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Kemp's triacid attached to octa-*O*-methyl resorc[4]arenes: conformations in solution and comparative binding studies with various 2-amino pyridines

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Abstract

We synthesized the new supramolecular host molecules **7** and **13** based on functionalized resorcarenes bearing Kemp's triacid. Conformations in solution have been investigated and the influence of intra- and intermolecular hydrogen bonds from the triacid was shown by low temperature and DOSY NMR experiments. The results of host **7** are supported by DFT calculations. The binding behaviour of **7** towards different 2-amino pyridines in chloroform has been investigated by NMR titrations. The association constants reach from K=207 M^{-1} for 2-amino-5-cyano pyridine to K=1551 M^{-1} for 2-amino-4-methyl pyridine. The association constants of the formed complexes of **7** with 2-amino pyridines were compared with those of the simple host systems **14** and **15** in order to evaluate the influence of the attached resorcarene host.

Keywords: Calixarenes; Supramolecular chemistry; 2-Amino pyridine; Hydrogen bonds

1. Introduction

Kemp's triacid[1] is a well known building block in supramolecular chemistry. The concave molecule shape was used for constructing various systems capable for molecular recognition such as rigid molecular clefts[2] and flexible receptors[3] with convergent functional groups of different size. In addition, the interaction of aromatic imides based on Kemp's triacid with adenine was investigated in polar and non-polar solvents and the role of π-stacking and hydrogen bonding in molecular recognition was determined.[4] These recognition phenomena are supplemented by substrate orientation which becomes very meaningful in catalysis.[5] Resorc[4]arenes,[6] a special type of calix[4]arene derived from resorcinol, are known to form molecular capsules of various size in the solid state[7,8] and in solution.[9] For example, these giant hexameric capsules have been reported to encapsulate various guest molecules even in the gas phase in addition to the formation of smaller complexes depending on the conditions used.[10,11]

Cavitands[12] and carcerands[13] are additional examples of resorc[4]arene based supramolecular host systems. Whereas non-functionalized resorc[4]arenes are dominated by hydrogen bonding as driving force for complex formation and aggregation for the latter ones the resorcinol hydroxyl groups are functionalized and therefore π-interaction and electron donation become more important in their host–guest chemistry. Cavitands and carcerands are conformationally fixed contrary to octa-*O*-methyl resorc[4]arenes giving rise to more flexible cavities. In a combination of these two components, the calixarene platform and the triacid moiety, a few systems are known with different host–guest interactions depending on the dimension of their cavities.[14–16] Analogously, our approach was to use

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the triacid for molecular recognition and orientation by hydrogen bonding and to investigate the utilization of the resorc[4]arene cavity for further recognition phenomena by the above described properties. In this work we present the synthesis of two host systems **7** and **13** with a flexible resorc[4]arene cavity combined with Kemp's triacid. We also present studies on the conformation of the host systems in solution and on the formation of complexes of **7** with various 2-amino pyridines.

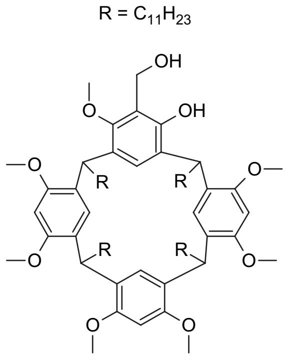
2. Results and discussion

2.1. Synthesis

2.1.1. Synthesis of the host system 7

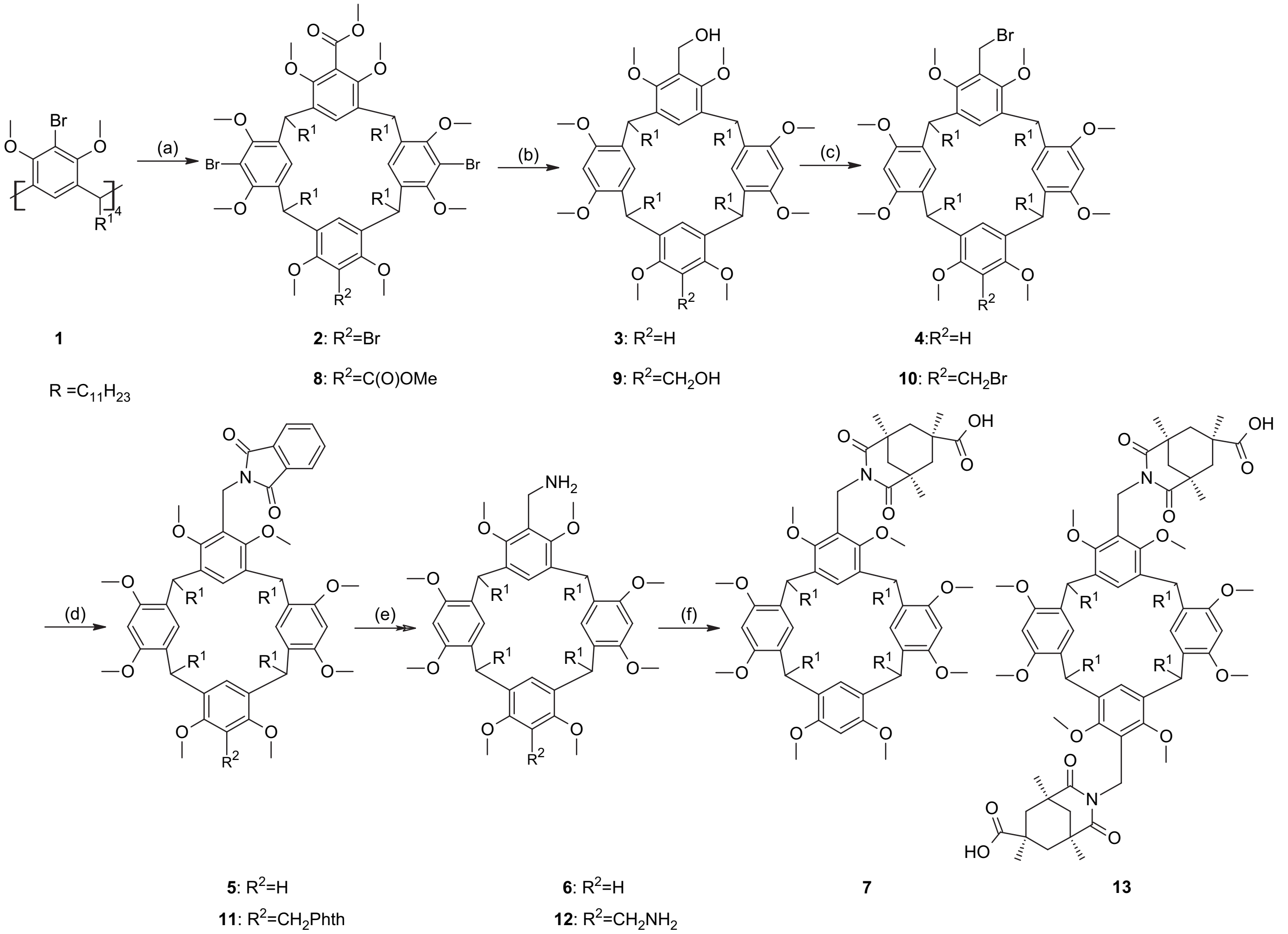
Starting from *C*-undecyltetrabromooctahydroxy-resorc[4]arene[17] **1** the host system **7** is prepared by a six-step synthesis (Scheme 1).[18,19] Treatment of **1** with 1 equiv *n*-butyllithium followed by reaction with methyl chloroformate leads to the mono functionalized resorc[4]arene **2**. The reduction of the methyl ester in the next step is crucial. Beside the formation of desired benzylic alcohol **3** a side reaction emerges by selective cleavage of only one of the methoxy groups leading to the phenolic alcohol **3b** as byproduct (Scheme 2). By treatment of the crude product with diazomethane in a mixture of chloroform/methanol the alcohol **3** is obtained exclusively.

In the next step the benzylic alcohol is substituted by bromine using phosphorus tribromide in very good yield. Resorc[4]arene **4** gives the benzylic phthalimide **5** and afterwards the



3b

Scheme 2. Byproduct **3b**.



Scheme 1. Synthesis of host systems **7** and **13**. (a) (i) *n*-butyllithium, THF, −78 °C, 2 h; (ii) methyl chloroformate, 12 h, rt; (b) (i) $LiAlH_4$, THF, 3.5 h, 60 °C; (ii) 12 h, rt; (c) PBr_3, CH_2Cl_2, 2 h, rt; (d) potassium phthalimide, hexadecyltributylphosphonium bromide, toluene, 2 h reflux; (e) $H_2NNH_2\cdot H_2O$, EtOH/THF (17:3), reflux, 12 h; (f) 5-(chloroformyl)-*cis*,*cis*-1,3,5-trimethylcyclohexane-1,3-dicarboxylic anhydride, DMAP, pyridine, 17 h, 90 °C.

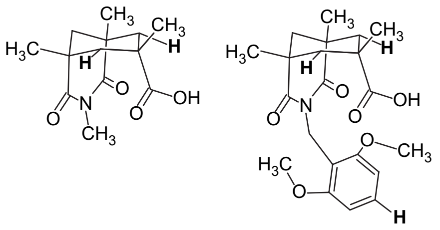
corresponding amine **6**. Kemp's triacid was prepared by a procedure known from the literature[20,21] and transformed to 5-(chloroformyl)-*cis*,*cis*-1,3,5-trimethylcyclohexane-1,3-dicarboxylic anhydride[1] to give **7** by condensation with the amine **6**. Crystals of **7** were obtained from ethanol but an X-ray analysis was not successful so far.

2.1.2. Synthesis of host **13**

The resorcarene based host **13** was prepared analogously to host **7**. In the first step the resorcarene is functionalized twofold by treatment with 2 equiv *n*-butyllithium. The reaction mixture is equilibrated for 2 h to give exclusively the oppositely functionalized arenes. In the next step no cleavage of a methoxy group occurs. This reaction was carried out several times for **3** and **9** and only for the mono functionalized resorcarene **3** bond cleavage happens. Further reaction steps take place in good yields to give host **13**. Also single crystals of host **13** were obtained from acetone but an X-ray analysis was not successful.

2.1.3. Synthesis of reference hosts **14** and **15**

For host–guest studies (see Section 3) two further host molecules were synthesized (Scheme 3). Compound **14** was prepared using a slightly different procedure as reported in the literature.[22] Compound **15** was prepared analogously to **7**. Single crystals of **15** were obtained from chloroform/methanol 1:1 and the X-ray analysis shows an intermolecular hydrogen bond in the solid state (Fig. 1).



14 **15**

Scheme 3. Molecular host systems **14** and **15**. Bold protons are monitored for the determination of association constants (see Section 3).

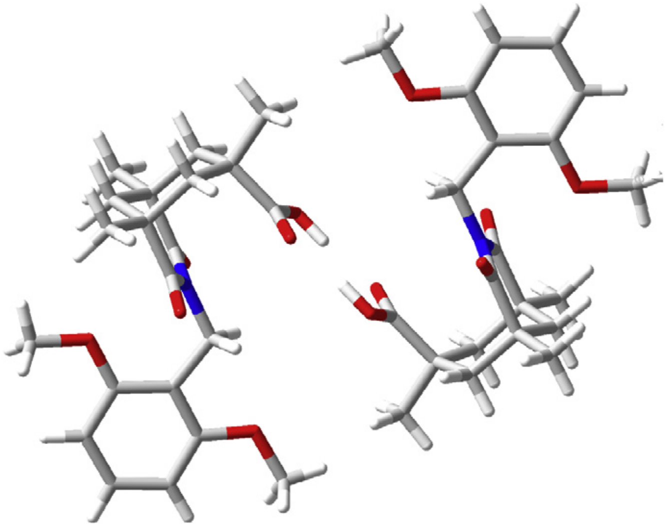


Figure 1. X-ray structure of **15**.

Summarizing, these three compounds (**7**, **14** and **15**) provide a scale of host molecules to study different modes of complexation by different host amplifications of the triacid moiety.

2.2. Host conformations in solution

2.2.1. Resorcarene **7**: an intramolecular hydrogen bond

The *rccc*-resorc[4]arene moiety of host **7** provides a flexible cavity of which various conformations have been well described earlier.[23–25] The ^{1}H NMR spectra of **7** are in agreement with a C_s symmetry. The resonances of the three *upper rim* aromatic protons are in a 2:1 distribution with very small differences in the chemical shift (0.015 ppm) and the resonances of the four *lower rim* aromatic protons show a 2:1:1 ratio.

There are also two triplets of respective two chemical identical methine protons with only very small difference of the chemical shift (0.03 ppm). We assume that an equilibrium geometry of host **7** is made up of two interconverting boat conformations giving in average a cone like conformation at the NMR time scale as it is commonly reported for resorc[4]arenes (Fig. 2a and b).

The most favourable conformations of the model **7a** corresponding to the above mentioned interconversion process have been calculated at the DFT (RI-BP-86) level of approximation. The *lower rim* *n*-undecyl groups were replaced by methyl

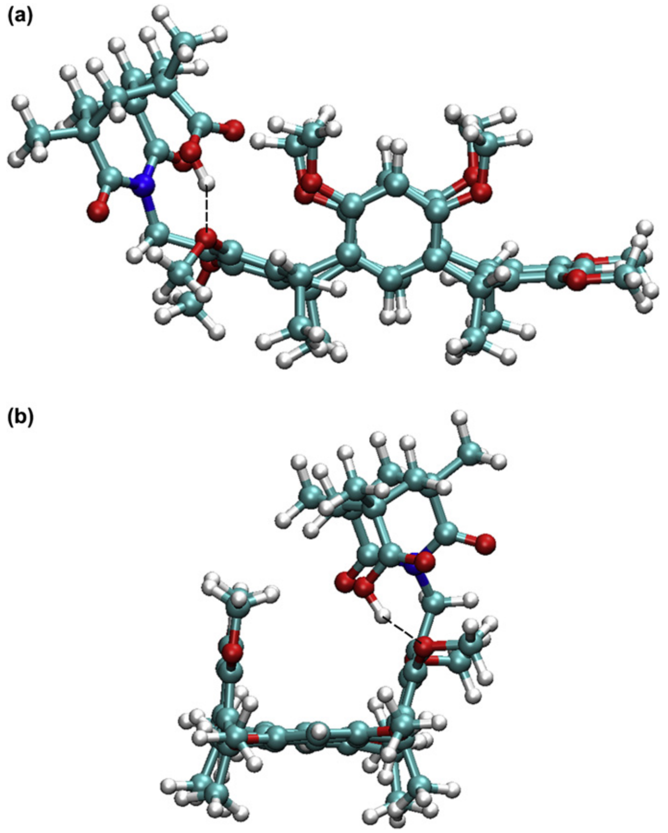


Figure 2. (a) Calculated structure **7a-1** as model for a conformer of **7**; (b) calculated structure **7a-2** as model for a conformer of **7**. A hydrogen bond from the carbon acid to a methoxy oxygen is pictured by the dashed line.

groups. Herein, the conformation **7a-1** is slightly preferred. The total energy of the alternative conformation **7a-2** is only 1.8 kcal/mol higher. For both conformers a formation of an intramolecular C(O)O–H···O hydrogen bond has been revealed. Beyond the hydrogen bonds illustrated in Figure 2a and b (**7a-1** and **7a-2**), conformations with intramolecular hydrogen bonds to the vicinal resorcinol methoxy oxygens are also important (**7b**). The structure **7b** (Fig. 3) is only 0.5 kcal/mol higher in energy as the structure **7a-1**.

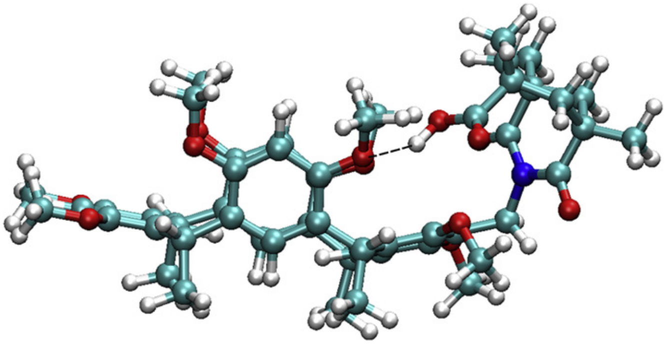
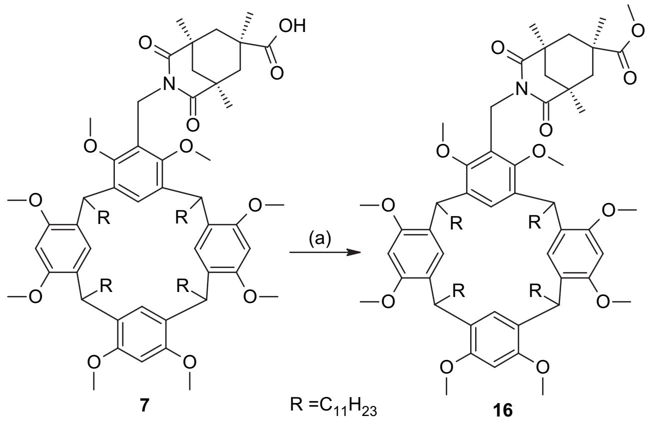


Figure 3. Calculated structure **7b** as model for a conformer of **7**. A hydrogen bond from the acid to a vicinal resorcinol methoxy oxygen is pictured by the dashed line.

To investigate the influence of the intramolecular hydrogen bonds the analogous carboxylic methyl ester **16** has been synthesized (Scheme 4). As expected the methyl ester **16** shows C_s symmetry at the ^{1}H NMR time scale as well. Interestingly both compounds show a remarkable difference in the temperature dependence of the conformations formed in solution.



Scheme 4. Synthesis of the acid ester **16**. (a) MeOH/CHCl$_3$ (1:1), CH$_2$N$_2$.

The temperature dependence of the ^{1}H NMR spectra of **7** is given in Figure 4. Only the aromatic region of the spectrum is shown. At room temperature the spectrum shows the above described profile, the chemical shifts are given in Section 5.

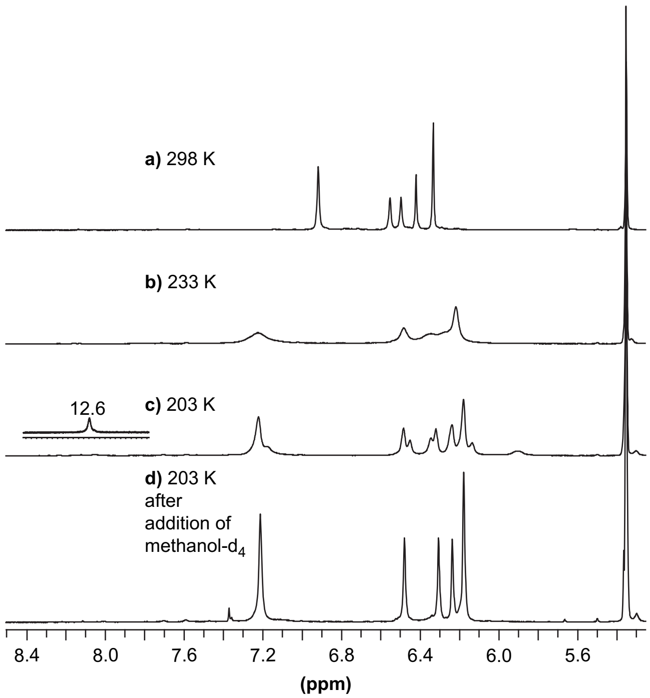


Figure 4. Aromatic region of the ^{1}H NMR spectra of **7** (600 MHz, CD$_2$Cl$_2$) at (a) 298 K; (b) 233 K; (c) 203 K, left: down field region of spectrum (c); (d) 203 K, after addition of a small amount of methanol-d_4.

With decreasing temperature (233 K) the signals are extremely broadened due to the slow dynamics of the interconversion process between the different conformers. At 203 K a peak at very low field (12.66 ppm) appears. This indicates a low electron density of the corresponding proton and is assigned to an intramolecular hydrogen bond between the carboxylic acid and an oxygen of a methoxy group. At 203 K the interconversion of different conformers becomes separated at the NMR time scale and the signal sets are adjusted. The ^{1}H NMR spectra at 203 K seem to consist of more than just two isomers. Because of the not clear assignment of the signals at this temperature we were not able to quantify the energy of the interconversion barrier of **7**.

To avoid intramolecular hydrogen bonding a small amount of methanol is added. The spectrum is sharpened again and almost matches the spectrum at room temperature (Fig. 4d). For comparison the ^{1}H NMR spectrum in acetone, which is known to avoid intramolecular hydrogen bonding, is given in Section 5 as well. The ^{1}H NMR spectrum of the methyl ester **16** at

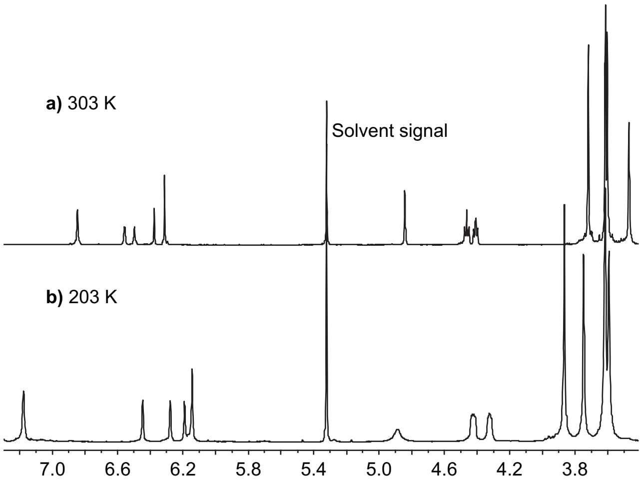


Figure 5. ^{1}H NMR spectra of **16** (600 MHz, CD$_2$Cl$_2$) at (a) 303 K; (b) 203 K.

room temperature and at 203 K is given in Figure 5. The resonances at low temperature are broadened and shifted but the original shape of the spectrum is still remained. In conclusion, the carboxylic acid resorcarene **7** shows a relatively high interconversion barrier in comparison to the ester **16** and we assume that this is caused by intermolecular hydrogen bonds. In these conformations the acid moiety points towards the resorcarene cavity and the resorcarene exhibits a boat conformation with C_s symmetry.

A similar influence on the conformation of other hydrogen-bonded supramolecular systems was reported by Chung et al. as well.[26]

2.2.2. *Resorcarene **13**: intermolecular hydrogen bonding*

The resorcarene **13** also provides an interesting behaviour in solution. At room temperature in chloroform no evidence for intramolecular hydrogen bonding to a methoxy oxygen or to the opposite carboxylic acid was found. The spectrum almost matches the spectrum in acetone which is known to avoid hydrogen bonding. At room temperature a white solid slowly precipitates from the satd acetone soln. This precipitate can be dissolved in chloroform or dichloromethane and shows a remarkable different NMR spectrum (Figs. 6 and 7). The difference is most demonstrative for the methoxy groups which appear from 3.0 to 4.0 ppm.

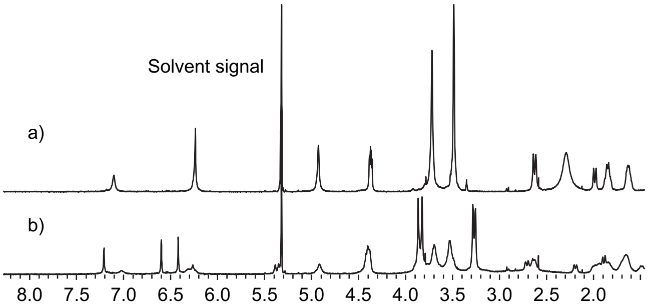


Figure 6. ^{1}H NMR spectra of **13** (500 MHz, CD_2Cl_2) (a) 16 h after addition of a small amount of methanol-d_4; (b) precipitate from acetone dissolved in methylene chloride.

After addition of a small amount of methanol the spectrum can be transferred into the origin shape. This proves that no reaction occurred and that the interaction is driven by hydrogen bonding. To investigate whether intra- or intermolecular hydrogen bonding takes place DOSY NMR experiments were carried out. For a better comparability to the literature the DOSY experiments were carried out in chloroform. The ^{1}H NMR spectrum in chloroform is broadened in comparison to the dichloromethane spectrum but the similar shape remains (Fig. 7). Even though, without methanol addition the spectrum merges within few days the spectrum of the monomer of **13**.

DOSY NMR measurements of spectra (b) and (c) in chloroform were carried out at 295.4 K. For spectrum (b) a diffusion coefficient of 0.35×10^{-5} cm^2 s^{-1} was determined and for spectrum (a) after methanol addition a diffusion coefficient of 0.62×10^{-5} cm^2 s^{-1}. These diffusion coefficients are in a typical magnitude of resorcarenes and resorcarene assemblies.[27]

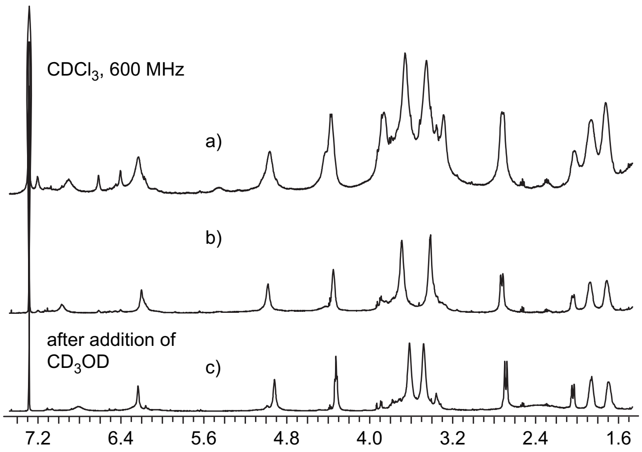


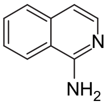
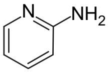
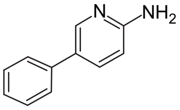
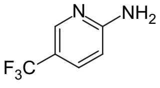
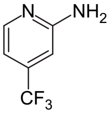
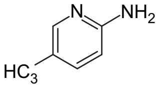
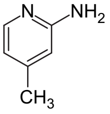
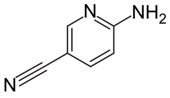
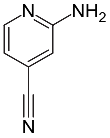
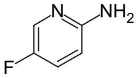
Figure 7. (a) ^{1}H NMR spectra of **13** (600 MHz, $CDCl_3$); (b) after one week in chloroform solution; (c) 16 h after addition of a small amount of methanol-d_4.

Since an intramolecular hydrogen bond would not change the diffusion coefficient upon addition of methanol these results clearly indicate intermolecular aggregation of **13**. Due to the broadened resonances apparently a dynamic equilibrium prevails in solution. This might happen between intermolecular hydrogen bond aggregates of different size. Therefore on the NMR time scale only an average diffusion coefficient was detected.

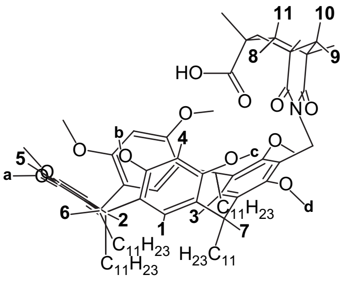
3. Host–guest chemistry in solution. NMR titrations: quantitative binding studies

Association constants for the complex formation of the hosts **7**, **14** and **15** with various 2-amino pyridines in chloroform were determined by NMR titrations. The guest molecules for host–guest studies were commercially purchased (for details see Section 5) besides amino pyridine **17** which was prepared according to the literature.[28,29] The determined binding constants are summarized in Table 1. For all titrations the coefficient of determination is higher than 0.99 and the given errors are the twofold standard deviation. For host **7** the resonances used for monitoring are the two magnetic equivalent equatorial protons of the Kemp's triacid moiety (H_{Kemp}), which appear at 2.64 ppm and the *lower rim* proton of the resorcarene scaffold (H_{arom}), which appears at 6.47 ppm in the ^{1}H NMR spectrum. A graphic assignment can be found in Section 5 (Scheme 5). The determined association constants for the different protons are in good agreement within the experimental error and prove the experimental consistency with one exception (see below). In case of 2-amino pyridines the largest association constants are obtained for the more electron rich guests up to K_a=1551 M^{-1} (2-amino-4-methyl pyridine). The association constants for less electron rich amino pyridines range from 200 to 600 M^{-1}, they are significantly smaller than for the amino pyridines without electronegative substituents. The substitution pattern of the guests does not affect the association constants in a distinct way as shown for the methyl and trifluoromethyl substituted 2-amino pyridines. Within the experimental error, they do not vary significantly.

Table 1
Association constants for the complex formation of hosts **7**, **14** and **15** with various 2-amino pyridines (K/M^{-1})

Guest	7		14	15	
	H_{arom}	H_{Kemp}	H_{Kemp}	H_{arom}	H_{Kemp}
	No	Consistency	6290±812	7905±1424	6591±1730
	1176±100	1018±116	1872±324	1035±156	1287±188
 **17**	—	558±54	1493±130	918±152	843±100
	—	356±34	823±152	362±50	361±82
	296±52	345±42			
	1377±98	1382±110			
	1551±62	1446±100			
	—	207±46			
	413±18	—			
	301±54	271±34			

However, the association constant for 2-amino-4-cyano pyridine is twice as large as for 2-amino-5-cyano pyridine. Not for all titrations both host protons can be fitted due to small change in chemical shift and the larger relative experimental error.



Scheme 5. Graphical assignment of the ^{1}H NMR of host **7**.

For comparison the association constants for complexes of host **14** and **15** with selected amino pyridines are determined as well. In general, the complexes of host **14** with 2-amino pyridines show the largest association constants. The fitted protons are the magnetic equivalent equatorial protons of the triacid at 2.62 ppm (H_{Kemp}) (see Scheme 3, bold). The complexes of **15** with 2-amino pyridines also exceed the complexes of **7** but the association constants are notably smaller than for the complexes of **14**. Again the resonances used for monitoring are the equatorial Kemp's triacid protons at 2.67 ppm (H_{Kemp}) and the aromatic proton at 7.08 ppm (H_{arom}) (bold protons in Scheme 3), which were in good agreement within the experimental error. The association constants for the complexes with 1-amino isoquinoline must be treated carefully. The experimentally determined association constants for the different protons of host **7** are not consistent. Therefore isomeric complexes have to be taken into account for **7**. In this case microscopic binding constants cannot be determined. Despite these limitations it can be established that 1-amino isoquinoline is the strongest binding partner for the hosts **14** and **15** of the complexes studied here. In conclusion, the largest association constants for all three host systems are obtained for the complexes with electron rich guests. The influence of the substitution pattern of the 2-amino pyridines plays a minor role.

Also NMR titration experiments of the monomer of host **13** with 2-aminopyrimidines were carried out. Surprisingly, by the shape of the binding isotherm a 1:1 complex of the host **13** and an aminopyrimidine can be excluded (Fig. 9). In consideration of the results of the titration experiments with host **7** and the difficult evaluation of higher complex stoichiometries in equilibrium these experiments were not pursued.

4. Conclusion

We presented the synthesis of a mono and a distal functionalized octamethoxy resorcarene attached to Kemp's triacid. The conformation of the hosts **7** and **13** in solution has been investigated. It is shown by low temperature NMR and by comparison with the corresponding methyl ester **16** that intramolecular hydrogen bonding from the triacid to the resorcarene is crucial for the structure of host **7** in solution. The results are supported by DFT calculations. We also have shown by DOSY NMR experiments that host **13** forms aggregates in solution driven by intermolecular hydrogen bonding.

The association constants for the complexes of **7** with various 2-amino pyridines in chloroform have been determined by NMR titration clearly showing the influence of electron donating and electron withdrawing substituents over a large scale of guest molecules. Association constants for complexes of selected 2-amino pyridines with smaller host molecules **14** and **15** were determined as well. The initial idea was to pre-organize a host–guest complex by hydrogen bonding of the triacid moiety to the guest molecule and to investigate the influence of the attached host, i.e., the resorcarene to provide a pocket like cavity for the guest. A cooperative binding of the triacid moiety and the attached host would have increased the association constant for at least one order of magnitude. However, based on our measurements we certainly can exclude such a cooperative binding by the triacid and the resorcarene or dimethoxy resorcinol moieties.

5. Experimental section

5.1. General methods

5.1.1. General procedure for NMR titrations

A solution of the host system was prepared in deuterated chloroform (c=3×10^{-3} M). Deuterated chloroform was purchased from Acros Organics and used as received. 0.7 mL of the host solution was transferred to a 5×178 mm NMR tube and a ^{1}H NMR spectrum was recorded on a Bruker Avance 600 spectrometer with internal standard (CHCl$_3$, 7.24 ppm). Then aliquots of a 0.1 M stock solution of an amino pyridine were added and spectra were recorded after each addition until complex saturation. The obtained titration curves were solved by non-linear fitting by iterative solution of Eq. 1.

$$\delta_{\mathrm{obs}} = \frac{(\delta_{\mathrm{H}} - \delta_{\mathrm{C}})}{[\mathrm{H}]_0}\frac{1}{2}\left([\mathrm{H}]_0 + [\mathrm{G}] + \frac{1}{K} - \sqrt{\left([\mathrm{H}]_0 + [\mathrm{G}] + \frac{1}{K}\right)^2 - 4[\mathrm{H}]_0[\mathrm{G}]}\right) - \delta_{\mathrm{H}} \quad (1)$$

Eq. 1 describes the relation between the observed chemical shift δ_{obs} and the association constant K. $[\mathrm{H}]_0$ is the host concentration and [G] the guest concentration. The chemical shift of the host δ_{H} was measured in absence of a guest. The chemical shift of the formed complex δ_{C} was treated as floating parameter. An elaborated derivation of Eq. 1 and further information are reported in the literature.[30–32] As an example the titration curve for the complex formation of **7** with 2-amino pyridine is shown in Figure 8. The shape of the binding isotherms for all titrations clearly shows a 1:1 complex stoichiometry, which is assured by a representative Job-plot[33] for the complex of **7** with 2-amino pyridine (Fig. 8, insertion).

Experiments were carried out at 300 K. Spectra were recorded at a guest/host ratio of 0.2, 0.4, 0.6, 0.8, 1, 2, 3, 4, 5, 7, 9, 11, 13, 15, 20, 25 and 45. In the case of 2-amino-4-cyano pyridine and 2-amino-5-cyano pyridine 0.05 M stock solutions were prepared due to the weak solubility. Because of the limited volume of the NMR tube only 25 guest equivalents were added but complex saturation was reached. Amino pyridines were commercially purchased from Alfa Aeser (2-amino-5-methyl pyridine (99%), 2-amino-4-methyl pyridine (98%), 2-amino-5-(trifluoro)methyl pyridine (97%), 2-amino-4-(trifluoro)methyl pyridine (99%), 2-amino-5-cyano pyridine (98%), 2-amino-4-cyano pyridine (97%) and 2-amino-5-fluoro pyridine (97%)) and Aldrich (2-Amino pyridine (99%) and 1-amino isoquinoline (99%)) and used as received. For the Job-plot stock solutions (c=4.3×10^{-3} M) of the host **7** and 2-amino pyridine were

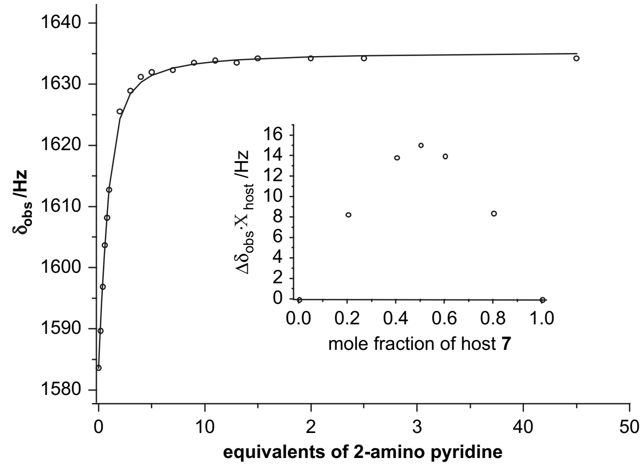


Figure 8. Measured (⌋) and calculated (solid line) chemical shift of the host resonances of **7** upon addition of 2-amino pyridine (initial c_{host}=3×10^{-3} M) in deuterated chloroform. Insertion: Job-plot for the complex of **7** with 2-amino pyridine (c_{overall}=4.3×10^{-3} M).

prepared. Aliquots of the host solution varying from 0 to 480 μl were transferred to NMR tubes. The stock solution of the guest was added to complete the volume to 600 μl. A spectrum was recorded for each sample on a Bruker DRX 500 spectrometer. For evaluation of NMR spectra Bruker 1D NMR software was used. For host–guest titrations of host **13** stock solutions with the same concentrations for the host and the guest as mentioned for the titrations of **7** were prepared in chloroform. Titrations were carried out with 2-aminopyrimidine, 2-amino-5-phenyl-aminopyrimidine and α-naphthyl-aminopyrimidine. The binding isotherm of the titration of host **13** with 2-aminopyrimidine is shown in Figure 9 which is representative for the shape of the isotherms of the other titrated aminopyrimidines.

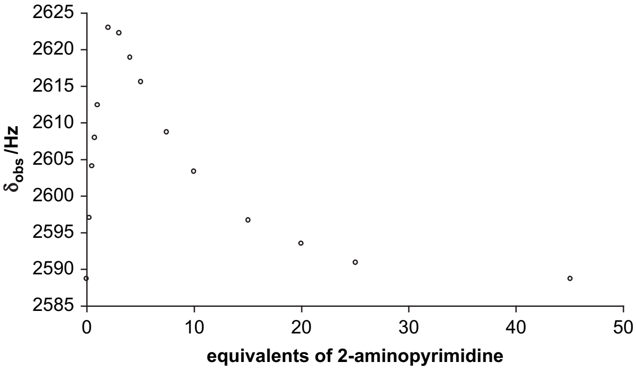


Figure 9. Measured chemical shift of host **13** upon addition of 2-aminopyrimidine (initial $c_{host}=3\times10^{-3}$ M) in deuterated chloroform.

5.1.2. Details of calculations

All calculations were performed with the TURBOMOLE set of programs.[34,35] Structures were optimized without any symmetry restrictions. The standard split-valence SV(P) basis sets[36] and DFT BP86[37,38] functional were used for calculations in combination with the high integration accuracy (grid=5) and convergence criterion (scfconv=1×10^{-8}). For more performance, the RI (Resolution of the Identity)[39–41] algorithm was employed for all calculation routines. No vibration frequency calculations were made, due to the large size of the investigated structures. The single-point energy calculations were performed with the optimized structures using the TZV basis sets of triple-zeta quality suggested by Ahlrichs et al.:[36] (11s6p)/[5s3p] for C, N, O and F contracted as {62111/411} and (5s)/[3s] for H with contraction {311}. The basis sets were expanded by addition of the polarization functions (the TZVP basis sets standard within the TURBOMOLE packet) formed as the TZV basis sets plus one set of three p-functions for hydrogen and one set of five d-functions for the other elements. The VMD program packet[42] was used for the graphical presentation of the calculated structures.

5.2. Synthetic procedures

5.2.1. *rccc*-5,11,17,23-Tetrabromo-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (1)

Sodium hydride (60%) in paraffin (5.2 g, 3.0 g pure sodium hydride, 127 mmol) under argon was washed with *n*-pentane (3×). Dry DMF (250 mL) was added and following a solution of *rccc*-5,11,17,23-tetrabromo-2,8,14,20-tetra-(*n*-undecyl)-resorc[4]arene[18,43] (15.4 g, 10.8 mmol) and iodomethane (12.2 mL, 27.6 g, 195 mmol) in dry DMF was added slowly to keep the temperature below 35 °C. The mixture was stirred for 1 day at room temperature. Iodomethane (5 mL, 11.4 g, 80 mmol) was added and the mixture was stirred at 50 °C for additional 1 day. At room temperature ethanol (20 mL) was added to dispose the excess of sodium hydride. The solvent was removed in vacuo and the residue was dissolved in chloroform (500 mL) and satd NH_4Cl soln (300 mL). The aqueous phase was extracted with chloroform (2×) and the organic layer was washed with water (3×) and dried over $MgSO_4$. The solvent was removed in vacuo and after recrystallization from 2-propanol the pure product was obtained as colourless crystals (15 g, 9.78 mmol, yield: 91%). Mp: 79 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.50 (br s, 4H, ArH), 4.43 (t, ^3J=7.4 Hz, 4H, ArCHAr), 3.64 (s, 24H, $COOCH_3$), 1.88–1.78 (m, 8H, $CHCH_2$), 1.36–1.17 (m, 72H, CH_2), 0.84 (t, ^3J=7.0 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=154.3, 134.6, 125.5, 113.1, 60.6, 38.6, 35.0, 31.9, 29.8, 29.8, 29.7, 29.7, 29.7, 29.4, 28.4, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{80}H_{124}O_8Br_4+NH_4$ $[M+NH_4]^+$ 1546.63680; found 1546.63432; IR (KBr): $\tilde{\nu}$ = 2923, 2855, 1468, 1418, 1392, 1327, 1296, 1229, 1189, 1151, 1090, 1039, 1003, 967, 917, 896, 777, 720 cm^{-1}.

5.2.2. *rccc*-5,11,17-Tribromo-23-[methoxycarbonyl]-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (2)

A solution of resorc[4]arene (**1**) (1.19 g, 0.78 mmol) in 50 mL anhydrous THF under argon-atmosphere was cooled to −78 °C and *n*-butyllithium (0.49 mL of a 1.6 M solution in hexanes, 0.78 mmol) was added rapidly. After 2 h methyl chloroformate (1 mL, 12.9 mmol) was added and the mixture was allowed to warm to room temperature within 12 h. Methanol (5 mL) was added and the solvent was removed in vacuo. The residue was dissolved in $CHCl_3$ and the organic layer was washed with water (3×), and was dried over anhydrous $MgSO_4$. Evaporation gave the crude product as yellow oil. After column chromatography (SiO_2, cyclohexane/ethyl acetate, 4:1) the pure product was obtained as colourless solid (0.8 g, 0.53 mmol, yield: 68%). Mp: 62–64 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.61 (br s, 2H, ArH), 6.55 (br s, 2H, ArH), 4.45 (t, ^3J=7.5 Hz, 2H, ArCHAr), 4.40 (t, ^3J=7.5 Hz, 2H, ArCHAr), 3.89 (s, 3H, $COOCH_3$), 3.63 (br s, 12H, OCH_3), 3.61 (br s, 12H, OCH_3), 1.87–1.79 (m, 8H, $CHCH_2$), 1.34–1.16 (m, 72H, CH_2), 0.84 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=167.5, 154.3, 154.3, 153.9, 134.6, 128.0, 125.5, 125.5, 122.5, 113.2, 113.1, 61.9, 60.6, 60.5, 52.5, 38.5, 37.8, 35.1, 35.1, 31.9, 29.8, 29.7, 29.7, 29.3, 28.4, 28.4, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{82}H_{128}O_{10}Br_3+H^+$ $[M+H]^+$ 1509.70521; found 1509.70431; IR (KBr): $\tilde{\nu}$ = 2956, 2922, 2851, 1736, 1580, 1470, 1456, 1420, 1396, 1291, 1261, 1039, 1009, 800 cm^{-1}.

*5.2.3. rccc-5-Hydroxymethyl-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**3**)*

A mixture of resorc[4]arene (**2**) (1 g, 0.66 mmol) and $LiAlH_4$ (150 mg, 4 mmol) in anhydrous THF (30 mL) under argon-atmosphere was refluxed for 3.5 h and additional $LiAlH_4$ (100 mg, 2.6 mmol) was added. The mixture was stirred for 12 h at room temperature and treated with methanol (10 mL). HCl (2 M) was added until the mixture became acidic. The mixture was extracted with $CHCl_3$ (3×). The organic layer was washed with satd $NaHCO_3$ soln and brine, and was dried over anhydrous $MgSO_4$. After evaporation the product (0.71 g, 0.57 mmol, yield: 86%) was obtained as white solid. The product can be recrystallized from acetone. Mp: 87–89 °C; ^{1}H NMR ($CDCl_3$, 600 MHz, 27 °C): δ=6.95 (s, 1H, ArH), 6.91 (s, 1H, ArH), 6.42 (s, 2H, ArH), 6.32 (s, 2H, ArH), 6.14 (s, 1H, ArH), 4.56 (s, 2H, $ArCH_2$), 4.48 (t, ^3J=7.4 Hz, 2H, ArCHAr), 4.42 (t, ^3J=7.4 Hz, 2H, ArCHAr), 3.76 (s, 6H, OCH_3), 3.75 (s, 6H, OCH_3), 3.46 (s, 6H, OCH_3), 3.26 (s, 6H, OCH_3), 1.87–1.72 (m, 8H, $CHCH_2$), 1.35–1.17 (m, 72H, CH_2), 0.85 (t, ^3J=7.2 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=155.9, 155.8, 155.4, 155.1, 133.1, 127.4, 126.6, 126.4, 126.2, 123.9, 96.0, 95.5, 61.3, 56.5, 56.2, 55.8, 55.4, 35.9, 35.3, 35.0, 34.7, 31.9, 30.0, 29.9, 29.8, 29.7, 29.4, 28.2, 28.2, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{81}H_{130}O_9+NH_4^+$ $[M+NH_4]^+$ 1265.00531; found 1265.00765; IR (KBr): $\tilde{\nu}$ = 3456, 2922, 2853, 1611, 1580, 1506, 1467, 1299, 1202, 1095, 1040, 904, 818, 722 cm^{-1}.

*5.2.4. rccc-5-Bromomethyl-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**4**)*

A solution of resorc[4]arene (**3**) (0.49 g, 0.39 mmol) in dry dichloromethane (20 mL) was treated with phosphonium tribromide (0.23 g, 0.85 mmol). The solution turned slightly pink. The reaction mixture was stirred for 2 h at room temperature and 2-propanol (5 mL) was added. The solution was washed with satd $NaHCO_3$ soln and brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded the product (0.47 g, 3.6 mmol, yield: 92%) as colourless solid. Mp: 79–80 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=7.03 (s, 1H, ArH), 6.96 (s, 1H, ArH), 6.44 (s, 2H, ArH), 6.28 (s, 2H, ArH), 6.15 (s, 1H, ArH), 4.57 (s, 2H, $ArCH_2$), 4.49 (t, ^3J=7.4 Hz, 2H, ArCHAr), 4.40 (t, ^3J=7.4 Hz, 2H, ArCHAr), 3.80 (s, 6H, OCH_3), 3.79 (s, 6H, OCH_3), 3.47 (s, 6H, OCH_3), 3.32 (s, 6H, OCH_3), 1.90–1.72 (m, 8H, $CHCH_2$), 1.42–1.13 (m, 72H, CH_2), 0.84 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=156.2, 155.9, 155.8, 155.1, 132.9, 128.3, 127.8, 126.4, 126.3, 126.2, 125.0, 122.8, 95.9, 95.3, 61.3, 56.2, 55.7, 55.1, 36.1, 35.6, 35.0, 34.4, 31.9, 30.0, 29.9, 29.8, 29.8, 29.7, 29.7, 29.7, 29.7, 29.4, 28.3, 28.1, 25.3, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{81}H_{129}O_8Br+NH_4^+$ $[M+NH_4]^+$ 1326.92091; found 1326.92150; IR (KBr): $\tilde{\nu}$ = 2921, 2852, 1611, 1582, 1506, 1467, 1299, 1202, 1042, 903, 811, 720 cm^{-1}.

*5.2.5. rccc-5-Phthalimidomethyl-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**5**)*

A mixture of the resorc[4]arene (**4**) (0.41 g, 0.31 mmol), potassium phthalimide (0.3 g, 1.62 mmol) and hexadecyltributylphosphonium bromide in toluene (20 mL) was refluxed for 3 h. The solvent was evaporated in vacuo and the residue dissolved in CH_2Cl_2. The solution was washed with 1 N NaOH and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (SiO_2, cyclohexane/ethyl acetate, 3:1) yielding a colourless solid (0.19 g, 0.14 mmol, yield: 45%). Mp: 56–58 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=7.87–7.61 (m, 4H, ArH), 6.70 (s, 1H, ArH), 6.66 (s, 1H, ArH), 6.57 (s, 2H, ArH), 6.30 (s, 2H, ArH), 6.27 (s, 1H, ArH), 4.84 (s, 2H, $ArCH_2$), 4.42 (t, ^3J=7.5 Hz, 4H, ArCHAr), 3.60 (s, 6H, OCH_3), 3.59 (s, 6H, OCH_3), 3.58 (s, 6H, OCH_3), 3.39 (s, 6H, OCH_3), 1.84–1.68 (m, 8H, $CHCH_2$), 1.33–1.10 (m, 72H, CH_2), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=167.9, 156.0, 155.7, 155.5, 134.3, 133.8, 133.5, 132.4, 126.8, 126.5, 126.2, 126.1, 125.7, 124.9, 123.6, 122.9, 120.8, 96.5, 95.5, 61.1, 56.2, 55.6, 36.1, 35.5, 25.4, 34.6, 33.2, 31.9, 30.0, 30.0, 29.9, 29.8, 29.7, 29.7, 29.4, 28.2, 28.1, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{89}H_{133}O_{10}N+Na^+$ $[M+Na]^+$ 1398.98217; found 1398.98139; IR (KBr): $\tilde{\nu}$ = 2924, 2854, 1719, 1655, 1499, 1459, 1439, 1398, 1351, 1299, 1201, 1040 cm^{-1}.

*5.2.6. rccc-5-Aminomethyl-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**6**)*

A solution of resorc[4]arene (**5**) (0.86 g, 0.62 mmol) in a mixture of ethanol and THF (17:3, 50 mL) was treated with hydrazine hydrate (2 mL, approx. 27 mmol pure hydrazine) and refluxed for 12 h. The solution was cooled to 0 °C and concd HCl (1.5 mL) was added. The solution was stirred for additional 2 h under ice cooling and concd NaOH was added till pH>10. The precipitate was filtered off and washed with concd NaOH and cold ethanol. The colourless solid (0.7 g, 0.56 mmol, yield: 90%) was dried in vacuo. Mp: 125 °C; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.92 (s, 1H, ArH), 6.90 (s, 1H, ArH), 6.42 (s, 2H, ArH), 6.30 (s, 2H, ArH), 6.12 (s, 1H, ArH), 4.47 (t, ^3J=7.4 Hz, 2H, ArCHAr), 4.42 (t, ^3J=7.4 Hz, 2H, ArCHAr), 3.77 (s, 6H, OCH_3), 3.76 (s, 6H, OCH_3), 3.62 (s, 2H, $ArCH_2$), 3.46 (s, 6H, OCH_3), 3.19 (s, 6H, OCH_3), 1.90–1.70 (m, 8H, $CHCH_2$), 1.38–1.14 (m, 72H, CH_2), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=155.9, 155.7, 155.3, 155.1, 133.0, 129.6, 127.4, 126.8, 126.4, 125.3, 123.8, 96.0, 95.1, 60.9, 56.2, 55.7, 55.4, 36.8, 36.1, 35.3, 35.0, 34.7, 31.9, 30.0, 30.0, 29.9, 29.8, 29.7, 29.4, 28.2, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{81}H_{131}NO_8+H^+$ $[M+H]^+$ 1246.99475; found 1246.99483; IR (KBr): $\tilde{\nu}$ = 3449, 2922, 2852, 1610, 1579, 1507, 1466, 1400, 1299, 1200, 1097, 1039, 903, 819, 720 cm^{-1}.

*5.2.7. Kemp's acid resorc[4]arene (**7**)*

A solution of the resorc[4]arene (**6**) (0.7 g, 0.56 mmol), 5-(chloroformyl)-*cis*,*cis*-1,3,5-trimethylcyclohexane-1,3-dicarboxylic anhydride (0.18 g, 70 mmol) and a catalytic amount of 4-dimethylamino pyridine in pyridine (20 mL) was heated to 90 °C for 17 h. The solvent was removed in vacuo and the residue was dissolved in $CHCl_3$. The organic layer was washed with 2 N

HCl and 2 N NaOH and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (SiO$_2$, cyclohexane/ethyl acetate, 1:1) yielding a colourless solid (0.34 g, 0.23 mmol, yield: 41%). Mp: 79–81 °C; ^{1}H NMR (CDCl$_3$, 500 MHz, 27 °C): δ=6.67 (s, 2H, ArH, *lower rim*, **H1**), 6.53 (s, 1H, ArH, *lower rim*, **H2**), 6.47 (s, 1H, ArH, *lower rim*, **H3**), 6.29 (s, 2H, ArH, *upper rim*, **H4**), 6.27 (s, 1H, ArH, *upper rim*, **H5**), 4.84 (s, 2H, ArCH$_2$R), 4.41 (t, ^3J=7.4 Hz, 2H, ArCHAr, **H6**), 4.38 (t, ^3J=7.4 Hz, 2H, ArCHAr, **H7**), 3.62 (s, 6H, OCH$_3$ **a**), 3.55 (s, 6H, OCH$_3$ **b**), 3.53 (s, 6H, OCH$_3$ **c**), 3.35 (s, 6H, OCH$_3$ **d**), 2.64 (d, ^2J=13.8 Hz, 2H, Kemp's acid CH$_2$ eq, **H8**), 1.97 (d, ^2J=12.6 Hz, 1H, Kemp's acid CH$_2$ eq, **H9**), 1.89–1.63 (m, 8H, CHC*H*$_2$), 1.40–1.13 (m, 76H, CH$_2$; Kemp's acid CH$_2$ ax, **H10**, CH$_3$ Kemp's acid), 1.18 (s, 6H, CH$_3$ Kemp's acid), 1.10 (d, ^2J=14.4 Hz, 2H, Kemp's acid CH$_2$ ax, **H11**), 0.85 (t, ^3J=6.9 Hz, 12H, CH$_3$) ppm; ^{1}H NMR ((CD$_3$)$_2$CO, 500 MHz, 27 °C): δ=10.79 (br, 1H, COOH), 6.92 (s, 2H, ArH, *lower rim*), 6.61 (s, 1H, ArH, *lower rim*), 6.54 (s, 1H, ArH, *lower rim*), 6.52 (s, 1H, ArH, *upper rim*), 6.45 (s, 2H, ArH, *upper rim*), 4.89 (s, 2H, ArCH$_2$), 4.56 (t, ^3J=7.5 Hz, 2H, ArCHAr), 4.48 (t, ^3J=7.5 Hz, 2H, ArCHAr), 3.74 (s, 6H, OCH$_3$), 3.60 (s, 6H, OCH$_3$), 3.58 (s, 6H, OCH$_3$), 3.49 (s, 6H, OCH$_3$), 2.57 (d, ^2J=13.2 Hz, 2H, Kemp's acid CH$_2$ eq), 1.97 (d, ^2J=12.6 Hz, 1H, Kemp's acid CH$_2$ eq), 1.90–1.67 (m, 8H, CHC*H*$_2$), 1.43 (d, ^2J=12.6 Hz, 1H, Kemp's acid CH$_2$ ax), 1.37–1.21 (m, 74H, CH$_2$; Kemp's acid CH$_2$ ax), 1.20 (s, 3H, CH$_3$ Kemp's acid), 1.18 (s, 6H, CH$_3$ Kemp's acid), 0.86 (t, ^3J=6.9 Hz, 12H, CH$_3$) ppm; ^{1}H NMR (CD$_2$Cl$_2$, 600 MHz, 27 °C): δ=6.88 (s, 2H, ArH, *lower rim*), 6.52 (s, 1H, ArH, *lower rim*), 6.46 (s, 1H, ArH, *lower rim*), 6.39 (s, 1H, ArH, *upper rim*), 6.30 (s, 2H, ArH, *upper rim*), 4.86 (s, 2H, ArCH$_2$), 4.46 (t, ^3J=7.5 Hz, 2H, ArCHAr), 4.40 (t, ^3J=7.9 Hz, 2H, ArCHAr), 3.74 (s, 6H, OCH$_3$), 3.60 (s, 6H, OCH$_3$), 3.58 (s, 6H, OCH$_3$), 3.50 (s, 6H, OCH$_3$), 2.61 (d, ^2J=13.5 Hz, 2H, Kemp's acid CH$_2$ eq), 1.98 (d, ^2J=12.9 Hz, 1H, Kemp's acid CH$_2$ eq), 1.92–1.56 (m, 8H, CHC*H*$_2$), 1.41–1.20 (m, 78H, CH$_2$; Kemp's acid CH$_2$ ax, CH$_3$, Kemp's acid CH$_2$ ax), 1.16 (s, 6H, CH$_3$ Kemp's acid), 0.87 (t, ^3J=6.9 Hz, 12H, CH$_3$) ppm; ^{1}H NMR (CD$_2$Cl$_2$, 600 MHz, −70 °C): δ=12.66, 7.18, 6.44, 6.41, 6.31, 6.28, 6.19, 6.14, 6.09, 5.87, 5.26, 4.87, 4.51, 4.43, 4.36, 4.31, 4.23, 4.16, 4.09, 3.87, 3.74, 3.62, 3.59, 3.52, 3.44, 3.37, 2.54, 2.36, 2.24, 2.14, 1.99, 1.92, 1.83, 1.78, 1.49, 1.45, 1.12, 0.78 ppm; ^{13}C NMR (CDCl$_3$, 125 MHz, 27 °C): δ=177.4, 175.7, 156.1, 155.7, 155.6, 155.2, 133.9, 126.4, 126.1, 125.5, 125.5, 125.4, 122.5, 97.0, 95.4, 61.1, 56.2, 55.7, 44.3, 43.1, 41.7, 40.4, 36.1, 35.4, 35.0, 34.6, 31.9, 30.4, 30.0, 29.9, 29.9, 29.8, 29.7, 29.4, 28.2, 28.0, 25.9, 22.7, 14.1 ppm; HRMS: *m*/*z* calcd for $C_{93}H_{145}NO_{12}+Na^+$ $[M+Na]^+$ 1491.06590; found 1491.06629; IR (ATR): $\tilde{\nu}$ = 3477 (br), 3194 (br), 2963, 2852, 1730, 1705, 1678, 1611, 1582, 1502, 1462, 1378, 1297, 1201, 1164, 1091, 1039, 817, 755 cm^{-1}.

5.2.8. *rccc-5,17-Dibromo-11,23-bis-[methoxycarbonyl]-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**8**)*

A solution of resorc[4]arene (**1**) (10.1 g, 6.6 mmol) in anhydrous THF (450 mL) under argon-atmosphere was cooled to −78 °C and *n*-butyllithium (9 mL of a 1.6 M solution in hexanes, 14.4 mmol) was added rapidly. After 2 h methyl chloroformate (8 mL, 103.2 mmol) was added and the mixture was allowed to warm to room temperature within 12 h. Methanol (10 mL) was added and the solvent was removed in vacuo. The residue was dissolved in CHCl$_3$ and the organic layer was washed with water (3×), and was dried over anhydrous MgSO$_4$. Evaporation gives the crude product as yellow oil. After column chromatography (SiO$_2$, cyclohexane/ethyl acetate, 4:1) the pure product was obtained as colourless solid (4.7 g, 3.2 mmol, yield: 48%). Mp: 76 °C; ^{1}H NMR (CDCl$_3$, 500 MHz, 27 °C): δ=6.75 (br s, 2H, ArH), 6.46 (br s, 2H, ArH), 4.43 (t, ^3J=7.5 Hz, 4H, ArCHAr), 3.92 (s, 6H, COOCH$_3$), 3.69 (s, 12H, OCH$_3$), 3.54 (s, 12H, OCH$_3$), 1.87–1.79 (m, 8H, CHC*H*$_2$), 1.34–1.16 (m, 72H, CH$_2$), 0.84 (t, ^3J=6.9 Hz, 12H, CH$_3$) ppm; ^{13}C NMR (CDCl$_3$, 125 MHz, 27 °C): δ=167.5, 154.6, 153.7, 133.8, 128.1, 125.5, 122.5, 113.3, 62.0, 60.5, 52.6, 37.7, 35.1, 31.9, 29.8, 29.7, 29.7, 29.7, 29.4, 28.4, 22.7, 14.1 ppm; HRMS: *m*/*z* calcd for $C_{84}H_{130}O_{12}Br_2+Na^+$ $[M+Na]^+$ 1511.78212; found 1511.78396; IR (KBr): $\tilde{\nu}$ = 2924, 2852, 1727, 1584, 1467, 1438, 1421, 1333, 1296, 1279, 1265, 1233, 1197, 1154, 1118, 1090, 1063, 1031, 1002, 909, 892, 722 cm^{-1}.

5.2.9. *rccc-5,17-Bis-(hydroxymethyl)-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**9**)*

A mixture of LiAlH$_4$ (190 mg, 5 mmol) and resorc[4]arene (**8**) (3.62 g, 2.43 mmol) in anhydrous THF (100 mL) was stirred at room temperature for 0.5 h and subsequently at 60 °C for 4 h. Additional LiAlH$_4$ (190 mg, 5 mmol) was added and stirred for 4 h at 60 °C. At room temperature methanol (10 mL) and hydrochloric acid (2 M) were added until the mixture became acidic. The mixture was extracted with CHCl$_3$ (3×). The organic layer was washed with satd NaHCO$_3$ soln and brine and was dried over anhydrous MgSO$_4$. After evaporation the product (2.18 g, 2.14 mmol, yield: 88%) was obtained as white solid. The product can be recrystallized from acetone. Mp: 72 °C; ^{1}H NMR (CDCl$_3$, 500 MHz, 27 °C): δ=6.97 (s, 2H, ArH), 6.42 (s, 2H, ArH), 6.35 (s, 2H, ArH), 4.53 (s, 4H, ArCH$_2$), 4.48 (t, ^3J=7.2 Hz, 4H, ArCHAr), 3.77 (s, 12H, OCH$_3$), 3.40 (s, 12H, OCH$_3$), 1.87–1.72 (m, 8H, CHC*H*$_2$), 1.36–1.17 (m, 72H, CH$_2$), 0.85 (t, ^3J=6.9 Hz, 12H, CH$_3$) ppm; ^{13}C NMR (CDCl$_3$, 125 MHz, 27 °C): δ=155.6, 155.4, 133.0, 126.9, 126.5, 126.5, 126.3, 95.4, 61.5, 56.3, 55.7, 35.7, 35.1, 31.9, 29.3, 29.9, 29.8, 29.7, 29.4, 28.1, 22.7, 14.1 ppm; HRMS: *m*/*z* calcd for $C_{82}H_{132}O_{10}+Na^+$ $[M+Na]^+$ 1299.97127; found 1299.97187; IR (KBr): $\tilde{\nu}$ = 3531, 3437, 2923, 2854, 1704, 1613, 1582, 1503, 1466, 1426, 1401, 1366, 1298, 1262, 1202, 1090, 1028, 904, 876, 805, 720, 686 cm^{-1}.

5.2.10. *rccc-5,17-Bis-(bromomethyl)-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**10**)*

A solution of resorcarene (**9**) (1.14 g, 0.89 mmol) in dry dichloromethane (50 mL) was treated with phosphonium tribromide (0.96 g, 3.55 mmol). The reaction mixture was stirred for

2 h at room temperature and 2-propanol (5 mL) was added. The solution was washed with satd $NaHCO_3$ soln and brine and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo and the crude product was recrystallized from acetone to afford the product (1.00 g, 0.71 mmol, yield: 80%) as colourless solid. Mp: 101 °C; ^1H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.96 (s, 2H, ArH), 6.62 (s, 2H, ArH), 6.38 (s, 2H, ArH), 4.54 (s, 4H, $ArCH_2$), 4.51 (t, ^3J=7.2 Hz, 4H, ArCHAr), 3.71 (s, 12H, OCH_3), 3.57 (s, 12H, OCH_3), 1.90–1.72 (m, 8H, $CHCH_2$), 1.36–1.13 (m, 72H, CH_2), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=155.8, 155.7, 133.6, 128.0, 126.1, 125.7, 125.0, 95.8, 61.4, 55.6, 35.9, 35.5, 31.9, 29.9, 29.8, 29.8, 29.7, 29.4, 28.2, 24.5, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{82}H_{130}O_8Br_2+Na^+$ $[M+Na]^+$ 1423.80247; found 1423.80506; IR (KBr): $\tilde{\nu}$ = 2925, 2855, 1614, 1574, 1503, 1468, 1424, 1402, 1301, 1229, 1201, 1145, 1120, 1082, 1034, 1007, 898, 821, 771, 720, 629 cm^{-1}.

*5.2.11. rccc-5,17-Bis-[(phthalimido)-methyl]-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**11**)*

A mixture of resorcarene (**10**) (420 mg, 0.30 mmol), potassium phthalimide (175 mg, 0.94 mmol) an 18-crown-6 (34 mg, 0.18 mmol) in THF (50 mL) was refluxed for 12 h. Water (50 mL) was added and the aqueous phase extracted with chloroform (3×). The organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed and the crude product filtrated over silica gel (cyclohexane/ethyl acetate, 3:2). After recrystallization from acetone the product was obtained as colourless solid (258 mg, 0.17 mmol, yield: 56%). Mp: 197–198 °C; ^1H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=7.82–7.78 (m, 4H, ArH), 7.67–7.63 (m, 4H, ArH), 6.87 (s, 2H, ArH), 6.49 (s, 2H, ArH), 6.21 (s, 2H, ArH), 4.95 (s, 2H, $ArCH_2$), 4.40 (t, ^3J=7.2 Hz, 4H, ArCHAr), 3.60 (s, 12H, OCH_3), 3.47 (s, 12H, OCH_3), 1.88–1.65 (m, 8H, $CHCH_2$), 1.35–1.05 (m, 72H, CH_2), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=168.0, 156.0, 155.4, 134.6, 133.5, 132.4, 126.6, 126.1, 125.0, 123.0, 120.9, 96.6, 61.2, 55.5, 36.1, 35.7, 33.3, 31.9, 29.9, 29.8, 29.7, 29.7, 29.4, 28.2, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{98}H_{138}O_{12}N_2+NH_4^+$ $[M+NH_4]^+$ 1553.05880; found 1553.05859; IR (KBr): $\tilde{\nu}$ = 2920, 2851, 1772, 1713, 1610, 1580, 1499, 1465, 1389, 1324, 1296, 1199, 1087, 1036, 1006, 953, 900, 819, 796, 714, 532, 502 cm^{-1}.

*5.2.12. rccc-5,17-Bis-(aminomethyl)-4,6,10,12,16,18,22,24-octa-O-methyl-2,8,14,20-tetra-(n-undecyl)-resorc[4]arene (**12**)*

A solution of resorcarene (**11**) (1.04 g, 0.68 mmol) in a mixture of THF and ethanol (7:3, 50 mL) was treated with hydrazine hydrate (3 mL, ca. 40 mmol pure hydrazine) and refluxed for 12 h. At room temperature concd HCl (1.5 mL) was added and stirred for 2 h. Under ice cooling concd NaOH was added until pH>10. The THF was removed in vacuo and the precipitate was filtered off and washed with concd NaOH and cold ethanol to afford the product as colourless solid (816 mg, 0.64 mmol, yield: 94%). Mp: 97 °C; ^1H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.86 (s, 2H, ArH), 6.50 (s, 2H, ArH), 6.40 (s, 2H, ArH), 4.50 (t, ^3J=7.5 Hz, 4H, ArCHAr), 3.73 (s, 12H, OCH_3), 3.64 (s, 2H, $ArCH_2$), 3.38 (s, 12H, OCH_3), 1.89–1.70 (m, 8H, $CHCH_2$), 1.36–1.13 (m, 72H, CH_2), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=155.4, 155.2, 133.2, 128.8, 126.4, 126.3, 125.5, 95.5, 61.1, 55.7, 36.7, 35.7, 35.4, 31.9, 29.9, 29.8, 29.8, 29.7, 29.4, 28.1, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{82}H_{134}O_8N_2+H^+$ $[M+H]^+$ 1276.02130; found 1276.02343; IR (KBr): $\tilde{\nu}$ = 2918, 2849, 1658, 1609, 1578, 1503, 1465, 1296, 1197, 1087, 1032, 1011, 891, 821, 720, 513 cm^{-1}.

*5.2.13. Kemp's acid resorc[4]arene (**13**)*

A solution of the resorc[4]arene (**12**) (92 mg, 0.07 mmol), 5-(chloroformyl)-*cis,cis*-1,3,5-trimethylcyclohexane-1,3-dicarboxylic anhydride (44 mg, 0.17 mmol) and a catalytic amount of 4-dimethylamino pyridine in pyridine (30 mL) was refluxed for 5 h. The solvent was removed in vacuo and the residue was dissolved in $CHCl_3$. The organic layer was washed with 2 N HCl and 2 N NaOH and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, cyclohexane/ethyl acetate, 7.5%) yielding a colourless solid (102 mg, 0.06 mmol, yield: 86%). Mp: 140–145 °C; ^1H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.94 (s, 2H, ArH), 6.15 (s, 2H, ArH), 6.13 (s, 2H, ArH), 4.95 (s, 4H, $ArCH_2$), 4.31 (t, ^3J=6.9 Hz, 4H, ArCHAr), 3.65 (s, 12H, OCH_3), 3.36 (s, 12H, OCH_3), 2.68 (d, ^2J=13.8 Hz, 4H, Kemp's acid CH_2 eq), 2.00 (d, ^2J=13.2 Hz, 2H, Kemp's acid CH_2 eq), 1.77–1.90 (m, 4H, CH_2), 1.59–1.73 (m, 4H, CH_2), 1.02–1.42 (m, 96H, CH_2, Kemp's acid CH_2 ax, CH_3 Kemp's acid), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 27 °C): δ=177.8, 175.7, 156.3, 154.7, 135.2, 126.5, 125.1, 124.4, 122.5, 97.3, 61.1, 55.6, 44.4, 43.2, 41.8, 40.4, 36.5, 35.4, 35.1, 31.9, 30.5, 30.0, 29.9, 29.8, 29.7, 29.4, 28.2, 26.0, 22.7, 14.1 ppm. HRMS: *m/z* calcd for $C_{106}H_{162}O_{16}N_2+H^+$ $[M+H]^+$ 1720.19971; found 1720.19918; IR (KBr): $\tilde{\nu}$ = 3512 (br), 3196 (br), 2921, 2851, 1728, 1703, 1678, 1612, 1581, 1506, 1461, 1378, 1297, 1262, 1202, 1167, 1090, 1035, 1011, 804, 755, 729 cm^{-1}.

*5.2.14. 1,3,5,7-Tetramethyl-2,4-dioxo-3-aza-bicyclo[3.3.1]-nonane-7-carboxylic acid (**14**)*

5-(Chloroformyl)-*cis,cis*-1,3,5-trimethylcyclohexane-1,3-dicarboxylic anhydride (0.14 g, 54 mmol), methyl ammonium chloride (0.85 mg, 1.3 mmol) and a catalytic amount of 4-dimethylamino pyridine in pyridine (10 mL) were heated to 60 °C for 3 h. The solvent was evaporated in vacuo and the precipitate was dissolved in 6 N HCl and extracted with overall 35 mL chloroform (5×). The solvent was removed and the obtained solid was recrystallized from acetone to afford colourless crystals (0.52 g, 19 mmol, yield: 35%); ^1H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=2.92 (s, 3H, NCH_3), 2.62 (d, ^2J=13.2 Hz, 2H, Kemp's acid CH_2 eq), 1.94 (d, ^2J=13.2 Hz, 1H, Kemp's acid CH_2 eq), 1.36 (d, ^2J=13.3 Hz, 1H, Kemp's acid CH_2 ax), 1.25 (s, 6H, CH_3), 1.25 (s, 3H, CH_3), 1.17 (d, ^2J=13.3 Hz, 2H, Kemp's acid CH_2 ax) ppm; IR (ATR):

$\tilde{\nu}$ = 2964, 2930, 1701, 1668, 1467, 1449, 1427, 1408, 1378, 1358, 1379, 1273, 1233, 1209, 1116, 1094, 941, 886, 841, 795, 754, 620, 585, 563 cm^{-1}.

5.2.15. 3-(2,6-Dimethoxy)benzyl-1,5,7-trimethyl-2,4-dioxo-3-aza-bicyclo[3.3.1]nonane-7-carboxylic acid (**15**)

5-(Chloroformyl)-*cis*,*cis*-1,3,5-trimethylcyclohexane-1,3-dicarboxylic anhydride (0.11 g, 43 mmol), 2,6-dimethoxy benzyl amine (0.11 mg, 0.43 mmol) and a catalytic amount of 4-dimethylamino pyridine in pyridine (10 mL) were heated to 60 °C for 3 h. The solvent was evaporated in vacuo and the precipitate was dissolved in $CHCl_3$. The organic layer was washed with 2 N HCl (3×) and the solvent was removed in vacuo. The resulting precipitate was recrystallized from chloroform/methanol (1:1) to afford colourless crystals (44 mg, 11 mmol, yield: 26%); ^{1}H NMR ($CDCl_3$, 600 MHz, 27 °C): δ=7.08 (t, ^3J=8.3 Hz, 1H, ArH), 6.45 (d, ^3J=8.3 Hz, 2H, ArH), 4.85 (s, 2H, NCH_2R), 3.73 (s, 6H, OCH_3), 2.67 (d, ^2J=13.2 Hz, 2H, Kemp's acid CH_2 eq), 1.87 (d, ^2J=12.9 Hz, 1H, Kemp's acid CH_2 eq), 1.31 (d, ^2J=12.8 Hz, 1H, Kemp's acid CH_2 ax), 1.26 (s, 3H, CH_3), 1.23 (s, 6H, CH_3), 1.14 (d, ^2J=14.0 Hz, 2H, Kemp's acid CH_2 ax) ppm; ^{1}H NMR (MeOD, 500 MHz, 27 °C): δ=7.12 (t, ^3J=8.2 Hz, 1H, ArH), 6.54 (d, ^3J=8.2 Hz, 2H, ArH), 4.83 (s, 2H, NCH_2R), 3.73 (s, 6H, OCH_3), 2.56 (d, ^2J=13.2 Hz, 2H, Kemp's acid CH_2 eq), 1.85 (d, ^2J=12.6 Hz, 1H, Kemp's acid CH_2 eq), 1.45 (d, ^2J=13.2 Hz, 1H, Kemp's acid CH_2 ax), 1.24 (d, ^2J=13.8 Hz, 2H, Kemp's acid CH_2 ax), 1.20 (s, 3H, CH_3), 1.19 (s, 6H, CH_3) ppm; ^{13}C NMR (MeOD, 125 MHz, 27 °C): δ=178.9, 178.1, 159.8, 129.0, 114.4, 105.1, 56.1, 45.2, 43.9, 42.9, 41.4, 35.4, 30.8, 26.1 ppm; HRMS: *m*/*z* calcd for $C_{21}H_{27}NO_6+Na^+$ $[M+Na]^+$ 412.17306; found 412.17313; IR (ATR): $\tilde{\nu}$ = 2982, 2962, 2932, 1724, 1697, 1678, 1590, 1464, 1381, 1361, 1324, 1278, 1245, 1213, 1175, 1106, 1034, 1002, 973, 948, 767, 707, 659, 617, 586, 534 cm^{-1}. Crystal size 0.30×0.28×0.19 mm^3, monoclinic, $P2_1/c$, a=15.5794(3), b=8.5107(2), c=15.7755(3) Å, β= 108.5925(12)°, Z=4, V=1982.53(7) $Å^3$, ρ_{calcd}=1.305 mg m^{-3}, Θ_{max}=27.5°, μ=0.095 mm^{-1}, F(000)=832, 361 parameters, $R1$=0.0368, $wR2$=0.0946 (for 3844 reflections $[I>2\sigma(I)]$), R=0.0446, $wR(F^2)$=0.0998 (for 4519 unique reflections), R(int)=0.033, $\Delta\rho$(min/max)=−0.262/0.342 e $Å^{-3}$. CCDC 664625 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data via www.ccdc.cam.ac.uk/data_request/cif.

5.2.16. Kemp's acid ester resorc[4]arene (**16**)

A solution of resorc[4]arene (**7**) (7 mg, 4.8 μmol) in $CHCl_3$/MeOH (1:1, 5 mL) was treated with a 0.02 M solution of diazomethane in diethyl ether (0.2 mL, 4 mmol) and stirred for 30 min at room temperature. Acetic acid (0.05 mL) was added and the organic layer was washed with satd $NaHCO_3$ soln. The solvent was removed in vacuo to give the product as colourless solid (7 mg, 4.7 μmol, yield: 98%); ^{1}H NMR (CD_2Cl_2, 600 MHz, 27 °C): δ=6.85 (s, 2H, ArH, *lower rim*), 6.56 (s, 1H, ArH, *lower rim*), 6.50 (s, 1H, ArH, *lower rim*), 6.38 (s, 1H, ArH, *upper rim*), 6.31 (s, 2H, ArH, *upper rim*), 4.84 (s, 2H, $ArCH_2$), 4.46 (t, ^3J=7.5 Hz, 2H, ArCHAr), 4.41 (t, ^3J=7.2 Hz, 2H, ArCHAr), 3.72 (s, 6H, OCH_3), 3.62 (s, 6H, OCH_3), 3.61 (s, 6H, OCH_3), 3.47 (s, 6H, OCH_3), 2.61 (d, ^2J=13.2 Hz, 2H, Kemp's acid CH_2 eq), 1.95 (d, ^2J=12.2 Hz, 1H, Kemp's acid CH_2 eq), 1.88−1.63 (m, 8H, $CHCH_2$), 1.41−1.18 (m, 79H, CH_2; Kemp's acid CH_2 ax, CH_3 Kemp's acid, $COOCH_3$), 1.18 (s, 6H, CH_3 Kemp's acid), 1.12 (d, ^2J=13.8 Hz, 2H, Kemp's acid CH_2 ax), 0.87 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{1}H NMR (CD_2Cl_2, 600 MHz, −70 °C): δ=7.18 (s, 2H, ArH), 6.45 (s, 1H, ArH), 6.28 (s, 1H, ArH), 6.19 (s, 1H, ArH), 6.14 (s, 2H, ArH), 4.89 (s, 2H, $ArCH_2$), 4.42 (2H, ArCHAr), 4.32 (2H, ArCHAr), 3.86 (s, 6H, OCH_3), 3.75 (s, 6H, OCH_3), 3.62 (s, 6H, OCH_3), 3.59 (s, 6H, OCH_3), 2.54 (2H, Kemp's acid CH_2 eq), 1.93 (1H, Kemp's acid CH_2 eq), 1.90−1.70 (m, 8H, $CHCH_2$), 1.36−0.93 (m, 87H, CH_2; Kemp's acid CH_2 ax, CH_3 Kemp's acid, $COOCH_3$, CH_3 Kemp's acid, Kemp's acid CH_2 ax), 0.79 (12H, CH_3) ppm; ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=6.62 (s, 2H, ArH, *lower rim*), 6.57 (s, 1H, ArH, *lower rim*), 6.51 (s, 1H, ArH, *lower rim*), 6.29 (s, 2H, ArH, *upper rim*), 6.25 (s, 1H, ArH, *upper rim*), 4.82 (s, 2H, $ArCH_2$), 4.43−4.36 (m, 4H, ArCHAr), 3.59 (s, 6H, OCH_3), 3.57 (s, 6H, OCH_3), 3.56 (s, 6H, OCH_3), 3.30 (s, 6H, OCH_3), 2.65 (d, ^2J=13.8 Hz, 2H, Kemp's acid CH_2 eq), 1.95 (d, ^2J=12.6 Hz, 1H, Kemp's acid CH_2 eq), 1.85−1.65 (m, 8H, $CHCH_2$), 1.35−1.12 (m, 76H, CH_2; Kemp's acid CH_2 ax, CH_3 Kemp's acid), 1.18 (s, 6H, CH_3 Kemp's acid), 1.17 (s, 3H, $COOCH_3$), 1.12 (d, ^2J=13.8 Hz, 2H, Kemp's acid CH_2 ax), 0.85 (t, ^3J=6.9 Hz, 12H, CH_3) ppm; ^{13}C NMR (CD_2Cl_2, 125 MHz, 27 °C): δ=176.0, 175.9, 156.5, 156.2, 155.9, 155.5, 134.8, 126.9, 126.4, 126.3, 125.4, 125.3, 124.5, 123.4, 96.8, 96.1, 77.9, 56.2, 56.1, 55.8, 52.3, 44.6, 43.3, 42.4, 40.6, 36.3, 36.3, 35.4, 35.2, 35.2, 32.3, 30.5, 30.3, 30.2, 30.1, 30.1, 30.0, 29.8, 28.6, 28.4, 26.1, 23.0, 14.2 ppm; HRMS: *m*/*z* calcd for $C_{94}H_{147}NO_{12}+Na^+$ $[M+Na]^+$ 1505.08155; found 1505.08308.

5.2.17. 5-Phenyl-2-amino pyridine (**17**)

2-Amino-5-chloro pyridine (1 g, 7.78 mmol), boronic acid (1.42 g, 11.7 mmol, 1.5 equiv) and potassium phosphate were solved in toluene and have been degassed by pump−freeze−thaw (three cycles). Palladium acetate (17.5 mg, 0.078 mmol, 1%) and dicyclohexyl-(2,6-dimethoxy-biphenyl-2-yl)-phosphane (63.9 mg, 0.16 mmol, 2%) were added and the suspension was degassed by additional two pump−freeze−thaw cycles. The suspension was heated in a sealed tube to 100 °C for 17 h and filtrated. The precipitate was washed with ethyl acetate (2×) and the filtrate was washed with 2 N NaOH (3×) and satd NaCl soln and the solvent was removed in vacuo. The crude product was purified by column chromatography (SiO_2, cyclohexane/ethyl acetate, 3:2) yielding a colourless solid (0.95 g, 5.6 mmol, yield: 72%); ^{1}H NMR ($CDCl_3$, 500 MHz, 27 °C): δ=8.31 (d, ^4J=2.5 Hz, 1H), 7.65 (dd, ^3J=8.8 Hz, ^4J=2.5 Hz, 1H), 7.49 (d, ^3J=6.9 Hz, 2H), 7.40 (dd, ^3J=8.2 Hz, ^3J=8.2 Hz, 2H), 7.29 (t, ^3J=7.5 Hz, 1H), 6.56 (d, ^3J=8.8 Hz, 1H), 4.53 (s, 2H, NH_2) ppm.

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