Macro-Rings Designed for Uncharged Molecule Complexation. Synthesis, Complex Formation, and Structural Studies of New Pyridino Crowns Incorporating Resorcinol and Hydroquinone Building Blocks. X-Ray Crystal and Molecular Structure of a 22-Membered Pyridino Crown

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The crystal structure of the pyridino crown (**2**) containing a resorcinol group is reported. Two crystallographically independent molecules of compound (**2**) with considerably different conformations are present in the crystal. Both molecules provide a potential cavity, but have other steric factors highly unfavourable for complex formation. Also, there is no free space in the crystal lattice for accommodation of a guest molecule. Based on this result, three pyridino crowns of different ring size incorporating two resorcinol units in different positions (**5a–c**) have been synthesized, together with the hydroquinone-group-containing analogues (**6a–c**). The host properties of the new macro-rings were determined. It was found that compound (**6c**) forms crystalline inclusion complexes with a number of dipolar aprotic and rather apolar organic guests such as nitromethane, acetonitrile, DMF, or dioxane, while the other compounds are inefficient. Host–guest relationships are discussed and conclusions for future host design are drawn.

There is considerable current interest in host compounds capable of selective complex formation with uncharged organic molecules both in solution and in the crystalline state.[1–5] Aryl-condensed pyridino crowns and related macro-rings have grown into a broad family of hosts endowed with these properties.[6] Nevertheless, it appeared that host behaviour in this class of compounds may strongly depend on each single constituent of the macro-ring, and may also depend on positional isomers of a given building block. For instance, the 21-membered tribenzopyridino macro-ring (**1c**) readily forms crystalline inclusion complexes with organic guests, among them alcohols and dipolar aprotic molecules.[7] Constitutional modifications of compound (**1c**), such as in structures (**2**) or (**3**), extinguish the facility for complex formation.[8] These compounds have only one of the three catechol units of compound (**1c**) (the middle one) replaced by an isomeric resorcinol or hydroquinone group.[9] A smaller ring compound (**4**) comprising catechol and resorcinol units is also inefficient in complex formation.[6] Its crystal structure showed that compound (**4**) has a ring size unfavourable towards molecular inclusion.[10]

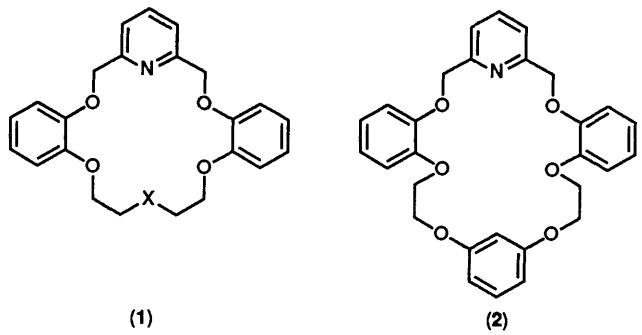
In order to gain more knowledge of the potential complexation behaviour of 1,3- or 1,4-benzo-condensed pyridino crowns, we became interested in the macro-rings of type (**5**) and (**6**). They are characterized by two lateral resorcinol or hydroquinone units with reference to the pyridine nucleus. We now report the synthesis and complexation properties of crown compounds (**5a–c**) and (**6a–c**). A structural study of resorcinol-modified macro-ring (**2**) is also included in this paper. The crystal structure of compound (**2**) was undertaken to rationalize the difference in inclusion behaviour between compounds (**1c**) and (**2**), and to establish guidelines for future host design such as that shown here.

Results and Discussion

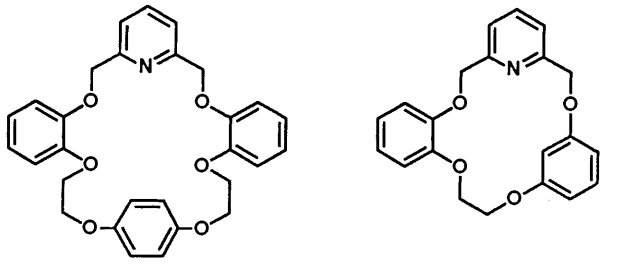
Crystal and Molecular Structure of Compound (**2**).—The final positional parameters of the non-hydrogen atoms for compound (**2**) are listed in Table 1. Selected bonding parameters are given in Table 2. There are two molecules (A and B) in the asymmetric unit, and these differ significantly from each other. Considering both molecules, A is more distorted than B.

Figures 1 and 2 show different views of the ring conformations of molecules A and B. In both cases, the overall geometry is different from the 'chair' form usually found for this class of compounds.[11,12] The torsion angles of the macrocyclic rings are expected to be *anti* (for C–X–C–C, X = O, N), ±*gauche* (for O–C–C–O), and *syn* (at 1,2-disubstituted benzene) as is usually observed for benzocrown compounds.[13] However, molecule A reveals a number of unusual endocyclic torsion angles of ± 130 ± 10° [denoted by * in Figure 1(*a*)]. They are specified in Table 2. Starting from the N(1)–C(2) bond, the macrocycle A [Figure 1(*a*)] has the conformation $aaxg^{-}saag^{+}asaasag^{+}xxsxaaa$ (where $x = 130 \pm 10°$), while molecule B [Figure 1(*b*)] has $aaag^{-}saag^{+}aaaaaag^{-}aasg^{+}aaa$. Thus, macro-ring A shows a fairly unsymmetrical structure, unlike ring B which has approximate mirror symmetry running through the pyridine atoms N(1) and C(24) and bisecting the opposite benzene ring (III).

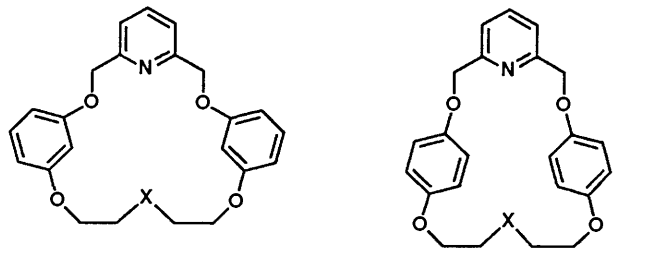
It is informative to draw a comparison with the all-1,2-phenylene analogous crown (**1c**). Here the macro-ring exists in a so-called 'dentist's chair' cavity-like conformation.[11] However, as Figures 2(*a*) and 2(*b*) illustrate, the A molecules have a 'distorted-boat' and the B molecules a 'distorted dentist's chair' conformation. The side views indicate that both types of molecule still provide a cavity, but the pyridino nitrogen (which is supposed to be the most efficient hydrogen-bond acceptor at complex formation) is in an unfavourable position for each molecule. In structure B, the pyridine N atom points away to the convex side of the molecule, while in molecule A the pyridino nitrogen and the C(12) atom of the opposite benzene ring (III) are pointing out in the same direction. These unfavourable steric factors prevent any hydrogen-bonded host–guest interaction. Also, the heteroatoms are not coplanar as for compound (**1a**).[11] A significant structural detail indicating the difference in shape of molecules A and B is the distance between the two end



(1) (2)

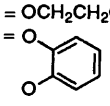


(3) (4)



(5) (6)

a; X = O
b; X = OCH_2CH_2O
c; X =



atoms C(24) and C(31) (Figure 2). For molecule A it is 4.0 Å, for molecule B 7.5 Å, nearly twice the distance in A.

There are two aliphatic C–C bonds in both molecules (A and B), namely the C(8)–C(9) and C(15)–C(16) bonds, whose mean lengths are significantly shorter (Table 2) than the normal values of 1.537 Å,[14] which can be attributed to the 'macrocyclic effect'.[8,13] The other mean bond lengths and angles (Table 2) are in good agreement with those of structures (**1**).[11] The non-bonded intramolecular distances for O-atoms in molecules A and B are 2.651(3) and 2.705(4) Å for O(4) ··· O(7), 2.952(4) and 2.714(4) Å for O(7) ··· O(10), 2.861(4) and 2.768(4) Å for O(14) ··· O(17), and 2.550(5) and 2.687(4) Å for O(17) ··· O(20), respectively. The value 2.550(5) Å is short compared with the van der Waals O ··· O non-bonded contact distance of 2.8 Å and it reflects the conformational strain of the macrocycle A. Considerable ring strain could be seen at C(2), C(5), C(6), C(11), C(13), C(18), and C(19) for both molecules.

The lattice structure (Figure 3) is such that molecules gear together to form a close package where parts of one molecule fill

* In some sense, this structure may be understood as a self-inclusion complex (pseudo-host–guest aggregate) where one macro-ring acts as the host for the other (guest). Both species differ by conformation (molecules A and B).

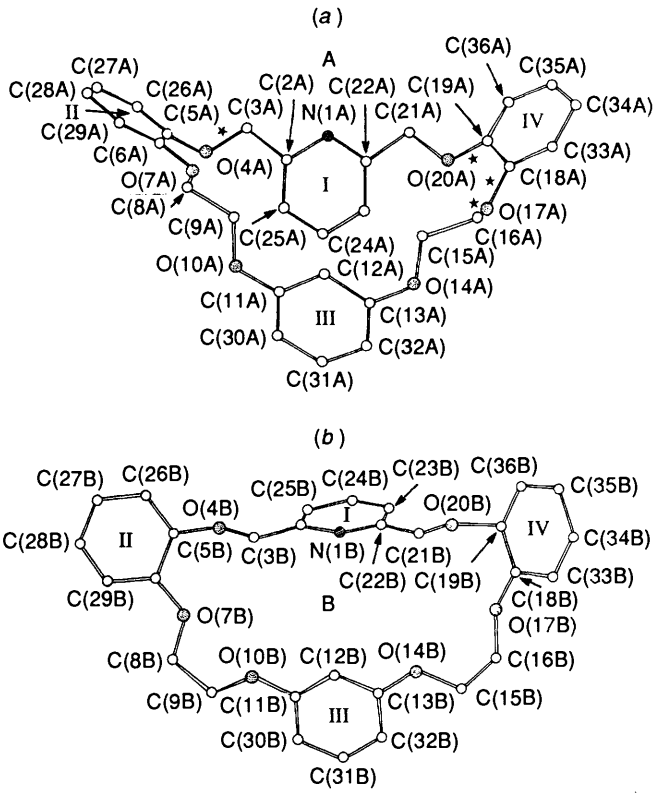


Figure 1. Structures of the two independent molecules of compound (**2**) (A and B) in the unit-cell [(*a*) and (*b*), respectively; top view] with the atom-numbering scheme (O atoms dotted, N atoms hatched, H atoms are omitted). The asterisks in (*a*) mark unusual torsion of molecule A.

the cavity space of its crystallographically independent counterpart. Consequently, no free lattice space for any guest species is available.* Also, there is no stacking either between pyridine nuclei or between any of the aromatic rings of neighbouring molecules, which stacking is normally a typical property of crystalline inclusion complexes of related pyridino hosts.[6,8,9b] Hence, the whole lattice structure simply follows a close packing motif and we may assume that the different conformations of compound (**2**) revealed in this structure are an implication of this.

This feature supports our chemical studies which showed that compound (**2**) could not be co-crystallized with the usual guest molecules.[8] The question arises as to whether this behaviour is general for a resorcinol group substituted at any position in a given host molecule. The same question applies to hydroquinone as the substituting building block in pyridino crowns [*cf.* structure (**3**)].[8] For that reason we undertook syntheses of macro-rings (**5a–c**) and (**6a–c**) which are pyridino crowns of various ring size with two resorcinol or hydroquinone building blocks in a different position [*cf.* structures (**2**) and (**3**)] and studied their capability of forming crystalline complexes with uncharged organic molecules.

Synthesis.—The new macro-rings were prepared by the procedure shown in Scheme 1. This involves reaction of monobenzyl-protected resorcinol (**9**) or hydroquinone (**10**) with the respective dichlorides (**8a–c**) to give the corresponding bis-benzyl ethers (**11a–c**) and (**12a–c**) in 50–60% yields [(**11c**) in 30%]. From former studies[8,9] it appeared that Cs_2CO_3 in dry dimethylformamide (DMF) is a favourable base system for Williamson-type reactions such as these shown here. Hydrogenolysis of compounds (**11a–c**) and (**12a–c**) gave the

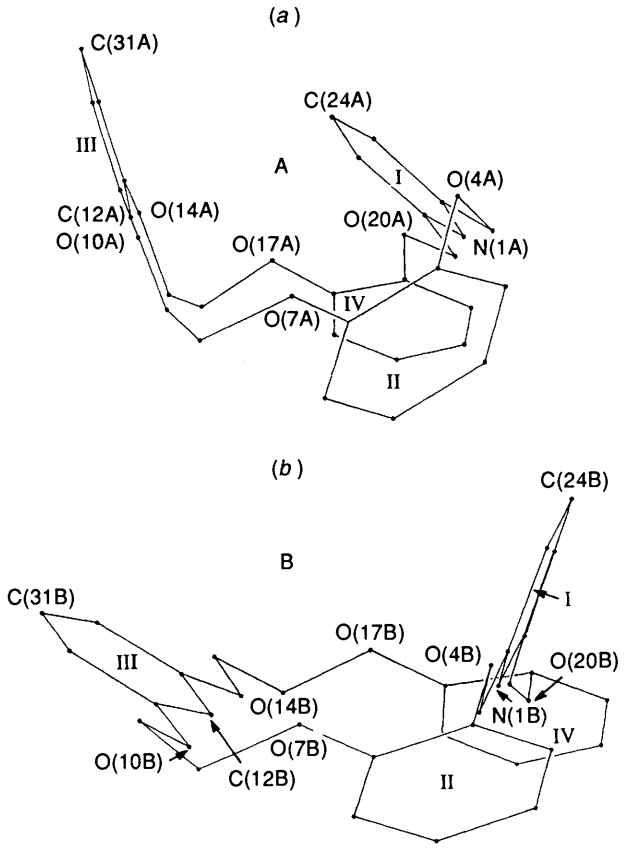


Figure 2. Side view (line drawing) of the A and B molecules of compound (**2**) [(*a*) and (*b*), respectively]. Relevant atoms are specified with numbers.

Table 1. Fractional atomic co-ordinates of non-hydrogen atoms for compound (**2**) (esds are in parentheses).

Atom	*x*	*y*	*z*
N(1A)	0.429 1(3)	0.182 5(2)	0.223 0(2)
C(2A)	0.424 1(3)	0.234 5(3)	0.287 5(2)
C(3A)	0.458 5(4)	0.170 0(3)	0.352 9(2)
O(4A)	0.436 7(2)	0.227 2(2)	0.424 2(1)
C(5A)	0.361 7(4)	0.188 9(3)	0.489 8(2)
C(6A)	0.230 3(3)	0.214 9(3)	0.503 8(2)
O(7A)	0.185 5(2)	0.273 5(2)	0.448 5(1)
C(8A)	0.050 2(4)	0.309 5(4)	0.463 8(2)
C(9A)	0.026 1(4)	0.359 8(4)	0.390 3(2)
O(10A)	0.051 9(3)	0.459 1(2)	0.386 7(1)
C(11A)	0.058 7(4)	0.507 6(4)	0.316 3(2)
C(12A)	0.032 5(4)	0.465 6(4)	0.252 4(2)
C(13A)	0.050 9(4)	0.519 3(4)	0.182 6(2)
O(14A)	0.035 3(3)	0.482 6(2)	0.115 0(1)
C(15A)	0.006 6(4)	0.384 3(4)	0.114 9(2)
C(16A)	0.030 8(4)	0.348 5(4)	0.032 1(2)
O(17A)	0.164 8(3)	0.327 8(3)	−0.000 8(2)
C(18A)	0.220 6(3)	0.238 9(3)	−0.039 8(2)
C(19A)	0.326 8(4)	0.188 9(3)	−0.021 6(2)
O(20A)	0.364 7(3)	0.230 7(2)	0.036 0(2)
C(21A)	0.408 1(4)	0.171 1(3)	0.091 7(2)
C(22A)	0.400 9(3)	0.234 8(3)	0.161 8(2)
C(23A)	0.365 8(3)	0.338 8(3)	0.161 8(2)
C(24A)	0.361 8(4)	0.391 3(3)	0.228 6(2)
C(25A)	0.390 3(3)	0.338 8(3)	0.292 6(2)
C(26A)	0.419 0(4)	0.132 4(3)	0.542 7(2)
C(27A)	0.343 7(6)	0.098 5(4)	0.608 5(3)
C(28A)	0.214 4(5)	0.121 3(3)	0.622 9(2)
C(29A)	0.155 9(4)	0.180 3(3)	0.570 1(2)
C(30A)	0.095 1(4)	0.600 5(4)	0.312 6(2)
C(31A)	0.108 6(4)	0.651 8(4)	0.242 9(2)
C(32A)	0.087 6(4)	0.611 6(4)	0.177 3(2)
C(33A)	0.179 0(4)	0.201 3(4)	−0.098 5(3)
C(34A)	0.247 0(4)	0.115 7(3)	−0.140 2(2)
C(35A)	0.353 1(5)	0.067 3(4)	−0.122 3(3)
C(36A)	0.394 4(5)	0.103 2(4)	−0.062 7(3)
N(1B)	0.202 2(3)	0.835 8(2)	0.714 9(2)
C(2B)	0.137 5(4)	0.847 9(3)	0.789 5(2)
C(3B)	0.217 9(4)	0.823 1(3)	0.847 1(2)
O(4B)	0.137 2(3)	0.838 8(2)	0.924 6(1)
C(5B)	0.199 8(5)	0.826 8(3)	0.983 8(2)
C(6B)	0.266 1(4)	0.733 2(3)	0.999 1(2)
O(7B)	0.263 4(2)	0.653 1(2)	0.954 3(2)
C(8B)	0.346 6(4)	0.559 4(4)	0.958 1(3)
C(9B)	0.325 8(4)	0.488 2(4)	0.901 2(3)
O(10B)	0.356 7(3)	0.531 3(2)	0.824 8(2)
C(11B)	0.330 9(4)	0.485 2(3)	0.764 4(3)
C(12B)	0.341 2(3)	0.538 4(3)	0.695 8(2)
C(13B)	0.317 9(4)	0.496 2(3)	0.632 2(3)
O(14B)	0.333 2(2)	0.553 3(2)	0.5659 (2)
C(15B)	0.314 9(4)	0.513 8(3)	0.496 7(3)
C(16B)	0.347 1(4)	0.585 9(4)	0.432 6(3)
O(17B)	0.257 1(2)	0.680 9(2)	0.452 3(2)
C(18B)	0.283 8(3)	0.763 4(3)	0.410 0(2)
C(19B)	0.224 6(4)	0.858 5(3)	0.445 6(2)
O(20B)	0.148 7(2)	0.863 1(2)	0.521 4(1)
C(21B)	0.223 8(4)	0.840 8(3)	0.578 1(2)
C(22B)	0.141 0(4)	0.856 8(3)	0.658 1(2)
C(23B)	0.011 0(5)	0.886 5(6)	0.674 8(3)
C(24B)	−0.054 6(6)	0.899 1(8)	0.751 9(3)
C(25B)	0.008 2(5)	0.877 5(6)	0.811 0(3)
C(26B)	0.190 7(6)	0.909 9(4)	1.029 2(3)
C(27B)	0.251 1(7)	0.898 2(5)	1.091 3(3)
C(28B)	0.317 2(6)	0.805 5(5)	1.105 1(3)
C(29B)	0.325 8(5)	0.721 4(4)	1.061 2(3)
C(30B)	0.297 8(4)	0.390 7(3)	0.770 6(3)
C(31B)	0.275 3(5)	0.350 2(4)	0.706 0(3)
C(32B)	0.283 2(4)	0.401 4(3)	0.636 9(3)
C(33B)	0.364 9(4)	0.759 0(4)	0.335 3(2)
C(34B)	0.381 2(5)	0.846 7(5)	0.297 1(3)
C(35B)	0.319 7(5)	0.940 5(5)	0.329 6(2)
C(36B)	0.242 0(5)	0.945 4(4)	0.405 6(3)

Table 2. Important bonding parameters for compounds (**2**) (esds are in parentheses).

Selected torsional angles/°	
C(2A)–C(3A)–O(4A)–C(5A)	126.86(34)
C(15A)–C(16A)–O(17A)–C(18A)	131.62(42)
C(16A)–O(17A)–C(18A)–C(19A)	−133.52(39)
C(18A)–C(19A)–O(20A)–C(21A)	137.55(40)
Mean values of bond distances/Å	
C–C(A)	1.497(6)
C–C(B)	1.493(6)
C=C(A)	1.374(6)
C=C(B)	1.381(7)
$C(sp^2)$–O(A)	1.369(5)
$C(sp^2)$–O(B)	1.371(5)
$C(sp^3)$–O(A)	1.418(5)
$C(sp)^3$–O(B)	1.430(5)
Mean values of bond angles/°	
C–O–C(A)	117.9(3)
C–O–C(B)	116.6(3)
C–N–C(Py) (A)	118.1(3)
C–N–C(Py) (B)	119.9(3)
C–C–C(Ph) (A)	119.9(4)
C–C–C(Ph) (B)	119.9(5)

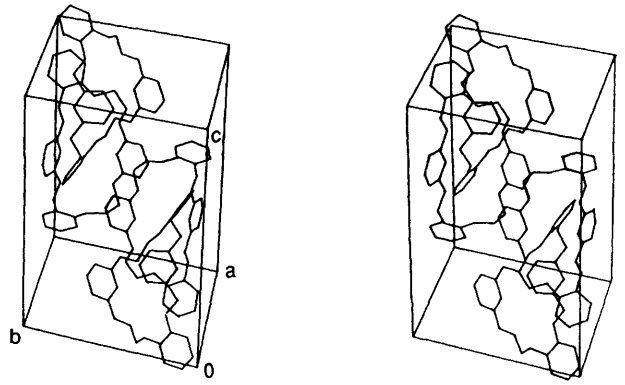
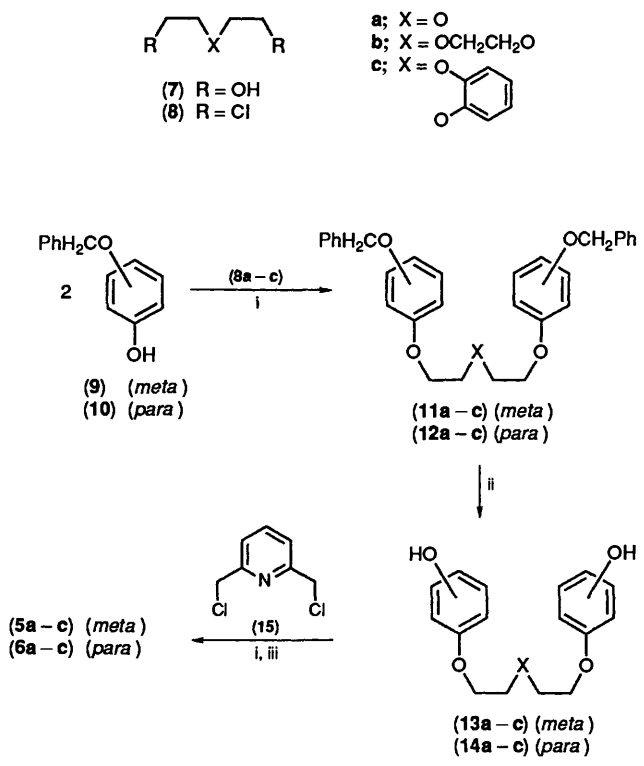


Figure 3. Simplified stereo view of the unit-cell packing of compound (**2**).



Scheme 1. Preparation of the intermediates and macrocycles. *Reagents and conditions:* i Cs_2CO_3–DMF, 60–70 °C; ii, H_2, Pd/C, EtOH or ethyl acetate, room temperature; iii, high dilution.

diphenols (**13a–c**) and (**14a–c**), which were cyclized with 2,6-bis(chloromethyl)pyridine (**15**) under high-dilution conditions[15] using Cs_2CO_3 in dry DMF to yield the macro-rings (**5a–c**) and (**6a–c**) in 40–60% yield.

Complex Formation.—A variety of solvents including protic, aprotic dipolar (mainly), and apolar compounds [see Table 3(*a*)] were used to investigate the crystalline complex formation (inclusion) capability of potential host compounds (**5a–c**) and (**6a–c**). The results are shown in Table 3(*b*). Of all the six macro-rings, only compound (**6c**), which is the 25-membered pyridino-crown comprising two flanking hydroquinone groups and one diametric catechol group with reference to the pyridino constituent, showed host properties. This was a rather unexpected finding since in the parent all-catechol series (**1a–c**) all members form inclusion compounds though to different extents and with different solvents.[6] In the present case, however, both the catechol-free compound (**6b**) and the lower-ring analogue (**6a**) are inefficient. Compared with the afore mentioned all-catechol series,[6] compounds (**6c**) and (**1a**) are similar, but differences are also apparent.[16] Both of them yield crystalline uncharged-molecule complexes with dipolar aprotic guests such as nitromethane, acetonitrile, DMF *etc.* [see Table 3(*b*)]. Beyond that, compound (**1a**) is capable of crystalline complex formation with some protic compounds (ethanol, epichlorohydrin, ethylene glycol),[16] but compound (**6c**) completely failed to do this. On the other hand, compound (**6c**) co-crystallized with dioxane, while compound (**1a**) did not, thus making contrasts between host (**6c**) and parent compound (**1a**) evident.

Table 3. (*a*) Solvent compounds tested for inclusion formation with hosts (**5a–c**) and (**6a–c**). (*b*) Crystalline inclusion compounds isolated.[a]

(*a*) Methanol, ethanol, propan-1-ol, propan-2-ol

nitromethane, nitroethane, nitrobenzene, acetonitrile, chloroacetonitrile, benzonitrile, DMF, tetramethylurea (TMU), DMSO

1,4-dioxane, toluene.

(*b*) (**6c**): nitromethane (1:2), nitroethane (1:1), acetonitrile (1:2), chloroacetonitrile (1:1), DMF (1:1), TMU (2:1), DMSO (*ca.* 2:1), 1,4-dioxane (*ca.* 2:1).

[a] See the Experimental section for method of preparation, drying standard, and characterization; stoicheiometric ratios (host:guest) are given in parentheses.

Another remarkable difference between compounds (**6c**) and (**1a**) relates to the host:guest stoicheiometry which by preference is 2:1 (with some 1:1 and 3:2) for compound (**1a**),[16] while compound (**6c**) shows almost equally 2:1, 1:1, and 1:2 stoicheiometry [Table 3(*b*)]. However, the individual host:guest stoicheiometries found in the crystalline complexes of compound (**6c**) look as if spatial requirements of both host and guest play an important role. For instance, the small guest nitromethane is complexed with 1:2 stoicheiometry, whereas the larger guest nitroethane has 1:1 stoicheiometry. The same behaviour was seen for acetonitrile and chloroacetonitrile, which involved 1:2 and 1:1 stoicheiometry, respectively. Other guests of comparably large size [tetramethylurea, dimethyl sulphoxide (DMSO), dioxane] require two host molecules for complex formation in the crystal. In view of the spatial relationship, it is also remarkable that aromatic substrates, neither as substituents nor as separate aromatic entities, were found to act as guest molecules.

Whether the discussed spatial relations refer to the cavity of the individual host molecule (**6c**) or to interstitial crystal voids or to both, proportionately, is a problem for crystal-structure determination. Unfortunately, all complexes of compound (**6c**) failed to afford suitable X-ray-quality crystals. Nevertheless, some general lines for future host design based on pyridino-crowns, defined in the following conclusions, are deducible.

Conclusions.—Considering the present and previous[8,10] results, it is obvious that resorcinol is an inefficient building block for the generation of macrocyclic pyridino hosts. By way of contrast, the hydroquinone unit is efficient, being similar to the catechol group. However, while the catechol unit has been found to be an all-round design module in pyridino host chemistry,[6] the hydroquinone group is not of equal value. Whether a host compound is formed or not on using the hydroquinone unit strongly depends on the position at which this building block is introduced into the macro-ring and also on the ring size of the target macrocycle. It is also important whether or not an additional catechol group is present. Examples are the pairs of pyridino crowns (**6c**) *vs.* (**3**),[8] (**6c**) *vs.* (**6a**), and (**6c**) *vs.* (**6b**), illustrating the different factors mentioned above [compounds (**3**), (**6a**), and (**6b**) give no complexes].

In the last analysis, the hydroquinone unit may be useful for the synthesis of other selective host molecules according to the modular-design principle,[6] though with certain restrictions.

Experimental

General Methods and Materials.—M.p.s were taken on a Reichert hot-stage apparatus and are uncorrected. ^{1}H NMR spectra were measured, unless otherwise stated, for $CDCl_3$ solutions (Me_4Si as internal standard) on a Varian EM-360 (60 MHz) spectrometer. Mass spectra were recorded on a A.E.I. MS-50 instrument. Crystal-structure determination was performed on a Nonius CAD-4 diffractometer. Elemental analyses were carried out by the Microanalytical Laboratory of the Institut für Organische Chemie und Biochemie, Bonn. For column chromatography, Al_2O_3 (Brockmann, grade II–III) and silica gel (0.063–0.1 mm, Merck) were used. Starting materials were purchased from Janssen. A 10% Pd/C catalyst of type E10N (Degussa) was used in catalytic hydrogenations. All solvents were of reagent quality or were purified by distillation before use.

Dichlorides (**8a**) and (**8b**) were prepared from the corresponding diols (**7a**) and (**7b**) with thionyl chloride in toluene–pyridine as described.[17,18]

1,2-*Bis*(2-*chloroethoxy*)*benzene* (**8c**).—This compound was prepared as above using compound (**7c**).[19] The crude product was recrystallized from heptane to give *compound* (**8c**) (68%) as crystals, m.p. 50–52 °C (Found: C, 51.5; H, 5.25. $C_{10}H_{12}Cl_2O_2$ requires C, 51.09; H, 5.14%); δ 3.58–4.20 (2 m, 8 H) and 6.86 (m, 4 H); *m/z* 236 (M^+, ^{37}Cl).

3-(*Benzyloxy*)*phenol* (**9**).—This compound was synthesized according to the literature procedure[20] to yield the crude product as a viscous oil. We found that purification was more effective by column chromatography on SiO_2 (eluant $CHCl_3$) than by distillation.[20] The purified product (26%) had m.p. 49–50 °C (lit.,[20] 50–51 °C) (Found: C, 77.8; H, 6.0. Calc. for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04%); δ 4.98 (s, 2 H), 5.15 (s, 1 H), 6.20–6.70 (m, 3 H), and 6.90–7.50 (m, 6 H); *m/z* 200 (M^+).

4-(*Benzyloxy*)*phenol* (**10**).—This compound was obtained by the literature method[21] (30%), m.p. 120–121 °C (lit.,[21] 121 °C); δ 4.78 (s, 1 H), 5.10 (s, 2 H), and 6.60–7.75 (m, 9 H).

Dibenzyl Ethers (**11a–c**) *and* (**12a–c**).—A mixture of benzyloxyphenol (**9**) or (**10**) (10.0 g, 50 mmol) of the corresponding dichloride (**8a–c**) (25 mmol), and caesium carbonate (8.15 g, 25 mmol) in dry DMF (150 cm^3) was stirred at 80 °C for 7–8 h. The cold reaction mixture was poured into water (500 cm^3) and extracted with CH_2Cl_2 (3 × 100 cm^3). The extract was washed with water and dried (Na_2SO_4). The solvent was removed and the residue was recrystallized. Specific details are given for each compound.

3,3′-[*Oxybis*(*ethyleneoxy*)]*diphenol Dibenzyl Ether* (**11a**). Dichloride (**8a**) and phenol (**9**) were used; recrystallization from MeOH yielded *compound* (**11a**) (59%) as crystals, m.p. 75–77 °C (Found: C, 76.45; H, 6.6. $C_{30}H_{30}O_5$ requires C, 76.57; H, 6.43%); δ 3.61–3.90 (m, 4 H), 4.07–4.30 (m, 4 H), 5.02 (s, 4 H), and 6.40–6.78 and 7.02–7.63 (2 m, 18 H); *m/z* 470 (M^+).

3,3′-[*Ethylenebis*(*oxyethyleneoxy*)]*diphenol Dibenzyl Ether* (**11b**). Dichloride (**8b**) and phenol (**9**) were used; recrystallization from MeOH yielded *compound* (**11b**) (62%) as crystals, m.p. 59–61 °C (Found: C, 74.5; H, 6.85. $C_{32}H_{34}O_6$ requires C, 74.69; H, 6.66%); δ 3.68 (s, 4 H), 3.60–4.20 (m, 8 H), 5.02 (s, 4 H), and 6.40–6.75 and 7.02–7.61 (2 m, 18 H); *m/z* 514 (M^+).

3,3′-[1,2-*Phenylenebis*(*oxyethyleneoxy*)]*diphenol Dibenzyl Ether* (**11c**). Dichloride (**8c**) and phenol (**9**) were used; recrystallization from EtOH yielded *compound* (**11c**) (30%) as crystals, m.p. 79–81 °C (Found: C, 77.25; H, 6.2. $C_{36}H_{34}O_6$ requires C, 76.84; H, 6.09%); δ 4.28 (m, 8 H), 4.98 (s, 4 H), and 6.35–6.70 and 6.90–7.50 (2 m, 22 H); *m/z* 562 (M^+).

4,4′-[*Oxybis*(*ethyleneoxy*)]*diphenol Dibenzyl Ether* (**12a**). Dichloride (**8a**) and phenol (**10**) were used; recrystallization from $CHCl_3$ yielded *compound* (**12a**) (59%) as crystals, m.p. 131–133 °C (Found: C, 76.4; H, 6.5. $C_{30}H_{30}O_5$ requires C, 76.57; H, 6.43%); δ 3.81–3.94 (m, 4 H), 4.02–4.20 (m, 4 H), 5.03 (s, 4 H), and 6.85–6.98 and 7.23–7.57 (2 m, 18 H); *m/z* 470 (M^+).

4,4′-[*Ethylenebis*(*oxyethyleneoxy*)]*diphenol Dibenzyl Ether* (**12b**). Dichloride (**8b**) and phenol (**10**) were used; recrystallization from MeOH yielded *compound* (**12b**) (60%) as crystals, m.p. 106–109 °C (Found: C, 74.6; H, 6.8. $C_{32}H_{34}O_6$ requires C, 74.69; H, 6.66%); δ 3.78 (s, 4 H), 3.78–3.99 (m, 4 H), 4.02–4.23 (m, 4 H), 5.02 (s, 4 H), and 6.94–7.03 and 7.28–7.61 (2 m, 18 H); *m/z* 514 (M^+).

4,4′[1,2-*Phenylenebis*(*oxyethyleneoxy*)]*diphenol Dibenzyl Ether* (**12c**). Dichloride (**8c**) and phenol (**10**) were used; recrystallization from CCl_4 yielded *compound* (**12c**) (53%) as crystals, m.p. 105–106 °C (Found: C, 76.6; H, 5.9. $C_{36}H_{34}O_6$ requires C, 76.84; H, 6.09%); δ 4.32 (m, 8 H), 5.00 (s, 4 H), and 6.80–7.04 and 7.20–7.55 (2 m, 22 H); *m/z* 562 (M^+).

Diphenols (**13a–c**) *and* (**14a–c**).—A mixture of the corresponding dibenzyl ether (**11a–c**) or (**12a–c**) (25 mmol) and Pd/C (10%; 1.0 g) in the solvent given below was hydrogenolysed in a Parr apparatus for 3 h at 3 atm and room temperature. The reaction mixture was filtered, washed with $CHCl_3$, evaporated under reduced pressure, and recrystallized. Specific details are given for each compound.

3,3′-[*Oxybis*(*ethyleneoxy*)]*diphenol* (**13a**). From compound (**11a**) in EtOH; recrystallization from $CHCl_3$ yielded *compound* (**13a**) (62%) as crystals, m.p. 124–126 °C (Found: C, 66.1; H, 6.3. $C_{16}H_{18}O_5$ requires C, 66.20; H, 6.26%); δ($CDCl_3$–[$^2H_6$]DMSO) 3.67–4.22 (m, 8 H), 5.50 (br, 2 H), and 6.25–6.60 and 6.85–7.50 (2 m, 8 H); *m/z* 290 (M^+).

3,3′-[*Ethylenebis*(*oxyethyleneoxy*)]*diphenol* (**13b**). From compound (**11b**) in EtOH; recrystallization from $CHCl_3$ yielded *compound* (**13b**) (76%) as crystals, m.p. 90–93 °C (Found: C, 64.9; H, 6.4. $C_{18}H_{22}O_6$ requires C, 64.66; H, 6.63%); δ($CDCl_3$–[$^2H_6$]DMSO) 3.66 (s, 4 H), 3.60–4.20 (m, 8 H), 5.50 (br, 2 H), and 6.30–7.50 (m, 8 H); *m/z* 334 (M^+).

3,3′-[1,2-*Phenylenebis*(*oxyethyleneoxy*)]*diphenol* (**13c**). From compound (**11c**) in ethyl acetate; recrystallization from $CHCl_3$ yielded *compound* (**13c**) (58%) as crystals, m.p. 123–125 °C (Found: C, 69.0; H, 5.85. $C_{22}H_{22}O_6$ requires C, 69.09; H, 5.79%); δ($CDCl_3$–[$^2H_6$]DMSO) 4.28 (m, 8 H), 6.25–6.62 and 6.80–7.38 (2 m, 12 H), and 8.62 (br, 2 H); *m/z* 562 (M^+).

4,4′-[*Oxybis*(*ethyleneoxy*)]*diphenol* (**14a**). From compound (**12a**) in EtOH; recrystallization from MeOH yielded *compound* (**14a**) (75%) as crystals, m.p. 100–102 °C (Found: C, 66.1; H, 6.4. $C_{16}H_{18}O_5$ requires C, 66.20; H, 6.25%); δ($CDCl_3$–[$^2H_6$]DMSO) 3.78–4.22 (m, 8 H), 6.66–6.95 (m, 8 H), and 8.60 (br, 2 H); *m/z* 290 (M^+).

4,4′-[*Ethylenebis*(*oxyethyleneoxy*)]*diphenol* (**14b**). From compound (**12b**) in EtOH; recrystallization from MeOH yielded *compound* (**14b**) (77%) as crystals, m.p. 115–118 °C (Found: C, 64.9; H, 6.85. $C_{18}H_{22}O_6$ requires C, 64.66; H, 6.63%); δ($CDCl_3$–[$^2H_6$]DMSO) 3.78 (s, 4 H), 3.78–3.99 (m, 4 H), 4.02–4.23 (m, 4 H), 6.70–6.87 (m, 8 H), and 8.50 (s, 2 H); *m/z* 334 (M^+).

4,4′-[1,2-*Phenylenebis*(*oxyethyleneoxy*)]*diphenol* (**14c**). From compound (**12c**) in ethyl acetate; recrystallization from EtOH yielded *compound* (**14c**) (72%) as crystals, m.p. 178–180 °C

(Found: C, 69.25; H, 6.05. $C_{22}H_{22}O_6$ requires C, 69.09; H, 5.79%); δ($CDCl_3$–[$^2H_6$]DMSO) 4.12–4.38 (m, 8 H), 6.70–7.04 (m, 12 H), and 8.42 (br, 2 H); *m/z* 382 (M^+).

2,6-Bis(chloromethyl)pyridine (**15**) was obtained from reaction of 2,6-bis(hydroxymethyl)pyridine with thionyl chloride.[22]

Macro-rings (**5a–c**) *and* (**6a–c**).—The respective diphenol (**13a–c**) or (**14a–c**) (10 mmol) and 2,6-bis(chloromethyl)pyridine (**15**) (1.76 g, 10 mmol) in separate portions (250 cm^3) of dry DMF were simultaneously added during 10 h under N_2 to a vigorously stirred suspension of caesium carbonate (3.26 g, 10 mmol) in dry DMF (350 cm^3) at 70 °C. The mixture was stirred for a further 3 h at the same temperature. The solvent was then removed under reduced pressure, and the residue was partioned between water and CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and evaporated. Purification by column chromatography on Al_2O_3 and recrystallization gave the title compounds. Specific details are given for each compound.

1,4,7,14,23-*Pentaoxa*[7](1,3)*benzeno*[2](2,6)*pyridino*[2](1,3)*benzenophane* (**5a**). Diphenol (**13a**) was used; eluant $CHCl_3$–heptane (4:1); recrystallization from MeOH yielded *compound* (**5a**) (49%) as crystals, m.p. 163–165 °C (Found: C, 69.9; H, 5.8; N, 3.5. $C_{23}H_{23}NO_5$ requires C, 70.21; H, 5.89; N, 3.56%); δ 3.72–3.90 (m, 4 H), 3.98–4.12 (m, 4 H), 5.30 (s, 4 H), and 6.28–7.61 (m, 11 H); *m/z* 393 (M^+).

1,4,7,10,17,26-*Hexaoxa*[10](1,3)*benzeno*[2](2,6)*pyridino*[2](1,3)*benzenophane* (**5b**). Diphenol (**13b**) was used; eluant $CHCl_3$–heptane (4:1); recrystallization from MeOH yielded *compound* (**5b**) (44%) as crystals, m.p. 91–92 °C (Found: C, 68.1; H, 6.2; N, 3.35. $C_{25}H_{27}NO_6$ requires C, 68.64; H, 6.22; N 3.20%); δ 3.66 (s, 4 H), 3.60–4.20 (m, 8 H), 5.30 (s, 4 H), and 6.40–7.82 (m, 11 H); *m/z* 437 (M^+).

1,4,11,14,21,30-*Hexaoxa*[4](1,2)*benzeno*[4](1,3)*benzeno*[2](2,6)*pyridino*[2](1,3)*benzenophane* (**5c**). Diphenol (**13c**) was used; eluant $CHCl_3$–heptane (5:1); recrystallization from light petroleum (b.p. 60–95 °C) yielded *compound* (**5c**) (15%) as crystals, m.p. 104–105 °C (Found: C, 71.6; H, 6.0; N, 3.0. $C_{29}H_{27}NO_6$ requires C, 71.72; H, 5.61; N, 2.88%); δ 4.20 (m, 8 H), 5.21 (s, 4 H), and 6.28–7.68 (m, 15 H); *m/z* 485 (M^+).

1,4,7,14,23-*Pentaoxa*[7](1,4)*benzeno*[2](2,6)*pyridino*[2](1,4)*benzenophane* (**6a**). Diphenol (**14a**) was used; eluant $CHCl_3$–heptane (6:1); recrystallization from EtOH yielded *compound* (**6a**) (53%) as crystals, m.p. 135–137 °C (Found: C, 69.9; H, 5.8; N, 3.5. $C_{23}H_{23}NO_5$ requires C, 70.21; H, 5.89; N, 3.56%); δ 3.62–3.79 (m, 4 H), 4.01–4.17 (m, 4 H), 5.20 (s, 4 H), and 6.58–7.60 (m, 11 H); *m/z* 393 (M^+).

1,4,7,10,17,26-*Hexaoxa*[10](1,4)*benzeno*[2](2,6)*pyridino*[2](1,4)*benzenophane* (**6b**). Diphenol (**14b**) was used; eluant $CHCl_3$–heptane (10:1); recrystallization from EtOH yielded *compound* (**6b**) (62%) as crystals, m.p. 109–110 °C (Found: C, 69.0; H, 6.4; N, 3.1. $C_{25}H_{27}NO_6$ requires C, 68.64; H, 6.22; N, 3.20%); δ 3.74 (s, 4 H), 3.80–3.94 (m, 4 H), 3.97–4.07 (m, 4 H), 5.24 (s, 4 H), and 6.63–7.78 (m, 11 H); *m/z* 437 (M^+).

1,4,11,14,21,30-*Hexaoxa*[4](1,2)*benzeno*[4](1,4)*benzeno*[2](2,6)*pyridino*[2](1,4)*benzenophane* (**6c**). Diphenol (**14c**) was used; eluant $CHCl_3$; recrystallization from EtOH yielded *compound* (**6c**) (39%) as crystals, m.p. 164–166 °C (Found: C, 71.4; H, 5.45; N, 2.95. $C_{29}H_{27}NO_6$ requires C, 71.74; H, 5.60; N, 2.88%); δ 4.22 (m, 8 H), 5.22 (s, 4 H), and 6.72–7.73 (m, 15 H); *m/z* 485 (M^+).

Preparation of Crystalline Complexes.—Host compound (**6c**) was dissolved under heating in a minimum amount of the respective guest solvent. The solution was prevented from cooling too rapidly. 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 stoicheiometry was determined by NMR integration. Data for each compound are given in Table 3(*b*).

X-Ray Structure Analysis.—Crystals of (**2**) were obtained from EtOH solution by slow evaporation at room temperature. A colourless, needle-shaped crystal was chosen for X-ray structure analysis. The crystal density was measured by the floatation method.

Crystal data: $C_{29}H_{27}NO_6$, M = 485.5, triclinic, a = 11.076(1), b = 13.459(1), c = 17.619(1) Å, α = 87.97(1), β = 75.57(1), γ = 78.17(1)°, V = 2 489.4 Å^3, refined cell parameters from 25 reflections in the range θ < 35°, space group $P\bar{1}$, Z = 4, D_m = 1.29 g cm^{-3}, D_x = 1.30 g cm^{-3}, T = 293 K, crystal dimensions 0.5 × 0.3 × 0.3 mm, $F(000)$ = 1 024, μ = 7.0 cm^{-1}.

Three-dimensional intensity data were collected on a Nonius CAD-4 diffractometer with graphite-monochromated Cu-K_α radiation (λ 1.5418 Å). 6 275 Reflections with h 0–11, k −13 to 13, l −15 to 15, and $2\theta_{max}$ 110° were measured in the ω/2θ scan mode. Three standard reflections remeasured after every 200 reflections showed no significant variation. 4 065 Reflections were considered as observed with $I > 2.0\sigma(I)$. Data were corrected for Lorentz and polarization effects but not for absorption.

The phase problem was solved by direct methods with MULTAN 80.[23] An *E*-map generated from the phase set (500 reflections), with the highest combined figure-of-merit, located most of the non-hydrogen atoms; the remaining atoms were found by difference Fourier synthesis. The structure was refined by the full-matrix least-squares method (SDP/VAX11-730)[24] where the function minimized was $w(|F_o| - |F_c|)^2$, with the weights (w) derived from counting statistics. During the refinement of the structure, three of the atoms [C(23B), C(24B), and C(25B)] of the pyridino ring showed a large temperature factor ($B \approx 20$ Å^2), suggesting conformational disorder of the ring system. To probe this, we left out these three atoms from structure-factor calculations and computed a difference Fourier. However, the difference Fourier did not show possible alternative sites for these atoms except that the peaks corresponding to these atoms were slightly long and drawn out. Hence anisotropic thermal prameters were applied to these atoms along with the other non-hydrogen atoms. Most of the hydrogen atoms were obtained from difference Fourier and the remaining hydrogen atoms were fixed geometrically. The hydrogen atoms were included in the refinement and they were given isotropic temperature factors corresponding to the atoms to which they were bonded. The refinement converged at R = 0.062 and R_w = 0.087. Highest parameter shift to esd ratio was 0.04 and S was 2.20. The max. and min. peak heights in the final difference Fourier map were +0.29 and −0.25 e Å^{-3} respectively. The atomic scattering factors were taken from International Tables for X-Ray Crystallography (ref. 14). Atomic co-ordinates of non-hydrogen atoms are listed in Table 1, and important geometric parameters are given in Table 2.*

* *Supplementary data* (see section 5.6.3 of Instructions for Authors, in the January issue). Lists of bond lengths and bond angles, fractional atomic co-ordinates for H atoms, anisotropic thermal parameters, and least-squares plane calculations have been deposited with the Cambridge Crystallographic Data Centre.

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