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Synthesis of mono- and bibrachial naphthalene-based macrocycles with pyrene or ferrocene units for anion detection

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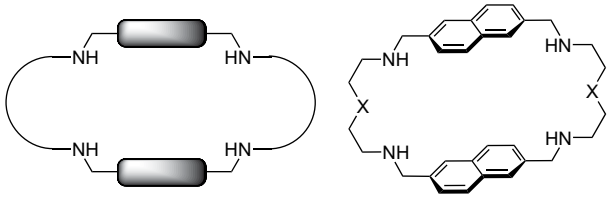
ABSTRACT

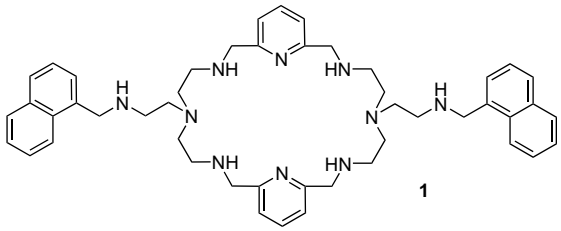
Three bibrachial cyclobisintercaland-type macrocycles with a 2,6-naphthylene scaffold and pyrene, ferrocene, or primary amino groups in side chains were synthesized by a [2+2]-cyclocondensation of functionalized diethylenetriamine derivatives with naphthalene-2,6-dialdehyde, whereas their monobrachial counterparts were prepared by a [1+1]-cyclocondensation of polyamines with a corresponding dialdehyde building block. The pyrene-functionalized macrocycles are able to bind orthophthalate and terephthalate anions in aqueous medium, as monitored by the changes in their fluorescence (excimer or monomer) properties.

1. Introduction

Macrocyclic compounds represent an important scaffold in coordination and supramolecular chemistry.[1,2] Among the vast number of macrocyclic compounds, which have been described, particularly interesting are the cyclobisintercaland compounds (**CBI**), which consist of two large aromatic units bridged by polyammonium chains. Similar to inclusion of aromatic drugs between the base pairs in nucleic acids (intercalation), the aromatic units in such macrocycles are situated at a distance suitable for intercalation of aromatic guest molecules. In fact, it was shown that naphthalene derivatives of this kind (**BisNP-O** and **BisNP-N**) are capable of inclusion of aromatic dicarboxylate anions, such as isomeric phthalate ions, as well as nucleotides, with a strong preference for purine derivatives.[3,4] Similar behavior was also observed for the Cu(II) complex of **BisNP-N**.[5] Moreover, these macrocyclic compounds exhibit rather unusual biochemical properties, for example, **BisNP-N** induces destabilization of double-helical DNA, presumably by binding to single-stranded loop or bulge regions of DNA.[6] Recently, we reported that **BisNP-O** selectively binds to mismatched base pairs in double-stranded DNA, with a strong preference to pyrimidine–pyrimidine mismatches, and is able to compete with a DNA enzyme for binding to its mismatched DNA target.[7]



CBI X = O: **BisNP-O** X = NH: **BisNP-N**



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In terms of molecular recognition, it is desirable that the binding of the guest molecule is accompanied by marked changes in the receptor's properties, which may be rapidly and conveniently monitored, e.g., fluorescence or electrochemical characteristics. For instance, the intrinsic fluorescence of naphthalene units in **BisNP-N** is efficiently quenched upon inclusion of nucleotides.[4] However, naphthalene units emit in the short-wavelength region of the spectrum, which suffers from background fluorescence of many biomolecules (λ <350 nm). Moreover, quenching of fluorescence is not desired for detection technologies, since it may be caused by the other stimuli affecting the fluorescence lifetime (oxygen, compounds with functional groups, which assist the intersystem crossing, etc.) Therefore, we decided to introduce reporting groups

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into the macrocyclic scaffold, which would give a fluorescence or electrochemical signal upon association of the macrocycle with guest molecules or upon binding to nucleic acids.

The synthesis of macrocyclic compounds bearing additional functional units is challenging.[2,8] A number of symmetrical macrocycles bearing one (*monobrachial*) or two pendant arms (*bibrachial macrocycles*) with amino, hydroxyl, or aromatic functional groups have been described. However, in most cases these groups are attached to small crown-ether fragments by short linkers. An illustrative example is given by compound **1**, which selectively binds citrate anions and signals the binding event by switching from excimer to monomer emission of naphthalene units.[9]

In our case, we decided to introduce longer pendant arms, to minimize the influence of bulky reporting units on the guest-binding properties of the cyclobisintercaland receptor. We envisaged that bibrachial macrocycles of this type may be obtained by the [2+2]-type condensation of an aromatic dialdehyde with diethylenetriamine derivatives, bearing a side chain with a reporting unit already attached to the central nitrogen atom (Scheme 1). This approach has been already applied for the synthesis of macrocycle **1**[10] and a few other related derivatives.[11,12]

However, the synthesis of monobrachial macrocycles bearing one pendant arm appeared to be more complex. Although several examples of unsymmetrical macrocycles, produced by a fragment-to-fragment assembly of building blocks, i.e., dialdehydes and diamines, are known, the final [1+1]-type condensation, resulting in formation of the macrocycle, is much less efficient and requires structural complementarity of the building blocks.[11] Moreover, to the best of our knowledge, unsymmetrical cyclobisintercaland-type macrocycles have not been described. Therefore, we developed the synthesis of naphthalene-based macrocycles of this type from a key building block, i.e., protected dialdehyde, and a diethylenetriamine derivative bearing a side-chain arm with a functional unit (Scheme 1). Moreover, we present the synthesis of the macrocycles with a primary amino group in the side chain, which gives a possibility for introduction of functional units *after* the macrocyclization step. Herein, we describe our approaches toward the synthesis of mono- and bibrachial macrocycles, derivatives of **BisNP-N**, incorporating fluorescent (pyrene), electrochemically-active (ferrocene), or reactive (primary amino group) substituents in the side arms.

2. Results and discussion

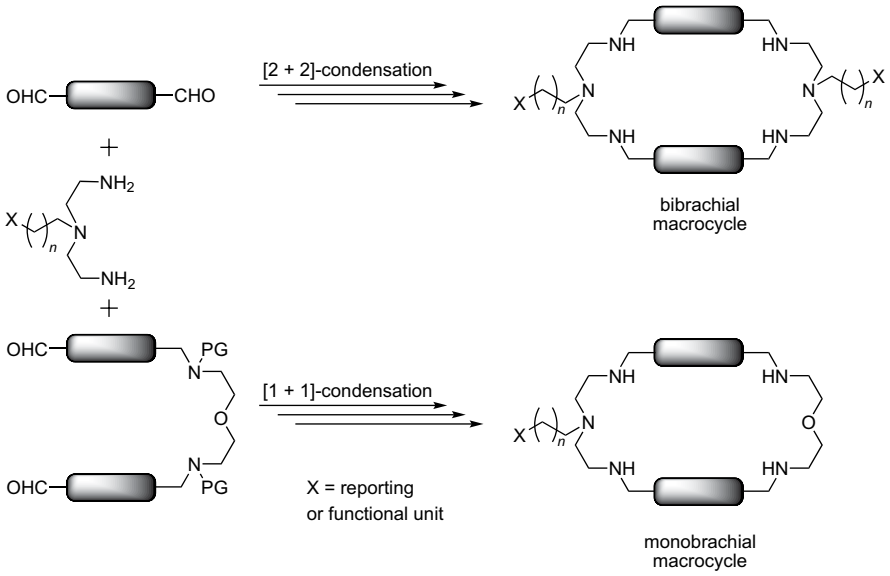
2.1. Synthesis of the dialdehyde building block 10

The starting material for the synthesis of the building block **10** was the commercially available unsymmetrically disubstituted naphthalene derivative, 6-bromo-2-naphtoic acid **2** (Scheme 2). After quantitative esterification and reduction of the methyl ester **3** with DIBAL-H, the alcohol **4** was oxidized with pyridinium chlorochromate to give 6-bromo-2-naphthaldehyde **5** in near-quantitative yield. The aldehyde group was protected using the $ZrCl_4$-catalyzed reaction with 1,3-propanediol in the presence of triethyl orthoformate as water scavenger,[13] to give the acetal **6** in high yield. To introduce the second aldehyde function, we performed halogen–lithium exchange with *n*-BuLi, followed by reaction of the lithio derivative with *N*-formylpiperidine. This method allowed us to obtain the key intermediate, the mono-protected dialdehyde **7**, in 65% yield. Notably, when DMF was employed as the source of formyl residue, the yield of **7** was significantly lower (25%), which is in agreement with the observations made for other substrates.[14,15]

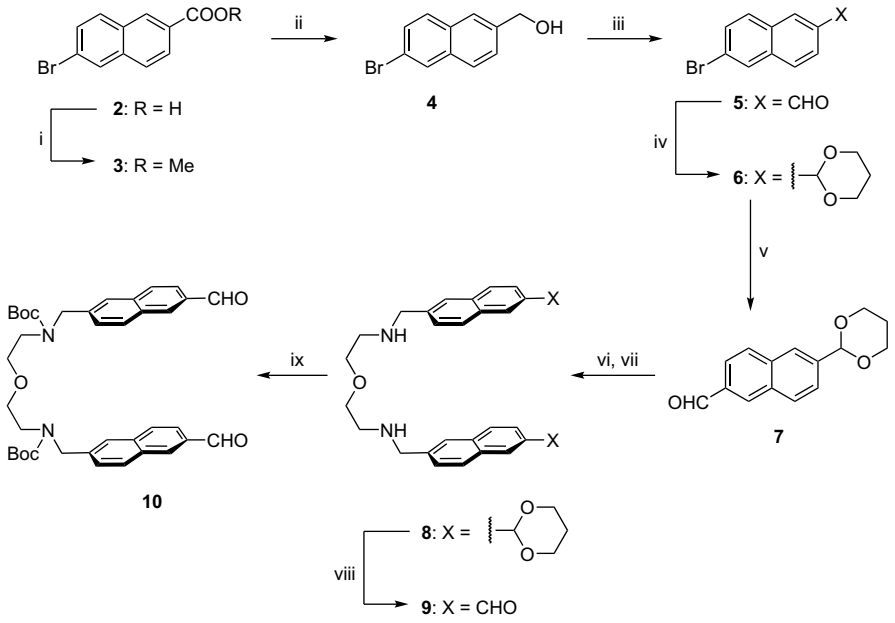
The dimeric derivative **8** was prepared in nearly quantitative yield by a two-step reductive amination of the intermediate **7** with 2,2′-oxydiethylamine. Notably, the removal of the two acetal protecting groups in **8** required rather harsh acidic treatment (6 M HCl, 60 °C) due to the presence of two basic nitrogen atoms in the molecule. The dialdehyde **9** was relatively unstable at room temperature and polymerization was observed after 24 h at 0 °C; therefore, crude **9** was converted to the di-*N*-Boc-protected building block **10**, which could be stored without appreciable decomposition for long periods.

2.2. Synthesis of the mono-protected polyamine 14

Although mono-protected derivatives of tris(2-aminoethyl)-amine (TREN) have been described,[16,17] we chose to prepare the TREN homologue **14** with a Boc-protected primary amino group in the side chain, longer than the two-carbon chains, which take part in formation of the macrocyclic framework. This approach should allow better separation of the side-chain functionality from the macrocyclic core. The polyamine **14** was readily prepared from the commercially available diethanolamine derivative **11** (Scheme 3).

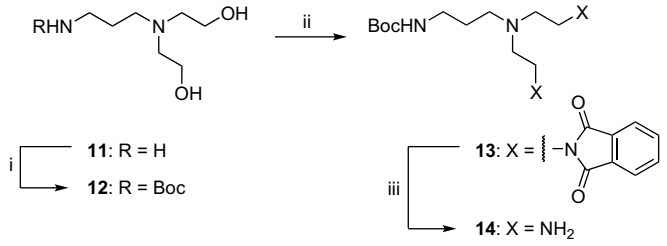


Scheme 1. General approach to mono- and bibrachial macrocycles.



Scheme 2. Synthesis of the building block **10**. Reagents and conditions: (i) MeOH, $HC(OMe)_3$, H_2SO_4, reflux, 100%; (ii) DIBAL-H, THF, rt, 40 h, 99%; (iii) PCC, CH_2Cl_2, reflux, 1 h, 98%; (iv) $HO(CH_2)_3OH$, $HC(OEt)_3$, $ZrCl_4$, CH_2Cl_2, rt, 96%; (v) *N*-formylpiperidine, *n*-BuLi, THF, −90 °C, 65%; (vi) $(H_2NCH_2CH_2)_2O$, benzene, reflux, 16 h; (vii) $NaBH_4$, MeOH, rt, 2 h, 97% over two steps; (viii) 6 M HCl, H_2O–dioxane, 60 °C, 4 h, 78%; (ix) Boc_2O, NEt_3, DMAP, CH_2Cl_2, rt, 18 h, 65%.

After initial Boc-protection of the amino group, the hydroxy groups of the diol **12** were substituted by primary amino groups using a Mitsunobu reaction with phthalimide, followed by cleavage of phthalimide groups with hydrazine to give the mono-Boc-protected polyamine **14** in 49% yield. We found that, for optimal yield of the product, this procedure may be performed using the 'one-pot' method, i.e., without isolation of the orthogonally protected derivative **13** before treatment with hydrazine. However, in a separate run a sample of compound **13** was isolated and characterized.



Scheme 3. Synthesis of the protected amine **14**. Reagents and conditions: (i) Boc_2O, CH_2Cl_2, 89%; (ii) phthalimide, PPh_3, DIAD, THF, rt, 16 h; (iii) H_2NNH_2, MeOH, reflux, 6 h, 49% over two steps.

2.3. Synthesis of the ferrocene-substituted polyamine 19

To obtain the ferrocene-modified polyamine **19**, we envisaged a reductive amination of 3-ferrocenylpropanal **18** with TREN (Scheme 4), since reductive amination is the preferred method for the synthesis of monofunctionalized derivatives of TREN.[18] Although the direct synthesis of aldehyde **18** by reaction of ferrocenylmethanol with an organomercuric derivative has been described previously,[19] the low yield and potential hazards of the published procedure prompted us to obtain this aldehyde via an alternative route. Thus, we prepared 3-ferrocenylpropanol **15** from ferrocenecarboxaldehyde in high yield by a modification of a published procedure.[20] However, the oxidation of this alcohol either by pyridinium chlorochromate at 40 °C or by activated DMSO at −60 °C (Swern method) were unsuccessful. The observed decomposition of the ferrocene unit and formation of ferric oxides indicated incompatibility of ferrocene derivatives with oxidizing agents.

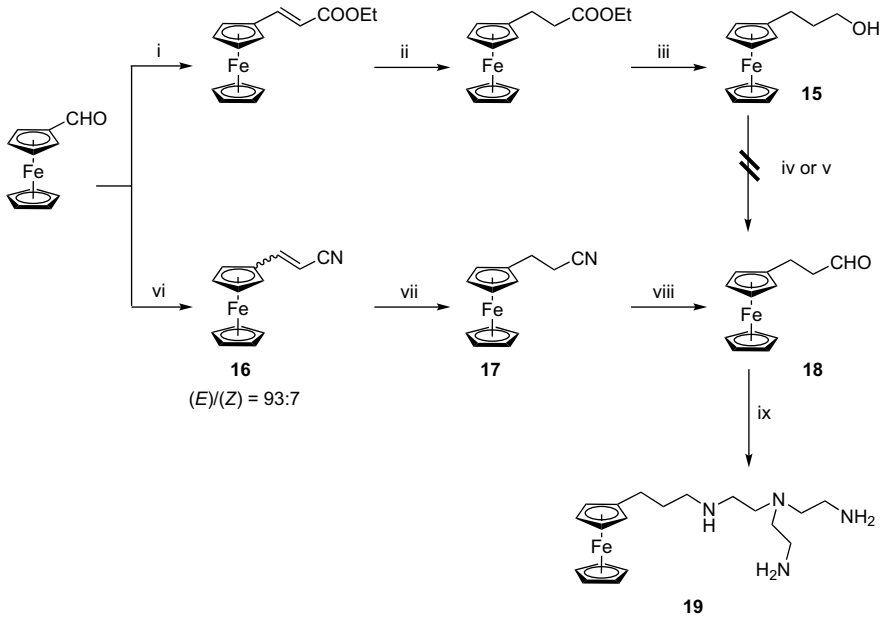
In another approach, we prepared 3-ferrocenylpropionitrile **17** by a Wittig–Horner reaction of ferrocenecarboxaldehyde with diethyl cyanomethylphosphonate, followed by hydrogenation of the resulting olefin **16**. This two-step procedure appeared less labor-intensive and much more efficient than the direct synthesis of nitrile **17** by alkylation of ferrocene with acrylonitrile.[21,22] The reduction of **17** with DIBAL-H readily gave the desired aldehyde **18**, which was made to react with a 10-fold excess of TREN, to afford, after reduction with $NaBH_4$ and purification by flash chromatography, the polyamine **19** in 79% yield.

2.4. Synthesis of the pyrene-substituted polyamine 23

The synthesis of the pyrene-modified polyamine **23** was accomplished in essentially analogous fashion as the ferrocene analogue **19**. In this case (Scheme 5), methyl 4-(1-pyrenyl)butyrate **20**, prepared from the commercially available 1-pyrenebutyric acid,[23] was quantitatively reduced with DIBAL-H to the alcohol **21**, which was further oxidized by the Swern reagent to 4-(1-pyrenyl)butanal **22**. Reductive amination of this aldehyde with an excess of TREN gave the pyrene-substituted polyamine **23** in 61% yield after purification by flash chromatography.

2.5. Synthesis of bibrachial macrocycles

The synthesis of symmetrical, bibrachial macrocycles **BisNP-2NH$_2$**, **BisNP-2FC**, and **BisNP-2PY** was performed by the [2+2]-type macrocyclization reaction between the readily available naphthalene-2,6-dialdehyde and polyamines **14**, **19**, and **23**, respectively (Scheme 6). In the case of Boc-protected polyamine **14**, the macrocyclic tetraimine **24** was formed in high yield (87%), but the purity of the isolated product was only about 85% (as determined by ^{1}H NMR spectroscopy), and attempts to purify this intermediate failed due to instability of the polyimine. To obtain the pure final product, the tetraimine **24** was reduced with $NaBH_4$ and the resulting amine was treated with excess Boc_2O to give the per-Boc-protected macrocyclic polyamine **25**, which could be readily purified by flash chromatography on silica. The ^{1}H and ^{13}C NMR



Scheme 4. Synthesis of the ferrocene-substituted amine **19**. Reagents and conditions: (i) $(EtO)_2P(O)CH_2COOEt$, NaOEt, EtOH, 0 °C, 1 h, 99%; (ii) H_2, 1 bar, Pd/C, AcOEt, 1 h, 99%; (iii) DIBAL-H, THF, rt, 20 h, 99%; (iv) PCC, CH_2Cl_2, reflux, 3 h; (v) $(COCl)_2$, DMSO, CH_2Cl_2, −60 °C, 15 min; (vi) $(EtO)_2P(O)CH_2CN$, K_2CO_3, EtOH, reflux, 1 h, 70%; (vii) H_2, 1 bar, Pd/C, EtOH, 4 h, 98%; (viii) DIBAL-H, CH_2Cl_2, rt, 30 min, 57%; (ix) $N(CH_2CH_2NH_2)_3$ (10 equiv), MeOH, $NaBH_4$, 18 h, 79%.

spectra of **25** showed very broad signals due to conformational restrictions imposed by the macrocyclic scaffold and numerous bulky Boc groups, but mass spectrometry confirmed the structure of the per-Boc-protected derivative. After removal of the protecting groups with HCl in EtOH, the macrocycle **BisNP-2NH$_2$** was obtained as pure hexahydrochloride salt.

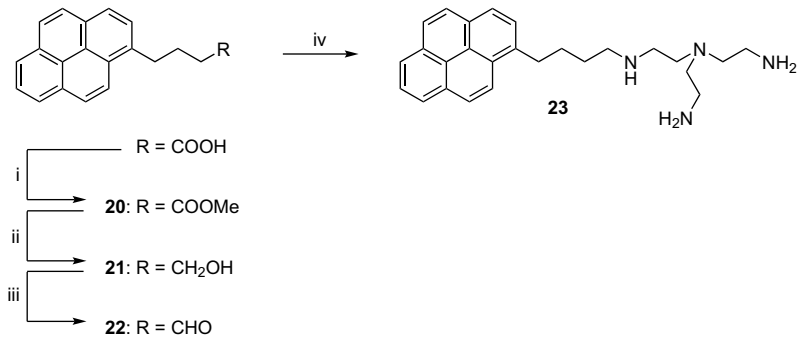
In analogous fashion, the ferrocene derivative **19** gave the corresponding macrocyclic tetraimine **26**. We were pleased to find that **26** required no additional purification and, after reduction with $NaBH_4$, the macrocyclic polyamine was converted to the hydrochloride salt, then recrystallized to give the bis-ferrocene-substituted macrocycle **BisNP-2FC×6HCl** in analytically pure form.

Finally, in the case of reaction with the pyrene derivative **23**, the macrocyclic tetraimine was not obtained in pure form. However, after reduction with $NaBH_4$, the macrocyclic polyamine **BisNP-2PY** could be readily purified by normal-phase flash chromatography using gradient elution with an increasing concentration of NH_4OH. After conversion to the hydrochloride salt, the macrocycle was recrystallized to give analytically pure **BisNP-2PY×6HCl**. The structures and purity of all macrocycles were confirmed by ^1H and ^{13}C NMR spectroscopy, mass spectrometry, elemental analysis, and HPLC analysis data.

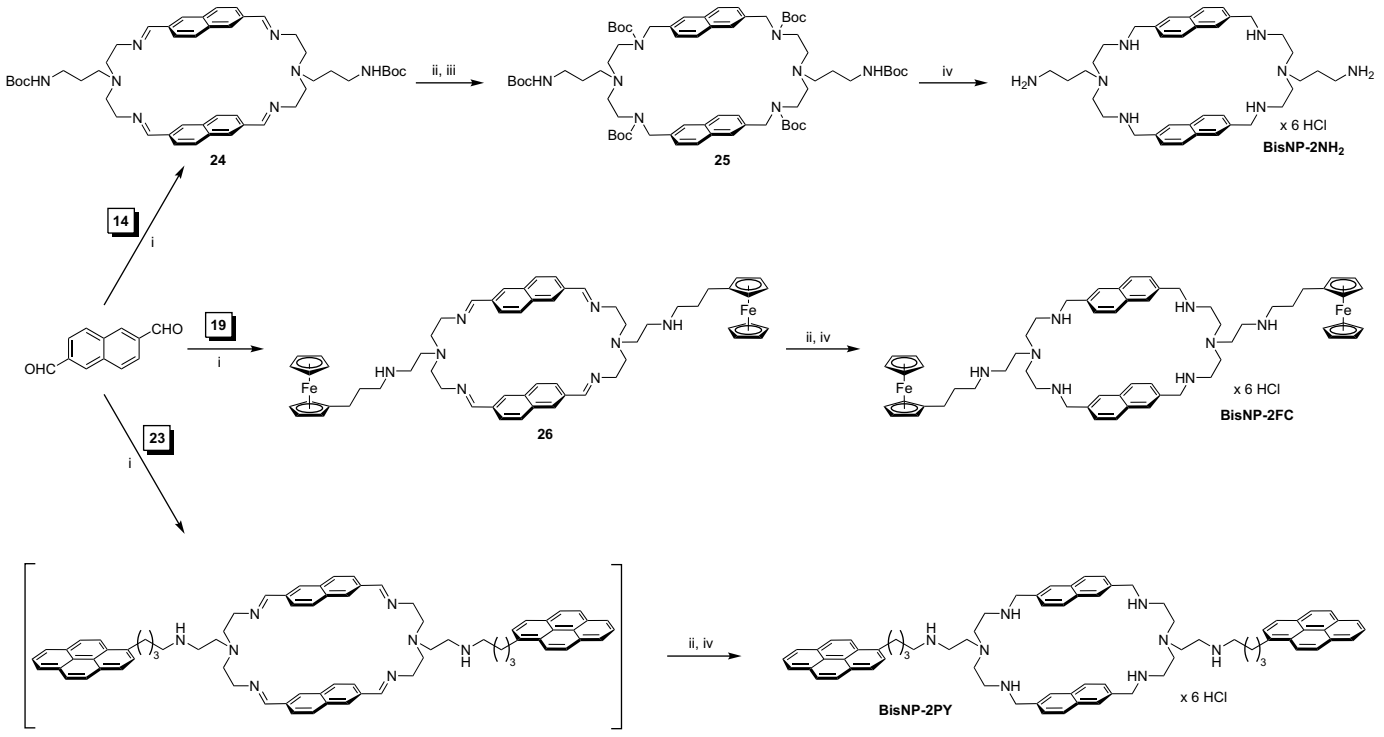
Altogether, these results indicate that the [2+2]-type macrocyclization reaction with naphthalene-2,6-dialdehyde readily proceeds with various derivatives of diethylenetriamine, and is essentially unaffected by the nature of the substituent at the central nitrogen atom. However, the substituent in the side chain has an influence on the purity of the intermediate tetraimine and on the method of choice for the purification of the final macrocycles. Thus, while pure ferrocene-substituted tetraimine **26** precipitated from the reaction medium, the *N*-Boc- and pyrene-substituted analogues were much less pure. In the latter case, the presence of the lipophilic pyrene units rendered the purification of the macrocycle **BisNP-2PY** by normal-phase flash chromatography feasible; however, in the case of **BisNP-2NH$_2$** it was necessary to achieve purification via the per-Boc-protected intermediate **25**.

2.6. Synthesis of monobrachial macrocycles

The synthesis of unsymmetrical, monobrachial macrocycles **BisNP-1NH$_2$** and **BisNP-1FC** was performed by the [1+1]-type cyclocondensation of dialdehyde **10** with polyamines **14** and **19**, respectively (Scheme 7). In contrast to the [2+2]-condensation, this type of macrocyclization was much less efficient, and the resulting



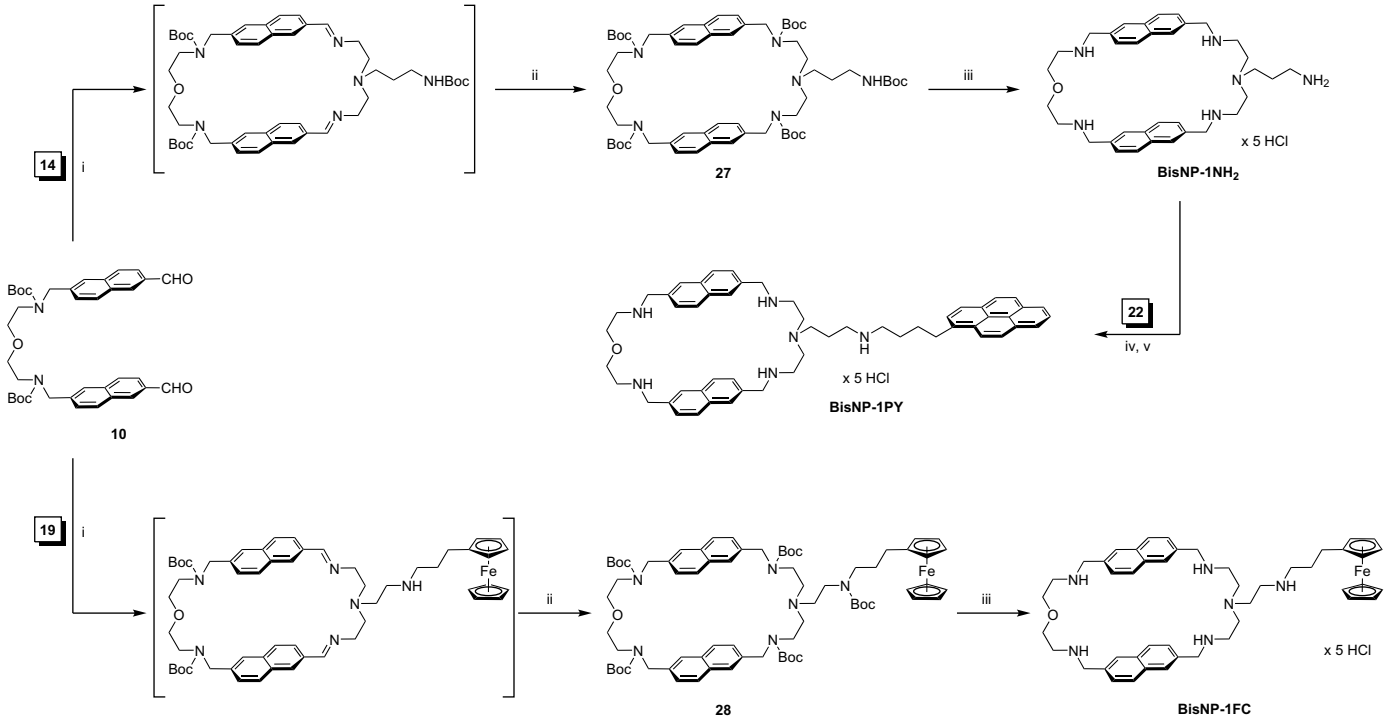
Scheme 5. Synthesis of the pyrene-substituted amine **23**. Reagents and conditions: (i) MeOH, H_2SO_4, reflux, 97%; (ii) DIBAL-H, THF, rt, 20 h, 99%; (iii) $(COCl)_2$, DMSO, CH_2Cl_2, −80 °C, 40 min, 90%; (iv) $N(CH_2CH_2NH_2)_3$ (10 equiv), MeOH, $NaBH_4$, 18 h, 61%.



Scheme 6. Synthesis of bibrachial macrocycles **BisNP-2NH$_2$**, **BisNP-2FC**, and **BisNP-2PY**. Reagents and conditions: (i) MeCN, rt, 2–5 days, 87% for **24**, 73% for **26**; (ii) $NaBH_4$, CH_2Cl_2–MeOH, rt, 3 h; (iii) Boc_2O, $NEt(^iPr)_2$, DMAP, CH_2Cl_2, 18 h; 51% for **25**; (iv) HCl, EtOH, reflux, 96% for **BisNP-2NH$_2$**, 79% for **BisNP-2FC**, 30% for **BisNP-2PY**.

macrocyclic diimines were not obtained in pure state. To obtain pure final products, the macrocyclic polyamines, obtained by reduction of the crude diimines with $NaBH_4$, were treated with excess of Boc_2O, and the resulting per-Boc-protected macrocycles **27** and **28** were isolated and purified by normal-phase flash chromatography on silica. As previously, the ^1H and ^{13}C NMR spectra of these compounds showed very broad signals, but mass spectrometry unambiguously confirmed their structure. After removal of the protecting groups by treatment with HCl in EtOH, the final compounds, macrocycles **BisNP-1NH$_2$×5HCl** and **BisNP-1FC×5HCl** were obtained; their structure and purity were confirmed by ^1H and ^{13}C NMR spectroscopy, mass spectrometry, elemental analysis, and HPLC analysis data.

To demonstrate that the primary amino group of the monobrachial macrocycle **BisNP-1NH$_2$** may be employed for introduction of various functional units, we synthesized the pyrene-containing



Scheme 7. Synthesis of monobrachial macrocycles **BisNP-1NH$_2$**, **BisNP-1PY**, and **BisNP-1FC**. Reagents and conditions: (i) MeCN, rt, 5–6 days; (ii) $NaBH_4$, CH_2Cl_2–MeOH, rt, 3 h, then Boc_2O, $NEt(^iPr)_2$, DMAP, CH_2Cl_2, 18 h, 27% for **27**, 41% for **28**; (iii) HCl, EtOH, reflux, 96% for **BisNP-1NH$_2$**, 61% for **BisNP-1FC**; (iv) MeOH, 18 h, then $NaBH_4$, 73%; (v) HCl, MeOH.

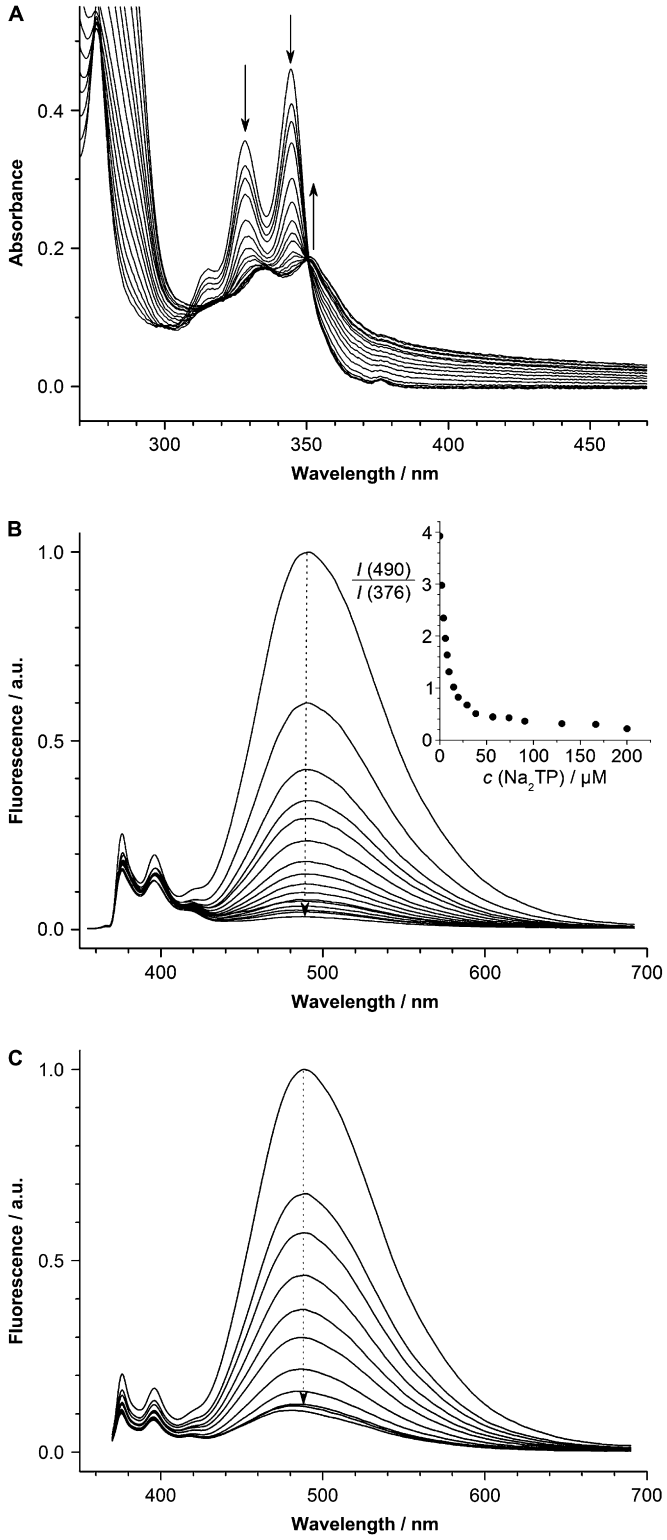


Figure 1. (A) Spectrophotometric titration of **Na_2TP** (0–610 μM) to a solution of **BisNP-2PY** (10 μM in sodium cacodylate buffer, pH 6.0). (B and C) Spectrofluorimetric titrations of **Na_2TP** (B, 0–200 μM) and **K_2OP** (C, 0–250 μM) to a solution of **BisNP-2PY** (2 μM), λ_{ex}=350 nm. The inset in (B) shows the changes of the ratio of fluorescence intensities at 490 nm (excimer) and 376 nm (monomer) as function of concentration of **Na_2TP**.

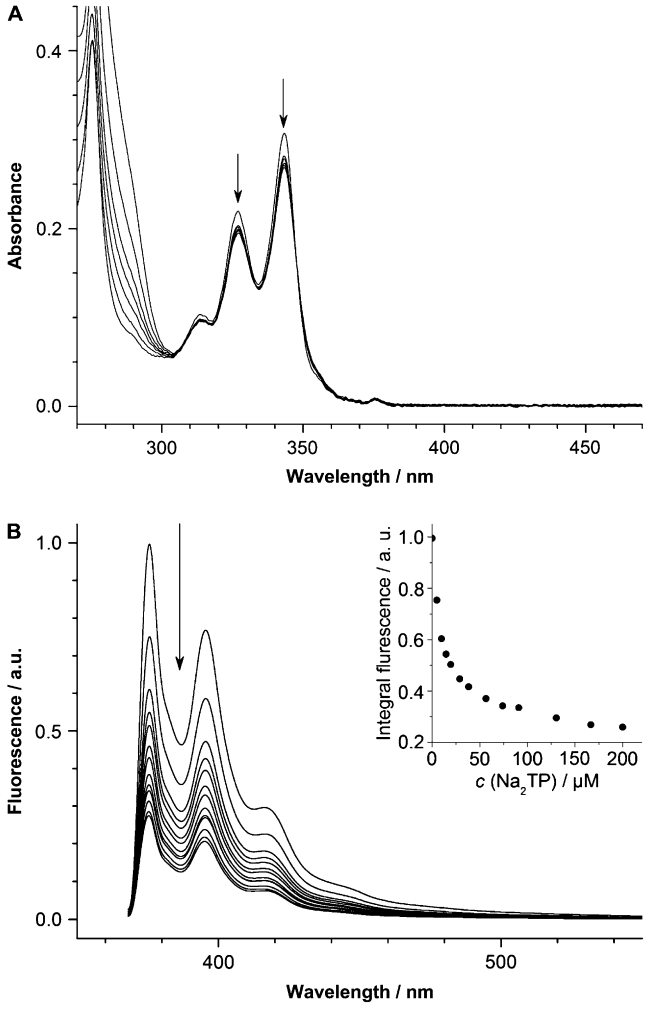


Figure 2. (A) Spectrophotometric titration of **Na_2TP** (0–300 μM) to a solution of **BisNP-1PY** (10 μM in sodium cacodylate buffer, pH 6.0). (B) Spectrofluorimetric titration of **Na_2TP** (0–200 μM) to a solution of **BisNP-1PY** (2 μM), λ_{ex}=348 nm. The inset shows the changes of integral fluorescence intensity as function of concentration of **Na_2TP**. The arrows show changes in the spectra in the course of titrations.

macrocycle **BisNP-1PY** by reductive amination of the aldehyde **22**. Indeed, this one-pot procedure gave the macrocycle **BisNP-1PY** in 73% yield after isolation by flash chromatography; for complete characterization this compound was converted to the hydrochloride salt **BisNP-1PY×5HCl**.

2.7. Interaction of BisNP-1PY and BisNP-2PY with orthophthalate and terephthalate ions

Since the ability of the macrocycles **BisNP-O** and **BisNP-N** to act as hosts for orthophthalate and terephthalate ions was demonstrated,[3,4] we investigated the capability of the pyrene derivatives **BisNP-1PY** and **BisNP-2PY** to function as fluorescent sensors for these analytes. Spectrophotometric titration of disodium terephthalate (**Na_2TP**) to solution of **BisNP-2PY** revealed pronounced hypochromic effect on the absorption spectrum of pyrene units, as well as a red shift of the absorption bands (Fig. 1A). This observation suggests formation of a ground-state complex of terephthalate anions with the receptor, which leads to the interaction of at least one pyrene ring with the guest. Moreover, the long-wavelength isosbestic point was conserved in the used range of concentration of the analyte, which gives evidence that one type of host–guest complex is formed in these conditions. Essentially the same changes in absorption spectrum were observed when a solution of **BisNP-2PY** was titrated with dipotassium orthophthalate (**K_2OP**; data not shown).

The fluorescence spectrum of **BisNP-2PY** revealed a strong broad band with a maximum at around 490 nm, corresponding to formation of an excimer between two pyrene units, accompanied with minor well-resolved bands at shorter wavelengths due to monomer emission of pyrene. This behavior is different from the one of compound **1**, which displays much weaker excimer emission from the pendant naphthalene residues, although they are separated by shorter linking chains than the pyrene units in **BisNP-2PY**.[9,10] The more efficient excimer fluorescence in the case of **BisNP-2PY** is presumably due to larger size of pyrene groups, compared with the naphthalene units in **1**, which assists their aggregation in aqueous medium. Addition of **Na_2TP** or **K_2OP** led to efficient quenching of excimer fluorescence, while the monomer emission remained much less affected (Fig. 1B and C). This behavior is useful for a ratiometric detection of concentration of the analyte (inset in Fig. 1B). Fitting of titration data to a 1:1-type complex[24] gave the value of the binding constant of $\log K$=5.7 (for terephthalate) and 4.9 (for phthalate ions). Interestingly, these values are larger than the ones determined for the parent macrocycle **BisNP-N** by means of NMR titrations ($\log K$=5.2 and 3.6, respectively), but the preferential binding of terephthalate over orthophthalate is retained.

In contrast, almost no changes were observed in the absorption spectrum of the monobrachial analogue **BisNP-1PY** upon addition of terephthalate (Fig. 2A). However, in the case of this compound, interaction with terephthalate led to quenching of monomeric fluorescence of the pyrene group (Fig. 2B), although this effect was less pronounced than quenching of the excimer emission of **BisNP-2PY**. Altogether, these results demonstrate that both functionalized macrocycles represent useful fluorescent probes, which respond in a different manner and may complement each other.

3. Conclusion

In summary, we have demonstrated that naphthalene-based bibrachial macrocycles with various functional units in side arms are available through the [2+2]-cyclocondensation, whereas the monobrachial, monofunctionalized macrocycles may be accessed via the [1+1]-cyclocondensation with the corresponding dialdehyde building block. Both types of cyclocondensation reaction tolerate various substituents in the side chains, however, the degree of purity of the resulting labile macrocyclic imine depends on the substrate. Although the problem of purification of polyamine macrocycles is seldom addressed in the literature, we showed that preparative-scale purification may be achieved by normal-phase chromatography, either by masking the amino groups of the macrocycle with Boc residues or by performing chromatography in alkaline conditions (NH_4OH). Moreover, we showed that the reactivity of the amino group in the side chain may be employed for facile preparation of macrocycles with other functional groups.

In addition, we demonstrated that the pyrene-functionalized macrocycles **BisNP-2PY** and **BisNP-1PY** represent fluorescent probes (with excimer and monomer emission of pyrene units, respectively), which sense the interaction of the receptor with guest molecules, e.g., isomeric phthalate anions, by changes in their fluorescent properties. Further investigations of these receptors, as well as of their electrochemically-active counterparts **BisNP-2FC** and **BisNP-1FC**, are in progress.

4. Experimental part

4.1. General remarks

All commercially available chemicals were reagent grade and used without further purification. Solvents were purified and dried according to standard procedures. The melting points were measured with an Electrothermal IA 9100 digital melting point instrument (Barnstead International) and are uncorrected. Mass spectra (ESI in the positive-ion mode) were recorded with a Waters ZQ LC-MS instrument (source voltage 50–75 kV). NMR spectra were measured on a Bruker Avance 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) spectrometer at 25 °C; chemical shifts are given in parts per million (δ) values (internal standards methanol, δ_H=3.34, δ_C=49.5 ppm, for D_2O,[25] and TMS for the other solvents); multiplicities of ^{13}C NMR signals were determined by means of DEPT-135 experiments. Elemental microanalyses of the new compounds were performed by the *Service de Microanalyse*, CNRS–ICSN, Gif-sur-Yvette, France. The purity of the final compounds was determined by HPLC analysis (Waters Alliance 2695 equipped with a Waters XTerra MS C_{18}-5 μm column and Waters 2998 photodiode array detector; eluent A: water with 0.05% trifluoroacetic acid, eluent B: MeCN, gradient elution with 10–100% of eluent B).

4.2. Synthesis of building block 10

4.2.1. *Methyl 6-bromo-2-naphthoate (**3**)*

A mixture of 6-bromo-2-naphthoic acid **2** (5.78 g, 23.0 mmol), trimethyl orthoformate (10 mL), concd H_2SO_4 (5 mL) in methanol (100 mL) was heated under reflux for 48 h. After cooling, the mixture was concentrated in vacuo to approx. 25 mL, poured into saturated aqueous solution of $NaHCO_3$ (100 mL), and extracted with dichloromethane (3×50 mL). The combined organic layers were washed with water and brine, dried over anhyd Na_2SO_4, and the solvent was removed in vacuo to give 6.10 g (quant.) of off-white solid, mp 125–127 (lit.[26] 123–125 °C). ^{1}H NMR ($CDCl_3$): δ=3.98 (s, 3H), 7.61 (dd, J=8.8, 1.8 Hz, 1H), 7.77–7.82 (m, 2H), 8.04 (s, 1H), 8.08 (dd, J=8.7, 1.5 Hz), 8.56 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=52.3 (CH_3), 122.6 (C_q), 126.3 (CH), 127.2 (CH), 127.8 (C_q), 129.9 (CH), 130.2 (CH), 130.8 (CH), 130.9 (CH+C_q), 136.4 (C_q), 166.9 (C_q).

4.2.2. *6-Bromo-2-(hydroxymethyl)naphthalene (**4**)*

To a solution of DIBAL-H in hexanes (0.7–1.3 M, 52 mL), kept at 0 °C under argon, a solution of **3** (4.51 g, 17.0 mmol) in anhyd THF (40 mL) was added dropwise within 30 min. The reaction mixture was allowed to warm to room temperature and stirred for 40 h. MeOH (10 mL) was carefully added, followed by 6 M aq HCl (40 mL) and Et_2O (40 mL). The aqueous phase was saturated with solid NH_4Cl, separated, and extracted with Et_2O (2×40 mL). The combined organic layers were washed with water (50 mL), brine and dried over anhyd $MgSO_4$. The solvent was removed in vacuo to give 3.99 g (99%) of white solid. ^{1}H NMR (DMSO-d_6): δ=4.66 (d, J=5.6 Hz, 2H), 5.37 (t, J=5.6 Hz, 1H, OH), 7.52 (d, J=9 Hz, 1H), 7.60 (dd, J=8.7, 1.9 Hz, 1H), 7.85–7.88 (m, 3H), 8.17 (d, J=1.5 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ=62.8 (CH_2), 118.5 (C_q), 124.2 (CH), 126.3 (CH), 126.8 (CH), 128.9 (CH), 129.3 (CH), 129.8 (CH), 131.4 (C_q), 133.2 (C_q), 140.9 (C_q).

4.2.3. *6-Bromo-2-naphthaldehyde (**5**)*

To a suspension of pyridinium chlorochromate (5.42 g, 25.1 mmol) in anhyd CH_2Cl_2 (55 mL), vigorously stirred at reflux temperature, a suspension of **4** (3.97 g, 16.7 mmol) in anhyd CH_2Cl_2 (80 mL) was added in one portion. The reaction mixture was stirred under reflux for 1 h, cooled to room temperature and poured into Et_2O (260 mL). The mixture was triturated until the black oil solidified, filtered through a pad of silica, and thoroughly eluted with Et_2O. The filtrate was concentrated in vacuo to give 3.85 g (98%) of off-white solid, mp 116–118 °C (lit.[27] oil). ^{1}H NMR ($CDCl_3$): δ=7.66 (dd, J=8.7, 1.7 Hz, 1H), 7.83–7.88 (m, 2H), 7.98 (dd, J=8.6, 1.0 Hz, 1H), 8.07 (d, J=1.7 Hz, 1H), 8.30 (s, 1H), 10.15 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=123.5 (C_q), 123.9 (CH), 128.1 (CH), 130.2 (CH), 130.6 (CH), 130.9 (CH), 131.0 (C_q), 134.0 (CH), 134.2 (C_q), 137.2 (C_q), 191.7 (CH).

*4.2.4. 6-Bromo-2-(1,3-dioxan-2-yl)naphthalene (**6**)*

A solution of **5** (1.98 g, 8.42 mmol), 1,3-propanediol (1.03 g, 13.5 mmol), triethyl orthoformate (1.50 g, 10.1 mmol), and $ZrCl_4$ (40 mg, 0.17 mmol) in anhyd CH_2Cl_2 (25 mL) was stirred at room temperature under argon for 2 h and then poured into 10% aq solution of NaOH (40 mL). The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (3×40 mL) and the organic layers were combined, washed with water (2×40 mL), brine, and dried over anhyd Na_2SO_4. The solvent was removed in vacuo to give 2.38 g (96%) of off-white solid, mp 120–122 °C (cyclohexane); R_f=0.57 (cyclohexane–AcOEt 7:3). ^{1}H NMR ($CDCl_3$): δ=1.46–1.53 (m, 1H), 2.20–2.36 (m, 1H), 4.00–4.10 (m, 2H), 4.30–4.35 (m, 2H), 5.65 (s, 1H), 7.54 (dd, J=8.7, 1.7 Hz, 1H), 7.63 (d, J=8.5, 1 Hz, 1H), 7.71–7.77 (m, 2H), 7.94 (s, 1H), 7.99 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=25.7 (CH_2), 67.4 (CH_2), 101.3 (CH), 120.2 (C_q), 124.8 (CH), 125.2 (CH), 127.1 (CH), 129.4 (CH), 129.7 (CH), 129.9 (CH), 131.3 (C_q), 134.5 (C_q), 136.5 (C_q); MS (ESI$^+$): m/z (%)=314 (100) [M+Na]$^+$, 293 (25) [M+H]$^+$, 213 (78) [M−Br]$^+$. Anal. Calcd (%) for $C_{14}H_{13}BrO_2$: C, 57.36; H, 4.47. Found: C, 57.53; H, 4.61.

*4.2.5. 6-(1,3-Dioxan-2-yl)-2-naphthaldehyde (**7**)*

A solution of the acetal **6** (2.36 g, 8.05 mmol) in anhyd THF (70 mL) was cooled to −90 °C under argon. *n*-BuLi (1.6 M in hexanes, 6.0 mL, 9.6 mmol) was added dropwise within 30 min, while pale-yellow precipitate has formed. The suspension was stirred at −90 °C for further 30 min. *N*-Formylpiperidine (1.35 mL, 1.37 g, 12.1 mmol) was added dropwise within 15 min at this temperature, and the reaction was stirred at −90 °C for 30 min and then allowed to warm to room temperature and left for 16 h. Saturated aqueous solution of NH_4Cl (50 mL) was added and the mixture was vigorously stirred for 15 min at room temperature. The organic layer was separated and the aqueous layer was extracted with AcOEt (3×40 mL). The organic layers were combined, washed with satd NH_4Cl solution (2×40 mL) and brine, and dried over anhyd Na_2SO_4. The solvents were removed in vacuo and the residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–AcOEt 7:3). The aldehyde **25** (1.27 g, 65%) was obtained as white solid, mp 144–146 °C (lit.[28] 141–144 °C); R_f=0.39 (cyclohexane–AcOEt 7:3). ^{1}H NMR ($CDCl_3$): δ=1.48–1.54 (m, 1H), 2.20–2.36 (m, 1H), 4.02–4.11 (m, 2H), 4.31–4.36 (m, 2H), 5.69 (s, 1H), 7.71 (dd, J=8.7, 1.7 Hz, 1H), 7.95–8.03 (m, 4H), 8.32 (s, 1H), 10.15 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=25.9 (CH_2), 67.7 (CH_2), 101.2 (CH), 123.1 (CH), 125.2 (CH), 125.6 (CH), 129.7 (CH), 129.8 (CH), 132.9 (C_q), 134.3 (CH), 134.5 (C_q), 136.3 (C_q), 139.5 (C_q), 192.4 (CH); MS (ESI$^+$): m/z (%)=265 (100) [M+Na]$^+$, 243 (79) [M+H]$^+$, 215 (8) [M−CO]$^+$.

*4.2.6. 2,2′-Oxybis{N-[(6-(1,3-dioxan-2-yl)naphth-2-yl)-methyl]ethylamine} (**8**)*

A solution of the aldehyde **7** (751 mg, 3.10 mmol) and 2,2′-oxydiethylamine (162 mg, 1.55 mmol) in benzene (10 mL) was heated under reflux for 18 h and then evaporated to dryness, leaving the *diimine* in quantitative yield as a pale-yellow solid, which was used without further purification. ^{1}H NMR ($CDCl_3$): δ=1.48–1.52 (m, 1H), 2.21–2.37 (m, 1H), 3.84 (br s, 4H), 4.02–4.11 (m, 2H), 4.31–4.36 (m, 2H), 5.67 (s, 1H), 7.59 (dd, J=8.5, 1.3 Hz, 1H), 7.74–7.77 (m, 2H), 7.87–7.92 (m, 3H), 8.36 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=26.0 (CH_2), 61.3 (CH_2), 67.6 (CH_2), 70.6 (CH_2), 101.6 (CH), 124.1 (CH), 124.4 (CH), 125.4 (CH), 128.9 (2CH), 129.7 (CH), 133.3 (C_q), 134.2 (C_q), 134.4 (C_q), 137.4 (C_q), 162.9 (CH). The diimine was dissolved in a mixture of CH_2Cl_2 (5 mL) and MeOH (5 mL), cooled in an ice bath, and $NaBH_4$ (171 mg, 4.50 mmol) was added. The solution was stirred at room temperature for 2 h and evaporated to dryness. Aq NaOH (1 M, 20 mL) was added to the residue, and the mixture was extracted with CH_2Cl_2 (5×10 mL), the combined organic layers were washed with 5% aq Na_2CO_3, dried over K_2CO_3, and evaporated in vacuo to give **8** (841 mg, 97%) as a pale-yellow solid, which was used without further purification, mp 127–129 °C (cyclohexane–benzene). ^{1}H NMR ($CDCl_3$): δ=1.47–1.51 (m, 1H), 1.82 (br s, 1H, NH), 2.20–2.36 (m, 1H), 2.84 (t, J=5.1 Hz, 2H), 3.59 (t, J=5.1 Hz, 2H), 3.95 (s, 2H), 4.01–4.10 (m, 2H), 4.30–4.35 (m, 2H), 5.65 (s, 1H), 7.43 (dd, J=8.4, 1.2 Hz, 1H), 7.57 (dd, J=8.5, 1.3 Hz, 1H), 7.73–7.80 (m, 3H), 7.92 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=26.0 (CH_2), 48.9 (CH_2), 54.1 (CH_2), 67.6 (CH_2), 70.5 (CH_2), 101.9 (CH), 124.0 (CH), 125.2 (CH), 126.4 (CH), 126.9 (CH), 128.1 (CH), 128.7 (CH), 132.4 (C_q), 133.7 (C_q), 135.9 (C_q), 138.2 (C_q); MS (ESI$^+$): m/z (%)=557 (100) [M+H]$^+$. Anal. Calcd (%) for $C_{34}H_{40}N_2O_5$: C, 73.36; H, 7.24; N, 5.03. Found: C, 73.31; H, 7.17; N, 4.79.

*4.2.7. 2,2′-Oxybis{N-[(6-formylnaphth-2-yl)methyl]ethylamine} (**9**)*

A solution of the diacetal **8** (379 mg, 681 μmol) in a mixture of 1,4-dioxane (5 mL) and 6 M aq HCl (10 mL) was heated at 60 °C for 2 h. The solution was evaporated to dryness, dissolved in water, and aq solution of Na_2CO_3 was added to pH ∼10. The mixture was extracted with $CHCl_3$ (3×40 mL), the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2; gradient elution with CH_2Cl_2–MeOH–NEt_3 98:2:0 to 85:15:0.5) to give **27** (235 mg, 78%) as a sticky pale-yellow oil, which polymerized upon standing overnight. ^{1}H NMR ($CDCl_3$): δ=1.84 (br s, 2H, NH), 2.87 (t, J=5.1 Hz, 4H), 3.63 (t, J=5.1 Hz, 4H), 4.01 (s, 4H, CH_2N), 7.56 (d, J=8.4 Hz, 4H), 7.82–7.93 (m, 8H), 8.28 (s, 2H), 10.13 (s, 2H); ^{13}C NMR ($CDCl_3$): δ=49.0 (CH_2), 54.0 (CH_2), 70.6 (CH_2), 123.2 (CH), 126.6 (CH), 127.9 (CH), 128.9 (CH), 129.8 (CH), 131.9 (C_q), 134.0 (C_q), 134.3 (CH), 136.7 (C_q), 141.8 (C_q), 192.3 (CH); MS (ESI$^+$): m/z (%)=441 (100) [M+H]$^+$.

*4.2.8. 2,2′-Oxybis{N-(tert-butoxycarbonyl)-N-[(6-formylnaphth-2-yl)methyl]ethylamine} (**10**)*

To a solution of crude **9** (630 mg, 1.43 mmol) in CH_2Cl_2 (10 mL), Boc_2O (0.94 g, 4.29 mmol), NEt_3 (0.40 mL), and DMAP (5 mg) were added. The reaction mixture was stirred at room temperature for 18 h, diluted with CH_2Cl_2 (50 mL), washed with 2% aq $KHSO_4$ (2×40 mL), brine, dried over anhyd $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–MTBE 6:4) to give **10** (600 mg, 65%) as pale-yellow oil. ^{1}H NMR (Me_2CO-d_6): δ=1.36 (br s, 9H), 1.49 (br s, 9H), 3.38 (br m, 2H), 3.49 (br m, 2H), 3.58 (br s, 4H), 4.71 (br s, 4H), 7.55 (dd, J=8.5, 1.5 Hz, 2H), 7.82 (br s, 2H), 7.90 (dd, J=8.5, 1.5 Hz, 2H), 7.98 (d, J=8.5 Hz, 2H), 8.10 (d, J=8.5 Hz, 2H), 8.48 (s, 2H), 10.16 (s, 2H); ^{13}C NMR (Me_2CO-d_6): δ=28.5 (CH_3), 47.5 (CH_2), 52.2 (CH_2), 70.3 (CH_2), 80.1 (C_q), 123.5 (CH), 126.6 (CH), 127.7 (CH), 129.6 (CH), 130.6 (CH), 132.9 (C_q), 135.0 (CH), 135.2 (C_q), 137.2 (C_q), 156.0 (C_q), 192.7 (CH); MS (ESI$^+$): m/z (%)=541 (80) [M−^{t}BuOCO]$^{\bullet+}$, 641 (31) [M+H]$^+$, 663 (100) [M+Na]$^+$.

4.3. Synthesis of polyamine 14

*4.3.1. N-(3-tert-Butoxycarbonylaminopropyl)diethanolamine (**12**)*

A solution of *N*-(3-aminopropyl)diethanolamine **11** (6.49 g, 40.0 mmol) and Boc_2O (10.5 g, 48.0 mmol) in CH_2Cl_2 (100 mL) was stirred at room temperature for 18 h. The solvent was removed in vacuo, the residue was dissolved in water (150 mL), and 5% aq $KHSO_4$ was added to adjust pH to ∼7 (approx. 10 mL). The solution was extracted with hexane (4×50 mL) and the organic phases were discarded. The aqueous phase was made strongly alkaline with NaOH (pH ∼14) and extracted with CH_2Cl_2 (7×30 mL). The combined organic layers were washed with satd aq Na_2CO_3, dried over K_2CO_3, and evaporated in vacuo to give **12** (9.29 g, 89%) as colorless viscous oil, which solidified on standing. ^{1}H NMR (D_2O): δ=1.42 (br s, 9H), 1.62–1.71 (m, 2H), 2.57–2.62 (m, 2H), 2.71 (t, J=6.3 Hz, 4H), 3.07 (t, J=6.6 Hz, 2H), 3.69 (t, J=6.3 Hz, 4H); ^{13}C NMR (D_2O): δ=26.2 (CH_2), 28.3 (CH_3), 38.9 (CH_2), 52.1 (CH_2), 55.6 (CH_2), 59.3 (CH_2), 81.4

(C_q), 158.9 (C_q); MS (ESI^+): *m/z* (%)=263 (95) $[M+H]^+$, 285 (100) $[M+Na]^+$.

4.3.2. *N-(3-tert-Butoxycarbonylaminopropyl)-N,N-bis-(2-aminoethyl)amine (**14**)*

A mixture of **12** (10.5 g, 40.0 mmol), phthalimide (12.9 g, 88.0 mmol), and triphenylphosphine (23.1 g, 88.0 mmol) in anhyd THF (320 mL) was cooled to 0 °C under argon, and diisopropyl azodicarboxylate (17.3 mL, 17.8 g, 88.0 mmol) was added from a syringe within 30–40 min. The homogeneous mixture was allowed to warm to room temperature, and stirred overnight. After evaporation in vacuo, the residue was dissolved in warm Et_2O (90 mL) and cyclohexane (90 mL) was added. The crystallization was induced and the flask was left at 0 °C for 18 h. The precipitated crystalline solid (complex of Ph_3PO and diisopropyl hydrazodicarboxylate) was filtered and washed with a mixture of cyclohexane and Et_2O (1:1, approx. 40 mL). The filtrate was concentrated in vacuo to give the crude *N-(3-tert-butoxycarbonylaminopropyl)-N,N-bis(2-phthalimidoethyl)amine (**13**)*. It was dissolved in MeOH (300 mL) and hydrazine hydrate (22.0 mL) was added. The mixture was stirred under reflux for 6 h, while voluminous white precipitate of phthalhydrazide had formed. After cooling to room temperature, it was filtered off and thoroughly washed with MeOH and CH_2Cl_2. The filtrate was concentrated in vacuo and then twice evaporated with toluene (100 mL) to remove excess hydrazine. To the residue, CH_2Cl_2 (100 mL) was added; the mixture was sonicated and filtered to remove the remaining phthalhydrazide, which was washed with CH_2Cl_2 (2×10 mL). The filtrate was concentrated in vacuo and dissolved in water (300 mL). Aq HCl (1 M) was added to adjust pH to 4–5 and the mixture was extracted with CH_2Cl_2 (4×50 mL); these organic fractions were discarded. The aqueous phase was made strongly alkaline with solid NaOH and extracted with CH_2Cl_2 (8×100 mL); the combined organic phases were dried over NaOH, filtered, and concentrated in vacuo to give 15.6 g of oil, which was purified by column chromatography (SiO_2; eluent: MeOH–aq 28% NH_3 9:1). The fraction containing the product were evaporated, the residue was dissolved in benzene, filtered to remove the remaining SiO_2, and evaporated in vacuo to give **14** (5.08 g, 49%) as colorless viscous oil. ^1H NMR (CD_3OD): δ=1.43 (br s, 9H), 1.64 (qi, *J*=7 Hz, 2H), 2.46–2.53 (m, 6H), 2.69 (t, *J*=6.2 Hz, 4H), 3.08 (t, *J*=6.8 Hz, 2H); ^{13}C NMR (CD_3OD): δ=28.4 (CH_2), 28.8 (CH_3), 39.6 (CH_2), 40.0 (CH_2), 53.1 (CH_2), 57.3 (CH_2), 79.9 (C_q), 158.5 (C_q); HRMS (ESI^+): *m/z* calcd for $C_{12}H_{29}N_4O_2$ $[M+H^+]$ 261.2285, found: 261.2284.

A small portion of crude **13** was purified by flash chromatography on SiO_2 (eluent: cyclohexane–AcOEt 55:45), followed by column chromatography on Al_2O_3 (activity grade III, eluent: cyclohexane–AcOEt 70:30) to give pure **13** as white solid, mp 79–81 °C. ^1H NMR ($CDCl_3$): δ=1.40 (s, 9H), 1.52 (qi, *J*=6.4 Hz, 2H), 2.56 (t, *J*=6.8 Hz, 2H), 2.76 (t, *J*=6.4 Hz, 4H), 2.95 (m, 2H), 3.71 (t, *J*=6.4 Hz, 4H), 5.00 (br s, 1H), 7.66–7.74 (m, 8H); ^{13}C NMR ($CDCl_3$): δ=27.3 (CH_2), 28.4 (CH_3), 35.7 (CH_2), 38.2 (CH_2), 50.9 (CH_2), 51.9 (CH_2), 78.8 (C_q), 123.1 (C_q), 132.1 (CH), 133.7 (CH), 156.0 (C_q), 168.2 (C_q); MS (ESI^+): *m/z* (%)=521 (100) $[M+H]^+$.

4.4. Synthesis of the ferrocene-modified polyamine 19

4.4.1. *3-Ferrocenylpropanol (**15**)*

To a solution of DIBAL-H (0.7–1.3 M hexanes, 27 mL), stirred at 0 °C under argon, a solution of ethyl 3-ferrocenylpropanoate (prepared from in two steps from ferrocenecarboxaldehyde)[20] (2.60 g, 9.09 mmol) in anhyd THF (30 mL) was added from a syringe within 15 min. The mixture was allowed to warm to room temperature and was stirred for 20 h. MeOH (5 mL) was added, followed by water (5 mL), aq 6 M HCl (15 mL), and Et_2O (20 mL). The aqueous phase was saturated with solid NH_4Cl, separated, and extracted with Et_2O (2×30 mL). The combined organic phases were washed with water and brine (15 mL each), dried over $MgSO_4$, and the solvent was removed in vacuo to give **15** (2.19 g, 99%) as orange oil. ^1H NMR ($CDCl_3$): δ=1.30 (s, 1H), 1.74–1.83 (m, 2H), 2.43 (t, *J*=7.5 Hz, 2H), 3.67 (t, *J*=6.4 Hz, 2H), 4.05–4.07 (m, 4H), 4.10 (s, 5H); characterization data corresponded to the ones reported previously.[20,29]

4.4.2. *(E,Z)-3-Ferrocenylacrylonitrile (**16**)*

A mixture of ferrocenecarboxaldehyde (2.57 g, 12.0 mmol), diethyl cyanomethylphosphonate (2.33 mL, 2.55 g, 14.4 mmol), and solid K_2CO_3 (4.97 g, 36.0 mmol) in abs EtOH (40 mL) was stirred under reflux in argon atmosphere for 1 h, cooled to room temperature, and the solvent was removed in vacuo. The residue was partitioned between water and Et_2O (40 mL each), the organic layer was separated, and the aqueous layer was extracted with Et_2O (3×30 mL). The combined organic layers were washed with water, 0.5 M aq HCl, water, and brine, dried over anhyd $MgSO_4$, and concentrated in vacuo. The red-brown residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–MTBE 9:1) to give **16** (2.02 g, 71%) as dark-red solid, mp 89–90 °C (lit.[30] 90–92 °C). ^1H NMR ($CDCl_3$): δ=4.18 (s, 5H), 4.45 (br s, 4H), 5.43 (d, *J*=16 Hz, 1H), 7.27 (d, *J*=16 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ=68.1 (CH), 69.8 (CH), 71.4 (CH), 78.0 (C_q), 91.7 (CH), 119.1 (C_q), 151.6 (CH); MS (ESI^+): *m/z* (%)=237 (100) $[M^+]$. The product contained 7% (by ^1H NMR) of the (*Z*)-isomer, which was not isolated.

4.4.3. *3-Ferrocenylpropionitrile (**17**)*

A solution of **16** (2.01 g, 8.48 mmol) in abs EtOH (50 mL) was hydrogenated at atmospheric pressure in the presence of Pd catalyst (0.15 g, 5% on charcoal, Degüssa-type with water content 50%) for 2 h (the reaction was monitored by TLC on SiO_2-covered plates, eluent: cyclohexane–MTBE 8:2). After completion of reaction, the mixture was filtered and the solvent was removed in vacuo to give pure **17** (1.99 g, 98%) as yellow solid, mp 68–71 °C. ^1H NMR ($CDCl_3$): δ=2.52 (t, *J*=7.4 Hz, 2H), 2.71 (t, *J*=7.4 Hz, 2H), 4.09–4.14 (m, 9H); ^{13}C NMR ($CDCl_3$): δ=19.1 (CH_2), 26.0 (CH_2), 67.8 (CH), 67.9 (CH), 68.6 (CH), 85.1 (C_q), 119.5 (C_q); MS (ESI^+): *m/z* (%)=199 (18) $[M-CH_2CN]^+$, 239 (100) $[M^+]$.

4.4.4. *3-Ferrocenylpropanal (**18**)*

To a solution of nitrile **17** (1.79 g, 7.50 mmol) in anhyd CH_2Cl_2 (60 mL), stirred at room temperature under argon, DIBAL-H (0.7–1.3 M in hexanes, 11.5 mL) was added within 5 min via syringe. The reaction mixture was stirred for 30 min at room temperature and MeOH (5 mL) was added, followed by water (5 mL) and aq HCl (6 M, 30 mL). The aqueous phase was extracted with CH_2Cl_2 (2×40 mL); the combined organic phases were washed with water, 5% aq $NaHCO_3$, water, and brine (40 mL each), dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–MTBE 9:1) to give **18** (1.04 g, 57%) as orange oil, which has crystallized on standing, mp 50–52 °C (lit.[31] 48–51 °C). ^1H NMR ($CDCl_3$): δ=2.68 (s, 4H), 4.07 (s, 4H), 4.11 (s, 5H), 9.81 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=22.2 (CH_2), 45.3 (CH_2), 67.6 (CH), 68.1 (CH), 68.7 (CH), 87.4 (C_q), 202.1 (CH); MS (ESI^+): *m/z* (%)=214 (11) $[M-CO]^+$, 242 (100) $[M^+]$.

4.4.5. *N,N-Bis(2-aminoethyl)-N′-(3-ferrocenylpropyl)-ethylenediamine (**19**)*

A stirred solution of tris(2-aminoethyl)amine (5.12 g, 35.0 mmol) in MeOH (60 mL) was deoxygenated by a stream of argon, and a solution of 3-ferrocenylpropanal **18** (847 mg, 3.50 mmol) in a mixture of MeOH (30 mL) and $CHCl_3$ (10 mL) was added dropwise at room temperature. The reaction mixture was stirred at room temperature for 5 h, cooled in an ice bath, and $NaBH_4$ (0.30 g, 7.9 mmol) was added. After 20 min at room

temperature, aq NaOH (2 M, 10 mL) was added. The mixture was evaporated to dryness, toluene (50 mL) was added, and the mixture was evaporated again. After addition of the same volume of toluene and solid anhyd K_2CO_3, the mixture was stirred, filtered, and the inorganic material was thoroughly washed with toluene. The filtrate was evaporated and the orange residue was purified by flash chromatography (SiO_2; eluent: CH_2Cl_2–MeOH–28% aq NH_3 70:25:5). The fractions containing the product were evaporated, the residue was dissolved in benzene, filtered to remove remaining SiO_2, and evaporated in vacuo to give **19** (1.02 g, 79%) as bright-orange oil, which solidified on standing at +4 °C. ^{1}H NMR (CD_3OD): δ=1.74 (qi, J=7.5 Hz, 2H), 2.40 (t, J=7.5 Hz, 2H), 2.50–2.72 (m, 14H), 4.04–4.09 (m, 9H); ^{13}C NMR (CD_3OD): δ=28.5 (CH_2), 31.9 (CH_2), 40.1 (CH_2), 48.1 (CH_2), 50.5 (CH_2), 54.8 (CH_2), 57.9 (CH_2), 68.2 (CH), 69.1 (CH), 69.5 (CH), 89.8 (C_q); MS (ESI$^+$): m/z (%)=373 (100) [M+H]$^+$.

4.5. Synthesis of the pyrene-modified polyamine 23

4.5.1. 4-(1-Pyrenyl)butanol (*21*)

Alcohol **21** was prepared by reduction of methyl 4-(1-pyrenyl)butyrate[23] **20** with DIBAL-H as described for **15** in 99% yield; dark-yellow oil, which solidified on standing. ^{1}H NMR ($CDCl_3$): δ=1.27 (br s, 1H); 1.69–1.78 (m, 2H), 1.88–1.98 (m, 2H), 3.66 (t, J=7.6 Hz, 2H), 3.69 (t, J=6.5 Hz, 2H), 7.85 (d, J=7.8 Hz, 1H), 7.95–8.16 (m, 7H), 8.26 (d, J=9.3 Hz, 1H); characterization data corresponded to the ones reported previously.[32]

4.5.2. 4-(1-Pyrenyl)butanal[33] (*22*)

To a solution of oxalyl chloride (1.20 mL, 1.71 g, 13.5 mmol) in anhyd CH_2Cl_2 (26 mL), stirred at −90 °C under argon, a mixture of DMSO (2.7 mL) and CH_2Cl_2 (4 mL) was added dropwise. The mixture was stirred at −80 to −90 °C for 10 min, and a solution of the alcohol **21** (2.65 g, 9.66 mmol) in a mixture of DMSO (2.7 mL) and CH_2Cl_2 (4 mL) was added dropwise. The mixture was stirred for 40 min, while voluminous precipitate has formed. Triethylamine (6.7 mL) was added and the mixture was allowed to warm to room temperature, stirred for 2 h, and poured into water (40 mL). The organic phase was separated and extracted with CH_2Cl_2 (3×40 mL). The combined organic phases were washed with water, brine, dried over $MgSO_4$, and the solvent was removed in vacuo. The residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–CH_2Cl_2 50:50) to give **22** (2.36 g, 90%) as pale-yellow solid, mp 67–71 °C. ^{1}H NMR ($CDCl_3$): δ=2.19 (qi, J=7.4 Hz, 2H), 2.57 (dt, J=7.4, 1 Hz, 2H), 3.38 (t, J=7.6 Hz, 2H), 7.84 (d, J=7.8 Hz, 1H), 7.96–8.06 (m, 3H), 8.10–8.18 (m, 4H), 8.28 (d, J=9.3 Hz, 1H), 9.80 (s, 1H); ^{13}C NMR ($CDCl_3$): δ=24.0 (CH_2), 32.6 (CH_2), 43.4 (CH_2), 123.2 (CH), 124.8 (2CH), 125.0 (CH), 125.1 (C_q), 125.9 (CH), 126.8 (CH), 127.3 (CH), 127.4 (CH), 127.5 (CH), 128.7 (C_q), 130.0 (C_q), 130.9 (C_q), 131.4 (C_q), 135.5 (C_q), 202.2 (CH); MS (ESI$^+$): m/z (%)=255 (100) [M−17] *unassigned*, 273 (52) [M+H]$^+$, 295 (7) [M+Na]$^+$.

4.5.3. N,N-Bis(2-aminoethyl)-N′-[4-(1-pyrenyl)butyl]-ethylenediamine (*23*)

Polyamine **23** was prepared from **22** and tris(2-aminoethyl)-amine analogously to **19** in 61% yield after purification by flash chromatography (SiO_2; eluent: CH_2Cl_2–MeOH–28% aq NH_3 70:25:5) as pale-yellow solid. ^{1}H NMR (CD_3OD): δ=1.57–1.67 (m, 2H), 1.79–1.89 (m, 2H), 2.39–2.48 (m, 6H), 2.53–2.62 (m, 8H), 3.30–3.35 (t, overlap with CHD_2OD, 2H), 7.84 (d, J=7.8 Hz, 1H), 7.93–8.16 (m, 7H), 8.26 (d, J=9.3 Hz, 1H); ^{13}C NMR (CD_3OD): δ=30.4 (CH_2), 30.7 (CH_2), 34.2 (CH_2), 40.0 (CH_2), 48.0 (CH_2), 50.5 (CH_2), 54.7 (CH_2), 57.7 (CH_2), 124.4 (CH), 125.8 (CH), 125.9 (CH), 126.0 (CH), 126.1 (C_q), 126.2 (C_q), 127.0 (CH), 127.6 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 129.8 (C_q), 131.2 (C_q), 132.3 (C_q), 132.8 (C_q), 137.9 (C_q); MS (ESI$^+$): m/z (%)=403 [M+H]$^+$.

4.6. Synthesis of bibrachial macrocycles

4.6.1. Synthesis of ***BisNP-2NH$_2$***

*4.6.1.1. Tetraimine **24**.* To a solution of the amine **14** (781 mg, 3.00 mmol) in anhyd MeCN (150 mL), stirred at room temperature under argon, a solution of naphthalene-2,6-dialdehyde[7,34] (553 mg, 3.00 mmol) in anhyd MeCN (150 mL) was added dropwise within 4 h. The mixture was stirred at room temperature for 5 days, while pale-yellow precipitate separated. The mixture was concentrated in vacuo at ambient temperature to a volume of 100 mL, sonicated, and the solid was separated, washed with MeCN, and dried in vacuo to give the crude di-*N*-Boc-protected cyclic tetraimine **24** (1.07 g, 87%), as pale-yellow solid, which was used without further purification. ^{1}H NMR ($CDCl_3$): δ=1.38 (s, 18H), 1.81 (qi, J=6.3 Hz, 4H), 2.63 (t, J=6.3 Hz, 4H), 2.82 (t, J=5 Hz, 8H), 3.37–3.43 (m, 4H), 3.72 (t, J=5 Hz, 8H), 5.94 (br m, 2H, NH), 7.27 (s, 4H), 7.31 (d, J=8 Hz, 4H), 7.59 (d, J=8 Hz, 4H), 8.13 (s, 4H); ^{13}C NMR ($CDCl_3$): δ=26.8 (CH_2), 28.5 (CH_3), 38.2 (CH_2), 50.4 (CH_2), 53.4 (CH_2), 58.7 (CH_2), 78.5 (C_q), 123.0 (CH), 128.3 (CH), 129.8 (CH), 133.4 (C_q), 134.2 (C_q), 156.5 (C_q), 161.9 (CH); MS (ESI$^+$): m/z (%)=818 (100) [M+H]$^+$, 840 (45) [M+Na]$^+$.

*4.6.1.2. Per-Boc-protected macrocycle **25**.* A portion of the crude cyclic tetraimine **24** (490 mg, 0.60 mmol) was dissolved in a mixture of CH_2Cl_2 (10 mL) and MeOH (10 mL), and $NaBH_4$ (340 mg, 9.00 mmol) was added. After stirring at room temperature for 2 h, the solvents were removed in vacuo and 2 M aq NaOH (40 mL) was added. The mixture was extracted with CH_2Cl_2 (4×40 mL); the combined organic phases were washed with satd aq Na_2CO_3, dried over K_2CO_3, and concentrated to a volume of 5 mL. To this solution, Boc_2O (1.05 g, 4.80 mmol) and DMAP (10 mg) were added. The reaction mixture was stirred at room temperature for 18 h, concentrated in vacuo, and the residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–MTBE 6:4) to give the hexa-Boc-protected macrocyclic amine **25** (378 mg, 51%) as a fluffy white solid, which gave a single spot on TLC; the NMR spectrum revealed very broad signals, which were difficult to assign. MS (ESI$^+$): m/z (%)=1126.0 (12) [M−^{t}BuOCO]$^+$, 1226.0 (100) [M+H]$^+$, 1248.1 (48) [M+Na]$^+$.

*4.6.1.3. Macrocycle **BisNP-2NH$_2$×8HCl**.* The derivative **25** was dissolved in abs EtOH (5 mL) and a solution of HCl in dioxane (4 M, 5 mL) was added. The mixture was stirred under reflux for 4 h and then evaporated to dryness to give **BisNP-2NH$_2$×8HCl** as a very hygroscopic white solid. ^{1}H NMR (CD_3OD): δ=1.86–2.00 (m, 4H), 2.89 (t, J=7 Hz, 4H), 2.97–3.06 (m, 12H), 3.22–3.27 (m, 12H), 4.09 (s, 8H), 7.48 (d, J=8.5 Hz, 4H), 7.88 (s, 4H), 7.90 (d, J=8.5 Hz, 4H); ^{13}C NMR (CD_3OD): δ=22.8 (CH_2), 38.2 (CH_2), 43.6 (CH_2), 48.8 (CH_2), 50.8 (CH_2), 51.5 (CH_2), 128.7 (CH), 129.8 (C_q), 130.4 (CH), 131.0 (CH), 133.9 (C_q); MS (ESI$^+$): m/z (%)=625.5 (100) [M+H]$^+$; purity (HPLC peak area) 97%.

4.6.2. Synthesis of ***BisNP-2FC***

*4.6.2.1. Tetraimine **26**.* This macrocycle was prepared from amine **19** and naphthalene-2,6-dialdehyde, following the procedure described for the synthesis of **24** and obtained in 73% yield after 2 days of reaction time as yellow solid. ^{1}H NMR ($CDCl_3$): δ=1.91–1.91 (m, 4H), 2.51 (t, J=8 Hz, 4H), 2.74 (t, J=5.5 Hz, 4H), 2.79–2.90 (m, 16H), 3.69 (br s, 8H), 4.11–4.13 (m, 18H, Fc-H), 7.20 (s, 4H), 7.26 (d, J=8 Hz, 4H), 7.62 (d, J=8 Hz, 4H), 8.15 (s, 4H); ^{13}C NMR ($CDCl_3$): δ=27.8 (CH_2), 31.9 (CH_2), 47.4 (CH_2), 50.5 (CH_2), 53.5 (CH_2), 58.2 (CH_2), 67.3 (CH), 68.2 (CH), 68.6 (CH), 88.8 (C_q), 122.4 (CH), 128.4 (CH), 130.2 (CH), 133.2 (C_q), 134.2 (C_q), 162.5 (CH); MS (ESI$^+$): m/z (%)=522 (12) [M+2H]$^{2+}$, 1042 (100) [M+H]$^+$.

*4.6.2.2. Macrocycle **BisNP-2FC×6HCl**.* A portion of the crude cyclic tetraimine **26** (208 mg, 0.20 mmol) was dissolved in a mixture of CH_2Cl_2 (5 mL) and MeOH (5 mL), and $NaBH_4$ (76 mg, 2.0 mmol) was added. After stirring at room temperature for 3 h, the solvents were removed in vacuo and 2 M aq NaOH (20 mL) was added. The mixture was extracted with CH_2Cl_2 (4×40 mL); the combined organic phases were washed with satd aq Na_2CO_3, dried over K_2CO_3, and evaporated to dryness. The residue (orange oil) was dissolved in EtOH (5 mL) and HCl (7.5 M in EtOH, 5 mL) was added. The mixture was evaporated and the solid residue was recrystallized from EtOH–water to give **BisNP-2FC×6HCl** (200 mg, 79%) as yellow microcrystalline powder; decomp. at 170 °C. ^{1}H NMR (CD_3OD): δ=2.05–2.20 (m, 4H), 2.44 (t, J=7 Hz, 4H), 2.77–2.92 (m, 12H), 3.10 (t, J=7.5 Hz, 4H), 3.24–3.31 (m, 6H, overlap with CHD_2OD), 4.11–4.18 (m, 18H), 4.42 (s, 8H), 7.60 (d, J=8.4 Hz, 4H), 7.79 (d, J=8.4 Hz, 4H), 8.10 (s, 4H); ^{13}C NMR (CD_3OD): δ=27.7 (CH_2), 28.6 (CH_2), 46.8 (CH_2), 47.1 (CH_2), 49.6 (CH_2), 52.2 (CH_2), 52.7 (CH_2), 53.0 (CH_2), 68.7 (CH), 69.3 (CH), 70.0 (CH), 89.7 (C_q), 129.5 (CH), 130.5 (CH), 130.8 (C_q), 132.3 (CH), 134.6 (C_q); MS (ESI$^+$): m/z (%)=1050 (100) $[M+H]^+$. Anal. Calcd (%) for $C_{62}H_{80}Fe_2N_8\times6HCl\times6H_2O$ (1375.9): C, 54.12; H, 7.18; N, 8.17; Cl, 15.46. Found: C, 54.21; H, 6.95; N, 8.17; Cl, 15.46; purity (HPLC peak area) 98%.

*4.6.3. Synthesis of **BisNP-2PY***

To a solution of the amine **23** (443 mg, 1.10 mmol) in anhyd MeCN (60 mL), stirred at room temperature under argon, a solution of naphthalene-2,6-dialdehyde (203 mg, 1.10 mmol) in a mixture of anhyd MeCN (60 mL) and anhyd CH_2Cl_2 (10 mL) was added dropwise within 4 h. Colorless oil separated on the walls of the flask, which then solidified as the stirring was continued for 6 days. The pale-yellow precipitate was collected, washed with MeCN, and dried in vacuo to give 494 mg of the cyclic tetraimine derivative containing impurities. It was dissolved in a mixture of CH_2Cl_2 (15 mL) and MeOH (15 mL), and $NaBH_4$ (209 mg, 5.50 mmol) was added. After stirring for 3 h at room temperature, the mixture was evaporated, 1 M aq NaOH (30 mL) was added, and the mixture was extracted with CH_2Cl_2 (5×20 mL). The combined organic fractions were washed with satd aq Na_2CO_3 solution, dried over anhyd K_2CO_3, and evaporated in vacuo. The residue was purified by flash chromatography (SiO_2; eluent: CH_2Cl_2–MeOH–aq 28% NH_3 80:20:1 to 80:20:3) to give **BisNP-2PY** (177 mg, 30%) as a low-melting pale-yellow solid. ^{1}H NMR ($CDCl_3$): δ=1.23–1.33 (m, 4H), 1.44–1.54 (m, 4H), 1.77 (br s, NH), 2.40 (t, J=7.3 Hz, 4H), 2.51–2.58 (m, 16H), 2.72–2.75 (m, 8H), 2.93 (m, J=7.7 Hz, 4H), 3.74 (s, 8H), 7.14 (d, J=8.3 Hz, 4H), 7.21 (d, J=8.3 Hz, 4H), 7.46 (s, 4H), 7.60 (d, J=7.8 Hz, 2H), 7.93–8.05 (m, 12H), 8.12 (d, J=7.8 Hz, 4H); ^{13}C NMR ($CDCl_3$): δ=29.5 (CH_2), 30.3 (CH_2), 33.2 (CH_2), 47.8 (CH_2), 47.9 (CH_2), 50.2 (CH_2), 53.9 (CH_2), 54.5 (CH_2), 123.6 (CH), 124.7 (CH), 124.8 (CH), 124.9 (CH), 125.1 (C_q), 125.2 (C_q), 125.8 (CH), 125.9 (CH), 126.5 (CH), 126.6 (CH), 127.1 (CH), 127.2 (CH), 127.6 (CH), 127.9 (CH), 128.6 (C_q), 129.8 (C_q), 131.0 (C_q), 131.6 (C_q), 132.7 (C_q), 137.0 (C_q), 137.7 (C_q); MS (ESI$^+$): m/z (%)=555.7 (100) $[M+2H]^{2+}$, 1109.7 $[M+H]^+$. To prepare the hydrochloride salt, the amine was dissolved in MeOH, treated with excess concentrated aq HCl, the suspension was evaporated, and the residue was recrystallized from DMF–water to give **BisNP-2PY×6HCl** (183 mg) as white solid, mp (decomp.) 310–315 °C; purity (HPLC peak area) 97%. Anal. Calcd (%) for $C_{76}H_{84}N_8\times6HCl\times3H_2O$ (1382.3): C, 66.03; H, 7.00; N, 8.11; Cl, 15.39. Found: C, 66.01; H, 7.09; N, 8.26; Cl, 15.23.

4.7. Synthesis of monobrachial macrocycles

*4.7.1. Synthesis of **BisNP-1NH$_2$***

*4.7.1.1. Per-Boc-protected macrocycle **27**.* To a solution of the amine **14** (521 mg, 2.00 mmol) in anhyd MeCN (150 mL), stirred at room temperature under argon, a solution of the dialdehyde **10** (1.28 g, 2.00 mmol) in anhyd MeCN (150 mL) was added dropwise within 4 h. The reaction mixture was stirred at room temperature for six days; no precipitation was observed. The solvent was removed in vacuo, and the residue was dissolved in a mixture of CH_2Cl_2 (20 mL) and MeOH (10 mL). $NaBH_4$ (760 mg, 20 mmol) was added; the reaction mixture was stirred at room temperature for 18 h and then evaporated to dryness. To the residue, aq NaOH (2 M, 70 mL) was added and the mixture was extracted with CH_2Cl_2 (4×50 mL). The combined organic phases were washed with satd Na_2CO_3 solution, dried over anhyd K_2CO_3, and concentrated in vacuo to a volume of 10 mL. To this solution, Boc_2O (2.18 g, 10.0 mmol), $NEt(^iPr)_2$ (1.4 mL, 8.00 mmol), and DMAP (10 mg) were added. The reaction mixture was stirred at room temperature for 18 h, concentrated in vacuo, and the residue was purified by flash chromatography (SiO_2; eluent: cyclohexane–MTBE 5:5) to give the penta-Boc-protected macrocyclic amine **27** (583 mg, 27%) as a fluffy white solid, which gave a single spot on TLC; the NMR spectrum displayed very broad signals, which were difficult to assign. MS (ESI$^+$): m/z (%)=1013.6 (9) $[M-{}^t\mathrm{Bu}]^+$, 1069.6 (65) $[M+H]^+$, 1091.6 (100) $[M+Na]^+$.

*4.7.1.2. Macrocycle **BisNP-1NH$_2$×5HCl**.* The derivative **27** was dissolved in abs EtOH (10 mL) and a solution of HCl in dioxane (4 M, 5 mL) was added. The mixture was stirred under reflux for 4 h and cooled to room temperature. The precipitate was separated, washed with abs EtOH, and dried in vacuo to give **BisNP-1NH$_2$×5HCl** (391 mg, 96% from **27**) as very hygroscopic white solid. ^{1}H NMR (CD_3OD): δ=1.86–2.00 (m, 2H), 2.81 (t, J=7 Hz, 2H), 2.99–3.04 (m, 6H), 3.41 (t, J=5 Hz, 4H), 3.47 (t, J=4.5 Hz, 4H), 3.92 (t, J=4.5 Hz, 4H), 4.40 (s, 4H), 4.42 (s, 4H), 7.63 (dd, J=8.5, 1.5 Hz, 2H), 7.69 (dd, J=8.5, 1.5 Hz, 2H), 7.85 (d, J=8.5 Hz, 2H), 7.90 (d, J=8.5 Hz, 2H), 8.04 (s, 2H), 8.10 (s, 2H); ^{13}C NMR (CD_3OD): δ=21.5 (CH_2), 38.8 (CH_2), 46.5 (CH_2), 48.2 (CH_2), 48.6 (CH_2), 50.0 (CH_2), 52.3 (CH_2), 52.6 (CH_2), 66.6 (CH_2), 128.6 (CH), 129.0 (CH), 130.2 (CH), 130.4 (CH), 130.6 (CH), 131.0 (CH+C_q), 131.1 (C_q), 134.2 (C_q), 134.3 (C_q); MS (ESI$^+$): m/z (%)=285 (100) $[M+2H]^{2+}$, 559 (60) $[M+H]^+$; purity (HPLC peak area) 98%.

*4.7.2. Synthesis of **BisNP-1FC***

*4.7.2.1. Per-Boc-protected macrocycle **28**.* Compound **28** was prepared from the amine **19** and dialdehyde **10**, following the procedure described for the synthesis of **27** in 41% yield after purification by flash chromatography (SiO_2, eluent: cyclohexane–MTBE 6:4) as fluffy yellow solid, which gave a single spot on TLC; the NMR spectrum gave very broad signals, which were difficult to assign. MS (ESI$^+$): m/z (%)=1282 (92) $[M+H]^+$, 1304 (100) $[M+Na]^+$.

*4.7.2.2. Macrocycle **BisNP-1FC×5HCl**.* The derivative **28** (259 mg, 0.20 mmol) was dissolved in abs EtOH (5 mL) and a solution of HCl in dioxane (4 M, 5 mL) was added. The mixture was stirred under reflux for 4 h, evaporated to dryness, and the residue was recrystallized from MeOH–water to give **BisNP-1FC×5HCl** (117 mg, 61% from **28**) as hygroscopic yellow solid, decomp. at 190 °C. ^{1}H NMR (CD_3OD): δ=2.00–2.05 (m, 2H), 2.47 (t, J=7 Hz, 2H), 2.90–3.00 (m, 6H), 3.10 (t, J=7.5 Hz, 2H), 3.27 (m, 2H), 3.35–3.45 (m, 8H), 3.89 (s, 4H), 4.10–4.16 (m, 9H, Fc-H), 4.41 (s, 8H), 7.64 (d, J=8 Hz, 2H), 7.73–7.84 (m, 6H), 8.06 (s, 2H), 8.14 (s, 2H); ^{13}C NMR (CD_3OD): δ=27.5 (CH_2), 28.5 (CH_2), 45.7 (CH_2), 47.0 (CH_2), 48.4 (CH_2), 49.3 (CH_2), 51.0 (CH_2), 51.7 (CH_2), 52.4 (CH_2), 53.0 (CH_2), 66.8 (CH_2), 68.7 (CH), 69.4 (CH), 70.0 (CH), 89.8 (C_q), 128.8 (CH), 129.5 (CH), 130.2 (CH), 130.7 (CH), 131.0 (CH), 131.1 (C_q), 131.2 (C_q), 131.7 (CH), 134.5 (C_q), 134.6 (C_q); MS (ESI$^+$): m/z (%)=391 (100) $[M+2H]^{2+}$, 781 (95) $[M+H]^+$. Anal. Calcd (%) for

$C_{47}H_{60}FeN_6O\times5HCl\times2H_2O$ (999.2): C, 56.50; H, 6.96; N, 8.41; Cl, 17.74. Found: C, 56.71; H, 6.71; N, 8.27; Cl, 17.93; purity (HPLC peak area) 94%; a peak corresponding to **BisNP-1(FC$^+$)** (m/z=780 [M$^+$]) was also detected by HPLC (5% peak area).

*4.7.3. Synthesis of **BisNP-1PY***

To a suspension of **BisNP-1NH$_2$×5HCl** (75.0 mg, 100 μmol) in MeOH (25 mL), ion-exchange resin (IRA-420, OH$^-$) was added and the suspension was shaken until the salt dissolved. The mixture was filtered and the resin was thoroughly washed with MeOH. The filtrate was concentrated to a volume of 5 mL and molecular sieves (3 Å) were added. To the gently stirred mixture, a solution of the aldehyde **22** (27.0 mg, 100 μmol) in a mixture of MeOH (1 mL) and $CHCl_3$ (1 mL) was added dropwise. After stirring for 18 h at room temperature, $NaBH_4$ (20 mg, 530 μmol) was added and, after reacting for 1 h, the mixture was diluted with CH_2Cl_2 (5 mL), filtered, the filtrate was evaporated in vacuo, and the residue was purified by flash chromatography (SiO_2, eluent: CH_2Cl_2–MeOH–aq 28% NH_3 80:20:1 to 80:20:3) to give **BisNP-1PY** (60.0 mg, 73%) as yellow oil. ^{1}H NMR ($CDCl_3$): δ=1.38–1.48 (m, 2H), 1.57–1.66 (m, 4H), 2.36 (t, J=7 Hz, 2H), 2.46 (t, J=6.8 Hz, 2H), 2.52 (t, J=6.9 Hz, 2H), 2.61 (t, J=5 Hz, 4H), 2.79–2.85 (m, 8H), 3.13 (t, J=7.6 Hz, 2H), 3.69 (t, J=5 Hz, 4H), 3.78 (s, 4H), 3.86 (s, 4H), 7.19 (dd, J=8.4, 1 Hz, 4H), 7.29 (d, J=8.4 Hz, 2H), 7.33 (d, J=8.4 Hz, 2H), 7.50 (s, 2H), 7.53 (s, 2H), 7.74 (d, J=7.8 Hz, 1H), 7.95–8.19 (m, 8H); ^{13}C NMR ($CDCl_3$): δ=27.0 (CH_2), 29.3 (CH_2), 29.9 (CH_2), 33.2 (CH_2), 47.5 (CH_2), 48.3 (CH_2), 49.0 (CH_2), 49.8 (CH_2), 52.0 (CH_2), 53.3 (CH_2), 53.8 (CH_2), 54.5 (CH_2), 69.8 (CH_2), 123.4 (CH), 124.6 (CH), 124.7 (CH), 124.8 (CH), 125.0 (C_q), 125.7 (CH), 125.8 (CH), 125.9 (CH), 126.4 (C_q), 126.5 (3CH), 127.1 (CH), 127.5 (CH), 127.8 (CH), 127.9 (CH), 128.5 (C_q), 129.7 (C_q), 130.9 (C_q), 131.4 (C_q), 132.5 (2C_q), 136.8 (C_q), 137.3 (C_q), 137.4 (C_q); MS (ESI$^+$): m/z (%)=413 (63) [M+2H]$^{2+}$, 825 (100) [M+H]$^+$. To prepare the hydrochloride salt, the amine was dissolved in MeOH, treated with excess concentrated aq HCl, the suspension was evaporated, and the residue was recrystallized from water to give **BisNP-1PY×6HCl** as white solid, mp (decomp.) 305–308 °C; purity (HPLC peak area) 96%. Anal. Calcd (%) for $C_{55}H_{64}N_6O\times5HCl\times2H_2O$ (1043.5): C, 63.31; H, 7.05; N, 8.05; Cl, 16.99. Found: C, 63.42; H, 6.77; N, 7.94; Cl, 16.90.

4.8. Spectrophotometric and spectrofluorimetric titrations

Absorption spectra were recorded with a double-beam spectrophotometer (UVIKON XL) in 1-mL quartz cells with a path length of 1 cm, whereas fluorescence spectra were recorded with a HORIBA Jobin-Yvon FluoroMax-3 fluorimeter in 1-mL quartz cells with a cross-section of 1 cm×0.5 cm, using bandwidths of 2 nm. All measurements were performed in sodium cacodylate buffer (10 mM $NaAsO_2Me_2$, 10 mM NaCl, pH 6.0). Stock solution of **BisNP-2PY×6HCl** (1 mM) was prepared in a mixture DMSO–H_2O (1:1 v/v). Stock solutions of **BisNP-1PY×5HCl** (1 mM), dipotassium phthalate (**K$_2$OP**, 0.1 M), and disodium terephthalate (**Na$_2$TP**, 0.1 M) were prepared in deionized water. The excitation wavelengths for fluorimetric titrations (348 nm for **BisNP-1PY** and 350 nm for **BisNP-2PY**) correspond to the isosbestic points, found from the corresponding spectrophotometric titrations.

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