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An upper-rim-substituted calix[4]arene tetracarboxylic acid forms hydrogen-bonded duplexes with lower-rim-substituted tetra(4-pyridyl)- and tetra(3-pyridyl)calix[4]arenes in chloroform. The formation of these adducts was studied by extraction experiments. The association constants determined via $^1$H NMR dilution experiments in CDCl$_3$ are $7.6 \times 10^4$ and $1.3 \times 10^4$ M$^{-1}$ for the 4-pyridyl and the 3-pyridyl derivative, respectively. IR studies in the solid state and in solution indicate that the interaction is based on hydrogen bonding and that the degree of proton transfer is negligible. VPO measurements support the formation of 1:1 adducts.

Introduction

In recent years there has been an increased interest in the construction of noncovalently bonded aggregates.$^{10}$ Since material characteristics are determined by the structure and organization of the individual components, a careful study of molecular self-organization and self-assembly should provide information about how molecular functionalities are translated into macroscopic functions. The relatively small size (of many) of the assemblies of well-defined shape, size, and dimensionality may lead to novel properties.$^8$ The resulting materials may find application in the fields of nonlinear optics, electronics, photonics, and information storage and processing.

Calix[4]arenes$^8$ have proved to be very useful building blocks in the synthesis of receptors for cations,$^9$ anions,$^7$ and neutral molecules.$^6$ The cyclic skeleton provides substantial preorganization, and this, in combination with the many possibilities of selective functionalization, makes it possible to tune the molecule toward the desired application.

The preorganization of functional units not only plays a very important role in molecular recognition but is also of premier importance in the self-assembly of larger structures.$^{10}$ In other words, the specific positioning of moieties that are able to interact on an associative basis is part of the information that is needed in the self-assembly process.

Even though calix[4]arenes seem to meet the prerequisites needed for a molecule to be of any interest in the construction of well-defined aggregates, very little effort has been devoted to the behavior of calix[4]arenes in noncovalent aggregation processes.$^{11}$

The first hydrogen-bonded aggregates of calix[4]arenes were described only a few years ago by our group.$^{12}$ A calix[4]arene fixed in the cone conformation substituted with a self-complementary pyridone moiety dimerizes in chloroform with a dimerization constant of 100 M$^{-1}$, comparable to that of simple pyridones.$^{13,14}$ However, attaching a second pyridone moiety to the calix[4]arene did not give rise to well-defined dimers; instead, a mixture of oligomers was obtained. The second example was described by Shinkai et al.$^{15}$ A hydrogen-bonded duplex was formed through the interaction between a calix[4]arene with four carboxyl groups and a calix[4]arene with four stilbazole moieties. Recently, Pochini et al.$^{16}$ described the formation of a hydrogen-bonded dimer in CDCl$_3$ based on the self-complementarity of carboxylic acids.$^{18}$ In these three cases described above, all hydrogen-bonding groups are located at the upper rim.$^{17}$

In this paper we describe the first well-defined hydrogen-bonded aggregates in which a calix[4]arene substi-

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tuted with hydrogen-bonding groups at the upper rim interacts with calix[4]arenes substituted with complementary hydrogen-bonding groups at the lower rim. The hydrogen bonding interaction used is that between carboxylic acids and pyridines, the effectiveness of which in supramolecular chemistry has been described by several groups.18

Results and Discussion

Synthesis. To investigate the interaction between upper rim- and lower rim-substituted calix[4]arenes compounds 2, 5, 7a,b, and 8a–c were synthesized (Chart 1). These compounds make it possible to compare the 2-fold functionalized calix[4]arene derivatives (2 and 7a,b) with the 4-fold functionalized derivatives 5 and 8a–c. This is expected to provide information about the strength and stoichiometry of the interaction, while the different points of attachment of the pyridine moieties should give insight in geometrical aspects and the nature of the interaction.

Calix[4]arenediarylcacidic acid 2 was prepared in 61% yield by oxidation of 4formylcalix[4]arene 19 with sodium chlorite and sulfamic acid.10 Calix[4]arene-tetraarylcarboxylic acid 5 was synthesized starting from

\[ R_2 \quad R_3 \quad R_4 \]

\[ R_1 \quad \text{Et} \quad \text{O} \quad R_2 \quad H \quad R_3 \quad \text{CHO} \]

\[ R_1 \quad \text{Et} \quad \text{O} \quad R_2 \quad R_3 \quad \text{COOH} \]

\[ R_1 \quad \text{CHO} \quad R_2 \quad R_3 \quad \text{CHO} \]

\[ R_1 \quad \text{CHO} \quad R_2 \quad R_3 \quad \text{COOH} \]

\[ R_1 \quad \text{H} \quad R_2 \quad R_3 \quad \text{CHO} \]

The dipyridylcalix[4]arenes 7a and 7b were synthesized in 32% and 66% yield, respectively, by reaction of bisbenzoxylcalix[4]arene 6 with a large excess (10 equiv) of the HCl salt of the corresponding picolyl chloride under strongly basic conditions (NaOH, 25 equiv) in DMF, similar to the procedure described by Pappalardo et al. for the preparation of tetrpyridylcalix[4]arene 8e.22 The easily accessible bis(benzoxyl)calix[4]arene 6b was used in order to avoid undesirable interactions of the pyridine nitrogens with the phenolic hydroxyls and to allow for a good comparison with the tetrpyridylcalix[4]arenes 8a–c. The latter were synthesized according to the procedure of Pappalardo et al.22 The yields were 53% and 71% for 8a and 8b, respectively. The structure of the synthesized compounds was determined by 1H NMR, 13C NMR, FAB-MS, and elemental analyses.

1H NMR Studies. In order to investigate the interactions between dicarboxylic acid 2 and dipyridyl 7a and 7b, equimolar amounts of 2 and the corresponding dipyridyl derivative were mixed in CDCl3 at a concentration of 5 mM. In the 1H NMR spectra of these mixtures no changes were observed compared with the 1H NMR spectra of the free compounds. From this it was concluded that the interaction between the dipyridyl 7a,b and dicarboxylic acid 2 is too weak to compete effectively with the dimerization of 2.24 Similarly, no changes were observed in the spectra of equimolar mixtures of dicarboxylic acid 2 and tetrpyridyl 8a–c. Also, in this case strong dimerization most probably prevents the hydrogen-bonded interaction of 2 with 8a–c.

Contrary to the above, the mixtures of tetracarboxylic acid 5 and tetrpyridyls 8a–c show much more interesting behavior. The solubility of 5 in chloroform is very low, even though the lower rim is substituted with four octyl chains. However, after a 1:1 mixture of 5 was warmed with tetra(4-pyridyl) 8a, a clear solution was obtained, even at concentrations higher than 0.02 M, and this solubilization is accompanied by downfield shifts of the aromatic protons of 8a. When less than 1 equiv of 8a was added, 1H NMR analysis of the obtained suspensions showed that the amount of carboxylic acid which had dissolved is equal to that of the amount of 8a added. The results of this extraction series are depicted in Figure 1. These results strongly suggest the formation of a 1:1 complex of tetracarboxylic acid 5 and tetra(4-pyridyl) 8a (Chart 2, 9a).

Virtually identical results were obtained for mixtures of 5 and tetra(3-pyridyl) 8b (Figure 2). Again, upfield


(21) The route via the tetraformyl derivative has the advantage over the procedure described by Regen et al. of being clean and producing the tetracarboxylic acid in good yield after very simple purification, especially on a larger scale. Conner, M.; Johnt, V.; Regen, S. L. J. Org. Chem. 1993, 57, 3744.


(24) Dicarboxylic acid 2 is quite soluble in chloroform and is assumed to be present as a strongly hydrogen-bonded dimer in apolar solvents like chloroform, since such behavior was established recently for a closely related compound: (a) Arduini, A.; Pabbi, M.; Manteroni, M.; Mirone, L.; Pochini, A.; Secchi, A.; Ungaro, R. J. Org. Chem. 1995, 60, 1454.
shifts for the aromatic protons of 8b are observed in the 1H NMR spectra, and an extraction series indicates the formation of a 1:1 adduct.

When more than 1 equiv of tetra pyridyl 8a (or 8b) was added, the downfield shifts of the aromatic protons of the tetrapyridyl 8a (or 8b) decreased as the concentration of tetra pyridyl increased. A decrease in the changes of these shifts is also observed when a 1:1 solution of the tetracarboxylic acid 5 and the tetrapyridyl are diluted. The results of these dilution experiments are depicted in Figures 3 and 4. The hyperbolic shape of the curves in Figures 3 and 4 indicates that the interaction between the tetracarboxylic acid 5 and the tetrapyridyls 8a and 8b is of an associative nature and is not the result of simple proton transfer from acid to base. Proton transfer was also not expected based on the estimated $pK_a$ of the components.[26,27]

When the data of Figures 3 and 4 are treated as dilution curves for 1:1 association of the molecules, complexation constants of $7.6 \times 10^3$ and $1.3 \times 10^3$ M$^{-1}$ for the association of tetracarboxylic acid 5 with tetrapyridyls 8a and 8b, respectively, can be calculated by the method of Horn and Drex.[26,28] The somewhat stronger interaction of 5 with tetra(4-pyridyl) 8a as

(26) Investigations on solid state mixtures of pyridine and chloroacetic acids using IR spectroscopy and $^{35}$Cl NMR spectroscopy indicated that the degree of proton transfer is strongly correlated with the difference in $pK_a$ of the two components in water. For $\Delta pK_a$ smaller than 2.0 the interaction is mainly of the neutral hydrogen bond type. Similar characteristics have been found for the interaction between carboxylic acids and pyridine in chloroform. It was further shown that there is a critical $\Delta pK_a$ of 3.7 above which the solid state adducts are predominantly ionized and below which the adducts are predominantly un-ionized.[a] (a) Dega-Stefan, Z.; Greeh, E.; Naudet-Barcizewiska, M. Z.; Stafran, M. J. Chem. Soc., Perkin Trans. 2 1975, 250. (b) Chihara, H.; Nakamura, N. Bull. Chem. Soc. Jpn. 1971, 44, 1980. (c) Barrow, G. M. J. Am. Chem. Soc. 1956, 78, 5502. (d) Johnson, S. L.; Rumon, K. A. J. Phys. Chem. 1965, 69, 74.
expressed by the relative magnitudes of the $K$ values is most probably the result of the higher basicity of the 4-pyridyl derivative compared to the 3-pyridyl derivative.

![Figure 5](image_url)

The interaction between tetracarboxylic acid 5 and tetra(2-pyridyl) 8c differs largely from that between 5 and tetrapyridyl 8a or 8b. Even after reflushing, no solutions were obtained for mixtures with less than 1.75 equiv of 8c (Figure 5). The latter result was somewhat expected on the basis of studies of CPK molecular models of the complexes: it is not possible for all four nitrogens of tetra(2-pyridyl) 8c to interact simultaneously with the four carboxyl groups of 5. The CPK models indicated that tetracarboxylic acid 5 in the cone conformation can interact with tetra(4-pyridyl) 8a and tetr(3-pyridyl) 8b by formation of four hydrogen bonds, schematically depicted as 9a and 9b, respectively. In complex 9b the rotation of the pyridine rings, which is necessary to orient the pyridine nitrogens correctly, also causes the pyridines to diverge slightly, making the molecule compatible with the cone conformation of 5, in which the carboxylic acid groups are slightly divergent.

The inability of tetra(2-pyridyl) 8c to solubilize 1 equiv of tetracarboxylic acid 5 together with the observation that at least 6 equiv of 4-picoline is needed to solubilize tetracarboxylic acid 5 at room temperature (Figure 6) further illustrates the cooperative nature of the interaction of the four pyridine moieties of tetra(4-pyridyl) 8a and tetra(3-pyridyl) 8b with tetracarboxylic acid 5.

An important feature of the mixtures of tetracarboxylic acid 5 and all of the pyridyl compounds (including 4-picoline) is that two separate signals, at 6.7 and 8.0 ppm, are present for the aromatic protons of 5. The two resonances have the same chemical shift as the two sharp resonances that appear upon cooling of a solution of 5 in CDCl$_3$:CDCl$_3$ to $-4 \degree C$ and are at equal distance from the singlet that is observed for these protons at 100 $\degree C$.

The two signals observed at low temperature can be associated with the tetracarboxylic acid 5 being present in the pinched cone conformation, in which two of the aromatic units become parallel while the other two become more divergent. This observation indicates that the interaction of the tetracarboxylic acid 5 with the tetrapyridyl 8a and 8b slows down the interconversion between the two equivalent pinched cone conformations.

In other words, the intermolecular hydrogen bonding influences the flexibility of the calix[4]arene skeleton of the tetracarboxylic acid 5 substantially.

The observation of the pinched cone conformation of tetracarboxylic acid 5 could in principle be also explained by the formation of an intramolecular hydrogen bond in addition to two intermolecular hydrogen bonds, i.e. the intramolecular hydrogen bond causes the pinching of the tetracarboxylic acid 5, while the remaining carboxyl groups are available for intermolecular association. Another possibility is that two tetracarboxylic acids adopt a pinched cone conformation and self-associate in the manner that was described by Pochini et al. for a corresponding calix[4]arene dicarboxylic acid and that the remaining four divergent carboxyl groups interact with pyridine moieties of tetrapyridyl 8a and 8b in a 2:2 fashion.

In the two cases described above, only two of the four pyridine moieties of the tetrapyridyls are involved in the intermolecular interaction with the tetracarboxylic acid. However, the ratio of the components in these complexes is the same as those depicted in Chart 2, i.e., 1:1. This prompted the investigation of the interaction between tetracarboxylic acid 5 and the dipyriddylic[4]arenes 7a and 7b.

Extraction experiments in CDCl$_3$ showed that in the case of 7a at least 2 equiv of the dipyriddylic[4]arene is needed to completely solubilize tetracarboxylic acid 5, and in the case of 7b 3 equiv of the dipyriddylic[4]arene is required (Figures 7 and 8, respectively). These observations further support the formation of 1:1 adducts of tetracarboxylic acid 5 and tetrapyridyls 8a and 8b as a result of simultaneous hydrogen bonding between the...
Figure 7. Extraction of 5 in CDCl₃ by 7a. ○ = fraction of 5 dissolved; = expected for 1:1 complex; --- = expected for 1:2 complex.

Figure 8. Extraction of 5 in CDCl₃ by 7b. ○ = fraction of 5 dissolved; --- = expected for 1:1 complex; --- = expected for 1:2 complex.

four carboxyl groups and the four pyridine moieties. These duplexes are then stabilized by two strong and two weak hydrogen bonds, strong with parallel COOH groups and weak with divergent COOH groups.

Vapor Pressure Osmometry. The association between 5 and 8a and between 5 and 8b were further characterized by vapor pressure osmometric measurements in chloroform. For the 5-8a associate a molecular weight of 2004 ± 200 g/mol was determined, whereas for the 5-8b associate a molecular weight of 2179 ± 120 g/mol was determined. Both values agree well with the expected molecular weight for a 1:1 complex, which is 2063 g/mol.

Infrared Spectroscopy. To investigate the nature of the interaction the tetracarboxylic acid 5 with the tetra(4-pyridyl) 8a and the tetra(3-pyridyl) 8b infrared spectroscopy was used. The interaction was studied both in the solid phase (KBr) and in solution (tetrachloroethane, 10 mM). For the former, the 1:1 mixtures of the tetracarboxylic acid 5 and the corresponding tetrapyridyl in chloroform were concentrated to dryness under reduced pressure. When the solid phase IR spectrum of the mixture of 5 and 8a is compared to those of the free carboxylic acid and the free tetra(4-pyridyl) 8a a broad signal of medium intensity appears around 1942 cm⁻¹. This signal has been assigned to the OH of carboxylic acids which are involved in hydrogen bonding to pyridine derivatives. Moreover, no change is observed for the C=O frequency of the carboxyl groups, which suggests that the carboxyls are not involved in the association process. Moreover, the fact that the carbonyl stretch is observed at 1702 cm⁻¹ indicates that indeed no proton transfer occurs. Similar observations were made in solution. Again, a broad signal is present at 1921 cm⁻¹, and no shifts were noticed for the carbonyl frequencies at 1700 cm⁻¹.

The results from the IR spectroscopic measurements of the interaction between the tetracarboxylic acid 5 and the tetra(3-pyridyl) 8b are almost identical to those for the 5-8a complex. In KBr the broad hydrogen bonding OH-signal appears at 1921 cm⁻¹, while the carbonyl frequency remains unchanged at 1702 cm⁻¹. In tetrachloroethane the broad OH-signal appears at 1921 cm⁻¹ and the carbonyl stretch frequency is stable at 1699 cm⁻¹. From the above results, it can be concluded that the hydroxyl group of the tetracarboxylic acid 5 is involved in hydrogen-bonded interaction with both tetrapyridyl 8a and 8b and that no proton transfer occurs.

Conclusions

It has been shown by ¹H NMR and IR spectroscopy, together with VPO measurements, that the interaction between the calix[4]arenetetracarboxylic acid 5 leads to formation of well-defined hydrogen-bonded 1:1 associates with the tetra(4-pyridyl)calix[4]arene 8a and the tetra(3-pyridyl)calix[4]arene 8b. For geometrical reasons the formation of such an aggregate is not possible with the tetra(2-pyridyl)calix[4]arene 8c. That the interaction involves the simultaneous formation of four hydrogen bonds was demonstrated by comparison with the dipyridyl derivatives 7a and 7b. No interaction was observed between the pyridylcalix[4]arenes and the dicarboxylic acid 2, due to the strong self-association of the latter.

At first glance the results obtained for the combinations of the tetracarboxylic acid 5 and the tetra(4-pyridyl)- (8a) and the tetra(3-pyridyl)calix[4]arene (8b) are in line with those reported by Shinkai et al. for the association of a tetracarboxylic acid calix[4]arene and a tetrastilbazolocalix[4]arene. The authors, however, did not report association constants, so no comparison can be made with the associates described in this paper with regard to the strength of the association. Furthermore, they did not observe any changes in chemical shift in the ¹H NMR spectra for either the tetracarboxyl component or the tetrastilbazole component. The main structural difference between the associate described by Shinkai et al. and the associates described in this paper is that the former consists of two calix[4]arenes which are both substituted at the upper rim, while the latter combine lower rim substituted tetrapyridylcalix[4]arenes with an upper rim substituted tetracarboxyliccalix[4]arene. To the best of our knowledge this is the first example of a hydrogen-bonded calix[4]arene duplex that involves both the upper and the lower rim.

Experimental Section

Melting points are uncorrected. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ (unless otherwise stated) using residual solvent protons as internal reference. Mass spectra were recorded using m-NBA as a matrix. Hexanes (referring to petroleum ether with bp 60–80 °C), CH₂Cl₂, and EtOAc were distilled from KMnO₄. CHCl₃ was distilled from CaCl₂. DMF was dried over molecular sieves (4 Å) for at least 3 days. NaH was a 55–65% dispersion in mineral oil. Other chemicals were of reagent grade and were used without further purification. Flash column chromatography was performed with silica gel 60 (0.040–0.063 mm, 230–400 mesh) from Merck. All reactions were carried out in an argon atmosphere unless...

otherwise stated. The presence of solvent in the analytical samples was confirmed by H NMR spectroscopy. Diformyl-(1),10-tetrakis(octylxoyl)-8,11-bis(benzoyloxy)-8,11,16,19-tetraacetic acid[4]arene (8e) was synthesized accordingly to literature procedures.

25.26,27,28-Tetraakis[2-ethoxyethoxy]calix[4]arene[5]-17-Diaryloxyacetic Acid (2). To a solution of diformyl[4]arene (4) (0.25 g, 0.33 mmol) in CHCl₃ (10 mL) and acetone (20 mL) were added a solution of H₂N₂SO₃H (0.14 g, 1.4 mmol) in H₂O (1.0 mL) and a solution of NaN₃ClO₃ (0.12 g, 1.5 mmol) in H₂O (1.0 mL). The solution was stirred at rt for 3 h and concentrated under reduced pressure. The residue was taken up in CH₂Cl₂ (100 mL), washed with 1 N HCl (3 × 60 mL) and brine (50 mL), dried over MgSO₄, and concentrated under reduced pressure. The residue was recrystallized from MeOH to give the product in 61% yield: mp 273–275 °C; H NMR δ 7.16 (d, 4 H, J = 7.4 Hz), 7.1–7.0 (m, 2 H), 6.75 (s, 4 H), 4.46 and 3.15 (Abq, 8 H, J = 15.7 Hz), 4.27 (4 H, J = 6.5 Hz), 3.94 (t, 4 H, J = 4.7 Hz), 3.57 (t, 4 H, J = 6.3 Hz), 3.75 (t, 4 H, J = 4.7 Hz), 3.58, 3.51 (q, 4 H, J = 7.0 Hz), 1.23 (t, 6 H, J = 7.0 Hz), 1.16 (6, 6 H, J = 7.0 Hz); ¹³C NMR δ 172.0, 169.2, 157.7, 136.3, 135.8, 139.7, 139.3, 123.0, 123.0, 73.9, 72.9, 69.4, 68.5, 65.6, 66.5, 58.2, 18.1, 15.3, 15.2; FAB-MS m/z 900.0 (M⁺, calc 898.4); IR (KBr) 1697 cm⁻¹. Anal. Calcd for C₈₉H₅₉O₉: C, 88.98; H, 6.75. Found: C, 87.84; H, 6.58.

25.26,27,28-Tetraakis[1-oxo-3,9-dichloro-6,10-dimethyl-1,4-oxa-8,13-dione[4]arene[5]-17-Diaryloxyacetic Acid (4). To a solution of 1,2-dichloro-3,9-dichloro-6,10-dimethyl-1,4-oxa-8,13-dione[4]arene (3) (1.00 mL, 1.15 mmol) in dry CH₂Cl₂ (20 mL) was added dropwise over 5 min. The reaction was stirred without heating and brine (20 mL), dried over MgSO₄, and concentrated under reduced pressure. The residue was recrystallized from CH₂Cl₂/MeOH to give the product in 66% yield: mp 273–275 °C; H NMR δ 7.16 (d, 4 H, J = 7.4 Hz), 7.1–7.0 (m, 2 H), 6.75 (s, 4 H), 4.46 and 3.15 (Abq, 8 H, J = 15.7 Hz), 4.27 (4 H, J = 6.5 Hz), 3.94 (t, 4 H, J = 4.7 Hz), 3.57 (t, 4 H, J = 6.3 Hz), 3.75 (t, 4 H, J = 4.7 Hz), 3.58, 3.51 (q, 4 H, J = 7.0 Hz), 1.23 (t, 6 H, J = 7.0 Hz), 1.16 (6, 6 H, J = 7.0 Hz); ¹³C NMR δ 172.0, 169.2, 157.7, 136.3, 135.8, 139.7, 139.3, 123.0, 123.0, 73.9, 72.9, 69.4, 68.5, 65.6, 66.5, 58.2, 18.1, 15.3, 15.2; FAB-MS m/z 900.0 (M⁺, calc 898.4); IR (KBr) 1697 cm⁻¹. Anal. Calcd for C₈₉H₅₉O₉: C, 88.98; H, 6.75. Found: C, 87.84; H, 6.58.

25.11,17,23-Tetraakis[1,1-dimethyl-1,4-oxa-8,13-dione[4]arene[5]-25,26,27,28-tetraakis[2-ethoxyethoxy]calix[4]arene[5]-25-benzoxyl[4,2-bis(4-pyridylmethylene)oxacyclo[4]arene (8a). p-tert-Butylcalix[4]arene (0.74 g, 1.0 mmol) was added to a suspension of Na₂O (2.0 g, 50 mmol, 60% in oil, washed with hexanes) in dry DMF (50 mL) and stirred overnight. After the precipitate was filtered off, the filtrate was washed with CH₂Cl₂ (100 mL) and with brine (2 × 50 mL). After the organic layer was dried over MgSO₄, the solvent was removed by evaporation under reduced pressure. Recrystallization from CH₂Cl₂/hexanes gave 8a as a white crystalline material in 59% yield: mp 255–257 °C; H NMR δ 8.64 and 7.21 (Abq, 8 H, J = 6.5 Hz), 6.75 (s, 6.13, 4.85 (s, 8 H), 6.91, 6.15, 2.71, 1.75, 0.84 (t, 12 H, J = 7.0 Hz); ¹³C NMR δ 171.9, 169.3, 135.6, 135.4, 132.9, 129.4, 128.3, 73.9, 72.9, 69.4, 68.5, 66.5, 58.2, 18.1, 15.3, 15.2; FAB-MS m/z 1013.8 (M⁺, calc 1013.8); IR (KBr) 1697 cm⁻¹. Anal. Calcd for C₈₉H₅₉O₉·0.5H₂O: C, 78.79; H, 7.89; N, 4.58. Found: C, 78.79; H, 7.89; N, 4.58.

5.11,17,23-Tetraakis[1,1-dimethyl-1,4-oxa-8,13-dione[4]arene[5]-25,26,27,28-tetraakis[2-ethoxyethoxy]calix[4]arene[5]-25-benzoxyl[4,2-bis(4-pyridylmethylene)oxacyclo[4]arene (8b) was synthesized following the same procedure as described for 8a, using 3-picolyl chloride hydrochloride instead of 4-picolyl chloride hydrochloride: yield 71%; mp 255–257 °C; H NMR δ 8.58 (s, 4 H), 8.50–8.51 (m, 4 H), 7.49 (d, 4 H, J = 7.8 Hz), 7.15–7.10 (m, 4 H), 6.73 (s, 8 H), 4.84 (s, 4 H), 3.96 and 2.80 (Abq, 8 H, J = 12.6 Hz), 1.06 (s, 36 H); ¹³C NMR δ 151.7, 150.9, 149.2, 145.3, 136.9, 133.7, 125.2, 122.9, 74.0, 33.9, 31.4, 31.1; FAB-MS m/z 1013.8 (M⁺ + H⁺), 1013.4 (M⁺ + Na⁺). Anal. Calcd for C₈₉H₅₉O₉·0.5H₂O: C, 78.79; H, 7.89; N, 4.58. Found: C, 78.79; H, 7.89; N, 4.58.

Extraction of Tetracarbonyl Acid 5 by Tetrapyriddy[8] and [8] in CDC₅. To eight vials containing tetracarbonyl acid (5, 0.5 mg, 5 μmol) were added increasing amounts (0.14–0.5 mL) of a 10 mM solution of tetrakis[1,1-dimethyl-1,4-oxa-8,13-dione[4]arene[5]-25,26,27,28-tetraakis[2-ethoxyethoxy]calix[4]arene[5]-25-benzoxyl[4,2-bis(4-pyridylmethylene)oxacyclo[4]arene (8a) and added the total volume to 1.0 mL. To obtain mixtures above the 1:1 stoichiometry, increasing aliquots of the 1.0 mM solution of 8a were added to a 1:1:5 mixture of 5 and 8a. The mixtures were sonicated for 15 min and heated at reflux for 5 min in the closed vials, and after the mixture was cooled to room temperature the 1H NMR spectra of the mixtures were recorded. To determine the fraction of 5 that had dissolved eq 1 was used

\[ \text{X}_5 = \left( \frac{1}{1 + \frac{[5]}{[8]}} \right) \]
\( X_A = \) fraction dissolved carboxylic acid (5)

\( I_A = \) integral of equatorial methylene bridge protons of 5

\( I_N = \) integral of equatorial methylene bridge protons of 8a (or 8b)

\( A_N = \) total amount of 5 present in mixture

\( P_N = \) total amount of 8a (or 8b) present in mixture

The fraction of dissolved carboxylic acid 5 was calculated using the integral at 3.3 ppm (A(\text{CH}_3\text{Ar})) for the tetracarboxylic acid and the integral at 3.0 ppm (A(\text{CH}_3\text{Ar})) for 8a. For 8b the integral at 4.9 ppm (OCH)_3 was used.

**Extraction of Tetracarboxylic Acid 5 by Tetra(2-pyridyl) 8c in CDCl_3.** To seven vials containing \( \sim 4.20 \) mg of tetracarboxylic acid 5 were added increasing amounts (0.15, 0.30, 0.45, 0.60, 0.75, 0.90, and 1.05 mL) of a 6.68 mM solution of 8c in CDCl_3, and extra CDCl_3 was added to bring the total volume to 1.00 mL. The closed vials were heated at reflux for 10 min and stirred at 50 \(^\circ\)C for at least 1 h, after which the \(^1\)H NMR spectra of the mixtures were recorded. The fraction of dissolved 5 was calculated with eq 1 using the integral at 0.86 ppm (CH) for the carboxylic acid and the integral at 5.0 ppm (OCH) for 8c. The results were normalized for the mixture with 1.75 equiv (1.05 mL) of 8c, since in that case a clear solution (at rt) was obtained, indicating 100% solubilization of 8. Due to overlap the bridging methylene protons could not be used in this case.

**Extraction of Tetracarboxylic Acid 5 by 4-Picoline in CDCl_3.** To eight vials containing \( \sim 4.30 \) mg of 5 were added increasing amounts (0.15, 0.25, 0.37, 0.50, 0.63, 0.75, 0.87, and 1.00 mL) of a 32 mM solution of 4-picoline (dried over molecular sieves) in CDCl_3, and extra CDCl_3 was added to bring the total volume to 1.00 mL. In the closed vials the mixtures were heated at reflux for 10 min and stirred at 50 \(^\circ\)C for at least 1 h and at rt for at least 30 min, after which the \(^1\)H NMR spectra of the mixtures were recorded. The fraction of dissolved 5 was calculated with eq 1 using the integral at 0.9 ppm (CH) for the carboxylic acid and the integral at 8.4 ppm (2,6-pyH) for 4-picoline. Only the mixture containing 8 equiv of 4-picoline gave a clear solution at rt.

**Extraction of Tetracarboxylic Acid 5 by Dipyrindyl 7a and 7b in CDCl_3.** To eight vials containing \( \sim 4.20 \) mg of tetracarboxylic acid 5 were added increasing amounts (0.08, 0.13, 0.25, 0.37, 0.51, 0.62, 0.75, and 1.00 mL) of a 16 mM solution of dipyrindyl 7a in CDCl_3, and extra CDCl_3 was added to bring the total volume to 1.00 mL. The closed vials were sonicated for 5 min, heated at reflux for 10 min, and stirred overnight at 40 \(^\circ\)C, after which the \(^1\)H NMR spectra of the mixtures were recorded. The fraction of dissolved 5 was calculated with eq 1 using the integral at 8.0 ppm (ArH) for the carboxylic acid and the integral at 8.4 ppm (2,6-pyH) for 7a. For determination of the interaction between 5 and 7b the aliquots of a 16 mM solution of 7b were 0.13, 0.25, 0.37, 0.50, 0.65, 0.75, and 1.00 mL. For the carboxylic acid the integral at 6.8 ppm (ArH) was used and for the dipyrindyl the integral at 6.4 ppm (ArH).

**Vapor Pressure Osmometry.** The vapor pressure osmometric measurements were carried out in CHCl_3 on a Genotec SA-70 vapor pressure osmometer, operated at 29 \(^\circ\)C. The CHCl_3 was of analytical grade, and the residual ethanol was removed by passing it over an Al_2O_3 column (50 g/100 mL). The calibration standard, polystyrene, \( M_w = 4000, M_p/M_w = 1.05 \), was obtained from Polysciences, Inc. For the molecular weight determination five solutions of a 1:1 mixture of the tetracarboxylic acid 5 and the tetrapyrindyl (8a or 8b) of concentrations between 20 and 4 mM were measured.

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