Preorganized Macrocyclic Receptors Featuring *endo*-Carboxylic Acid Groups. Host Synthesis and Inclusion Compounds with Alcohol and Amine Guests

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Abstract. The synthesis and characterization of four new macrocyclic host compounds **1**–**4** having modified diphenylmethane units as bridging elements and two *endo*-orientated carboxylic acid groups attached to aromatic building blocks are described. The complexation properties of the macrocycles towards amines and alcohols are reported, showing that the ability to form convergent inclusion compounds depends on the type of the spacer element. For the dicarboxylic hosts **1** and **2** *endo*-complexation of guest molecules based on hydrogen bonding to the acid functions is proved using ^{1}H NMR investigation and X-ray crystal structure analysis.

Macrocyclic host compounds, now as ever, play an important part in supramolecular chemistry [1, 2]. Many structural concepts such as lying behind the crown ethers and cryptands [3], the calixarenes [4] or other cyclophane-type macrocycles [5] have been developed to examine the selective binding of ions and uncharged guest species in a molecular cavity [6, 7]. In cases of the inclusion of neutral guest compounds it proved satisfactory to attach binding sites in a preorganized manner inside a well fitting cavity that meets complementary with regard to the size, the shape and the functionalities of the guest molecule [8]. H-bonding is certainly one of the most important and most frequently used noncovalent interactions [9]. In this field, an advantage is that H-bonds enable a variety of well defined binding modes [10]. With reference to the H-donor functionality they mainly involve hydroxy, amine and to a certain degree amide groups [11]. On the other hand, carboxylic groups are only scarcely used in artificial receptors, as contrasted with biological systems [12]. In particular, examples of macrocyclic hosts containing this very group in an *endo*-oriented way are rare in the literature [13, 14]. A reason for this fact is perhaps the crux compelling this active group into a cavity which needs a

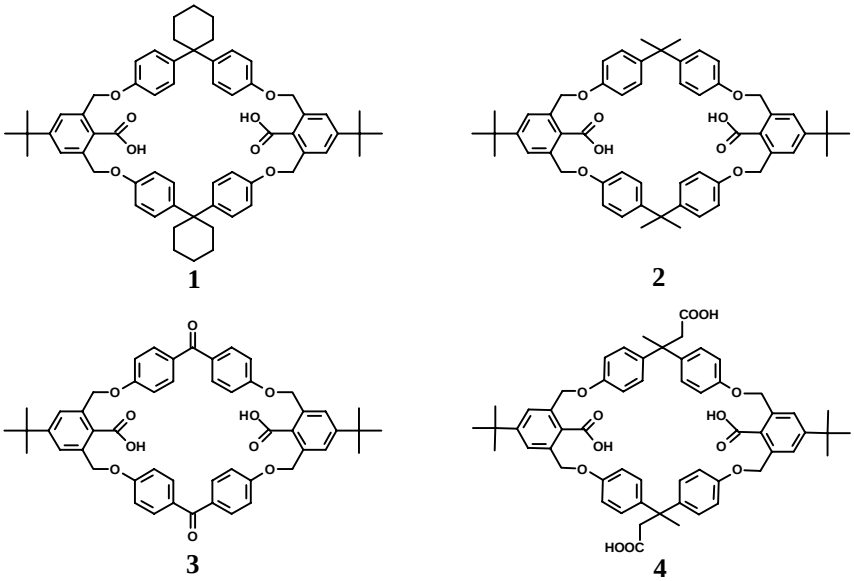

Fig. 1 Synthesized macrocyclic receptors **1**–**4**

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macroring of reasonable size but which is rigid enough to prevent this group from getting out or forming transannular interactions such as carboxylic dimers at the expense of selective guest binding.

Here we demonstrate a possible solution of these difficulties and report on the synthesis of four macrocylic host compounds (**1**–**4**; Fig. 1) providing two *endo*-preorganized carboxylic acid functions. They are based on an unique rigid framework allowing modification of bridging elements. The inclusion behaviour of these host compounds regarding amines and alcohols as guest molecules is reported including conformational studies of the host–guest complexes with amines by ^{1}H NMR technique as well as X-ray crystal structures of three complexes with ethanol.

Results and Discussion

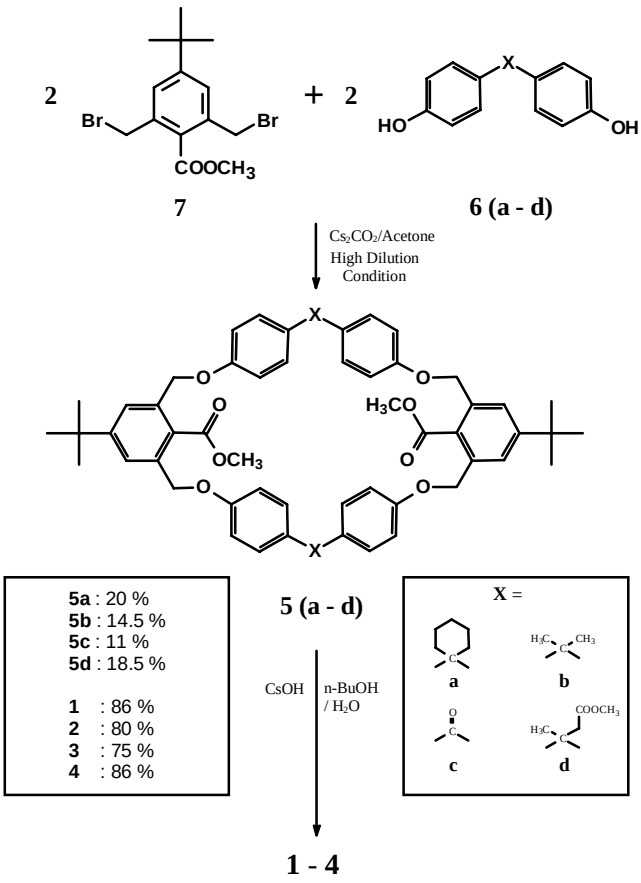
Host Design and Synthesis

Starting point of the present host design was to bring apart two carboxylic acid groups inside of a macroring in order to prevent an intramolecular dimerization of these groups. With regard to that, rigid spacers or bridging elements are required. At the same time the bridging units should serve a suitable distance inside of the cavity and between the two carboxy groups to allow a guest complexation *via* H-bonding. Previous molecular mechanics calculations (MM2) of bis(4-hydroxyphenyl)methane derivatives [15] show the expected roof-like arrangement of the phenyl rings, and the distance between both OH-groups suggests this structural element as a favourable unit for the host design [14, 16]. As a suitable building block for the intended macrocyclization containing the carboxy group, 4-*tert*-butylbenzoic acid having two extra functional substituents in 2,6-position of the aromatic ring was selected. This all ensures the deliberate preoganization of the macroring with *endo*-orientation of the carboxy functions. The large and lipophilic *tert*-butyl substituent was also introduced to improve the solubility in organic solvents such as chloroform or dichloromethane.

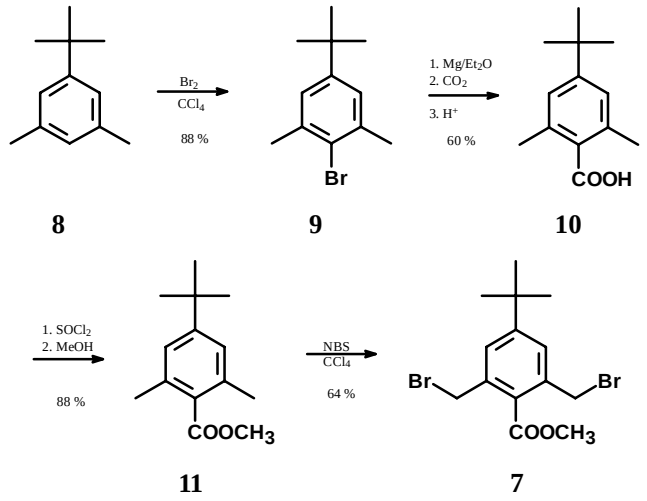
Key steps of the syntheses are the ring closure reactions to yield the macrocyclic esters **5a**–**d** which were done by ether bond formation between **7** and **6a**–**d**, as shown in Scheme 1.

Based on a series of experiments for optimizing the reaction conditions, high dilution [17], cesium carbonate as the base [18] and acetone as the solvent proved most advantageous. Using these conditions gave **5a**–**d** in rather good yields (11%–20%), considering the formations of four bonds during cyclization. Hydrolysis of the esters **5a**–**d** to yield the target molecules **1**–**4** turned out best in the solvent/base system *n*-butanol/cesium hydroxide (10M in H_2O), whereas the use of ethanol or *i*-propanol as solvent was found to require much longer reaction times, and normally hydrolysis is not complete.

The cyclization component **7** was prepared as illustrated in Scheme 2. Starting with 5-*tert*-butyl-*m*-xylene (**8**), aromatic bromination (**9**), Grignard carboxylation (**10**), esterification (**11**) and a side-chain bromination were performed following literature procedures [19–21]. Compounds **6**, **6b** and **6c** are commercial available



Scheme 1 Synthesis of host molecules **1**–**4**



Scheme 2 Synthesis of cyclization component **7**

while **6a** and **6d** have been synthesized using well described condensation reactions between phenol and the corresponding ketones (cyclohexanone and methyl acetoacetate, respectively) [22, 23].

Solid Host-guest Complexes

Apart from the self-complementary carboxy group [24], other well known complementary functions as H-bonding partners for a carboxylic acid site are given with the hydroxy group such as in alcohols [25] or the amino and amide groups provided by acyclic, heterocyclic and heteroaromatic amines or amides [8, 11]. Moreover, to obtain an *endo*-cyclic inclusion, a suitable size and shape of the potential guest species with regard to the dimensions of the host cavity is required. Coming from these considerations, selected compounds to be testet as potential guest molecules are small alcohols and amines while carboxylic acids and their amide derivatives are dropped for reasons of too much space taken by these compounds when hydrogen bonded [11, 26]. Specifications of the solid host-guest complexes formed with amines and alcohols are given in Tables 1 and 2, respectively. These complexes were obtained by simple recrystallization from a liquid guest or by using a co-solvent (chloroform) for recrystallization in cases of low solubility of the solid host in the liquid guest or if the guest compound is a solid itself. The host–guest ratios of the complexes were determined by ^{1}H NMR integration of the dissolved complexes.

Molecular Recognition of Amines

A disadvantage of the complexes of **1**–**3** formed with prim. and most of the sec. amines is that they are only slightly soluble in organic solvents and often they show a non-stoichiometrical ratio between host and guest (*cf.* Table 1). Also the complexes of **4** with two of the four carboxy groups laterally attached to the macroring, in general, were found very similar in this behaviour and showed salt-character. Therefore, we focused on mono-, bi- and tertiary amines including mono- and bicyclic as well as heterocyclic species of compounds, the complexes of which with **1**–**3** have a much better solubility in organic solvents. As being suggested from Table 1, the host:guest ratio depends on the number of

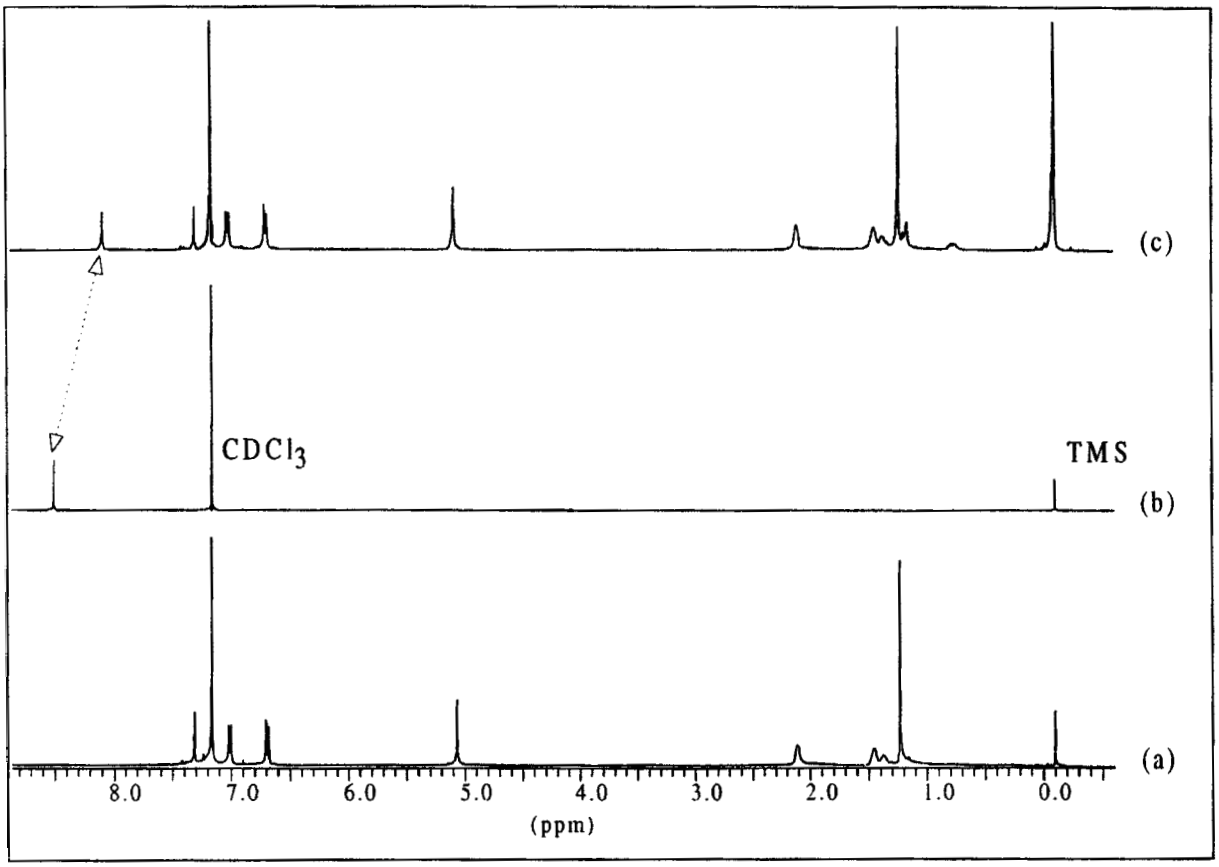
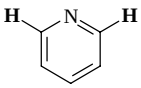
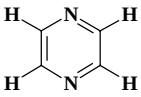
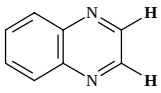
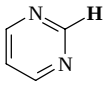
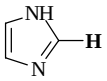
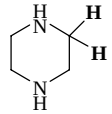
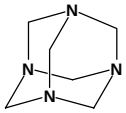


Fig. 2 Examples of NMR spectra (in $CDCl_3$) showing the shift effect of a macrocring indicative of complexation: (a) 5',28'-Di-*tert*-butyl-1',10',24',33'-tetraoxa-dispiro[cyclohexane-1,17'-([2](1,3)benzeno[2]-(1,4)benzeno[1](1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzeno-phane)-40',1''-cyclohexane]-8',31'-dicarboxylic acid (**1**); (b) uncomplexed pyrazine; (c) **1**·pyrazine (1:1).

Table 1 Host–guest complexes with amines [a]) (stoichiometric ratios, and ^{1}H NMR shifts of guest protons, as specified in the formular drawings, in $CDCl_3$ solution of the complexes relative to the uncomplexed case)

Host	**1**		**2**		**3**	
Guest	ratio	$\Delta\delta$ ppm	ratio	$\Delta\delta$ ppm	ratio	$\Delta\delta$ ppm
Pyridine 	1:2	−0.12	1:2	<−0.05	[b)]	[b)]
Pyrazine 	1:1	−0.48	1:1	−0.15	1:1	+0.25
Quinoxaline 	1:1	−0.36	1:1	−0.27	[b)]	[b)]
Pyrimidine 	1:1	−0.40	1:1	−0.25	1:1	+0.20
Imidazole 	1:1	−1.15	1:1	−0.95	1:1	+0.15
Piperazine 	1:1	−1.10	1:1	−1.00	[b)]	[b)]
DABCO 	1:1	−1.20	1:1	−1.05	1:1	+0.65
Hexamethylene tetramine 	–	–	–	[b)]	[b)]	
Triethylamine NEt_3	1:2	−0.90	1:2	−0.65	[b)]	[b)]

[a]) Aniline, 1,4-phenylene diamine, diethylamine or pyrrolidine yielded only complexes of low solubility unsuitable for NMR integration.
[b]) Not tested.

Table 2 Inclusion compounds with alcohols [a])

Host Cpd	Guest alcohol			
	CH_3OH	C_2H_5OH	2-C_3H_7OH	1-C_3H_7OH
1	1:2	1:2	1:2	[b])
2	1:2	1:2	1:2	1:2
3	1:3	1:3	1:3	1:3
4	1:4	1:4	1:4	[b])

[a]) 1-Butanol, 2-butanol, ethylene glycol, *tert*.-butanol, cyclohexanol, 1,4-cyclohexanediol or hydroquinone yielded no inclusion compounds with **1**–**3**, except for **3** which forms a non-stoichiometric inclusion compound with 1-butanol; **4** gave non-stoichiometric complexes with all alcohols specified here.
[b]) Non-stoichiometric complexes.

amino groups of the guest molecules. Moreover, a size selection with reference to the amine is seen, in particular when hosts **1** and **2** are used. Both compounds, *e.g.*, are able to give a solid 1:1 complex with diazabicyclooctane (DABCO), but not either such complex could be isolated with hexamethylene tetramine or any interaction between the two components is deducible from the ^{1}H NMR experiment in solution of $CDCl_3$ (Table 1).

On the other hand, the solution ^{1}H NMR spectra of the amine complexes with **1** and **2** show significant upfield chemical shifts for the protons of the guest molecules while the complexes of **3** with the amines give

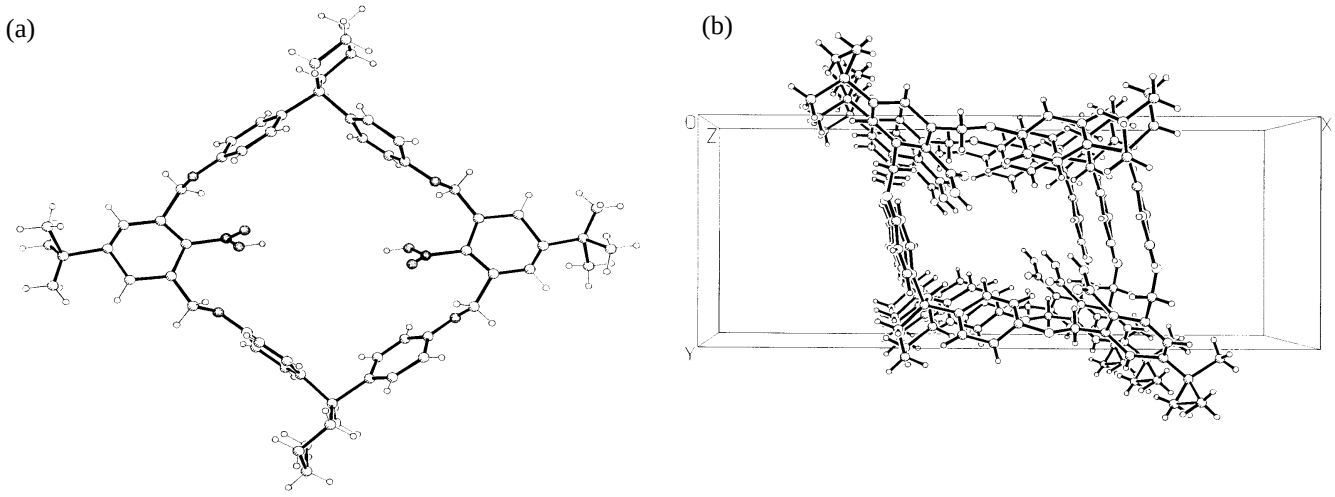


Fig. 3 X-ray crystal structure of 5',28'-Di-*tert*-butyl-1',10',24',33'-tetraoxa-dispiro[cyclohexane-1,17'-([2](1,3)benzeno[2]-(1,4)benzeno[1](1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzenophane)-40',1''-cyclohexane]-8',31'-dicarboxylic acid (**1**)•2 EtOH: (a) Molecular plot (guest molecules were not determined); (b) excerpt of the packing structure showing the channel formation.

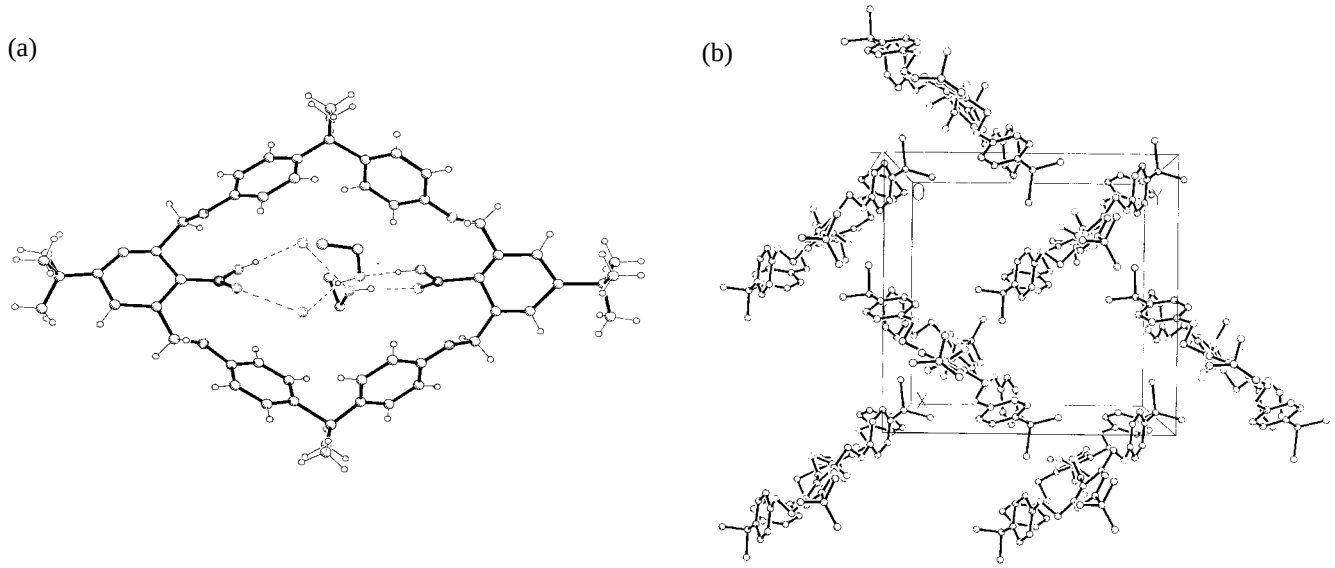


Fig. 4 X-ray crystal structure of 5,28-Di-*tert*-butyl-17,17,40,40-tetramethyl-1,10,24,33-tetraoxa-[2](1,3)benzeno[2](1,4) benzeno[1](1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzenophane-8,31-dicarboxylic acid (**2**) •2 EtOH•2 H_2O: (a) Molecular plot; (b) packing structure (guest molecules are omitted).

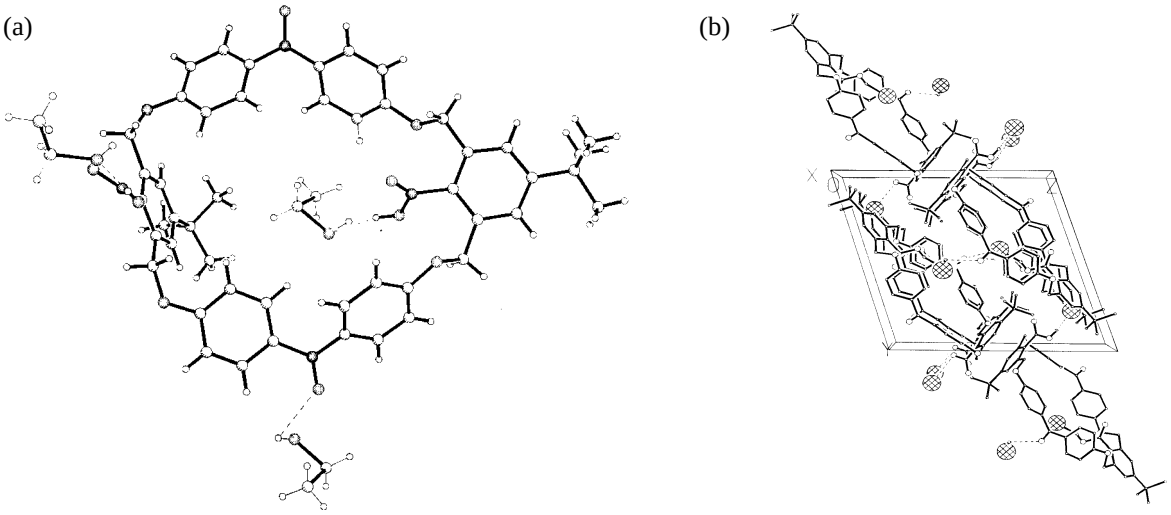


Fig. 5 X-ray crystal structure of 5,28-Di-*tert*-butyl-17,40-dioxo-1,10,24,33-tetraoxa-[2](1,3)benzeno[2](1,4)benzeno[1](1,4)-benzeno[2](1,3)benzeno[2](1,4)benzeno[1](l,4)benzenophane-8,31-dicarboxylic acid (**3**) ·3 EtOH: (a) Molecular plot; (b) packing structure (guest molecules represented as spheres).

rise to 'normal' shifts to higher ppm values (Table 1). An example of this shift behaviour is illustrated in Fig. 2 showing the ^{1}H NMR spectra of the free host compound **1**, of uncomplexed pyrazine (signal at 8.60 ppm) and of the inclusion complex **1**·pyrazine (1:1), leading to an upfield shifted signal for the guest located at 8.12 ppm. Obviously, the guest protons are shielded by the macrocyclic ring of the host compound, demonstrating accommodation of the guest molecule inside the host cavity. By comparison, the particular arrangement of the benzophenone bridging units in host compound **3**, where a distortion of the aromatic rings is very likely [27], does not allow to serve convergent binding sites. Considering the X-ray crystal structures of the ethanol inclusion complexes (see below) there is every reason to believe in this interpretation.

Inclusion Compounds with Alcohols

In principle, as follows from Table 2, crystalline inclusion compounds containing alcohols as guests were obtained from all host molecules (**1**–**4**). Nevertheless, they refer to rather small alcohols while large alcohols failed to form crystalline complexes, giving rise to a distinct differentiation between alcohols according to their size (cf. Table 2). Another remarkable effect is the clear stoichiometric ratio (host:guest) provided by each host compound in its complexes, being 1:2 for **1** and **2**, 1:3 for **3** and 1:4 for **4**, in the strict sense. For **1**, **2** and **4** this behaviour correlates with the number of carboxylic groups involved in the host structure, while **3** having two carboxylic and two simple carbonyl groups is an intermediate case.

The ^{1}H NMR data of the dissolved complexes show only small shifts relative to the individual compounds including the hydrogen atoms of the alcohol attached to the carbon atom that contains the hydroxy group. Actually these hydrogen atoms are shifted upfield between 0.1 and 0.2 ppm for all complexes of **1** and **2**, whereas **3** and **4** cause small downfield shifts (0.05–0.2 ppm). From the sign of the shifts, this is well in keeping with the above complexes of the amines, suggesting similar conditions concerning the orientation of the binding sites of the hosts in both types of complexes. Hence, the crystal structures successfully performed of three host–guest complexes with alcohols including different hosts but the same guest, namely **1**·2 EtOH, **2**·2 EtOH·2 H_2O and **3**·3 EtOH, are of particular relevance.

Crystals of these complexes suitable for x-ray crystal study were obtained from ethanol solutions of the host compounds by slow solvent concentration. Unfortunately, in case of the **1**·2 EtOH complex the crystals decompose so quickly that the guest molecules could not be determined in the structure preventing from refinement to convergence. Nevertheless, the crystal structure furnishes a first model of the macrocycle explaining its conformation. Molecular structures and packing excerpts of the three complexes are illustrated in Figs. 3–5.

With reference to Figs. 3a and 4a, the most remarkable point is the orientation of the carboxy groups being *endo* in the two host molecules **1** and **2**. The distance between the intra-host carboxy groups [OH··O=C] in **1**·2 EtOH of 6.34 Å is far from allowing acid dimerization. Thus it is highly probable that the two ethanol molecules are inserted between these groups and are held fixed by hydrogen bonding in accordance with the structure of **2**·2 EtOH·2 H_2O. In the crystal of the **2**·2 EtOH·2 H_2O inclusion compound a cyclic hydrogen bond system is found in the molecular center. This hydrogen bonded ring is formed by an alternating arrangement of

two ethanol, two water oxygens and the two carboxylic groups (the distance of OH_{hos} *t* ·· O=C_{host} is 7.23 Å). The $\underline{CH_2}$ units of the ethanol molecules are inside the host cavity while the $\underline{CH_3}$ groups are located outside of the plane of the macroring. These facts are in good agreement with the upfield shifts found in the solution ^{1}H NMR spectra. Although the acid functions are used for binding the alcohol in the cavity and do not take part in other way, the packing of the complexes **1**·2 EtOH (Fig. 3b) and **2**·2 EtOH·2 H_2O (Fig. 4b) are rather different. Host **1** accommodates the guest molecules in infinite channels which pass through the crystal like a system of parallel tubes. Easy diffusion of the guest molecules is enabled, thus explaining the fast solvent loss of the crystals during the measurement. The tubules are held together only by van-der-Waals forces. In the ternary inclusion compound of **2** with ethanol and water, **2** forms discrete complexes with the guest species. It is particularly interesting to see the two water and two alcohol molecules separately bound to opposing -COOH groups in the same cavity. This particular feature holds for both molecules of the asymmetric unit. The two hosts are placed in the unit cell such that they are roughly rectangular to each other with the ring middle always covered by the apolar *tert*-butyl groups of the other neighbouring hosts. The so placed macrorings yield a packing structure which consists of two layers. As before only van-der-Waals intermolecular interactions stabilize this crystal structure.

The molecular structure of compound **3** differs from **1** and **2** in the arrangement of the phenyl rings of the benzophenone spacer element (Fig. 5a). As a consequence, one of the carboxy groups is *endo*-oriented while the other has an *exo*-orientation. For this reason, the hydroxy groups of the guest molecules in the **3**·3 EtOH crystal interact separatly with the carboxylic acid functions resulting in isolated host:guest hydrogen bonds and *endo*/*exo*-binding of the two independent ethanol guest molecules. In addition, the third alcohol molecule forms a hydrogen bond to one of the carbonyl groups of the host. Again no inter-associate hydrogen bonding can be detected between the discrete **3**·3 EtOH complexes. As obvious from the packing diagram, primarily $\pi-\pi$ interactions between neighbouring macrorings stabilize the layers in this structure. The $\pi-\pi$ interactions, due to the exposed aromatic surfaces, not only influence and make use of the molecular conformation. They are also obviously decisive in the lattice buildup analogously to some nine- and six-membered calixarene hosts with heteroaromatic spacers [28].

In summary, development of the present host design leads to new cyclophane receptors containing inward preorganized carboxylic acid groups. They were obtained using a modular strategy where 2,6-disubstituted benzoic acid and diphenylmethane analogous building blocks are combined to form the macrocycles. As shown for the macrorings **1** and **2**, molecular recognition of suitable guest molecules including alcohols and amines takes place inside of the host cavity involving both of their carboxy groups as binding sites in a clear *endo* mode. This particular inclusion behaviour is promising to a range of potential applications such as catalysis [1b, 29], selective compound extraction and transport [14, 30, 31] or sensing [32, 33]. Moreover, with reference to the modular strategy the concept is capable of development yielding other *endo*-dicarboxylic receptors having variable shapes and sizes of the host cavity on varying the bridging elements.

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Experimental

Synthesis. Melting points (uncorrected): Kofler melting point apparatus. – IR spectra: Perkin-Elmer FT-IR-1600 spectrometer. – NMR spectra: Bruker AC-200 (200 MHz – ^{1}H, 50 MHz – ^{13}C; δ values in ppm relative to tetramethylsilane as internal standard). – Mass spectra: Cratos Concept 1H (FAB). – Elemental analyses: Heraeus CHN–O-Rapid. All reagents were commercial products and were utilized without further purification. The solvents used were purified or dried by common literature procedures.

Starting materials: 2,2-Bis(4-hydroxyphenyl)propane (**6b**) and 4,4'-dihydroxybenzophenone (**6c**) are commercially available (Aldrich) while 1,1-bis(4-hydroxyphenyl)cyclohexane (**6a**) [22] and methyl 3,3-bis(4-hydroxyphenyl)butyrate (**6d**) [23] were prepared by literature procedures. 2,6-Dimethyl-4-*tert*-butylbenzoic acid (**10**) was obtained analogously to mesitoic acid [19] from 4-*tert*-butyl-m-xylene (**8**) by bromination to give 4-*tert*-butyl-2,6-dimethylbromobenzene (**9**) (88%, *m.p*. 48 – 49 °C) which was converted to the carboxylic acid **10** by Grignard reaction with carbon dioxide (60%, *m.p*. 167–168 °C). Compound **10** was stirred with a threefold excess of thionyl chloride for 12 h at room temperature. The reaction mixture was cooled to 0 °C and quenched with an excess of absolute methanol. Evaporation of methanol and distillation of the resulting residue yielded 88% methyl 4-*tert*-butyl-2,6-dimethylbenzoate (**11**) (*m.p*. 38 – 40 °C) [20]. NBS-bromination of the methyl ester **11** by refluxing 2.1 equivalents of NBS and a trace of AIBN in tetrachloromethane for 3 h followed by usual workup (recrystallization from *n*-pentane) gave 65% of methyl 2,6-bis(bromomethyl)-4-*tert*-butylbenzoate (**7**) (*m.p*. 94 – 96 °C) [21].

Macrocyclic Ester Derivatives 5a – d (General Procedure)

Under an atmosphere of argon 13.03 g (40 mmol) of cesium carbonate and 5 g of molecular sieve (0.4 Å, both dried for 12 h at 200 °C) was suspended in 1250 ml of dry acetone. The stirred suspension was heated to reflux, and a mixture of

20 mmol **7** and 20 mmol of the corresponding bisphenol **6a**–**d** in 500 ml of dry acetone was added dropwise over 8 h. After heating and stirring for additional 3 h, the reaction mixture was cooled to room temperature and filtered. Evaporation of the solvent gave a yellow oily residue which was taken up in chloroform (50 ml) and thoroughly filtered through silica gel (6 cm × 10 cm^2). After removal of the solvent under reduced pressure the oily residue was dissolved in acetone and allowed to stand at 8 °C for several days (3–10 d). The colourless solid which formed was collected and recrystallized from acetone. Specific details for each compound are given below.

Dimethyl 5',28'-di-tert-butyl-1',10',24',33'-tetraoxa-dispiro[cyclohexane-1,17'-([2](1,3)benzeno[2]-(1,4)benzeno[1] (1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1] (1,4)benzenophane)-40' 1''-cyclohexane]-8',31'-dicarboxylate (**5a**)

Reaction of 7.56 g **7** and 5.37 g **6a** yielded 1.95 g (20.1%) **5a** as a colourless solid, *m.p.* > 300 °C. – IR (KBr): ν/cm^{-1} = 2935, 2860, 1731, 1609, 1508, 1279, 1242, 881, 824. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 1.24 (s, 18H), 1.42 (m, 12H), 2.13 (m, 8H), 2.80 (s, 6H), 5.00 (s, 8H), 6.89 (d, 8H, J = 9 Hz), 7.07 (d, 8H, J = 9 Hz), 7.35 (s, 4H). – ^{13}C NMR (50 MHz, CD_2Cl_2): δ/ppm = 23.38, 26.78, 31.22, 35.07, 37.23, 45.12, 51.22, 69.34, 114.07, 126.49, 128.17, 130.56, 136.03, 142.24, 153.54, 156.78, 168.72.

$C_{64}H_{72}O_8$	Calcd.: 968.52	Found: 968.5 (MS, FAB).
$C_{64}H_{72}O_8 \cdot H_2O$ (987.29)	Calcd.: C 77.86	H 7.55
	Found: C 77.90	H 7.30.

Dimethyl 5,28-di-tert-butyl-17,17,40,40-tetramethyl-1,10,24,33-tetraoxa-[2](1,3)benzeno[2] (1,4)benzeno[1] (1,4) benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzenophane-8,31-dicarboxylate (**5b**)

Reaction of 7.56 g **7** and 4.57 g **6b** yielded 1.29 g (14.5%) of **5b** as a colourless solid, *m.p.* > 300 °C. – IR (KBr): ν/cm^{-1} = 2934, 2856, 1727, 1607, 1509, 1225, 900, 824. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 1.35 (s, 18H), 1.66 (s, 12H), 3.03 (s, 6H), 5.13 (s, 8H), 6.74 (d, 8H, J = 8.4 Hz), 7.08 (d, 8H, J = 8.4 Hz), 7.38 (s, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 30.17, 31.14, 34.83, 41.37, 51.11, 69.49, 113.81, 126.01, 127.43, 130.18, 135.82, 143.75, 153.13, 156.85, 168.77.

$C_{58}H_{64}O_8$	Calcd.: 888.45	Found: 888.4 (MS, FAB).
$C_{58}H_{64}O_8 \cdot H_2O$ (907.10)	Calcd.: C 76.79	H 7.11
	Found: C 76.83	H 7.25.

Dimethyl 5,28-di-tert-butyl-17,40-dioxo-1,10,24,33-tetraoxa-[2](1,3)benzeno[2](1,4)benzeno[1](1,4)-benzeno[2](1,3) benzeno[2](1,4)benzeno[1](l,4)benzenophane-8,31-dicarboxylate (**5c**)

Reaction of 7.56 g **7** and 4.28 g **6c** yielded 0.97 g (11.2%) **5c** as a colourless solid. **5c** dec. > 280 °C. – IR (KBr): ν/cm^{-1} = 2959, 1715, 1645, 1599, 1505, 1286, 851, 767. – ^{1}H NMR (200 MHz, $CDC1_3$/DMSO-d6): δ/ppm = 1.15 (s, 18H), 3.26 (s, 6H), 5.34 (s, 8H), 6.86 (d, 8H, J = 8.5 Hz), 7.35 (s, 4H), 7.56 (d, 8H, J = 8.5 Hz). – ^{13}C NMR (50 MHz, $CDC1_3$/DMSO-d6): δ/ppm = 30.28, 34.26, 51.61, 68.08, 114.01, 123.20, 125.76, 130.32, 131.46, 135.47, 153.53, 161.24, 167.90, 193.64.

$C_{54}H_{52}O_{10}$	Calcd.: 860.35	Found: 860.4 (MS, FAB).
$C_{54}H_{52}O_{10} \cdot H_2O$ (879.01)	Calcd.: C 73.79	H 6.19
	Found: C 73.54	H 6.15.

Dimethyl 2,2'-[5,28-di-tert-butyl-17,40-dimethyl-8,31-bis(methoxycarbonyl-[2](1,3)benzeno[2](1,4)benzeno [1](1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4) benzenophane-17,40-diyl]-diacetate (**5d**)

Reaction of 7.56 g **7** and 5.73 g **6d** yielded 1.86 g (18.5%) of **5d** as a colourless solid, *m.p.* 221–223 °C. – IR (KBr): ν/cm^{-1} = 2952, 1733, 1610, 1509, 1245, 884, 831. – ^{1}H NMR (200 MHz, $CDC1_3$): δ/ppm = 1.33 (s, 18H), 1.83 (s, 6H), 3.03 (s, 6H), 3.10 (s, 4H), 3.46 (s, 6H), 5.24 (s, 8H), 6.72 (d, 8H, J = 8.8 Hz), 7.03 (d, 8H, J = 8.8 Hz), 7.38 (s, 4H). – ^{13}C NMR (50 Mhz, $CDC1_3$): δ/ppm = 27.24, 31.00, 34.67, 43.64, 45.62, 50.96, 51.12, 69.36, 113.74 , 125.88, 127.48, 129.94, 135.56, 141.32, 152.95, 156.86, 168.59,171,72.

$C_{62}H_{68}O_{12}$	Calcd.: 1004.47	Found: 1004.4 (MS, FAB).
$C_{62}H_{68}O_{12} \cdot H_2O$ (1023.23)	Calcd.: C 72.78	H 6.90
	Found: C 72.66	H 6.83.

Macrocyclic Carboxylic Acids 1–4 (General Procedure)

1 mmol of the diesters **5a**–**5c** or of the tetraester **5d** was suspended in 50 ml *n*-butanol. After addition of a tenfold excess (per ester function) of a 10 molar aqueous cesium hydroxide solution, the reaction mixture was heated under reflux until a clear solution was obtained. Heating was continued for 3 h, and the solvent removed under reduced pressure. The solid residue was suspended in 50 ml of 1N hydrochloric acid and stirred at room temperature for 1 h. The aqueous suspension was extracted three times with 50 ml chloroform.The combined organic layers were dried over Na_2SO_4 and the solvent evaporated. The crude products were purified by recrystallization from benzene. Specific details for each compound are given below.

5',28'-Di-tert-butyl-1',10',24',33'-tetraoxa-dispiro[cyclohexane-1,17'-([2](1,3)benzeno[2]-(1,4)benzeno[1](1,4) benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzenophane)-40',1''-cyclohexane]-8',31'-dicarboxylic acid (**1**)

2.45 g (2.53 mmol) **5a** yielded 2.04 g (85.7%) **1** as a colourless solid, *m.p.* > 300 °C. – IR (KBr): ν/cm^{-1} = 2935, 2860, 1703, 1608, 1509, 1243, 884, 824. – ^{1}H NMR (200 MHz; $CDCl_3$): δ/ppm = 1.26 (s, 18H), 1.51 (m, 12H), 2.18 (m, 8H), 5.17 (s, 8H), 6.76 (d, 8H, J = 8.5 Hz), 7.06 (d, 8H, J = 8.5 Hz), 7.41 (s, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$/DMSO-d6): δ/ppm = 22.38, 25.87, 30.81, 34.32, 35.98, 43.76, 78.81, 113.68, 125.64, 127.06, 127.45, 134.38, 140.70, 151.42, 155.94, 169.02.

$C_{62}H_{68}O_8$	Calcd.: 940.49	Found: 940.4 (MS, FAB).
$C_{62}H_{68}O_8 \cdot 3H_2O$ (995.26)	Calcd.: C 74.82	H 7.49
	Found: C 74.96	H 7.79.

5,28-Di-tert-butyl-17,17,40,40-tetramethyl-1,10,24,33-tetraoxa-[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzenophane-8,31-dicarboxylic acid (**2**)

1.84 g (2.07 mmol) **5b** yielded 1.45 g (80.5%) **2** as a colourless solid, *m.p.* > 300 °C.). – IR (KBr): ν/cm^{-1} = 2962, 2878, 1724, 1608,1509, 1228, 883, 830. – ^{1}H NMR (200 MHz;

$CDCl_3$/DMSO-d_6): δ/ppm = 1.29 (s, 18H), 1.60 (s, 12H), 5.06 (s, 8H), 6.69 (d, 8H, J = 8.8 Hz), 7.05 (d, 8H, J = 8.8 Hz), 7.34 (s, 4H).
$C_{56}H_{60}O_8$ Calcd.: 860.43 Found: 860.5 (MS, FAB).
$C_{56}H_{60}O_8 \cdot 3H_2O$ (915.14) Calcd.: C 73.50 H 7.27 Found: C 73.71 H 6.96.

5,28-Di-tert-butyl-17,40-dioxo-1,10,24,33-tetraoxa-[2](1,3)benzeno[2](1,4)benzeno[1](1,4)-benzeno[2] (1,3)benzeno[2](1,4)benzeno[1](l,4)benzenophane-8,31-dicarboxylic acid (**3**)

1.44 g (1.67 mmol) **5c** yielded 1.05 g (75.5%) **3** as a colourless solid, *m.p.* > 300 °C. – IR (KBr): ν/cm^{-1} = 2955, 1702, 1642, 1600, 1507, 1227, 849, 768. – ^{1}H NMR (200 MHz; $CDCl_3$/ DMSO-d_6): δ/ppm = 1.21 (s, 18H), 5.52 (s, 8H), 6.98 (d, 8H, J = 10.4 Hz), 7.39 (s, 4H), 7.70 (d, 8H, J = 10.4 Hz).
$C_{52}H_{48}O_{10}$: Calcd.: 832.32 Found: 833.3 (M^++H; MS, FAB).
$C_{52}H_{48}O_{10} \cdot H_2O$ (850.97) Calcd.: C 73.40 H 5.92 Found: C 73.47 H 5.65.

2,2'-[5,28-Di-tert-butyl-17,40-dimethyl-8,31-bis(methoxycarbonyl-[2](1,3)benzeno[2](1,4) benzeno[1](1,4)benzeno[2](1,3)benzeno[2](1,4)benzeno[1](1,4)benzenophane-17,40-diyl]-diacetic acid (**4**)

1.56 g (1.55 mmol) **5d** were hydrolyzed as given above. Different from the general procedure, extraction with chloroform is not applicable. Instead of this, the crude acid was filtered off and washed thoroughly with cold water. Recrystallization from ethanol yielded 1.27 g (86.2%) **4** as a colourless solid, *m.p.* 249–252 °C. – IR (KBr): ν/cm^{-1} = 2964, 1707, 1609, 1509, 1242, 883, 832. – ^{1}H NMR (200 MHz; DMSO-d_6): δ/ppm = 1.30 (s, 18H), 1.81 (s, 6H), 3.08 (s, 4H), 5.10 (s, 8H), 6.74 (d, 8H, J = 8.8 Hz), 7.10 (d, 8H, J = 8.8 Hz), 7.52 (s, 4H). – ^{13}C NMR (50 MHz, DMSO-d_6): δ/ppm = 26.52, 30.92, 34.52, 42.96, 45.16, 68.62, 113.91, 125.81, 127.36, 132.09, 134.71, 141.14, 151.65, 156.51, 169.13, 172.45.
$C_{58}H_{60}O_{12}$: Calcd.: 948.41 Found: 948.3 (MS, FAB).
$C_{58}H_{60}O_{12} \cdot 3\,H_2O$ (1003.15) Calcd.: C 69.45 H 6.63 Found: C 69.66 H 6.47.

Crystalline Inclusion Compounds

The alcoholic host–guest complexes (Table 2) were obtained by recrystallization from a saturated host solution in the respective alcohol. For preparation of the inclusion complexes with amines (Table 1) host and guest were dissolved in separate volumes of solvent (chloroform or dichloromethane for hosts **1**–**3** and ethanol for **4**). Combining the two solutions (solution of the guest in excess) and slow concentration yielded the stoichiometric complexes. The compounds were isolated by suction filtration, washed with the respective solvent and dried for 15 min at 18 Torr. Yields obtained for the alcohol and amine complexes are between 80–95%. The host:guest stoichiometric ratios were determined by ^{1}H NMR integration of the compounds in $CDCl_3$ solution.

X-ray Crystal Structure Analyses

Crystals of **1**·2 EtOH, **2**·2 EtOH·2 H_2O and **3**·3 EtOH suitable for crystallographic studies were obtained by slow concentration of solutions of **1**, **2** and **3** in ethanol, respectively. The diffraction data were collected on an Enraf-Nonius CAD-4 instrument. The data sets of **1**·2 EtOH and **2**·2 EtOH·2H_2O were measured at T = 130 K (CuKα-radiation, λ = 1.54178) using an ω-2θ scan technique, and the measurement of **3**·3 EtOH was performed at T = 293 K (CuKα-radiation, λ = 1.54178, ω scan technique). The crystals of **1**·2 EtOH decomposed so quickly that the positions of ethanol guest molecules could not be determined. The structure was therefore not refined satisfactorily (no R value is given) and only a rough model of the host structure could be obtained. The models of the other two inclusion compounds were obtained using SHELXS-86 [34] and were refined to convergence at the respective R values.

Crystal data for **1**·2 EtOH: $C_{66}H_{80}O_{10}$; M = 1033.34; ρ = 1.025 g/cm^3; space group $P2_1/n$; a = 26.632(3), b = 10.636(1), c = 11.850(1) Å; α = 90, β = 93.91(1), γ = 90°; V = 3349 Å^3; Z = 2; F(000) = 1112; μ = 0.510 mm^{-1}.

Crystal data for **2**·2 EtOH·2 H_2O: $C_{60}H_{76}O_{12}$; M = 989.25; crystal dimensions = 0.20 × 0.08 × 0.08 mm, ρ =1.165 g/cm^3; space group $P2_1/n$; a = 14.638(3), b = 15.227(3), c = 25.127(5) Å; β = 91.13(3)°; V = 5600 Å^3; Z = 4 ; F(000) = 2100; μ = 0.649 mm^{-1}; number of reflections 8227 (measured), 7872 (independend), 880 (observed) [2σ(I)]; refined parameters 650; R = 0.1028, wR = 0.2647.

Crystal data for **3**·3 EtOH: $C_{58}H_{66}O_{13}$; M = 971.15; crystal dimensions = 0.25 x 0.35 x 0.40 mm; ρ = 1.182 g/cm^3; space group $P\bar{1}$; a = 11.466(2), b = 15.875(2), c = 16.028(2) Å; α = 73.14(1), β = 86.60(1), γ = 77.77(1)°; V = 2727 Å^3; Z = 2; F(000) = 1036; μ = 0.640 mm^{-1}; number of reflections 8554 (measured), 8083 (independent), 5658 (observed) [3σ(I)]; refined parameters 598; R = 0.1098, wR = 0.1430.

Supplementary material. Lists of the structure factors, atomic coordinates and thermal components for non-hydrogen atoms and hydrogen atom parameters are available from E. W. on request.

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