 (s, 12 H, $ArCH_3$), 5.59 (s, 4 H, Ar_3CH), 6.12 (s, 4 H, ArH, ortho to OH), 6.23 (bs, 4 H, ArH, meta to OH), 6.60 (d, J = 7.6 Hz, 8 H, ArH, meta to CH_3), 6.77 (d, J = 7.6 Hz, 8 H, ArH, ortho to CH_3), 8.46 (bs, 8 H, OH); MS (16 eV) m/e 848 (M^+, 100). Anal. Calcd for $C_{56}H_{48}O_8 \cdot 1.5H_2O$: C, 76.78; H, 5.98. Found (after drying 24 h at 150 °C and 10^{-5} Torr): C, 76.78; H, 5.85.

2,8,14,20-Tetrakis(4-bromophenyl)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-dodecaene-4,6,10,12,16,18,22,24-octol (Stereoisomer) (26) (Run 22). Procedure III applied to resorcinol and 4-bromobenzaldehyde gave **26** (reaction time 21 days). The amount of C_{4v} isomer of this compound varied dramatically with time and scale. A large scale reaction required 35 days for complete conversion to the C_{4v} isomer. Residual C_{2v} isomer was removed from the desired C_{4v} isomer by suspending the acid-free isomeric mixture in refluxing absolute ethanol for 1 h and filtering and mixture rapidly while hot. The C_{4v} isomer remained undissolved and gave a 43% yield; mp >390 °C: ^1H NMR ($(CD_3)_2SO$) δ 5.60 (s, 4 H, Ar_3H), 6.18 (s, 4 H, ArH, ortho to OH), 6.2–6.8 (vbs, 4 H, ArH, meta to OH), 6.57 (d, J = 8.1 Hz, 8 H, ArH, ortho to Br), 7.18 (d, J = 8.1 Hz, 8 H, ArH, ortho to Br), 8.68 (s, 8 H, OH); MS (16 eV) m/e 1108 ($M^+ + 4$, 34; 1:4:6:4:1 Br_4 isotope pattern centered as indicated). Anal. Calcd for $C_{52}H_{36}Br_4O_8 \cdot 1.5H_2O$: C, 54.57; H, 3.52. Found (after drying 24 h at 175 °C and 10^{-5} Torr): C, 54.58; H, 3.56.

Runs 23 to 29. In these runs (Table II) employing other aromatic aldehydes and resorcinol as starting materials, the products that precipitated from the reaction mixture were analyzed by ^1H NMR, making use of the differences of the resonances of the resorcinol-derived protons from the C_{4v} and C_{2v} isomers by analogy with the above differences in the two isomers of **26**.

Crystal Structures. Compound **2** crystallizes from CH_3CN as colorless platelets in the triclinic system $P\bar{1}$ as the solvate $2 \cdot 2.5CH_3CN \cdot 3H_2O$. Unit cell dimensions are as follows: a = 11.229 (1), b = 11.297 (1), and c = 15.078 Å, α = 74.996 (3)°, β = 87.087 (3)°, γ = 75.294 (4)°, V = 1793 Å^3, Z = 2. The crystal was examined on a modified Picker FACS-1 diffractometer, Mo K_α radiation, at 295 K. The structure was determined by direct methods. Refinement of 206 parameters (2917 reflections with $I > 3\sigma(I)$) has an agreement value, R, currently at 0.083. One acetonitrile is disordered about a crystallographic center of symmetry. Extensive hydrogen bonding links octols to water and to other octols.

Compound **5** crystallizes from ethanol/acetone as large colorless parallelepipeds in the monoclinic system $P2_1/n$ as the solvate $5 \cdot EtOH \cdot (CH_3)_2CO \cdot H_2O$. Unit cell dimensions are as follows: a = 14.446 (2), b = 21.705 (3), and c = 15.265 (2) Å, β = 106.848 (4)°, V = 4603 Å^3, Z = 4. The crystal was examined on a modified Picker FACS-1 diffractometer, Mo K_α radiation, at 295 K. The structure was determined by direct methods. Refinement of 296 parameters (5086 reflections with $I > 3\sigma(I)$) has an agreement value, R, currently at 0.068. Ethanol, water, and other octols are hydrogen bonded to each octol.

Further crystallographic details will be published elsewhere.

Registry No. **2**, 74708-10-4; **3**, 118600-17-2; **4**, 118600-18-3; **5**, 118600-19-4; **6**, 118629-59-7; **7**, 116780-43-9; **8**, 118600-20-7; **9**, 118600-21-8; **10**, 118629-60-0; **11**, 118629-61-1; **12**, 118600-22-9; **13**, 118600-23-0; **14**, 118600-24-1; **15**, 113379-32-1; **16**, 118655-57-5; **21**, 118600-25-2; **22**, 118600-26-3; **23**-C_{4v}, 74410-61-0; **23**-C_{2v}, 74378-21-5; **24**, 118600-27-4; **25**, 118600-36-5; **26**, 118600-28-5; **27**-C_{4v}, 118600-29-6; **27**-C_{2v}, 118711-36-7; **28**-C_{4v}, 118712-52-0; **28**-C_{2v}, 118600-30-9; **29**-C_{4v}, 118600-31-0; **29**-C_{2v}, 118711-37-8; **30**-C_{4v}, 118600-32-1; **30**-C_{2v}, 118712-53-1; **31**, 118600-33-2; **32**, 118600-34-3; **33**, 118600-35-4; 4-$CH_3OC_6H_4CHO$, 123-11-5; 4-$AcNHC_6H_4CHO$, 122-85-0; 4-$C_6H_5C_6H_4CHO$, 3218-36-8; 4-$HO_2CC_6H_4CHO$, 619-66-9; 4-NCC_6H_4CHO, 105-07-7; 4-$(CH_3)_3CC_6H_4CHO$, 939-97-9; resorinol, 108-46-3; dihydrocinnamaldehyde, 104-53-0; hexanal, 66-25-1; dodecanal, 112-54-9; ethanal, 75-07-0; propanal, 123-38-6; butanal, 123-72-8; pentanal, 110-62-3; 3-methylbutanal, 590-86-3; 5-hydroxypentanal, 4221-03-8; 6-chlorohexanal, 52387-36-7; phenylethanal, 122-78-1; 4-nitrodihydrocinnamaldehyde, 80793-24-4; 4-bromodihydrocinnamaldehyde, 80793-25-5; 2-methylresorcinol, 608-25-3; 2-nitroresorcinol, 601-89-8; *p*-anisaldehyde, 123-11-5; 4-ethylbenzaldehyde, 4748-78-1; benzaldehyde, 100-52-7; 4-methylbenzaldehyde, 104-87-0; 4-bromobenzaldehyde, 1122-91-4.