165. New Cyclophanes as Initiator Cores for the Construction of Dendritic Receptors: Host-Guest Complexation in Aqueous Solutions and Structures of Solid-State Inclusion Compounds

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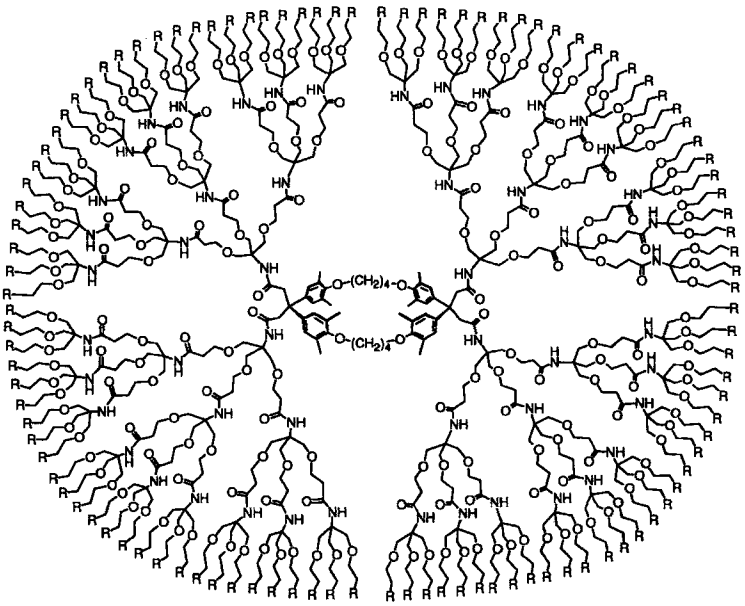
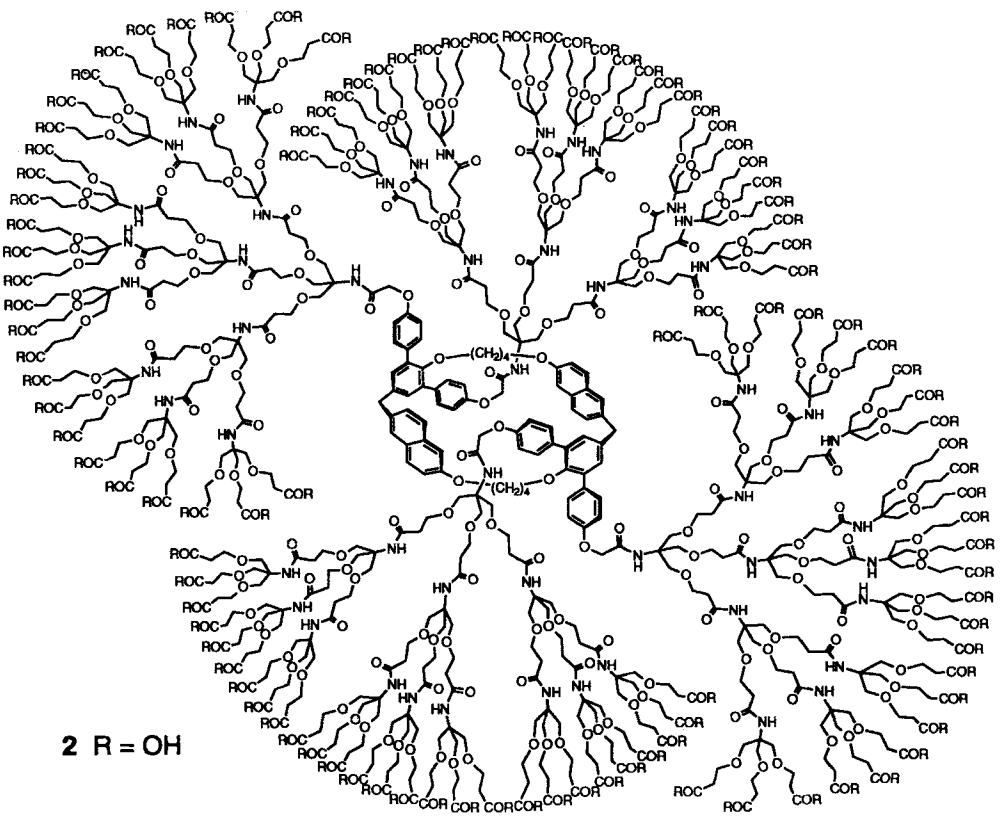
Cyclophanes **3** and **4** were prepared as initiator cores for the construction of dendrophanes (*dend*ritic cyclo*phanes*) **1** and **2**, respectively, which mimic recognition sites buried in globular proteins. The tetraoxy[6.1.6.1]paracyclophane **3** was prepared by a short three-step route (*Scheme 1*) and possesses a cavity binding site shaped by two diphenylmethane units suitable for the inclusion of flat aromatic substrates such as benzene and naphthalene derivatives as was shown by ^{1}H-NMR binding titrations in basic D_2O phosphate buffer (*Table 1*). The larger cyclophane **4**, shaped by two wider naphthyl(phenyl)methane spacers, was prepared in a longer, ten-step synthesis (*Scheme 2*) which included as a key intermediate the tetrabromocyclophane **5**. ^{1}H-NMR Binding studies in basic borate buffer in D_2O/CD_3OD demonstrated that **4** is an efficient steroid receptor. In a series of steroids (*Table 1*), complexation strength decreased with increasing substrate polarity and increasing number of polar substituents; in addition, electrostatic repulsion between carboxylate residues of host and guest also affected the binding affinity strongly. The conformationally flexible tetrabromocyclophane **5** displayed a pronounced tendency to form solid-state inclusion compounds of defined stoichiometry, which were analyzed by X-ray crystallography (*Fig. 2*). 1,2-Dichloroethane formed a cavity inclusion complex **5a** with 1:1 stoichiometry, while in the 1:3 inclusion compound **5b** with benzene, one guest is fully buried in the macrocyclic cavity and two others are positioned in channels between the cyclophanes in the crystal lattice. In the 1:2 inclusion compound **5c**, two toluene molecules penetrate with their aromatic rings the macrocyclic cavity from opposite sides in an antiparallel fashion. On the other hand, *p*-xylene (= 1,4-dimethylbenzene) in the 1:1 compound **5d** is sandwiched between the cyclophane molecules with its two Me groups penetrating the cavities of the two macrocycles. In the 1:2 inclusion compound **5e** with tetralin (= 1,2,3,4-tetrahydronaphthalene), both host and guest are statically disordered. The shape of the macrocycle in **5a–e** depends strongly on the nature of the guest (*Fig. 4*). Characteristic for these compounds is the pronounced tendency of **5** to undergo regular stacking and to form channels for guest inclusion; these channels can infinitely extend across the macrocyclic cavities (*Fig. 6*) or in the crystal lattice between neighboring cyclophane stacks (*Fig. 5*). Also, the crystal lattice of **5c** displays a remarkable zig-zag pattern of short Br ··· O contacts between neighboring macrocycles (*Fig. 7*).

1. Introduction. – Over the past two decades, water-soluble, nanometer-sized cyclophanes have attracted large interest as synthetic receptors for apolar substrates [1–3] and, after suitable functionalization, as artificial enzymes [4]. They contain wide open, solvent-exposed apertures by which hydrophobic guests penetrate, often in a nearly diffusion-controlled way [1b], into the binding site, and, therefore, possess model character for hydrophobic pockets and clefts at the surface of proteins. To improve the model character of these artificial receptors for binding sites that are more deeply buried within globular proteins, we recently took advantage of the rapidly developing dendrimer technology [5] and introduced cyclophane receptors as initiator cores into globular dendrimers [6]. The central recognition sites in the resulting dendrophanes (*dend*ritic cyclo*phanes*) such as the third-generation compounds **1** and **2** are spherically surrounded



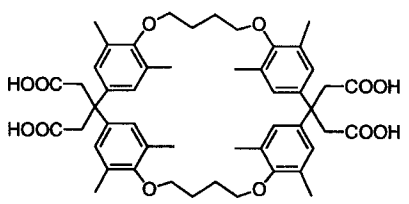
1 R = COOH

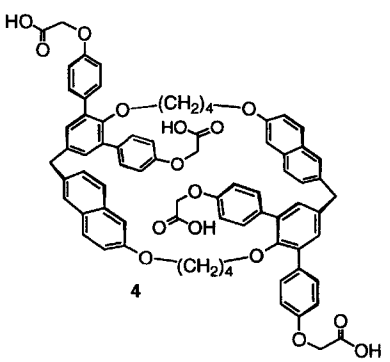


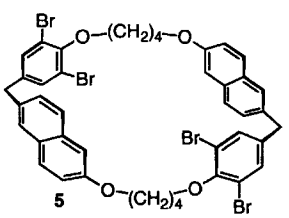
2 R = OH

by the dendritic branches which bear terminal carboxylate groups to ensure water solubility.

In this first paper in a series of two, we report the synthesis and binding properties of the new functionalized water-soluble cyclophanes **3** and **4** that serve as the initiator cores for the construction of the dendritic receptors [7–12] **1** and **2**. Whereas **3** complexes flat aromatic substrates [1], compound **4**, with its more spacious cavity, is suitable for the inclusion complexation of steroids [13–16]. We also describe the remarkable channel and clathrate-forming properties of tetrabromocyclophane **5**, a precursor to **4**. In the directly following paper [17], the synthesis of dendrophanes **1** and **2** by divergent and semi-convergent growth methodology is described, and the receptor properties of these macromolecules with molecular weight up to 20000 D are analyzed.

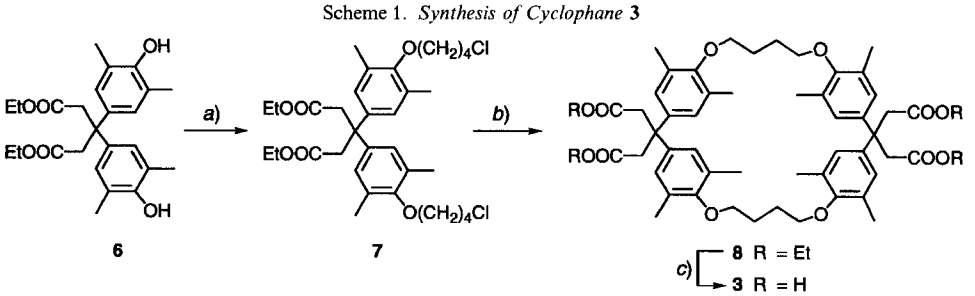






2. Results and Discussion. – 2.1. *Synthesis of Cyclophane* **3**. The synthesis of **3** (*Scheme 1*) closely followed a method previously described for the preparation of a bis[(1*H*-imidazol-1-yl)methyl]-substituted cyclophane that catalyzes the hydrolysis of activated esters [18]. The dichloro derivative **7** was cyclized (Cs_2CO_3/MeCN) with diphenol **6** [19] to give cyclophane tetraester **8** which was characterized by X-ray crystallogra-

Scheme 1. *Synthesis of Cyclophane* **3**

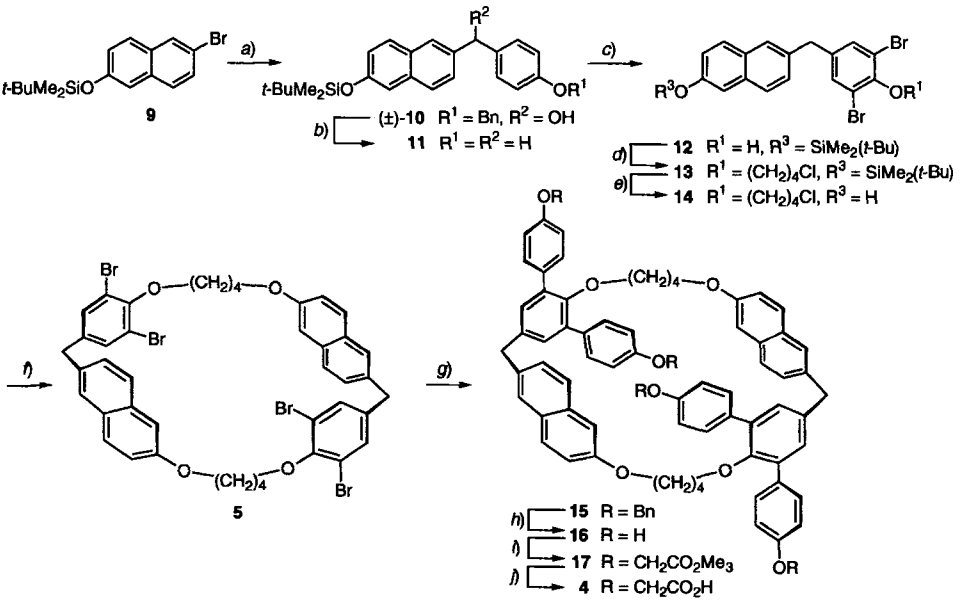


a) Cs_2CO_3, K_2CO_3, $Cl(CH_2)_4Cl$, DMF, 24 h, 90°; 46%. *b*) Cs_2CO_3, MeCN, 55 h, reflux; 25%. *c*) 20% aq. NaOH soln., MeOH/THF, 6 h, 90°; 56%.

phy [6b]. The crystal-structure analysis showed an open 8.0×9.5 Å wide rectangular cavity (distances between the centers of opposite benzene rings) suitable for the incorporation of flat aromatic substrates. Hydrolysis of **8** (NaOH/MeOH) afforded the initiator core **3** for the construction of dendrophanes.

2.2. *Synthesis of Cyclophane* **4**. The synthesis of initiator core **4** started with silyl-protected **9** (*Scheme 2*), which was prepared from 6-bromo-2-naphthol (*t*-BuMe$_2$SiCl, Et$_3$N, DMAP (= 4-(dimethylamino)pyridine)). *Grignard* addition to 4-(phenylmethoxy)-benzaldehyde [20] yielded alcohol (±)-**10** which was reduced by catalytic hydrogenation [21] to the naphthyl(phenyl)methane derivative **11**. Regiospecific *ortho*-bromination at low temperature [22] gave phenol **12** which was alkylated with a large excess of 1,4-dichlorobutane to yield **13**. Deprotection to naphthol **14** and macrocyclization afforded the poorly soluble tetrabromocyclophane **5**.

Scheme 2. *Synthesis of Cyclophane* **4**



a) Mg, THF, then 4-(phenylmethoxy)benzaldehyde, 12 h, r.t. *b*) H_2, 10% Pd/C, MeOH, 6 d, r.t.; 70% (from **9**). *c*) Br_2, *t*-BuNH$_2$, PhMe, 4 h, −40°. *d*) Cl(CH$_2$)$_4$Cl, K_2CO_3, acetone, 1 d, reflux. *e*) Bu$_4$NF, THF/CH_2Cl_2, 10 min, 0°; 69% (from **11**). *f*) Cs_2CO_3, MeCN, 5 d, 80°; 17%. *g*) [Pd(PPh$_3$)$_4$], 4-(phenylmethoxy)-phenylboronic acid, Na_2CO_3, PhMe/EtOH/THF/H_2O, 6 d, 80°; 77%. *h*) HCO_2NH_4, 10% Pd/C, MeOH/THF, 30 min, reflux; 98%. *i*) $BrCH_2CO_2Me$, K_2CO_3, DMF, 3 d, 70°; 63%. *j*) 1N aq. LiOH, THF/MeOH, 2 d, r.t.; 99%.

Four-fold Pd^0-catalyzed *Suzuki* cross-coupling [23] of **5** with 4-(phenylmethoxy)phenylboronic acid [24] gave **15** in 77% yield. Removal of the benzyl protecting groups by hydrogenolysis [25] provided tetraphenol **16** which was alkylated with methyl 2-bromoacetate in DMF to give tetraester **17**. Basic hydrolysis finally yielded the cyclophane initiator core, tetraacid **4**.

2.3. *Complexation of Apolar Substrates by Cyclophanes* **3** *and* **4** *in Aqueous Solutions.* ^{1}H-NMR Binding titrations at fast host-guest exchange were performed to determine the inclusion complexation properties of the new receptors **3** and **4**. Association constants K_a

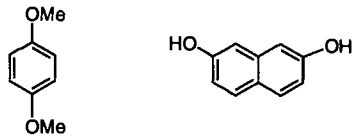
and binding free energies ΔG° were determined by nonlinear least-squares curve-fitting analysis [26] of the changes in chemical shift recorded for protons of the binding partner held at constant concentration during the titration. Concentration ranges were chosen to reach 70–90% saturation binding. The comparison of the binding properties of **3** and **4** to those of dendrophanes such as **1** and **2** was expected to clarify specific effects from dendritic branching on kinetics and thermodynamics of substrate inclusion at the dendritic core [17]. Since the complexation ability of [6.1.6.1]paracyclophanes such as **3** in aqueous solution is well-established [1][18], only a few binding titrations were performed with this receptor. The stability constants of the 1:1 complexes formed by 1,4-dimethoxybenzene (**18**; *Table 1, Entry 1*) and naphthalene-2,7-diol (**19**; *Entry 2*) in 0.066M phosphate buffer in D_2O (pD 8.4) containing 2.7% (*v/v*) $(CD_3)_2SO$ were found in the ranges expected from previous work. Inclusion complexation was indicated in each case by differential, complexation-induced upfield shifts of the guest protons, upfield shifts of the protons in the $-O(CH_2)_4O-$ bridges of the cyclophane, and a downfield shift of the aromatic resonance of **3** [1]. In the titrations, the shift of the aromatic resonance of **3** was evaluated which, in the complex of **19**, amounted to $\Delta\delta_{sat} = +0.29$ ppm at saturation binding. However, ^{1}H-NMR or fluorescence titration data with the fluorescence probe 6-toluidinonaphthalene-2-sulfonate (TNS) [17] could not be fitted to a 1:1 inclusion complexation model; presumably, the two aromatic moieties of this guest penetrate each a cyclophane cavity under formation of a 1:2 host-guest complex.

The complexation properties of receptor **4** could not be evaluated in a pure aqueous solution (0.2M borate buffer in D_2O, pD 10.5) due to significant self-aggregation [1]. In a 1:1 mixture of borate buffer in D_2O and CD_3OD, the self-association tendency was considerably reduced; nevertheless, some of the resonances of the 1,1′:3′1″-terphenyl moieties of **4** still showed concentration-dependent chemical shifts. Thus, in the concentration range between 0.1 and 4.0 mM, the aromatic resonances shifted upfield by 0.05–0.15 ppm. Therefore, we investigated the complexation of testosterone (**20**) by two ^{1}H-NMR titration modes in which either the concentration of the host or of the guest

Table 1. *Association Constants* K_a *and Complexation Free Enthalpies* ΔG° *Determined by* ^{1}*H-NMR Binding Titrations for Complexes of* **3** *and* **4**

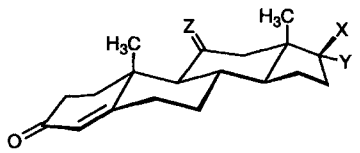
Entry	Host	Guest	Conditions	K_a [1 mol^{-1}]	ΔG° [kcal mol^{-1}][a]
1	**3**	**18**	[b] [c]	500	−3.7
2	**3**	**19**	[b] [c]	4300	−5.0
3	**4**	**20**	[d] [e]	1300	−4.2
4	**4**	**20**	[d] [f]	1350	−4.3
5	**4**	**21**	[d] [e]	1500	−4.3
6	**4**	**22**	[d] [e]	380	−3.5
7	**4**	**24**	[d] [e]	260	−3.3
8	**4**	**23**	[d] [e]	75	−2.6[g]
9	**4**	**25**	[d] [e]	40	−2.2[g]

[a]) Uncertainties in ΔG°: ±0.1 kcal mol^{-1}. [b]) In 0.066M phosphate buffer (pD 8.4) in $D_2O/(CD_3)_2SO$ 97.3:2.7; *T* 300 K. [c]) Constant [host] = 0.5–1.0 mM, variable [guest] = 0.25–2.5 mM. [d]) In a 1:1 mixture of basic 0.2 mM borate buffer (pD 10.5) in D_2O and CD_3OD; *T* 298 K. [e]) Constant [host] = 0.2–0.5 mM, variable [guest] = 0.4–5.0 mM. [f]) Constant [guest] = 0.37 mM, variable [host] = 0.15–2.87 mM. [g]) Values with higher uncertainties since only up to 40% saturation binding reached during the titration.

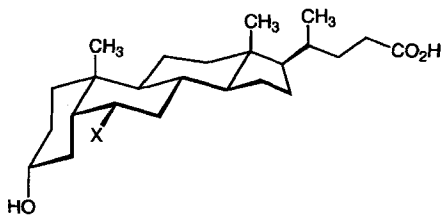


18

19



Steroid	X	Y	Z
20 testosterone	OH	H	H,H
21 progesterone	COMe	H	H,H
22 cortisone	$COCH_2OH$	OH	O
23 hydrocortisone	$COCH_2OH$	OH	β-OH,H



Steroid	X
24 lithocholic acid	H
25 hyodeoxycholic acid	OH

was kept constant (*Table 1*, *Entries 3* and *4*). If self-aggregation of **4** induced a significant error, different K_a values would probably be obtained by inverse titrations. However, both studies gave nearly identical results demonstrating that the weak self-aggregation of the receptor did hardly interfere with stoichiometric host-guest complexation. When the downfield shifts ($\Delta\delta_{sat} = +0.35$ to $+0.50$ ppm) of the aromatic 1,1′:3′,1″-terphenyl resonances *s*, d_1, and d_2 of **4** (*Fig. 1*) were evaluated in a titration at constant host concentration, a stability constant for the 1:1 complex with testosterone of $K_a = 1300 \pm 100\ l\ mol^{-1}$ was obtained (*Table 1*, *Entry 3*). In the inverse titration, at constant guest concentration, evaluation of the complexation-induced upfield shifts of the Me(19) ($\Delta\delta_{sat} = -0.81$ ppm) and Me(18) ($\Delta\delta_{sat} = -0.24$ ppm) resonances of **20** yielded $K_a = 1350\ l\ mol^{-1}$ for the formed 1:1 complex (*Entry 4*). The observed changes in chemical shift, in combination with *Corey-Pauling-Koltum* (CPK) molecular model examinations, suggest that testosterone is axially included in the cavity of **4** (*Fig. 1*) as had been previously proposed for steroid complexes of other cyclophane receptors shaped by two naphthyl(phenyl)methane units [14][27].

Remarkably, in the titration at constant host concentration, the signals *s*, d_1, and d_2 of **4**, after some broadening, started to split into a total of six sharp signals ($s \neq s'$, $d_1 \neq d_1'$, $d_2 \neq d_2'$) near saturation, indicating that the barrier of rotation about the biphenyl-type axes in the 1,1′:3′,1″-terphenyl moieties becomes slow on the NMR time scale as a result of the axial inclusion of testosterone. A linear *van't Hoff* regression analysis ($r^2 = 0.99$) of variable-temperature ^{1}H-NMR titrations at 293, 300, 307, and 314 K yielded $\Delta H^\circ = -5.0$ kcal mol^{-1} and $T\Delta S = -0.8$ kcal mol^{-1} (298 K) for the complexation of testosterone in D_2O buffer/CD_3OD 1:1 [13][14b], demonstrating the enthalpic driving force for the association process.

A series of ^{1}H-NMR titrations with various steroids revealed that cyclophane **4** discriminates efficiently between substrates of different polarity (*Table 1*, *Entries 3* and *5–9*) [14]. In these titrations at constant host concentration, the complexation-induced

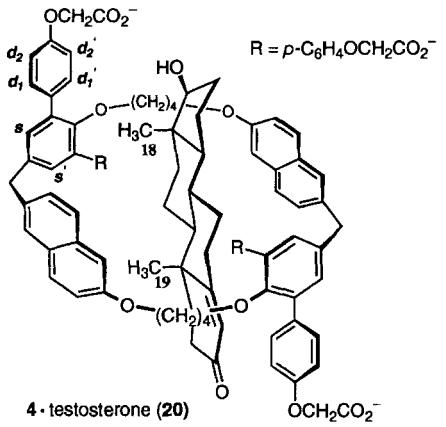


Fig. 1. *Schematic drawing of the axial inclusion complex of testosterone* (**20**) *with cyclophane* **4**. Protons that were monitored during ^{1}H-NMR binding titrations are labeled.

downfield shifts ($\Delta\delta_{sat}$ = + 0.36 and + 0.58 ppm) of the two aromatic resonances of the C_6H_4–OCH_2COO^- moieties of **4** were evaluated. Complexation strength decreased from progesterone (**21**), to testosterone (**20**), to cortisone (**22**), to lithocholate (**24**), to hydrocortisone (**23**), and to hyodeoxycholate (**25**). The stability of the inclusion complexes was lowered by increasing steroid polarity resulting from increasing numbers of polar substituents and by electrostatic repulsion [28] between the carboxylate residues of the binding partners.

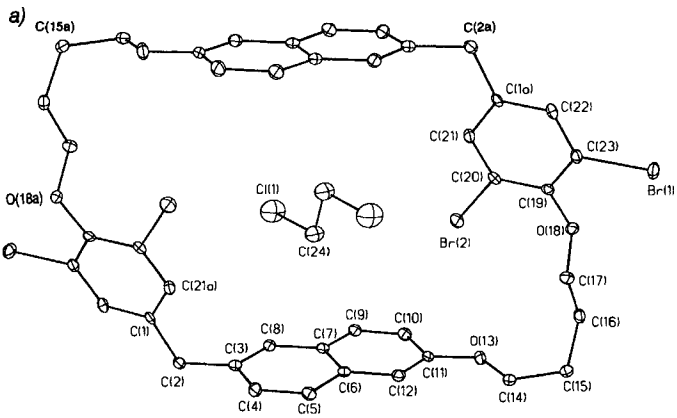
2.4. *X-Ray Crystal-Structure Analysis of Five Inclusion Compounds Formed by Tetrabromocyclophane* **5**. In crystalline inclusion complexes [29] of a macrocyclic host, a guest can be included intramolecularly within the cavity of the host or intermolecularly between host molecules in the crystal lattice. The former inclusion type resembles a classical host-guest complex whereas the latter is referred to as a clathrate [30–32]. The distinction between a molecular host-guest complex and a clathrate can be problematic, since macrocyclic receptors frequently not only shape an intramolecular cavity binding site for guest inclusion, but also assemble in the crystal in a way leading to cage-, layer-, or channel-type interstices for intermolecular guest incorporation. Such dual modes of crystalline guest inclusion are well documented for cyclodextrins [33], cyclophanes [34][35], and calixarenes [36].

Five crystalline inclusion compounds of different stoichiometry were obtained when cyclophane **5** was dissolved in various solvents and crystallization was induced by slow diffusion of hexane into these solutions. The inclusion compounds formed by 1,2-dichloroethane (→ **5a**) and *p*-xylene (1,4-dimethylbenzene; → **5d**) have 1:1 stoichiometry, those of toluene (→ **5c**) and tetralin (= 1,2,3,4-tetrahydronaphthalene; → **5e**) display 1:2 host-guest stoichiometry, and the one of benzene (→ **5b**) 1:3 host-guest stoichiometry. The molecular structures are depicted in *Fig. 2*, and the experimental details of the structure analyses are summarized in *Table 2*.

2.4.1. *Geometry of the Cyclophane*. In all five inclusion compounds, cyclophane **5** adopts a structure of a molecular box whose corners might be defined by the inversion-symmetry-related atom pairs C(2)/C(2a) and C(15)/C(15a) (for numbering, see *Fig. 2*).

Table 2. *Experimental Details of the X-Ray Diffraction Measurements for the Inclusion Compounds* **5a–e**

		5a	**5b**	**5c**	**5d**	**5e**
Empirical formula		$1/2(C_{42}H_{36}Br_4O_4)$ $1/2(C_2H_4Cl_2)$	$1/2(C_{42}H_{36}Br_4O_4)$ $1+1/2(C_6H_6)$	$1/2(C_{42}H_{36}Br_4O_4)$ (C_7H_8)	$1/2(C_{42}H_{36}Br_4O_4)$ $1/2(C_8H_{10})$	$1/2(C_{42}H_{36}Br_4O_4)$ $(C_{10}H_{12})$
Temperature of data collection [K]		138	188	230	218	148
Crystal dimensions [mm]		$\sim 0.3 \times 0.3 \times 0.3$	$\sim 0.2 \times 0.2 \times 0.25$	$\sim 0.2 \times 0.2 \times 0.2$	$\sim 0.2 \times 0.2 \times 0.2$	$\sim 0.4 \times 0.4 \times 0.5$
Space group		$P2_1/c$	$P\bar{1}$	$P\bar{1}$	$P2_1/n$	$P2_1/c$
Cell dimensions	a [Å]	12.663(4)	8.598(3)	10.029(2)	8.798(1)	11.772(8)
	b [Å]	12.775(6)	11.079(3)	10.520(3)	21.136(6)	9.320(4)
	c [Å]	13.257(7)	14.225(8)	12.590(3)	12.195(5)	24.858(11)
	α [°]	90	83.23(3)	78.26(2)	90	90
	β [°]	108.55(3)	75.70(4)	80.42(2)	90.41(2)	102.31(4)
	γ [°]	90	81.65(3)	70.67(2)	90	90
Formula weight		512.4	579.9	554.3	515.2	594.4
D_c [g/cm^3]		1.67	1.49	1.51	1.51	1.48
$2 \sin\theta/\lambda$ [Å^{-1}] max		1.10	1.15	1.28	1.15	0.96
Scan mode		ω/θ	ω/θ	ω/θ	ω/θ	ω/θ
No. of unique reflections		2811	4017	5298	3668	2456
No. of obs. reflections ($I > 3\sigma I$, **5a–d**) ($I > 2\sigma I$, **5e**)		2139	2732	3702	2318	1702
No. of variables in final least-square analysis		330	342	312	287	335
Type of refinement F		F	F	F	F	F
Exponentially modified weight factor r [Å^2]		5.0	5.0	5.0	5.0	5.0
Extinction correction		isotropic	isotropic	isotropic	isotropic	isotropic
R (F)		0.027	0.041	0.043	0.029	0.055
R_w (F)		0.035	0.047	0.050	0.036	0.067


a)
C(15a)
C(2a)
C(1a)
C(22)
C(21)
C(23)
C(20)
Br(1)
C(19)
O(18a)
Cl(1)
C(24)
Br(2)
O(18)
C(17)
C(21a)
C(9)
C(10)
C(16)
C(1)
C(8)
C(7)
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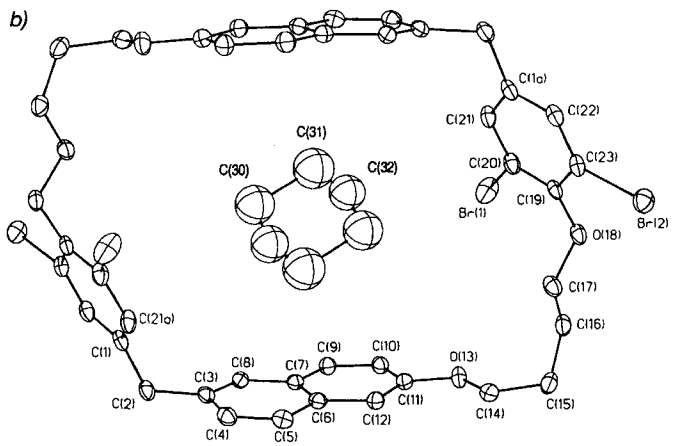
C(12)
C(15)
C(14)
C(4)
C(5)


b)
C(1a)
C(31)
C(21)
C(22)
C(30)
C(32)
C(20)
C(23)
Br(1)
C(19)
Br(2)
O(18)
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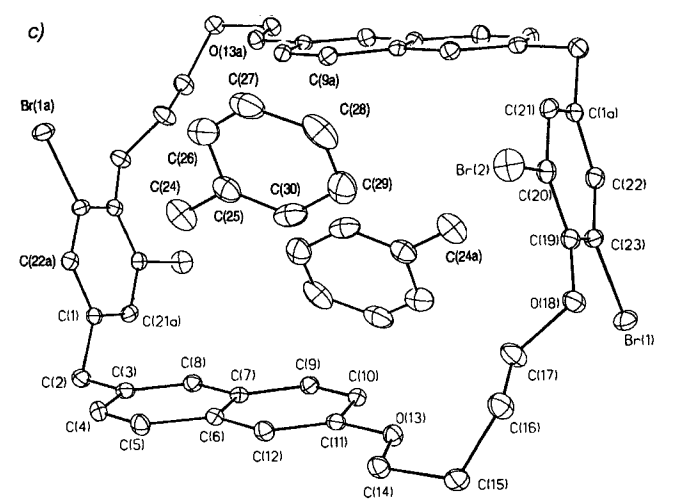
C(15)
C(14)
C(4)
C(5)


c)
O(13a)
C(27)
C(9a)
Br(1a)
C(28)
C(21)
C(1a)
C(26)
Br(2)
C(24)
C(30)
C(29)
C(22)
C(25)
C(20)
C(19)
C(24a)
C(23)
C(22a)
O(18)
C(1)
C(21a)
Br(1)
C(17)
C(2)
C(3)
C(8)
C(7)
C(9)
C(10)
C(4)
O(13)
C(16)
C(5)
C(6)
C(11)
C(12)
C(14)
C(15)

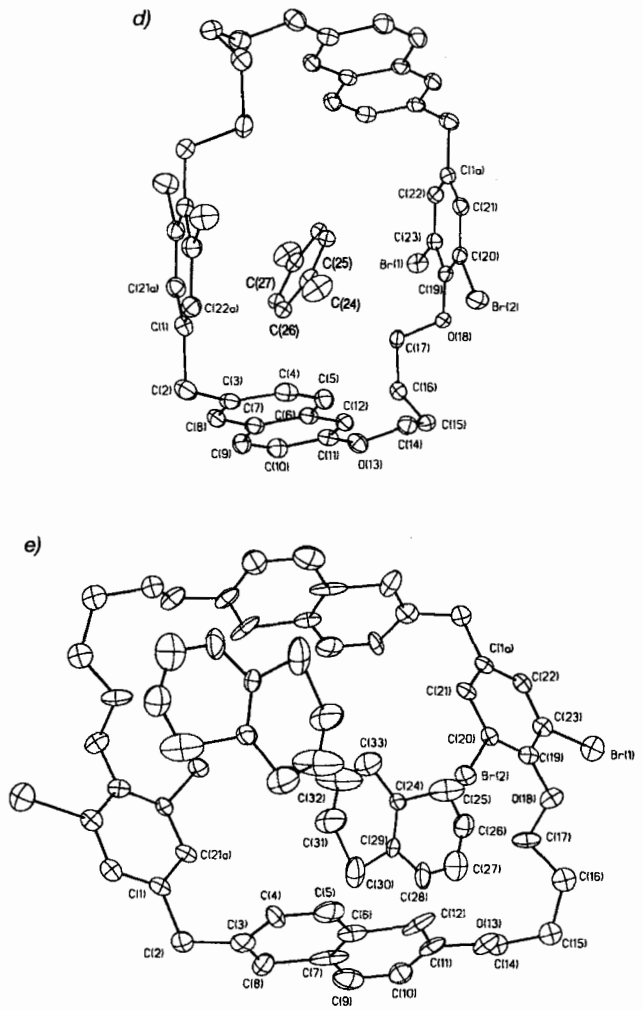


Fig. 2. *Molecular structures of inclusion compounds* **5a–e** *in views on the best plane through the cyclophane skeleton.* Arbitrary numbering; displacement ellipsoids are shown at the 30% probability level. In structure **5b**, the benzene at the center is highly disordered, and the two benzene molecules outside the cavity (see. *Fig. 5*) are omitted for clarity.

The edges of the box are separated by nearly equal distances in four of the five structures: the distances C(2) ··· C(15) and C(15) ··· C(2a) in **5a–c** and **5e** amount to *ca.* $10.0 \times 9.0 \pm 0.1$ Å; only the box in the *p*-xylene clathrate **5d** is slightly smaller (10.1×8.5 Å; see below). The distance O(13) ··· O(18a), which characterizes the opening of the naphthyl(phenyl)methane spacers, is also similar in all five structures and varies between 11.2 and 11.8 Å. There is no particular strain in the macrocycle, and bond angles adopt regular and characteristic values in all five inclusion compounds (*Fig. 3*). All bond lengths, except in the disordered structure of **5e**, are also in the expected ranges.

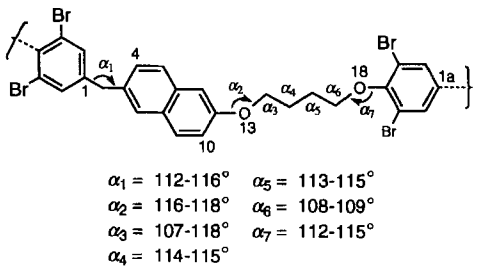


Fig. 3. *Characteristic bond angles of cyclophane* **5** *in the inclusion compounds* **5a**–**d**. The values of the less accurate structure of **5e** are omitted. For numbering, see *Fig. 2*.

Although the dimensions of the cyclophane box, as defined above, are similar in all structures, size and shape of the cyclophane cavity vary substantially among the various inclusion compounds (*Fig. 4*).

An analysis of the dihedral angles (*Table 3*) shows that the similar edge dimensions of the cyclophane box are mainly the result of similar conformations of the bridging $-O(CH_2)_4O-$ chains, whereas the differences in size and shape of the cyclophane cavity are predominantly determined by the conformation of the aromatic rings in the naphthyl(phenyl)methane spacers. In all structures, the first two dihedral angles ϕ_3 and ϕ_4 in the bridges are antiperiplanar (*ap*) which leads to a nearly identical box length C(2) $\cdots$ C(15) of *ca.* 10.0 $\pm$ 0.1 Å. The other dihedral angles $\phi_5-\phi_9$ have similar absolute values in **5a**–**c**, with a sequence of *sc-sc-ap-ap-sc* relationships (*sc* = synclinal), yielding *ca.* 9.0 $\pm$ 0.1 Å for the second edge (C(15) $\cdots$ C(2a)) of the box. In the *p*-xylene clathrate **5d**, a sequence of three *sc* conformations ($\phi_5-\phi_7$) leads to the shortening of the box dimension by *ca.* 0.5 Å. The *gauche* dihedral angle ϕ_9 (78–97°) in all structures results from the steric interactions between $H_2C(17)$ and the two *o*-bromo substituents on the adjacent benzene ring; similar dihedral angles are also observed in the crystal structures of other, structurally related cyclophane hosts with *o*-disubstituted aromatic rings, such as **8** [6b][37].

In contrast to the conformations of the bridges, those of the aromatic rings in **5**, as defined by the dihedral angles ϕ_1 and ϕ_2 (*Table 3*), differ substantially among the various structures. Thus, the two dibromobenzene rings in **5a** (and in **5e**; values not given here) are largely turned into the cavity ($\phi_1 = -19°$), leading to a sizeable reduction in free cavity space (*Fig. 4*). As a result of the different orientations of the aromatic rings, the macrocyclic cavity adopts either open rectangular (**5c**) or square (**5b** and **5d**) shapes or nearly closed ones (**5a** and **5c**) (*Fig. 4*). A rough estimate of the reduction in question can be obtained by comparing the orthogonal distances between the mean planes of the two naphthalene rings (A_1) and the mean planes of the two phenyl rings (A_2), which vary from $A_1 \times A_2 = 6.4 \times 11.3$ Å (**5c**), to 8.9×9.4 Å (**5b**), to 8.1×8.8 Å (**5d**), to 8.5×5.0 Å (**5a**), and to 8.6×5.5 Å (**5e**).

2.4.2. *Host-Guest Interactions in the Inclusion Compounds.* A full guest inclusion in the macrocyclic cavity is observed for 1,2-dichloroethane in **5a** and for one of the three benzene molecules in **5b**. The other guests either penetrate the cavity of **5** only partially or are located, in a clathrate-type fashion, entirely outside the cavity. In **5a** (*Fig. 2,a*), the two dibromobenzene rings of the macrocycle are turned into the cavity, reducing its size

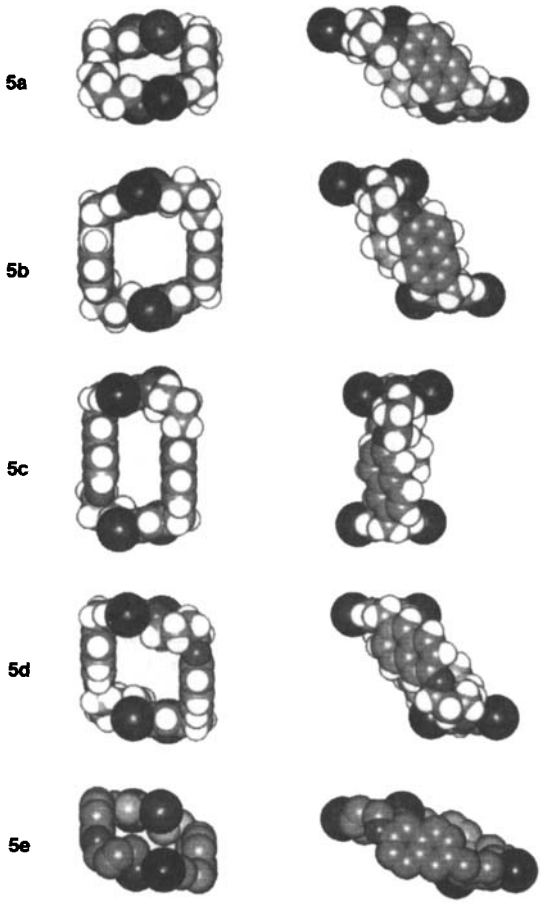
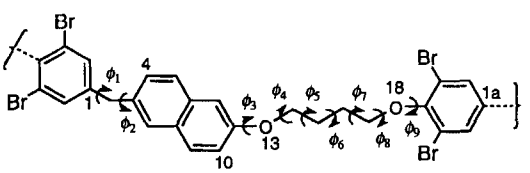


Fig. 4. *CPK Model representations of cyclophane* **5** *in the five inclusion compounds* **5a**–**e** *showing the different shapes of the cavity*. On the left side, the view is approximately parallel to the four aromatic-ring planes. On the right side, the view is approximately parallel to the dibromobenzene-ring planes. The Br-atoms are shown in dark, the H-atoms in light shading. The H-atoms in the tetralin clathrate were not refined and are not shown.

Table 3. *Characteristic Dihedral Angles* θ [°] *in Inclusion Compounds* **5a**–**d**. The less accurate data for the tetralin derivative **5e** are omitted. For numbering, see *Fig. 2*.

	ϕ_1	ϕ_2	ϕ_3	ϕ_4	ϕ_5	ϕ_6	ϕ_7	ϕ_8	ϕ_9
5a	−19	87	178	−173	52	58	−171	163	97
5b	−49	84	177	−178	64	60	168	156	−90
5c	−80	129	−175	178	68	−58	−162	−155	−78
5d	−122	64	171	−166	58	62	65	180	−84



to fit the small guest. Short intermolecular C–H $\cdots$ π contacts [38] exist between the CH_2 groups of the guest and the naphthalene rings (C(24) $\cdots$ C(7) = 3.56 Å); additional short Cl $\cdots$ H–C contacts, which can be considered as very weak H-bonds [39][40], are observed between the two Cl-atoms of the guest and naphthalene H–C groups (Cl(1) $\cdots$ C(8) = 3.73 Å, Cl(1) $\cdots$ C(21a) = 3.71 Å).

A disordered benzene molecule occupies the center of the nearly square cyclophane in **5b** (*Fig. 2,b*), whereas two ordered ones (related by inversion symmetry) are located between neighboring cyclophane stacks (*Fig. 5*). The cavity of **5** shaped by two naphthyl(phenyl)methane units apparently is too large to provide high geometric complementarity to the enclosed benzene molecule which, therefore, is disordered. In contrast, an ordered benzene molecule was previously found at the center of the cavity in a smaller tetraoxo[6.1.6.1]paracyclophane, which is shaped by two diphenylmethane spacers and structurally closely related to **3** [34]. The clathrated benzene molecules in **5b** undergo parallel-shifted stacking along the channel axis (shortest C $\cdots$ C distance, 3.34 Å) and are involved in C–H $\cdots$ π interactions with the naphthalene rings of neighboring cyclophanes.

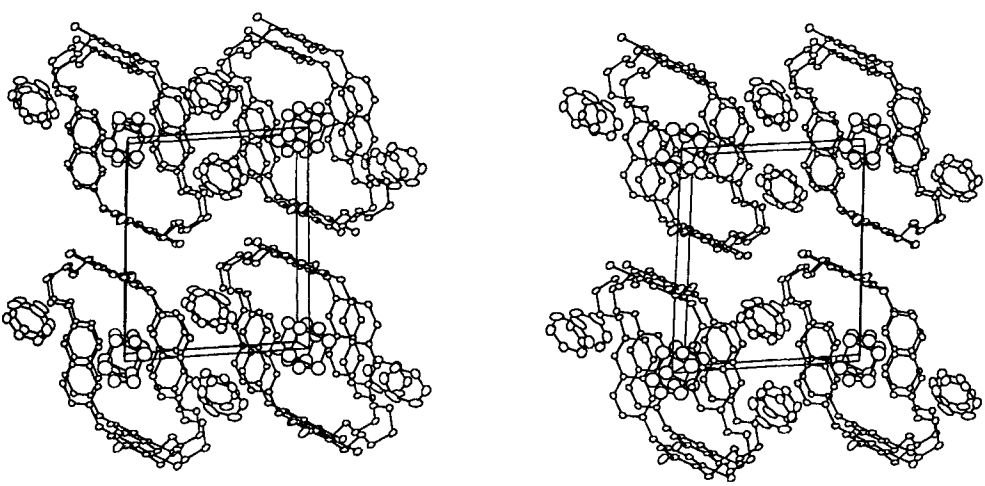


Fig. 5. *Crystal packing of the 1:3 benzene inclusion compound* **5b** *viewed along the* a*-axis*

Two antiparallel toluene molecules, related by inversion symmetry, penetrate the cyclophane cavity from opposite sides in inclusion compound **5c** (*Fig. 2,c*). Whereas they do not show short intermolecular contacts among themselves, they undergo weak C–H $\cdots$ π interactions with the macrocycle, *i.e.*, the toluene rings interact with the naphthalene protons (C(25) $\cdots$ C(9a) = 3.69 Å (C $\cdots$ H–C angle, 125°)) and their Me groups are directed towards the π-electron cloud of the dibromobenzene moieties of **5** (C(24) $\cdots$ C(22a) = 3.70 Å).

The cyclophane molecules in **5d** (*Fig. 2,d*) stack along the *a*-axis, leading to typical channels (*Fig. 6*) [35b,c][38b][41], and the *p*-xylene guest is sandwiched between adjacent cyclophane molecules in the stack. The two Me groups of *p*-xylene penetrate into the cavities of two sandwiching hosts. A very similar structure had previously been

found for the 1:1 inclusion compound of *p*-xylene with a smaller tetraoxa[6.1.6.1]paracyclophane already mentioned above [34]. In **5d**, there are no short C ··· C contacts (< 4.0 Å) between host and guest, whereas the two *p*-xylene Me groups, which penetrate from opposite sides into a cavity, are approximately at *van der Waals* distance ($H_3C \cdots CH_3$ = 3.8 Å).

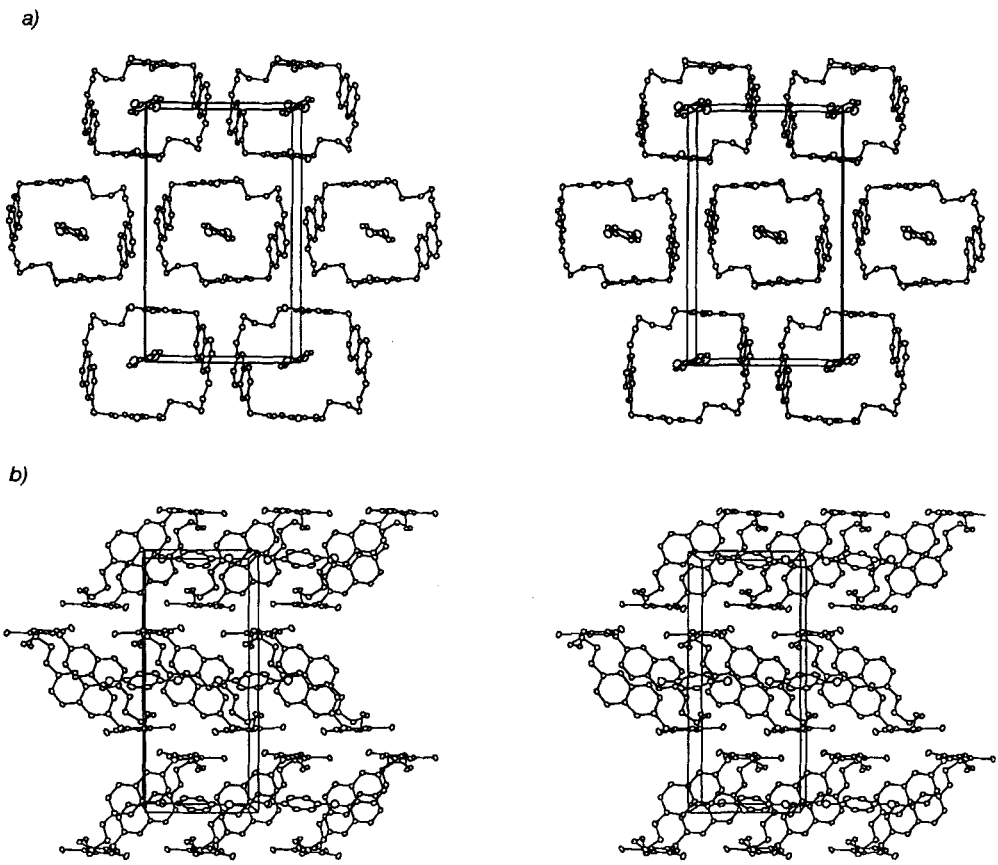


Fig. 6. *Crystal packing of the 1:1 inclusion compound* **5d** *with* p-*xylene viewed* a) *along the* a-*axis and* b) *along the* c-*axis*

In the 1:2 inclusion compound **5e** with tetralin (*Fig. 2,e*), both cyclophane and guest molecules are statically disordered. Two tetralin molecules in symmetry-related antiparallel orientations approach the narrow cavity of macrocycle **5** from opposite sides. The extensive disorder in the tetralin molecules did not permit to differentiate unambiguously between the alicyclic and the aromatic rings and, therefore, the intermolecular host-guest contacts cannot be discussed with confidence.

2.4.3. *Crystal Packing*. The regular stacking of the macrocycles generates characteristic channel structures in all five inclusion compounds. This is nicely illustrated in *Fig. 6* for **5d**, in which *p*-xylene occupies the channel formed by the stacking macrocycles. In this inclusion compound, the stacking macrocycles fill the space in the crystal lattice

efficiently, not leaving interstices for additional guest inclusion. Characteristic contacts between neighboring stacks include $\pi \cdots \pi$ stacking between parallel shifted naphthalene rings, the shortest intermolecular C $\cdots$ C distance being *ca.* 3.50 Å. Short intermolecular π-π contacts are also observed in **5a–c** between the dibromobenzene rings (C $\cdots$ C distances between 3.48 and 3.59 Å) and the naphthalene rings (C $\cdots$ C distances between 3.44 and 3.86 Å) of neighboring macrocycles.

In contrast to **5d**, the stacked macrocycles in **5b** (*Fig. 5*) not only generate channels for benzene inclusion that extend across the macrocyclic cavities, but also channels for benzene inclusion between stacks of the cyclophane.

Of particular interest was the crystal lattice of the toluene inclusion compound **5c**. *Fig. 7* shows a layer of cyclophane molecules viewed along the direction of the *a*-axis. In addition to the intermolecular aromatic π-π contacts mentioned above, each cyclophane undergoes four identical Br $\cdots$ O interactions [39] (two symmetry-related pairs) to two neighboring molecules. The contacts Br(1) $\cdots$ O(13a′) and O(13) $\cdots$ Br(1a′) as well as Br(1a) $\cdots$ O(13″) and O(13a) $\cdots$ Br(1a″) generate a zig-zag pattern along the *c*-axis. The C–Br $\cdots$ O angles are 168°, and the Br $\cdots$ O distance (3.12 Å) is smaller than the sum of the *van der Waals* radii of O (1.52 Å) and Br (1.85 Å) [42]. These observations are in agreement with those made by *Hassel* and coworkers for Br $\cdots$ O contacts seen in adducts between Br_2 and MeOH [43a], Br_2 and 1,4-dioxane [43b], and oxalyl bromide and 1,4-dioxane [43c]; in these associations, the Br $\cdots$ O distances vary between 2.7 and 3.2 Å. More recent work has shown that short contacts between O- or N-atoms on one side and the halogen atoms Cl, Br, or I on the other are observed quite frequently in crystals and are attributed to polarization effects between these atoms [44]. Such contacts have also been described by means of electron donor-acceptor interactions [45].

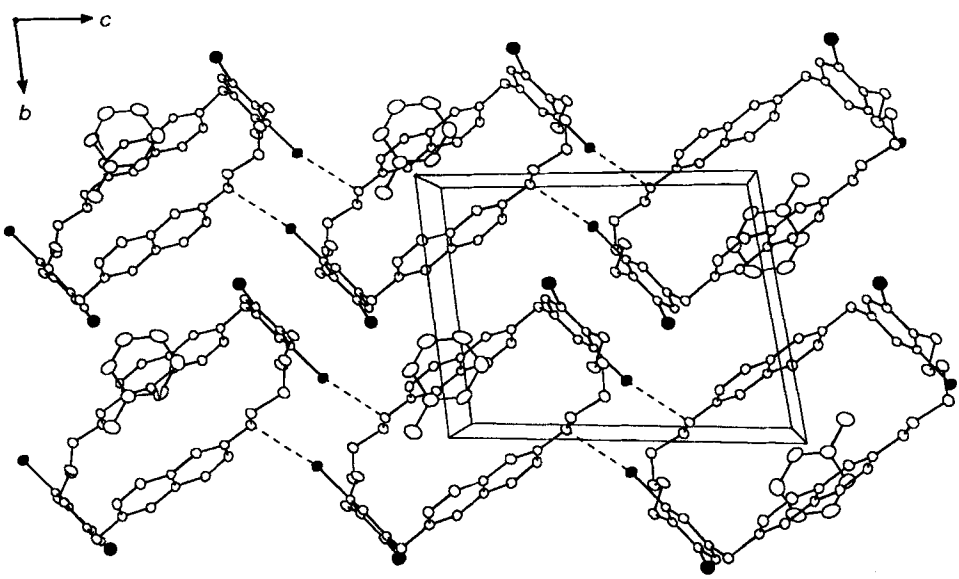


Fig. 7. *Crystal packing of the 1:2 inclusion compound* **5c** *with toluene viewed along the* a*-axis.* Only one of the two toluene molecules is shown for clarity. Br-Atoms are shown in dark.

The reasons why the conformation of cyclophane **5** and the mode of guest inclusion vary so much in the present compounds remain unclear. Macrocycle **5** is too large for a tightly fitting 1:1 cavity inclusion complexation with any of the guests of this study. Furthermore, it is highly flexible, and it can be assumed that both the energetics of the particular guest-inclusion modes as well as crystal-lattice effects largely determine its geometry. This was readily shown by computer modeling. Monte Carlo (MC) searches of conformational space using MacroModel v. 5.0 [46] were executed for free **5** with the AMBER* or MM2* force fields [47] in the gas phase or by using the GB/SA solvation model for $CHCl_3$ [48]. Starting geometries were either a constructed model of **5** with an open cavity or the structure of **5** in the benzene inclusion complex **5b**. In each search, up to 50 conformers were found within 3.0 kcal mol^{-1} of the global minimum, underlining the high conformational flexibility of the cyclophane. According to the MC searches (1000 to 10000 steps) with AMBER* in the gas phase and in $CHCl_3$ as well as with MM2* in the gas phase, fully collapsed structures are the only contributors to the *Boltzmann* distribution of populated conformers at room temperature. Macrocyclic collapse in these computed structures occurred in a way to generate short π-π contacts (shortest C $\cdots$ C distances between 3.4 and 3.8 Å) either between the naphthalene and dibromobenzene rings or between the naphthalene rings of opposite naphthyl-(phenyl)methane units. In these searches, geometries of **5** with an open cavity such as those observed in the inclusion compounds were only found at much higher energy ($>>$ 5 kcal mol^{-1}). Only the MC search with the MM2* force field in $CHCl_3$ showed at *ca.* 2 kcal mol^{-1} above the global minimum open geometries resembling those seen in the inclusion compounds. In view of the conformational flexibility of **5** and its size, more extended computational attempts to rationalize the formation of the observed solid-state structures **5a–e** [49] do not seem appropriate at this stage.

3. Conclusion. – With the two cyclophanes **3** and **4** bearing four divergent carboxylate side chains, ideal initiator cores for the construction of dendrophanes were prepared. Their incorporation into globular dendrimers of various generations, such as the third-generation derivatives **1** and **2** is reported in the directly following paper [17]. ^{1}H-NMR Binding titrations in basic aqueous buffers confirmed the expected tendency of the smaller derivative **3** to form cavity inclusion complexes with flat benzene and naphthalene derivatives and of the larger macrocycle **4** to axially incorporate steroidal substrates. Tetrabromocyclophane **5**, a precursor in the synthesis of **4**, showed a high propensity to form inclusion complexes of varying stoichiometry in the solid state, which were studied by X-ray crystallography. In the solid-state structures, the box-type macrocycles form regular stacks which, in return, generate two kinds of channels for guest inclusion. One type of channel extends within a stack of cyclophanes across the macrocyclic cavities, and a second type is formed between cyclophane stacks in the crystal lattice. Different guest inclusion modes were observed in the X-ray crystal structures, varying from full cavity inclusion (1,2-dichloroethane, benzene) to partial cavity inclusion (toluene, *p*-xylene, tetralin), to clathrate-type lattice inclusion (benzene). Macrocycle **5** is highly flexible and changes its shape as a function of the nature of the guest and the energetics of the crystal packing. The size of the macrocyclic cavity is adjusted largely by conformational changes of the aromatic rings which can turn substantially into the cavity, thereby reducing its size. The main host-guest as well as host-host interactions

in the inclusion compounds are π-π stacking and C–H $\cdots$ π interactions, the 1:2 inclusion compound with toluene displaying additional short intermolecular Br $\cdots$ O contacts between neighboring cyclophanes. In contrast to the more or less open cavities seen in the X-ray crystal structures of the inclusion compounds, computer modeling of individual molecules of **5** (gas phase or in $CHCl_3$) showed a high preference for fully collapsed conformations with a closed macrocyclic cavity in the absence of suitable guest molecules. These findings demonstrate nicely the importance of guest and crystal packing effects for the macrocyclic geometries found in the solid state.

Experimental Part

General. Reagents and solvents were reagent-grade commercials and were used without further purification. THF, Et_2O, and PhMe were freshly distilled from sodium benzophenone ketyl; CH_2Cl_2 was distilled over CaH_2. For cyclization reactions, MeCN (*p.a.*) was dried over molecuar sieves (3 Å). Evaporation was done at water-aspirator pressure and drying under high vacuum (h.v.) at $5 \cdot 10^{-5}$ Torr. Column chromatography: SiO_2 *60* (230–400 mesh, 0.040–0.063 mm) from *E. Merck*. Thin layer chromatography (TLC): plastic sheets precoated with SiO_2 *G* UV_{254} from *Macherey-Nagel* and glass-backed SiO_2 *60* F_{254} from *Merck*, visualization by UV light. Melting points: *Büchi Smp-20*; uncorrected. UV/VIS Spectra: *Varian-Cary-5* spectrophotometer; λ_{max} in nm (log ε). IR Spectra (cm^{-1}): *Perkin-Elmer 1600-FTIR*. NMR Spectra: *Bruker AM 500* (^{13}C) and *Varian Gemini 300* or *200* (^1H) at 296 or 300 K; Me_4Si or solvent peaks as reference. EI-MS: *Hitachi-Perkin-Elmer-RMU-6M* spectrometer; 70 eV. FAB-MS (*m/z* (%)): *VG-ZAB-2-SEQ* instrument; 3-nitrobenzyl alcohol as matrix and positive-ion mode if not indicated otherwise. Elemental analyses were performed by the 'Mikrolabor' at the Laboratorium für Organische Chemie, ETH-Zürich.

^1H-NMR Binding Titrations. Deuterated borate buffer (pD 10.5) for the titrations was prepared as described [50a]. Deuterated phosphate buffer (pD 8.4) was prepared by mixing 0.066M aq. KH_2PO_4 (5.5 ml) and 0.66M aq. Na_2HPO_4 (94.5 ml) [50b]. H/D Exchange of the buffer occurred by evaporation of the aq. buffer soln. (50 ml) followed by three cycles of dissolution of the residue in D_2O and evaporation. At the end, the residue was dissolved in D_2O (50 ml, 99.8% D-atoms) [50a]. Preparation of samples for the titrations and evaluation of the titration data [26] were done according to published protocols [14b] [51].

Diethyl 3,3-Bis[4-(4-chlorobutoxy)-3,5-dimethylphenyl]pentanedioate (**7**). A stirred mixture of **6** (20 g, 47 mmol), Cs_2CO_3 (30 g, 92 mmol), K_2CO_3 (28 g, 0.2 mol), and 1,4-dichlorobutane (110 ml) in DMF (100 ml) was heated to 90° for 24 h. The formed precipitate was filtered off, the solvent was evaporated, and the resulting oil dissolved in CH_2Cl_2 and washed with H_2O. Evaporation and chromatography (SiO_2, CH_2Cl_2) afforded **7** (13.2 g, 46%). Colorless viscous oil. ^1H-NMR (300 MHz, $CDCl_3$): 0.94 (*t*, *J* = 7.0, 6 H); 1.85–2.05 (*m*, 8 H); 2.18 (*s*, 12 H); 3.41 (*s*, 4 H); 3.64 (*t*, *J* = 6.0, 4 H); 3.75 (*t*, *J* = 5.9, 4 H); 3.85 (*q*, *J* = 7.0, 4 H); 6.72 (*s*, 4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.93; 16.52; 27.84; 29.51; 42.51; 44.94; 46.00; 59.79; 71.08; 127.83; 129.73; 141.44; 154.07; 171.59. FAB-MS: 608.1 (14, M^+).

Tetraethyl 5,14,20,21,29,32,33,37-Octamethyl-7,12,22,27-tetraoxapentacyclo[26.2.2.2^{3,6}.2^{13,16}.2^{18,21}]octatriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-2,2,17,17-tetraacetate (**8**). A soln. of **6** (4.21 g, 9.84 mmol) and **7** (6.0 g, 9.84 mmol) in MeCN (200 ml) was added dropwise over 7 h to a refluxing suspension of Cs_2CO_3 (10.6 g, 32.5 mmol) in dry MeCN (800 ml). After heating to reflux for 48 h and cooling, the formed precipitate was filtered off and the resulting oil chromatographed (SiO_2, CH_2Cl_2/AcOEt 96:4): **8** (2.5 g, 25%). Colorless powder which was recrystallized from AcOEt. M.p. 210°. IR (KBr): 3428*w*, 2950*m*, 1732*s*, 1590*w*, 1484*s*. ^1H-NMR (200 MHz, $CDCl_3$): 0.90 (*t*, *J* = 7.1, 12 H); 1.90–1.20 (*m*, 8 H); 2.11 (*s*, 24 H); 3.43 (*s*, 8 H); 3.75–3.90 (*m*, 16 H); 6.65 (*s*, 8 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 13.63; 16.37; 26.76; 41.62; 45.30; 59.54; 71.87; 127.34; 129.42; 141.30; 153.53; 171.29. FAB-MS: 965.4 (M^+). Anal. calc. for $C_{56}H_{76}O_{12}$ (965.23): C 72.17, H 7.94, O 19.89; found: C 71.68, H 7.63, O 20.03. X-Ray: see [6b].

5,14,20,21,29,32,33,37-Octamethyl-7,12,22,27-tetraoxapentacyclo[26.2.2.2.^{3,6}.2^{13,16}.2^{18,21}]octatriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-2,2,17,17-tetraacetic Acid (**3**). A suspension of **8** (0.15 g, 0.155 mmol) in 20% aq. NaOH soln. (1.5 ml), MeOH (4 ml), and THF (1.5 ml) was heated to 90°. After stirring for 6 h at 90° and cooling, the org. solvents were evaporated. The residual aq. soln. was acidified with 6M HCl and extracted with Et_2O (3 ×), the combined org. phase dried ($MgSO_4$) and evaporated, and the residue recrystallized from MeOH: **3** (72 mg, 56%). Colorless powder. M.p. > 275°. IR (KBr): 3000 (br.), 2929*m*, 1733*s*, 1704*s*, 1485*m*. ^1H-NMR (200 MHz, $(CD_3)_2SO$): 1.80–1.90 (*m*, 8 H); 2.06 (*s*, 24 H); 3.41 (*s*, 8 H); 3.70–3.80 (*m*, 8 H); 6.76

(*s*, 8 H); 11.85 (br. *s*, 4 H). ^{13}C-NMR (50 MHz, $(CD_3)_2SO$): 16.09; 25.88; 43.83; 71.15; 126.58; 128.71; 141.60; 152.98; 172.16 (1 peak masked by solvent peak). FAB-MS: 852.3 (M^+). Anal. calc. for $C_{50}H_{60}O_{12}$ (853.02): C 70.40, H 7.09, O 22.51; found: C 70.24, H 7.36, O 22.26.

[(6-Bromonaphthalen-2-yl)oxy](1,1-dimethylethyl)dimethylsilane (**9**). To a soln. of 6-bromonaphthalen-2-ol (60.0 g, 269 mmol) and DMAP (366 mg, 3.0 mmol) in dry Et_3N (81.0 g, 800 mmol) and CH_2Cl_2 (100 ml), a soln. of *t*-BuMe_2SiCl (42.5 g, 282 mmol) in CH_2Cl_2 (100 ml) was added dropwise over 5 min while the temp. was kept below 30°. After stirring for 16 h at r.t., CH_2Cl_2 (400 ml) was added, the soln. washed successively with sat. aq. solns. (800 ml each) of NH_4Cl, $NaHCO_3$ (800 ml), and NaCl, dried (Na_2SO_4), and evaporated, and the residue recrystallized from MeOH (500 ml): **9** (81.6 g, 90%). Colorless platelets. R_f 0.74 (SiO_2, hexane/AcOEt 10:1). M.p. (MeOH): 63.0–63.5. IR ($CHCl_3$): 3018*m*, 2958*m*, 2886*w*, 2859*m*, 1626*m*, 1589*s*, 1495*s*, 1464*m*, 1364*m*, 1329*w*, 1270*s*, 1260*s*, 1150*m*, 1119*w*, 1058*w*, 1000*w*, 970*s*, 924*s*, 848*s*, 838*s*, 796*s*, 790*s*. ^{1}H-NMR (500 MHz, CD_3OD): 0.30 (*s*, 6 H); 1.07 (*s*, 9 H); 7.16 (*dd*, *J* = 8.8, 2.4, 1 H); 7.25 (*d*, *J* = 2.4, 1 H); 7.53 (*dd*, *J* = 8.8, 2.0, 1 H); 7.68 (*d*, *J* = 8.8, 1 H); 7.75 (*d*, *J* = 8.8, 1 H); 8.00 (*d*, *J* = 2.0, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): −4.34; 18.25; 25.63; 114.89; 117.28; 123.08; 128.32; 128.44; 129.42; 129.60; 130.28; 133.09; 153.90. EI-MS: 338 (40, M^+), 281 (100, $[M - C_4H_9]^+$). Anal. calc. for $C_{16}H_{21}BrOSi$ (337.33): C 56.97, H 6.27, Br 23.69; found: C 57.10, H 6.25, Br 23.89.

6-{[(1,1-Dimethylethyl)dimethylsilyl]oxy}-α-4-[(phenylmethoxy)phenyl]naphthalene-2-methanol ((±)-**10**). To a flame-dried flask was added 1/10 of a soln. of **9** (total 70.5 g, 209 mmol) in abs. THF (total 320 ml) together with Mg powder (5.34 g, 220 mmol). The reaction was started by addition of a few drops of Br_2 and heating. The residual soln. of **9** was subsequently added over 1 h to the suspension which was maintained at reflux. After heating to reflux for an additional hour and cooling to r.t., 4-(phenylmethoxy)benzaldehyde [20] (43.0 g, 202 mmol) in THF (100 ml) was added dropwise over 30 min. The mixture was stirred at r.t. overnight, then sat. aq. NH_4Cl soln. (400 ml) was added at 4°, and stirring was continued for 20 min. The aq. phase was washed with Et_2O (200 ml), the combined org. phase washed with sat. aq. NaCl soln. (400 ml), dried ($MgSO_4$), and evaporated and the residue dried at 90°/h.v.: yellow viscous oil (95 g) which was used for the next step without further purification. For anal. purposes, chromatography (SiO_2, hexane/CH_2Cl_2/AcOEt 18:3:1) and recrystallization from hexane (2×) afforded pure (1±)-**10**. Colorless powder. R_f 0.35 (SiO_2, hexane/AcOEt 4:1). M.p. 81–82° (hexane). IR ($CHCl_3$): 3610*w*, 3021*m*, 2959*w*, 2860*w*, 1638*w*, 1606*m*, 1509*m*, 1480*m*, 1385*m*, 1375*m*, 1261*s*, 1240*m*, 1184*m*, 1110*w*, 1030*m*, 988*w*, 958*w*, 915*m*, 850*m*, 822*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 0.24 (*s*, 6 H); 1.02 (*s*, 9 H); 2.25 (*d*, *J* = 3.6, 1 H); 5.03 (*s*, 2 H); 5.91 (*d*, *J* = 3.6, 1 H); 6.90–6.95 (*m*, 2 H); 7.07 (*dd*, *J* = 8.8, 2.4, 1 H); 7.16 (*d*, *J* = 2.4, 1 H); 7.29–7.34 (2*m*, 3 H); 7.34–7.38 (*m*, 3 H); 7.39–7.42 (*m*, 2 H); 7.63 (*d*, *J* = 8.6, 1 H); 7.70 (*d*, *J* = 8.8, 1 H); 7.78 (br. *s*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): −4.35; 18.25; 25.71; 70.02; 75.89; 114.82; 114.84; 122.32; 124.68; 125.09; 127.05; 127.43; 127.93; 128.01; 128.56; 128.97; 129.43; 134.03; 136.37; 136.95; 139.27; 153.61; 158.27. EI-MS: 470 (16, M^+), 91 (100, $C_7H_7^+$). Anal. calc. for $C_{30}H_{34}O_3Si$ (470.68): C 76.56, H 7.28; found: C 76.73, H 7.35.

4-[(6-{[(1,1-Dimethylethyl)dimethylsilyl]oxy}naphthalen-2-yl)methyl]phenol (**11**). An intensively stirred soln. of crude **10** (95.0 g, *ca.* 200 mmol) in MeOH (1.2 l) was hydrogenated at 5 atm H_2 with 10% Pd/C (10.0 g) for 6 d at r.t. The catalyst was removed by filtration over *Celite*, and evaporation yielded the oily crude product which was dried at r.t./h.v. and then filtered over SiO_2 (1.55 kg, hexane/AcOEt 6:1 → 5:1). Upon further drying at 70°/h.v., **11** (51.4 g, 70% from **9**) slowly crystallized. For anal. purposes, recrystallization from hexane afforded a fluffy colorless solid. R_f 0.47 (SiO_2, hexane/AcOEt 4:1). M.p. 89–90° (hexane). IR ($CHCl_3$): 3598*w*, 3330*w*, 3040*w*, 2942*m*, 2930*m*, 2859*m*, 1604*s*, 1513*s*, 1479*m*, 1435*w*, 1374*w*, 1334*w*, 1261*s*, 1185*m*, 1100*w*, 910*w*, 976*m*, 956*m*, 884*m*, 844*s*, 816*m*. ^{1}H-NMR (500 MHz, CD_3OD): 0.28 (*s*, 6 H); 1.06 (*s*, 9 H); 4.02 (*s*, 2 H); 6.74 (*m*, 2 H); 7.05–7.09 (*m*, 3 H); 7.18 (*d*, *J* = 2.4, 1 H); 7.27 (*dd*, *J* = 8.5, 1.8, 1 H); 7.56 (br. *s*, 1 H); 7.63 (*d*, *J* = 8.5, 1 H); 7.69 (*d*, *J* = 9.0, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): −4.50; 18.35; 25.72; 41.01; 114.81; 115.28; 122.13; 126.65; 126.85; 127.88; 128.88; 129.37; 130.15; 133.15; 133.50; 136.83; 153.07; 153.77. EI-MS: 364 (85, M^+), 307 (95, $[M - C_4H_9]^+$), 107 (100, $C_7H_7O^+$). Anal. calc. for $C_{23}H_{28}O_2Si$ (364.56): C 75.78, H 7.74; found: C 75.97, H 7.83.

2,6-Dibromo-4-[(6-{[(1,1-dimethylethyl)dimethylsilyl]oxy}naphthalen-2-yl)methyl]phenol (**12**). A soln. of *t*-BuNH_2 (36.0 g, 492 mmol) in abs. PhMe (550 ml) was cooled under N_2 to −35°, and Br_2 (34.8 g, 218 mmol) was slowly added dropwise while keeping the temp. inside the flask below −25°. After cooling to −80°, a soln. of **11** (36.7 g, 101 mmol) in PhMe (80 ml) was added dropwise over 30 min while the temp. was maintained below −60°. After warming to −40° over 4 h and to 0° over 1 h, the formed suspension was poured into 0.1N aq. $Na_2S_2O_3$ (250 ml). The org. phase was washed with 6M aq. HCl (3 × 200 ml) and sat. aq. NaCl soln. (200 ml), dried (Na_2SO_4), and evaporated. The residual oil (53 g) was dried at r.t./h.v. until crystallization occurred. The crude product was used in the next step without further purification. For anal. purposes, recrystallization from hexane afforded **12** as a mildly rose solid. R_f 0.63 (SiO_2, hexane/AcOEt 4:1). M.p. 99–100° (hexane). IR ($CHCl_3$):

3510*w*, 3020*w*, 2944*m*, 2931*m*, 2859*w*, 1635*w*, 1604*m*, 1565*w*, 1505*w*, 1475*s*, 1437*w*, 1408*w*, 1374*w*, 1324*w*, 1270*s*, 1262*s*, 1160*m*, 1123*w*, 1010*w*, 980*m*, 962*m*, 935*w*, 870*m*, 846*m*, 834*m*, 815*m*. ^{1}H-NMR (500 MHz, CD_3OD): 0.28 (*s*, 6 H); 1.06 (*s*, 9 H); 4.00 (*s*, 2 H); 7.07 (*dd*, *J* = 8.7, 2.4, 1 H); 7.20 (*d*, *J* = 2.4, 1 H); 7.26 (*dd*, *J* = 8.8, 1.8, 1 H); 7.35 (*s*, 2 H); 7.59 (br. *s*, 1 H); 7.67 (*d*, *J* = 8.8, 1 H); 7.72 (*d*, *J* = 8.7, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): −4.34; 18.25; 25.71; 40.44; 109.76; 114.79; 122.39; 126.92; 127.22; 127.47; 128.94; 129.29; 132.29; 133.37; 135.11; 135.93; 147.68; 153.40. EI-MS: 522 (45, M^+), 465 (100, $[M - C_4H_9]^+$), 265 (31, $C_7H_5Br_2O^+$). Anal. calc. for $C_{23}H_{26}Br_2O_2Si$ (522.35): C 52.89, H 5.02, Br 30.59; found: C 52.96, H 5.11, Br 30.70.

[(6-{[3,5-Dibromo-4-(4-chlorobutoxy)phenyl]methyl}naphthalen-2-yl)oxy](1,1-dimethylethyl)dimethylsilane (**13**). A mixture of crude **12** (53 g, *ca.* 101 mmol), 1,4-dichlorobutane (127.0 g, 1.0 mol), and anh. K_2CO_3 (35.0 g, 253 mmol) in dry acetone (150 ml) was heated to reflux for 24 h. After cooling, the inorg. salts were removed by filtration and washed with CH_2Cl_2 (100 ml), and the filtrate was evaporated. The brownish oily residue (50 g) was dried under h.v. and used without further purification in the next step. For anal. purposes, chromatography (SiO_2, hexane/AcOEt 5:1) afforded a colorless viscous oil. R_f 0.77 (SiO_2, hexane/PhMe 1:1). IR ($CHCl_3$): 3056*w*, 2957*m*, 2931*m*, 2859*m*, 1636*w*, 1604*s*, 1543*m*, 1502*m*, 1479*s*, 1458*s*, 1382*m*, 1342*w*, 1261*s*, 1172*w*, 1154*w*, 1121*w*, 975*m*, 958*m*, 931*m*, 865*m*, 840*s*, 776*m*. ^{1}H-NMR (500 MHz, CD_3OD): 0.29 (*s*, 6 H); 1.07 (*s*, 9 H); 1.99–2.05 (*m*, 2 H); 2.06–2.12 (*m*, 2 H); 3.72 (*t*, *J* = 6.4, 2 H); 4.05 (*t*, *J* = 6.0, 2 H); 4.08 (*s*, 2 H); 7.11 (*dd*, *J* = 9.0, 2.4, 1 H); 7.22 (*d*, *J* = 2.4, 1 H); 7.29 (*dd*, *J* = 8.5, 1.8, 1 H); 7.47 (*s*, 2 H); 7.64 (br. *s*, 1 H); 7.70 (*d*, *J* = 8.5, 1 H); 7.76 (*d*, *J* = 9.0, 1 H). ^{13}C-NMR (125 MHz, CD_3OD): −4.25; 19.11; 26.28; 28.43; 30.54; 41.23; 45.56; 73.47; 115.77; 119.07; 123.22; 128.03; 128.26; 128.68; 130.17; 130.92; 134.17; 134.85; 136.74; 142.11; 152.67; 154.63. EI-MS: 612 (98, M^+), 476 (42), 249 (86), 91 (40, $C_7H_7^+$), 73 (43, $C_3H_9Si^+$), 55 (100, $C_4H_7^+$). HR-MS: 612.0285 (M^+, $C_{27}H_{33}{}^{79}Br^{81}BrClO_2Si^+$; calc. 612.0284).

6-{[3,5-Dibromo-4-(4-chlorobutoxy)phenyl]methyl}naphthalen-2-ol (**14**). To a soln. of crude **13** (50 g, ≤ 81 mmol) in dry CH_2Cl_2 (250 ml), 1M Bu_4NF in THF was added at 0° (→green). After addition of 80 ml over 10 min, TLC showed quantitative conversion. The soln. was washed with H_2O (2 × 300 ml), dried (Na_2SO_4), filtered over cotton-wool, and evaporated first *in vacuo*, then under h.v./r.t. The resin-like crude product was filtered over SiO_2 (1.50 kg, PhMe/AcOEt 33:1 → 15:1): **14** (35.3 g, 69 % starting from **11**). Red light-sensitive resin. R_f 0.22 (SiO_2, hexane/AcOEt 4:1). IR ($CDCl_3$): 3592*m*, 3300*w*, 3025*w*, 1638*m*, 1608*s*, 1543*m*, 1510*m*, 1458*s*, 1440*m*, 1384*m*, 1261*s*, 1173*s*, 1143*m*, 954*w*, 920*w*, 902*w*, 856*m*. ^{1}H-NMR (500 MHz, CD_3OD): 2.01–2.08 (*m*, 2 H); 2.09–2.16 (*m*, 2 H); 3.72 (*t*, *J* = 6.5, 2 H); 4.03 (*t*, *J* = 6.0, 2 H); 4.05 (*s*, 2 H); 7.09 (*dd*, *J* = 8.7, 2.4, 1 H); 7.10 (*d*, *J* = 2.4, 1 H); 7.23 (*dd*, *J* = 8.4, 1.8, 1 H); 7.46 (*s*, 2 H); 7.59 (br. *s*, 1 H); 7.62 (*d*, *J* = 8.4, 1 H); 7.70 (*d*, *J* = 8.7, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 27.36; 29.21; 40.58; 44.90; 72.27; 109.41; 118.06; 118.17; 126.96; 127.19; 127.92; 128.99; 129.51; 132.94; 133.35; 134.65; 139.91; 151.38; 153.29. EI-MS: 498 (7, M^+), 408 (16, $[M - C_4H_7Cl]^+$), 91 (83, $C_7H_7^+$), 55 (100, $C_4H_7^+$). HR-MS: 497.9416 (M^+, $C_{21}H_{19}{}^{79}Br^{81}BrClO_2^+$; calc. 497.9420).

18,37,40,44-Tetrabromo-11,16,30,35-tetraoxaheptacyclo[34.2.2.2^{17,20}.1^{3,7}.1^{6,10}.1^{22,26}.1^{25,29}]hexatetraconta-3,5,7(46),8,10(45),17,19,22,24,26(42),27,29(41),36,38,39,43-hexadecaene (**5**). To a refluxing suspension of anh. Cs_2CO_3 (50.0 g, 153 mmol) in dry MeCN (3.5 l) under N_2, a soln. of **14** (11.70 g, 23.5 mmol) in MeCN (500 ml) was added dropwise over 1 h. After stirring at 80° for 5 d, the hot suspension was filtered over *Celite*, and the filtrate was evaporated. This reaction was repeated three times, and the combined crude product was chromatographed (SiO_2 (200 g), hot PhMe under mild pressure). Evaporation gave a brownish solid (11 g) which was dissolved in warm CH_2Cl_2 (50 ml), and upon standing, the crude product (4.05 g) crystallized out and was isolated by filtration. Two repeats of this purification procedure by redissolving the respective residue in CH_2Cl_2 (15 ml, then 5 ml) and recrystallization afforded additional 1.35 g of product. The last mother liquor was evaporated, and chromatography (SiO_2 (100 g), CCl_4/CH_2Cl_2 5:2 → 3:2) yielded additional product. The combined crude products (5.9 g) were recrystallized from PhMe to give **5** (5.53 g, 17%). Colorless crystals. R_f 0.63 (SiO_2, hexane/AcOEt 4:1). M.p. > 240° (PhMe). UV (CH_2Cl_2): 265 (12900), 275 (13200), 284 (9300), 321 (3000), 335 (3600). IR (KBr): 3055*w*, 3022*w*, 2949*m*, 1632*m*, 1605*s*, 1542*m*, 1506*m*, 1474*s*, 1455*s*, 1391*s*, 1262*s*, 1223*s*, 1262*s*, 1223*s*, 1178*s*, 1120*w*, 1206*m*, 998*m*, 951*m*, 850*s*, 806*m*, 740*s*. ^{1}H-NMR (500 MHz, CD_2Cl_2): 2.04–2.12 (*m*, 8 H); 3.93 (*s*, 4 H); 4.00 (*t*, *J* = 6.1, 4 H); 4.21 (*t*, *J* = 6.5, 4 H); 7.06 (*d*, *J* = 2.5, 2 H); 7.08 (*dd*, *J* = 8.8, 2.5, 2 H); 7.11 (*dd*, *J* = 8.4, 1.8, 2 H); 7.27 (*s*, 4 H); 7.51 (br. *s*, 2 H); 7.54 (*d*, *J* = 8.4, 2 H); 7.61 (*d*, *J* = 8.8, 2 H). ^{13}C-NMR (125 MHz, CD_2Cl_2): 25.44, 25.91; 40.92; 67.15; 73.01; 107.20; 118.31; 119.72; 127.27; 127.54; 127.93; 129.19; 129.26; 133.21; 133.64; 135.43; 140.81; 151.91; 157.30. FAB-MS: 924 (9, M^+), 136 (100), 107 (52, $C_7H_7O^+$). Anal. calc. for $C_{42}H_{36}Br_4O_4$ (924.36): C 54.57, H 3.93, Br 34.58, O 6.92; found: C 54.55, H 4.09, Br 34.68, O 6.87.

18,37,40,44-Tetrakis[4-(phenylmethoxy)phenyl]-11,16,30,35-tetraoxaheptacyclo[34.2.2.2^{17,20}.1^{3,7}.1^{6,10}.1^{22,26}.1^{25,29}]hexatetraconta-3,5,7(46),8,10(45),17,19,22,24,26(42),27,29(41),36,38,39,43-hexadecaene (**15**). To $[Pd(PPh_3)_4]$ (1.00 g, 0.86 mmol), **5** (3.50 g, 3.79 mmol), 4-(phenylmethoxy)phenylboronic acid [24] (5.20 g,

22.8 mmol), and Na_2CO_3 (32.0 g, 300 mmol) in a flask flushed thoroughly with Ar were added Ar-saturated PhMe (320 ml), EtOH (50 ml), THF (80 ml), and H_2O (200 ml). The yellow mixture was heated to 80° under intense stirring, and a stream of Ar was bubbled through for 2 h until the color changed to grey. After stirring for 3 d at 80°, additional [$Pd(PPh_3)_4$] (1.00 g) and 4-(phenylmethoxy)phenylboronic acid (5.20 g) were added, the suspension was saturated again with Ar, and stirring was continued at 80° for 3 d. After cooling, the aq. layer was extracted with PhMe (50 ml), the combined org. phase diluted with warm CH_2Cl_2 (1 l), then rapidly filtered over *Celite*, and evaporated, and the brownish residue (8 g) chromatographed (SiO_2 (250 g), warm PhMe under mild pressure). The crude product (4.8 g) was recrystallized from CH_2Cl_2 (300 ml) and dried at 80°/h.v. to give **15** (3.88 g, 77%). Colorless powder. R_f 0.27 (SiO_2, PhMe/hexane 5:1). M.p. > 240° (CH_2Cl_2). UV (CH_2Cl_2): 256 (112000), 337 (5000). IR (CD_2Cl_2): 3033*w*, 2933*w*, 1607*m*, 1510*m*, 1451*w*, 1380*w*, 1240*m*, 1178*w*, 994*m*, 970*s*, 958*s*, 884*s*. ^{1}H-NMR (500 MHz, CD_2Cl_2): 1.44–1.59 (*m*, 8 H); 3.17 (*t*, *J* = 6.0, 4 H); 3.34 (*t*, *J* = 6.0, 4 H); 4.02 (*s*, 4 H); 5.14 (*s*, 8 H); 6.70 (*d*, *J* = 2.4, 2 H); 6.88 (*dd*, *J* = 8.9, 2.4, 2 H); 7.00–7.04 (*m*, 8 H); 7.12 (*s*, 4 H); 7.27 (*dd*, *J* = 8.5, 1.7, 2 H); 7.32–7.42 (*m*, 12 H); 7.45–7.52 (*m*, 16 H); 7.56–7.59 (*m*, 6 H). ^{13}C-NMR (125 MHz, CD_2Cl_2): 24.75, 25.16; 42.03; 65.59; 70.43; 71.07; 106.68; 114.82; 119.40; 126.85; 127.34; 127.93; 128.13; 128.36; 128.96; 129.00; 129.20; 130.33; 131.07; 132.00; 133.44; 135.90; 137.10; 137.66; 138.03; 152.54; 157.12; 158.48. FAB-MS: 1337 (100, M^+). Anal. calc. for $C_{94}H_{80}O_8$ (1337.67): C 84.40, H 6.03; found: C 84.30, H 6.05.

4,4',4'',4'''-(11,16,30,35-Tetraoxaheptacyclo[34.2.2.2^{17,20}.1^{3,7}.1^{6,10}.1^{22,26}.1^{25,29}]hexatetraconta-3,5,7(46),8,10(45),17,19,22,24,26(42),27,29(41),36,38,39,43-hexadecaen-18,37,40,44-tetrayl)tetrakisphenol (**16**). To a suspension of HCO_2NH_4 (2.00 g, 31.7 mmol) and **15** (3.86 g, 2.88 mmol) in MeOH (100 ml), and THF (1.5 l) at 0° was added under Ar slowly 10% Pd/C (2.0 g), and the mixture was heated to reflux for 30 min. Hot filtration over *Celite*, evaporation, and chromatography (SiO_2 (100 g), loading with PhMe, then eluting with hot PhMe/AcOEt 3:1 under mild pressure) yielded **16** (2.74 g, 98%) which, for anal. purposes, was recrystallized from EtOH. Colorless sparingly soluble powder. R_f 0.32 (PhMe/AcOEt 3:1). M.p. > 240° (EtOH). IR (KBr): 3533*m*, 3416*s*, 3015*w*, 2938*m*, 1634*m*, 1607*s*, 1513*s*, 1462*m*, 1451*m*, 1415*m*, 1386*m*, 1262*s*, 1224*s*, 1174*s*, 1005*m*, 957*m*, 834*s*, 558*m*. ^{1}H-NMR (500 MHz, $(CD_3)_2SO$): 1.30–1.38 (*m*, 4 H); 1.49–1.57 (*m*, 4 H); 3.02 (*t*, *J* = 5.9, 4 H); 3.33 (*t*, *J* = 5.9, 4 H); 3.98 (*s*, 4 H); 6.74 (*d*, *J* = 2.4, 2 H); 6.84 (*d*, *J* = 8.6, 8 H); 6.88 (*dd*, *J* = 8.9, 2.4, 2 H); 7.07 (*s*, 4 H); 7.25–7.31 (*m*, 10 H); 7.64–7.68 (*m*, 6 H); 9.56 (*s*, 4 H). ^{13}C-NMR (125 MHz, $(CD_3)_2SO$): 23.63; 24.08; 40.60; 64.32; 69.61; 105.87; 114.91; 118.63; 125.98; 126.90; 127.74; 128.27; 128.61; 128.80; 129.17; 130.17; 132.46; 135.10; 136.71; 137.47; 151.20; 155.98; 155.59. FAB-MS: 976 (100, M^+), 663 (20), 550 (59), 522 (75). Anal. calc. for $C_{66}H_{56}O_8$ (977.17): C 81.12, H 5.78; found: C 80.69, H 5.84.

Tetramethyl 2,2',2'',2'''-[(11,16,30,35-Tetraoxaheptacyclo[34.2.2.2^{17,20}.1^{3,7},1^{6,10}.1^{22,26}.1^{25,29}]hexatetraconta-3,5,7(46),8,10(45),17,19,22,24,26(42),27,29(41),36,38,39,43-hexadecaen-18,37,40,44-tetrayl)tetrakis(4,1-phenyleneoxy)]tetrakisacetate (**17**). To a suspension of **16** (2.66 g, 2.72 mmol) and K_2CO_3 (2.50 g, 18.1 mmol) in abs. DMF (15 ml), methyl 2-bromoacetate (5.0 ml, 8.30 g, 54.0 mmol) was added and the mixture was stirred at 70° under Ar for 3 d. The suspension was poured on $CHCl_3$ (100 ml) and the resulting mixture heated to reflux for 10 min and then extracted with H_2O (50 ml). Evaporation and chromatography (SiO_2 (250 g), $CHCl_3$/AcOMe) of the crude product (3.5 g) afforded **17** (2.16 g, 63%). Colorless solid. R_f 0.20 (SiO_2, $CHCl_3$/AcOMe 30:1). M.p. > 240° ($CHCl_3$/AcOMe). IR ($CDCl_3$): 3025*w*, 2955*m*, 1760*s*, 1605*s*, 1510*s*, 1440*m*, 1380*m*, 1295*m*, 1265*m*, 1180*s*, 1085*m*, 1010*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.42–1.48 (*m*, 4 H); 1.53–1.62 (*m*, 4 H); 3.14 (*t*, *J* = 5.8, 4 H); 3.35 (*t*, *J* = 5.8, 4 H); 3.82 (*s*, 12 H); 4.01 (*s*, 4 H); 4.71 (*s*, 8 H); 6.73 (*d*, *J* = 2.4, 2 H); 6.90 (*dd*, *J* = 8.8, 2.4, 2 H); 6.94–6.98 (*m*, 8 H); 7.09 (*s*, 4 H); 7.24 (*dd*, *J* = 8.4, 1.6, 2 H); 7.46–7.50 (*m*, 8 H); 7.56 (br. *s*, 2 H); 7.58 (*d*, *J* = 8.8, 2 H); 7.61 (*d*, *J* = 8.4, 2 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 24.28; 24.63; 41.75; 52.34; 64.86; 65.39; 70.59; 106.26; 114.19; 119.03; 126.52; 127.04; 127.93; 128.75; 128.78; 130.28; 130.84; 132.50; 133.04; 135.25; 136.52; 137.47; 152.02; 156.68; 157.02; 169.41. FAB-MS: 1264 (10, M^+), 1051 (43), 307 (100). Anal. calc. for $C_{78}H_{72}O_{16}$ (1265.42): C 74.04, H 5.73; found: C 73.90, H 5.87.

2,2',2'',2'''-[(11,16,30,35-Tetraoxaheptacyclo[34.2.2.2^{17,20}.1^{3,7},1^{6,10}.1^{22,26}.1^{25,29}]hexatetraconta-3,5,7(46),8,10(45),17,19,22,24,26(42),27,29(41),36,38,39,43-hexadecaen-18,37,40,44-tetrayl)tetrakis(4,1-phenyleneoxy)]-tetrakis(acetic Acid) (**4**). A suspension of **17** (2.00 g, 1.58 mmol) and 1N aq. LiOH (20 ml, 20 mmol) in THF/MeOH 4:1 (10 ml) was heated for 48 h at r.t., yielding a clear soln. after 24 h. Subsequently, 1N aq. HCl (21 ml) saturated with NaCl was added under ice-cooling, leading to the precipipation of most of the product. The org. solvents were evaporated, and sat. aq. NaCl soln. (40 ml) was added to the residual aq. suspension, which was subsequently extracted with warm AcOMe (160 ml). Evaporation of the combined org. phases and extensive drying under h.v. of the residue afforded **4** (1.89 g, 99%). Colorless powder, highly insoluble in most org. solvents. M.p. > 240° (AcOMe). IR (KBr): 3500–2200*m*, 1731*s*, 1630*m*, 1606*s*, 1509*s*, 1433*m*, 1384*m*, 1223*s*, 1180*s*, 1115*w*, 1078*m*, 1002*w*, 995*w*, 831*s*. ^{1}H-NMR (500 MHz, $(CD_3)_2SO$): 1.25–1.33 (*m*, 4 H); 1.41–1.48 (*m*, 4 H); 3.04 (*t*, *J* = 5.5, 4 H); 3.40 (*t*, *J* = 5.5, 4 H); 3.98 (*s*, 4 H); 4.72 (*s*, 8 H); 6.79 (*d*, *J* = 2.4, 2 H); 6.88 (*dd*, *J* = 8.9, 2.4, 2 H); 6.96

(*d*, J = 8.8, 8 H); 7.11 (*s*, 4 H); 7.30 (*dd*, J = 8.5, 1.5, 2 H); 7.36 (*d*, J = 8.8, 8 H); 7.63 (*d*, J = 8.5, 2 H); 7.64 (*d*, J = 8.9, 2 H); 7.67 (br. *s*, 2 H). ^{13}C-NMR (125 MHz, $(CD_3)_2SO$): 24.41; 24.74; 41.09; 65.05; 65.24; 70.87; 106.82; 114.58; 119.14; 126.53; 127.47; 128.25; 128.83; 129.10; 130.14; 130.64; 131.46; 133.06; 135.21; 137.05; 138.13; 151.80; 156.52; 157.50; 170.60. FAB-MS (glycerol, neg.-ion mode): 1208 (10, M^-), 1150 (3, $[M - C_2H_2O_2]^-$), 275 (34), 183 (100), 91 (73).

X-Ray Crystal-Structure Analyses. The X-ray measurements were made on a *Nonius-CAD4* diffractometer equipped with graphite monochromator (MoK_α radiation, λ 0.7107 Å) and a *Nonius* gas-stream low-temperature device. Cyclophane **5** was dissolved in the different solvents, and upon diffusion of hexane into these solns., plate-like crystals of **5a–e** were obtained; they were cut and embedded in epoxy resin to avoid evaporation of cocrystallized solvent. Inclusion compounds **5a**, **5d**, and **5e** crystallized in the monoclinic space group $P2_1/c$ ($P2_1/n$), while **5b** and **5c** crystallized in the triclinic space group $P\bar{1}$. All cyclophane skeletons had a crystallographic center of symmetry. In **5a**, the ratio between cyclophane and solvent was 1:1, the 1,2-dichloroethane sitting at the inversion center. In **5b**, the corresponding ratio was 1:3, with one (disordered) benzene sitting at the inversion center and two clathrated benzene molecules (related by symmetry). In cyclophanes **5c**, **5d**, and **5e**, the ratio between cyclophane and solvent was 1:2, 1:1, and 1:2, resp.

The structures were solved by direct methods and refined by full-matrix least-squares analysis (SHELXTL PLUS) using an isotropic extinction correction and an exponentially modified weight factor [52]. For **5a–d**, all heavy atoms were refined anisotropically, H-atoms isotropically and with H-positions based on stereochemical considerations. The structure of **5e**, including solvent is disordered; the disorder could be partially resolved within the aliphatic chains bridging the naphthyl(phenyl)methane moieties, *i.e.*, for the fragment C(14)–C(15)–C(16), two sets of atoms were refined with isotropic U values and half weights (only one orientation is shown in *Fig. 2,e*). The remaining heavy atoms were refined anisotropically (H-atoms omitted). Additional experimental details are summarized in *Table 2*, and further details of the crystal-structure analyses are available on request from the Director of the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB12 1EZ (UK), on quoting the full journal citation.

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