# Synthesis, Conformational Analysis, and Binding Properties of Molecular Clips with Two Different Side Walls

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A new general route toward the synthesis of diphenylglycoluril clips with two different side walls starting from the new precursor **6b** and the known compound **2b** is described. A variety of clips are accessible in this way, some of them containing metal binding ligand systems, *viz.* phenanthroline, pyridine, salophen, and porphyrin for future applications as supramolecular catalysts. The physical and binding properties of the new clips are presented and discussed.

## Introduction

There is currently great interest in the fields of host−guest chemistry and in catalysis of reactions using simple enzyme mimics.[1] The focus of this interest has been primarily on the design and construction of molecules possessing a binding site for a substrate, which is positioned nearby a catalytically active center. In the case of enzymes, the enzyme−substrate complex formation is generally dominated by hydrophobic effects with additional, relatively weak interactions such as hydrogen bonding, $\pi-\pi$ stacking, and dipolar interactions used to control substrate selectivity and orientation. The shape complementarity of the receptor site and the aforementioned weak interactions are of fundamental importance for achieving substrate selectivity and regio- and enantioselectivity in the reaction. Early research into this area has revealed that cyclodextrins are ideal building blocks for the construction of simple enzyme-like catalysts.[2] As in natural enzymes, substrate binding in these mimics is dominated by hydrophobic interactions.[3] Simple modifications of the cyclodextrin molecules with basic functionalities has provided catalysts that are active toward ester hydrolysis and transesterification reactions.[4] A more recent example of a water soluble molecule with a binding site is that of Diederich's cyclophane,[5] which when functionalized with a thiazolium[6] or a porphyrin group[7] proved also to be a good enzyme mimic. Organic chemists are not, like nature, confined to the use of water as a solvent, and consequently the enzyme approach can also be applied to molecular systems that are soluble in organic solvents. In these cases the main forces contributing to the complex stability are hydrogen bonding, electrostatic interactions, $\pi-\pi$ stacking interactions, and metal-to-ligand bonding. One of the more promising types of receptor molecules which are capable of binding guests in organic solvents are the tweezer-like or clip-shaped receptors. Zimmerman[8] and Whitlock[9] have constructed excellent examples of this type of molecules, showing high substrate binding and selectivity. The next step, however, to combine these types of receptors with a catalytically active site has received considerably less attention. The most commonly used catalysts described in the literature are porphyrins and salophenes, the former species often being found in natural enzymes. Several examples of bridged, capped, and fenced porphyrins as catalysts giving remarkable selectivities have been reported.[10] Only in a limited number of systems, is the porphyrin located nearby a substrate binding site.[11−13]

One of the major goals of research in our group has been the design and synthesis of new types of cleft-shaped host molecules that can be functionalized with catalytically active components and used consequently as enzyme mimics. Previous work toward this goal has led to the development of clip,[14] and basket-shaped[15] molecules

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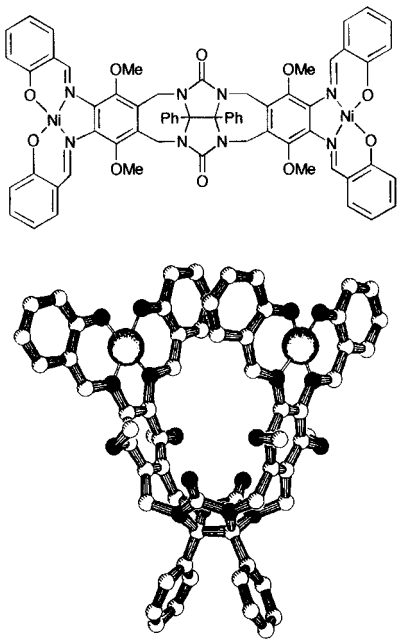

**Figure 1.** X-ray structure of the double nickel(II) salophene functionalized molecular clip (see ref 18).

based on diphenylglycoluril which were found to be ideal hosts for hydroxybenzene substrates. Subsequent functionalization of these baskets with metal centers positioned above the cavity *via* flexible spacers gave host molecules which were still able to bind dihydroxybenzenes, but in addition showed catalytic activity giving substrate selectivity[16] and enhancement of reaction rates.[17] Another approach used to construct biomimetic catalysts was to functionalize the side walls of a molecular clip with two metal salophene groups (Figure 1).[18] The obtained clip was unable, unfortunately, to bind guest molecules due to the steric hindrance of the methoxy groups blocking the cavity. In order to overcome the steric hindrance caused by the close proximity of two functionalized walls, it was necessary to design clip molecules with two different (aromatic) side walls which would facilitate the monofunctionalization with a metal center. In this paper the synthesis, characterization, and preliminary binding studies of these new clip molecules are described.

## Results and Discussion

**Synthesis.** Previously developed starting compounds derived from diphenylglycoluril (DPG) which have been used in the synthesis of other molecular receptors are cyclic ether **1**[14b] and the tetraacetoxy and the tetrachloro derivatives **2a** and **2b** (Chart 1).[14a] Clip **3a** can be synthesized from **1** by means of an acid-catalyzed amido alkylation reaction, and clips **3b**, **4**, and **5a** are accessible from the more reactive compound **2b**.

The first step in the synthesis of asymmetrically substituted clip molecules is the preparation of a monowalled intermediate. Subsequent reaction of this species with a second side wall will result in the desired compounds. In order to synthesize clip molecules functionalized with one ligand system, the monowalled species have to be nitrated before the second wall is attached (*vide infra*). These steps will be described later.

**Monowalled Molecules Based on DPG.** To obtain monowalled host **7**, cyclic ether **1** was reacted with 1 equiv of 1,4-dimethoxybenzene (1,4-DMB) in a mixture of acetic anhydride and TFA under a variety of different reaction conditions. In all cases the reaction product was a 1:1 mixture of **1** and **3a**, probably because the acetate functions in the intermediate **8** are activated by the attached aromatic wall toward a further amido alkylation reaction compared to the tetraacetate intermediate **2a**. Another possibility is that the first attached wall has a favorable preorganization effect on the second 1,4-DMB molecule. In order to overcome this problem, a new starting compound, **6b**, which has two sites of differing reactivity toward Friedel−Crafts alkylation was synthesized. Compound **6b** was obtained from **1** in two steps: (i) a partial reaction of **1** with acetic anhydride using *p*-toluenesulfonic acid as a catalyst and subsequent separation of **6a** from **1** by column chromatography, yielding **6a** in 65%; (ii) substitution of the acetyl groups with chloride groups by stirring **6a** overnight in a 1:1 mixture of $CH_2Cl_2$ and thionyl chloride. This gave crystalline **6b** (92% yield) which was moisture sensitive.

Reaction of **6b** with 1,4-DMB in 1,2-dichloroethane with $SnCl_4$ as a catalyst at both room temperature and at 0 °C again resulted in mixtures of **1** and **3a** as products. The reaction was performed at lower temperature, in order to better differentiate the reactivity of the sites of **6b**. To a 1:1 mixture of **6b** and 1,4-DMB in 1,2-dichloroethane at −35 °C was added $SnCl_4$, and the mixture was allowed to warm slowly to 0 °C overnight. The precipitate obtained was found to be **7** (88% yield). A similar reaction of the tetrachloro derivative **2b** yielded a mixture of **1**, **7**, and **3a** (molar ratio 1:4:1), which could be separated by column chromatography to give pure **7** (58%). An alternative approach to obtain **7** was by performing the reaction at room temperature but in high dilution. Slow addition of a solution of 1,4-DMB to an 1,2-dichloroethane solution of **2b** and $SnCl_4$ again yielded a mixture of **1**, **7**, and **3a** (1:4:1), which yielded **7** (52% after column chromatography).

2,7-Dimethoxynaphthalene (2,7-DMN) and 1,4-dimethoxynaphthalene (1,4-DMN) are less reactive toward attack by **2b** than 1,4-DMB. An equimolar mixture of **2b** and 2,7-DMN in 1,2-dichloroethane containing 4 equiv of $SnCl_4$ was heated under reflux to yield **9** in 71% after column chromatography. A similar reaction of **2b** with 1,4-DMN yielded **10** in 42%.

**Molecular Clips with Two Different Side Walls.** The monowalled molecules **7**, **9**, and **10** could now be used as starting materials for the preparation of several new clips containing two different aromatic side walls. Heating a mixture of **7** with hydroquinone in 1,2-dichloroethane with *p*-toluenesulfonic acid as a catalyst yielded **13** in 73%. This compound, which is insoluble in most organic solvents, was converted into a bright red compound **14** by aerial oxidation in DMSO using $Cu_2Cl_2$ as a catalyst (yield 77%). Reactions of **7** and **9** with 1,4-DMN in mixtures of acetic anhydride and TFA yielded **15** and **18** in 70 and 65%, respectively. Analogous reactions of **9** and **10** with 1,4-DMB yielded **17a** and **15** in 94 and 97%, respectively.

Nitration reactions were carried out in order to obtain clip molecules functionalized with a catalytic side wall.

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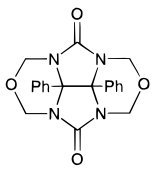
## Chart 1



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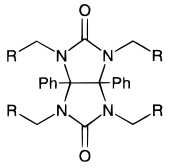
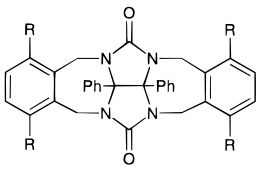
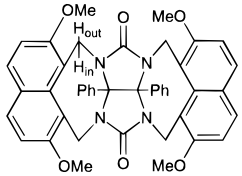


**2a** R= OAc
**2b** R= Cl



**3a** R=OMe
**3b** R=H



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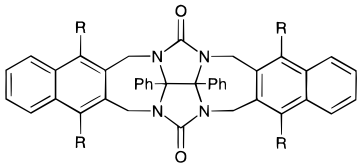
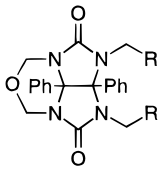
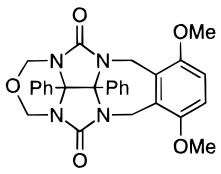


**5a** R=OMe
**5b** R=H



**6a** R=OAc
**6b** R=Cl



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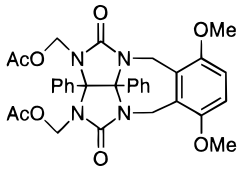

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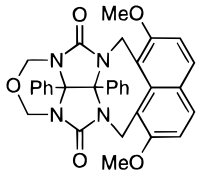

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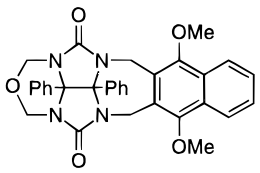

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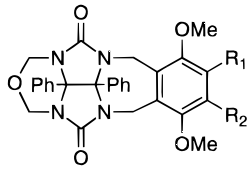
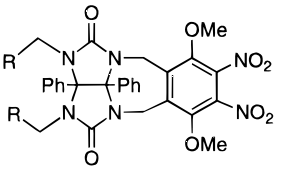
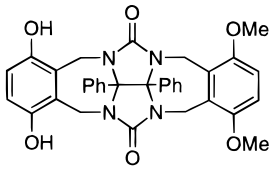


**11a:** $R_1 = NO_2$ $R_2 = H$
**11b:** $R_1 = NO_2$ $R_2 = NO_2$
**11c:** $R_1 = NH_2$ $R_2 = NH_2$



**12a** R = OAc
**12b** R = Cl



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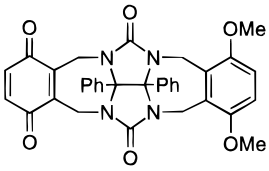

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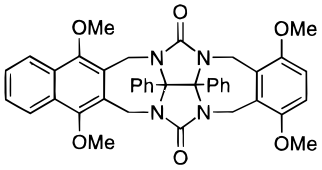

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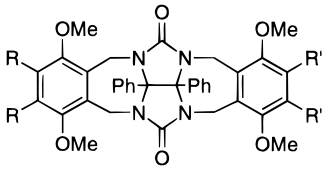
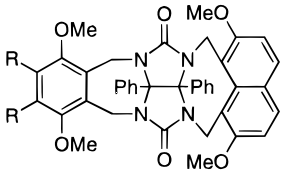
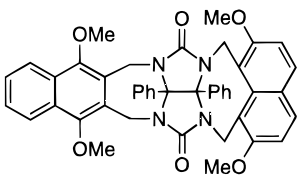


**16a** R=H, R'=$NO_2$
**16b** R=H, R'=$NH_2$
**16c** R,R'=$NO_2$
**16d** R,R'=$NH_2$



**17a** R=H
**17b** R=$NO_2$
**17c** R=$NH_2$



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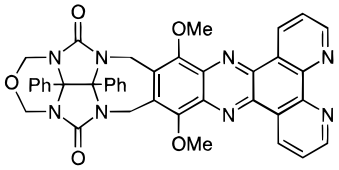

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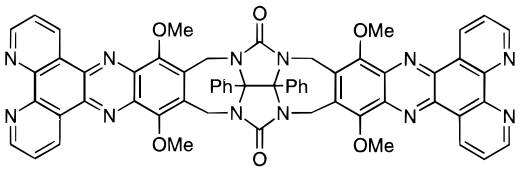

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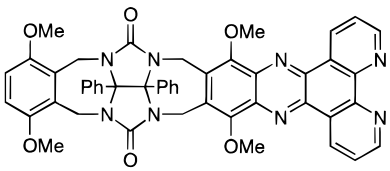

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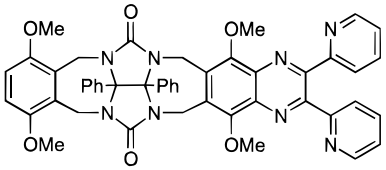

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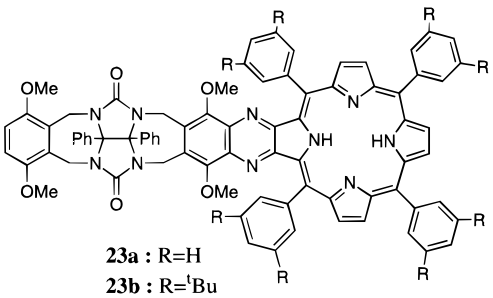
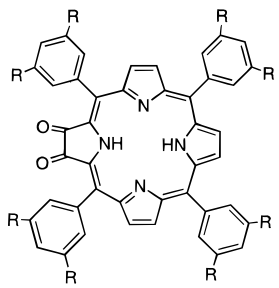
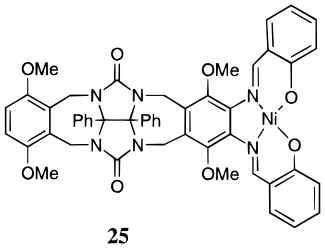


**23a :** R=H
**23b :** R=$^t$Bu



**24a :** R=H
**24b :** R=$^t$Bu

**Chart 1 (Continued)**



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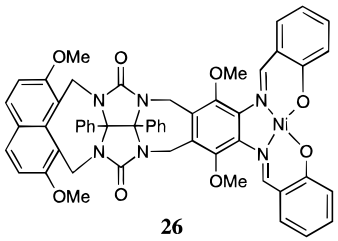

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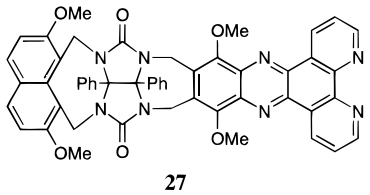
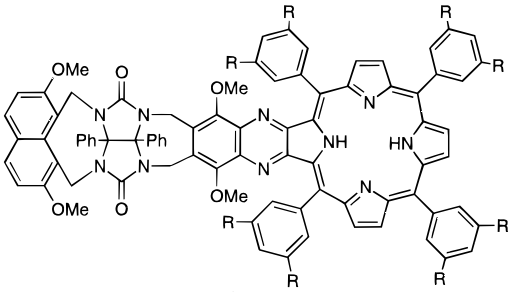


**27**



**28:** R= $^{t}$Bu

Stirring compound **7** in acetic anhydride with 2 equiv of nitric acid for 16 h gave the mononitro compound **11a** as a crystalline precipitate in 80% yield. The analogous reaction with a mixture of **1**, **7**, and **3a** (molar ratio 1:4:1) gave a precipitate which was proved to be pure **11a** (yield: 80% based on **7**). Subsequent reaction of **11a** in acetic anhydride with 4 equiv of nitric acid yielded the dinitro compound **11b** in 96%, after purification by column chromatography. Dinitro clip **16a** was prepared in 96% yield by amido alkylation of **11b** with 1,4-DMB in acetic anhydride/TFA. Several nitration reactions with **17a** were carried out in order to obtain dinitro clip **17b**. The clip molecule decomposed under the conditions necessary to nitrate the 1,4-DMB wall to give 2,7-dimethoxy-1,8-dinitronaphthalene as a side product. Compound **11b** was reacted, therefore, with acetic acid and *p*-toluenesulfonic acid to give compound **12a**, which was treated subsequently with thionyl chloride in $CH_2Cl_2$ to give **12b**. This compound was now sufficiently reactive to undergo a Friedel−Crafts reaction with 2,7-DMN to yield **17b** in 60% yield.

Dinitro compounds **11b**, **16a**, and **17b** were reduced to the corresponding diamines, **11c**, **16b**, and **17c**, using triethylammonium formate[19] as a hydrogen donor with Pd on carbon as a catalyst in a mixture of THF and methanol. These compounds were found to be very sensitive to oxidation and were used without further purification for subsequent synthesis.

**Clip Molecules Functionalized with Catalytic Side Walls.** All clips containing one or two walls functionalized with a ligand were obtained by a condensation reaction of **11c**, **16b**, **16d**, or **17c** with a diketone precursor or with salicylaldehyde. Heating **11c** with 1,10-phenanthroline-5,6-quinone[20] in a (1:1:1 (v/v)) mixture of MeOH/THF/$CH_2Cl_2$ over molecular sieves (3 Å) yielded **19** in 79% after purification by column chromatography. Similar reactions of **16b** with 1,10-phenanthroline-5,6-quinone, 2,2′-pyridil, and porphyrin diketone **24a**[21] gave compounds **21**, **22**, and **23a** in 75, 31, and 28% yields, respectively. The condensation reaction of **16b** and 2,2′-pyridil or porphyrin diketone **24** in pure dichloromethane resulted in significantly higher yields (52 and 92%, respectively). A clip molecule functionalized at one side with a salophene unit was obtained after a template condensation reaction of **16b** with salicylaldehyde and $Ni(OAc)_2 \cdot 4H_2O$, yielding **25** in 66% yield. Monofunctionalized clip molecules having an opposing 2,7-DMN side wall were obtained by similar condensation reactions using **17c** as the diamine precursor, resulting in clip molecules **26**−**28** (yields 31, 80, and 26%, respectively).

**NMR Conformational Analysis.** It has been shown previously[14a] by our group that a naphthalene moiety which is connected to the DPG framework at the 1- and 8-positions can adopt two orientations: (a) upward with respect to the phenyl ring on the convex side of the DPG unit (*anti*) and (b) downward (*syn*) with respect to this ring. Compound **4** which has two napthalene moieties connected exists in three conformations in solution, which interconvert slowly on the NMR time scale, *syn*−*syn* (7.7%), *syn*−*anti* (89.6%) and *anti*−*anti* (2.7%).

Compounds **9**, **17a**, and **18**, which have one naphthalene wall connected at the 1- and 8-positions, were expected to exist in solution in only two conformations, *viz. syn* and *anti*. The 400 MHz $^1$H NMR spectra of these compounds in $CDCl_3$ at 298 K confirmed this. Nearly all signals of the respective conformers could be assigned with the help of COSY spectra (see Table 1). The procedure that was followed for this assignment was similar to that described previously for **4**.[14a] The shielding effects of aromatic rings can be estimated with the help of the Johnson and Bovey tables.[22] It can be shown that the signals of the protons of the phenyl groups of the diphenylglycoluril framework on the *syn* side of one conformer are shifted upfield relative to the proton signals on the *anti* side. This method enables full assignment of the AX quartets of the $NCH_2$ protons and the signals of the wall protons for each of the conformers. The relative abundance of the different conformers of **9**,

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(20) (a) Smith, G.; Cagle, F. W., Jr. *J. Org. Chem.* **1947**, *12*, 781. (b) Koft, E.; Case, F. H. *J. Org. Chem.* **1962**, *27*, 865. (c) Dickeson, J.; Summers, L. *Aust. J. Chem.* **1970**, *23*, 1023.

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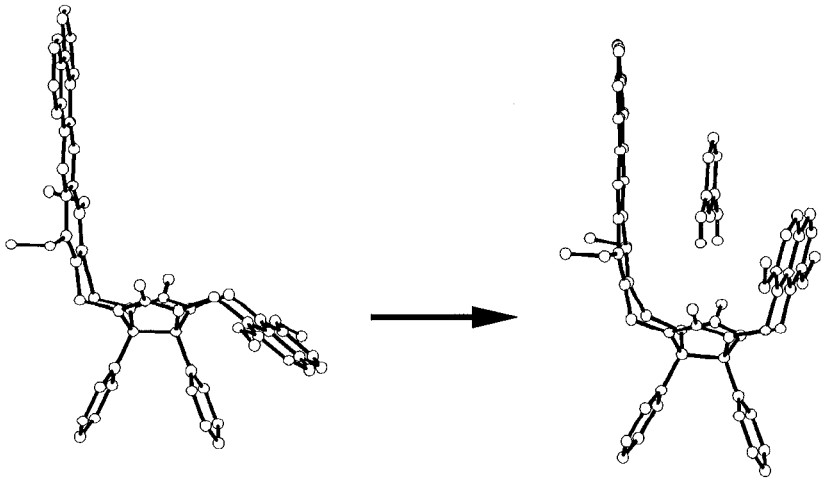

**Figure 2.** Binding of a resorcinol guest molecule by an "induced fit" mechanism in a clip containing an 1,8-connected naphthalene side wall.

**Table 1. Assignment of $^1$H NMR Signals to the Conformers of 9, 17a, and 18[a]**

| | **9** | | **17a** | | **18** | |
|---|---|---|---|---|---|---|
| proton signal | *anti* | *syn* | *anti* | *syn* | *anti* | *syn* |
| NC$H_2$O out[b] | 5.37 (11.0) | 5.66 (11.0) | | | | |
| NC$H_2$O in[b] | 4.29 (11.0) | 4.44 (11.0) | | | | |
| NC$H_2$Ph out[b] | | | 5.39 (15.8) | 5.68 (15.8) | | |
| NC$H_2$Ph in[b] | | | 3.85 (15.8) | 3.74 (15.8) | | |
| NC$H_2$Napht (2,7) out[b] | 5.98 (16.3) | 6.20 (16.5) | 5.98 (16.4) | 6.12 (16.4) | 5.97 (16.4) | 6.15 (14.8) |
| NC$H_2$Napht (2,7) in[b] | 4.19 (16.3) | 5.11 (16.5) | 4.10 (16.4) | 4.95 (16.4) | 4.09 d | 4.96 (14.8) |
| NC$H_2$Napht (1,4) out[b] | | | | | 5.63 (16.0) | 5.82 (15.9) |
| NC$H_2$Napht (1,4) in[b] | | | | | 3.84 (16.0) | 3.93 (15.9) |
| $OCH_3$ | 4.11 | 3.97 | 4.07<br>3.75 | 3.95<br>3.93 | 4.02<br>3.90 | 4.25<br>3.96 |
| Ph H-2,6[c] | *d* | 6.42(*s*) | *d* | 6.46(*s*) | *d* | 6.50(*s*) |
| Ph H-3,5[c] | *d* | 6.13(*s*) | d | 6.13(*s*) | d | 6.16(*s*) |
| Ph H-4[c] | d | 6.25(*s*) | *d* | 6.26(*s*) | d | 6.28(*s*) |
| Ph H-2,3[e] | | | 6.12 | 6.85 | | |
| Napht H-3 (2,7) | 7.19 (9.0) | 6.90 (9.0) | 7.14 (9.1) | 6.88 (9.1) | 7.11 (8.9) | 6.88 (8.9) |
| Napht H-4 (2,7) | 7.74 (9.0) | 7.30 (9.0) | 7.62 (9.1) | 7.26 (9.1) | 7.57 (8.9) | 7.26 (8.9) |
| Napht H-5,8 (1,4) | | | | | 7.95 | 8.11 |
| Napht H-6,7 (1,4) | | | | | 7.41 | 7.51 |

[a] Shifts are in ppm; *J* couplings (Hz) in parentheses; the designations (*s*) and (*a*) are used for the phenyl rings *syn* and *anti* with respect to the side walls. [b] The designations in and out are used as indicated in Chart 1. [c] Protons of the glycoluril framework. [d] No assignment could be made. [e] Protons of the 1,4-dimethoxybenzene side wall.

**17a**, and **18** were determined by integration of these signals: 23% of the molecules of **9** were in the *syn* conformation and 77% in the *anti* conformation in $CDCl_3$ at 298 K. In the case of **17a**, these values were 85 and 15%, and in the case of **18** 76 and 24%, respectively. This result is in agreement with the previously proposed idea that clip molecules with naphthalene walls connected at the 1,8-positions preferentially adopt a conformation in which the walls are optimally exposed to solvent molecules.[14a] For compound **4** this is achieved with the *syn*−*anti* conformation, for compound **9** with the *anti* conformation, and for compounds **17a** and **18** with the *syn* conformation. More details concerning these conformations will be presented in a separate paper.[24]

In addition to these model compounds, the conformational behavior of the monofunctionalized clip molecules **26**−**28** was also studied by $^1$H NMR (see Table 2). These molecules are important with respect to the overall goal of developing biomimetic catalytic systems. They were found to exist in two conformers with the *syn* conformers dominating: 68% for **26**, 68% for **27**, and 55% for **28**.

**Binding Properties.** It is known from our earlier studies that molecular clip **3a** is a good receptor for the complexation of dihydroxybenzenes, whereas **5a** is unable to bind such guests.[14d] This lack of binding of guest molecules was ascribed initially to the methoxy groups on the walls of **5a** which point inside the cavity and block the carbonyl functions from forming hydrogen bonds. Further studies indicate that, in addition to this steric effect, there is an unfavorable, *i.e.* repulsive, $\pi-\pi$ interaction between the aromatic guest and the naphthalene side walls which also results in a decrease in binding (*vide infra*).

Complexation studies with the guest olivetol (1,3-dihydroxy-5-pentylbenzene) were performed in order to obtain further insight into the influence of two different aromatic walls in the clip molecule, upon host−guest binding. The association constants ($K_a$'s) and complex-induced shift (CIS) values for a series of related clip molecules were determined by $^1$H NMR titrations as described previously.[14d] The trends in binding affinity of olivetol to selected clips are shown in Table 3. It can be seen that a large drop in $K_a$ is observed upon going from host molecules **3a** to **15** to **5a**. This highlights the fact that an 1,4-DMN wall (which can be considered as a functionalized 1,4-DMB wall) is unfavorable for guest binding compared with an 1,4-DMB wall. By comparing the association constant between olivetol and clip **3a** with that of clip **15** it can be seen that the presence of one 1,4-DMN side wall in a clip considerably reduces the binding strength (25×), but does not totally block the cleft for binding. The binding of olivetol to cyclic ether **1** ($K_a$ = 25 $M^{-1}$) increases when an 1,4-DMB wall is attached to this molecule (**7**, $K_a$ = 40 $M^{-1}$), but decreases when this wall is an 1,4-DMN aromatic surface (**10**, $K_a$ < 1 $M^{-1}$).

Clip molecules **17a** and **18** are able to bind an olivetol guest by an induced fit mechanism. The 2,7-DMN wall flips upon complexation of the guest molecule as depicted in Figure 2. The association constants for clips **17a** and

(24) Reek, J. N. H.; Elemans, J. A. A. W.; Engelkamp, H.; Rowan, A. E.; Nolte, R. J. M. *J. Am. Chem. Soc.*, submitted.

**Table 2. Assignment of $^1$H NMR Signals to the Conformers of 26, 27, and 28[a]**

| | 26 | | 27 | | 28 | |
|---|---|---|---|---|---|---|
| proton signal | *anti* | *syn* | *anti* | *syn* | *anti* | *syn* |
| NC*H*$_2$Ph | 5.50 | 5.65 | 5.89 | 6.08 | 5.85 | 6.13 |
| out[b] | (15.9) | (15.8) | (16.4) | (15.9) | (15.0) | (15.0) |
| NC*H*$_2$Ph | 3.88 | 3.86 | 3.96 | 4.01 | 3.82 | 3.95 |
| in[b] | (15.9) | (15.8) | (16.4) | (15.9) | (15.0) | (15.0) |
| NC*H*$_2$Napht (2,7) | 5.98 | 6.15 | 6.04 | 6.17 | 5.58 | 4.80 |
| out[b] | (15.9) | (14.7) | (16.4) | (14.9) | (15.0) | (15.0) |
| NC*H*$_2$Napht (2,7) | 4.09 | 4.98 | 4.12 | 4.98 | 3.96 | 2.70 |
| in[b] | (15.9) | (14.7) | (16.4) | (14.9) | (15.0) | (15.0) |
| OCH$_3$ | 4.03 | 3.97 | 4.34 | 4.72 | 3.96 | 3.91 |
| | 3.52 | 3.81 | 4.05 | 3.99 | 3.55 | 3.85 |
| Ph H-2,6[c] | 7.36−6.95 | 6.49 | 7.32−6.98 | 6.54 | 7−7.3 | 6.75(*s*) |
| | | (*s*) | | | | 7.23(*a*) |
| Ph H-3,5[c] | 7.36−6.95 | 6.19 | 7.32−6.98 | 6.25 | 7−7.3 | 6.15(*s*) |
| | | (*s*) | | | | 6.85(*a*) |
| Ph H-4[c] | 6.60 | 6.29 | 7.32−6.98 | 6.30 | 7−7.3 | 6.60(*s*) |
| | | (*s*) | | (7.3) | | 7.10(*a*) |
| Napht H-3 (2,7) | 7.17 | 6.89 | 7.02) | 6.90 | 6.8−7.3 | 6.8−7.3 |
| | (9.0) | (9.0) | (8.8) | (9.0) | | |
| Napht H-4 (2,7) | 7.59 | 7.28 | 7.47 | 7.28 | 6.8−7.3 | 6.8−7.3 |
| | (9.0) | (9.0) | (8.8) | (9.0) | | |
| Ar*H* | 7.36−6.95 | 7.36−6.95 | | | | |
| ArNC*H*Ar | 9.04 | 9.26 | | | | |
| Phenan*H* | | | 9.50 | 9.67 | | |
| | | | 9.22 | 9.29 | | |
| | | | 7.72 | 7.84 | | |
| porphyrin $\beta H$ | | | | | 8.94 | 8.94 |
| | | | | | 8.67 | 8.67 |
| porphyrin $\beta H$ | | | | | (5.0) | (5.0) |
| | | | | | 8.77 | 8.77 |
| porphyrin pyr *H* | | | | | −2.68 | −2.68 |
| porphyrin Ar*H* | | | | | 7.5−8.3 | 7.5−8.3 |
| porphyrin ArCC*H* | | | | | 1.5−1.7 | 1.5−1.7 |

[a] Shifts are in ppm; *J* couplings (Hz) in parentheses; the designations (s) and (*a*) are used for the phenyl rings *syn* and *anti* with respect to the side walls. [b] The designations in and out are used as indicated in Chart 1. [c] Protons of the glycoluril framework.

**Table 3. Association Constants and Complex-Induced Shift Values of Complexes between Olivetol and Different Clips[a]**

| clip | $K_a$/M$^{-1}$ | CIS/ppm[b] | clip | $K_a$/M$^{-1}$ | CIS/ppm[b] |
|---|---|---|---|---|---|
| **3a** | 1500 | −0.51 | **20** | <1 | |
| **15** | 55 | −0.43 | **21** | 210 | −0.36 |
| **5a** | <1 | | **22** | 125 | −0.31 |
| **1** | 25 | | **23a** | 30 | −0.34 |
| **7** | 40 | −0.34 | **5b** | 60[d] | |
| **10** | <1 | | **3b** | 175[d,e] | |
| **17a** | 1060[c] | | **25** | 920 | −0.44[f] |
| **18** | 90[c] | | **26** | 1200 | −0.40[f] |
| **19** | <1 | | | | |

[a] The errors in the association constants are 10−30%. [b] CIS values of the 1,4-dimethoxybenzene side walls. [c] Value taken from ref 24. [d] Association constant of the complex with resorcinol. [e] Value taken from ref 25. [f] CIS values of the imine protons.

**18** were determined by following the ratio of conformers as a function of the guest concentration.[14a] These experiments also revealed that the 1,4-DMN wall is very unfavorable for binding. A drop in association constant from $K_a$ = 1060 M$^{-1}$ (**17a**) to 90 M$^{-1}$ (**18**) was observed when the 1,4-DMB wall in the clip molecule was replaced by an 1,4-DMN wall (Table 3). Since the change to an 1,4-DMN wall had such a great influence upon the host−guest binding, it was decided to perform binding studies with **5b**, a molecule with naphthalene walls but without methoxy groups. In this case resorcinol (1,3-dihydroxybenzene) was chosen as the guest molecule in order that a comparison with previous studies could be made.[14d] Clip molecule **5b** was able to bind resorcinol ($K_a$ = 70 M$^{-1}$), but with a lower binding constant than was found for the clip with two benzene walls **3b** ($K_a$ = 175 M$^{-1}$). When the methoxy groups of clip molecule **5a** are removed, the cleft is no longer blocked; however, the binding is still relatively weak (compared with that of **3b**) because of unfavorable $\pi-\pi$ stacking interactions. These unfavorable $\pi-\pi$ interactions are caused by a repulsive electrostatic interaction according to calculations using the Hunter and Sanders model[23] (see also ref 25 ). The formation of the hydrogen bonds between host and guest forces the guest into a geometry in which the $\pi-\pi$ interaction with the aromatic side walls is very unfavorable.

Comparison of the complex-induced shift (CIS) value of clip **15** (−0.43 ppm) with that of **3a** (−0.51 ppm), indicates that in both complexes the guest molecule is positioned in a similar orientation. Calculations were carried out with a computer program based on the Johnson and Bovey tables of ring current shifts,[22] which suggested that the guest is less deeply bound in the cavity of clip **15** than in the cavity of clip **3a**.[14d] This might be important when a guest molecule has to be bound nearby a catalytically active site, *e.g.* a metal center bound to ligands **19**−**23**.

The binding properties of the ligand functionalized molecular clips **19**−**26** are of interest with respect to the aims outlined in the introduction. The monophenanthroline clip **21** is capable of binding olivetol ($K_a$ = 210 M$^{-1}$), whereas the diphenanthroline clip **20** is not a good host ($K_a$ < 1 M$^{-1}$). This is in line with the binding results obtained with clip molecules **3a**, **5a,** and **15** (*vide supra*) and is due to the repulsive nature of the two large electronegative side walls of **20**, and the steric effects of the methoxy groups which partly shield the carbonyl groups. Porphyrin clip **23a** and dipyridine clip **22** are also capable of binding olivetol in their clefts ($K_a$ = 30 and 125 M$^{-1}$, respectively). The observed binding constants are lower than the binding constant of monophen-

(25) Reek, J. N. H.; Priem, A. H.; Elemans, J. A. A. W.; Engelkamp, H.; Rowan, A. E.; Nolte, R. J. M. *J. Am. Chem. Soc.*, submitted.

anthroline clip **21** due to steric effects. In clip **22** the pyridyl groups are positioned orthogonally to the wall of the cleft, leading to steric congestion when the guest is bound. Porphyrin clip **23a** contains phenyl groups attached to the porphyrin ring which are pointing slightly into the cleft, as is evident from the X-ray structure of this molecule.[26] These phenyl groups cause steric repulsion, resulting in a lower association constant. Monowalled clip molecule **19** is not able to bind olivetol, which is in agreement with the binding properties of **10**. The CIS values of the complexes between the clips **21**, **22**, and **23** and olivetol suggest that the guest is bound with approximately the same geometry but less deeply than in clip **3a**.[14d]

It is clear from the binding studies with compounds **15** and **18** that 2,7-DMN side walls give rise to slightly higher binding constants than 1,4-DMB side walls. This is also the case for the clips containing a catalytically active nickel salophene side wall. Compound **25** binds olivetol with an association constant of $K_a = 920\ M^{-1}$, which is slightly lower than the $K_a = 1200\ M^{-1}$ measured for **26**. These binding constants are, however, both higher than those observed for the 1,4-DMN containing clips **15** and **18**. This is probably an effect of the lower electron density of the nickel salophene functionalized side wall, which reduces the electrostatic repulsion between this side wall and the aromatic ring of the bound guest molecule.

This new synthetic route enables the construction of a wide variety of novel clip molecules with different side walls, which can be easily monofunctionalized to give enzyme mimics. Further detailed binding studies with these new clip molecules as well as catalytic studies are reported in separate papers.[25,26]

## Experimental Section

**General.** Thionyl chloride and triethylammonium formate were distilled prior to use. THF and diethyl ether were distilled under nitrogen from sodium benzophenone ketyl. Dichloromethane and chloroform were distilled from $CaCl_2$. 1,2-Dichloroethane and methanol were distilled from $CaH_2$. All other solvents and chemicals were commercial materials and used as received. Merck silica gel (60H) was used for column chromatography and Merck silica gel $F_{254}$ plates for thin layer chromatography. Melting points were determined on a Jeneval polarization microscope THMS 600 hot stage and are uncorrected. IR spectra were recorded on a Perkin-Elmer FTIR 1720-X spectrometer. $^1$H NMR spectra were recorded on Bruker WH-90, Bruker AC-100, Bruker WM-200, and Bruker AM-400 instruments. Chemical shifts are reported in ppm downfield from internal $(CH_3)_4Si$. Abbreviations used are as follows: s, singlet; d, doublet; m, multiplet; br, broad. Assignments of proton signals in complicated NMR spectra were made with the help of 2D COSY techniques. FAB-MS spectra were recorded on a VG 7070E instrument; the matrix used was 3-nitrobenzyl alcohol. Field desorption (FD) mass spectrometry was carried out using a JEOL JMS SX/SX102A four-sector mass spectrometer, coupled to a JEOL MS-MP7000 data system; 10 $\mu$m tungsten wire FD emitters containing carbon microneedles with an average length of 30 $\mu$m were used. The samples were dissolved in methanol/water and then loaded onto the emitters with the dipping technique. An emitter current of 0−15 mA was used to desorb the samples. The ion source temperature was generally 90 °C. Elemental analyses were determined with a Carbo Erba Ea 1108 instrument.

**Compounds.** The syntheses and properties of compounds **1**, **2a**, **2b**, **3a**, **3b**, **4**, **5a**,[14] and **16c** and **16d**[18] have been described elsewhere. 1,10-Phenanthroline-5,6-quinone was synthesized from 1,10-phenanthroline monohydrate according to literature procedures.[20] 17,18-Dioxoporphyrins **24a** and **24b** were kindly provided by Prof. M. J. Crossley.[21]

**6,8,15,16b,16c,17-Hexahydro-16b,16c-diphenyl-7*H*,16*H*-6a,7a,15a,16a-tetraazanaphtho[5,6]azuleno[2,1,8-*ij*]naphtho[*f*]azulene-7,16-dione (5b).** To a suspension of 900 mg (16 mmol) of KOH in 2 mL of DMSO was added 300 mg (1.0 mmol) of diphenylglycoluril and 650 mg (2.7 mmol) of α,α′-dibromo-2,3-dimethylnaphthalene. The mixture was stirred for 16 h and then poured into 20 mL of water. The compound was extracted with 20 mL of $CH_2Cl_2$, and the organic layer was washed with aqueous 1 N NaOH and water and dried over $MgSO_4$. After evaporation of the solvent, the compound was purified by column chromatography (eluent $CH_2Cl_2$) and recrystallization from $CHCl_3$, yielding 184 mg of white powder (31%): mp >310 °C; $^1$H NMR ($CDCl_3$) $\delta$ 7.70 (s, 4H, Napht*H*), 7.70−7.60 and 7.45−7.30 (2m, 8H, Napht*H*), 7.18 (s, 10H, ArH), 5.01 and 4.27 (2d, 8H, NC$H_2$Ar, $J = 16.0$ Hz); FAB-MS $m/z$ 599 $(M + H)^+$. Anal. Calcd for $C_{40}H_{30}N_4O_2$: C, 80.25; H, 5.05; N, 9.36. Found: C, 80.56; H, 5.11; N, 8.99.

**Acetic Acid [3-(Acetoxymethyl)tetrahydro-1,4-dioxo-2a,7b-diphenyl-6-oxa-2,3,4a,7a-tetraazacyclopenta[*cd*]inden-2-yl]methyl Ester (6a).** A suspension of 3.18 g (8.40 mmol) of **1** and 80 mg (0.42 mmol) of *p*-toluenesulfonic acid monohydrate in 15 mL of acetic anhydride was heated to reflux. After the mixture became clear, it was instantly cooled in an ice bath. Diethyl ether (15 mL) was added, and the resulting precipitate was filtered off, washed with diethyl ether, and dried under vacuum. After column chromatography ($CH_2Cl_2$/MeOH, 99:1 v/v), 2.62 g (65%) of **6a** was obtained as a white solid: mp 228 °C; IR (KBr) 1756, 1737 (C═O), 1237 (COC); $^1$H NMR ($CDCl_3$) $\delta$ 7.20−6.95 (m, 10H, ArH), 5.65 and 4.47 (2d, 4H, NC$H_2$OAc, $J = 11.4$ Hz), 5.62 and 5.33 (2d, 4H, NC$H_2$O, $J = 11.1$ Hz), 2.07 (s, 6H, $COCH_3$); FAB-MS $m/z$ 481 $(M + H)^+$. Anal. Calcd for $C_{24}H_{24}N_4O_7$: C, 60.00; H, 5.03; N, 11.66. Found: C, 60.12; H, 4.99; N, 11.55.

**2,3-Bis(chloromethyl)dihydro-2a,7b-diphenyl-6-oxa-2,3,4,7a-tetraazacyclopenta[*cd*]indene-1,4-dione (6b).** Compound **6a** (1.11 g, 2.31 mmol) was stirred under nitrogen for 16 h in a mixture of 2 mL of $CH_2Cl_2$ and 3 mL (41 mmol) of $SOCl_2$. After addition of 5 mL of diethyl ether, the precipitate was filtered off, washed with diethyl ether, and dried under vacuum to yield 0.92 g (92%) of **6b** as a white hygroscopic solid: $^1$H NMR ($CDCl_3$) $\delta$ 7.28−6.92 (m, 10H, ArH), 5.40 and 5.33 (2d, 4H, NC$H_2$Cl, $J = 11.0$ Hz), 5.65 and 4.47 (2d, 4H, NC$H_2$O, $J = 11.1$ Hz); FAB-MS $m/z$ 397 $(M - Cl)^+$. Anal. Calcd for $C_{20}H_{18}N_4O_3Cl_2$: C, 55.44; H, 4.19; N, 12.93. Found: C, 55.58; H, 4.25; N, 12.72.

**Monowalled Compound 7. Method A.** A stirred suspension of 0.95 g (2.2 mmol) of **6a** and 0.30 g (2.2 mmol) of 1,4-dimethoxybenzene in 100 mL of 1,2-dichloroethane was cooled under nitrogen to −35 °C in an acetone/$CO_2$ bath. $SnCl_4$ (1 mL, 8 mmol) was added, and the mixture was allowed to warm slowly to 0 °C. A precipitate was formed, which was filtered at 0 °C, washed with diethyl ether, and redissolved in 100 mL of dichloromethane. The organic layer was washed with aqueous 1 N HCl and water, dried ($MgSO_4$), and concentrated *in vacuo* to yield 0.96 g (88%) of **7** as a white solid.

**Method B.** A stirred suspension of 1.07 g (2.2 mmol) of **2b** and 0.30 g (2.2 mmol) of 1,4-dimethoxybenzene in 100 mL of 1,2-dichloroethane was cooled under nitrogen to −35 °C in an acetone/$CO_2$ bath. $SnCl_4$ (1 mL, 8 mmol) was added. The mixture was allowed to warm slowly to 0 °C, and 10 mL of aqueous 6 N HCl was added. After the mixture was stirred 15 min, the organic layer was washed with water and concentrated *in vacuo*. A mixture of **1**, **7**, and **3a** was obtained (molar ratio 1:4:1) which could be separated by column chromatography ($CHCl_3$/MeOH, 197:3, v/v) to yield 0.63 g (58%) of **7**.

**Method C.** To a stirred solution of 1.0 g (2.0 mmol) of **2b** and 1 mL (8 mmol) of $SnCl_4$ in 200 mL of degassed 1,2-dichloroethane was slowly added (2 mL/min) a solution of 0.28 g (2.0 mmol) of 1,4-dimethoxybenzene in 100 mL of 1,2-dichloroethane. After the addition of 10 mL of 6 N aqueous HCl the mixture was stirred for another 15 min. The organic layer was washed with water and concentrated *in vacuo*. A

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mixture of **1**, **7**, and **3a** was obtained (molar ratio 1:4:1) which could be separated by column chromatography as described under method B to yield 0.52 g (51%) of **7**: mp 381 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 7.30−7.00 (m, 10H, ArH), 6.83 (s, 2H, ArH), 5.65 and 3.80 (2d, 4H, NC$H_2$Ar, $J$ = 15.8 Hz), 5.50 and 4.40 (2d, 4H, NC$H_2$O, $J$ = 11.0 Hz), 3.87 (s, 6H, $OCH_3$); FAB-MS $m/z$ 499 $(M + H)^+$. Anal. Calcd for $C_{28}H_{26}N_4O_5$: C, 67.46; H, 5.26; N, 11.24. Found: C, 67.63; H, 5.15; N, 11.18.

**Monowalled Compound 9**. A mixture of 2.0 g (4.1 mmol) of **2b**, 1.0 g (5.3 mmol) of 2,7-dimethoxynaphthalene, and 1.5 mL (12 mmol) of $SnCl_4$ was refluxed under nitrogen for 50 min in 100 mL of degassed 1,2-dichloroethane. After this period, 10 mL of aqueous 6 N HCl was added, and the mixture was refluxed for an additional 15 min. After cooling, $CH_2Cl_2$ (50 mL) was added, and the organic layer was washed with aqueous 1 N HCl, aqueous 1 N NaOH (2×), and water and concentrated *in vacuo*. Column chromatography ($CH_2Cl_2$/MeOH, 99:1 v/v) gave 1.6 g (71%) of **9** as a white solid: mp 315 °C dec; $^1$H NMR ($CDCl_3$) see Table 1; FAB-MS $m/z$ 549 $(M + H)^+$. Anal. Calcd for $C_{32}H_{28}N_4O_5$: C, 70.06; H, 5.14; N, 10.21. Found: C, 70.20; H, 5.22; N, 9.99.

**Monowalled Compound 10.** A mixture of 2.4 g (4.9 mmol) of **2b**, 1.1 g (5.9 mmol) of 1,4-dimethoxynaphthalene, and 1.5 mL (12 mmol) of $SnCl_4$ was refluxed under nitrogen for 5 min in 100 mL of degassed 1,2-dichloroethane. After this period 10 mL of aqueous 6 N HCl was added, and the mixture was refluxed for an additional 15 min. After cooling, $CH_2Cl_2$ (50 mL) was added and the organic layer was washed with aqueous 1 N HCl, aqueous 1 N NaOH (2×) and water, and concentrated *in vacuo*. Column chromatography ($CHCl_3$/EtOAc, 95:5 v/v) gave 1.1 g (42%) of **10** as a white solid: mp 377 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 8.10 (m, 2H, Napht H-5,8), 7.53 (m, 2H, Napht H-6,7), 7.27−7.00 (m, 10H, ArH), 5.81 and 4.03 (2d, 4H, NC$H_2$Ar, $J$ = 15.9 Hz), 5.52 and 4.43 (2d, 4H, NC$H_2$O, $J$ = 11.0 Hz), 4.20 (s, 6H, $OCH_3$); FAB-MS $m/z$ 549 $(M + H)^+$. Anal. Calcd for $C_{32}H_{28}N_4O_5$: C, 70.06; H, 5.14; N, 10.21. Found: C, 70.08; H, 5.18; N, 10.15.

**Mononitro Compound 11a**. To an ice-cooled suspension of **7** (0.49 g, 0.99 mmol) in 2 mL of acetic anhydride was *carefully* and *slowly* added 0.5 mL of aqueous 53% $HNO_3$. The resulting solution was allowed to warm to room temperature and stirred for 16 h. A crystalline precipitate was filtered off and washed with acetic acid and cold ethanol: yield 0.43 g (80%) of **11a** as a pale yellow solid; mp 303 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 7.39 (s, 1H, ArH), 7.22−7.03 (m, 10H, ArH), 5.69, 5.65, 3.95 and 3.84 (4d, 4H, NC$H_2$Ar, $J$ = 15.8 Hz), 5.51 and 4.43 (2 × br d, 4H, NC$H_2$O, $J$ = 11.0 Hz), 4.10 and 3.96 (2s, 6H, $OCH_3$); FAB-MS $m/z$ 544 $(M + H)^+$. Anal. Calcd for $C_{28}H_{25}N_5O_7$: C, 61.87; H, 4.64; N, 12.88. Found: C, 62.03; H, 4.67; 12.69.

**Dinitro Compound 11b**. To an ice-cooled suspension of **11a** (0.35 g, 0.65 mmol) in 2 mL of acetic anhydride was *carefully* and *slowly* added 1 mL of aqueous 53% $HNO_3$. The resulting solution was allowed to warm to room temperature. The mixture was stirred for 16 h and then poured into 100 mL of water. The product was extracted with 50 mL of $CH_2Cl_2$. The organic layer was washed twice with aqueous 1 N NaOH and with water and concentrated *in vacuo*. After purification by column chromatography ($CH_2Cl_2$/EtOH, 99:1 v/v), 0.35 g (94%) of **11b** was obtained as a pale yellow solid. The compound was recrystallized from acetic acid: mp 376 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 7.30−7.00 (m, 10H, ArH), 5.57 and 3.98 (2d, 4H, NC$H_2$Ar, $J$ = 15.8 Hz), 5.52 and 4.46 (2d, 4H, NC$H_2$O, $J$ = 11.0 Hz), 4.19 (s, 6H, $OCH_3$); FAB-MS $m/z$ 589 $(M + H)^+$. Anal. Calcd for $C_{28}H_{24}N_6O_9$·($CH_3COOH$): C, 55.54; H, 4.35; N, 12.96. Found: C, 55.68; H, 4.12; N, 13.05.

**Diamino Compound 11c**. Compound **11b** (0.10 g, 0.17 mmol) was suspended in a degassed mixture of 5 mL of methanol and 5 mL of THF. Palladium on carbon (25 mg) and 0.5 mL (3.4 mmol) of triethylammonium formate were added. The mixture was stirred under nitrogen for 16 h and filtered under nitrogen, and the residue was washed with $CH_2Cl_2$ (5 mL). The resulting solution of **11c** was used without purification for further synthesis. An aliquot of the solution was evaporated to dryness for analysis: $^1$H NMR ($CDCl_3$) $\delta$ 7.25−7.04 (m, 10H, ArH), 5.43 and 3.91 (2d, 4H, NC$H_2$Ar, $J$ = 15.8 Hz), 5.53 and 4.45 (2d, 4H, NC$H_2$O, $J$ = 11.1 Hz), 3.92 (s, 6H, $OCH_3$); the signals of the amino groups were too broad to be detected; FAB-MS $m/z$ 529 $(M + H)^+$. Due to the extreme instability of the compound, no satisfactory elemental analysis could be obtained.

**Monowalled Compound 12a.** A mixture of 0.43 g (0.73 mmol) of **11a**, 50 mg (0.26 mmol) of *p*-toluenesulfonic acid monohydrate, and 2 mL of acetic anhydride was stirred at 110 °C for 3 h. After cooling, 8 mL of methanol was added and the mixture was poured in 100 mL of aqueous 2 N NaOH. The product was extracted with 2 × 50 mL of $CH_2Cl_2$. The combined organic layers were washed with water, dried ($MgSO_4$), and evaporated to dryness to yield 0.48 g (95%) of **12a** as a pale yellow solid. The compound was recrystallized from acetic acid: mp 98−102°C; $^1$H NMR ($CDCl_3$) $\delta$ 7.34−6.82 (m, 10H, ArH), 5.63 and 5.28 (2d, 4H, NC$H_2$OAc, $J$ = 11.5 Hz), 5.62 and 3.92 (2d, 4H, NC$H_2$Ar, $J$ = 16.4 Hz), 4.17 (s, 6H, $OCH_3$), 2.02 (s, 6H, $COCH_3$); FAB-MS $m/z$ 631 $(M - OAc)^+$, 713 $(M + Na)^+$. Anal. Calcd for $C_{32}H_{30}N_6O_{12}$·0.5($CH_3$-COOH): C, 55.00; H, 4.48; N, 11.66. Found: C, 54.88; H, 4.63; N, 11.63.

**Monowalled Compound 12b.** Compound **12a** (0.48 g, 0.73 mmol) was stirred under nitrogen for 16 h in a mixture of 2 mL of $CH_2Cl_2$ and 4 mL of $SOCl_2$. The solvent was removed *in vacuo* to yield 0.45 g (100%) of **12b** as a pale yellow hygroscopic solid: $^1$H NMR ($CDCl_3$) $\delta$ 7.37−6.83 (m, 10H, ArH), 5.59 and 3.91 (2d, 4H, NC$H_2$Ar, $J$ = 16.0 Hz), 5.41 and 5.25 (2d, 4H, NC$H_2$Cl, $J$ = 11.5 Hz), 4.17 (s, 6H, $OCH_3$); FAB-MS $m/z$ 573 $(M - 2Cl + H)^+$. Anal. Calcd for $C_{28}H_{24}N_6O_8$-$Cl_2$: C, 52.27; H, 3.76; N, 13.06. Found: C, 52.47; H, 3.84; N, 12.78.

**5,7,12,13b,13c,14-Hexahydro-1,4-dihydroxy-8,11-dimethoxy-13b,13c-diphenyl-6*H*,13*H*-5a,6a,12a,13a-tetraazabenz[5,6]azuleno[2,1,8-*ija*]benz[*f*]azulene-6,13-dione (13).** A suspension of 0.77 g (1.5 mmol) of **7** and 0.61 g (3.2 mmol) of *p*-toluenesulfonic acid monohydrate in 10 mL of degassed 1,2-dichloroethane was refluxed under nitrogen for 10 min over molecular sieves (4 Å). To the resulting clear solution was added 0.34 g (3.1 mmol) of hydroquinone, and the mixture was refluxed over molecular sieves for an additional 1 h. After cooling, 5 mL of methanol was added, and the precipitate was collected by filtration and washed with methanol. After recrystallization from DMSO, 0.67 g (73%) of **13** was obtained as a white solid: mp 325 °C dec; $^1$H NMR (DMSO-$d_6$) $\delta$ 8.76 (s, 2H, OH), 7.28−6.90 (m, 10H, ArH), 6.77 and 6.44 (2s, 4H, ArH), 5.37, 5.26, 3.63 and 3.50 (4d, 8H, NC$H_2$-Ar, $J$ = 15.8 Hz), 3.69 (s, 6H, $OCH_3$); FAB-MS $m/z$ 591 $(M + H)^+$. Anal. Calcd for $C_{34}H_{30}N_4O_6$: C, 69.14; H, 5.12; N, 9.49. Found: C, 69.24; H, 5.19; N, 9.31.

**Clip Molecule 14.** Compound **13** (0.13 g, 0.22 mmol) was dissolved in 5 mL of DMSO. $Cu_2Cl_2$ (50 mg) and 0.5 mL of pyridine were added, and air was bubbled through the mixture for 2 h. The resulting red suspension was poured into 50 mL of aqueous 1 N HCl, and the product was extracted with 50 mL of $CHCl_3$. The organic layer was washed with aqueous 1 N HCl, 5% aqueous $NH_3$ (2×), and water (2×) and concentrated *in vacuo*. After purification by column chromatography ($CH_2Cl_2$/MeOH, 98:2 v/v), 0.10 g (77%) of **14** was obtained as a red solid: mp 312 °C dec; IR 1734, 1714 (C=O), 1655 (C=C); $^1$H NMR ($CDCl_3$) $\delta$ 7.35−6.85 (m, 10H, ArH), 6.72 and 6.65 (2s, 4H, ArH and CH), 5.64, 5.50, 3.77, and 3.67 (4d, 8H, NC$H_2$-Ar, $J$ = 15.8 Hz), 3.80 (s, 6H, $OCH_3$); FAB-MS $m/z$ 591 $(M + 4H)^+$. Anal. Calcd for $C_{34}H_{28}N_4O_6$·($CH_2Cl_2$): C, 62.41; H, 4.49; N, 8.32. Found: C, 62.29; H, 4.55; N, 8.38.

**Clip Molecule 15. Method A.** A solution of 0.27 g (0.49 mmol) of **10** and 75 mg (0.54 mmol) of 1,4-dimethoxybenzene in 1 mL of acetic anhydride and 1 mL of trifluoroacetic acid was heated for 1 h at 95 °C. After cooling, 4 mL of methanol was slowly added, and the resulting precipitate was filtered off, washed with diethyl ether, and dried under vacuum to yield 106 mg (97%) of **15** as a white solid.

**Method B.** A solution of 0.32 g (0.64 mmol) of **7** and 0.24 g (1.29 mmol) of 1,4-dimethoxynaphthalene in 2 mL of acetic anhydride and 2 mL of trifluoroacetic acid was heated for 3 h at 95 °C. After cooling, 8 mL of methanol was slowly added, and the resulting precipitate was filtered off, washed with diethyl ether, and dried under vacuum to yield 0.30 g (70%) of **15**: mp 263 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 8.05 (m, 2H, Napht

H-5,8), 7.48 (m, 2H, Napht H-6,7), 7.35−6.95 (m, 10H, ArH), 6.67 (s, 2H, ArH), 5.73, 5.59, 3.94, and 3.79 (4d, 8H, NC$H_2$Ar, $J$ = 16.0 Hz), 4.08 and 3.76 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 669 $(M + H)^+$. Anal. Calcd for $C_{40}H_{36}N_4O_6$: C, 71.84; H, 5.43; N, 8.38. Found: C, 72.07; H, 5.36; N, 8.21.

**5,7,12,13b,13c,14-Hexahydro-1,4,8,11-tetramethoxy-2,3-dinitro-13b,13c-diphenyl-6*H*,13*H*-5a,6a,12a,13a-tetraazabenz[5,6]azuleno[2,1,8-*ija*]benz[*f*]azulene-6,13-dione (16a).** With **11b** (0.35 g, 0.60 mmol) and 1,4-dimethoxybenzene (90 mg, 0.65 mmol) as starting materials, this compound was synthesized as described for **15** (method A) to yield 0.40 g (96%) of **16a** as a pale yellow solid. The compound was recrystallized from acetic acid: IR 1708 (C═O), 1546, 1358 (N−O); $^1$H NMR ($CDCl_3$) $\delta$ 7.30−6.95 (m, 10H, ArH), 6.85 (s, 2H, ArH), 5.61 and 3.80 (2d, 4H, NC$H_2$Ar, $J$ = 15.9 Hz), 5.52 and 3.88 (2d, 4H, NC$H_2$Ar, $J$ = 16.4 Hz), 4.07 and 3.82 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 709 $(M + H)^+$. Anal. Calcd for $C_{36}H_{32}N_6O_{10}\cdot(CH_3COOH)$: C, 59.36; H, 4.72; N, 10.94. Found: C, 59.61; H, 4.59; N, 10.82.

**5,7,12,13b,13c,14-Hexahydro-1,4,8,11-tetramethoxy-2,3-diamino-13b,13c-diphenyl-6*H*,13*H*-5a,6a,12a,13a-tetraazabenz[5,6]azuleno[2,1,8-*ija*]benz[*f*]azulene-6,13-dione (16b).** Compound **16a** (0.21 g, 0.30 mmol) was suspended in a degassed mixture of 10 mL of methanol and 10 mL of THF. Palladium on carbon (50 mg) and 1 mL (7 mmol) of triethylammonium formate were added. The mixture was stirred under nitrogen for 16 h and filtered under nitrogen, and the residue was washed with $CH_2Cl_2$ (10 mL). The resulting solution of **16b** was used without purification for further synthesis. An aliquot of the solution was evaporated to dryness for analysis: mp 311 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 7.18−6.92 (m, 10H, ArH), 6.71 (s, 2H, ArH), 5.60, 5.36, 3.83, and 3.78 (4d, 8H, NC$H_2$Ar, $J$ = 15.8 Hz), 5.0−4.0 (br s, 4H, $NH_2$), 3.82 and 3.77 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 649 $(M + H)^+$. Due to the extreme instability of the compound, no satisfactory elemental analysis could be obtained.

**Clip Molecule 17a.** With **9** (0.38 g, 0.69 mmol) and 1,4-dimethoxybenzene (0.11 g, 0.80 mmol) as starting materials, this compound was synthesized as described for **15** (method A) to yield 0.43 g (93%) of **17a** as a white solid: mp 317 °C dec; IR 1727, 1712 (C═O); $^1$H NMR ($CDCl_3$) see Table 1; FAB-MS $m/z$ 669 $(M + H)^+$. Anal. Calcd for $C_{40}H_{36}N_4O_6$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.85; H, 5.43; N, 8.37.

**Dinitro Compound 17b.** To a solution of 0.45 g (0.70 mmol) of **12b** and 0.26 g (1.4 mmol) of 2,7-dimethoxynaphthalene in 40 mL of degassed 1,2-dichloroethane was added 1 mL (8 mmol) of $SnCl_4$. The mixture was refluxed under nitrogen for 3 h. After cooling, 4 mL of aqueous 6 N HCl was added, and the mixture was refluxed for another 30 min. After cooling, 100 mL of aqueous 1 N HCl was added, and the product was extracted with 2 × 50 mL of $CH_2Cl_2$. The combined organic layers were washed with aqueous 1 N NaOH and with water. After evaporation of the solvent, the product was purified by column chromatography ($CH_2Cl_2$/MeOH, 199:1 v/v) to yield 0.32 g (60%) of **17b** as a pale yellow solid. The compound was recrystallized from acetic acid: mp 265 °C; $^1$H NMR ($CDCl_3$) *syn*-conformer (65%) $\delta$ 7.29 and 6.95 (2d, 4H, NaphtH, $J$ = 9.1 Hz), 7.20−6.95 (m, 5H, ArH), 6.45 and 6.18 (2d, 4H, ArH, $J$ = 7.0 Hz), 6.28 (t, 1H, ArH, $J$ = 7.0 Hz), 6.15 and 5.00 (2d, 4H, NC$H_2$Napht, $J$ = 14.5 Hz), 5.60 and 3.87 (2d, 4H, NC$H_2$Ph, $J$ = 16.4 Hz), 4.27 and 3.98 (2s, 12H, $OCH_3$); *anti*-conformer (35%) $\delta$ 7.69 and 7.16 (2d, 4H, NaphtH, $J$ = 9.1 Hz), 7.20−6.95 (m, 10H, ArH), 5.93 and 4.11 (2d, 4H, NC$H_2$-Napht, $J$ = 16.4 Hz), 5.41 and 3.78 (2d, 4H, NC$H_2$Ph, $J$ = 16.4 Hz), 4.04 and 3.89 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 759 $(M + H)^+$. Anal. Calcd for $C_{40}H_{34}N_6O_{10}\cdot(CH_3COOH)$: C, 61.61; H, 4.68; N, 10.26. Found: C, 61.71; H, 4.64; N, 10.20.

**Diamino Compound 17c.** Compound **17b** (0.26 g, 0.34 mmol) was suspended in a degassed mixture of 10 mL of THF and 10 mL of methanol. Palladium on carbon (200 mg) and 1 mL (6.8 mmol) of triethylammonium formate were added. The mixture was stirred under nitrogen for 24 h and filtered under nitrogen, and the residue was washed with 10 mL of $CH_2Cl_2$. The filtrate was evaporated to dryness to yield 0.24 g (100%) of **17c** as a pale yellow very hygroscopic solid: $^1$H NMR ($CDCl_3$) *syn*-conformer (70%) $\delta$ 7.30−6.80 (m, 5H, ArH), 7.10 and 6.88 (2d, 4H, NaphtH, $J$ = 9.0 Hz), 6.45 and 6.18 (2d, 4H, ArH, $J$ = 7.3 Hz), 6.28 (t, 1H, ArH, $J$ = 7.3 Hz), 6.16 and 4.98 (2d, 4H, NC$H_2$Napht, $J$ = 14.5 Hz), 5.46 and 3.80 (2d, 4H, NC$H_2$Ph, $J$ = 15.9 Hz), 4.01 and 3.96 (2s, 12H, $OCH_3$); *anti*-conformer (30%) $\delta$ 7.30−6.80 (m, 10H, ArH), 7.65 and 7.16 (2d, 4H, NC$H_2$Napht, $J$ = 9.0 Hz), 5.97 and 4.19 (2d, 4H, NC$H_2$-Napht, $J$ = 16.1 Hz), 5.38 and 3.72 (2d, 4H, NC$H_2$Ph, $J$ = 16.1 Hz), 4.05 and 3.69 (2s, 12H, $OCH_3$); the signals of the amino protons were too broad to be detected; FAB-MS $m/z$ 699 $(M + H)^+$. Due to the extreme instability of this compound, no satisfactory elemental analysis could be obtained, and the compound was immediately used for further reaction.

**Compound 18.** With **9** (0.20 g, 0.36 mmol) and 1,4-dimethoxynaphthalene (0.14 g, 0.72 mmol) as starting materials, this compound was synthesized as described for **15** (method B) to yield 0.17 g (65%) of **18** as a white solid: mp 322 °C dec; IR 1711 (C═O); $^1$H NMR ($CDCl_3$) see Table 1; FAB-MS $m/z$ 719 $(M + H)^+$. Anal. Calcd for $C_{44}H_{38}N_4O_6$: C, 73.52; H, 5.33; N, 7.79. Found: C, 73.87; H, 5.29; N, 7.72.

**Monowalled Phenanthroline Compound 19.** Compound **11b** (90 mg, 0.15 mmol) was reduced to **11c** as described above. To a solution of **11c** in a mixture of 5 mL of methanol, 5 mL of THF, and 5 mL of $CH_2Cl_2$ was added 56 mg (0.27 mmol) of 1,10-phenanthroline-5,6-quinone. The mixture was refluxed under nitrogen for 16 h, the condensed solvent running back over molecular sieves (3 Å). $CH_2Cl_2$ was added (25 mL), and the organic layer was washed with aqueous 1 N NaOH, water, and concentrated *in vacuo*. After purification by column chromatography ($CH_2Cl_2$/EtOH, 93:7 v/v), 84 mg (78%, based on **11b**) of **19** could be obtained as a yellow solid: mp > 400 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.60 (dd, 2H, PhenH, $J$ = 8.0 Hz, $J$ = 2.0 Hz), 9.27 (dd, 2H, PhenH, $J$ = 4.7 Hz, $J$ = 2.0 Hz), 7.81 (dd, 2H, PhenH, $J$ = 8.0 Hz, $J$ = 4.7 Hz), 7.36−7.03 (m, 10H, ArH), 6.03 and 4.09 (2d, 4H, $NCH_2$Ar, $J$ = 15.8 Hz), 5.53 and 4.45 (2d, 4H, $NCH_2O$, $J$ = 11.3 Hz), 4.64 (s, 6H, $OCH_3$); FAB-MS $m/z$ 703 $(M + H)^+$. Anal. Calcd for $C_{40}H_{30}N_8O_5\cdot(C_2H_6O)$: C, 66.14; H, 4.46; N, 14.70. Found: C, 66.39; H, 4.64; N, 14.57.

**Diphenanthroline Clip 20.** Compound **16c** (0.53 g, 0.66 mmol) was reduced to **16d** as described above. To a solution of **16d** in a mixture of 20 mL of methanol, 20 mL of THF, and 20 mL of $CH_2Cl_2$ was added 0.33 g (1.6 mmol) of 1,10-phenanthroline-5,6-quinone. The mixture was refluxed under nitrogen for 16 h, the condensed solvent running back over molecular sieves (3 Å). $CH_2Cl_2$ was added (100 mL), and the organic layer was washed with aqueous 1 N NaOH and water and concentrated *in vacuo*. After purification by column chromatography ($CHCl_3$/MeOH, 9:1 v/v), 0.45 g (66% based on **16c**) of **20** was obtained as a yellow solid: mp > 400 °C; $^1$H NMR ($CDCl_3$) $\delta$ 9.29 (dd, 4H, PhenH, $J$ = 8.2 Hz, $J$ = 2.0 Hz), 9.08 (dd, 4H, PhenH, $J$ = 4.5 Hz, $J$ = 2.0 Hz), 7.52 (dd, 4H, PhenH, $J$ = 8.2 Hz, $J$ = 4.5 Hz), 7.45−7.11 (m, 10H, ArH), 6.03 and 4.05 (2d, 8H, NC$H_2$Ar, $J$ = 16.0 Hz), 4.47 (s, 12H, $OCH_3$); FAB-MS $m/z$ 1027 $(M + H)^+$. Anal. Calcd for $C_{60}H_{42}N_{12}O_6\cdot CHCl_3$: C, 63.91; H, 3.78; N, 14.66. Found: C, 63.81; H, 3.92; N, 14.62.

**Monophenanthroline Clip 21.** Compound **16a** (0.56 g, 0.79 mmol) was reduced to **16b** as described above. To a solution of **16b** in a mixture of 20 mL of methanol, 20 mL of THF, and 20 mL of $CH_2Cl_2$ was added 0.25 g (1.2 mmol) of 1,10-phenanthroline-5,6-quinone. The mixture was refluxed under nitrogen for 16 h, the condensed solvent running back over molecular sieves (3 Å). $CH_2Cl_2$ was added (100 mL), and the organic layer was washed with aqueous 1 N NaOH and water, and concentrated *in vacuo*. After purification by column chromatography ($CH_2Cl_2$/EtOH, 93:7, v/v), 0.49 g (75% based on **16a**) of **21** was obtained as a yellow solid: mp 392 °C dec; IR 1714 (C═O); $^1$H NMR ($CDCl_3$) $\delta$ 9.49 (dd, 2H, PhenH, $J$ = 7.9 Hz, $J$ = 2.0 Hz), 9.20 (dd, 2H, PhenH, $J$ = 7.9 Hz, $J$ = 4.6 Hz), 7.65 (dd, $J$ = 7.9 Hz, $J$ = 4.6 Hz), 7.32−7.08 (m, 10H, ArH), 6.57 (s, 2H, ArH), 5.99, 5.62, 4.02 and 3.84 (4d, 8H, NC$H_2$Ar, $J$ = 15.8 Hz), 4.55 and 3.72 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 823 $(M + H)^+$. Anal. Calcd for $C_{48}H_{38}N_8O_6\cdot CH_2Cl_2$: C, 64.34; H, 4.44; N, 12.34. Found: C, 64.96; H, 4.47; N, 12.18.

**Monodipyridine Clip 22.** Compound **16a** (0.19 g, 0.27 mmol) was reduced to **16b** as described above. To a solution of **16b** in a mixture of 10 mL of methanol, 10 mL of THF, and 10 mL of $CH_2Cl_2$ was added 0.11 g (0.89 mmol) of 2,2′-pyridil.

The mixture was refluxed under nitrogen for 16 h, the condensed solvent running back over molecular sieves (3 Å). $CH_2Cl_2$ was added (50 mL), and the organic layer was washed with aqueous 1 N NaOH and water and concentrated *in vacuo*. After purification by column chromatography ($CHCl_3$/MeOH, 197:3 v/v), 69 mg (31% based on **16a**) of **22** was obtained as a yellow solid: mp 365 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 8.28−8.05 (m, 4H, PyH), 7.91−7.75 (m, 2H, PyH), 7.45−6.95 (m, 12H, PyH and ArH), 6.65 (s, 2H, ArH), 5.88, 5.56, 3.96 and 3.80 (4d, 8H, NC$H_2$Ar, $J$ = 15.8 Hz), 4.34 and 3.75 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 825 $(M + H)^+$. Anal. Calcd for $C_{48}H_{40}N_8O_6$: C, 69.89; H, 4.89; N, 13.58. Found: C, 70.14; H, 4.97; N, 13.24.

**Monoporphyrin Clip 23a.** Compound **16a** (0.18 g, 0.25 mmol) was reduced to **16b** as described above. The methanol and the THF was evaporated *in vacuo*. To a solution of **16b** in 10 mL of $CH_2Cl_2$ was added 0.10 g (0.16 mmol) of **24a**. The mixture was refluxed under nitrogen for 16 h over molecular sieves (3 Å). $CH_2Cl_2$ was added (50 mL), and the organic layer was washed with aqueous 1 N NaOH and water and concentrated *in vacuo*. After purification by column chromatography ($CH_2Cl_2$), 180 mg (92% based on **24a**) of **23a** was obtained as a purple solid: mp 262 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 8.85 and 8.69 (2d, 4H, $\beta$ pyrrole, $J$ = 5.0 Hz), 8.68 (s, 2H, $\beta$ pyrrole), 8.21 (m, 8H, Ar H-2,6 porphyrin), 7.84 (m, 8H, Ar H-3,5 porphyrin), 7.76 (m, 4H, Ar H-4 Porphyrin), 7.15 and 7.12 (2s, 10H, ArH), 6.62 (s, 2H, ArH), 5.90, 5.57, 3.89 and 3.80 (4d, 8H, NC$H_2$Ar, $J$ = 15.8 Hz), 3.86 and 3.75 (2s, 12H, $OCH_3$), −2.53 (br s, 2H, NH); FAB-MS $m/z$ 1257 $(M + H)^+$. Anal. Calcd for $C_{80}H_{60}N_{10}O_6$: C, 76.42; H, 4.81; N, 11.14. Found: C, 76.72; H, 4.95; N, 10.78.

**Monoporphyrin Clip 23b.** This molecule was synthesized in an analogous manner to **23a** using **24b** instead of **24a**: $^1$H NMR ($CDCl_3$) $\delta$ 8.91 and 8.54 (2d, 4 H, $J$ = 5.0 Hz, $\beta$ pyrrolic H), 8.65 (s, 2 H, $\beta$ pyrrolic H), 8.12 (s, 2 H, ArH porphyrin), 8.08 (s, 2 H, ArH porphyrin), 8.01 (s, 2 H, ArH porphyrin), 7.86 (s, 2 H, ArH porphyrin), 7.85 (s, 2 H, ArH porphyrin), 7.77 (s, 2 H, ArH porphyrin), 7.10 (m, 10 H, ArH diphenylglycoluril), 6.46 (s, 2 H, ArH), 5.90 and 3.93 (2d, 4 H, $J$ = 15.8 Hz, NC$H$HAr), 5.44 and 3.69 (2d, 4 H, $J$ = 15.8 Hz, NC$H_2$Ar) 3.73 (s, 6 H, $OCH_3$) 3.62 (s, 6 H, $OCH_3$), 1.52, 1.50, 1.41, and 1.26 (4s, 72 H, $CCH_3$), −2.50 (br s, 2H, NH); FAB-MS $m/z$ 1706 $(M)^+$. Anal. Calcd for $C_{112}H_{124}N_{10}O_6$: C, 78.84; H, 7.32; N, 8.21. Found: C, 78.99; H, 7.36; N, 8.02.

**Nickel Salophen Compound 25.** To a solution of 0.43 g (0.66 mmol) of **16b** in a mixture of 20 mL of THF and 20 mL of methanol were added 0.24 g (1.97 mmol) of 2-hydroxybenzaldehyde and a solution of 0.25 g of $Ni(OAc)_2 \cdot 4H_2O$ in 2 mL of methanol. The mixture was stirred under nitrogen for 64 h. The solvent was removed *in vacuo*, and the residue was suspended in 150 mL of methanol. After filtration, the residue was redissolved in 100 mL of $CHCl_3$. The organic layer was washed with water (3×), dried ($MgSO_4$), and concentrated *in vacuo* to yield 0.40 g (66%) of **25** as a red solid. A sample was recrystallized by slow diffusion of *n*-hexane in a solution of **25** in $CHCl_3$: mp 382 °C dec; $^1$H NMR ($CDCl_3$) $\delta$ 9.15 (s, 2H, NC$H$Ar), 7.32−7.03 (m, 16H, ArH), 6.70 (s, 2H, ArH), 6.62 (t, 2H, ArH, $J$ = 7.6 Hz), 5.62, 5.57, 3.86 and 3.77 (4d, 8H, NC$H_2$-Ar, $J$ = 15.8 Hz), 3.79 and 3.68 (2s, 12H, $OCH_3$); FAB-MS $m/z$ 913 $(M + H)^+$. Anal. Calcd for $C_{50}H_{42}N_6O_8Ni \cdot (CHCl_3)$: C, 59.30; H, 4.20; N, 8.14. Found: C, 59.33; H, 4.29; N, 8.01.

**Nickel Salophen Compound 26.** To a solution of compound **17c** (0.24 g, 0.34 mmol) in a mixture of 10 mL of THF and 10 mL of methanol were added 125 mg (1.02 mmol) of 2-hydroxybenzaldehyde and a solution of 127 mg (0.51 mmol) of $Ni(OAc)_2 \cdot 4H_20$ in 1 mL of methanol. The mixture was stirred under nitrogen for 64 h. The solvent was removed *in vacuo*, and the residue was suspended in 75 mL of methanol. After filtration, the residue was redissolved in 50 mL of $CHCl_3$. The organic layer was washed with water (3×), dried ($MgSO_4$) and concentrated *in vacuo* to yield 0.10 g (31%) of **26** as a red solid: mp 373 °C dec; $^1$H NMR see Table 2; FAB-MS $m/z$ 963 $(M + H)^+$; HRMS (field desorption) calculated for $C_{54}H_{44}N_6O_8$-Ni 962.257, found 962.253.

**Monophenanthroline Compound 27.** To a solution of 0.11 g (0.16 mmol) of **17c** in a mixture of 7 mL of THF and 7 mL of methanol was added 60 mg (0.29 mmol) of 1,10-phenathroline-5,6-quinone. The mixture was refluxed under nitrogen for 64 h over molecular sieves (3 Å). After cooling, the precipitate was filtered off and washed with diethyl ether. The product was purified by column chromatography ($CH_2$-$Cl_2$/MeOH, 93:7 v/v) to yield 0.11 g (80%) of **27** as a yellow solid: mp >400 °C; $^1$H NMR see Table 2; FAB-MS $m/z$ 873 $(M + H).^+$ Anal. Calcd for $C_{52}H_{40}N_6O_8 \cdot (CH_2Cl_2)$: C, 66.46; H, 4.42; N, 11.70. Found: C, 66.45; H, 4.45; N, 11.34.

**Monoporphyrin Compound 28.** To a solution of 0.10 g (0.15 mmol) of **17c** in 7 mL of $CH_2Cl_2$ was added 250 mg of **24b** (0.27 mmol). The mixture was refluxed over molecular sieves (3 Å) under nitrogen for 48 h. After cooling, the solvent was evaporated, and the product was purified by column chromatography ($CH_2Cl_2$) to yield 70 mg (26%) of **28** as a purple solid: mp >400 °C; $^1$H NMR see Table 2; FAB-MS $m/z$ 1760 $(M + 4H)^+$. Anal. Calcd for $C_{116}H_{128}N_{10}O_6$: C, 79.24; H, 7.34; N, 7.97. Found: C, 79.02; H, 7.57; N, 8.11.

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