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Functionalized binaphthyl salophen [a] crown ethers as models for the enzyme urease

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Abstract. Functionalized binaphthyl salophen crown ethers **2** and **3** containing a Lewis-acidic uranyl cation were prepared by the Ba^{2+}-templated cyclization of dialdehydes **15** and **22**, for which two convenient synthetic routes were developed, with diamines **23** and **24**. Intramolecular complexation of the amide groups in metallomacrocycles **2** and **3** was demonstrated by the isolation of two different forms of **2a**, which were observed to interconvert, by ^{1}H-NMR and IR spectroscopy and by electrochemical measurements. Use of diamine **24** during the cyclization resulted in the formation of two different stereoisomers of the monofunctionalized metallomacrocycles **3a-d** and in "sidedness" of the bisfunctionalized metallomacrocycles **3e** and **3f**. Solid complexes of urea and **2c** and **2d** were isolated, but no catalytic activity was observed for **2a** in the hydrolysis of urea in dioxane/water.

Introduction

The complexation of neutral guests by receptor molecules containing an electrophilic metal ion for coordination to the guest molecules is well documented[1]. Despite the important role that metal ions play in many enzymatic reactions, however, there are not many examples of supramolecular *metalloenzyme* models[2].

Previously, we have shown that the uranyl-containing salophen crown ethers **1** are well suited for the complexation of small, polar, neutral molecules such as urea, formamide, acetamide, etc[1b,c,e]. As especially urea[3] is complexed very well by these metallomacrocycles[1c], we decided to investigate the possibility of using these receptor molecules as models for the enzyme urease.

When the uranyl salophen crown ethers are considered as potential models for the enzyme urease, it becomes clear from consideration of the proposed mechanism (Figure 16, Ref. 4b), that some of the requirements are already fulfilled. The salophen crown ethers contain a metal ion for the complexation of urea by coordination to the carbonyl oxygen atom, although an uranyl ion is present instead of a nickel ion. The salophen crown ethers also contain partly negatively charged ether oxygen atoms, which should be able to fulfill the role of the negatively charged functionality in the active site of urease in stabilizing the metal-ion-coordination-induced positive charge on the amino groups of the urea molecule. Missing from the model are the nucleophile (a coordinated hydroxide ion in the active site of urease) and the general acid, which is required for the productive breakdown of the tetrahedral intermediate[4].

As a first approach, we have replaced an ethylene glycol unit of metallomacrocycles **1** by a 1,1′-binaphthol unit[1h], a building block which allows the incorporation of functional groups close to the cavity of the macrocycle. The isolation of solid complexes with urea[1h] and the enhanced rate of urea transport through a supported liquid membrane[5] showed that the resulting binaphthyl salophen crown ethers are indeed able to complex urea. Furthermore, molecular-mechanics calculations indicated that the metallomacrocycles have the appropriate geometry for positioning substituents in the 3- and 3′-positions of the binaphthyl moiety close to the complexed substrate molecules[1h].

Therefore, we decided to synthesize the functionalized binaphthyl salophen crown ethers **2** and **3**, which contain either one or two phenolic OH groups close to the complexed urea molecule. According to molecular-mechanics calculations, the carboxamide groups direct the phenolic OH groups, which may act as general acids during the breakdown of the tetrahedral intermediate formed during the hydrolysis of urea, towards the cavities of the metallomacrocycles. The acidity of these OH groups can be modified by the introduction of electron-donating or -withdrawing substituents (X).

In this paper, two routes are described for the synthesis of the functionalized binaphthyl salophen crown ethers **2** and **3**. The structures of these metallomacrocycles have been studied by molecular-mechanics calculations, ^{1}H-NMR spectroscopy, and electrochemistry. The hydrolysis of urea in the presence of metallomacrocycle **2a** has been investigated.

Results and discussion

Synthesis

In the synthesis of **2** and **3**, the macrocyclization reaction in which the rather labile Schiff bases are formed was

[a] Salophen = *N,N′*-phenylene(salicylideneiminate)

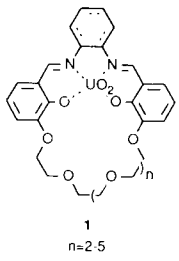


Chart 1.

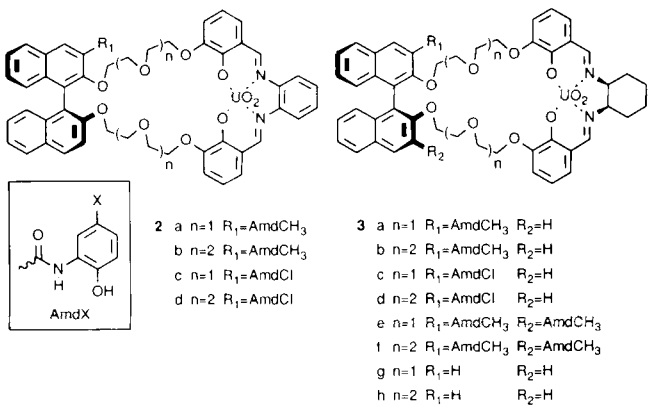
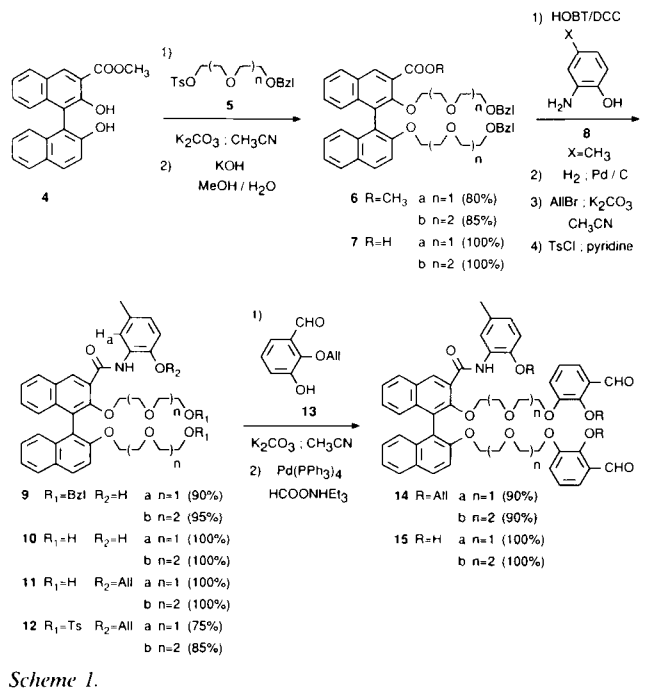


Chart 2.



Scheme 1.

performed as the last step. Two different routes for the preparation of the required bis(2-hydroxybenzaldehyde) derivatives **15** are described.

Linear synthesis. In the first approach (Scheme 1), the building blocks for the crown ether ring, the salophen unit, and the functional group are added step by step to the functionalized binaphthol. This approach gives rise to a linear synthesis, which is rather long but gives high yields for each step.

Binaphthol **4**[6a] was dialkylated with tosylates [b] **5**, prepared[1h] from the monobenzyl ethers of di- or triethylene glycol[7] by reaction with tosyl chloride in pyridine, to give esters **6** in good yield (80–85%). In the ^{1}H-NMR spectra, the singlets at 10.85 and 5.01 ppm for the OH groups of **4** have disappeared, demonstrating that O-alkylation has occurred. The IR spectra show absorptions at 1729 cm^{-1} for the ester group. The singlet for H-4 of the binaphthyl moiety, which is a useful diagnostic probe in the ^{1}H-NMR spectra, has shifted from 8.71 to 8.44 ppm. The C_2 symmetry of the binaphthyl unit of **6** is destroyed by the presence of the ester substituent in the 3-position. This lack of symmetry is clearly visible in the ^{1}H-NMR spectra from the non-equivalence of the polyethylene glycol substituents. Two singlets are observed for the benzylic protons of **5** in the ^{1}H-NMR spectra, *viz.* at 4.39 and 4.41 ppm (**6a**) and at 4.51 and 4.52 (**6b**) ppm.

Saponification of the esters **6** was carried out with KOH in a mixture of MeOH and H_2O. Hydrolysis of the esters was evident from the disappearance of the singlets for the OCH_3 groups at 3.95 ppm in the ^{1}H-NMR spectra of **7**. Incorporation of the required functional group in **7** was accomplished by reacting its carboxylic acid with the appropriate amine **8**. Several methods for the activation of the carboxylic acid of **7** were tried[8]. Although the yields for the different reactions were comparable, it was concluded that the active ester coupling (HOBT/DCC) [c] was most convenient, because this method was not very moisture-sensitive and gave easily reproducible yields.

In the ^{1}H-NMR spectra of amides **9**, a considerable downfield shift is observed for the amide NH protons (10.65 ppm), indicating that a hydrogen bond is formed between the amide group and (probably) the naphtholic ether oxygen atoms. This gives rise to a six-membered-ring intramolecular hydrogen bond, which is well known to be very stable[9], and which is also found in molecular-mechanics calculations. A downfield shift is also observed in the ^{1}H-NMR spectra for the phenolic OH groups of **9** (9.0 ppm). Probably, the phenolic OH groups form an intramolecular hydrogen bond with the neighboring carbonyl groups or with one of the polyethylene glycol oxygen atoms. Indications for hydrogen bonding to the carbonyl oxygen are observed in the IR spectra of **9**, which show two absorptions for the C=O group, *viz.* at 1665 cm^{-1} for the free and at 1643 cm^{-1} for the hydrogen-bonded carbonyl group.

Removal of the protective benzyl ethers was achieved by catalytic hydrogenation on Pd/C. It was observed that the hydrogenation should be stopped as soon as debenzylation was complete, because a by-product was formed if the hydrogenation mixture was left overnight. The presence of the by-product in the reaction mixture was indicated by additional signals at *e.g.* 10.66 (s, NH), 8.84 (s, BinC$_4$H), 2.7–2.9, 2.0–2.5, and 1.5–1.8 ppm in the ^{1}H-NMR spectra of **10**, which are consistent with partial reduction of the binaphthyl unit[10].

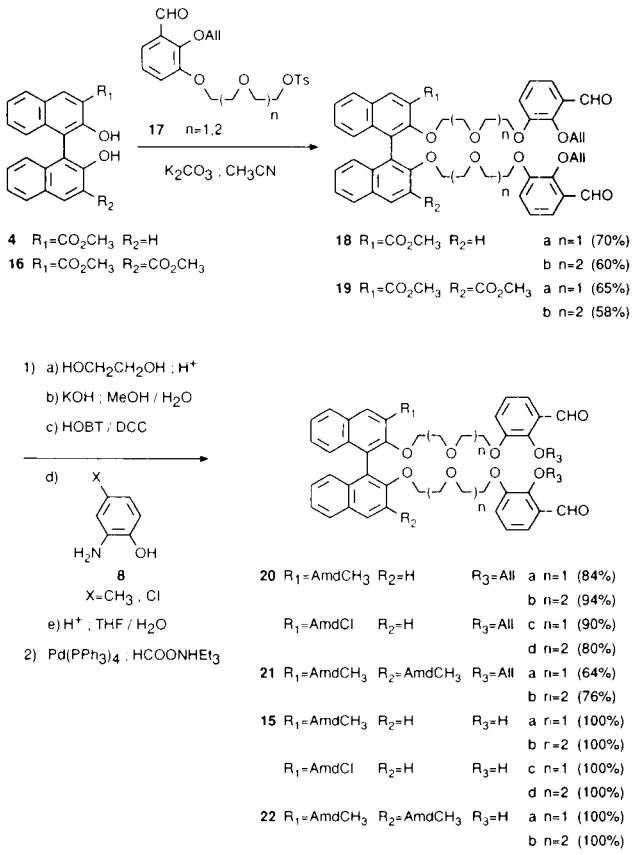
The phenolic OH groups of **10** were selectively protected by using the differences in acidity of the phenolic and aliphatic OH groups. Reaction of **10** with a slight excess of allyl bromide and K_2CO_3 in refluxing CH_3CN resulted in clean allylation of the phenolic OH groups. The reaction was monitored by TLC, using a $FeCl_3$ solution to indicate the presence of free phenolic OH groups. In the IR spectra of **11**, only one absorption is visible for the C=O group of the amides. The value of 1666 cm^{-1} indicates that the carbonyl groups are no longer hydrogen-bonded after alkylation of the phenolic OH groups. There is a remarkable downfield shift observed in the ^{1}H-NMR spectra for the signals due to protons H_a (Scheme 1),

[b] Tosyl = 4-toluenesulfonyl = 4-methylbenzenesulfonyl.

[c] HOBT = 1-hydroxybenzotriazole DCC = 1,3-dicyclohexylcarbodiimide.

which shift from around 7.1 ppm (**10**) to 8.54 ppm (**11**), indicating that the aromatic ring of the functional group changed its orientation after alkylation of the phenolic OH group.

Tosylation of diols **11** with tosyl chloride in pyridine at 0°C gave **12** in good yield (75–85%). In the IR spectra, absorptions at 1355 and 1177 cm^{-1} prove the presence of the sulfonate esters. Alkylation of the protected 2,3-dihydroxybenzaldehyde derivative **13**[1c] with ditosylates **12** afforded the protected dialdehydes **14** in high yield (90%). In the IR spectra, separate signals are observed for the amide carbonyl (1668 cm^{-1}) and for the aldehyde carbonyl groups (1687 cm^{-1}). Deprotection of **14** was achieved by reductive deallylation with $Pd(PPh_3)_4$ as the catalyst and $HCOONHEt_3$ as the reducing agent[11]. In spite of the small differences in R_f value of **14** and **15**, the reaction could easily be monitored by TLC if a $FeCl_3$ solution was used to indicate the appearance of the free phenolic OH groups. In the ^{1}H-NMR spectra of **15** no signals were observed for the allyl ethers. The OH groups of the 2-hydroxybenzaldehyde units show two singlets in the ^{1}H-NMR spectra at 10.87 and 10.83 ppm (**15a**) and at 10.82 and 10.79 ppm (**15b**). The large downfield shifts for the OH groups indicate that they are hydrogen-bonded to the aldehyde groups. The non-equivalence of the two OH groups is caused by the lack of C_2 symmetry of the molecule resulting from the substituent in the 3-position of the binaphthyl unit. This non-equivalence is observed both in ^{1}H-NMR and ^{13}C-NMR spectra. The OH groups of the amide substituents exhibit singlets around 9.0 ppm in the ^{1}H-NMR spectra, indicating that they are hydrogen-bonded. In the IR spectra only one absorption is observed for the carbonyl of both the amide and the aldehyde groups (1657 cm^{-1}).



Scheme 2.

Convergent synthesis. In the second approach, the building blocks for the crown ether ring and the salophen unit are attached to the functionalized binaphthol in one step (Scheme 2). The required functional groups are incorporated in the molecule in a separate reaction. The advantage of this route is that esters **18** and **19** are common intermediates for differently functionalized salophen crown ethers. After the introduction of the different functional groups, only a few steps are needed to prepare the aldehydes **15** and **22**, which are required for the cyclization reaction.

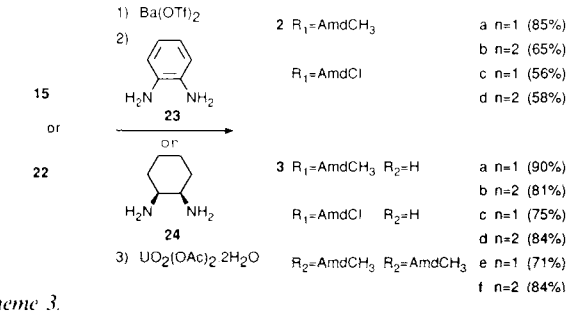
Functionalized binaphthols **4** and **16**[12] were dialkylated with tosylates **17**, prepared[1h] by alkylation of aldehyde **13** with the monotosylates of di- and triethylene glycol[13] and subsequent tosylation of the resulting alcohol with tosyl chloride in pyridine, to give esters **18** and **19** in good yield (60–70%). In the ^{1}H-NMR spectra of **18**, two signals are observed for the aldehyde groups around 10.4 ppm. As the diesters **19** have C_2 symmetry, only one aldehyde signal is observed in their ^{1}H-NMR spectra at 10.4 ppm. A singlet at 3.95 ppm in the ^{1}H-NMR spectra of **18** and **19** shows that the ester groups are still present. In the IR spectra, absorptions for both the ester carbonyl (1728 cm^{-1}) and for the aldehyde carbonyl groups (1687 cm^{-1}) are observed.

The conversion of the esters **18** and **19** into the amides **20** and **21** started with the protection of the aldehyde groups as acetals, as the aldehyde groups were expected to give side reactions both during the alkaline saponification of the esters (Cannizzarro reaction) and during the amide coupling (formation of Schiff bases). Acetalization was performed by refluxing a solution of **18** or **19** in $CHCl_3$ with a 20-fold excess of ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid over molecular sieves (3 Å) to remove the liberated water. In the ^{1}H-NMR spectra of the products, the signals around 10.4 ppm for the aldehyde groups have disappeared and new singlets are observed around 6.1 ppm for the acetal protons (O–CH–O).

The esters were saponified by refluxing a solution of the diacetals in $MeOH/H_2O$ (3:1) with a 20-fold excess of KOH. After careful acidification of the reaction mixture with citric acid, the carboxylic acids were isolated. In the ^{1}H-NMR spectra, the absence of the singlets at 3.95 ppm for the ester OCH_3 groups shows that hydrolysis has taken place. The protecting acetal groups are still intact after the acidification, as demonstrated by the signals around 6.1 ppm for the acetal protons (O–CH–O).

The carboxylic acids were converted into active esters with HOBT and DCC, which were reacted in situ with the appropriately substituted 2-aminophenol **8** to give amides **20** and **21** in good overall yield (64–94%), after hydrolysis of the protecting acetal groups with acidic aqueous THF and purification by column chromatography. The large downfield shifts in the ^{1}H-NMR spectra of the singlets for the NH protons reveal that they are strongly hydrogen-bonded to the naphtholic ether oxygen atoms. In the ^{1}H-NMR spectra the phenolic OH groups of the amide substituents show singlets around 9.1 ppm (X = CH_3) and 9.3 ppm (X = Cl). In the IR spectra, separate absorptions are observed for the aldehyde carbonyl (1686 cm^{-1}) and the amide-carbonyl groups (1644 cm^{-1}). The values of the amide-carbonyl absorptions suggest that the carbonyl is involved in a hydrogen bond.

Amides **20** and **21** were deallylated[11] with $Pd(PPh_3)_4$ and $HCOONHEt_3$ to give bis(2-hydroxybenzaldehyde) derivatives **15** and **22** in quantitative yield. For X = CH_3, the "normal" excess of 3 equiv of $HCOONHEt_3$ per allyl ether was used, but for X = Cl a smaller excess of 1.5 equiv was used and the reaction was carefully monitored by TLC, since it is known that both $Pd(PPh_3)_4$[14] and metallic Pd[15], which is often formed at the end of the



Scheme 3.

reductive deallylation by decomposition of the complex, can cleave aryl–halogen bonds in the presence of formate ions as a reducing agent. The products with X = CH_3 are identical with the aldehydes **15a** and **15b** obtained via the first route. Aldehydes **15c** and **15d** (X = Cl) show comparable spectroscopic properties to **15a** and **15b**. The presence of chlorine atoms in **15c** and **15d** after the reductive deallylation is demonstrated by the FAB mass spectra, which show M + 1 peaks at *m/z* 872.5 and 960.6, respectively, and by ^{1}H-NMR spectroscopy, which shows that protons H_a only have a *meta* coupling (1.3 and 2.3 Hz, respectively) and no *ortho* coupling.

Cyclization. Dialdehydes **15** and **22** were cyclized (Scheme 3) by the addition of 1 equiv of diamines **23** or **24** to a solution of **15** or **22** and 2 equiv of $Ba(OTf)_2$[16] in THF. The Ba^{2+} ions act as template ions[1a–c], bringing the two aldehyde groups of **15** or **22** close together by coordinating with the polyether oxygen atoms. Addition of $UO_2(OAc)_2$ gave the crude uranyl salophen crown ethers **2** and **3** after some washing steps to remove the barium salts and the acetic acid formed.

Metallomacrocycles **2a** and **2b** were purified by precipitation from a CH_2Cl_2 solution with cyclohexane. Salophen crown ethers **2c** and **2d** were purified by addition of a solution of excess urea in CH_3CN to a solution of **2c** and **2d** in refluxing CH_3CN. Upon cooling, the urea complexes of **2c** and **2d** precipitated. Metallomacrocycles **3b, 3d, 3e**, and **3f** were purified by flash column chromatography on silica gel, followed by precipitation from a solution in CH_2Cl_2 with cyclohexane. Salophen crown ethers **3a** and **3c** were purified by trituration with CH_2Cl_2. Attempts to purify these metallomacrocycles by column chromatography failed because they precipitated on the silica gel.

The solubility behavior of the metallomacrocycles **2** and **3** is rather peculiar. The salophen crown ethers with the largest rings (**2b, 2d, 3b**, and **3d**) and the bisfunctionalized salophen crown ethers **3e** and **3f** are quite soluble in CH_2Cl_2 and in DMSO. The smaller salophen crown ethers are quite insoluble in dry CH_2Cl_2. Their solubility is increased by the addition of MeOH or by saturating the organic solvent with water. They are not readily soluble in DMSO either, but they can be dissolved by heating them in this solvent for some time. After cooling, they do not precipitate from the DMSO solution.

The IR spectra of macrocycles **2** and **3** show absorptions for the imine bonds at 1602 cm^{-1} (**2**) or at 1615 cm^{-1} (**3**) and for the uranyl cations around 900 cm^{-1}. None or very weak absorptions are observed in the IR spectra for the amide carbonyl groups. The FAB mass spectra show M + 1 peaks for the salophen crown ethers, indicating that the uranyl cations are tightly bound. Some characteristic features of the ^{1}H-NMR and ^{13}C-NMR spectra will be discussed below.

Structural behavior

As the uranyl salophen crown ethers are known to complex with substrate molecules containing an amide functionality[1], the possibility of intramolecular complexation of the amide substituent in the 3-position of the binaphthyl unit was examined.

According to CPK models and molecular-mechanics calculations, coordination of the amide carbonyl oxygen atom to the uranyl cation is sterically possible, provided that the N substituent of the amide group is rotated through the crown ether ring. This interconversion is difficult, according to CPK models, for the smaller metallomacrocycles (**2a, 2c, 3a, 3c**, and **3e**), which should give rise to a slow rate of interconversion for these compounds, but it is relatively easy for the larger metallomacrocycles (**2b, 2d, 3b, 3d**, and **3f**).

If the ^{1}H-NMR spectrum of **2a** in $CDCl_3$ is examined, it is clear that two different types of molecules are present. Some characteristic signals are listed in Table I.

Although **2a** is not completely stable on silica gel and shows some decomposition, this metallomacrocycle can be fractionated by column chromatography, using EtOAc/CH_2Cl_2 (1 : 2) to elute form I and EtOAc/CH_2Cl_2/MeOH (8 : 16 : 1) to elute form II of the macrocycle. Although the ^{1}H-NMR spectra of both fractions are very different, they both exhibit all the characteristics which are expected for **2a**. In the FAB mass spectra, a M + 1 peak is observed at *m/z* 1192.6 for both forms. The IR spectra of $\mathbf{2a}_I$ and $\mathbf{2a}_{II}$ are very similar, but some distinct differences are observed in the region for the C=O stretch vibrations. Form I reveals an absorption at 1630 cm^{-1} and a shoulder around 1550 cm^{-1}, whereas form II shows a weak absorption around 1650 cm^{-1}.

If separate solutions of $\mathbf{2a}_I$ and $\mathbf{2a}_{II}$ were examined by TLC and ^{1}H-NMR spectroscopy after being left overnight, forms I and II were found to be present in both solutions. This proves that $\mathbf{2a}_I$ and $\mathbf{2a}_{II}$ are two forms of the same molecule, which interconvert very slowly[17].

The available evidence suggests that $\mathbf{2a}_I$ is the intramolecular amide complex and $\mathbf{2a}_{II}$ is the water complex. Evidence for these proposed structures comes from the ^{1}H-NMR spectra of the two forms of **2a**. Form I shows a very asymmetric salophen unit, which is in agreement with the fact that the amide substituent is very close to only one side of the salophen unit. In the ^{1}H-NMR spectrum of form II, a broad signal is observed at 5.3 ppm for a coordinated water molecule, which is absent in the spectrum of $\mathbf{2a}_I$. The shift in the IR spectrum of form I of the carbonyl stretch frequency to lower wavenumbers (1630 cm^{-1} for $\mathbf{2a}_I$ compared with 1650 cm^{-1} for $\mathbf{2a}_{II}$) is also in agreement with oxygen coordination in form I. The chromatographic behavior of forms I and II shows that $\mathbf{2a}_I$ has less interactions with the silica gel than $\mathbf{2a}_{II}$, which can be rationalized by the assumption that form I has a permanent intramolecular ligand coordinated to the fifth coordination site of the uranyl cation. Form II, on the other hand, has a water molecule coordinated to the uranyl cation, which may exchange with silanol groups of the silica gel. This compound only becomes mobile if an excess of guest (MeOH) is added to the eluent.

Table I Characteristic ^{1}H NMR signals for **2a** *(ppm, $CDCl_3$).*

	Form I	Form II
CONH	11.15	10.68
HC=N	9.43	9.40
HC=N	9.35	9.38
$BinC_4H$	9.12	8.96
$AmdCH_3$	1.89	2.03

The ^{1}H-NMR spectrum of **2b** in $CDCl_3$ resembles that of **2a**$_{II}$. The larger ring size of this macrocycle allows a much faster interconversion between the two possible forms of the salophen crown ether, which explains why only the most stable conformation is observed. Additional evidence for intramolecular coordination of the amide carbonyl group to the uranyl cation was obtained by IR spectroscopy. As has been mentioned earlier, only weak absorptions are observed in the IR spectra of **2** and **3** for the carbonyl groups of the amides around 1650 cm^{-1}. The frequency of the carbonyl stretch vibrations will be shifted to lower wavenumbers both by hydrogen bonding and by coordination to the metal ion. As a result of this, the absorptions of the amide carbonyl groups are obscured by those of the imine bonds.

Hydrogen bonding alone cannot be responsible for the disappearance of the amide carbonyl absorptions in the IR spectra, because strong absorptions are observed at 1650 cm^{-1} for the amide carbonyl groups and at 1625 cm^{-1} for the urea carbonyl group in the IR spectra of the urea complexes of **2c** and **2d** (*vide supra*). In these urea complexes, hydrogen bonding to the amide carbonyl is still possible. Coordination of the amide group to the uranyl cation can no longer occur, however, because the vacant coordination site of the uranyl cation is occupied by the urea molecule.

As the IR spectra were recorded in the solid state, both intra- and intermolecular coordination of the amide group to the uranyl cation is possible. Therefore, IR spectra of **3b** both in $CHCl_3$ and in DMSO were measured. The IR spectrum of **3b** in $CHCl_3$ only showed an absorption for the imine bonds at 1615 cm^{-1}. This shows that the amide group is coordinated to the uranyl cation. As the solution was quite dilute, intramolecular coordination is most likely. In DMSO, the solvent is expected to compete with the amide group for the coordination site of the uranyl cation, because DMSO is known to form complexes with salophen crown ethers[1c,e]. The IR spectrum of **3b** in DMSO shows strong absorptions at 1665 cm^{-1} for the amide carbonyl group and at 1615 cm^{-1} for the imine bonds, demonstrating that the amide group is no longer coordinated to the uranyl cation.

The ^{1}H-NMR spectrum of **3a** in DMSO-d_6 also indicates the presence of two different compounds, even after heating at 100°C for 30 min. The differences are much smaller, however, than for **2a**. The ratio of the two compounds is approximately 1 : 1.4. The two compounds could not be separated by TLC. As DMSO is a good ligand for the uranyl cation, it is not very likely that these compounds correspond to the intramolecular amide and the solvent complex, as was the case for **2a**. It is much more likely that the two compounds are diastereomers resulting from the "sidedness", which is introduced in the metallomacrocycles by the use of *cis*-1,2-cyclohexanediamine. The two compounds, one of which has the functional group and the cyclohexyl ring on the same side of the crown ether, while the other one has them on opposite sides, are expected to have very similar properties.

In the ^{1}H-NMR spectra of **3b**, no evidence is found for the presence of two different compounds. Presumably, the differences between the two compounds are so small because of the large distance between the binaphthyl unit and the salophen moiety.

The C_2 symmetry of the disubstituted binaphthyl unit of **3e** and **3f** is disrupted by the *cis*-1,2-cyclohexanediamine unit. This is clearly observed in the ^{1}H- and ^{13}C-NMR spectra of **3e** and **3f** in $CDCl_3$, which show two signals in the ratio 1 : 1 for virtually all atoms of the binaphthyl unit and of the functional groups. The ^{1}H- and ^{13}C-NMR spectra of **3e** and **3f** in DMSO-d_6 are much simpler and show only one signal for the different atoms of the binaphthyl unit and of the functional groups. Probably, DMSO decreases the interactions between the binaphthyl unit and the salophen unit by disrupting the hydrogen bonds, which rigidify the metallomacrocycles considerably.

Table II Reduction potentials of binaphthyl salophen crown ethers 3[18] *in DMSO.*

	R_1	R_2	n	E_c (V)
3g	H	H	1	−1.1615
3a	AmdCH$_3$	H	1	−1.0723
3e	AmdCH$_3$	AmdCH$_3$	1	−1.0226
3h	H	H	2	−1.1545
3b	AmdCH$_3$	H	2	−1.0965
3f	AmdCH$_3$	AmdCH$_3$	2	−1.0050

Electrochemistry

The intramolecular complexation of the amide groups to the uranyl cation in the binaphthyl salophen crown ethers with, respectively, zero, one, and two functional groups was also investigated by cyclic voltammetry. For each compound, series of cyclic voltammograms were recorded in DMSO at different scan rates (0.2, 0.5, 1.0, and 1.5 V/s) and at different urea concentrations (from 0 to 0.12 M).

The metallomacrocycles show very similar electrochemical behavior. A single reduction and a single oxidation step are observed. The distances between the cathodic and the anodic peaks (ΔE_p) are approximately 70–80 mV and are nearly independent of the scan rate. The i_p values are linear to the square roots of the scan rate, indicating a diffusion-controlled process.

The reduction potentials of the metallomacrocycles in the absence of urea, show a clear dependence on the structure of the compound (Table II), becoming progressively more positive on going from zero, to one, and to two amide substituents. It can be concluded from this shift, that there is decreasing DMSO complexation in this series, which might indicate that intramolecular complexation of the amide groups is increasingly effective.

Addition of urea to the solutions of the metallomacrocycles in DMSO shifts the reduction potential to more positive values (Figure 1), which suggests that there is a competition between urea and DMSO in the complexation reaction. Unfortunately, the shifts in DMSO are too small to estimate an association constant for the complexation of urea.

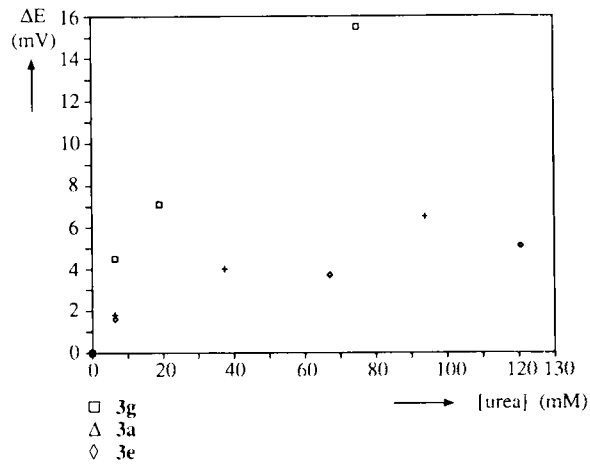


Figure 1. $\Delta E = E_c - E_{c,ligand}$ *as a function of the urea concentration.*

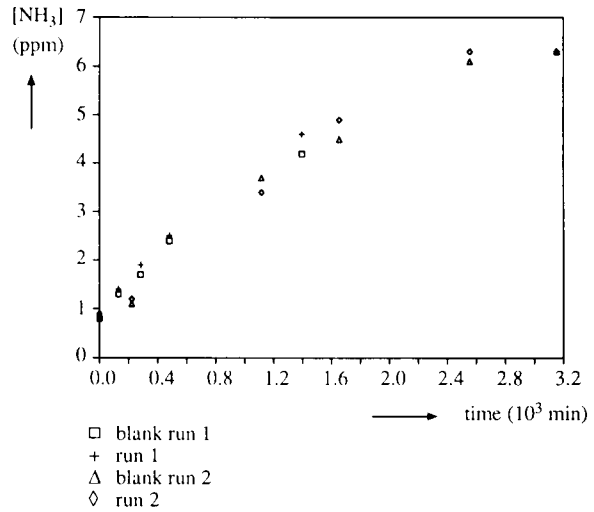


Figure 2. Concentration of NH_3 as a function of time, in the absence and presence of **2a**.

Hydrolysis experiments

To investigate whether the functionalized binaphthyl salophen crown ethers show catalytic activity, the rate of degradation of urea in the absence and presence of enzyme model was examined. The hydrolysis reactions were performed in dioxane/water 4:1 (v/v) at 80°C, which has the advantage that the spontaneous degradation of urea occurs at a measurable rate, so that catalytic activity of the enzyme model will show up as an observable rate increase.

Due to the composition of the reaction mixture, it was not possible to monitor the reaction by simply observing pH changes. Therefore, the ammonia formed by the degradation of urea was isolated from the reaction mixture. Of the available methods[19], microdiffusion[20] seemed to be the most convenient, because it is reasonably fast and it can be used to isolate small quantities of ammonia. Because the presence of dioxane in the samples interfered with colorimetric determination[21] of the ammonia concentration, the samples were analyzed by ion chromatography.

The results of two separate runs (blank: [urea] = 10 mM; exp: [urea] = 10 mM and [**2a**] = 3 mM) are shown in Figure 2.

These results clearly show that there is no significant difference in the rate of decomposition of urea in the absence and presence of **2a**. No difference in rate was observed when the concentration of urea in the reaction mixture was increased to 2.5 M. Furthermore, the downward curvature, which is observed in Figure 2, indicates that only degradation of urea to ammonium cyanate takes place in both cases. It is known[22], that the rate of degradation of urea under neutral conditions levels off with increasing conversion, because the reverse reaction, the formation of urea from ammonia and cyanic acid, becomes increasingly important. No reverse reaction occurs, however, if urea is hydrolyzed to ammonia and carbon dioxide.

There are many possible explanations for the lack of catalytic activity. The association constant of **2a** with urea may be too low at 80°C in the solvent mixture used, resulting in only a minor fraction of the urea molecules being complexed in the "active site" of the enzyme model. Another possibility is that oxygen coordination to the uranyl cation alone does not activate urea strongly enough to accelerate the hydrolysis reaction. Additional functional groups, such as a good nucleophile, might be necessary to catalyze the reaction.

Conclusions

As the functionalized binaphthyl salophen crown ethers, for which two convenient synthetic routes were developed, show no catalytic activity in the hydrolysis of urea, future research will be directed at the development of enzyme models containing two complexed metal ions for complexing with both the substrate molecule (urea) and with a nucleophilic solvent molecule.

Experimental

General methods

NMR spectra were recorded on a Bruker AC 250 spectrometer in $CDCl_3$ with Me_4Si as internal standard unless stated otherwise. Assignments of the NMR spectra are according to the numbering in Chart 3. Mass spectra were obtained with a Finnigan MAT 90 spectrometer. Positive-ion fast-atom bombardment (FAB) mass spectra were recorded using *m*-nitrobenzyl alcohol as matrix. IR spectra were recorded with a Nicolet 5 SCX FT spectrophotometer. Melting points were determined using a Reichert melting-point apparatus and are uncorrected. Elemental analyses were carried out by a Model 1106 Carlo Erba Strumentazione Elemental Analyzer. CH_2Cl_2, EtOAc, and hexane were distilled before use. CH_3CN was stored over molecular sieves (4 Å) prior to use. THF was distilled from sodium/benzophenone. DCC was distilled *in vacuo*. 2-Amino-4-methylphenol and 2-amino-4-chlorophenol were purified by sublimation. Other chemicals were of reagent grade and were used without purification. Column chromatography was performed with silica gel (Merck, 0.040–0.063 mm). All reactions were carried out under an argon atmosphere. Compounds **4**[6a], **5**[1h], **13**[1c], **16**[12], and **17**[1h] were prepared according to literature procedures. Care should be taken when handling uranyl-containing compounds because of their toxicity and radioactivity[23].

General procedure for the synthesis of esters **6**

A mixture of binaphthol **4** (1.72 g, 5 mmol), tosylate **5** (11 mmol), and K_2CO_3 (1.52 g, 11 mmol) in CH_3CN (25 ml) was refluxed overnight. The reaction mixture was cooled, diluted with CH_2Cl_2 (25 ml) and filtered through Celite. After removal of the solvent, the crude products were purified by flash column chromatography to give colorless oils.

2,2'-Bis[2-[2-(phenylmethoxy)ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxylic acid methyl ester (**6a**). Eluent EtOAc/hexane 2:3; yield 80%. ^1H NMR: δ 8.44 (s, 1H, $BinC_4H$); 7.92 (d, 1H, J 9.0 Hz, $BinC_{4'}H$); 7.87 (d, 1H, J 8.0 Hz, $BinC_5H$); 7.81 (d, 1H, J 7.8 Hz, $BinC_{5'}H$); 7.40 (d, 1H, J 9.0 Hz, $BinC_{3'}H$); 7.4–7.1 (m, 16H, ArH); 4.41 and 4.39 (s, 2×2H, $ArCH_2O$); 4.2–4.0 (m, 2H, CH_2O); 3.93 (s, 3H, OCH_3); 3.8–3.0 (m, 14H, CH_2O). ^{13}C NMR: δ 166.9 (s, C=O); 154.1, 153.2 (s, $BinC_{2,2'}$); 138.2, 138.1 (s, $BzlC_{1,1'}$); 135.7, 133.7 (s, $BinC_{8a,8a'}$); 132.5 (d, $BinC_4$); 129.9 (d, $BinC_{4'}$); 129.6, 129.0 (s, $BinC_{4a,4a'}$); 128.8 (d, $BinC_5$); 128.2 (d, Bzl); 127.8 (d, $BinC_{5'}$); 127.7, 127.6, 127.5 (d, Bzl); 114.5 (d, $BinC_{3'}$); 73.1–69.1 (t, CH_2O); 52.3 (q, OCH_3). IR (KBr): 1729 (OC=O) cm^{-1}. Ms (EI) m/z: 700.303 (M^+, calcd. for $C_{44}H_{44}O_8$ 700.304).

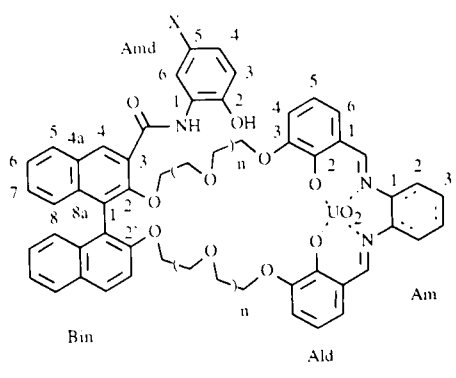


Chart 3.

2,2'-Bis[2-[2-[2-(phenylmethoxy)ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxylic acid methyl ester (**6b**). Eluent EtOAc/hexane 2:1; yield 85%. ^{1}H NMR: δ 8.46 (s, 1H, $BinC_4H$); 8.0–7.9 (m, 2H, $BinC_{4',5}H$); 7.82 (d, 1H, *J* 7.8 Hz, $BinC_{5'}H$); 7.40 (d, 1H, *J* 8.9 Hz, $BinC_{3'}H$); 7.4–7.1 (m, 16H, ArH); 4.52 and 4.51 (s, 2×2H, $ArCH_2O$); 4.2–4.1 (m, 2H, CH_2O); 3.95 (s, 3H, OCH_3); 3.8–3.0 (m, 22H, CH_2O). ^{13}C NMR: δ 166.9 (s, C=O); 154.1, 153.2 (s, $BinC_{2,2'}$); 138.1 (s, $BzlC_{1,1'}$); 135.7, 133.7 (s, $BinC_{8a,8a'}$); 132.5 (d, $BinC_4$); 129.9 (d, $BinC_{4'}$); 129.6, 129.0 (s, $BinC_{4a,4a'}$); 128.8 (d, $BinC_5$); 128.3 (d, Bzl); 127.8 (d, $BinC_{5'}$); 127.67, 127.66, 127.5 (d, Bzl); 114.4 (d, $BinC_{3'}$); 73.1–69.2 (t, CH_2O); 52.3 (q, OCH_3). IR (KBr): 1729 (OC=O) cm^{-1}. Ms (EI) *m/z*: 788.356 (M^+, calcd. for $C_{48}H_{52}O_{10}$ 788.355).

General procedure for the synthesis of acids **7**

To a solution of ester **6** (5 mmol) in MeOH (120 ml) was added a solution of KOH (5.6 g, 100 mmol) in H_2O (30 ml) and the mixture was refluxed until the product had disappeared according to TLC (SiO_2; EtOAc/hexane 1:1; *ca.* 1 h). The solvent was evaporated and the residue was divided between CH_2Cl_2 (100 ml) and 1N hydrochloric acid (100 ml). The organic layer was dried (Na_2SO_4) and filtered. Evaporation of the solvent gave the products as colorless oils in quantitative yield.

2,2'-Bis[2-[2-(phenylmethoxy)ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxylic acid (**7a**). ^{1}H NMR: δ 8.87 (s, 1H, $BinC_4H$); 8.00 (d, 1H, *J* 9.1 Hz, $BinC_{4'}H$); 7.95 (d, 1H, *J* 8.1 Hz, $BinC_5H$); 7.87 (d, 1H, *J* 7.9 Hz, $BinC_{5'}H$); 7.45 (d, 1H, *J* 9.1 Hz, $BinC_{3'}H$); 7.5–7.1 (m, 16H, ArH); 4.48 and 4.40 (s, 2×2H, $ArCH_2O$); 4.3–4.1 (m, 2H, CH_2O); 3.8–3.1 (m, 14H, CH_2O). ^{13}C NMR: δ 166.3 (s, C=O); 154.3, 152.4 (s, $BinC_{2,2'}$); 138.0 (s, $BzlC_{1,1'}$); 128.3, 127.71, 127.70, 127.5 (d, Bzl); 114.5 ($BinC_{3'}$); 73.2–69.1 (t, CH_2O). IR (KBr): 3209 (OH); 1728 (OC=O) cm^{-1}. Ms (EI) *m/z*: 686.288 (M^+, calcd. for $C_{43}H_{42}O_8$ 686.288).

2,2'-Bis[2-[2-[2-(phenylmethoxy)ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxylic acid (**7b**). ^{1}H NMR: δ 8.86 (s, 1H, $BinC_4H$); 8.0–7.9 (m, 2H, $BinC_{4',5}H$); 7.87 (d, 1H, *J* 7.6 Hz, $BinC_{5'}H$); 7.44 (d, 1H, *J* 9.0 Hz, $BinC_{3'}H$); 7.5–7.1 (m, 16H, ArH); 4.52 and 4.51 (s, 2×2H, $ArCH_2O$); 4.3–4.1 (m, 2H, CH_2O); 3.8–3.1 (m, 22H, CH_2O). ^{13}C NMR: δ 166.3 (s, C=O); 154.3, 152.4 (s, $BinC_{2,2'}$); 138.2, 138.1 (s, $BzlC_{1,1'}$); 128.3, 127.71, 127.69, 127.5 (d, Bzl); 114.5 ($BinC_{3'}$); 73.1–69.0 (t, CH_2O). IR (KBr): 3207 (OH); 1728 (OC=O) cm^{-1}. Ms (EI) *m/z*: 774.335 (M^+, calcd. for $C_{47}H_{50}O_{10}$ 774.340).

General procedure for the synthesis of amides **9**

To a solution of carboxylic acid **7** (5 mmol) in CH_2Cl_2 (25 ml) were added $HOBT.H_2O$ (0.84 g, 5.5 mmol) and DCC (1.13 g, 5.5 mmol) and the reaction mixture was stirred for 1 h at room temperature. Amine **8** (X = CH_3; 0.68 g, 5.5 mmol) was added and stirring was continued overnight. The reaction mixture was filtered to remove the precipitated DCU (*N,N'*-dicyclohexylurea), diluted with CH_2Cl_2 (25 ml), washed with 2N hydrochloric acid (2×50 ml), and dried (Na_2SO_4). After evaporation of the solvent, the crude products were purified by flash column chromatography to give colorless oils.

N-(2-Hydroxy-5-methylphenyl)-2,2'-bis[2-[2-(phenylmethoxy)ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxamide (**9a**). Eluent EtOAc/hexane 1:1; yield 90%. ^{1}H NMR: δ 10.66 (s, 1H, NH); 9.03 (s, 1H, AmdOH); 8.94 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 7.7 Hz, $BinC_{5'}H$); 7.46 (d, 1H, *J* 9.1 Hz, $BinC_{3'}H$); 7.5–7.1 (m, 17H, ArH); 7.0–6.8 (m, 2H, AmdH); 4.37 and 4.28 (s, 2×2H, $ArCH_2O$); 4.3–4.0 (m, 2H, CH_2O); 3.8–3.0 (m, 14H, CH_2O); 2.22 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 164.5 (s, C=O); 154.2, 152.1 (s, $BinC_{2,2'}$); 146.9 (s, $AmdC_2$); 138.0, 137.9 (s, $BzlC_{1,1'}$); 133.9 (d, $BinC_4$); 130.4 (d, $BinC_{4'}$); 128.3, 127.70, 127.67, 127.6, 127.5 (d, Bzl); 114.6 (d, $BinC_{3'}$); 73.5–69.1 (t, CH_2O); 20.4 (q, $AmdCH_3$). IR (KBr): 3302 (NH, OH); 1665, 1643 (NC=O) cm^{-1}. Ms (EI) *m/z*: 791.360 (M^+, calcd. for $C_{50}H_{49}NO_8$ 791.346).

N-(2-Hydroxy-5-methylphenyl)-2,2'-bis[2-[2-[2-(phenylmethoxy)ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxamide (**9b**). Eluent EtOAc/hexane 1:1; yield 95%. ^{1}H NMR: δ 10.67 (s, 1H, NH); 8.98 (s, 1H, AmdOH); 8.95 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 8.0 Hz, $BinC_{5'}H$); 7.45 (d, 1H, *J* 8.9 Hz, $BinC_{3'}H$); 7.4–7.1 (m, 17H, ArH); 7.0–6.8 (m, 2H, AmdH); 4.49 and 4.46 (s, 2×2H, $ArCH_2O$); 4.3–4.1 (m, 2H, CH_2O); 3.8–3.0 (m, 22H, CH_2O); 2.25 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 164.4 (s, C=O); 154.2, 152.1 (s, $BinC_{2,2'}$); 146.7 (s, $AmdC_2$); 138.1, 138.0 (s, $BzlC_{1,1'}$); 133.8 (d, $BinC_4$); 130.4 (d, $BinC_{4'}$); 128.3, 127.7, 127.58, 127.55 (d, Bzl); 114.7 (d, $BinC_{3'}$); 73.5–69.1 (t, CH_2O); 20.5 (q, $AmdCH_3$). IR (KBr): 3303 (NH, OH); 1665, 1643 (NC=O) cm^{-1}. Ms (EI) *m/z*: 879.421 (M^+, calcd. for $C_{54}H_{57}NO_{10}$ 879.398).

General procedure for the debenzylation of **9**. *Synthesis of* **10**

To a solution of the dibenzyl ether **9** (5 mmol) in a mixture of EtOAc (50 ml) and EtOH (50 ml) was added 10% Pd on carbon (0.2 g). The reaction mixture was stirred in a hydrogen atmosphere until the starting material had disappeared according to TLC (SiO_2; $EtOH/CH_2Cl_2$ 1:9). The hydrogen was removed and the mixture was filtered through Celite. Evaporation of the solvent gave products **10** as colorless oils in quantitative yield.

2,2'-Bis[2-(2-hydroxyethoxy)ethoxy]-N-(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3-carboxamide (**10a**). ^{1}H NMR: δ 10.51 (s, 1H, NH); 9.02 (s, 1H, AmdOH); 8.88 (s, 1H, $BinC_4H$); 8.1–8.0 (m, 2H, $BinC_{4',5}H$); 7.91 (d, 1H, *J* 7.8 Hz, $BinC_{5'}H$); 7.49 (d, 1H, *J* 9.0 Hz, $BinC_{3'}H$); 7.5–7.1 (m, 7H, ArH); 7.0–6.9 (m, 2H, AmdH); 4.4–4.2 (m, 1H, CH_2O); 4.1–4.0 (m, 1H, CH_2O); 3.9–3.8 (m, 1H, CH_2O); 3.7–3.0 (m, 13H, CH_2O); 2.74 (bs, 2H, OH); 2.28 (s, 3H, CH_3). ^{13}C NMR: δ 164.9 (s, C=O); 154.3, 151.9 (s, $BinC_{2,2'}$); 147.7 (s, $AmdC_2$); 133.6 (d, $BinC_4$); 115.2 (d, $BinC_{3'}$); 73.3–69.3 (t, CH_2O); 61.3 (t, CH_2OH); 20.5 (q, $AmdCH_3$). IR (KBr): 3410, 3397 (NH, OH); 1645 (NC=O) cm^{-1}. Ms (EI) *m/z*: 611.251 (M^+, calcd. for $C_{36}H_{37}NO_8$ 611.252).

2,2'-Bis[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]-N-(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3-carboxamide (**10b**). ^{1}H NMR: δ 10.63 (s, 1H, NH); 8.94 (s, 1H, AmdOH); 8.93 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.90 (d, 1H, *J* 7.5 Hz, $BinC_{5'}H$); 7.47 (d, 1H, *J* 9.1 Hz, $BinC_{3'}H$); 7.5–7.1 (m, 7H, ArH); 7.0–6.8 (m, 2H, AmdH); 4.3–4.1 (m, 2H, CH_2O); 3.9–3.1 (m, 24H, CH_2O + OH); 2.28 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 164.4 (s, C=O); 154.3, 152.1 (s, $BinC_{2,2'}$); 146.3 (s, $AmdC_2$); 133.7 (d, $BinC_4$); 114.7 (d, $BinC_{3'}$); 73.3–69.3 (t, CH_2O); 61.5 (t, CH_2OH); 20.6 (q, $AmdCH_3$). IR (KBr): 3319 (NH, OH); 1664, 1648 (NC=O) cm^{-1}. Ms (EI) *m/z*: 699.316 (M^+, calcd. for $C_{40}H_{45}NO_{10}$ 699.304).

General procedure for the allylation of **10**. *Synthesis of diols* **11**

A solution of phenol **10** (5 mmol), allyl bromide (0.73 g, 6 mmol), and K_2CO_3 (0.83 g, 6 mmol) in dry CH_3CN (50 ml) was refluxed until the reaction was completed according to TLC (SiO_2; $EtOH/CH_2Cl_2$ 1:9; *ca.* 3 h). The reaction mixture was cooled, diluted with CH_2Cl_2 (50 ml), and filtered through Celite to give the allylated phenols **11** as oils in quantitative yield.

2,2'-Bis[2-(2-hydroxyethoxy)ethoxy]-N-[5-methyl-2-(2-propenyloxy)phenyl]-[1,1'-binaphthalene]-3-carboxamide (**11a**). ^{1}H NMR: δ 10.41 (s, 1H, NH); 8.81 (s, 1H, $BinC_4H$); 8.54 (d, 1H, *J* 1.7 Hz, $AmdC_6H$); 8.1–8.0 (m, 2H, $BinC_{4',5}H$); 7.91 (d, 1H, *J* 7.9 Hz, $BinC_{5'}H$); 7.47 (d, 1H, *J* 9.0 Hz, $BinC_{3'}H$); 7.5–7.2 (m, 6H, ArH); 6.86 (dd, 1H, *J* 8.3 and 1.6 Hz, $AmdC_4H$); 6.78 (d, 1H, *J* 8.3 Hz, $AmdC_3H$); 6.0–5.7 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.4–4.9 (m, 2H, $OCH_2CH=C\underline{H}_2$); 4.51 (d, 2H, *J* 4.8 Hz, $OC\underline{H}_2CH=CH_2$); 4.3–4.1 (m, 2H, CH_2O); 3.9–3.0 (m, 14H, CH_2O); 2.48 (t, 1H, *J* 6.5 Hz, OH); 2.37 (s, 3H, $AmdCH_3$); 2.21 (t, 1H, *J* 6.2 Hz, OH). ^{13}C NMR: δ 164.0 (s, C=O); 154.0, 152.3 (s, $BinC_{2,2'}$); 145.2 (s, $AmdC_2$); 117.1 (t, $OCH_2CH=\underline{C}H_2$); 114.2 (d, $BinC_{3'}$); 111.5 (d, $AmdC_3$); 73.4–69.0 (t, CH_2O); 61.2 (t, CH_2OH); 21.0 (q, $AmdCH_3$). IR (KBr): 3419, 3339 (NH, OH); 1666 (NC=O) cm^{-1}. Ms (EI) *m/z*: 651.283 (M^+, calcd. for $C_{39}H_{41}NO_8$ 651.283).

2,2'-Bis[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]-N-[5-methyl-2-(2-propenyloxy)phenyl]-[1,1'-binaphthalene]-3-carboxamide (**11b**). ^{1}H NMR: δ 10.46 (s, 1H, NH); 8.81 (s, 1H, $BinC_4H$); 8.54 (s, 1H, $AmdC_6H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.90 (d, 1H, *J* 7.9 Hz, $BinC_{5'}H$); 7.47 (d, 1H, *J* 9.0 Hz, $BinC_{3'}H$); 7.5–7.2 (m, 6H, ArH); 6.9–6.8 (m, 1H, $AmdC_4H$); 6.77 (d, 1H, *J* 8.3 Hz, $AmdC_3H$); 6.0–5.7 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.4–4.9 (m, 2H, $OCH_2CH=C\underline{H}_2$); 4.51 (d, 2H, *J* 4.9 Hz, $OC\underline{H}_2CH=CH_2$); 4.3–4.1 (m, 2H, CH_2O); 3.8–2.9 (m, 24H, CH_2O + OH); 2.36 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 163.6 (s, C=O); 154.0, 152.0 (s, $BinC_{2,2'}$); 145.3 (s, $AmdC_2$); 117.1 (t, $OCH_2CH=\underline{C}H_2$); 114.3 (d, $BinC_{3'}$); 111.3 (d, $AmdC_3$); 73.4–69.1 (t, CH_2O); 61.3 (t, CH_2OH); 21.0 (q, $AmdCH_3$). IR (KBr): 3412, 3335 (NH, OH); 1666 (NC=O) cm^{-1}. Ms (EI) *m/z*: 739.330 (M^+, calcd. for $C_{43}H_{49}NO_{10}$ 739.336).

General procedure for the tosylation of diols **11**. *Synthesis of ditosylates* **12**

To a solution of diol **11** (5 mmol) in pyridine (10 ml) was added tosyl chloride (2.29 g, 12 mmol) in one portion at 0°C. The reaction

mixture was stirred at this temperature for 3 h. After addition of a small amount of ice, the reaction mixture was poured into a mixture of concentrated hydrochloric acid (100 ml) and ice. The hydrochloric acid solution was extracted with CH_2Cl_2 (3×50 ml) and the combined organic phases were washed with 2N hydrochloric acid (2×50 ml). After drying ($MgSO_4$), the solvent was evaporated to give the crude products, which were purified by flash column chromatography to give pure **12** as oils.

2,2'-Bis[2-[2-[[(4-methylphenyl)sulfonyl]oxy]ethoxy]ethoxy]-N-[5-methyl-2-(2-propenyloxy)phenyl]-[1,1'-binaphthalene]-3-carboxamide (**12a**). Eluent EtOAc/hexane 2:3; yield 75%. ^{1}H NMR: δ 10.38 (s, 1H, NH); 8.77 (s, 1H, $BinC_4H$); 8.51 (d, 1H, *J* 1.8 Hz, $AmdC_6H$); 8.0–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 7.8 Hz, $BinC_{5'}H$); 7.68 and 7.66 (d, 2×2H, *J* 8.3 Hz, $TsC_{2,2'}H$); 7.42 (d, 1H, *J* 9.1 Hz, $BinC_{3'}H$); 7.4–7.1 (m, 10H, ArH); 6.9–6.8 (m, 1H, $AmdC_4H$); 6.76 (d, 1H, *J* 8.3 Hz, $AmdC_3H$); 5.9–5.7 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.3–4.9 (m, 2H, $OCH_2CH=C\underline{H}_2$); 4.48 (d, 2H, *J* 4.8 Hz, $OC\underline{H}_2CH=CH_2$); 4.2–4.1 (m, 2H, CH_2O); 3.7–2.8 (m, 14H, CH_2O); 2.41 (s, 6H, $TsCH_3$); 2.36 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 163.2 (s, C=O); 153.9, 151.8 (s, $BinC_{2,2'}$); 145.1 (s, $AmdC_2$); 144.54, 144.51 (s, $TsC_{4,4'}$); 132.64, 132.60 (s, $TsC_{1,1'}$); 129.6 (d, $TsC_{3,3'}$); 127.6, 127.5 (d, $TsC_{2,2'}$); 117.0 (t, $OCH_2CH=\underline{C}H_2$); 114.2 (d, $BinC_{3'}$); 111.3 (d, $AmdC_3$); 73.5–67.7 (t, CH_2O); 21.4 (q, $TsCH_3$); 20.9 (q, $AmdCH_3$). IR (KBr): 3332 (NH); 1667 (NC=O); 1354, 1176 (SO_2-O) cm^{-1}. Ms (FAB) *m/z*: 960.1 ($[M+H]^+$, calcd. for $[C_{53}H_{53}NO_{12}S_2+H]$ 960.3).

2,2'-Bis[2-[2-[2-[[(4-methylphenyl)sulfonyl]oxy]ethoxy]ethoxy]ethoxy]-N-[5-methyl-2-(2-propenyloxy)phenyl]-[1,1'-binaphthalene]-3-carboxamide (**12b**). Eluent EtOAc/hexane 2:1; yield 85%. ^{1}H NMR: δ 10.56 (s, 1H, NH); 8.84 (s, 1H, $BinC_4H$); 8.56 (d, 1H, *J* 1.4 Hz, $AmdC_6H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 8.0 Hz, $BinC_{5'}H$); 7.73 (d, 4H, *J* 8.2 Hz, $TsC_{2,2'}H$); 7.5–7.1 (m, 7H, ArH); 7.27 (d, 4H, *J* 8.3 Hz, $TsC_{3,3'}H$); 6.9–6.7 (m, 2H, $AmdC_{3,4}H$); 6.0–5.8 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.4–4.9 (m, 2H, $OCH_2CH=C\underline{H}_2$); 4.48 (d, 2H, *J* 4.7 Hz, $OC\underline{H}_2CH=CH_2$); 4.16 (t, 2H, *J* 4.5 Hz, CH_2O); 4.0–2.8 (m, 22H, CH_2O); 2.37 (s, 6H, $TsCH_3$); 2.34 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 163.3 (s, C=O); 154.0, 151.9 (s, $BinC_{2,2'}$); 145.2 (s, $AmdC_2$); 144.6, 144.5 (s, $TsC_{4,4'}$); 132.6 (s, $TsC_{1,1'}$); 129.6 (d, $TsC_{3,3'}$); 127.6, 127.5 (d, $TsC_{2,2'}$); 116.9 (t, $OCH_2CH=\underline{C}H_2$); 114.2 (d, $BinC_{3'}$); 111.2 (d, $AmdC_3$); 73.4–68.0 (t, CH_2O); 21.3 (q, $TsCH_3$); 20.8 (q, $AmdCH_3$). IR (KBr): 3330 (NH); 1667 (NC=O); 1355, 1177 (SO_2-O) cm^{-1}. Ms (FAB) *m/z*: 1048.5 ($[M+H]^+$, calcd. for $[C_{57}H_{61}NO_{14}S_2+H]$ 1048.4).

General procedure for the synthesis of protected dialdehydes **14**

A mixture of aldehyde **13** (1.96 g, 11 mmol), ditosylate **12** (5 mmol), and K_2CO_3 (1.52 g, 11 mmol) in dry CH_3CN (50 ml) was refluxed overnight. The reaction mixture was cooled, diluted with CH_2Cl_2 (50 ml) and filtered through Celite. After evaporation of the solvent the crude products were obtained, which were purified by flash column chromatography to give colorless oils.

2,2'-Bis[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]-N-[5-methyl-2-(2-propenyloxy)phenyl]-[1,1'-binaphthalene]-3-carboxamide (**14a**). Eluent EtOAc/hexane 2:3; yield 90%. ^{1}H NMR: δ 10.55 (s, 1H, NH); 10.38 and 10.37 (s, 2×1H, CHO); 8.81 (s, 1H, $BinC_4H$); 8.53 (d, 1H, *J* 1.7 Hz, $AmdC_6H$); 8.00 (d, 1H, *J* 9.0 Hz, $BinC_{4'}H$); 7.98 (d, 1H, *J* 7.9 Hz, $BinC_5H$); 7.88 (d, 1H, *J* 7.9 Hz, $BinC_{5'}H$); 7.5–7.1 (m, 9H, ArH); 7.02 and 7.01 (t, 2×1H, *J* 7.9 Hz, $AldC_{5,5'}H$); 6.9–6.8 (m, 2H, $AldC_{4,4'}H$); 6.80 (dd, 1H, *J* 8.3 and 1.6 Hz, $AmdC_4H$); 6.71 (d, 1H, *J* 8.3 Hz, $AmdC_3H$); 6.1–5.8 (m, 3H, $OCH_2C\underline{H}=CH_2$); 5.4–4.9 (m, 6H, $OCH_2CH=C\underline{H}_2$); 4.5–4.4 (m, 6H, $OC\underline{H}_2CH=CH_2$); 4.2–4.1 (m, 2H, CH_2O); 3.8–3.1 (m, 14H, CH_2O); 2.32 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 190.5, 190.4 (d, CHO); 163.6 (s, C=O); 154.2, 152.1 (s, $BinC_{2,2'}$); 152.0, 151.4, 151.3 (s, $AldC_{2,2',3,3'}$); 145.4 (s, $AmdC_2$); 124.0 (d, $AldC_{5,5'}$); 119.50, 119.45, 119.23, 119.18 (d, $AldC_{4,4',6,6'}$); 118.6 (t, $AldOCH_2CH=\underline{C}H_2$); 117.2 (t, $AmdOCH_2CH=\underline{C}H_2$); 114.4 (d, $BinC_{3'}$); 111.5 (d, $AmdC_3$); 74.8–67.8 (t, CH_2O); 21.1 (q, $AmdCH_3$). IR (KBr): 3335 (NH); 1687 (HC=O); 1668 (NC=O) cm^{-1}. Ms (EI) *m/z*: 971.392 (M^+, calcd. for $C_{59}H_{57}NO_{12}$ 971.188).

2,2'-Bis[2-[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]ethoxy]-N-[5-methyl-2-(2-propenyloxy)phenyl]-[1,1'-binaphthalene]-3-carboxamide (**14b**). Eluent EtOAc/hexane 1:1; yield 90%. ^{1}H NMR: δ 10.53 (s, 1H, NH); 10.41 (s, 2H, CHO); 8.83 (s, 1H, $BinC_4H$); 8.55 (d, 1H, *J* 1.7 Hz, $AmdC_6H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 7.9 Hz, $BinC_{5'}H$); 7.5–7.1 (m, 9H, ArH); 7.1–7.0 (m, 4H, $AldC_{4,4',5,5'}H$); 6.9–6.8 (m, 1H, $AmdC_4H$); 6.75 (d, 1H, *J* 8.3 Hz, $AmdC_3H$); 6.1–5.8 (m, 3H, $OCH_2C\underline{H}=CH_2$); 5.4–4.9 (m, 6H, $OCH_2CH=C\underline{H}_2$); 4.7–4.6 (m, 4H, $OC\underline{H}_2CH=CH_2$); 4.49 (d, 2H, *J* 4.8 Hz, $OC\underline{H}_2CH=CH_2$); 4.16 (t, 2H, *J* 4.7 Hz, CH_2O); 4.1–2.9 (m, 22H, CH_2O); 2.35 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 190.5, 190.4 (d, CHO); 163.6 (s, C=O); 154.3, 152.2 (s, $BinC_{2,2'}$); 152.1, 151.5 (s, $AldC_{2,2',3,3'}$); 145.4 (s, $AmdC_2$); 124.0 (d, $AldC_{5,5'}$); 119.6, 119.4, 119.3 (d, $AldC_{4,4',6,6'}$); 118.8 (t, $AldOCH_2CH=\underline{C}H_2$); 117.2 (t, $AmdOCH_2CH=\underline{C}H_2$); 114.4 (d, $BinC_{3'}$); 111.4 (d, $AmdC_3$); 75.0–68.3 (t, CH_2O); 21.1 (q, $AmdCH_3$). IR (KBr): 3333 (NH); 1687 (HC=O); 1668 (NC=O) cm^{-1}. Ms (FAB) *m/z*: 1060.4 ($[M+H]^+$, calcd. for $[C_{63}H_{65}NO_{14}+H]$ 1060.4).

General procedure for the deallylation of protected dialdehydes **14**. *Synthesis of dialdehydes* **15**

A solution of **14** (2 mmol), $Pd(PPh_3)_4$ (11.5 mg, 10 μmol), and $HCOONHEt_3$ (2.65 g, 18 mmol) in a mixture of THF (20 ml), EtOH (20 ml), and H_2O (4 ml) was refluxed until the reaction was completed according to TLC (SiO_2; EtOAc/hexane 1:1; *ca.* 3 h). The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (100 ml) and washed with 1N hydrochloric acid (100 ml). The organic phase was dried ($MgSO_4$) and evaporated to give the products as oils in quantitative yield.

2,2'-Bis[2-[2-[3-formyl-2-hydroxyphenoxy]ethoxy]ethoxy]-N-(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3-carboxamide (**15a**). ^{1}H NMR: δ 10.87 and 10.83 (s, 2×1H, AldOH); 10.63 (s, 1H, NH); 9.88 and 9.87 (s, 2×1H, CHO); 8.97 (s, 1H, AmdOH); 8.92 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.89 (d, 1H, *J* 7.5 Hz, $BinC_{5'}H$); 7.5–6.8 (m, 16H, ArH); 4.3–4.1 (m, 2H, CH_2O); 3.9–3.2 (m, 14H, CH_2O); 2.17 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 196.1 (d, CHO); 164.4 (s, C=O); 154.1, 151.9 (s, $BinC_{2,2'}$); 151.7, 151.5 (s, $AldC_{3,3'}$); 147.1, 147.0, 146.7 (s, $AldC_{2,2'}+AmdC_3$); 120.92, 120.88 (s, $AldC_{1,1'}$); 120.2, 119.9, 119.43, 119.40 (d, Ald); 114.6 (d, $BinC_{3'}$); 73.4–68.4 (t, CH_2O); 20.3 (q, $AmdCH_3$). IR (KBr): 3423, 3303 (NH, OH); 1656 (C=O) cm^{-1}. Ms (EI) *m/z*: 851.284 (M^+, calcd. for $C_{50}H_{45}NO_{12}$ 851.294).

2,2'-Bis[2-[2-[2-[3-formyl-2-hydroxyphenoxy]ethoxy]ethoxy]ethoxy]-N-(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3-carboxamide (**15b**). ^{1}H NMR: δ 10.82 and 10.79 (s, 2×1H, AldOH); 10.66 (s, 1H, NH); 9.93 and 9.90 (s, 2×1H, CHO); 9.03 (s, 1H, AmdOH); 8.94 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 7.5 Hz, $BinC_{5'}H$); 7.5–6.8 (m, 16H, ArH); 4.3–3.0 (m, 24H, CH_2O); 2.23 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 195.9, 195.8 (d, CHO); 164.4 (s, C=O); 154.3, 152.0 (s, $BinC_{2,2'}$); 151.81, 151.79 (s, $AldC_{3,3'}$); 147.2, 147.1, 146.7 (s, $AldC_{2,2'}+AmdC_3$); 121.04, 120.98 (s, $AldC_{1,1'}$); 120.4, 119.4 (d, Ald); 114.5 (d, $BinC_{3'}$); 73.3–68.7 (t, CH_2O); 20.3 (q, $AmdCH_3$). IR (KBr): 3302 (NH, OH); 1657 (C=O) cm^{-1}. Ms (FAB) *m/z*: 940.2 ($[M+H]^+$, calcd. for $[C_{54}H_{53}NO_{14}+H]$ 940.3).

General procedure for the synthesis of esters **18** *and* **19**

A mixture of binaphthol **4** (1.72 g, 5 mmol) or **16** (2.01 g, 5 mmol), tosylate **17** (10 mmol), and K_2CO_3 (1.38 g, 10 mmol) in CH_3CN (50 ml) was refluxed overnight. The reaction mixture was cooled, diluted with CH_2Cl_2 (50 ml) and filtered through Celite. After removal of the solvent, the crude products were purified by flash column chromatography to give colourless oils.

2,2'-Bis[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxylic acid methyl ester (**18a**). Eluent EtOAc/CH_2Cl_2 1:9; yield 70%. ^{1}H NMR: δ 10.43 and 10.41 (d, 2×1H, *J* 0.6 Hz, CHO); 8.44 (s, 1H, $BinC_4H$); 8.0–7.9 (m, 2H, $BinC_{4',5}H$); 7.83 (d, 1H, *J* 7.5 Hz, $BinC_{5'}H$); 7.5–6.9 (m, 13H, ArH); 6.1–5.9 (m, 2H, $OCH_2C\underline{H}=CH_2$); 5.4–5.1 (m, 4H, $OCH_2CH=C\underline{H}_2$); 4.6–4.5 (m, 4H, $OC\underline{H}_2CH=CH_2$); 4.3–4.2 (m, 2H, CH_2O); 3.94 (s, 3H, OCH_3); 3.9–3.1 (m, 14H, CH_2O). ^{13}C NMR: δ 190.5, 190.4 (d, CHO); 166.8 (s, C=O); 154.2, 153.3, 152.2, 152.1, 151.6 (s, $BinC_{2,2'}+AldC_{2,2',3,3'}$); 135.8, 133.9 (s, $BinC_{8a,8a'}$); 133.3 (d, $OCH_2C\underline{H}=CH_2$); 132.6 (d, $BinC_4$); 130.0 (d, $BinC_{4'}$); 128.9 (d, $BinC_5$); 127.9 (d, $BinC_{5'}$); 123.9 (d, $AldC_{5,5'}$); 119.7, 119.40, 119.35 (d, $AldC_{4,4',6,6'}$); 118.7, 118.6 (t, $OCH_2CH=\underline{C}H_2$); 114.5 (d, $BinC_{3'}$); 75.0–68.3 (t, CH_2O); 52.3 (q, OCH_3). IR (KBr): 1728 (OC=O); 1687 (HC=O) cm^{-1}. Ms (EI) *m/z*: 840.314 (M^+, calcd. for $C_{50}H_{48}O_{12}$ 840.315).

2,2'-Bis[2-[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxylic acid methyl ester (**18b**). Eluent EtOAc/CH_2Cl_2 1:4; yield 60%. ^{1}H NMR: δ 10.441 and 10.436

(s, 2×1H, CHO); 8.47 (s, 1H, $BinC_4H$); 8.0–7.9 (m, 2H, $BinC_{4',5}H$); 7.84 (d, 1H, *J* 7.6 Hz, $BinC_{5'}H$); 7.5–7.0 (m, 13H, ArH); 6.1–5.9 (m, 2H, $OCH_2CH{=}CH_2$); 5.4–5.1 (m, 4H, $OCH_2CH{=}CH_2$); 4.7–4.6 (m, 4H, $OCH_2CH{=}CH_2$); 4.2–4.0 (m, 6H, CH_2O); 3.96 (s, 3H, OCH_3); 3.9–3.0 (m, 18H, CH_2O). ^{13}C NMR: 190.5 (d, CHO); 166.9 (s, C=O); 154.2, 153.3, 152.2, 151.5 (s, $BinC_{2,2'}$ + $AldC_{2,2',3,3'}$); 135.8, 133.8 (s, $BinC_{8a,8a'}$); 133.3 (d, $OCH_2CH{=}CH_2$); 132.6 (d, $BinC_4$); 130.0 (d, $BinC_{4'}$); 128.9 (d, $BinC_5$); 127.9 (d, $BinC_{5'}$); 124.0, 119.6, 119.4 (d, $AldC_{4,4',5,5',6,6'}$); 118.9 (t, $OCH_2CH{=}CH_2$); 114.6 (d, $BinC_{3'}$); 75.0–68.4 (t, CH_2O); 52.3 (q, OCH_3). IR (KBr): 1728 (OC=O); 1686 (HC=O) cm^{-1}. Ms (EI) *m/z*: 928.371 (M^+, calcd. for $C_{54}H_{56}O_{14}$ 928.367).

2,2'-Bis[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3,3'-dicarboxylic acid dimethyl ester (**19a**). Eluent EtOAc/CH_2Cl_2 1:9; yield 65%. ^1H NMR: δ 10.42 (s, 2H, CHO); 8.48 (s, 2H, $BinC_{4,4'}H$); 7.90 (d, 2H, *J* 7.9 Hz, $BinC_{5,5'}H$); 7.5–7.3 (m, 6H, ArH); 7.14 (d, 2H, *J* 9.0 Hz, $BinC_{8,8'}H$); 7.1–7.0 (m, 4H, ArH); 6.1–5.9 (m, 2H, $OCH_2CH{=}CH_2$); 5.3–5.1 (m, 4H, $OCH_2CH{=}CH_2$); 4.6–4.4 (m, 4H, $OCH_2CH{=}CH_2$); 4.1–4.0 (m, 4H, CH_2O); 3.94 (s, 6H, OCH_3); 3.9–3.2 (m, 12H, CH_2O). ^{13}C NMR: δ 190.5 (d, CHO); 166.7 (s, C=O); 153.4 (s, $BinC_{2,2'}$); 152.2, 151.6 (s, $AldC_{2,2',3,3'}$); 135.6 (s, $BinC_{8a,8a'}$); 133.3, 133.2 (d, $OCH_2CH{=}CH_2$ and $BinC_{4,4'}$); 130.2 (s, $AldC_{1,1'}$); 129.6 (s, $BinC_{4a,4a'}$); 123.9, 119.7, 119.4 (d, $AldC_{4,4',5,5',6,6'}$); 118.6 (t, $OCH_2CH{=}CH_2$); 74.9–68.3 (t, CH_2O); 54.4 (q, OCH_3). IR (KBr): 1729 (OC=O); 1686 (HC=O) cm^{-1}. Ms (EI) *m/z*: 898.325 (M^+, calcd. for $C_{52}H_{50}O_{14}$ 898.320).

2,2'-Bis[2-[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3,3'-dicarboxylic acid dimethyl ester (**19b**). Eluent EtOAc/CH_2Cl_2 1:4; yield 58%. ^1H NMR: δ 10.44 (d, 2H, *J* 0.4 Hz, CHO); 8.51 (s, 2H, $BinC_{4,4'}H$); 7.94 (d, 2H, *J* 8.0 Hz, $BinC_{5,5'}H$); 7.5–7.0 (m, 12H, ArH); 6.1–5.9 (m, 2H, $OCH_2CH{=}CH_2$); 5.4–5.1 (m, 4H, $OCH_2CH{=}CH_2$); 4.7–4.6 (m, 4H, $OCH_2CH{=}CH_2$); 4.10 (t, 4H, *J* 4.8 Hz, CH_2O); 4.1–3.9 (m, 2H, CH_2O); 3.96 (s, 6H, OCH_3); 3.73 (t, 4H, *J* 4.8 Hz, CH_2O); 3.7–3.1 (m, 14H, CH_2O). ^{13}C NMR: δ 190.5 (d, CHO); 166.8 (s, C=O); 153.4 (s, $BinC_{2,2'}$); 152.2, 151.6 (s, $AldC_{2,2',3,3'}$); 135.6 (s, $BinC_{8a,8a'}$); 133.33, 133.25 (d, $OCH_2CH{=}CH_2$ and $BinC_{4,4'}$); 130.2 (s, $AldC_{1,1'}$); 129.5 (s, $BinC_{4a,4a'}$); 124.0, 119.8, 119.5 (d, $AldC_{4,4',5,5',6,6'}$); 118.8 (t, $OCH_2CH{=}CH_2$); 75.0–68.6 (t, CH_2O); 52.4 (q, OCH_3). IR (KBr): 1729 (OC=O); 1687 (HC=O) cm^{-1}. Ms (EI) *m/z*: 986.347 (M^+, calcd. for $C_{56}H_{58}O_{16}$ 986.373).

Procedure for the synthesis of amides **20** *and* **21**

A mixture of ester **18** or **19** (2.5 mmol), ethylene glycol (3.1 g, 50 mmol), and a catalytic amount of *p*-toluenesulfonic acid in $CHCl_3$ (100 ml) was refluxed over molecular sieves (3 Å). After the starting dialdehyde had been converted completely to the diacetal according to TLC [SiO_2; EtOAc/CH_2Cl_2 1:9 (**18a** and **19a**) or 1:4 (**18b** and **19b**); *ca.* 2 h], the reaction mixture was cooled, washed with a dilute $NaHCO_3$ solution (50 ml) and water (2×100 ml), and dried with Na_2SO_4. After evaporation of the solvent, the residue was dissolved in MeOH (75 ml) and a solution of KOH (2.8 g, 50 mmol) in water (25 ml) was added (the diacetal partly separated from the solution as an oil). The reaction mixture was refluxed until the ester had disappeared according to TLC [SiO_2; EtOAc/CH_2Cl_2 1:9 (**18a** and **19a**) or 1:4 (**18b** and **19b**); *ca.* 2 h]. The methanol was evaporated and the residue was divided between CH_2Cl_2 (100 ml) and an aqueous solution of citric acid (100 ml, the final pH was 4–5). The organic layer was separated, dried with Na_2SO_4, filtered, and the solvent was evaporated. The residue was dissolved in CH_2Cl_2 (25 ml) and HOBT.H_2O [0.42 g, 2.75 mmol (**18**) or 0.84 g, 5.5 mmol (**19**)] and DCC [0.57 g, 2.75 mmol (**18**) or 1.13 g, 5.5 mmol (**19**)] were added. After stirring the reaction mixture for 1 h, the amine **8** (2.75 mmol [**18**] or 5.5 mmol [**19**]) was added and stirring was continued overnight. The reaction mixture was filtered and, after evaporation of the solvent, the residue was dissolved in THF (75 ml) to which 1N hydrochloric acid (25 ml) was added. After 1 h, the solvent was evaporated and the residue was dissolved in CH_2Cl_2 (100 ml), washed with 1N hydrochloric acid (100 ml), dried with Na_2SO_4, filtered, and evaporated to dryness. The crude products were purified by flash column chromatography to give **20** and **21** as oils.

2,2'-Bis[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]-N-(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3-carboxamide (**20a**). Eluent EtOAc/CH_2Cl_2 5:95; yield 84%. ^1H NMR: δ 10.64 (s, 1H, NH); 10.362 and 10.357 (d, 2×1H, *J* 0.7 Hz, CHO); 9.11 (s, 1H, AmdOH); 8.91 (s, 1H, $BinC_4H$); 8.03 (d, 1H, *J* 9.0 Hz, $BinC_4H$); 7.97 (d, 1H, *J* 8.0 Hz, $BinC_5H$); 7.90 (d, 1H, *J* 7.6 Hz, $BinC_{5'}H$); 7.47 (d, 1H, *J* 9.1 Hz, $BinC_3H$); 7.5–6.8 (m, 15H, ArH); 6.1–5.8 (m, 2H, $OCH_2CH{=}CH_2$); 5.3–5.0 (m, 4H, $OCH_2CH{=}CH_2$); 4.6–4.4 (m, 4H, $OCH_2CH{=}CH_2$); 4.3–4.1 (m, 2H, CH_2O); 3.8–3.1 (m, 14H, CH_2O); 2.14 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 190.3, 190.2 (d, CHO); 164.6 (s, C=O); 154.2, 152.02, 151.96, 151.8, 151.4, 151.3 (s, $BinC_{2,2'}$ + $AldC_{2,2',3,3'}$); 147.1 (s, $AmdC_3$); 119.6, 119.5, 119.43, 119.37 (d, $AldC_{4,4',6,6'}$); 118.5, 118.4 (t, $OCH_2CH{=}CH_2$); 114.6 (d, $BinC_{3'}$); 74.9–67.9 (t, CH_2O); 20.3 (q, $AmdCH_3$). IR (KBr): 3309 (NH); 1686 (HC=O); 1644 (NC=O) cm^{-1}. Ms (EI) *m/z*: 931.360 (M^+, calcd. for $C_{56}H_{53}NO_{12}$ 931.357).

2,2'-Bis[2-[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]ethoxy]-N-(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3-carboxamide (**20b**). Eluent EtOAc/hexane 3:2; yield 94%. ^1H NMR: δ 10.67 (s, 1H, NH); 10.42 and 10.40 (s, 2×1H, CHO); 9.10 (s, 1H, AmdOH); 8.95 (s, 1H, $BinC_4H$); 8.1–8.0 (m, 2H, $BinC_{4',5}H$); 7.89 (d, 1H, *J* 7.6 Hz, $BinC_{5'}H$); 7.5–6.8 (m, 16H, ArH); 6.2–5.8 (m, 2H, $OCH_2CH{=}CH_2$); 5.4–5.1 (m, 4H, $OCH_2CH{=}CH_2$); 4.7–4.5 (m, 4H, $OCH_2CH{=}CH_2$); 4.3–3.9 (m, 6H, CH_2O); 3.8–3.0 (m, 18H, CH_2O); 2.24 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 190.5, 190.4 (d, CHO); 164.6 (s, C=O); 154.2, 152.12, 152.08, 152.05, 151.50, 151.46 (s, $BinC_{2,2'}$ + $AldC_{2,2',3,3'}$); 147.2 (s, $AmdC_3$); 119.6, 119.5, 119.4 (d, $AldC_{4,4',6,6'}$); 118.83, 118.81 (t, $OCH_2CH{=}CH_2$); 114.7 (d, $BinC_{3'}$); 75.0–68.3 (t, CH_2O); 20.4 (q, $AmdCH_3$). IR (KBr): 3302 (NH); 1686 (HC=O); 1644 (NC=O) cm^{-1}. Ms (FAB) *m/z*: 1020.4 ($[M+H]^+$, calcd. for $[C_{60}H_{61}NO_{14}+H]$ 1020.4).

N-(5-Chloro-2-hydroxyphenyl)-2,2'-bis[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxamide (**20c**). Eluent EtOAc/CH_2Cl_2 5:95; yield 90%. ^1H NMR: δ 10.75 (s, 1H, NH); 10.36 and 10.35 (s, 2×1H, CHO); 9.34 (bs, 1H, AmdOH); 8.92 (s, 1H, $BinC_4H$); 8.04 (d, 1H, *J* 9.1 Hz, $BinC_4H$); 7.99 (d, 1H, *J* 8.0 Hz, $BinC_5H$); 7.90 (d, 1H, *J* 7.8 Hz, $BinC_{5'}H$); 7.46 (d, 1H, *J* 9.0 Hz, $BinC_3H$); 7.5–6.8 (m, 15H, ArH); 6.1–5.8 (m, 2H, $OCH_2CH{=}CH_2$); 5.3–5.0 (m, 4H, $OCH_2CH{=}CH_2$); 4.6–4.4 (m, 4H, $OCH_2CH{=}CH_2$); 4.3–4.1 (m, 2H, CH_2O); 3.9–3.1 (m, 14H, CH_2O). ^{13}C NMR: δ 190.34, 190.27 (d, CHO); 164.8 (s, C=O); 154.1, 151.9, 151.8, 151.7, 151.3, 151.1 (s, $BinC_{2,2'}$ + $AldC_{2,2',3,3'}$); 148.0 (s, $AmdC_3$); 119.44, 119.36 (d, Ald); 118.6, 118.5 (t, $OCH_2CH{=}CH_2$); 114.6 (d, $BinC_{3'}$); 74.9–67.9 (t, CH_2O). IR (KBr): 3301 (NH); 1688 (HC=O); 1643 (NC=O) cm^{-1}. Ms (EI) *m/z*: 951.289 (M^+, calcd. for $C_{55}H_{50}ClNO_{12}$ 951.302).

N-(5-Chloro-2-hydroxyphenyl)-2,2'-bis[2-[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxamide (**20d**). Eluent EtOAc/CH_2Cl_2 85:15; yield 80%. ^1H NMR: δ 10.77 (s, 1H, NH); 10.41 and 10.39 (s, 2×1H, CHO); 9.3 (bs, 1H, AmdOH); 8.94 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.89 (d, *J* 7.6 Hz, 1H, $BinC_{5'}H$); 7.5–7.0 (m, 15H, ArH); 6.96 (d, 1H, *J* 8.7 Hz, $AmdC_3H$); 6.1–5.9 (m, 2H, $OCH_2CH{=}CH_2$); 5.3–5.1 (m, 4H, $OCH_2CH{=}CH_2$); 4.7–4.5 (m, 4H, $OCH_2CH{=}CH_2$); 4.2–3.9 (m, 6H, CH_2O); 3.8–3.0 (m, 18H, CH_2O). ^{13}C NMR: δ 190.5, 190.4 (d, CHO); 164.9 (s, C=O); 154.2, 152.12, 152.08, 151.9, 151.50, 151.46 (s, $BinC_{2,2'}$ + $AldC_{2,2',3,3'}$); 148.1 (s, $AmdC_3$); 119.7, 119.6, 119.49, 119.45 (d, $AldC_{4,4',6,6'}$); 118.84, 118.82 (t, $OCH_2CH{=}CH_2$); 114.7 (d, $BinC_{3'}$); 75.0–68.3 (t, CH_2O). IR (KBr): 3308 (NH); 1685 (HC=O); 1646 (NC=O) cm^{-1}. Ms (FAB) *m/z*: 1040.4 ($[M+H]^+$, calcd. for $[C_{59}H_{58}ClNO_{14}+H]$ 1040.4).

2,2'-Bis[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]-N,N'-bis(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3,3'-dicarboxamide (**21a**). Eluent EtOAc/CH_2Cl_2 5:95; yield 64%. ^1H NMR: δ 10.48 (s, 2H, NH); 10.31 (s, 2H, CHO); 8.90 (s, 2H, $BinC_{4,4'}H$); 8.74 (bs, 2H, AmdOH); 8.06 (d, 2H, *J* 8.0 Hz, $BinC_{5,5'}H$); 7.6–7.4 (m, 4H, BinH); 7.36 (dd, 2H, *J* 7.9 and 1.5 Hz, $AldC_{6,6'}H$); 7.2–7.1 (m, 4H, $BinC_{8,8'}H$ and $AmdC_{6,6'}H$); 7.1–6.9 (m, 2H, $AldC_{5,5'}H$); 6.9–6.8 (m, 4H, AmdH); 6.83 (dd, 2H, *J* 8.1 and 1.5 Hz, $AldC_{4,4'}H$); 6.0–5.7 (m, 2H, $OCH_2CH{=}CH_2$); 5.2–5.0 (m, 4H, $OCH_2CH{=}CH_2$); 4.5–4.3 (m, 4H, $OCH_2CH{=}CH_2$); 3.9–3.2 (m, 16H, CH_2O); 2.18 (s, 6H, $AmdCH_3$). ^{13}C NMR: δ 190.2 (d, CHO); 164.1 (s, C=O); 152.4 (s, $BinC_{2,2'}$); 151.8, 151.1 (s, $AldC_{2,2',3,3'}$); 146.8 (s, $AmdC_{2,2'}$); 135.6 (s, $BinC_{8a,8a'}$); 135.0 (d, $BinC_{4,4'}$); 133.0 (d, $OCH_2CH{=}CH_2$); 123.4, 119.6, 119.5 (d, $AldC_{4,4',5,5',6,6'}$); 118.8 (t, $OCH_2CH{=}CH_2$); 75.1–68.1 (t, CH_2O); 20.4 (q, $AmdCH_3$). IR (KBr): 3310 (NH, OH); 1686 (HC=O); 1670, 1646 (NC=O) cm^{-1}. Ms (FAB) *m/z*: 1081.4 ($[M+H]^+$, calcd. for $[C_{64}H_{60}N_2O_{14}+H]$ 1081.4).

2,2'-Bis[2-[2-[2-[3-formyl-2-(2-propenyloxy)phenoxy]ethoxy]ethoxy]ethoxy]-N,N'-bis(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3,3'-dicarboxamide (**21b**). Eluent EtOAc/CH_2Cl_2 1:9; yield 76%. ^1H NMR: δ 10.54 (s, 2H, NH); 10.36 (s, 2H, CHO); 9.01 (s, 2H, $BinC_{4,4'}H$); 8.86 (s, 2H, AmdOH); 8.07 (d, 2H, *J* 8.0 Hz, $BinC_{5,5'}H$); 7.6–7.3 (m, 6H, BinH and AldH); 7.28 (s, 2H, $AmdC_{6,6'}H$); 7.19 (d,

2H, *J* 8.4 Hz, $BinC_{8,8'}H$); 7.1–7.0 (m, 4H, AldH); 7.0–6.8 (m, 4H, AmdH); 6.1–5.8 (m, 2H, $OCH_2CH{=}CH_2$); 5.3–5.1 (m, 4H, $OCH_2CH{=}CH_2$); 4.55 (d, 4H, *J* 6.1 Hz, $OCH_2CH{=}CH_2$); 4.0–3.2 (m, 24H, CH_2O); 2.26 (s, 6H, $AmdCH_3$). ^{13}C NMR: δ 190.3 (d, CHO); 164.1 (s, C=O); 152.5 (s, $BinC_{2,2'}$); 152.1, 151.4 (s, $AldC_{2,2',3,3'}$); 146.8 (s, $AmdC_{2,2'}$); 135.6 (s, $BinC_{8a,8a'}$); 134.9 (d, $BinC_{4,4'}$); 133.2 (d, $OCH_2CH{=}CH_2$); 118.8 (t, $OCH_2CH{=}CH_2$); 75.0–68.3 (t, CH_2O); 20.5 (q, $AmdCH_3$). IR (KBr): 3311 (NH, OH); 1686 (HC=O); 1669, 1645 (NC=O) cm^{-1}. Ms (FAB) *m/z*: 1169.5 ($[M+H]^+$, calcd. for $[C_{68}H_{68}N_2O_{16}+H]$ 1169.5).

General procedure for the deallylation of protected dialdehydes **20** *and* **21**. *Synthesis of dialdehydes* **15** *and* **22**

A solution of **20** or **21** (2 mmol), $Pd(PPh_3)_4$ (11.5 mg, 10 μmol), and $HCOONHEt_3$ [1.76 g, 12 mmol (**20a,b**, **21**), 0.88 g, 6 mmol (**20c,d**)] in a mixture of THf (20 ml), EtOH (20 ml), and H_2O (4 ml) was refluxed until the reaction was completed according to TLC (SiO_2; $EtOAc/CH_2Cl_2$ 1:9; *ca.* 3 h). The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (100 ml) and washed with 1N hydrochloric acid (100 ml). The organic phase was dried ($MgSO_4$) and evaporated to give the products as oils in quantitative yield.

N-(5-Chloro-2-hydroxyphenyl)-2,2'-bis[2-[2-(3-formyl-2-hydroxyphenoxy)ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxamide (**15c**). ^1H NMR: δ 10.92 and 10.84 (s, 2×1H, AldOH); 10.75 (s, 1H, NH); 9.85 and 9.83 (s, 2×1H, CHO); 9.09 (s, 1H, AmdOH); 8.90 (s, 1H, $BinC_4H$); 8.1–6.9 (m, 2H, $BinC_{4',5}H$); 7.87 (d, 1H, *J* 7.9 Hz, $BinC_{5'}H$); 7.64 (d, 1H, *J* 2.3 Hz, $AmdC_6H$); 7.5–6.7 (m, 15H, ArH); 4.3–4.1 (m, 2H, CH_2O); 3.9–3.1 (m, 14H, CH_2O). ^{13}C NMR: δ 196.1, 196.0 (d, CHO); 164.5 (s, C=O); 154.1, 151.8, 151.6, 151.3 (s, $BinC_{2,2'}+AldC_{3,3'}$); 147.2, 147.0, 146.9 (s, $AldC_{2,2'}+AmdC_3$); 120.84, 120.79 (s, $AldC_{1,1'}$); 119.7, 119.43, 119.38, 119.3 (d, $AldC_{4,4',6,6'}$); 114.5 (d, $BinC_{3'}$); 73.5–68.5 (t, CH_2O). IR (KBr): 3418, 3306 (NH, OH); 1656 (C=O) cm^{-1}. Ms (FAB) *m/z*: 872.5 ($[M+H]^+$, calcd. for $[C_{49}H_{42}ClNO_{12}+H]$ 872.2).

N-(5-Chloro-2-hydroxyphenyl)-2,2'-bis[2-[2-[2-(3-formyl-2-hydroxyphenoxy)ethoxy]ethoxy]ethoxy]-[1,1'-binaphthalene]-3-carboxamide (**15d**). ^1H NMR: δ 10.84 (bs, 2H, AldOH); 10.79 (s, 1H, NH); 9.91 and 9.88 (s, 2×1H, CHO); 9.20 (s, 1H, AmdOH); 8.93 (s, 1H, $BinC_4H$); 8.1–7.9 (m, 2H, $BinC_{4',5}H$); 7.88 (d, 1H, *J* 7.5 Hz, $BinC_{5'}H$); 7.61 (d, 1H, *J* 1.3 Hz, $AmdC_6H$); 7.5–6.8 (m, 15H, ArH); 4.3–4.0 (m, 6H, CH_2O); 3.9–3.0 (m, 18H, CH_2O). ^{13}C NMR: δ 196.1, 196.0 (d, CHO); 164.7 (s, C=O); 154.2, 152.0, 151.9 (s, $BinC_{2,2'}+AldC_{3,3'}$); 147.6, 147.3, 147.2 (s, $AldC_{2,2'}+AmdC_3$); 121.15, 121.10 (s, $AldC_{1,1'}$); 120.0, 119.5 (d, Ald); 114.6 (d, $BinC_{3'}$); 73.5–68.9 (t, CH_2O). IR (KBr): 3304 (NH, OH); 1658 (C=O) cm^{-1}. Ms (FAB) *m/z*: 960.6 ($[M+H]^+$, calcd. for $[C_{53}H_{50}ClNO_{14}+H]$ 960.3).

*2,2'-Bis[2-[2-[3-formyl-2-hydroxyphenoxy]ethoxy]ethoxy]-*N,N'*-bis(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3,3'-dicarboxamide* (**22a**). ^1H NMR: δ 10.86 (s, 2H, AldOH); 10.48 (s, 2H, NH); 9.83 (s, 2H, CHO); 8.96 (s, 2H, $BinC_{4,4'}H$); 8.69 (bs, 2H, AmdOH); 8.06 (d, 2H, *J* 8.0 Hz, $BinC_{5,5'}H$); 7.6–7.3 (m, 4H, BinH); 7.28 (s, 2H, $AmdC_{6,6'}H$); 7.18 (d, 2H, *J* 8.4 Hz, $BinC_{8,8'}H$); 7.10 (dd, 2H, *J* 6.6 and 2.7 Hz, AldH); 7.0–6.7 (m, 8H, ArH); 4.0–3.2 (m, 16H, CH_2O); 2.17 (s, 6H, $AmdCH_3$). ^{13}C NMR: δ 196.1 (d, CHO); 164.1 (s, C=O); 152.4 (s, $BinC_{2,2'}$); 151.5 (s, $AldC_{3,3'}$); 147.1 (s, $AldC_{2,2'}$); 146.6 (s, $AmdC_{2,2'}$); 135.6 (s, $BinC_{8a,8a'}$); 134.8 (d, $BinC_{4,4'}$); 121.0 (s, $AldC_{1,1'}$); 120.0, 119.6 (d, Ald); 73.9–68.6 (t, CH_2O); 20.4 (q, $AmdCH_3$). IR (KBr): 3308 (NH, OH); 1655 (C=O) cm^{-1}. Ms (FAB) *m/z*: 1001.2 ($[M+H]^+$, calcd. for $[C_{58}H_{52}N_2O_{14}+H]$ 1001.3).

*2,2'-Bis[2-[2-[2-[3-formyl-2-hydroxyphenoxy]ethoxy]ethoxy]ethoxy]-*N,N'*-bis(2-hydroxy-5-methylphenyl)-[1,1'-binaphthalene]-3,3'-dicarboxamide* (**22b**). ^1H NMR: δ 10.79 (s, 2H, AldOH); 10.53 (s, 2H, NH); 9.89 (s, 2H, CHO); 8.96 (s, 2H, $BinC_{4,4'}H$); 8.78 (bs, 2H, AmdOH); 8.07 (d, 2H, *J* 8.0 Hz, $BinC_{5,5'}H$); 7.6–7.3 (m, 6H, BinH and $AmdC_{6,6'}H$); 7.2–6.8 (m, 12H, ArH); 4.0–3.1 (m, 24H, CH_2O); 2.23 (s, 6H, $AmdCH_3$). ^{13}C NMR: δ 195.8 (d, CHO); 164.1 (s, C=O); 152.5 (s, $BinC_{2,2'}$); 151.8 (s, $AldC_{3,3'}$); 147.2 (s, $AldC_{2,2'}$); 146.5 (s, $AmdC_{2,2'}$); 135.5 (s, $BinC_{8a,8a'}$); 134.7 (d, $BinC_{4,4'}$); 121.2 (s, $AldC_{1,1'}$); 120.5, 119.5 (d, Ald); 73.9–68.0 (t, CH_2O); 20.5 (q, $AmdCH_3$). IR (KBr): 3309 (NH, OH); 1655 (C=O) cm^{-1}. Ms (FAB) *m/z*: 1089.3 ($[M+H]^+$, calcd. for $[C_{62}H_{60}N_2O_{16}+H]$ 1089.4).

General procedure for the cyclization of dialdehydes **15** *and* **22**. *Synthesis of the functionalized binaphthyl salophen crown ethers* **2** *and* **3**

A solution of dialdehyde **15** or **22** (2.5 mmol), $Ba(OTf)_2$ (2.18 g, 5.0 mmol), and either diamine **23** (270 mg, 2.5 mmol) or **24** (285 mg, 2.5 mmol) in THF (250 ml) was refluxed for 30 min. After cooling slightly, $UO_2(OAc)_2.2H_2O$ (1.59 g, 3.75 mmol) was added and refluxing was continued for about 30 min. The solvent was evaporated and the residue was dissolved in CH_2Cl_2 (200 ml) and washed with water (2×100 ml), an aqueous solution of Na_2SO_4 (50 ml), and water (100 ml) again. After drying ($MgSO_4$) and evaporation of the solvent the crude products were obtained, which were purified as described below.

[4,5,7,8,29,30,32,33-Octahydro-45,46-dihydroxy- N*-(2-hydroxy-5-methylphenyl)-10,14:23,27-dimethenobenzo[z]dinaphtho[2,1-h:1',2'-j][1,4,7,12,15,18,25,28]hexaoxadiazacyclotetratriacontine-2-carboxamidato(2-)-*$N^{16},N^{21},O^{45},O^{46}$*]dioxouranium* (**2a**). The product was purified by precipitation from CH_2Cl_2 with cyclohexane. Yield 85%; m.p. 262–264°C. Anal. Calcd. for $C_{56}H_{47}N_3O_{12}U\cdot C_6H_{12}\cdot 1.25H_2O$ (1298.744): C 57.34, H 4.77, N 3.24; found: C 57.15, H 4.41, N 3.30%. Karl Fisher titration calcd. for 1.25 H_2O: 1.73; found: 1.60.

The product was fractionated by flash column chromatography to give fraction I (elution with $EtOAc/CH_2Cl_2$ 1:2) and fraction II (elution with $EtOAc/CH_2Cl_2$/MeOH 8:16:1).

Fraction I: ^1H NMR: δ 11.15 (s, 1H, NH); 9.43 and 9.35 (s, 2×1H, HC=N); 9.12 (s, 1H, $BinC_4H$); 8.06 (d, 1H, *J* 9.0 Hz, BinH); 7.95 (d, 1H, *J* 7.9 Hz, BinH); 7.9–6.7 (m, 20H, ArH); 6.66 and 6.53 (t, 2×1H, *J* 7.8 Hz, $AldC_{5,5'}H$); 4.6–3.5 (m, 14H, CH_2O); 3.1–2.8 (m, 2H, CH_2O); 1.89 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 165.9, 165.6 (d, HC=N); 163.7 (s, C=O); 162.7, 161.2 (s, $AldC_{2,2'}$); 154.3, 152.6 (s, $BinC_{2,2'}$); 150.1, 149.9 (s, $AldC_{3,3'}$); 74.2–66.1 (t, CH_2O); 20.3 (q, $AmdCH_3$). IR (KBr): 1630 (m, NC=O); 1602 (s, HC=N); 896 (O-U-O) cm^{-1}. Ms (FAB) *m/z*: 1192.6 ($[M+H]^+$, calcd. for $[C_{56}H_{47}N_3O_{12}U+H]$ 1192.4).

Fraction II: ^1H NMR: δ 10.68 (s, 1H, NH); 9.40 and 9.38 (s, 2×1H, CH=N); 8.96 (s, $BinC_4H$); 8.42 (bs, 1H, AmdOH); 8.09 (d, 1H, *J* 8.1 Hz, BinH); 8.01 (s, 1H, $AmdC_6H$); 7.97 (d, 1H, *J* 9.1 Hz, $BinC_{4'}H$); 7.90 (d, 1H, *J* 8.0 Hz, BinH); 7.48 (d, 1H, *J* 9.1 Hz, $BinC_{3'}H$); 7.6–7.4 (m, 4H, AmH); 7.4–7.1 (m, 11H, ArH); 6.63 (t, 2H, *J* 7.8 Hz, $AldC_{5,5'}H$); 6.6–6.5 (m, 1H, $AmdC_4H$); 6.50 (d, 1H, *J* 8.1 Hz, $AmdC_3H$); 5.3 (bs, H_2O); 4.7–2.9 (m, 16H, CH_2O); 2.03 (s, 3H, $AmdCH_3$). ^{13}C NMR: δ 165.6, 165.5 (d, HC=N); 163.9 (s, C=O); 162.7, 162.1 (s, $AldC_{2,2'}$); 155.1, 152.3 (s, $BinC_{2,2'}$); 149.7, 149.6 (s, $AldC_{3,3'}$); 72.6–69.2 (t, CH_2O); 20.6 (q, $AmdCH_3$). IR (KBr): 1662 (w, NC=O); 1603 (s, HC=N); 903 (O-U-O) cm^{-1}. Ms (FAB) *m/z*: 1192.6 ($[M+H]^+$, calcd. for $[C_{56}H_{47}N_3O_{12}U+H]$ 1192.4).

[4,5,7,8,10,11,32,33,35,36,38,39-Dodecahydro-51,52-dihydroxy- N*-(2-hydroxy-5-methylphenyl)-13,17:26,30-dimethenobenzo[f,][1]dinaphth[2,1-k:1',2'-m][1,4,7,10,15,18,21,24,31,34]-octaoxadiazacyclotetracontine-2-carboxamidato(2-)-*$N^{19},N^{24},O^{51},O^{52}$*]dioxouranium* (**2b**). The product was purified by precipitation from CH_2Cl_2 with cyclohexane. Yield 65%; m.p. 203–206°C. Anal. calcd. for $C_{60}H_{55}N_3O_{14}U\cdot 0.5C_6H_{12}\cdot 2H_2O$ (1358.233): C 55.61, H 4.62, N 3.16; found: C 55.76, H 4.38, N, 3.32%. Karl Fisher titration calcd. for 2 H_2O: 2.03; found: 2.38. ^1H NMR (DMSO-d_6): δ 10.43 (s, 1H, NH); 9.86 (s, 1H, AmdOH); 9.62 (s, 2H, HC=N); 8.79 (s, 1H, $BinC_4H$); 8.25 (s, 1H, $AmdC_6H$); 8.2–8.1 (m, 2H, $BinC_{4',5}H$); 7.99 (d, 1H, *J* 7.4 Hz, $BinC_{5'}H$); 7.8–7.7 (m, 3H, $BinC_{3'}H$+AmH); 7.6–7.2 (m, 10H, ArH); 7.03 and 7.01 (d, 2×1H, *J* 8.2 Hz, $BinC_{8,8'}H$); 6.76 (s, 2H, $AmdC_{3,4}H$); 6.63 and 6.61 (t, 2×1H, *J* 7.8 Hz, $AldC_{5,5'}H$); 4.4–2.9 (m, 24H, CH_2O); 2.24 (s, 3H, $AmdCH_3$). ^{13}C NMR (DMSO-d_6): δ 166.6 (d, CH=N); 162.8 (s, C=O); 161.1 (s, $AldC_{2,2'}$); 154.1, 151.6 (s, $BinC_{2,2'}$); 150.34, 150.30 (s, $AldC_{3,3'}$); 146.8 (s, $AmC_{1,1'}$); 144.5 (s, $AmdC_2$); 132.2 (d, $BinC_4$); 121.1 (d, $AmdC_6$); 120.3 ($AmC_{2,2'}$); 116.0 (d, $AldC_{5,5'}$); 115.0 (d, $BinC_{3'}$); 114.6 ($AmdC_3$); 73.4–68.5 (t, CH_2O); 20.7 (q, $AmdCH_3$). IR (KBr): 1643 (w, NC=O); 1603 (HC=N); 905 (O-U-O) cm^{-1}. Ms (FAB) *m/z*: 1280.8 ($[M+H]^+$, calcd. 1280.4).

*[*N*-(5-Chloro-2-hydroxyphenyl)-4,5,7,8,29,30,32,33-octahydro-45,46-dihydroxy-10,14:23,27-dimethenobenzo[z]dinaphtho[2,1-h:1',2'-j]-[1,4,7,12,15,18,25,28]hexaoxadiazacyclotetratriacontine-2-carboxamidato(2-)-*$N^{16},N^{21},O^{45},O^{46}$*]dioxouranium.urea* (**2c**.urea). The product was purified as the urea complex by cooling a solution of **2c** in hot CH_3CN, containing excess urea. The urea complex slowly precipitated and was filtered off. Yield 56%; m.p. 257–259°C. Anal. calcd. for $C_{55}H_{44}ClN_3O_{12}U\cdot CH_4N_2O\cdot 1.25H_2O$ (1295.056): C 51.94, H 3.93, N 5.41; found: C 51.89, H 3.76, N 5.31%. Karl Fisher titration calcd. for 1.25 H_2O: 1.74; found: 1.76. ^1H NMR (DMSO-d_6): δ 10.60 and 10.57 (s, 2×1H, AmdOH and NH); 9.62 and 9.61 (s, 2×1H, HC=N); 8.76 (s, 1H, $BinC_4H$); 8.56 (d, 1H, *J* 2.5 Hz, $AmdC_6H$); 8.16 (d, 1H, *J* 8.0 Hz, BinH); 8.0–7.9 (m, 2H, BinH); 7.8–7.7 (m, 2H, AmH); 7.62 (d, 1H, *J* 9.1 Hz, $BinC_{3'}H$); 7.7–7.0 (m, 13H, ArH); 6.97 (d, 1H, *J* 8.6 Hz, $AmdC_3H$); 6.62 (t, 2H, *J* 7.8 Hz, $AldC_{5,5'}H$); 5.47 (bs, 4H, $(H_2N)_2C{=}O$); 4.5–3.2 (m, 16H, CH_2O). ^{13}C NMR (DMSO-d_6): δ 166.6, 166.4 (d, HC=N); 163.3 (s, C=O); 161.0, 160.9 (s,

AldC$_{2,2'}$); 154.6, 152.9 (s, BinC$_{2,2'}$); 150.1, 149.8 (s, AldC$_{3,3'}$); 146.8, 146.7 (s, AmC$_{1,1'}$); 145.6 (s, AmdC$_2$); 74.2–67.3 (t, CH$_2$O). IR (KBr): 3432, 3400, 3371, 3323, 3266 (NH); 1652 (NC=O); 1625 ((H$_2$N)$_2$C=O); 1602 (HC=N) cm^{-1}. Ms (FAB) *m/z*: 1272.1 ([M + urea + H]$^+$, calcd. for [C$_{55}$H$_{44}$ClN$_3$O$_{12}$U + CH$_4$N$_2$O + H] 1272.3); 1212.3 ([M + H]$^+$, calcd. 1212.3); (EI) *m/z*: 60.032 (M$^+$, calcd. for CH$_4$N$_2$O 60.032).

*[N-(5-Chloro-2-hydroxyphenyl)-4,5,7,8,10,11,32,33,35,36,38,39-dodecahydro-51,52-dihydroxy-13,17:26,30-dimethenobenzo[f$_1$]dinaphth-[2,1-k:1',2'-m][1,3,7,10,15,18,21,24,31,34]octaoxadiazacyclotetracontine-2-carboxamidato(2-)-N^{19},N^{24},O^{51},O^{52}]dioxouranium · urea (**2d** · urea)* The product was purified as the urea complex by cooling a solution of **2d** in hot CH$_3$CN, containing excess urea. The urea complex slowly precipitated and was filtered off. Yield 58%; m.p. 199–202°C. Anal. calcd. for C$_{59}$H$_{52}$ClN$_3$O$_{14}$U · CH$_4$N$_2$O · H$_2$O (1378.659): C 52.27, H 4.24, N 5.08; found: C 53.03, H 4.55, N, 5.39%. Karl Fisher titration calcd. for 1 H$_2$O: 1.31; found: 1.20. ^{1}H NMR (DMSO-d_6): δ 10.65 and 10.58 (s, 2H, AmdOH and NH); 9.61 (s, 2H, HC=N); 8.86 (s, 1H, BinC$_4$H); 8.60 (d, 1H, *J* 2.5 Hz, AmdC$_6$H); 8.22 (d, 1H, *J* 8.2 Hz, BinH); 8.16 (d, 1H, *J* 9.2 Hz, BinH); 7.99 (d, 1H, *J* 7.8 Hz, BinH); 7.8–7.7 (m, 2H, AmH); 7.70 (d, 1H, *J* 9.4 Hz, BinC$_{3'}$H); 7.6–6.9 (m, 13H, ArH); 6.90 (d, 1H, *J* 8.6 Hz, AmdC$_3$H); 6.62 and 6.60 (t, 2×1H, *J* 7.6 Hz, AldC$_{5,5'}$H); 5.48 (bs, 4H, (H$_2$N)$_2$C=O); 4.4–2.8 (m, 24H, CH$_2$O). ^{13}C NMR (DMSO-d_6): δ 166.5 (d, HC=N); 163.1 (s, C=O); 161.0 (s, AldC$_{2,2'}$); 154.0, 151.4 (s, BinC$_{2,2'}$); 150.3, 150.2 (s, AldC$_{3,3'}$); 146.8 (s, AmC$_{1,1'}$); 145.5 (s, AmdC$_2$); 73.4–68.4 (t, CH$_2$O). IR (KBr): 3431, 3425, 3328 (NH); 1648 (NC=O); 1623 ((H$_2$N)$_2$C=O); 1603 (HC=N) cm^{-1}. Ms (FAB) m/z: 1300.1 ([M + H]$^+$, calcd. 1300.4).

*[Cis-4,5,7,8,16a,17,18,19,20,20a,29,30,32,33-tetradecahydro-45,46-dihydroxy-N-(2-hydroxy-5-methylphenyl)-10,14:23,27-dimethenobenzo-[z]dinaphtho[2,1-h:1',2'-j][1,4,7,12,15,18,25,28]hexaoxadiazacyclotetratriacontine-2-carboxamidato(2-)-N^{16},N^{21},O^{45},O^{46}]dioxouranium (**3a**).* The product was purified by trituration with CH$_2$Cl$_2$. Yield 90%; m.p. > 300°C (dec). Anal. calcd. for C$_{56}$H$_{53}$N$_3$O$_{12}$U · 0.5 C$_6$H$_{12}$ · 0.5 H$_2$O (1249.199): C 56.73, H 4.84, N 3.36; found: C 56.56, H 4.73, N 3.31%. Karl Fisher titration calcd. for 0.5 H$_2$O: 0.72; found: 0.80. ^{1}H NMR DMSO-d_6): δ 10.46 and 10.44 (s, 1H, NH); 9.90 and 9.88 (s, 1H, AmdOH); 9.39 (s, 2H, HC=N); 8.75 (s, 1H, BinC$_4$H); 8.3–7.9 (m, 4H, AmdC$_6$H and BinC$_{4',5,5'}$H); 7.70 and 7.68 (d, 1H, *J* 9.1 Hz, BinC$_{3'}$H); 7.6–6.9 (m, 11H, ArH); 6.9–6.7 (m, 2H, AmdC$_{3,4}$H); 6.6–6.5 (m, 2H, AldC$_{5,5'}$H); 4.7–4.5 (m, 2H, AmC$_{1,1'}$H); 4.5–3.2 (m, 16H, CH$_2$O); 2.5–2.2 (m, 2H, AmC$_{2,2'}$H); 2.25 and 2.24 (s, 3H, AmdCH$_3$); 1.9–1.7 (m, 2H, AmC$_{2,2'}$H); 1.7–1.5 (m, 4H, AmC$_{3,3'}$H). ^{13}C NMR (DMSO-d_6): δ 167.6 (d, HC=N); 163.0, 162.9 (s, C=O); 159.9, 159.6 (s, AldC$_{2,2'}$); 154.6, 152.7 (s, BinC$_{2,2'}$); 149.99, 149.95, 149.7, 149.6 (s, AldC$_{3,3'}$); 144.7 (s, AmdC$_2$); 70.5 (d, AmC$_{1,1'}$); 73.8–67.1 (t, CH$_2$O); 27.5, 27.3 (t, AmC$_{2,2'}$); 21.5, 21.2 (t, AmC$_{3,3'}$); 20.7 (q, AmdCH$_3$). IR (KBr): 1613 (HC=N); 897 (O–U–O) cm^{-1}. Ms (FAB) *m/z*: 1198.4 ([M + H]$^+$, calcd. 1198.4).

*[Cis-4,5,7,8,10,11,19a,20,21,22,23,23a,32,33,35,36,38,39-octadecahydro-51,52-dihydroxy-N-(2-hydroxy-5-methylphenyl)-13,17:26,30-dimethenobenzo[f$_1$]dinaphth[2,1-k:1',2'-m][1,4,7,10,15,18,21,24,31,34]octaoxadiazacyclotetracontine-2-carboxamidato(2-)-N^{19}, N^{24}, O^{51}, O^{52}]dioxouranium (**3b**).* The product was purified by flash column chromatography (eluent MeOH/CH$_2$Cl$_2$ 5:95), followed by precipitation from CH$_2$Cl$_2$ with cyclohexane. Yield 81%; m.p. 196–198 °C. Anal. calcd. for C$_{60}$H$_{61}$N$_3$O$_{14}$U · 1.25H$_2$O (1308.737): C 55.07, H 4.89, N 3.21; found: C 55.42, H 4.79, N 3.18%. Karl Fisher titration calcd. for 1.25 H$_2$O: 1.72; found: 1.79. ^{1}H NMR (DMSO-d_6): δ 10.49 (s, 1H, NH); 9.96 (s, 1H, AmdOH); 9.42 (s, 2H, HC=N); 8.83 (s, 1H, BinC$_4$H); 8.30 (s, 1H, AmdC$_6$H); 8.3–8.1 (m, 2H, BinC$_{4',5}$H); 8.00 (d, 1H, *J* 7.8 Hz, BinC$_{5'}$H); 7.72 (d, 1H, *J* 9.2 Hz, BinC$_{5'}$H); 7.6–7.2 (m, 8H, ArH); 7.05 and 7.03 (d, 2H, *J* 8.1 Hz, BinC$_{8,8'}$ H); 6.9–6.7 (m, 2H, AmdC$_{3,4}$H); 6.62 and 6.60 (t, 2H, *J* 7.7 Hz, AldC$_{5,5'}$H); 4.7–4.5 (m, 2H, AmC$_{1,1'}$H); 4.4–2.9 (m, 24H, CH$_2$O); 2.5–2.2 (m, 2H, AmC$_{2,2'}$H); 2.26 (s, 3H, AmdCH$_3$); 2.0–1.7 (m, 2H, AmC$_{2,2'}$H); 1.7–1.5 (m, 4H, AmC$_{3,3'}$H). ^{13}C NMR (DMSO-d_6): δ 167.8 (d, HC=N); 162.8 (s, C=O); 159.8, 159.7 (s, AldC$_{2,2'}$); 154.1, 151.7 (s, BinC$_{2,2'}$); 150.11, 150.09 (s, AldC$_{3,3'}$); 144.5 (AmdC$_2$); 70.7, 70.5 (d, AmC$_{1,1'}$); 73.4–68.4 (t, CH$_2$O); 27.4 (t, AmC$_{2,2'}$); 21.3 (t, AmC$_{3,3'}$); 20.7 (q, AmdCH$_3$). IR (KBr): 3340, 3312 (NH, OH); 1662 (w, NC=O); 1615 (s, HC=N); 900 (O–U–O) cm^{-1}. Ms (FAB) *m/z*: 1286.9 ([M + H]$^+$, calcd. 1286.5).

*[N-(5-Chloro-2-hydroxyphenyl)-cis-4,5,7,8,16a,17,18,19,20,20a,29,30,32,33-tetradecahydro-45,46-dihydroxy-10,14:23,27-dimethenobenzo[z]-dinaphtho[2,1-h:1',2'-j][1,4,7,12,15,18,25,28]hexaoxadiazacyclotetratriacontine-2-carboxamidato(2-)-N^{16},N^{21},O^{45},O^{46}]dioxouranium (**3c**).* The product was purified by trituration with CH$_2$Cl$_2$. Yield 75%; m.p. > 300°C (dec). Anal. calcd. for C$_{55}$H$_{50}$ClN$_3$O$_{12}$U · 1.5H$_2$O (1245.551): C 53.08, H 4.29, N 3.37; found: C 53.27, H 4.32, N 3.12%. Karl Fisher titration calcd. for 1.5 H$_2$O: 2.17; found: 2.13. ^{1}H NMR (DMSO-d_6): δ 10.7–10.5 (m, 2H, AmdOH and NH); 9.41 (s, 2H, HC=N); 8.81 (s, 1H, BinC$_4$H); 8.56 (s, 1H, AmdC$_6$H); 8.3–7.9 (m, 3H, BinC$_{4',5,5'}$H); 7.70 (d, 1H, *J* 9.0 Hz, BinC$_{3'}$H); 7.6–6.9 (m, 12H, ArH); 6.58 (t, 2H, *J* 7.7 hz, AldC$_{5,5'}$H); 4.7–4.5 (m, 2H, AmC$_{1,1'}$H); 4.5–3.1 (m, 16H, CH$_2$O); 2.5–2.2 (m, 2H, AmC$_{2,2'}$H); 1.9–1.7 (m, 2H, AmC$_{2,2'}$H); 1.7–1.5 (m, 4H, AmC$_{3,3'}$H). ^{13}C NMR (DMSO-d_6): δ 167.5 (d, HC=N); 163.3, 163.2 (s, C=O); 159.8, 159.53, 159.45 (s, AldC$_{2,2'}$); 154.6, 152.7, 152.6 (s, BinC$_{2,2'}$); 150.0, 149.9, 149.7, 149.5 (s, AldC$_{3,3'}$); 145.6 (s, AmdC$_2$); 70.9, 70.3 (d, AmC$_{1,1'}$); 74.0–68.1 (t, CH$_2$O); 27.5 (t, AmC$_{2,2'}$); 21.5 (t, AmC$_{3,3'}$). IR (KBr): 1655 (NC=O); 1615 (HC=N); 898 (O–U–O) cm^{-1}. Ms (FAB) *m/z*: 1218.2 ([M + H]$^+$, calcd. 1218.4).

*[N-(5-Chloro-2-hydroxyphenyl)-cis-4,5,7,8,10,11,19a,20,21,22,23,23a,32,33,35,36,38,39-octadecahydro-51,52-dihydroxy-13,17:26,30-dimethenobenzo[f$_1$]dinaphth[2,1-k:1',2'-m][1,4,7,10,15,18,21,24,31,34]octaoxadiazacyclotetracontine-2-carboxamidato(2-)-N^{19},N^{24},O^{51},O^{52}]dioxouranium (**3d**).* The product was purified by flash column chromatography (eluent MeOH/CH$_2$Cl$_2$ 5:95), followed by precipitation from CH$_2$Cl$_2$ with cyclohexane. Yield 84%; m.p. 201–204°C. Anal. calcd. for C$_{59}$H$_{58}$ClN$_3$O$_{14}$U · H$_2$O (1324.651): C 53.50, H 4.57, N 3.17; found: C 53.48, H 4.67, N 2.92%. Karl Fisher titration calcd. for 1 H$_2$O: 1.36; found: 1.26. ^{1}H NMR (DMSO-d_6): δ 10.7–10.5 (m, 2H, AmdOH and NH); 9.41 (s, 2H, HC=N); 8.82 (s, 1H, BinC$_4$H); 8.54 (d, 1H, *J* 2.5 Hz, AmdC$_6$H); 8.3–8.1 (m, 2H, BinC$_{4',5}$H); 7.99 (d, 1H, *J* 7.9 Hz, BinC$_{5'}$H); 7.71 (d, 1H, *J* 9.2 Hz, BinC$_{3'}$H); 7.6–6.9 (m, 11H, ArH); 6.88 (d, 1H, *J* 8.6 Hz, AmdC$_3$H); 6.59 and 6.58 (t, 2H, *J* 7.8 Hz, AldC$_{5,5'}$H); 4.7–4.5 (m, 2H, AmC$_{1,1'}$H); 4.4–2.9 (m, 24H, CH$_2$O); 2.5–2.2 (m, 2H, AmC$_{2,2'}$H); 1.9–1.7 (m, 2H, AmC$_{2,2'}$H); 1.7–1.5 (m, 4H, AmC$_{3,3'}$H). ^{13}C NMR (DMSO-d_6): δ 167.8 (d, HC=N); 163.0 (s, C=O); 159.7 (s, AldC$_{2,2'}$); 154.1, 151.5 (s, BinC$_{2,2'}$); 150.09, 150.05 (s, AldC$_{3,3'}$); 145.5 (s, AmdC$_2$); 132.5 (d, BinC$_4$); 130.4, 129.4 (d, BinC$_{4',5}$); 128.1 (d, BinC$_{5'}$); 119.7 (d, AmdC$_6$); 115.7 (d, AmdC$_3$); 115.4 (d, AldC$_{5,5'}$); 114.9 (d, BinC$_{3'}$); 70.7, 70.5 (d, AmC$_{1,1'}$); 73.4–68.4 (t, CH$_2$O); 27.4 (t, AmC$_{2,2'}$); 21.4 (t, AmC$_{3,3'}$). IR (KBr): 1665 (NC=O); 1615 (HC=N); 901 (O–U–O) cm^{-1}. Ms (FAB) *m/z*: 1306.4 ([M + H]$^+$, calcd. 1306.4).

*[Cis-4,5,7,8,16a,17,18,19,20,20a,29,30,32,33-tetradecahydro-45,46-dihydroxy-N,N'-bis(2-hydroxy-5-methylphenyl)-10,14:23,17-dimethenobenzo[z]dinaphtho[2,1-h:1',2'-j][1,4,7,12,15,18,25,28]hexaoxadia-zacyclotetratriacontine-2,35-dicarboxamidato(2-)-N^{16},N^{21},O^{45},O^{46}]-dioxouranium (**3e**).* The product was purified by flash column chromatography (eluent MeOH/CH$_2$Cl$_2$ 3:97), followed by precipitation from CH$_2$Cl$_2$ with cyclohexane. Yield 71%; m.p. > 300°C (dec). Anal. calcd. for C$_{64}$H$_{60}$N$_4$O$_{14}$U · 0.5C$_6$H$_{12}$ · 0.75H$_2$O (1402.854): C 57.36, H 4.85, N 3.99; found: C 57.13, H 5.05, N 3.94%. Karl Fisher titration calcd. for 0.75 H$_2$O: 0.96; found: 1.03. ^{1}H NMR (CDCl$_3$): δ 10.83 and 10.63 (s, 2×1H, NH); 9.54 and 9.22 (bs, 2×1H, AmdOH); 9.24 and 9.20 (s, 2×1H, HC=N); 8.96 and 8.92 (s, 2×1H, BinC$_4$H); 8.2–8.0 (m, 4H, BinC$_{5,5'}$H + AmdC$_{6,6'}$H); 7.6–7.3 (m, 4H, BinC$_{6,6',7,7'}$H); 7.2–7.0 (m, 6H, ArH); 6.67 and 6.60 (t, 2×1H, *J* 7.8 Hz, AldC$_{5,5'}$H); 6.47 (s, 2H, AmdH); 6.42 (s, 2H, AmdH); 5.94 (bs, 2H, H$_2$O); 4.7–4.5 (m, 2H, AmC$_{1,1'}$H); 4.3–2.9 (m, 16H, CH$_2$O); 2.5–2.2 (m, 2H, AmC$_{2,2'}$H); 2.05 and 1.97 (s, 2×3H, AmdCH$_3$); 2.0–1.8 (m, 2H, AmC$_{2,2'}$H); 1.8–1.5 (m, 4H, AmC$_{3,3'}$H). ^{13}C NMR (CDCl$_3$): δ 167.7, 167.5 (d, HC=N); 163.4, 163.1 (s, C=O); 159.7, 159.2 (s, AldC$_{2,2'}$); 152.9, 152.6 (s, BinC$_{2,2'}$); 149.9, 149.7 (s, AldC$_{3,3'}$); 143.9 (s, AmdC$_{2,2'}$); 71.6, 71.4 (d, AmC$_1$); 73.8–68.7 (t, CH$_2$O); 27.7, 27.6 (t, AmC$_{2,2'}$); 21.7, 21.6 (t, AmC$_{3,3'}$); 20.7, 20.5 (q, AmdCH$_3$). IR (KBr): 1665 (NC=O); 1615 (HC=N); 902 (O–U–O) cm^{-1}. Ms (FAB) *m/z*: 1347.4 ([M + H]$^+$, calcd. 1347.5).

*[Cis-4,5,7,8,10,11,19a,20,21,22,23,23a,32,33,35,36,38,39-octadecahydro-51,52-dihydroxy-N,N'-bis(2-hydroxy-5-methylphenyl)-13,17:26,30-dimethenobenzo[f$_1$]dinaphth[1,2-k:1',2'-m][1,4,7,10,15,18,21,24,31,34]octaoxadiazacyclotetracontine-2,41-dicarboxamidato(2-)-N^{19},N^{24},-O^{51},O^{52}]dioxouranium (**3f**).* The product was purified by flash column chromatography (eluent MeOH/CH$_2$Cl$_2$ 5:95), followed by precipitation from CH$_2$Cl$_2$ with cyclohexane. Yield 84%; m.p. > 300°C (dec). Anal. calcd. for C$_{68}$H$_{68}$N$_4$O$_{16}$U · 0.5H$_2$O (1444.376): C 56.55, H 4.82, N 3.88; found: C 56.38, H 4.73, N 3.76%. Karl Fisher titration calcd. for 0.5 H$_2$O: 0.62; found: 0.72. ^{1}H NMR (CDCl$_3$): δ 10.73 and 10.61 (s, 2×1H, NH); 9.30 and 9.26 (s, 2×1H, HC=N); 8.95 and 8.93 (s, 2×1H, BinC$_{4,4'}$H); 8.13 (d, 2H, *J* 9.1 Hz, BinC$_{5,5'}$H); 8.07 and 7.81 (s, 2×1H, AmdC$_{6,6'}$H); 7.6–7.3 (m, 4H, BinC$_{6,6',7,7'}$H); 7.2–7.1 (m, 4H, AldH); 7.08 (d, 2H, *J* 8.1 Hz, BinC$_{8,8'}$H); 6.8–6.5 (m, 6H, ArH); 4.7–4.5 (m, 2H, AmC$_{1,1'}$H); 4.5–4.4 (m, 1H, CH$_2$O); 4.3–2.7 (m, 22H, CH$_2$O); 2.6–2.3 (m, 3H, CH$_2$O and AmC$_{2,2'}$H); 2.20 and 2.14 (s, 2×3H, AmdCH$_3$); 2.1–1.5 (m, 6H, AmC$_{2,2',3,3'}$H);

^{1}H NMR (DMSO-d_6): δ 10.16 (s, 2H, NH); 9.97 and 9.96 (s, 2×1H, AmdOH); 9.41 and 9.40 (s, 2×1H, HC=N); 8.81 (s, 2H, $BinC_{4,4'}H$); 8.26 (d, 2H, J 8.1 Hz, $BinC_{5,5'}H$); 8.10 (s, 2H, $AmdC_{6,6'}H$); 7.57 (t, 2H, J 7.5 Hz, $BinC_{6,6'}H$); 7.45 (t, 2H, J 7.6 Hz, $BinC_{7,7'}H$); 7.26 (d, 2H, J 7.9 Hz, AldH); 7.18 (d, 2H, J 7.7 Hz, AldH); 7.07 (d, 2H, J 8.4 Hz, $BinC_{8,8'}H$); 6.76 (d, 2H, J 8.1 Hz, $AmdC_{3,3'}H$); 6.7–6.6 (m, 2H, $AmdC_{4,4'}H$); 6.58 (t, 2H, J 7.8 Hz, $AldC_{5,5'}H$); 4.7–4.5 (m, 2H, $AmC_{1,1'}H$); 4.3–2.9 (m, 24H, CH_2O); 2.5–2.2 (m, 2H, $AmC_{2,2'}H$); 2.18 (s, 6H, $AmdCH_3$); 1.9–1.7 (m, 2H, $AmC_{2,2'}H$); 1.7–1.5 (m, 4H, $AmC_{3,3'}H$). ^{13}C NMR (DMSO-d_6): δ 167.9 (d, HC=N); 163.1 (s, C=O); 159.6 (s, $AldC_{2,2'}$); 151.5 (s, $BinC_{2,2'}$); 150.1 (s, $AldC_{3,3'}$); 144.7 (s, $AmdC_{2,2'}$); 134.7 (s, $BinC_{8a,8a'}$); 132.6 (d, $BinC_{4,4'}$); 129.9 (s, $BinC_{4a,4a'}$); 70.9, 70.3 (d, $AmC_{1,1'}$); 73.0–68.4 (t, CH_2O); 27.6, 27.2 (t, $AmC_{2,2'}$); 21.6, 21.1 (t, $AmC_{3,3'}$); 20.6 (q, $AmdCH_3$). IR (KBr): 1616 (HC=N); 899 (O–U–O) cm^{-1}. Ms (FAB) m/z: 1435.4 ([M + H]$^+$, calcd. 1435.5).

Calculations

Molecular-mechanics calculations were performed with CHARMm and the graphical QUANTA interface[24]. Force-field parameters were taken from CHARMm, except the electrostatic[1h] and the non-bonded parameters[1h] for the uranyl cation, which were determined to reproduce the experimental hydration geometry and enthalpy. The coordinates of the salophen units were taken from published structures[1c,e] and were kept constant by imposing constraints on the atomic positions.
With molecular-mechanics calculations, steric minima of the complexes were determined. Minimizations were terminated at *RMS* < 0.0001.

Electrochemistry

Cyclic voltammetry was carried out with an AUTOLAB-100 computerized system for electrochemistry (Eco Chemie, Utrecht, The Netherlands). The measurements were performed at a static mercury-drop electrode (Metrohm, 663 VA Stand). A Ag/AgCl reference electrode, filled with 0.1M Et_4NCl (Fluka, recrystallized from acetone) in DMSO (Merck, distilled), was used. The reference electrode was brought into contact with the sample via an electrolytic bridge filled with 0.35M Et_4NClO_4 (Fluka, purum) in DMSO. A glassy carbon rod was used as auxiliary electrode.
The sample concentrations were 0.36–0.56mM **3** in DMSO. Oxygen was expelled by bubbling with nitrogen (Hoekloos, very pure) for at least 12 min. Cyclic voltammograms for each compound were recorded at different scan rates (0.2, 0.5, 1.0, and 1.5 V/s) and at different urea concentrations (0–0.12M).

Hydrolysis experiments

The reactions were carried out in polypropylene vials with screw caps. In each vial, approximately 1.5 ml of the reaction mixture [10mM or 2.5M urea (crystallized from EtOH) in dioxane/water 4:1 (v/v) for the blank reaction; 10mM or 2.5M urea and 3mM **2a** in dioxane/water 4:1 (v/v) for the hydrolysis reaction] was heated at 80°C. After appropriate time intervals, the vials were removed from the heating bath and cooled to 0°C. 1.00 ml of the reaction mixture was transferred to the outer chamber of a Conway microdiffusion cell (which had been thoroughly cleaned with alkaline ethanol, diluted sulfuric acid, demineralized water, and ethanol, successively). Into the inner chamber 1.00 ml 2mM nitric acid was introduced from a burette. The diffusion cells were covered with glass plates and sealed with silicone grease. Through a small slit, approximately 1 ml of a saturated K_2CO_3 solution was added to the outer chamber. The liquids in the outer chamber were mixed by carefully rotating the diffusion cells approximately 20 times.
After 2 h at room temperature, the contents of the central chamber were removed and analyzed by ion chromatography, using a Waters 6000 A solvent delivery system and a Waters U6K injector together with one of the following columns:
1) Vydac 400 IC Cation (Metrohm, 50×4.6 mm) 2mM HNO_3, 2 ml/min
2) Hamilton PRP-X200 Cation (Applikon, 250×4.1 mm) 4mM HNO_3 in MeOH/H_2O 3:7 (v/v), 2 ml/min
3) IC-PAK C M/D (Waters, 150×3.9 mm) 3mM HNO_3 and 0.1mM EDTA, 1 ml/min.
The temperature of the columns was set at 35°C. The sample (25 μl) was injected with a Hamilton syringe.

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midazole), followed by aminolysis of the resulting acyl imidazolides gave products **9** in 70–80% yield. Converting the carboxylic acids **7** into the corresponding acid chlorides with oxalyl chloride and reacting these compounds with amide **8** in the presence of pyridine gave **9** in 40–90% yield. The higher yields were obtained if 5 equiv of oxalyl chloride were used for the synthesis of the acid chlorides instead of 2 equiv. Aminolysis of the active esters, formed by the reaction of carboxylic acids **7** with HOBT (*N*-hydroxybenzotriazole) and DCC (dicyclohexylcarbodiimide) with amine **8** afforded **9** in approximately 90% yield.

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[17] To investigate this interconversion in more detail, solutions of $\mathbf{2a}_{I}$ and $\mathbf{2a}_{II}$ in $CHCl_3$ with 5% of methanol were analyzed by HPLC (column: LiChrospher Si-60, 5 μ, 125×4 mm Merck 50820; eluent $MeOH/CH_2Cl_2$ 1.7:98.3, 1 ml/min; UV detection [254 nm]) after different time intervals.

$\mathbf{2a}_{I} \rightleftarrows \mathbf{2a}_{II}$ $\quad K_{eq} = [\mathbf{2a}_{I}]/[\mathbf{2a}_{II}]$

Although equilibrium was not yet reached after 28 h at room temperature, K_{eq} was estimated to be approximately 16. This means that, at equilibrium, **2a** is present in form I for 6% and in form II for 94%. At higher temperatures (50°C), the interconversion is much faster and a different equilibrium is reached (K_{eq} = 5).

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