A New Type of Calixarene: Octahydroxypyridine[4]arenes

Thorsten Gerkensmeier,[b] Jochen Mattay,*[a] and Christian Näther[c]

Abstract: A new type of calixarene has been synthesised. Like resorcinol and a number of resorcinol derivatives, 2,6-dihydroxypyridine has been proven to form cyclic tetramers in moderate yields with a number of aliphatic and two aromatic aldehydes in acidic media. The problem of the formation of configurational isomers can be reduced by increasing the reaction temperature and time. With electron-rich aromatic aldehydes, 2,6-dihydroxypyridine unexpectedly yields deep-coloured acyclic quinoid systems. The octahydroxypyridine[4]arenes may have a high potential as receptors for molecular recognition and self organisation.

Keywords: calixarenes · molecular container · pyridines · supramolecular chemistry

Introduction

In recent years, calixarenes have attracted much attention, which is documented in the large number of publications dealing with this class of compounds. Their accessibility and structural features made them the target of numerous complexation and inclusion studies. The most popular types of calixarene are obtained from 4-*tert*-butylphenol and formaldehyde, or from resorcinol derivatives and aldehydes except formaldehyde. In calixarene chemistry, pyridines play a negligible role. Unlike resorcinol or phenols, pyridines are not easily attacked by electrophilic reagents and therefore do not form cyclic oligomeric compounds with aldehydes. However, a few examples for the preparation of pyridinocalixarenes through alternative pathways have been reported. The first successful synthesis was performed by Newcome[1] by the dimerisation of pyridine dimers and later by Kral[2] by the carbene addition of the easily accessible calix[4]pyrroles. The bridging of the calixarene occurs at the 2- and 6-positions of the pyridine, thus the nitrogen is on the lower rim. With the aim of expanding the cavity of the calixarene by reversible complexation with suitable organic partner molecules, we planned to place the functionalisation on the upper rim.

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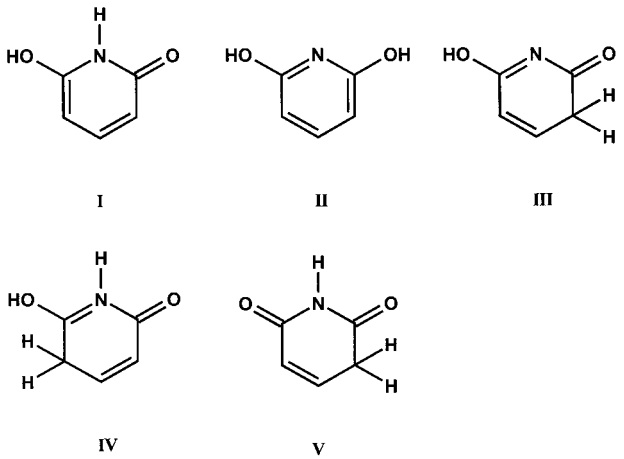
Since unsubstituted pyridine is not sufficiently reactive at the 3- and 5-positions, activating substituents such as hydroxyl groups are required. In conclusion, the 2,6-dihydroxypyridine should be suitable for cyclisation experiments. Its similarity to resorcinol is evident, but it is also capable of forming tautomers which may not react as desired. Already in the sixties, Katritzky and Spinner discussed solvent and substitution effects on the contributions of the five possible tautomers of 2,6-dihydroxypyridine, namely 6-hydroxy-2(1*H*)-pyridinone (**I**) 2,6-dihydroxypyridine (**II**), 6-hydroxy-2(3*H*)-pyridinone (**III**), 6-hydroxy-2(5*H*)-pyridinone (**IV**) and 2,6(1H; 3*H*)-pyridinedione (**V**).[3]. They found that the hydroxypyridone **I** is the predominant tautomer in water, ethanol and DMSO, while in dioxane the tautomer **V** is favoured and up to 13% of the dihydroxypyridine **II** could be detected. In most cases, tautomers **III** and **IV** appear only in trace amounts, or could not be detected at all. For that reason, 2,6-dihydroxy-



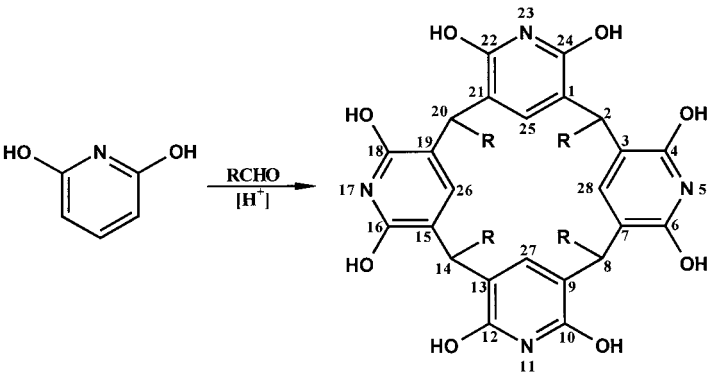
pyridine also features pyrimidine-base mimics. The bases, for example thymine or uracil, are known to form strong hydrogen-bonded complexes with complementary molecules. The pyridone tautomers may therefore be useful for the preparation and study of hydrogen-bonded complexes.

In this paper, unless otherwise stated, the term dihydroxypyridine is used for all isomers and substructures, ignoring the actual distribution of tautomers.

Results and Discussion

First attempts: A common method for the synthesis of resorc[4]arenes is the condensation of resorcinol and aldehydes in aqueous acidic media. Similar reaction conditions should lead to protonated and, therefore, unreactive 2,6-dihydroxypyridine. Nevertheless, reactions with electrophiles such as nitronium, diazonium cations, chlorine, and even β-ketoesters to yield 8-aza-7-hydroxy-4-alkylcoumarins under acidic conditions were reported. This is indicative of the fact that there is sufficient reactivity for electrophilic agents at the 3- and 5-positions.[4] Our first approach using ethanol and concentrated hydrochloric acid as solvent was not very successful. Depending on the aldehyde, we obtained amorphous and frequently less-soluble, colourless, bright yellow or orange compounds that quickly decomposed. However, for the condensation products of the aliphatic aldehydes from pentanal to dodecanal, the molecular masses of the cyclic tetramers were found by means of MALDI mass spectrometry. The complex signals in the NMR spectra of the more apolar and therefore soluble products suggested that a mixture of different configurational and/or conformational isomers of the cyclic tetramers were present. As a consequence, the formation of the calixarenes works in principle, although pure products were not obtained as was the case in many other calixarene-formation reactions (see Scheme 1 and Table 1: in the following we use the term *octahydroxypyridine[4]arene* rather than *5,11,17,23-tetraazaresorc[4]arene* in order to highlight the unique feature of this new type of calixarene).

2,6-Dihydroxypyridine and 3-methylbutanal—octahydroxytetraisobutylpyridine[4]arene: Based on the first promising results, we tried to force the mechanism of formation by adjusting the conditions of the thermodynamically controlled reactions. Therefore, prolonged heating for seven days was expected to eliminate the thermodynamically less stable isomers in favour of the *rccc* isomer, which is expected to be the thermodynamically more stable cyclic compound. We attempted to cyclise 3-methylbutanal with dihydroxypyridine in this way, but isomeric mixtures were still found. The obtained material revealed only the molecular peak of the cyclic tetramer in the MALDI spectra, but the NMR spectra demonstrated that the product still consisted of a mixture of isomers. The macrocycles are poorly soluble in most organic solvents except for DMF, DMSO and THF, hence most nonmacrocyclic impurities can easily be removed by washing the raw product with ethanol and acetone. The acidic properties of the amphoteric 2,6-dihydroxypyridines are responsible for their sensitivity towards bases. Basic solutions of pyridine[4]arenes are quickly oxidised when exposed to air. The following experiments showed that the separation of the diastereomers is not easy. For example, crystallisation from THF/water yielded a crystalline mixture of the same composition. Also, separation by HPLC on Si-60 silica gel with mixtures of ethyl acetate and cyclohexane, as well as on RP18-material with THF and water, failed owing to strong tailing effects. The raw product was therefore converted into the benzoyl derivative in order to obtain more apolar compounds that could then be separated by column chromatography.



VI

Scheme 1. Acid-catalyzed synthesis of 4,6,10,12,16,18,22,24-octahydroxy-2,8,14,20-tetra-R-pyridine[4]arene **VI** from 2,6-dihydroxypyridine and aldehydes.

Table 1. Survey of the prepared pyridine[4]arenes **1**–**5**, **8** and **9** and methylidenepyridinones **6** and **7**. R in both cases denotes the substituent of the aldehyde.

R	Compound	Isolated yield [%]	Notes[a]
2′-methylpropyl	*rctt*-**1**	4 (2 steps)	i), identified as perbenzoylated *rctt* isomer, X-ray crystal structure
2′-methylpropyl	*rcct*-**1**	25 (2 steps)	i), identified as perbenzoylated *rcct* isomer
2′-methylpropyl	*rccc*-**1**	11 (2 steps)	i), identified as perbenzoylated *rccc* isomer, X-ray crystal structure
2′-methylpropyl	**2**	72	ii), *rccc* isomer, X-ray crystal structure
n-butyl	**3**	55	ii)
methyl	**4**	39 (2 steps)	ii), identified as perbenzoylated *rccc* isomer, X-ray crystal structure
n-undecyl	**5**	47	ii), *rccc* isomer
4 – -nitrophenyl	**8**	49 (2 steps)	ii), X-ray-crystal-structure of the peracetylated *rctt* isomer
phenyl	**9**	25 (2 steps)	ii), *rccc* isomer
2′-thienyl	**6**	93	i), for the structure see Scheme 7
4′-octyloxyphenyl	**7**	91	ii), for the structure see Scheme 7

[a] Cyclisation conditions: i) solvent: hydrochloric acid, water, ethanol; reflux. ii) solvent: hydrochloric acid, glycol monoisopropyl ether; reflux. For detailed information see the Experimental Section.

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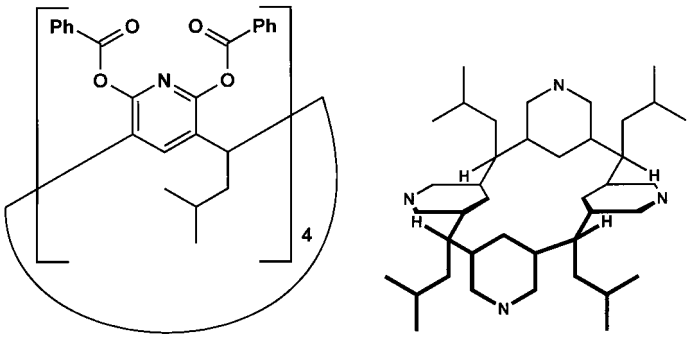
Three distinct fractions were isolated and identified. The first fraction contained the *rctt* isomer **1** (Scheme 2) in 4% overall yield and revealed C_{2h} symmetry in the NMR spectra. As opposed to the NMR spectrum of the *rccc* isomer with C_{4v} symmetry, all the observed signals of the *rctt* isomer are



1 *rctt*-**1**

Scheme 2. 4,6,10,12,16,18,22,24-Octakis(benzoyloxy)-2,8,14,20-tetraisobutylpyridine[4]arene (*rctt*-**1**) and a schematic representation of the *rctt* isomer in its chair-conformation (benzoyloxy substituents, hydrogen atoms, except for methine protons, and double bonds are omitted for clarity).

doubled except for signals for the diarylmethine protons. Instead of the triplet, a doublet of doublets is observed, a consequence of the different chemical environments of the neighbouring protons of the methylene moiety. Suitable crystals for X-ray analysis were grown by the slow evaporation of chloroform/ethanol and the structural assignment was confirmed (Figure 1).

The third fraction of **1** contained the *rccc* isomer (Scheme 3) isolated in 12% overall yield. Coalescence effects broaden all the signals in the ^{1}H NMR spectrum, and even the

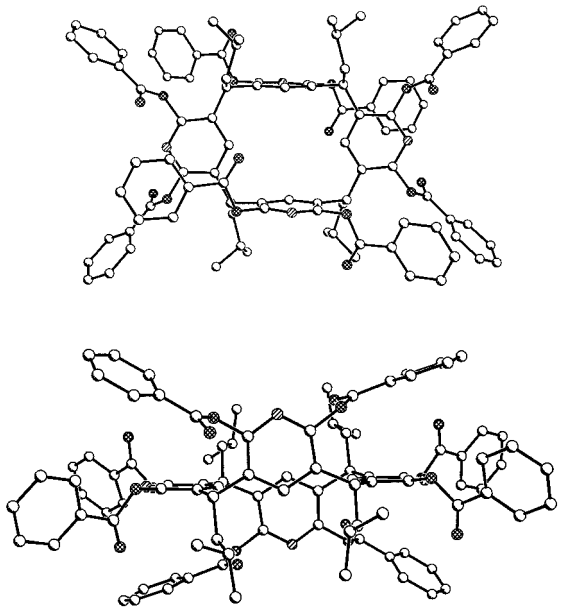
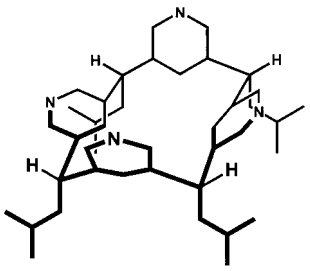


Figure 1. Top (above) and side view (below) of the X-ray crystal-structure of *rctt*-4,6,10,12,16,18,22,24-octakis(benzoyloxy)-2,8,14,20-tetraisobutylpyridine[4]arene (**1**).

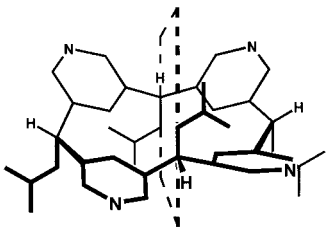


rccc-**1**

Scheme 3. Schematic representation of *rccc*-2,8,14,20-tetraisobutylpyridine[4]arene **1** (the benzoyloxy substituents in the 4,6,10,12,16,18,22,24-positions and the hydrogen atoms are omitted, and double bonds are not displayed).

^{13}C NMR spectrum shows broad resonances for the pyridine carbon atoms, while all the other carbon atoms are well resolved. However, the C_{4v} symmetry is clearly exhibited in high-temperature measurements at 80 °C. The exact mass determination gave satisfactory results. Crystals were grown from chloroform and ethanol, but the quality was too low for a crystal-structure determination.

The main product was found in the second fraction in 25% overall yield. Owing to tailing effects of the previous fraction, its isolation required a second purification step by column chromatography. By comparison to the other isomers of the perbenzoylated tetraisobutylpyridine[4]arenes, mass spectrometric analysis also showed the formation of the perbenzoylated macrocycle. On the other hand, the multiplicities of all the resonances observed in the ^{1}H and ^{13}C NMR spectra are quite complicated. The exact assignment of all resonances has not been achieved, but the important features are discussed. The benzoyloxy substituents are the most complicated moieties, since numerous signals are hidden in overlapping bands. Ten carbon signals are observed for the pyridine systems, indicating that two groups are chemically equivalent at a time. Two-dimensional HSQC and HMBC ^{1}H,^{13}C-coupling experiments revealed that these pyridine groups are adjacent. The isobutyl substituents show equal signal patterns for each hydrogen and carbon atom, all in a 2:1:1 ratio. This symmetry is in accordance with the *rcct* isomer of **1** (Scheme 4) and allows two residues to be chemically equivalent. Furthermore, the two equal isobutyl moieties bear distinguishable methyl groups and methylene hydrogens. These properties can only be possessed by a *rcct*-configured calixarene that features a molecular conformation with

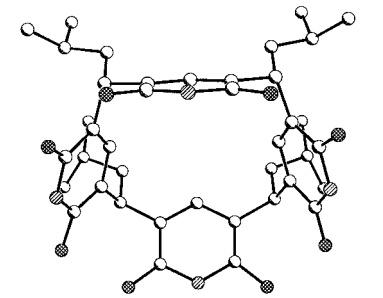


rcct-**1**

Scheme 4. Schematic representation of *rcct*-tetraisobutylpyridine[4]arene **1** (benzoyloxy moieties are omitted and the hydrogen atoms, except for the methine protons, and double bonds are not displayed for clarity). The symmetry plane is shown as a dotted line.

a symmetry plane perpendicular to the calixarene plane which crosses the two chemically different isobutyl groups (Scheme 4).

Interestingly, resorc[4]arenes usually do not tend to form this isomer in large quantities, althought exceptions to the rule are known.[5] Since it is not the thermodynamically most stable compound, prolonged heating of the reaction mixture at higher temperatures should lead to better yields of the *rccc* isomer. Glycol monoisopropyl ether has been explored for the cyclisation, because it dissolves the reagents, is quite stable to high concentrations of hydrochloric acid and allows the reaction mixture to reach a temperature of about 145 °C. In addition, the desired product should be insoluble in this solvent. In fact, heating a mixture of 2,6-dihydroxypyridine hydrochloride and 3-methylbutanal in glycol monoisopropyl ether and hydrochloric acid for 7–10 days produced the *rccc* isomer **2** in a moderate yield. In some cases, the ^{1}H NMR spectra showed traces of configurational isomers or tautomers. Recrystallisation from THF and water gave single crystals suitable for X-ray crystallography (Figure 2). In



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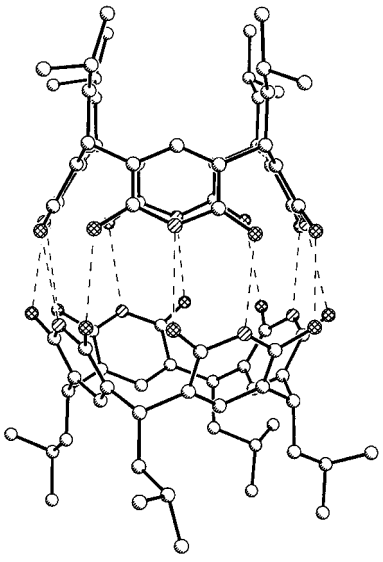


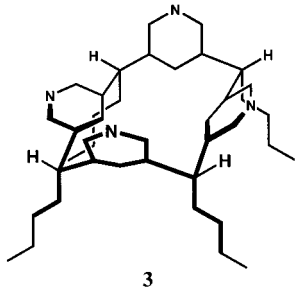
Dimer of **2**

Figure 2. X-ray crystal structure of *rccc*-4,6,10,12,16,18,22,24-octahydroxy-2,8,14,20-tetraisobutylpyridine[4]arene (**2**) and its head-to-head dimer.

contrast to many *rccc*-resorc[4]arenes which favour the *boat* conformation, the pyridine[4]arene has a perfect *cone* conformation. Unlike the benzoyloxypyridine[4]arenes **1**, the octahydroxypyridine[4]arene **2** does not show the typical pyridine geometry: The C–N–C angle of the octahydroxypyridine group is 120.6°, whereas in the benzoyloxypyridine moiety it is 115.8°; The C–N bond lengths are 136 pm and 132 pm. This may be explained by the influence of the pyridone tautomer. The analysis also shows the formation of a calixarene dimer. Two calixarenes are orientated upper rim to upper rim, establishing 12 hydrogen bonds. The two pyridine[4]arenes are twisted about 30° along the *z* axis to optimise the strength of the hydrogen bonding. The dimer does not appear to be very stable. Neither MALDI mass spectrometry nor vapour-pressure osmometry in THF at 30 °C supports the existence of the dimeric container rather than the monomeric molecules.

In general, self-assembling systems have attracted much attention in recent years[6] and specially modified calixarenes have been prepared to explore their aggregation behaviour.[7] Similar to our results (Figure 2) mostly dimer formations were observed,[7b,c, 8] but occasionally large hexameric aggregates were also found both in the solid state and in solution.[9] This structure is another example of calixarene dimers, which may have potential in the controlled formation of dimeric molecular containers.

2,6-Dihydroxypyridine and *n*-alkanals—further examples of octahydroxypyridine[4]arenes: *n*-Pentanal also yielded the *rccc*-configured octahydroxypyridine[4]arene **3** (Scheme 5)



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Scheme 5. Schematic representation of *rccc* isomer of pyridine[4]arene **3** obtained from the acidic condensation of 2,6-dihydroxypyridine and *n*-pentanal. Double bonds, hydroxy and acetoxy groups, as well as hydrogen atoms, except for methine protons, are omitted.

under comparable conditions. There was a small amount of configurational isomers or tautomers present, indicated by two additional small signals in the aromatic region of the ^{1}H NMR spectrum, and by another triplet for the methine proton. These signals could be diminished by the addition of trifluoroacetic acid (TFA) or by heating. This pyridine[4]arene crystallised as needles from hot DMSO and is the most polar yet soluble calixarene that we explored. Aldehydes with shorter alkyl chains led to insoluble materials. In order to check the formation of *rccc* isomers in the case of unsubstituted or short-chain alkanals, the same procedure was first applied to formaldehyde and ethanal as described above for the synthesis of the more soluble perbenzoylated octahydroxypyridine[4]arene **1**. Attempts with formaldehyde gave rise to an insoluble, amorphous, colourless powder that could not be analyzed by means of NMR spectroscopy or by MALDI mass

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spectrometry. The raw product of the cyclisation step with ethanal was perbenzoylated and crystallised from chloroform/ethanol. The colourless, crystalline substance showed the mass of the expected benzoylated cyclic tetramer **4**. The NMR spectra were complicated by coalescence effects both in ^{1}H and ^{13}C NMR measurements, similar to those found with compound *rccc*-**1**. High-temperature ^{1}H NMR spectroscopy confirmed the *rccc*-configuration of **4** and the crystal-structure analysis was the final proof (Figure 3).

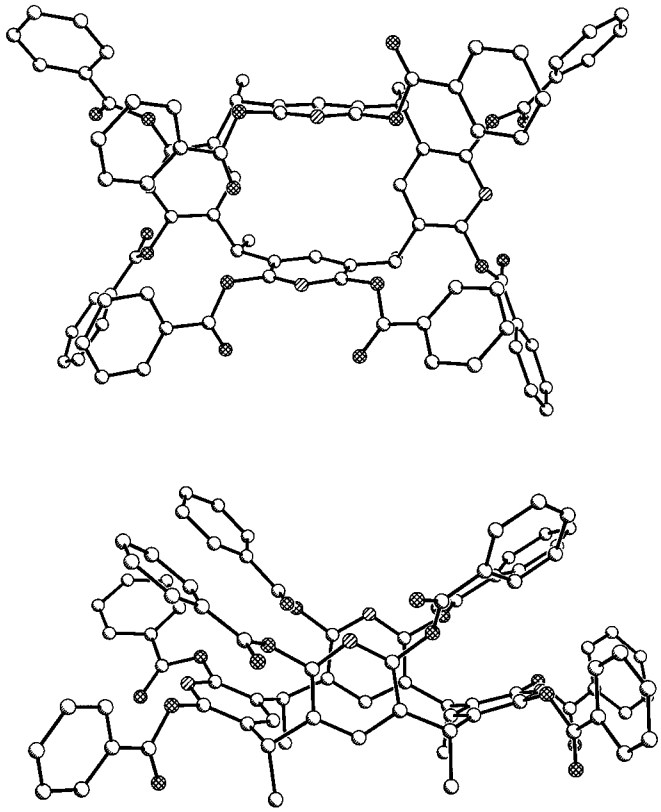
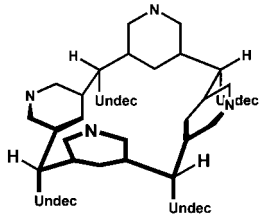


Figure 3. Top (above) and side view (below) of the X-ray crystal structure of *rccc*-4,6,10,12,16,18,22,24-octakis(benzoyloxy)-2,8,14,20-tetramethylpyridine[4]arene (**4**).



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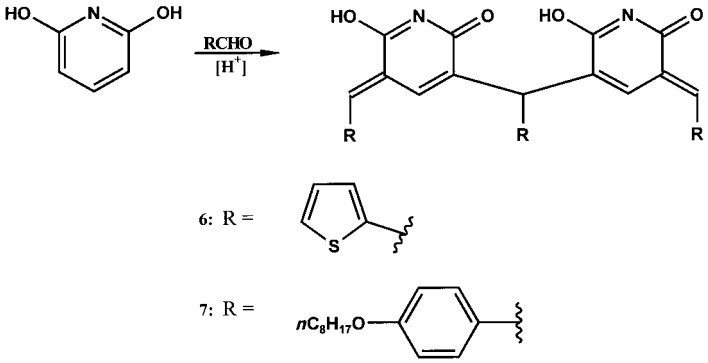
Scheme 6. Schematic representation of *rccc* isomers of pyridine[4]arene **5** obtained from the acidic condensation of 2,6-dihydroxypyridine and *n*-dodecanal. Double bonds, hydroxy and acetoxy groups, as well as hydrogen atoms, except for methine protons, are omitted.

The applicability of the cyclisation procedure in glycol monoisopropyl ether was also examined for very apolar long-chain aldehydes. *n*-Dodecanal yielded a waxlike clot of condensation products. Trituration with acetone and crystallisation of the remaining solid from chloroform and ethanol yielded a pale yellow, crystalline solid in 47% yield. Spectroscopic data showed the formation of the *rccc*-octahydroxytetraundecylpyridine[4]arene **5** (Scheme 6). The ^{13}C NMR spectrum revealed interesting details about the tautomers existing in solution. Altogether eight aromatic signals were recorded in chloroform. Three were hardly detectable, and five main peaks of large intensity were observed. Considering Spinner's and Katritzky's work,[3] the symmetry and the chemical shifts of the spectrum, it seemed reasonable to assign the five main peaks to the pyridone tautomer. The decreased symmetry of the pyridone had no effect on the aliphatic region, which is crowded with overlapping resonances. Although it is difficult to assign all the individual signals, the terminal ethyl and the methine moiety can easily be identified. These resonances are singlets, indicating that the molecule retains the C_4 symmetry evidently caused by the fast interchange of pyridone-pyridol tautomers and by their orientation. The three small peaks probably belong to the pyridinediol tautomer. The intensity of these resonances increases on addition of trifluoroacetic acid to a solution of **5** in chloroform, and in very polar solvents such as [D_6]DMSO the pyridol bands are dominant. A similar effect can be observed in the ^{1}H NMR spectra. Shoulders or additional peaks of low intensity can be found around the aromatic and the methine signals, especially in apolar solvents such as chloroform and tetrachloroethane. However, they decrease in intensity or even disappear upon heating and addition of acid.

2,6-Dihydroxypyridine and aromatic aldehydes—scope and limitation: Aromatic aldehydes were also employed in the condensation process. Depending on the nature of the aldehyde, colourless, yellow or even orange materials were obtained. These compounds were nearly insoluble in all common solvents (even in DMSO and DMF) and decomposed within hours or days. 4-Cyano-, 4-methyl- and 4-acetamidobenzaldehyde and 2-, 3- and 4-pyridinecarboxaldehyde were subjected to the cyclisation procedure, but no proof for the formation of cyclic tetramers was found. 4-Octyloxybenzaldehyde and thiophene-2-carboxaldehyde were exceptions, since they led to bright yellow, stable precipitates that were isolated and fully characterised as products **6** and **7**, respectively (Scheme 7). The analysis showed, that the main



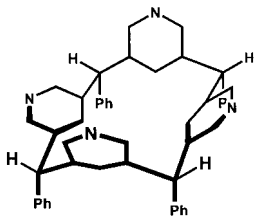
Scheme 7. Condensation of 2,6-dihydroxypyridine with electron-rich aromatic aldehydes and formation of quinoid pyridone structures.

products of the reactions contained two methylidenepyridinone substructures, which are remarkably stable considering the harsh conditions of their formation. The reason for this unexpected stability could result from the comparably electron-rich alkyloxyphenyl or thiophene substituent. The *E*

configuration of the methide structure was confirmed by NOESY experiments. The orientation of the double bonds in the pyridinone system and the position of the hydroxyl groups cannot be deduced from the present analytical data.

Attempts to crystallise both compounds were not successful. In the case of **6**, the structure appears to be unstable. Upon heating in DMF or DMSO, a number of new, unassigned, well-resolved resonances appeared in the ^{1}H NMR spectrum at $\delta = 11.43$, 11.46, 8.14, 8.13, 8.11, 7.99, 7.82, 7.80, 7.54, 7.57, 7.29, 7.26, 7.24, 7.11 and 7.02, all in a 1:1 ratio, while the other signals of **6** decreased. Similar effects were observed on addition of TFA. This process was not visible in the mass spectra, because only the mass of the parent condensate **6** was found. Storage of the compound for days under vacuum reversed this effect. These results suggest, that the observed "decomposition" might be a reversible rearrangement. Although the deep colour suggests the presence of quinoid moieties, a structure comparable with **6** or **7** does not apply to the other condensation products of aromatic aldehydes and 2,6-dihydroxypyridine. Neither mass spectrometry nor ^{1}H NMR spectroscopy could confirm the dimeric methylidenepyridone or the calixarene structures. When the more reactive 4-nitrobenzaldehyde was used in the cyclisation reaction, glistening, pale yellow leaves of low solubility were obtained. In order to improve the solubility in apolar media, peracetylation was performed. The product of this reaction (compound **8**) was sufficiently soluble to complete the characterisation, and single crystals were isolated from chloroform which were subjected to X-ray analysis. In accordance with NMR spectroscopic and mass spectrometric data, **8** was found to be the peracetylated cyclic calixarene tetramer of the condensation of 2,6-dihydroxypyridine and 4-nitrobenzaldehyde. Similar to resorc[4]arenes, the *rctt* isomer adopts a chair conformation (Figure 4).

The reaction of benzaldehyde led to a brown, insoluble precipitate under cyclisation conditions. Acetylation afforded an insoluble residue as the main product, which decomposed upon heating in DMSO to give a blue solution and some chloroform-soluble, colourless, crystalline material, which was fully characterised. The spectra showed that the peracetylated *rccc* isomer of the tetraphenylpyridine[4]arene **9** (Scheme 8) was obtained in 25% overall yield. This is quite unusual, since aromatic aldehydes prefer to form the *rctt* configuration with C_{2h} symmetry.



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Scheme 8. Schematic representation of the *rccc* isomer of pyridine[4]arene **9** obtained from the acidic condensation of 2,6-dihydroxypyridine and benzaldehyde. Double bonds, hydroxy and acetoxy groups, as well as hydrogen atoms, except for methine protons, are omitted.

General features: The pyridine[4]arenes are generally crystalline, stable compounds at room temperature, sensitive only to bases and to exposure to direct sunlight. Since the calixarenes are probably isolated as hydrochlorides from the reaction mixture, their solubility in organic solvents, except for DMF and DMSO, is mostly low. Long-chain aldehydes led to pyridine[4]arenes soluble in chloroform and other apolar media. When dried under vacuum for days, the solubility and the NMR spectra changed, probably owing to the loss of hydrochloric acid and a to change in the distribution of tautomeric structures. The use of DMSO as solvent favoured the pyridol tautomer, which may exist in a protonated or unprotonated state, while apolar pyridinarenes favoured the pyridone tautomer in chloroform. Elemental analyses were also performed, but as is the case with many other calixarenes, the pyridine[4]arenes presented here did not easily crystallise solvent-free.

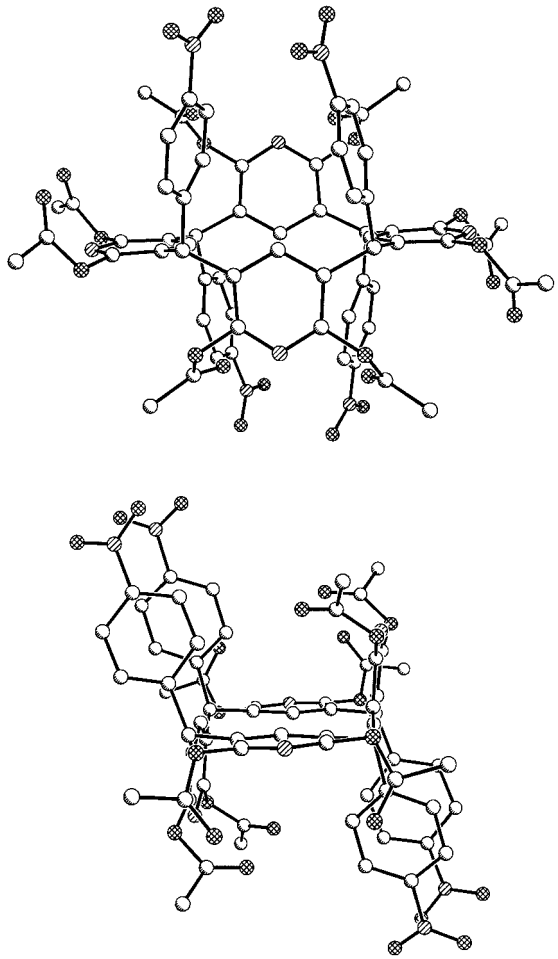

Figure 4. Top (above) and side view (below) of the X-ray crystal structure of *rctt*-4,6,10,12,16,18,22,24-octakis(acetoxy)-2,8,14,20-(*p*-nitrophenyl)pyridine[4]arene (**8**).

The most important feature of these calixarenes may be their ability to form aggregates and complexes. We are currently pursuing the ability of the pyridine[4]arenes to bind metal cations and anions. Earlier attempts with strongly hydrogen-bonded complexes were performed with complementary molecules. Our first choice was 2,6-diaminopyridine. When hot solutions of **5** and 2,6-diaminopyridine in toluene were mixed, an instant precipitation of a colourless, amorphous substance was observed. This compound may be a complex, but the nature of the binding is yet unknown, since it was insoluble and unstable and turned into a black solid upon storage over a few hours. In order to keep the complex in solution, more apolar and soluble complexation partners

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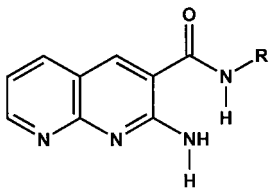
should be applied. Among these are Reinhoudt's diaminodiazinecalix[4]arenes, [8e, f] 2-aminonaphthyridines, guanines, melamine derivatives and many others. These topics are still under investigation, but preliminary results have already been achieved.



10

In the case of **10**, a mixture with **5** in hot toluene yielded a clear, viscous solution upon cooling to 5 °C. An important feature of this gel was its dependence on the ratio of the complex partners. Rheologic experiments revealed a thixotropic behaviour, and freeze-fracture transmission electron microscopy will be applied to this system and the results will be published soon.[10]

Conclusion

These results open a pathway to a new type of calixarene based on the acidic condensation of 2,6-dihydroxypyridine and aldehydes. The reactivity of 2,6-dihydroxypyridine is lower than that of resorcinol or 2-hydroxyresorcinol, so harsher conditions must be applied, but the cyclisation reactions are, in principle, comparable. Mixtures of configurational isomers of cyclic tetramers were found, unless the conditions favoured the thermodynamically stable *rccc* isomer by prolonged heating at elevated temperatures. Aliphatic aldehydes were converted into the *rccc*-shaped calixarenes. Aromatic aldehydes were less suitable for the cyclisation. Unstable, coloured compounds were frequently obtained. In the case of the less reactive 4-octyloxybenzaldehyde and thiophene carboxaldehyde a bright yellow product was isolated and identified as methylidenepyridinones **6** and **7**, respectively, which were quite stable. When the reactive 4-nitrobenzaldehyde was used, a *rctt*-configured, nearly insoluble calixarene isomer was found. Benzaldehyde yielded the *rccc* isomer as well as some less soluble materials. The calixarenes derived from aromatic aldehydes are even less soluble than their aliphatic relatives, therefore derivatisation is necessary in order to perform analyses and for further utilisation. The ability of the dihydroxypyridines to form tautomers depends on the solvent, the temperature and acidity of the medium, as well as on their amphoteric properties. The identification was therefore complicated since they were monitored by NMR spectroscopic techniques. Further functionalisation and the use of the tautomerism of 2,6-dihydroxypyridine derivatives may offer a route to strongly hydrogen-bonded complexes with a view to larger defined aggregates. One example was inadvertently found in the X-ray crystal structure of the octahydroxytetraisobutylpyridine[4]arene **2**. This is a further molecular container based on calixarenes. We are currently studying the complexation behaviour of these octahydroxypyridine[4]arenes, which may lead to new materials of interesting macroscopic properties.

Experimental Section

General: All solvents used were of p.a. quality or were purified by distillation. Chloroform was distilled over $CaCl_2$, and THF over $LiAlH_4$. All melting points were determined on a Büchi B-540 and are uncorrected. The ^1H NMR spectra were measured on a Bruker AC200 (200.13 MHz) or an ARX300 (300.13 Mhz) spectrometer, and the ^{13}C NMR on a Bruker AC200 (50.32 MHz), an ARX300 (75.47 MHz) or a DRX500 (125.77 Mhz) spectrometer. MALDI-TOF spectra were recorded on a LAZARUS III DE by Dr. H. Luftmann, University of Münster, ionisation by N_2-Laser 337 nm, 3 ns pulse, 16 kV, 1 m flight-distance. ESI-MS was performed on a Finnigan TSQ7000 triple-quadrupole tandem mass spectrometer with electron-spray ionisation. Exact mass determination was measured on a Bruker FTMS4.7T BioApexII and on a Finnigan MAT8200. UV measurements were conducted on a Perkin–Elmer Lambda14 spectrometer and IR spectra were recorded on a Perkin–Elmer Paragon1000 FT-IR (s = strong, m = medium, w = weak, br = broad) spectrometer. Merck Si-60 DC plates were used for TLC experiments. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-143792 (Compound **1**), CCDC-143791 (Compound **2**), CCDC-143790 (Compound **4**) and CCDC-143793 (Compound **8**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Preparation of *rctt*-1, *rccc*-1 and *rcct*-1: A solution of 2,6-dihydroxypyridine hydrochloride (6.00 g, 40.8 mmol) in ethanol (30 mL), water (30 mL) and hydrochloric acid (conc., 15 mL) was added dropwise to 3-methyl-1-butanal (3.51 g, 4.38 mL, 40.8 mmol) at RT under argon. After addition of the aldehyde, the mixture was heated at reflux for 5 d. The reaction was cooled to RT, the colourless precipitate was separated, washed with ethanol and acetone, and dried under vacuum. The remaining solid (6.70 g, 92 %) was a colourless powder, which was soluble in DMF, DMSO, and THF, and consisted of at least three diastereomers. MALDI-TOF-MS (matrix α-cyano-4-hydroxycinnamic acid, cations): m/z: 717 $[M]^+$; 739 $[M+Na]^+$. The mixture of diastereomers (1.50 g, 2.09 mmol) was heated at reflux for 3 h in benzoyl chloride (10 mL) and pyridine (3 mL), and then cautiously hydrolysed with water at RT. The precipitated benzoic acid was removed by washing with hot water. The residue was collected on a Buchner funnel, washed with ethanol and dried under vacuum. The reaction yielded the perbenzoylated raw product (2.70 g, 89 %) as a grey powder, which was soluble in chloroform. Absorption on silica gel Si-60 and elution with cyclohexane/ethyl acetate (4:1) gave three fractions.

Fraction 1: *rctt*-4,6,10,12,16,18,22,24-octakis(benzoyloxy)-2,8,14,20-tetraisobutylpyridine[4]arene (*rctt*-1): The compound was recrystallised from chloroform/ethanol. Slow evaporation yielded single crystals (120 mg, 4 %) suitable for X-ray crystal structure analysis. $R_f = 0.48$ (cyclohexane/ethyl acetate 4:1); m.p. 311–312 °C; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.60$ (d, $^3J = 6.5$ Hz, 12H; CH_3), 0.89 (d, $^3J = 6.5$ Hz, 12H; CH_3), 1.46 (br m, 4H; $CH_2CH(CH_3)_2$), 1.55–1.67 (m, 8H; CH_2), 4.56 (dd, $^3J = 12$, 3 Hz, 4H; $(Ar)_2CH$), 6.81 (s, 2H; $CH_{pyridine}$), 7.34 (br t, 8H; $CH_{ar,meta}$), 7.54 (br m, 12H; $CH_{ar,meta,para}$), 7.65 (m, 4H; $CH_{ar,\ para}$), 7.73 (dd, $^3J = 8.4$, 1.3 Hz, 8H; $CH_{ar,ortho}$), 8.04 (dd, $^3J = 7.7$, 1.4 Hz, 8H; $CH_{ar,ortho}$), 8.08 (s, 2H; $CH_{pyridine}$); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 20.81$ (CH_3), 23.8 (CH_3), 25.78 (CH_3CHCH_3), 35.47 ($CH(CH_3)_2$), 42.99 (CH_2), 126.39 ($C_{pyridine,meta}$), 128.25 ($C_{pyridine,meta}$), 128.37 ($CH_{phenyl,meta}$), 128.60 (*C*C=O), 128.64 ($CH_{phenyl,meta}$), 130.17 ($CH_{phenyl,ortho}$), 130.31 (*C*C=O), 130.57 ($CH_{phenyl,ortho}$), 133.74 ($CH_{phenyl,para}$), 134.09 ($CH_{phenyl,para}$), 138.57 ($CH_{pyridine}$), 140.35 ($CH_{pyridine}$), 152.17 (NCO), 154.95 (NCO), 163.84 (C=O), 164.35 (C=O); UV/Vis (CH_2Cl_2, 8.8×10^{-6} mol L^{-1}): λ_{max} ($\log(I_o/I)$) = 232 (1.143), 271 nm (0.430); IR: $\tilde{\nu} = 3448$ (br s, N–H), 3078 (w, CH_{ar}), 2957 (m, CH), 1749 (s, C=O), 1583 (m, C=C), 1452 (m), 1432 (m), 1238 (s), 1216 (s, C–O), 1175 (m), 1154 (m), 1127 (w), 1084 (s, C–O), 1052 (s), 1023 (m), 704 cm^{-1} (s, $CH_{ar,monosubst}$); MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid, cations): *m/z*: 1550 $[M]^+$, 1572 $[M+Na]^+$, 1588 $[M+K]^+$; exact mass calcd for $C_{96}H_{85}N_4O_{16}$: 1549.5961; found 1549.5952. X-ray crystal-structure analysis (*rctt*-**1**): formula $C_{96}H_{84}N_4O_{16} \cdot 4\,CHCl_3 \cdot 0.5\,C_2H_5OH$, $a = 13.003(1)$, $b = 13.473(1)$, $c = 17.150$ (1) Å, $\alpha = 67.19$ (1), $\beta = 87.58$ (1), $\gamma = 66.44$ (1)°, $V = 2516.0(4)$ Å^3, $T = 180$ K, $\rho_{calcd} = 1.353$ g cm^{-3}, $\mu = 0.4$ mm^{-1}, triclinic, space group $P\bar{1}$ (No. 2), $Z = 1$, STOE imaging plate diffraction system, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, 19698 measured reflections in the range of $4° \leq 2\vartheta \leq 48°$, 7476

independent reflections used for refinement and 5739 reflections with $I \geq 2\sigma(I)$. Structure solution was performed using SHELXS-86. Structure refinement against F^2 using SHELXL-93. 623 refined parameters, R for all reflections with $I \geq 2\sigma(I) = 0.0797$, w$R2$ for all reflections = 0.2488, GoF = 1.047, residual electron density: 0.58/ − 0.97 e Å^{-3}, All non-hydrogen atoms were refined by using anisotropic displacement parameters. The hydrogen atoms were positioned with idealised geometry and refined with isotropic displacement parameters by using the riding model. The solvent molecules are disordered and were refined using a split model.

Fraction 2: *rcct*-4,6,10,12,16,18,22,24-octakis(benzoyloxy)-2,8,14,20-tetraisobutylpyridine[4]arene (*rcct*-1): The compound was purified twice by chromatography and recrystallised from chloroform/ethanol. Yield: 740 mg (25 %); $R_f = 0.42$ (cyclohexane/ethylacetate 4:1); m.p. 204 – 208 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 0.73$ (d, $^3J = 6.7$ Hz, 6H; CH_3), 0.74 (d, $^3J = 6.7$ Hz, 6H; CH_3), 0.84 (d, $^3J = 6.6$ Hz, 6H; CH_3), 0.89 (d, $^3J = 6.7$ Hz, 6H; CH_3), 1.45 (m, 1H; $(CH_3)_2CH$), 1.50 (m, 1H; $(CH_3)_2CH$), 1.62 (m, 2H; $(CH_3)_2CH$), 1.66 (t, $^3J = 7.2$ Hz, 2H; CH_2), 1.94 (ddd, $^2J = 14.4$ Hz, $^3J = 5.8$, 8.5 Hz, 2H; CH_2), 2.04 (ddd, $^2J = 15.2$ Hz, $^3J = 5.1$, 9.8 Hz, 2H; CH_2), 2.05 (dd, $^3J = 8.5$ Hz, 8.6 Hz, 2H; CH_2), 4.46 (dd, $^3J = 7.7$, 7.7 Hz, 1H; Ar_2CH), 4.49 (dd, $^3J = 5.9$ Hz, 9.6 Hz, 2H; Ar_2CH), 4.70 (t, $^3J = 8.0$ Hz, 1H; Ar_2CH), 7.21 (s, 2H; $CH_{pyridine}$), 7.27, 7.32, 7.52, 7.52, 7.55, 7.64, 7.77, 7.83, 7.84, 8.10 (m, 40H; $CH_{benzoyl}$), 8.18 (s, 2H; $CH_{pyridine}$); ^{13}C NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 21.85$ (CH_3), 22.31 (CH_3), 22.32 (CH_3), 22.90 (CH_3), 25.61 (CH_3CH), 25.81 (CH_3CH), 25.92 (CH_3CH), 33.47 (Ar_2CH), 34.55 (Ar_2CH), 37.04 (Ar_2CH), 43.43 (CH_2), 43.44 (CH_2), 44.39 (CH_2), 128.46, 128.49, 128.50, 128.66 ($CH_{phenyl,meta}$), 130.22, 130.39, 130.45, 130.66 ($CH_{phenyl,meta}$), 133.07, 133.71, 133.71, 134.02 ($CH_{phenyl,para}$), 164.10, 164.18, 164.53, 164.57 (C=O); UV/Vis (CH_2Cl_2, 1.2×10^{-5} mol L^{-1}): λ_{max} (log(I_o/I)) = 235 (1.46), 272 nm (0.470); IR: $\tilde{\nu} = 3448$ (br s, N−H), 3063 (w, CH_{ar}), 2956 (m, CH), 2868 (m, CH), 1748 (s, C=O), 1600 (m, C=C), 1582 (m, C=C), 1492 (w), 1452 (m), 1433 (m), 1387 (w), 1368 (w), 1238 (s), 1217 (s, C−O), 1176 (m), 1154 (m), 1128 (w), 1081 (s, C−O), 1050 (s), 1022 (m), 865 (w), 796 (w), 704 cm^{-1} (s, $CH_{ar,monosubst}$); MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid, cations): m/z: 1550 $[M]^+$, 1572 $[M+Na]^+$; exact mass calcd for $C_{96}H_{85}N_4O_{16}$: 1549.5961; found 1549.5957.

Fraction 3: *rccc*-4,6,10,12,16,18,22,24-octakis(benzoyloxy)-2,8,14,20-tetraisobutylpyridine[4]arene (*rccc*-1): As for the compounds isolated from fractions 1 and 2, compound *rccc*-**1** was crystallised from chloroform/ethanol. Crystals were obtained in this way (340 mg, 11 %), but gave poor results in the X-ray crystal structure determination. $R_f = 0.35$ (cyclohexane/ethyl acetate 4:1); m.p. 350 – 352 °C (chloroform/ethanol); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.60 - 0.95$ (br, 24H; CH_3), 1.30 – 2.30(br, 12H; $CH_2CH(CH_3)_2$), 4.56 (t, $^3J = 7.4$ Hz, 4H; $(Ar)_2CH$), 7.25 – 8.10 (br m, 11H; $CH_{aromatic}$); ^{1}H NMR (200 MHz, CD_2Cl_4, 70 °C): $\delta = 0.85$ (d, $^3J = 6.4$ Hz, 24H; CH_3), 1.61 (m, 4H; $CH(CH_3)_2$), 1.99 (t, $^3J = 6.7$ Hz, CH_2), 4.62 (t, $^3J = 7.4$ Hz, $(Ar)_2CH$), 7.43 (t, $^3J = 7.5$ Hz, 16H; $CH_{phenyl,meta}$), 7.53 (s, 4H; $CH_{pyridine}$), 7.64 (t, $^3J = 7.4$ Hz, $CH_{phenyl,para}$), 7.90 (d, $^3J = 7.3$ Hz, 16H; $CH_{phenyl,ortho}$); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 164.0$ (C=O), ∼153 (br, NCO), ∼138 (br, $CH_{pyridine}$), 133.8 ($CH_{phenyl,meta}$), ∼132 (br, $C_{pyridine,meta}$), 130.6 ($CH_{phenyl,para}$), 128.2 ($C_{phenyl,q}$, $CH_{phenyl,ortho}$), 43.4 (Ar_2CH), 34.9 (CH_2), 26.9 ($CH(CH_3)_2$), 25.8 (CH_3); UV/Vis (CH_2Cl_2, 9.0×10^{-5} mol L^{-1}): λ_{max} (log(I_o/I)) = 233 (1.50), 271 nm (0.433); IR: $\tilde{\nu} = 3448$ (br s, N$^+$−H), 3076 (w, CH_{ar}), 2957 (m, CH), 1749 (s, C=O), 1583 (m, C=C), 1452 (m), 1432 (m), 1238 (s), 1216 (s, C−O), 1175 (m), 1154 (m), 1127 (w), 1085 (s, C−O), 1052 (s), 1023 (m), 704 cm^{-1} (s, $CH_{ar,monosubst}$); MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid, cations): m/z: 1550 $[M]^+$, 1572 $[M+Na]^+$; 1588 $[M+K]^+$; exact mass calcd for $C_{96}H_{85}N_4O_{16}$: 1549.5961; found 1549.5954. 710 mg were collected as mixed fractions of *rctt*-**1** and *rcct*-**1** and *rcct*-**1** and *rccc*-**1**, both containing predominantly *rcct*-**1**.

Preparation of *rccc*-4,6,10,12,16,18,22,24-octahydroxy-2,8,14,20-tetraisobutylpyridine[4]arene (2): 3-Methyl-1-butanal (5.85 g, 7.30 mL, 68.0 mmol) was added dropwise to a solution of 2,6-dihydroxypyridine hydrochloride (10.0 g, 68.0 mmol) in glycol monoisopropyl ether (50 mL) and hydrochloric acid (conc., 25 mL). The reaction mixture was heated at reflux for 10 d under argon. After 20 h, the product began to precipitate. After cooling to RT, the precipitate was filtered off, washed with water, ethanol and acetone, and dried under vacuum. The raw material yielded a yellowish powder (11 g) which could be crystallised from THF/acetone to give a crystalline colourless powder. One batch of the product was dissolved in THF/water and allowed to evaporate slowly over a period of one week to give some single crystals for X-ray crystal structure analysis. Another sample was benzoylated and the product gave the same analytical data as fraction 3 of the preceding experiment containing *rccc*-**2**. Yield: 8.90 g (72 %); m.p. 243 – 245 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.96$ (d, $^3J = 6.5$ Hz, 24H; CH_3), 1.44 (m, 12H; $CH(CH_3)_2$), 2.05 (t, $^3J = 7.0$ Hz, 8H; CH_2), 4.13 (t, $^3J = 7.8$ Hz, $(Ar)_2CH$), 7.61 (s, 4H; $CH_{aromatic}$), 12.6 (br, 1H; OH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 158.3$ (NCO), 136.8 ($CH_{pyridine}$), 116.7 ($C_{pyridine,meta}$), 67.0, 30.9 (Ar_2CH), 25.9 (CH_2), 25.1, 22.5 (CH_3); UV/Vis (CH_2Cl_2, 9.0×10^{-5} mol L^{-1}): λ_{max} (log(I_o/I)) = 341 (0.72), 244 nm (0.20); IR: $\tilde{\nu} = 3440$ (br m, N−H, O−H), 2955 (m, CH), 1632 (s, C=O), 1586 (s, C=C), 1466 (m), 1367 (w), 1297 (m), 1209 (w), 870 (br m), 606 (w), 533 cm^{-1} (w); MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid, cations): m/z: 717 $[M]^+$, 738 $[M+Na]^+$; exact mass calcd for $C_{40}H_{53}N_4O_8$: 717.38634; found 717.38578. X-ray crystal-structure analysis of **2**: formula $C_{40}H_{52}N_4O_8 \cdot (CH_3)_2CO \cdot 1.5(CH_2)_4O$, $a = 22.197(2)$, $b = 15.790(1)$, $c = 28.780(3)$ Å, $\beta = 106.79(1)°$, $V = 9657(2)$ Å^3, $T = 180$ K, $\rho_{calcd} = 1.215$ g cm^{-3}, $\mu = 0.09$ mm^{-1}, monoclinic, space group $P2_1/c$ (No. 14), $Z = 8$, STOE imaging plate diffraction system, $\lambda(Mo_{K\alpha}) = 0.71073$ Å), 41983 measured reflections in the range of $4° \leq 2\theta \leq 45°$, 12150 independent reflections used for refinement and 9500 reflections with $I \geq 2\sigma(I)$. Structure solution was performed using SHELXS-86. Structure refinement against F^2 using SHELXL-93. 1151 refined parameters, R for all reflections with $I \geq 2\sigma(I) = 0.0840$, w$R2$ for all reflections = 0.2514, GoF = 1.054, residual electron density: 0.62/0.45 e Å^{-3}. All non-hydrogen atoms, except some of the atoms of the solvent molecules, were refined by using anisotropic displacement parameters. The hydrogen atoms were positioned with idealised geometry and refined with isotropic displacement parameters by using the riding model. Some of the isopropyl groups and some of the solvent molecules are disordered and were refined with isotropic displacement parameters using a split model.

Synthesis of *rccc*-4,6,10,12,16,18,22,24-octahydroxy-2,8,14,20-tetra-*n*-butylpyridine[4]arene (3): 2,6-Dihydroxypyridine (2.00 g, 13.6 mmol) in glycol monoisopropyl ether (10 mL) and hydrochloric acid (conc., 5 mL) was added dropwise to distilled *n*-pentanal (1.17 g, 1.45 mL, 13.6 mmol) and heated at reflux under argon for 7 d. The product began to precipitate after 24 h. After cooling to RT, the oily side-products were dissolved in acetone (50 mL). The remaining solid was filtered off, washed with acetone and recrystallised from DMSO to give pale yellow, glistening needles (1.35 g, 55 %). M.p. 250 – 252 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 0.89$ (t, $^3J = 7.19$ Hz, 12H; CH_3), 1.1 – 1.5 (m, 16H; CH_2), 2.1 – 2.35 (m, 8H; $CHCH_2$), 3.99 (t, $^3J = 7.36$ Hz, 4H; $CH_{methine}$), 7.61 (s, 4H; $CH_{pyridine}$), 12.5 (br s, 4H; NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 14.1$ (CH_3), 22.1 (CH_2CH_3), 29.1 ($CH_2CH_2CH_2$), 29.9 (($CH_3)_2CH$), 33.0 (Ar_2CH), 56.5, 116.5 (C_{meta}), 136.5 ($CH_{pyridine}$), 158.3 (COH); MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid, cations): m/z: 718 $[M+H]^+$, 740 $[M+Na]^+$; exact mass: calcd for $C_{40}H_{53}N_4O_8$: 717.3864; found 717.3858; elemental analysis calcd (%) for $C_{40}H_{52}N_4O_8 \cdot 1$ DMSO: C 63.37, H 7.47, N 7.04; found C 62.65, H 7.42, N 6.74.

Preparation of *rccc*-4,6,10,12,16,18,22,24-octakis(benzoyloxy)-2,8,14,20-tetramethylpyridine[4]arene (4): A suspension of 2,6-dihydroxypyridine (2.00 g, 13.6 mmol) in glycol monoisopropyl ether (10 mL) and hydrochloric acid (5 mL) was mixed with distilled ethanal (0.600 g, 0.760 mL) and heated at 50 °C for 5 h and then at reflux for 7 d under argon. (The apparatus was closed with a balloon to avoid losses of the aldehyde). Within 20 h, a colourless precipitate formed. After cooling to RT, the solid was collected and washed with acetone to leave a colourless powder of low solubility (1.01 g, 54 %). M.p. 282 – 284 °C. A sample of the raw material (1.00 g, 1.82 mmol), benzoyl chloride (10 mL) and distilled pyridine (2 mL) were heated at reflux for 2 h. After cooling to RT, water (40 mL) was added and the mixture was stirred until the organic layer had dissolved. The solid was separated and triturated three times with hot ethanol (20 mL). The residue was dried and recrystallised from chloroform/ethanol to yield colourless, crystalline plates (1.68 g, 39 %), which were soluble in THF, acetone and chloroform and insoluble in ethanol and cyclohexane. M.p. 400 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 8.30 - 7.25$ (br, 44H; $H_{ar.}$), 4.54 (q, $^3J = 7.1$ Hz, 4H; $CHCH_3$), 1.70 (d, $^3J = 7.4$ Hz, 12H; CH_3); ^{1}H NMR (200 MHz, DMSO, 80 °C): $\delta = 1.78$ (d, $^3J = 7.2$ Hz, 12H; CH_3), 4.45 (q, $^3J = 7.2$ Hz, 16H; $CHCH_3$), 7.53 (t, $^3J = 7.2$ Hz, 8H; $CH_{phenyl,meta}$), 7.65 – 7.85 (m, 24H; $CH_{phenyl,ortho,para}$), 7.94 (s, 4H; $CH_{pyridine}$); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta = 164.0$ (C=O), ∼157 (br, NCO), ∼138 (br, $CH_{pyridine}$), 133.8 ($CH_{phenyl,meta}$), ∼132 (br, $C_{pyridine,meta}$), 130.6 ($CH_{phenyl,para}$), 128.4 ($C_{phenyl,q}$, $CH_{phenyl,ortho}$), 32.0 (Ar_2CH), 20.4 (CH_3);

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MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid): *m/z*: 1420 $[M+K]^+$, 1403 $[M+Na]^+$, 1382 $[M+H]^+$, 1381 $[M]^+$; elemental analysis calcd (%) for $C_{84}H_{60}N_4O_{16}\cdot 2\,EtOH$: C 71.1, H 4.93, N 3.80; found C 71.9, H 5.09, N 3.64. X-ray crystal structure analysis: formula $C_{84}H_{60}N_4O_{16}\cdot 1.5\,CHCl_3$, $a=21.775(1)$, $b=11.861(1)$, $c=31.461(2)$ Å, $\beta=99.48(1)^\circ$, $V=8014.9(8)$ Å^3, $T=180$ K, $\rho_{calcd}=1.293$ g cm^{-3}, $\mu=0.23$ mm^{-1}, monoclinic, space group $P2_1/n$ (No. 14), $Z=4$, STOE imaging plate diffraction system, $\lambda(Mo_{K\alpha})=0.71073$ Å, 31970 measured reflections in the range of $4^\circ\le 2\theta\le 45^\circ$, 10304 independent reflections used for refinement and 7798 reflections with $I\ge 2\sigma(I)$. Structure solution was performed using SHELXS-86. Structure refinement against F^2 using SHELXL-93. 1040 refined parameters, R for all reflections with $I\ge 2\sigma(I)=0.0694$, w$R2$ for all reflections = 0.2231, GoF = 1.071, residual electron density: 0.80/ – 0.81 e Å^{-3}, All non-hydrogen atoms, except some of the atoms of the solvent molecules, were refined by using anisotropic displacement parameters. The hydrogen atoms were positioned with idealised geometry and refined with isotropic displacement parameters by using the riding model. One of the solvent molecules is disordered and was refined isotropically by using a split model.

Preparation of *rccc*-4,6,10,12,16,18,22,24-octahydroxy-2,8,14,20-tetra-*n*-undecylpyridine[4]arene (5): A suspension of 2,6-dihydroxypyridine hydrochloride (8.00 g, 54.4 mmol) in glycol monoisopropyl ether (40 mL) and hydrochloric acid (conc., 20 mL) was mixed with *n*-dodecanal (10.0 g, 54.4 mmol) and heated at reflux for 7 d under argon. After the solution had cleared, a wax-like, yellow to reddish mass began to precipitate within 5 h. The raw product was filtered off after cooling, taken up in acetone (250 mL) and treated with ultra-sound for 30 min. The resulting amorphous, pale yellow powder was separated, washed with acetone and ethanol, and dried. Recrystallisation from chloroform and ethanol afforded pale yellow leafy crystals (7.15 g, 47%). M.p. 170–172 °C; ^{1}H NMR (500 MHz, $CDCl_3$, CF_3COOD, 25 °C): $\delta=0.89$ (t, $^3J=7.1$ Hz, 12H; CH_3), 1.10–1.50 (m, 72H; CH_2), 2.14 (dt, $^3J=8.0$, 7.2 Hz, 8H; $CHCH_2CH_2$), 4.27 (t, $^3J=8.1$ Hz, 4H; $CH_{methine}$), 7.44 (s, 4H; $CH_{pyridine}$); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=14.1$ (CH_3), 22.1 (CH_2CH_3), 27.7 ($CHCH_2$), 29.4, 29.55, 29.63, 29.70, 29.73, 29.75, 31.94 ($CH_{2partialoverlap}$), 109.8 ($COHC$), 117.0 ($CCOH_{pyridinediol\ tautomer}$), 136.1 ($CH_{pyridinediol\ tautomer}$), 124.0 (C=O*C*), 153.5 (COH), 157.8 ($COH_{pyridinediol\ tautomer}$), 163.3 (C=O); ESI-MS (toluene/methanol): *m/z* (%): = 1109.8 $[M]^+$ (100), 1167.9 (8), 1184.9 (5); MALDI-TOF-MS (matrix 2,5-dihydroxybenzoic acid, cations): *m/z*: 1109 $[M]^+$; exact mass calcd for $C_{68}H_{109}N_4O_8$: 1109.8246; found 1109.8238; UV/Vis (CH_2Cl_2, 1.5×10^{-5} mol L^{-1}): λ_{max} ($\log(I_o/I)$) = 240 (0.241), 328 nm (0.677); IR: $\tilde{\nu}=3458$ (br m, N–H), 3116 (br w, CH_{ar}), 2923 (s, CH), 2851 (s, CH), 1633 (s, C=O), 1593 (m, C=C), 1466 (m), 1400 (w), 1370 (w), 1303 (m, OH), 1211 (w), 867 (m, CH), 608 (w), 538 cm^{-1} (w).

Preparation of *rctt*-4,6,10,12,16,18,22,24-octakis(acetoxy)-2,8,14,20-tetra-(4′,4″,4‴,4⁗nitrophenyl)pyridine[4]arene (8): 2,6-Dihydroxypyridine hydrochloride (2.00 g, 13.6 mmol) was dissolved in glycol monoisopropyl ether (10 mL) and hydrochloric acid (conc., 5 mL), mixed with 4-nitrobenzaldehyde (2.05 g, 13.6 mmol) and heated at reflux for 7 d under argon. After 4 h, a yellowish-grey solid began to precipitate. After cooling to RT the substance was collected, dispersed in hot acetone, filtered off and dried under vacuum to give a reddish, insoluble powder (2.67 g). The raw material was heated at reflux in acetic anhydride (20 mL) and *N*,*N*-dimethylaminopyridine (10 mg) for 3 h. The suspension did not clear throughout the experiment. After cooling, the reaction mixture was carefully dissolved in ethanol and a pale yellow, shimmering solid (2.20 g, 49%) was separated. Although still poorly soluble, a few mg could be dissolved in hot chloroform. Slow evaporation of the solvent gave crystals suitable for X-ray crystal-structural analysis. M.p. >340 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta=2.16$ (s, 12H; CH_3), 2.22 (s, 12H; CH_3), 5.59 (s, 4H; $(Ar)_2CH$), 6.32 (s, 2H; $CH_{pyridine}$), 6.71 (s, 2H; $CH_{pyridine}$), 6.96 (d, $^3J=6.8$ Hz, 8H; CH_{meta}), 7.96 (d, $^3J=6.8$ Hz, 8H; CH_{ortho}); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=20.74$ (CH_3), 43.46 ($(Ar)_2CH$), 123.85 ($C_{ar,ortho}$), 125.84 ($CH_{pyridine}$), 126.75 ($CH_{pyridine}$), 129.59 ($C_{ar,meta}$), 141.71 ($C_{pyridine}$), 143.20 ($C_{pyridine}$), 144.49 ($C_{ar,para}$), 147.19 ($C-NO_2$), 153.69 (NCO), 153.81 (NCO), 167.62 (C=O), 168.64 (C=O); UV/Vis (CH_2Cl_2, 7.6×10^{-6} mol L^{-1}). λ_{max} ($\log(I_o/I)$): 272 nm (0.977). IR: $\tilde{\nu}=3448$ (br s, N^+–H), 3078 (w, CH_{ar}), 1775 (s, C=O), 1606 (m, C=C), 1581 (s, C=C), 1518 (s, C=C), 1436 (s), 1371 (s), 1353 (s, N–O), 1310 (m), 1249 (w), 1168 (s, C–O), 1075 (s, C–O), 1010 (m), 951 (w), 938 (w), 889 (m), 863 (m), 837 (m, $CH_{ar,1,4\ disubst.}$), 733 (w), 586 (w), 480 cm^{-1} (w); ESI-MS (DMF, cations): *m/z*: 1313.28 $[M]^+$, 1330.31 $[M+NH_4]^+$, 1335.23 $[M+Na]^+$, 1351.23 $[M+K]^+$; elemental analysis calcd (%) for $C_{64}H_{48}N_8O_{24}$: C 58.5, H 3.68, N 8.54; found C 58.0, H 3.64, N 8.36. X-ray crystal-structure analysis of **8**: formula $C_{64}H_{48}N_8O_{24}\cdot 2\,CHCl_3$, $a=14.088(1)$, $b=17.122(1)$, $c=15.756(1)$ Å, $\beta=112.66(1)^\circ$, $V=3507.3(4)$ Å^3, $T=180$ K, $\rho_{calcd}=1.469$ g cm^{-3}, $\mu=0.33$ mm^{-1}, monoclinic, space group $P2_1/n$ (No. 14), $Z=2$, STOE imaging plate diffraction system, $\lambda(Mo_{K\alpha})=0.71073$ Å, 13006 measured reflections in the range of $4^\circ\le 2\theta\le 52^\circ$, 6303 independent reflections used for refinement and 4979 reflections with $I\ge 2\sigma(I)$. Structure solution was performed using SHELXS-86. Structure refinement against F^2 using SHELXL-93. 483 refined parameters, R for all reflections with $I\ge 2\sigma(I)=0.0433$, w$R2$ for all reflections = 0.1169, GoF = 0 1.032, residual electron density: 0.41/ – 0.42 e Å^{-3}, All non-hydrogen atoms, except some of the atoms of the solvent molecules, were refined by using anisotropic displacement parameters. The hydrogen atoms were positioned with idealised geometry and refined with isotropic displacement parameters by using the riding model. One of the solvent molecules is disordered and was refined by using a split model.

Preparation of *rccc*-4,6,10,12,16,18,22,24-octakis(acetoxy)-2,8,14,20-tetraphenylpyridine[4]arene (9): A slurry of dihydroxypyridine hydrochloride (2.50 g, 16.9 mmol), distilled benzaldehyde (1.80 g, 1.72 mL, 16.9 mmol), and conc. hydrochloric acid (4 mL) in glycol monoisopropyl ether (10 mL) was heated at reflux under argon for 48 h. After 1 h, a white substance began to precipitate. The reaction mixture was cooled to RT, and the residue was collected, washed with water and acetone to leave a grey material (3.64 g) which was almost insoluble in all tested solvents (water, ethanol, THF, dioxane, chloroform, toluene, pentane, DMF, DMSO). A sample of the raw material (700 mg) was heated at reflux in acetic anhydride (5 mL) and *N*,*N*-dimethylaminopyridine (10 mg) for 6 h under argon. The suspension did not clear during the reaction. After cooling to RT, the reaction mixture was carefully dissolved in with a small amount of ethanol and then poured into ethanol (50 mL). The solid was filtered off, washed with ethanol and then extracted with hot chloroform (3 × 20 mL). The combined chloroform solutions were evaporated to dryness to leave a yellowish solid that could be recrystallised from chloroform/ethanol to yield small, pale yellow scales (227 mg, 25%). M.p. 323–324 °C (decomp); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.14 (m, 3H; CH_{phenyl}), 6.69 (m, 2H; CH_{phenyl}), 6.54 (t, $^6J=0.64$ Hz, 1H; $CH_{pyridine}$), 5.39 (s, 1H; $CH_{methine}$), 2.09 (br, 6H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): $\delta=167.9$ (C=O), 153.2 (NCO), 138.5 ($C_{pyridine,meta}$), 128.8 ($CH_{phenyl,meta}$), 128.1 ($C_{pyridine,meta}$), 127.4 ($CH_{phenyl,para}$), 126.9 ($C_{phenyl,q}$, $CH_{phenyl,ortho}$), 44.0 (Ar_2CH), 20.6 (CH_3); UV/Vis (CH_2Cl_2, 8.8×10^{-6} mol L^{-1}): λ ($\log(I_o/I)$) = 275 (0.380), 268 (0.345), 263 nm (0.278); IR: $\tilde{\nu}=3448$ (br s, N^+–H), 3050 (w, CH_{ar}), 1778 (s, C=O), 1581 (m, C=C), 1496 (w), 1434 (m), 1370 (m), 1230 (w), 1168 (s, C–O), 1071 (s, C–O), 1010 (m), 1023 (m), 953 (w), 899 (w), 874 (w), 703 (w), 587 cm^{-1} (w); MS (EI, 70 eV, cations): *m/z* (%): 1091 $[M-Ac+H]^+$ (3), 1051 $[M-2Ac+H+H]^+$ (19), 1009 $[M-3Ac+2H+H]^+$ (26), 966 $[M-4Ac+3H+H]^+$ (20), 924 $[M-5Ac+4H+H]^+$ (17), 882 $[M-6Ac+5H+H]^+$ (20); 840 $[M-7Ac+6H+H]^+$ (13), 797 $[M-8Ac+7H+H]^+$ (26), 685 (13), 486 (76), 440 (71), 398 $[M-8Ac+6H+2H]^+$ (100), 380 (22), 352 (34), 328 (45), 325 (15), 288 (63), 241 (63), 215 (28), 198 (62), 154 (24), 152 (37), 135 (27), 125 (26), 115 (76); MS (CI, 70 eV, isobutyl chloride, cations): *m/z* (%): 1134 $[M+H]^+$ (3), 531 (2), 487 (6), 441 (8), 332 (6), 290 (36); 242 (76); 200 (63); 153 (100); 113 (17); 72 (12); elemental analysis calcd (%) for $C_{64}H_{52}N_4O_{16}\cdot 2\,CH_3COOH$: C 65.17, H 4.83, N 4.47; found C 64.82, H 4.83, N 4.83.

Synthesis of 6-hydroxy-5-{{6-hydroxy-5-{(*E*)-[4-(octyloxy)phenyl]methylidene}-2-oxo-2,5-dihydro-3-pyridinyl}[4-(octyloxy)phenyl]methyl}-3-{(*E*)-[4-(octyloxy)phenyl]methylidene}-2(3H)-pyridinone (7): A solution of 2,6-dihydroxypyridine hydrochloride (5.00 g, 34.0 mmol) in glycol monoisopropyl ether (20 mL) and hydrochloric acid (conc., 10 mL) was added dropwise to 4-octyloxybenzaldehyde (7.97 g, 34.0 mmol) at RT and then heated at reflux under argon for 24 h. A bright yellow precipitate formed some minutes after the addition of the aldehyde. After cooling to RT, acetone (50 mL) was added. The solid was filtered off and washed with acetone and ethanol. Recrystallisation from chloroform/ethanol afforded a bright yellow solid (6.70 g, 91%), which was soluble in chloroform, less soluble in acetone, and insoluble in cyclohexane and ethanol. M.p 244–245 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta=0.88$ (t, $^3J=7.2$ Hz, 3H; $CH_{3\ mid}$), 0.89 (t, $^3J=7.2$ Hz, 6H; CH_3), 1.24–1.38 (m, 24H; $12CH_2$), 1.41–1.48 (m, 6H; $3CH_2(CH_2)_2O$), 1.74–1.82 (m, 6H; CH_2CH_2O), 3.95 (t, $^3J=6.4$ Hz, 4H; $2CH_2O$), 3.96 (t, $^3J=6.3$ Hz, 2H; CH_2O_{mid}), 5.58 (s, 1H;

$CH_{methine}$), 6.82 (d, $^3J = 8.9$ Hz, 4H; $CH_{phenyl,ortho}$), 6.89 (d, $^3J = 8.8$ Hz, 2H; $CH_{phenyl,ortho,mid}$), 7.10 (dd, $^3J = 8.8$ Hz, $^6J = 0.5$ Hz, 2H; $CH_{phenyl,meta,mid}$), 7.24–7.27 (m, 4H; $CH_{phenyl,meta}$), 7.26 (t, $^3J = 1.0$ Hz, 2H; $CH_{pyridine}$), 8.05 (s, 2H; $CH_{methylidene}$), 8.39 (s, 2H; NH/OH); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): $\delta = 14.1$ (CH_3), 22.7 (CH_2), 26.0 (CH_2), 26.1 (CH_2), 29.1 (CH_2), 29.2 (CH_2), 29.26 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 31.81 ($CH_2CH_2O_{mid}$), 31.84 (CH_2CH_2O), 43.9 ($CH_{methine}$), 68.2 (CH_2O_{mid}), 68.4 (CH_2O), 114.9 ($CH_{phenyl,ortho,mid}$), 115.1 ($CH_{phenyl,ortho}$), 121.7 (C_q), 126.2 (C_q), 129.7 ($CH_{phenyl,meta,mid}$), 130.4 (C_q), 132.3 (C_q), 133.1 ($CH_{phenyl,meta}$), 135.9 ($CH_{pyridine}$), 147.0 ($C_{methide}$), 158.3 ($C_{q,pyridine}$), 161.93 ($C_{q,pyridine}$), 163.80 (COH), 164.39 (C=O); UV/Vis (CH_2Cl_2, 2.5×10^{-5} mol L^{-1}): λ_{max} ($\log(I_o/I)$) = 233 (0.91), 255 (0.98), 284 (0.0.31), 393 nm (1.58). IR: $\tilde{\nu}$ = 3163.9 (m, NH/OH), 3061.0 (m, $CH_{pyridone}$, CH_{methid}), 2923.4 (s, CH_2, CH_3), 2853.5 (s, CH_2, CH_3), 1690.2 (s, C=O), 1664.1 (s, NH), 1594.0 (m, C=C_{ar}), 1574.1 (s, C=C_{ar}), 1555.9 (s, C=C_{ar}), 1508.5 (s), 1467.1 (w), 1420.1 (m), 1378.3 (m), 1306.6 (w), 1258.5 (s, C–O), 1176.5 (s), 1022.7 (w), 828.7 (s, CH_{ar}), 724.3 (w), 564.5 (m), 531.6 cm^{-1} (m); MALDI-MS (matrix 2,5-dihydroxybenzoic acid): m/z: = 871 $[M+H]^+$, 893 $[M+Na]^+$, 909 $[M+K]^+$; exact mass calcd for $C_{55}H_{70}N_2O_7$: 870.51831; found 870.51810; exact mass calcd for $C_{54}{}^{13}CH_{70}N_2O_7$: 871.52167, found 871.52120.

Synthesis of 6-hydroxy-5-{[6-hydroxy-2-oxo-5-[(*E*)-2-thienylmethylidene]-2,5-dihydro-3-pyridinyl}(2-thienyl)methyl}-3-[(*E*)-2-thienylmethylidene]-2(3H)-pyridinone (6): A solution of dihydroxypyridine hydrochloride (2.00 g, 13.6 mmol) and thiophene-2-carboxaldehyde (1.50 g, 13.5 mmol) in ethanol (20 mL) and hydrochloric acid (conc., 10 mL) was heated at reflux under nitrogen. Within 1 h, an orange precipitate began to form. After 6 h, the reaction mixture was filtered while still hot, and the remaining solid was washed with ethanol and dried under vacuum to yield a fine, yellow powder (3.20 g, 93%). M.p. 314–316 °C (decomp); ^{1}H NMR (300 MHz, [D6]DMSO, 25 °C): $\delta = 11.55$ (s, 2H; OH), 8.17 (s, 2H; $CH_{pyridinone}$), 7.98 (dt, $^3J = 5.1$, 1.1 Hz, 2H; $CH_{thiophene}$), 7.85 (dt, $^3J = 3.4$, 1.1 Hz, 2H; $CH_{thiophene}$), 7.67 (t, $^4J = 0.9$ Hz, 2H; $CH_{methide}$), 7.56 (dd, $^3J = 5.1$, 1.2 Hz, 1H; $CH_{thiophene,mid}$), 7.25 (dd, $^3J = 5.1$ Hz, 3.7 Hz, 2H; $CH_{thiophene}$), 7.12 (dd, $^3J = 5.1$, 3.5 Hz, 1H; $CH_{thiophene,mid}$), 7.06 (dt, $^3J = 3.4$, 1.1 Hz, 1H; $CH_{thiophene,mid}$), 5.83 (s, 1H; $CH_{aliphatic,mid}$); ^{13}C NMR (75 MHz, [D_6]DMSO, 25 °C): $\delta = 164.1$ (C=O), 163.8 (COH), 141.9 ($C_{thiophene}$), 139.6 ($C_{pyridinone}$), 139.2 ($C_{thiophene,mid}$), 137.4 ($C_{pyridinone}$), 137.0 ($CH_{pyridinone}$), 136.9 ($CH_{thiophene}$), 135.4 ($CH_{methide}$), 133.1 ($CH_{thiophene}$), 128.8 ($CH_{thiophene}$), 127.7 ($CH_{thiophene,mid}$), 127.2 ($CH_{thiophene,mid}$), 126.1 ($CH_{thiophene,mid}$), 119.8 ($C_{pyridinone}$); UV/Vis (acetone, 3.6×10^{-5} mol L^{-1}): λ_{max} ($\log(I_o/I)$) = 384 nm (1.19); IR: $\tilde{\nu}$ = 3440 (br s, NH/OH), 3177 (m), 3062 (m, CH_{ar}), 1673 (s, C=O) 1617 (m), 1565 (m, C=C), 1433 (m), 1378 (m), 1317 (m), 1236 (m), 1211 (m), 1052 (w), 844 (w), 715 (m), 579 (w), 552 (w), 542 (w), 518 cm^{-1} (w); MS (CI, isobutane, cations): m/z (%): 505.0 $[M+H]^+$ (74), 302.0 (79), 206.0 (100); MS (EI, 70 eV, cations): m/z (%): 504.0 $[M]^+$ (100), 301 (17), 205 (11), 121 (55); exact mass calcd for $C_{25}H_{16}N_2O_4S_3$: 504.02722; found 504.02690; exact mass calcd for $C_{24}{}^{13}CH_{16}N_2O_4S_3$: 505.03058; found 505.03060.

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[1] G. R. Newcome, J. Y. Joo, F. R. Frontzek, *J. Chem. Soc. Chem. Commun.* **1987**, 854–856.

[2] a) V. Kral, P. A. Gale, P. Anzenbacher, K. Jursikova, V. Lynch, J. L. Sessler, *Chem. Commun.* **1998**, 9–10; b) V. Kral, J. L. Sessler, T. V. Shishkanova, P. A. Gale, R. Volf, *J. Am. Chem. Soc.* **1999**, *121*, 8771–8775.

[3] a) A. R. Katritzky, F. D. Popp, J. D. Rowe, *J. Chem. Soc. B* **1966**, 562–564; b) E. Spinner, J. C. B. White, *J. Chem. Soc. B* **1966**, 991–995; c) E. Spinner, G. B. Yeoh, *Aust. J. Chem.* **1971**, *24*, 2557–2573.

[4] a) L. Gattermann, A. Skita, *Ber. Dtsch. Chem. Ges.* **1916**, *49*, 494–501; b) R. L. Atkins, D. E. Bliss, *J. Org. Chem.* **1978**, *43*, 1975–1980.

[5] An excellent paper is found in F. Weinelt, H. J. Schneider, *J. Am. Chem. Soc.* **1991**, *56*, 5527–5535.

[6] Some examples: a) G. M. Whitesides, J. P. Mathias, C. T. Seto, *Science* **1991**, *254*, 1312–1319; b) R. G. Chapman, J. C. Sherman, Tetrahedron **1997**, *53*, 15911–15945; c) G. A. Ozin, *Chem. Commun.* **2000**, 419–432; d) M. Fujita, D. Oguro, M. Miyazawa, H. Oka, K. Yamaguchi, K. Ogura, *Nature* **1995**, *378*, 469–471; e) J. Rebek, Jr., *Acc. Chem. Res.* **1999**, *32*, 278–286.

[7] a) P. Timmermann, R. H. Vreekamp, R. Hulst, W. Verboom, D. N. Reinhoudt, K. Rissanen, K. A. Udachin, J. Ripmester, *Chem. Eur. J.* **1997**, *3*, 1823–1832; b) R. H. Vreekamp, W. Verboom, D. N. Reinhoudt, *Rec. Trav. Chim. Pays-Bas* **1996**, *115*, 363–370; c) R. H. Vreekamp, J. P. M. van Duynhoven, M. Hubert, W. Verboom, D. N. Reinhoudt, *Angew. Chem.* **1996**, *108*, 1306–1309; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1215–1218; d) O. Danny Fox, M. G. B. Drew, P. D. Beer, *Angew. Chem.* **2000**, *112*, 139–144; *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 135–140.

[8] Some examples include: a) J. Scheerder, R. H. Vreekamp, J. F. J. Engbersen, W. Verboom, J. P. M. van Duynhoven, D. N. Reinhoudt, *J. Org. Chem.* **1996**, *61*, 3477–3481; b) K. Koh, K. Araki, S. Shinkai, *Tetrahedron Lett.* **1994**, *35*, 8255–8258; c) O. Struck, W. Verboom, W. J. J. Smeets, A. L. Spek, D. N. Reinhoudt, *J. Chem. Soc. Perkin Trans. 2* **1997**, 223–227; d) M. H. B. Grote Gansey, F. J. Steemers, W. Verboom, D. N. Reinhoudt, *Synthesis* **1997**, 643–648; e) K. A. Jolliffe, M. C. Calama, R. Fokkens, N. M. M. Nibbering, P. Timmermann, D. N. Reinhoudt, *Angew. Chem.* **1998**, *110*, 1294–1297; *Angew. Chem. Int. Ed.* **1998**, *37*, 1247–1251; f) K. A. Jolliffe, P. Timmermann, D. N. Reinhoudt, *Angew. Chem.* **1999**, *111*, 983–986; *Angew. Chem. Int. Ed. 1999*, *38*, 933–937; g) R. K. Castanello, D. M. Rudkevich, J. Rebek, Jr., *J. Am. Chem. Soc.* **1996**, *118*, 10002–10003; h) B. C. Hamann, K. D. Shimizu, J. Rebek, Jr, *Angew. Chem.* **1996**, *108*, 1425–1427; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1326–1329; i) O. Mogck, V. Böhmer, W. Vogt, *Tetrahedron* **1996**, *52*, 8489–8496; j) O. Mogck, E. F. Paulus, V. Böhmer, I. Thondorf, W. Vogt, *Chem. Commun.* **1996**, 2533–2534; k) F. Inokuchi, S. Shinkai, *J. Chem. Soc. Perkin Trans. 2* **1996**, 601–605; l) M. S. Brody, C. A. Schalley, D. M. Rudkevich, J. Rebek, Jr., *Angew. Chem.* **1999**, *111*, 1738–1742, *Angew. Chem. Int. Ed.* **1999**, *38*, 1640–1644; m) J. Rebek, Jr., *J. Chem. Soc. Chem. Comm.* **2000**, 637–643; n) S. K. Körner, F. T. Tucci, D. M. Rudkevich, T. Heinz, J. Rebek, Jr., *Chem. Eur. J.* **2000**, *6*, 187–195; o) M. M. Conn, J. Rebek, Jr., *Chem. Rev.* **1997**, *97*, 1647–1668.

[9] a) L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469–472; b) T. Gerkensmeier, W. Iwanek, C. Agena, R. Fröhlich, S. Kotila, C. Näther, J. Mattay, *Eur. J. Org. Chem.* **1999**, 2257–2262.

[10] T. Gerkensmeier, M. Schwertfeger, W. Buchheim, J. Mattay, unpublished results.

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