Macroring–Neutral Molecule Complexation. Synthesis of Biconcave Pyridino Hosts, Complex Formation, and X-ray Crystal Structures of Two Inclusion Compounds

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A series of pyridino macrocycles **1–3(a–e)** incorporating rigid bi- and triaryl ether segments in different ring positions have been synthesized. The effect of incorporation of these building blocks into a given macroring framework on the host properties for uncharged-molecule inclusion has been studied. Symmetric 21-membered macrorings **1c**, **1d**, or **2c**, **2d** with tri-*o*-phenylene, tri-2,3-naphthylene, or mixed phenylene naphthylene ether units are efficient hosts in solid-state complexation of dipolar–aprotic and apolar guests such as nitro compounds and nitriles as well as DMF, DMSO, THF, dioxane, or benzene. X-ray analyses of the solid-state complexes of **1d** with $PhNO_2$ (1:1) and MeCN (1:1) have been studied. It is shown that the presence of the triaryl ether segment induces a biconcave nonequally sided host conformation suitable for guest inclusion. The packing characterizes the host–guest topologies of the two inclusion compounds to be of (H-bonded) cavitate-type for the MeCN case and of interstitial channel type for the $PhNO_2$ case. A comparative discussion of the present and previous results support the interpretation of hemispherand preorganization for the new host structures.

There is considerable recent interest in weak molecular interactions due to their importance in biochemical processes[1] and in the design of organic superstructures[2] and recognition systems.[3] Host–guest complexes between crown compounds and uncharged organic molecules have proven to be satisfactory models for the study of these type of interactions[4] and for the development of molecular sensors.[5] Aryl-condensed pyridino crowns have grown into a broad family of host compounds endowed with these properties.[6] They provide rather rigid conformations with a well-defined arrangement of the binding sites; one (the basic pyridine N) is a strong acceptor group for H bonds. This makes comparison between differently substituted hosts easy and allows predictions. Unlike the simple 18-crown-6 with identical ring faces,[7] less symmetric aryl-condensed pyridino crowns have the opportunity to use different faces for substrate binding.

Recently, we reported on the host properties of the 21-membered tribenzopyridino crown **1c**[8] to guest molecules $MeNO_2$ and MeCN. In the solid state, they select different faces of the biconcave host for complexation.[9] A promising approach to obtaining different selectivities of organic guest molecules is to alter the cavities of either or both faces of the host molecule. Thus we made it our object to substitute the phenylenes of **1c** by naphthylene or ethylene units which are known[10] to provide high and low steric shielding, respectively. The corresponding macrocycles are **1b–d**, **2b–d**, **3a**, **3c**, and **3e**. Here we report the synthesis and complexation (solid-state inclusion) properties of the new macrorings, including that of the parent host **1c**, and present the structures of **1d**·MeCN (1:1) and **1d**·$PhNO_2$ (1:1), i.e. inclusion complexes of **1d** with dipolar guest species of different size and shape.

Results and Discussion

Synthesis. All macrocycles studied here **1b–d**, **2b–d**, **3a**, **3c**, and **3e** (Chart I) were assembled from building blocks specified in Chart II using blocking/deblocking[11] and ring-formation techniques.[12] Intermediates and components important for the ring formation step are shown in Chart III. Ring closure reactions to yield the given macrocycles **1–3** (see above) were accomplished between 2,6-bis(chloromethyl)pyridine (**4**)[13] and appropriate

Chart I

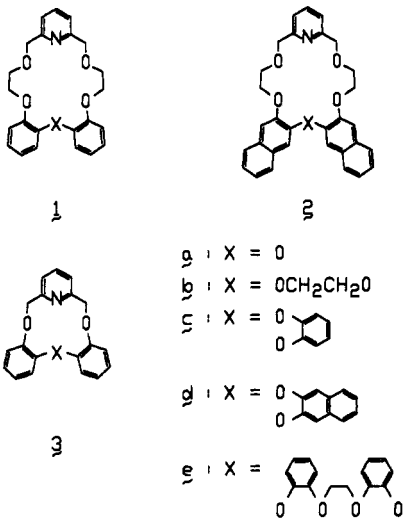

Chart II

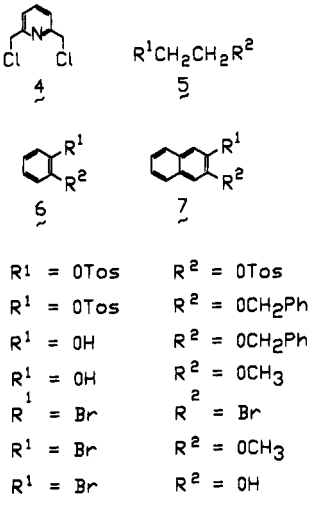

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Table I. Crystalline Inclusion Compounds[a]

guest compd	host						
	1b	**1c**	**1d**	**2b**	**2c**	**2d**[b]	**3e**
$MeNO_2$	–	1:1	1:1	–	1:2	1:1	–
$EtNO_2$	–	–	1:1	–	–	1:1	–
$PhNO_2$	–	–	1:1	1:1	1:1 ($0.5H_2O$)	–	1:1
MeCN	–	1:2	1:1	–	1:1	1:1	–
$ClCH_2CN$	1:2	1:1	1:1	–	1:1 ($0.5H_2O$)	1:1	–
$PhCH_2CN$	–	–	–	1:1	–	–	–
PhCN	–	–	1:1	1:1	1:1	–	–
DMF	–	–	1:1	–	–	1:2	–
DMSO	–	–	2:1	1:1	1:2 ($1H_2O$)	1:1	–
THF	–	–	1:1 ($1H_2O$)	–	1:1	–	–
dioxane	–	–	1:1	–	–	–	–
benzene	–	–	–	–	1:2 ($1H_2O$)	–	–
toluene	–	–	–	–	–	–	–

[a] Stoichiometric ratio host:guest, including analyzed water in the crystal. [b] In addition 1:1 complex with CH_2Cl_2.

Chart III

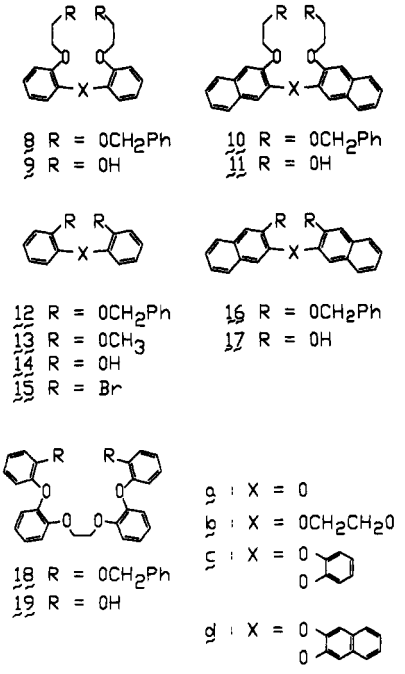
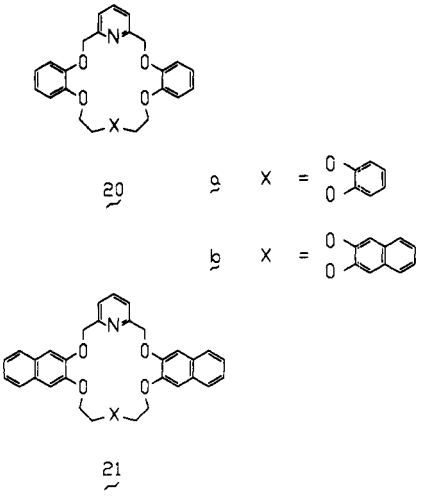


Chart IV



alcoholic and phenolic compounds, that is **9b–d**, **11b–d**, **14a**, **14c**, and **19**. For ring closure including alcoholic components (**9** and **11**), we used NaH in THF and applied high dilution conditions.[14] Phenolic compounds (**14** and **19**) were reacted with Cs_2CO_3 in dry DMF.[15]

The hydroxylic/phenolic components **9b–d**, **11b–d**, **14a**, **14c**, and **19** were obtained by deblocking (debenzylation or demethylation)[11,15b] of the corresponding ethers **8b–d**, **10b–d**, **13a**, **13c**, and **18**. Ethers **8b–d** and **10b–d** were

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Table II. Endocyclic Torsion Angles[a] in the Macrorings of Host–Guest Complexes 1d•$PhNO_2$ (1:1) and 1d•MeCN (1:1)

atoms	angle, deg		
	1d·$PhNO_2$ (1:1)	1d·MeCN (1:1)	$\Delta\tau$[b]
O(1)–C(1)–C(33)–N(1)	−169.8 (2)	−65.1 (4)	104.7
C(33)–C(1)–O(1)–C(2)	177.0 (2)	−172.7 (3)	10.3
C(1)–O(1)–C(2)–C(3)	−83.0 (3)	−179.3 (3)	96.3
O(1)–C(2)–C(3)–O(2)	82.0 (3)	75.0 (3)	7.0
C(2)–C(3)–O(2)–C(4)	175.3 (2)	168.2 (2)	7.1
C(3)–O(2)–C(4)–C(9)	−177.6 (2)	−168.5 (3)	9.1
O(2)–C(4)–C(9)–O(3)	−2.2 (3)	1.0 (4)	3.2
C(4)–C(9)–O(3)–C(10)	179.0 (2)	−156.7 (3)	24.3
C(9)–O(3)–C(10)–C(19)	73.0 (3)	61.4 (3)	11.6
O(3)–C(10)–C(19)–O(4)	−4.4 (4)	1.4 (4)	5.8
C(10)–C(19)–O(4)–C(20)	−176.7 (2)	−170.4 (2)	6.3
C(19)–O(4)–C(20)–C(25)	−109.1 (3)	−109.0 (3)	0.1
O(4)–C(20)–C(25)–O(5)	8.0 (4)	4.2 (4)	3.8
C(20)–C(25)–O(5)–C(26)	−172.4 (3)	179.6 (3)	8.0
C(25)–O(5)–C(26)–C(27)	177.5 (3)	−171.6 (3)	11.1
O(5)–C(26)–C(27)–O(6)	−169.6 (3)	−80.7 (3)	88.9
C(26)–C(27)–O(6)–C(28)	−179.9 (3)	−165.4 (3)	14.5
C(27)–O(6)–C(28)–C(29)	−77.0 (4)	−170.8 (3)	93.8
O(6)–C(28)–C(29)–N(1)	78.0 (4)	64.3 (4)	13.7
C(28)–C(29)–N(1)–C(33)	179.7 (3)	−179.5 (3)	0.8
C(1)–C(33)–N(1)–C(29)	179.0 (3)	175.2 (3)	5.8

[a] Estimated standard deviations given in parentheses in units of the least significant digit. [b] Difference in torsion angles.

synthesized from diphenols **14b–d** and **17b–d**, respectively, by reaction with tosylate **5b**. The bi- and triaryl building blocks **13c**, **13d**, **16c**, and **16d** were prepared by Ullmann coupling[16] of the monoblocked phenols/naphthols **6d** and **7c** with dibromides **6e** and **7e**, respectively. Intermediate **18** was synthesized via Ullmann reaction of **15b** with **6c**; **12b**, **15b**, and **16b** were obtained from dibromoethane (**5e**) or ethylene glycol ditosylate (**5a**) and the corresponding phenols/naphthols **6c**, **6g**, and **7c**.

Complex Formation. A variety of solvents differing in molecular size, shape, and polarity, such as alcohols, nitro compounds, nitriles, aromatic compounds, and heterocycles (cf. Table I), were used to investigate the solid-state complexation properties of potential host compounds **1b–d**, **2b–d**, **3a**, **3c**, and **3e**.

Unlike the isomeric hosts **20a**[17] and **20b**[18] (Chart IV) with separated aromatic units and other analogues previously studied,[17b] none of the present macrorings proved capable of forming a solid-state complex with alcohols. Also, the present macrorings show no host properties to amines. This is a somewhat unexpected behavior considering the presence of a pyridine N which is a potential receptor site for strong H bonds to alcohols and amines. However, some related pyridino crowns **21a** and **21b** with separated naphthalino moieties[19] behave in the same way, suggesting unfavorable ring conformation for the pyridine N. Aside from this fact, the majority of the new macrorings are rather efficient hosts for different solvents with dipolar–aprotic and apolar properties (Table I). They include various nitro compounds and nitriles, DMF, DMSO, THF, dioxane, CH_2Cl_2, benzene, and toluene. Nevertheless, each host has a characteristic level of selectivity. Macrorings **1d** and **2c** form a broad range of solid-state complexes while others allow only very few (**1c**, **2b**) or single complexes (**1b**, **3e**). As shown in Table I, complexation specifity is primarily a matter of discrimination between polar and less polar solvents; the latter being accommodated or not (cf. **1c** with **1d**, or **2c** with **2d**). Macrocycles **3a** and **3c** (12- and 15-membered rings, respectively) failed to form complexes (all other rings are 21-membered).

The results in Table I yield further details. Macroring **1c** not only yields very few complexes with dipolar aprotic compounds but also favors small molecules of the particular solvent classes (nitro compounds and nitriles); aromatic compounds are not complexed. Conversely **2b** favors the bulkier aromatic representatives of the given solvent classes. Although macroring **2d** is broader with reference to the solvent types, discrimination between aliphatic and aromatic compounds is distinct; only aliphatic molecules are complexed. A special feature of **2c** is the presence of stoichiometric amounts of water in some of the crystals which seems to add stability to the complexes. The only other hydrated complex is that of **1d** with THF.

The stoichiometric ratios of the complexes (Table I) range from 1:1 (host:guest), which is the most frequent, to 1:2 and 2:1, depending on the components. Remarkably, some exhibit varying ratios if the same guest molecule is involved (cf. $MeNO_2$, MeCN, and DMSO complexes). This is an important observation since all host molecules provide the same ring size (21-membered), and in some of them the only modification is replacement of phenylenes by naphthylenes which should not greatly alter the ring conformations.

Previous structural studies on $MeNO_2$ and MeCN complexes of **1c** (phenylene-condensed host) indicate a biconcave conformation with the guest molecules related to either the one or the other cavity which gives rise to particular packing modes in the crystals.[8,9] The $MeNO_2$ complex of **1c** is a cage-type H-bonded inclusion species. The other, MeCN complex of **1c**, shows channel topology and involves MeCN molecules with a different H-bonding pattern. There is evidence from Table I that the presence and the type of aromatic ring incorporated in the macrocycles are decisive factors controlling the complexation/inclusion properties of the new hosts. In order to find out the particular effect of the naphtho substitution, we studied the X-ray crystal structures of two complexes/inclusion compounds of **1d** (naphtho analogue of **1c**), namely 1d·$PhNO_2$ (1:1) and 1d·MeCN (1:1). They refer to dipolar protic guest molecules having different size and shape.

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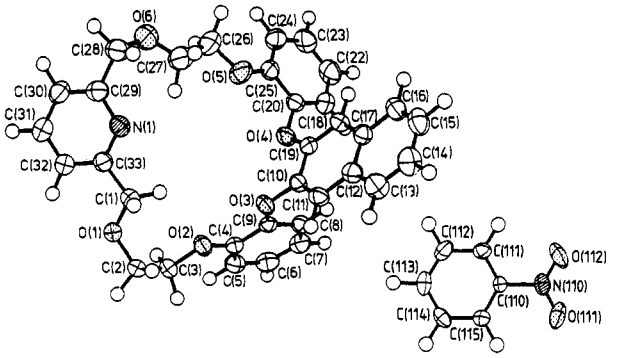

Figure 1. Molecular structure of **1d**·$PhNO_2$ (1:1), showing the atom numbering scheme. Heteroatoms are shaded.

X-ray Analysis: Structure Description of 1d·$PhNO_2$ (1:1) and 1d·MeCN (1:1). Views of the molecular and packing structures are presented in Figures 1–4. A complete numbering scheme of the host atoms and the $PhNO_2$ is given in Figure 1; MeCN is included in Figure 3. Endocyclic torsion angles in the macrorings are listed in Table II. Positional and thermal parameters of the atoms, bond distances, and bond angles (Tables V–X) are available as Supplementary Material.

1d·$PhNO_2$ (1:1). The macroring adopts a fairly unsymmetrical conformation in this complex (torsion code: $aag^-g^+aasag^+sag^-saaag^-g^+aa$) and reveals several noticeable torsion angles (Table II) owing to the rigid geometry of the aryl ether segment.[20] This yields the particular conformation of the macroring with both benzylic oxygens turned outward (one is more outward than the other) and two hydrogens pointing inward (Figure 1). The shape of the host molecule may be regarded as biconcave, with a deep cleft involving the central macroring and the naphthalene unit, and a shallower bowl-shaped cavity formed by the macroring, the lateral phenylenes, and the pyridine nucleus. These two cavities are on different sides of the macroring (see Figure 2).

The guest molecule $PhNO_2$ adopts the expected planar conformation which is found in crystalline $PhNO_2$.[21] Unlike crystalline $PhNO_2$, in the present $PhNO_2$ molecules the NO_2 group is unsymmetric [N(110)–O(111) = 122.6 pm and N(110)–O(112) = 117.5 pm vs 120.8 pm for crystalline $PhNO_2$; C(110)–N(110)–O(111) = 116.0° and C(110)–N(110)–O(112) = 119.3° vs 118° for crystalline $PhNO_2$]. The distortion is attributed to packing forces. The guest molecules lie as parallel pairs about a center of inversion, with an interplanar distance of 339 pm. There is a close contact between O(111) and C′(115) on the aromatic ring, explaining the asymmetry of the nitro moiety.

The pairs of guest molecules occupy channels formed by opposing host macrocycles (Figure 2). For channel building, the host molecules use their deep V-shaped cleft giving rise to a nearly rectangular cross-section of the channel (van der Waals dimension 5 × 8 Å). The planar $PhNO_2$ molecules are oriented along the channels. The lower cleft of the host molecule not including the naphthylene unit, however, is effective for packing in that macrorings and phenylene groups of different hosts interlock. As evident from Figure 2, packing motifs are also responsible for the irregular host conformation.

1d·MeCN (1:1). The macroring **1d** in the MeCN complex provides expected[20] torsion code $g^-aag^+aasag^+sag^-saag^-aag^+aa$ (cf. Table II), thereby adopting a relatively symmetric unstrained conformation (Figure 3). All oxygens point inward and the hydrogens are located outside.

As before, the macrocycle uses the V-shaped deep cleft involving the naphthylene unit for guest accommodation. However, the host–guest aggregate now exhibits the character of an intramolecular inclusion (cavitate or more precisely specified as aediculate type)[22] rather than a lattice void inclusion.[23] The rod-shaped MeCN molecule points lengthwise with the Me terminal into the cleft with orientation nearly perpendicular to the best plane defined by the heteroatoms N(1), O(1), O(2), O(3), and O(6) of the macroring. The intermolecular distances between the Me group of MeCN [C(111)] and these heteroatoms are 327, 348, 346, 323, and 338 pm for N(1), O(1), O(2), O(3), and O(6), respectively. Among these parameters, only the O(3) contact has a reasonable geometry for a potential H bond interaction [H(C111)···O(3) = 225.4 pm, C(111)–H(C111)···O(3) = 150.3°]. However, to designate this contact as a weak C–H···O hydrogen bond[24] is very doubtful[25,26] and not warranted, at least for the temperature conditions of this study. Instead, rotational disorder of the methyl H atoms about the MeCN axis is suggested,[25b] indicating that no strong orienting influence is present. Indeed, assuming a tetrahedral geometry of the methyl C, no orientation of the methyl group is possible where all three hydrogens are reasonably positioned for potential H bonds. A similar situation is found for the MeCN complexes of dibenzo-18-crown-6[25c] and of related pyridino crowns.[9,27] For geometrical reasons, we can also rule out bifurcated C–H:::$(O)_2$ hydrogen bonds.[25a]

Comparative Discussion of the Two Structures Including Previous Structural Results. The present inclusion structures reveal that macroring **1d** is suitable as a host for guest molecules of different shape and chemical nature [$PhNO_2$ is planar[21] and highly polar (4.0 D)[28] while MeCN is rod-shaped[9,25] and less polar (3.44 D)[28]]. This requires of the host some structural adaptation manifested in a conformational rearrangement, when going from **1d**·$PhNO_2$ to **1d**·MeCN.

An illustration is given in Figure 4 showing the superimposed macroring conformations of **1d** of both complexes. It is also evident from Table II when considering $\Delta\tau$ (difference of corresponding torsion angles for both complexes) with numerical values as high as 104.7°. In particular, in the MeCN complex all oxygens of the macrocycle are turned inward, whereas the macroring conformation of the $PhNO_2$ complex has the benzylic oxygens outside or partly outward (Figure 4). Conformational rearrangement around the benzylic O-positions noticeably affects the pyridine ring in its orientation. While in the $PhNO_2$ complex the pyridine ring is nearly antiparallel to the naphthylene unit, in the MeCN complex these aromatic groups are at an obtuse angle one with another. By way of contrast, conformation of the triaryl ether segment is less affected in both complexes.

In the previously studied MeCN and $MeNO_2$ complexes of **1c**[8,9] (phenylene analogue of **1d**), overall conformations of the macrorings resemble that of **1d** in the present MeCN

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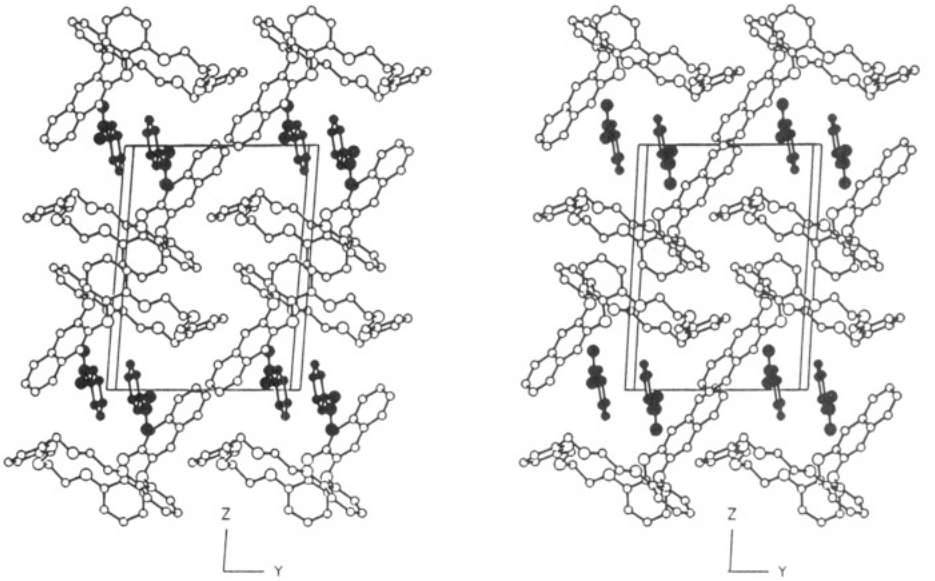

Figure 2. Stereoscopic packing illustration of **1d**·$PhNO_2$ (1:1). For clearness, H atoms are omitted; $PhNO_2$ molecules are shaded.

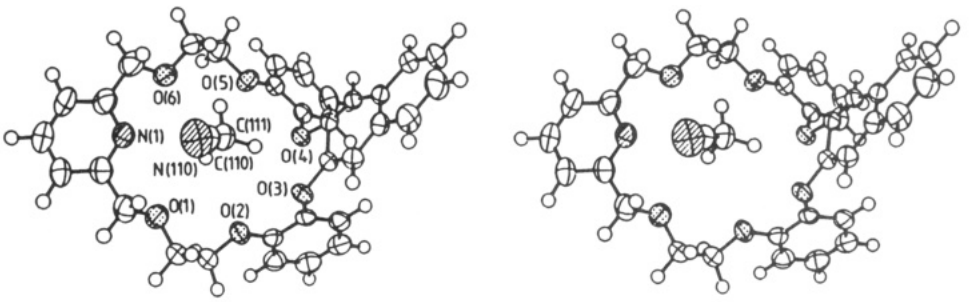

Figure 3. Molecular structure of **1d**·MeCN (1:1). Heteroatoms are shaded. Numbering scheme of the macroring atoms corresponds to Figure 1.

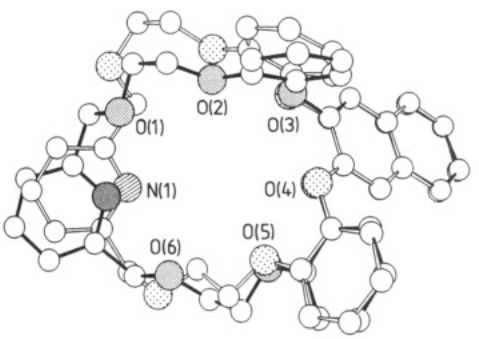

Figure 4. Superimposed macroring conformations corresponding to the $PhNO_2$ and MeCN complexes of **1d**, specified with unfilled und filled bond lines, respectively. Heteroatoms are shaded.

complex, except for the orientation of the pyridine ring (the pyridine rings are antiparallel with reference to the diametric aromatic unit in the **1c** complexes; **1d**·MeCN see above. Consequently, the cavity shapes are different for both macrocycles which is reflected in different geometries of the MeCN complexes of **1c** and **1d** in that MeCN is complexed at different host faces relative to the triaryl ether segment.

It is typical of uncomplexed macrocycles of this ring size to adopt asymmetrical conformations in the solid state with some heteroatoms pointing outward and consequently with some hydrogens inside the ring in order to avoid an unfavorably large empty hole and to reduce the high negative potential in the cavity if all oxygens point inward.[29] However, symmetrical conformations with a large cavity and all heteroatoms pointing inward dominate complexes stabilized by attractive interactions between host and guest molecules.[20] From that point of view, the MeCN complex of **1d**, and also the MeCN and $MeNO_2$ complexes of **1c**, relate to aggregations stabilized by some kind of attractive interactions between host and guest (weak H bonds or Coulomb-type interactions)[24-27] while the macroring conformation of **1d** in the $PhNO_2$ complex is suggestive of a rather unaffected host species.[20,29] Thus the structure of **1d**·MeCN (1:1) is phenotypical of a partially successful inclusion complex and that of **1d**·$PhNO_2$ (1:1) points to a crystal structure of **1d** with $PhNO_2$ as solvent of crystallization.

Conclusions

The present results show that macrorings incorporating a 2,6-fused pyridino unit and triaryl ether segments are a rich source of crystalline inclusion hosts (Table I). Whether inclusion compounds are formed with these molecules, and if so, what type is formed and which guest molecules are involved, depends on the ring size, the position of the mentioned building blocks, and the particular arylene subunits being used (1,2-phenylene or 2,3-naphthylene). A general trend evident from Table I is as follows: Variation of X in **1** and **2**, such as going from ethylene to 1,2-phenylene or 2,3-naphthylene, enhances inclusion formation with dipolar–aprotic and apolar

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molecules. This shows the general advantage of a triaryl ether segment in macrorings intended as inclusion hosts.

It is clear from the crystal structures (see Figures 1–4 and refs 8 and 9) that these triaryl ether segments are useful building blocks to lock a macroring into a biconcave conformation suitable for guest inclusion. Thus, the effect of enhanced rigidity of the triarylether moiety supports the principle of preorganization.[2b,6,30] Due to the aliphatic ether moieties, the present macrorings still have a reasonable degree of conformational freedom, as manifested in the crystal structures, which relate them to the hemispherand class of host molecules.[30,31]

The triaryl ether unit not only induces biconcave behavior of a host macroring but also establishes two unequal faces or sides for binding. Which side of a given macroring is complexed depends on the guest species,[8,9] but is also subject to packing relations[3b] and therefore difficult to predict. Another conclusion from the crystal structures is that the basic pyridine N is only rarely involved in direct host–guest interaction.[8] Also, from previous studies,[19,27] it became apparent that lateral naphthalene groups may support the formation of interstitial lattice inclusions rather than molecular complexes because of unintentional gearing effects between host molecules.

Considering these facts, a future host design based on oligoaryl ether supported macrocycles of the present type may involve exchange of the pyridine unit for a more efficient binding site[4] and the use of substituents[32] specifically attached to the lateral naphthalenes.

Experimental Section

General. For column chromatography Al_2O_3 (Brockmann, grade II–III; Woelm) and silica gel (0.063–0.1 mm; Merck) were used. A 10% Pd/C catalyst of type E10N (Degussa) was used in catalytic hydrogenations. Spectroscopic (^1H NMR, MS) and elemental analytical data for all new compounds are given in the supplementary material (Table III).

2,6-Bis(chloromethyl)pyridine (**4**),[13] 1,2-ethanediyl bis(*p*-toluenesulfonate) (**5a**),[33] 2-(benzyloxy)ethyl *p*-toluenesulfonate (**5b**),[34] 2-(benzyloxy)ethanol (**5c**)[35] 2-(benzyloxy)phenol (**6c**),[36] 3-(benzyloxy)-2-naphthol (**7c**),[37] and 2,3-dibromonaphthalene (**7e**)[38] were prepared according to the reported procedures.

2,2′-Oxydiphenol Bis(methyl ether) (13a). Ullmann condensation[39] between **6d** and **6f**: 49% colorless crystals (from EtOH/H_2O); mp 77–78 °C (lit.[40] mp 77–79 °C).

2,2′-(1,2-Phenylenedioxy)diphenol Bis(methyl ether) (13c). Ullmann condensation[34a,41] between **6d** and **6e**: 50% colorless crystals (from *n*-heptane); mp 103–104 °C (lit.[41] mp 103–104 °C).

2,2′-(2,3-Naphthylenedioxy)diphenol Bis(methyl ether) (13d). A mixture of **6d** (27.3 g, 220 mmol), **7e** (30.0 g, 105 mmol), Cu_2O (20.5 g, 143 mmol, dried at 100 °C), and 1,3-dimethylimidazolin-2-one (200 mL) was heated at 170–180 °C for 46 h and evaporated. Extractive workup of the residue (hot $CHCl_3$; washing with diluted HCl, then aqueous KBr solution) and chromatography (SiO_2; eluent $CHCl_3$/petroleum $CHCL_3$/petroleum ether 60–95 °C, 2:1) yielded 14.0 g (35.8%) of colorless crystals; mp 143–146 °C (from petroleum ether 60–95 °C).

Demethylation to the Diols 14a, 14c, and 14d. General Procedure. To a stirred solution of 75 mmol of the corresponding dimethyl ether (**13a**, **13c**, and **13d**) in 100 mL of dry CH_2Cl_2 at 0 °C was added via syringe under N_2–BBr_3 (28 mL, 300 mmol). The mixture was kept for 3 h at the same temperature, cooled to −50 °C, and quenched with MeOH. The mixture was evaporated with MeOH (4 × 50 mL), and the reside was dissolved in hot toluene and extracted with aqueous NaOH (2 N). The aqueous layer was separated and acidified (H_2SO_4), which precipitates the phenol. Recrystallization from *n*-heptane yielded colorless crystals. Details for the individual compounds are given below.

14a: 94%; mp 121–123 °C (lit.[40] mp 122–123 °C).

14c: 95%; mp 92–93 °C (lit.[41] mp 92–94 °C).

14d: 97%; mp 161–162 °C.

1,2-Bis[(2-bromophenyl)oxy]ethane (15b). To the sodium salt of **6g** [from **6g** (17.3 g, 100 mmol) and NaOH (4.0 g, 100 mmol)] in 130 mL of EtOH was added **5e** (9.40 g, 50 mmol). The mixture was refluxed for 7 h and subjected to standard workup including extraction (CH_2Cl_2) and recrystallization (MeOH) to yield 47% of colorless crystals with mp 117–118 °C.

3,3′-(1,2-Ethylenedioxy)bis-2-naphthol Bis(benzyl ether) (16b). From **7c** (12.5 g, 50 mmol), **5a** (7.41 g, 25 mmol), and Cs_2CO_3 (8.15 g, 25 mmol) in dry DMF analogous to the preparation of benzyl ethers **8** and **10** (see below). Recrystallization from $CHCl_3$/EtOH yielded 87% of colorless crystals with mp 157 °C.

3,3′-(1,2-Phenylenedioxy)bis-2-naphthol Bis(benzyl ether) (16c) and 3,3′-(2,3-Naphthylenedioxy)bis-2-naphthol Bis(benzyl ether) (16d). 3-(Benzyloxy)-2-naphthol (**7c**) (25.0 g, 100 mmol), **6e** (11.8 g, 50 mmol) or **7e** (14.3 g, 50 mmol), and Cu_2O (7.15 g, 50 mmol) in 200 mL of quinoline were reacted under the conditions described for **13d**.

16c: 31% cream-colored powder; mp 159–162 °C (from petroleum ether 60–95 °C).

16d: 27% cream-colored crystals; mp 73 °C.

2,2′-[1,2-Ethanediylbis(oxy-2,1-phenyleneoxy)]bisphenol Bis(benzyl ether) (18). A mixture of **15b** (18.6 g, 50 mmol), **6c** (20.0 g, 100 mmol), Cu_2O (4.2 g, 30 mmol), and K_2CO_3 (16.6 g, 120 mmol) in 300 mL of dry pyridine was refluxed under N_2 for 24 h. Workup as given for **13d**. Chromatography (Al_2O_3; eluent $CHCl_3$/*n*-heptane, 1:2) yielded 35% colorless crystals; mp 75–77 °C (from *n*-heptane).

Synthesis of Benzyl Ethers 8b, 8c, 8d, 10b, 10c, and 10d. General Procedure. A stirred mixture of 20 mmol of the respective diphenol (**14b–d**, **17b–d**) and of Cs_2CO_3 (6.51 g, 20 mmol) in 100 mL of dry DMF was heated at 80 °C for 1 h. Tosylate **5b** (12.3 g, 40 mmol) in 30 mL of dry DMF was added dropwise. Heating was continued for additional 6 h. The mixture was concentrated and poured into 300 mL of H_2O. Extractive workup ($CHCl_3$) and chromatography yielded the pure products. Details for the individual compounds are given below.

8b: Al_2O_3, eluent $CHCl_3$; 76% colorless crystals; mp 80–83 °C (from EtOH).

8c: Al_2O_3, eluent $CHCl_3$/*n*-heptane (1:1); 73% viscous oil.

8d: SiO_2, eluent $CHCl_3$; 81% highly viscous oil.

10b: SiO_2, eluent CH_2Cl_2; 87% colorless crystals; mp 134 °C (from EtOH).

10c: SiO_2, eluent CH_2Cl_2; 78% colorless crystals; mp 133–135 °C (from EtOH).

10d: Al_2O_3, eluent $CHCl_3$/petroleum ether 60–95 °C (1:1); 62% highly viscous oil which solidifies on standing; mp 103–104 °C.

Catalytic Hydrogenation to the Diols 9b–d and 11b–d and Diphenols 14b, 17b–d, and 19. General Procedure. A suspension of 25 mmol of the corresponding dibenzyl ether (**8b–d**, **10b–d**, **12b**, **16b–d**, and **18**, respectively) and 10% Pd/C (1.5–2.0 g) in 100–200 mL of EtOAc (unless otherwise stated) was hydrogenated in a Parr apparatus at 3 atm of H_2 and at 25 °C for 4 h. Recrystallization yielded colorless crystals. Details for the individual compounds are given below.

9b: 85%; from $CHCl_3$; mp 66–68 °C (lit.[14] mp 66–68 °C).

9c: 88%; from *n*-heptane; mp 97–99 °C.

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Table IV. Experimental Data of the X-ray Structure Analyses

	1d·$PhNO_2$ (1:1)	1d·MeCN (1:1)
(a) Crystal Data		
formula	$C_{39}H_{34}N_2O_8$	$C_{35}H_{32}N_2O_6$
formula wt, amu	658.71	576.65
crystal system	triclinic	monoclinic
space group	$P\bar{1}$ (no. 2)	$P2_1/n$ (no. 14)
lattice parameters		
a, pm	1058.9 (2)	1029.6 (3)
b, pm	1166.5 (3)	943.9 (2)
c, pm	1482.1 (4)	3146.3 (11)
α, deg	82.45 (2)	90.0
β, deg	79.30 (3)	97.59 (2)
γ, deg	67.73 (2)	90.0
V, nm^3	1.661	3.031
Z	2	4
D_{calcd}, g cm^{-3}	1.318	1.264
absorption coefficient (Mo Kα), cm^{-1}	0.55	0.60
(b) Data Collection		
intensity data measured/$2\theta_{max}$, deg	7639/54.0	6690/54.0
reflections observed	6661	5211
unique reflections/R_m	6345/0.009	4923/0.025
reflections suppressed with $\sigma(I)/I \geq$	0.50	0.66
(c) Structure Refinement		
parameters refined	451	397
reflections used	4957	3691
ratio reflections/parameter	10.99	9.30
R value, unique weights	6.17	5.14
rest electron density, e $Å^{-3}$	0.62	0.20

9d: 82%; from EtOAc; mp 127–129 °C.

11b: 86%; from EtOH; mp 155–156 °C.

11c: 83%; from EtOAc; mp 158–160 °C.

11d: 76%; from EtOH; mp 162–163 °C.

14b: 93%; from $CHCl_3$/petroleum ether 40–60 °C; mp 115–116 °C (lit.[42] mp 115–116 °C).

17b: in 50 mL of DMF; 92%; from $CHCl_3$; mp 265–266 °C.

17c: 71%; from $CHCl_3$/petroleum ether 60–95 °C; mp 190–191 °C.

17d: in 50 mL of DMF; 56%; from $CHCl_3$/MeOH; mp 210–213 °C.

19: 90%; from EtOH; mp 133–135 °C.

Synthesis of Macrocycles 1b–d and 2b–d. General Procedure. Ten millimoles of the respective diol (**9b–d** and **11b–d**) and 2,6-bis(chloromethyl)pyridine (**4**) (1.76 g, 10 mmol) in separate 250-mL portions of dry THF were simultaneously added under N_2 over a period of 10 h to a vigorously stirred refluxing suspension of NaH (1.5 g, 60 mmol) in 750 mL of dry THF (high dilution conditions).[14] After being boiled for an additional 4 h, the mixture was allowed to cool to room temperature and was quenched with MeOH. The solvent was removed, the resulting residue was extracted (hot CH_2Cl_2), and the extract was subjected to column chromatography (Al_2O_3). Recrystallization yielded colorless crystals. Details for the individual compounds are given below.

1b: eluent CH_2Cl_2; 44%; from *n*-heptane; mp 99–100 °C.

1c: eluent Et_2O; 45%; from MeOH; mp 105–106 °C.

1d: eluent $CHCl_3$; 52%; from *n*-heptane; mp 111–113 °C.

2b: eluent $CHCl_3$; 36%; from EtOH; mp 154 °C.

2c: eluent $CHCl_3$; 54%; from *n*-heptane; mp 129–131 °C.

2d: eluent CH_2Cl_2; 38%; from CH_2Cl_2/petroleum ether 60–95 °C; mp 143–144 °C.

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Synthesis of Macrocycles 3a, 3c, and 3e. General Procedure. Ten millimoles of the respective diphenol (**14a, 14c, 19**) and 2,6-bis(chloromethyl)pyridine (**4**) (1.76 g, 10 mmol) in separate 250-mL portions of dry DMF were simultaneously added over a period of 10 h under N_2 to a vigorously stirred suspension of Cs_2CO_3 (3.26 g, 10 mmol) in 350 mL of dry DMF at 70 °C. Stirring was continued for 4 h at the same temperature; workup and purification as before. Details for the individual compounds are given below.

3a: eluent $CHCl_3$; 36%; from *n*-heptane; mp 190–192 °C.

3c: eluent $CHCl_3$/*n*-heptane (3:1); from petroleum ether 60–95 °C; mp 129–131 °C.

3e: eluent $CHCl_3$; 50%; from *n*-heptane; mp 194–196 °C.

Preparation of the Crystalline Inclusion Complexes. General Procedure. The corresponding host compound was dissolved under heating in a minimum amount of the respective guest solvent. After storage for 12 h at room temperature, the crystals which formed were collected by suction filtration, washed with MeOH, and dried (1 h, room temperature, 15 Torr). Host:guest stoichiometry was determined by ^1H NMR integration. Data for each compound are given in Table I.

Crystallography. (a) Sample Preparation and Data Collection. Single crystals of **1d**·MeCN (1:1) and **1d**·$PhNO_2$ (1:1) were obtained from a solution of **1d** in MeCN and $PhNO_2$, respectively, as described above. Lattice parameters and reflection intensities were determined on a Enraf Nonius CAD4 diffractometer with Mo Kα radiation and graphite monochromator at 298 K. Correction for Lorentz polarization and intensity variations of three control reflections were applied, but no absorption correction.

(b) Structure Analysis and Refinement. All calculations were made on a Micro VAX II 630Q. Structures were solved by direct methods (SHELX 86)[43] and refined by block-diagonal least-squares methods (SHELX 76).[44] All atoms but hydrogens were refined with anisotropic displacement factors; hydrogens were put in calculated positions (C–H, 108.0 pm) and treated as riding on their parent C atoms. Illustrations were done by using KPLOT[45] and ORTEP[46] programs. The most important experimental data of the structure analyses are summarized in Table IV. Final atomic coordinates, thermal parametes, and bonding dimensions are listed in Tables V–X (supplementary material).

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Supplementary Material Available: Spectroscopic and elemental analytical data of the new compounds (Table III), positional paramaters and anisotropic temperature factors of the non-hydrogen atoms (Table V and VI), positional parameters and isotropic temperature factors for the hydrogen atoms (Table VII and VIII), and bond lengths and bond angles involving non-hydrogen atoms (Table IX and Table X) (13 pages). Ordering information is given on any current masthead page. A listing of observed and calculated structure factors is available directly from the author.

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