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Conformational restriction of flexible molecules in solution by a semirigid bis-porphyrin molecular tweezer

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ABSTRACT

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A semirigid bisporphyrin molecular clip with a glycoluril backbone has been synthesized. The clip provides an adaptable molecular cavity for binding of diamines. Binding constants for diamines of $10^4 - 10^7 \text{ M}^{-1}$ are orders of magnitude higher than those for monoamines of 10^3 M^{-1} , indicating a preference to bidentate binding. NMR studies confirmed that binding of bidentate guests occurs inside the clip. Short- and medium-size acyclic molecular guests are locked into a single, extended conformation, and also guests with longer flexible chains exhibit considerably less conformational mobility than when free in solution. The size of the cavity adapts to the guest size, as indicated by modeling studies and self diffusion constants of the complexes.

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1. Introduction

Metallated bisporphyrins are regarded as interesting hosts for the ditopic binding of organic guest molecules. A variety of spacers have been used to connect two porphyrin units, providing molecular clips of varying conformational flexibility.¹ This has been exploited, e. g., for the size-selective complexation of guest molecules in bisporphyrins with rigid spacers,² or for the determination of absolute stereochemistry using bisporphyrins with flexible spacers.³ Dimeric porphyrins with various topologies have been reported as model systems for enzymes⁴ and the photosynthetic reaction center. The guest molecule requires the presence of preferably two Lewis-basic functional groups to interact with the bisporphyrin metal ions, with ditopic binding providing stronger interaction as well as conformational restriction.^{5,6}

In this context, we found it interesting to address the effect of binding between acyclic diamines of varying chain length and semirigid bisporphyrin clips, regarding both conformational restriction of the guest, and adaptation of clip size (i. e., the volume of the molecular cleft) to the guest volume. For the spacer of such a semirigid bisporphyrin clip we chose the glycoluril backbone.^{7,8}

In this paper, we present the synthesis of a new symmetric zinc(II)porphyrin-terminated glycoluril clip **1** (Scheme 1), and a survey of its host-guest interaction with a series of diamino compounds.

Scheme 1. Molecular structure of clips **1**, **2** and previously reported clip **3**.⁸

2. Results and Discussion

2.1 Synthesis and characterization of bis-porphyrin glycoluril clips.

Using the same strategy as for our recently reported glycoluril-based clip **3** (Scheme 1),⁸ Zn-porphyrin clip **1** and free-base porphyrin clip **2** were prepared from the corresponding porphyrin dione (**8** or **9**) and the air-sensitive tetraamino backbone component **6** (Scheme 2). Compound **6** was synthesized in two steps from the glycoluril derivative **4**,⁹ prepared by condensation of urea and benzil.^{7c} Zinc-porphyrin dione **9** was obtained by metallation of its free-base dione **8**, which was prepared in several steps starting from porphyrin **7**. Alternative literature procedures towards synthesizing the porphyrin dione, e.g., hydroxylation of β -nitroporphyrin using sodium benzaloximate,¹⁰ or dihydroxylation using OsO_4 ¹¹ did not work in our hands. Likewise, dihydroxylation attempts of Zn(II) **7** using RuO_4 , produced *in situ* from RuCl_3 and NaIO_4 ,¹² did not yield any dioxo compound.

Scheme 2. Reagents and conditions: a: $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$, $\text{MeOH}/\text{CHCl}_3$, reflux, 3 h; b: THF/MeOH 1:1, reflux, 16 h.

Purification of **1** and **2** was challenging. Clip **1** was subjected to several flash chromatographic separations with a consecutive series of eluents (CHCl_3 , a mixture of CH_2Cl_2 and MeOH at different ratios, and toluene). Inclusion of solvent molecules contributes to purification difficulties, a common problem not only in porphyrin synthesis but also encountered for some glycoluril compounds.^{13,14,15} In particular, removal of traces of toluene was very difficult, indicating the formation of inclusion compounds. The purification of free-base clip **2** was even more challenging as several ^1H NMR signals for the porphyrin NH protons at negative chemical shifts were always observed, indicating a mixture of porphyrin tautomers that could not be resolved even by HPLC. Considering that the clip possesses two porphyrin units with no through-bond conjugation, the observation is not unexpected but still potentially problematic in our intended NMR application that benefits from a high degree of symmetry in the host. Metallation of the mixture of clip **2** tautomers with $\text{Zn}(\text{II})$ resulted in clean formation of clip **1** as a single compound.

Glycoluril-based clips may exist in three conformational isomers, interchanged by rotation of the single bonds of the elbow CH_2 (marked in Scheme 1), with substantial differences in the cavity opening, the closed (aa or anti-anti) is the desired one and also the most commonly observed in this class of molecular hosts (Figure 1).¹³ The conformational isomers are easily assigned by analysis of coupling constants and NOE effects in the elbow region.⁸ ^1H NMR analysis of **1** confirmed that the closed form was the only isomer present. However, the elbow region is still conformationally dynamic: At r.t., the proton signals for the methoxy group and elbow CH_2 (marked as H_a and H_b in Scheme 1) are broad, whereas the signals for the porphyrin units and the backbone phenyls are sharp. At lower temperatures the signals of the porphyrin units become broader. At higher temperatures, the elbow signals are significantly sharper whereas some of the signals from the porphyrin units are broadened. These non-uniform temperature-dependent effects are different from the quite uniform concentration-dependent aggregation effects, with sharper signals at lower (10^{-5} M) and broader at higher (10^{-3} M) concentrations, and are most likely due to dynamics in the elbow region that significantly influences the inter-porphyrin wall to wall distance at the rim of the clip (see supplementary information).

To probe the rigidity of the molecular cleft provided by clip **1** in its closed (aa) conformation, an energy minimization with the semiempirical PM3 method was performed, with Zn-Zn distances constrained to a series of fixed values. The resulting potential curve of Zn-Zn distance vs. relative potential energy shows a minimum at a Zn-Zn distance of 6.25 Å (Figure 1). The energy drop at distances below 8 Å might indicate the onset of attractive forces due to close contacts between phenyl rings on opposite clip walls (*vide infra*). Overall, there appears to be a considerable variability of wall to wall distance from 5 Å to 13.5 Å at relatively low (up to ca. 50 kJ/mol) energy cost. Typical binding enthalpies of the axial nitrogen ligands on Zn porphyrins have been shown to be around 30 kJ/mol to

57 kJ/mol per single interaction for heteroaromatic and aliphatic diamines, respectively.¹⁶ Thus, the binding energy of a ditopic ligand to clip **1** should be sufficient to push apart the clip walls. It should also be noted that the open (as) conformer has considerably higher energy than the closed (aa) conformations shown.

Figure 1. Potential energy vs. Zn-Zn distance for clip **1**, and corresponding structures with closed (aa) conformation, with the distance indicated below each structure. The energy minimized open (as) conformer is also shown (Zn-Zn distance ca. 22.8 Å).

NMR analysis in toluene- d_8 solution allowed the assignment of all protons in the porphyrin unit. Rotation of the *meso* phenyl groups is hindered, yielding two pairs of signals for the eight *ortho* protons (a/a' and b/b', Figure 2). The activation enthalpy was determined as $\Delta G^\ddagger = 47 \text{ kJ K}^{-1} \text{ mol}^{-1}$, which is comparable to values reported for other metalloporphyrins.¹⁷

Figure 2. Expansion from the ^1H NMR spectrum of clip **1** (500 MHz, toluene- d_8 solution, 25°C) with assignments of porphyrin protons (cf. Scheme 1).

Glycoluril clips possess several potential binding sites. In addition to the Lewis-acidic Zn(II) sites, there are Lewis-basic sites on the pyrrolic nitrogens, in the backbone glycoluril unit and at the pyrazoline imines. The clip also possesses several potential sites for π - π or π -cation interactions that normally are considerably weaker than the Lewis acid-base interactions. In clip **3**, the pyrazoline unit dominated over all other binding sites in interactions with cations and hydrogen-bond-donors, but the inner *meso* phenyls of the porphyrin units in **1** and **2** should efficiently block this coordination site. In line with this reasoning, the very minor effects on ^1H NMR shifts observed upon addition of silver and ammonium cations was as expected,⁸ and the pronounced red-shift in the UV-Vis absorption spectrum upon addition of strong acid to **1** is thus most likely caused by protonation at pyrrolic nitrogens¹⁸ that eventually may lead to demetallation of the clip.

2.2 Complexation with organic guests with Lewis-base character

Of particular interest was to investigate if guests of varying size might be bound and if a preference to binding inside the clip would be observed.¹⁹ This would require a not too steep energy profile of metal-metal distance vs. potential energy (Figure 1) allowing variations in the amount of cavity opening. Guest molecules were chosen to cover a range of sizes, and include both rigid and flexible molecules. Chelation of Lewis bases, in particular amines and imines, to Lewis-acidic complexed metal ions is well documented both for monoporphyrin^{20,21} and bis-porphyrin systems. The extended aromatic structure would provide the desired NMR complexation-induced shifts (CISs) of the bound guests.

The results of the UV-Vis titration studies are summarized in Table 1. As expected, 1:1 complexation with binding constants in the range of $10^4 - 10^6 \text{ M}^{-1}$ were observed for diamines, whereas K_a for monoamines and amino alcohols were several orders of magnitude weaker. The data for clip **1** + guest, with red-shift of all bands and clear isosbestic points suggests that only one complex is formed in each case (Figure 3).

Figure 3. A representative UV-Vis titration of clip **1** + guest (here 2,3,4-tri-*O*-methyl-1,5-diaminopentane **17**) with arrows indicating changes in absorbance.

Table 1. K_a measured by UV-Vis titration of clip **1** + guests.

Guest	K_a / M^{-1}
Pyridine ^a	10^3
Octylamine ^a	10^3
2-aminoethanol ^a	10^3
2-aminobutanol ^a	10^3
N-methyl-2-aminoethanol ^a	10^3
DABCO 10 ^a	10^6
4,4'-bipyridine 11 ^b	10^7
1,6-diaminohexane 12 ^a	10^6
1,8- diaminooctane 13 ^b	10^6
1,12- diaminododecane 14 ^b	10^6
1,20- diaminoeicosane 16 ^b	10^5
2,3,4-tri- <i>O</i> -methyl-1,5-diaminopentane 17 ^b	10^4
2,3,4,5-tetra- <i>O</i> -methyl-1,6-diaminohexane 18 ^b	10^4

^aCHCl₃ solution. ^bCH₂Cl₂ solution.

Diffusion studies provided further information about the complexation of various guests with clip **1** (Table 2).^{14e,22} As expected, clip **1** has a lower diffusion coefficient ($D = 7.0 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$) than the free guests ($D = 9.3 \times 10^{-10} - 14 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$). In each of the complexes, clip **1** and the bound guest have essentially the same diffusion coefficient, indicating the absence of any equilibrium between bound and free diamine. Furthermore, diffusion coefficients of the complexes with smaller guests (DABCO **10**, 2,3,4-tri-*O*-methyl-1,5-diaminopentane **17**²³ and 2,3,4,5-tetra-*O*-methyl-1,6-diaminohexane **18**²³) were found to be identical to the free clip (i. e., $D = 7.0 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$). For the complexes with larger guests (1,12-diamine **14** and 1,20-diamine **16**), diffusion was found to be slower ($D = 4.7 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$) than for the free clip. However, the decrease of D was substantially larger than would be expected if it was related to the Stokes radius *via* the molecular weight. This indicates an alteration of clip shape, i. e., the larger guests push the clip walls farther apart. Since diffusion coefficients depend on the hydrodynamic radius rather than the molecular weight of molecules in solution,²⁴ this guest-dependent variation of wall distance for clip **1** would account for the observed diffusion behavior.²²

Table 2. Diffusion coefficients for free species and $\approx 1:1$ complexes.

Species	D ($\text{m}^2 \text{s}^{-1}$)	r_H ($\text{\AA}$)	MW
DABCO 10	2.1×10^{-9}	1.9	112.0
2,3,4-tri- <i>O</i> -methyl-1,5-diaminopentane 17	1.4×10^{-9}	2.9	193.2
2,3,4,5-tetra- <i>O</i> -methyl-1,6-diaminohexane 18	1.4×10^{-9}	2.9	237.2
1,12-diaminododecane 14	1.4×10^{-9}	2.9	200.4
1,20-diaminoeicosane 16	9.3×10^{-10}	4.3	312.6
Clip 1	7.0×10^{-10}	5.8	2018.0
Clip 1:10	7.0×10^{-10}	5.8	2130.0
Clip 1: 17	7.0×10^{-10}	5.8	2211.2
Clip 1: 18	7.0×10^{-10}	5.8	2255.2
Clip 1:14	4.7×10^{-10}	8.6	2218.4
Clip 1:16	4.7×10^{-10}	8.6	2523.8

Diffusion coefficients were measured by NMR LEDPGSE experiments, 500 MHz, in CDCl_3 solutions at 25°C with residual CHCl_3 as reference ($2.33 \times 10^{-9} \text{m}^2 \text{s}^{-1}$).

^1H NMR analysis of **1** with diamines provided clear evidence that the guests are bound inside the clip. The number of signals for the bound guests corresponds to symmetrical 1:1 complexes, the structures of which are shown in Scheme 3. For the C_{12} and C_{20} diamines, only one of multiple conformations is shown.

Scheme 3. Structures of inclusion compounds of clip **1** with various guests, from semi empirical calculations (PM3).

^a Extended conformation (i. e., aaaaa). ^b aagagaa conformer. ^c gggggagaggg conformer. ^d gggaaggaaggagaggagg conformer.

2.3 Binding of guests with fixed N-N distance

Clip flexibility for the binding of guests of varying size was investigated by adding aliquots of 1,4-diazabicyclo[2.2.2]octane (DABCO) (**10**, $d_{\text{N,N}} = 2.60 \text{ \AA}$), and 4,4'-bipyridyl (**11**, $d_{\text{N,N}} = 7.15 \text{ \AA}$) to clip **1** in CDCl_3 solution. The ^1H NMR signals of CH_3O and elbow protons became sharper, indicating reduced conformational mobility in this region upon complexation, and an alteration of the overall shape of the complex compared to that of pure **1** in accordance with the calculated structures. Addition of 4,4'-bipyridyl **11** resulted in moderate chemical shift changes for the porphyrin signals and negative CIS values for the guest, i. e., $\Delta\delta = -2.67$ (H-3) and $\Delta\delta = -6.35$ (H-2). Only two bipyridyl proton signals were observed for mixtures where the clip was in excess proving a symmetric binding in the cleft. When the guest was present in excess, separate broad peaks for both bound and free bipyridyl protons were observed, the broadening being due to ligand exchange. On addition of DABCO **10**, the signal for the guest protons exhibited a pronounced CIS ($\Delta\delta \approx -7.20$). Only one signal was observed for the bound guest, indicating ditopic binding in the clip cavity. NOEs between bound **10** and the porphyrin phenyl protons of **1** provide further proof for binding.

The negative CIS for all porphyrin pyrrolic protons and positive CIS for the elbow H_a protons are attributable to a closer equilibrium wall to wall distance in the complex than in the free clip, as has previously been observed for clip **3**.⁸ When an excess of clip was present, two distinct sharp signals for bound and free clip, respectively, were observed. Thus, although the binding constants for the two guests are in the same range, the exchange between free and (internally) bound guest on the NMR timescale is moderate for **11** and very slow for **10**. The differences could be due to electronic differences between the aliphatic amine **10** and the aromatic imine **11** but, more likely to the favorable close porphyrin-porphyrin interaction which is more pronounced in the complex with **10** than in the free clip or in the complex with **11**.

2.4 Flexible diamine ligands: Conformational restriction.

The absence of exchange broadening of the ligand signals was observed for mixtures of clip **1** and 1,6-diaminohexane **12** ($d_{N,N} = 8.83 \text{ \AA}$ for extended conformer). The observation of only four ligand signals, with pronounced negative CIS values, proves binding in the clip cavity. NOEs between 1,6-diaminohexane protons ($\text{NOE}_{(i, i+2)}$ but not $\text{NOE}_{(i, i+3)}$) indicate an extended, i. e., all-*trans*, conformation of **12** in the complex (Figure 4, Figure 5).¹ In contrast to its complex with Zn(II)TPP,²⁵ the stronger binding to clip **1**, indicated by absence of exchange broadening, also illustrates the importance of cooperative binding to two sites, i. e., the two metal centers.

Figure 4. Expected NOEs for two conformers of 1,6-diaminohexane (**12**) protons. For *anti* bonds: $a = \text{NOE}_{(i, i+2)}$, $b = \text{NOE}_{(i, i+1)}$; for *gauche* bonds: $c = \text{NOE}_{(i, i+3)}$.

Figure 5. Expansion from ROESY spectrum of clip **1** with 1,6-diaminohexane **12** (500 MHz, CDCl_3 solution, 25°C), guest/clip ≈ 1 , mixing time = 0.5s.

As the binding of 1,6-diaminohexane **12** is ditopic, resulting in stretching of the alkyl chain, it is interesting to study longer diamines. Thus, 1,8-diaminooctane **13** ($d_{N,N} = 11.34 \text{ \AA}$ for all-*trans* conformer) binds to clip **1**, with

similar effects on signal widths and chemical shifts as for 1,6-diaminohexane **12** (Figure 6, Figure 7). However, in contrast to the latter, a larger variety of NOEs between protons of 1,8-diaminooctane **13** (i. e., $\text{NOE}_{(i,i+1)}$, $\text{NOE}_{(i,i+2)}$, $\text{NOE}_{(i,i+3)}$) indicates the presence of *gauche* bonds, i. e., its longer chain is no longer stretched out into the all-*trans* conformation (Figure).

For the even longer alkyl chains of 1,12-diaminododecane **14** ($d_{\text{N,N}} = 16.53 \text{ \AA}$ for all-*trans* conformer) and 1,20-diaminoeicosane **16** ($d_{\text{N,N}} = 26.61 \text{ \AA}$ for all-*trans* conformer), 7 and 11 ligand signals are observed, respectively. This proves location inside the cavity also for guests that are without possibility of adopting an all-*trans* conformation upon ditopic binding. NOE patterns for **14** and **16** are also more complex as for 1,8-diaminooctane i.e., $\text{NOE}_{(i,i+1)}$, $\text{NOE}_{(i,i+2)}$, and $\text{NOE}_{(i,i+3)}$ are observed.

In alkyl chains, transforming an anti conformer to a *gauche* conformer increases the conformational energy by only 3 – 4 kJ/mol,²⁶ which is lower than typical binding energies between Zn(II)TPP and amines, i. e., 57 kJ/mol per single interaction for aliphatic diamines.¹⁶

Thus, for the interaction between clip **1** and guests **12**, **13**, **14** and **16** with K_a of 10^5 - 10^7 M^{-1} , only a small energy penalty, including the opening of the clip, has to be paid.

Figure 6. Expansion from ^1H NMR spectra of clip **1** with 1,8-diaminooctane **13** (500 MHz, CDCl_3 solution, 25°C). a: only guest **13**; b: guest/clip: ≈ 1 .

Figure 7. Expansion from ROESY spectrum (mixing time 0.5 s) of clip **1** with 1,8-diaminooctane **13** (500 MHz, CDCl_3 solution, 25°C), guest/clip ≈ 1 .

The ditopic binding of diamines to clip **1** is only possible in a “head-on” fashion with the porphyrin units in opposite positions, in contrast to a recently reported bisporphyrin system where, due to its flexible link, a distinction between this and an alternative “side-on” mode with sideways dislocation of the porphyrin units, accommodating all-*trans* conformations of the guests, was not possible.²⁷

3. Conclusion

The semirigid bisporphyrin clip **1** binds diamine guests of varying size ditopically inside of its molecular cleft. Shorter acyclic guests (carbon chain $\leq C_6$) bind in an all-anti, i. e., zig-zag conformation, whereas longer acyclic guests (carbon chain $\geq C_8$) bind in a conformation including gauche kinks. The adaptation of the clip to increasing guest size is indicated by diffusion data. Conformational restriction of acyclic guest molecules with several stereogenic centers should be a useful method to determine their relative stereochemistry, as we have shown in a parallel study.²³

4. Experimental

UV-Vis titrations were carried out on a Varian Cary 3 Bio spectrophotometer using 10 mm or 5 mm quartz cuvettes at r.t. with CH_2Cl_2 or $CHCl_3$, filtered over basic aluminium oxide, as solvent. K_a for diamines was determined utilizing the iterative fitting program (in Matlab R2012b) recently published by P. Thordarsson.²⁸ A 1:1 complexation model and global fitting to several datasets was applied, K_a is calculated by (eqn. 1). The standard error (SE_y) is estimated by (eqn. 2). For monoamines line fitting using Origin software was utilized to calculate K_a . 1H and ^{13}C NMR spectra were recorded on a Varian Unity Inova (1H at 499.94 MHz, ^{13}C at 125.7 MHz) spectrometer. Chemical shifts are reported in ppm referenced to tetramethylsilane via the residual solvent signal ($CDCl_3$, 1H at 7.26 and ^{13}C at 77 ppm; toluene- d_8 , 1H at 2.36 and ^{13}C at 21.5 ppm; $CH_3COOH-d_4$, 1H at 2.09 and ^{13}C at 20.4 ppm). Signal assignments were derived from P.E.COSY,²⁹ gHSQC,³⁰ gHMBC,³¹ gNOESY,³² ROESY,³³ and TOCSY³⁴ spectra. For NMR titrations, aliquots of a guest solution were added to a solution of clip **1** in an NMR tube using an Eppendorf pipette. Diffusion coefficients were determined from LED-PGSE experiments,³⁵ using z-gradients, acquiring a series of 10-20 spectra for an array of gradient pulse strengths (0 to 20 gauss/cm). Typically, a relaxation delay of 1 s, 9 ms gradient pulse duration, 100 ms diffusion delay, and 5 ms storage delay were used. The LED-PGSE spectra were evaluated by plotting the square of the gradient strength against the natural logarithm of the signal amplitude, resulting in a straight line with a slope proportional to $-D$ (diffusion coefficient). The actual value for D was obtained by relating this slope to that of a compound with known diffusion coefficient, measured under the same conditions. In the present investigation, we have used the residual $CHCl_3$ signal in $CDCl_3$ ($D = 2.33 \times 10^{-9} m^2 s^{-1}$).³⁶ Diffusion coefficients (D) were calculated by (eqn. 3) and the hydrodynamic radius (r_H) by (eqn. 4). The activation energy for phenyl rotation was determined by full lineshape fitting using gNMR 5.0.6.³⁷ MALDI-TOF spectra were recorded using a Bruker Daltonics Ultraflex II MALDI-TOF mass spectrometer using an α -cyano-4-hydroxycinnamic acid matrix. HRMS was acquired using a Thermo Scientific LTQ Orbitrap Velos apparatus in infusion mode. Analytical TLC was performed using Merck precoated silica gel 60 F₂₅₄ plates. For column chromatography Matrex silica gel (60 Å, 35-70 μm) was used. Melting points were determined using a Stuart Scientific melting point apparatus SMP10 and are uncorrected. Computations of clip energies were performed with Titan 1.0.5 (Wavefunction, Inc.) using semi-empirical PM3. Elemental analysis was performed by Eurofins Mikrokemi AB, Uppsala, Sweden. Commercially available compounds were used without purification. meso-Tetraphenylporphyrin (TPPH₂) **7** was purchased from Porphyrin Systems GbR, Germany, or prepared according to literature procedures³⁸ and transformed into beta-nitroTPPH₂ as previously reported.^{10a} Dry solvents were obtained by distillation from sodium and benzophenone (diethyl ether, THF) or CaH_2 (CH_2Cl_2).

$$[HG] = \frac{1}{2} \left\{ \left([G]_0 + [H]_0 + \frac{1}{K_a} \right) - \sqrt{\left([G]_0 + [H]_0 + \frac{1}{K_a} \right)^2 - 4[H]_0[G]_0} \right\} \quad (\text{Eqn. 1})$$

$$SE_y = \sqrt{\frac{\sum(y_{data} - y_{calc})^2}{N - k}} \quad (\text{Eqn. 2})$$

$$D = \frac{m(\text{obs}) \times D(\text{ref})}{m(\text{ref})} \quad (\text{Eqn. 3})$$

$$r_H = \frac{k_b T}{6\pi\eta D} \quad (\text{Eqn. 4})$$

4.1. 5,7,12,13b,13c,14-Hexahydro-1,4,8,11-tetramethoxy-13b,13c-diphenyl-6H,13H-5a,6a,12a,13a-tetraazabenz[5,6]azuleno[2,1,8-ija]benz[f]azulene-6,13-dione (**4**) was prepared following literature procedures.^{7c}

4.2. 5,7,12,13b,13c,14-Hexahydro-1,4,8,11-tetramethoxy-2,3,9,10-tetranitro-13b,13c-diphenyl-6H,13H-5a,6a,12a,13a-tetraazabenz[5,6]azuleno[2,1,8-ija]benz[f]azulene-6,13-dione (**5**) was prepared as previously reported.⁹

4.3. 5,7,12,13b,13c,14-Hexahydro-1,4,8,11-tetramethoxy-2,3,9,10-tetraamino-13b,13c-diphenyl-6H,13H-5a,6a,12a,13a tetraazabenz[5,6]azuleno[2,1,8-ija]benz[ff]azulene-6,13-dione (**6**) was prepared via a slightly modified procedure as previously reported.⁹

4.4. 2,3-Dioxo-5,10,15,20-tetrakisphenylchlorine (**8**)⁴⁰

TPPNO₂ (prepared from TPP **7**, using a literature procedure)^{10a} (367 mg, 0.56 mmol) was dissolved in dry CH₂Cl₂ (30 mL), and to this tin(II)chloride dihydrate (1.26 g, 5.6 mmol) and conc. HCl (3.5 mL) were added. The reaction mixture was stirred under argon atmosphere for 3.5 days in the dark, upon which CH₂Cl₂ (100 mL) and water (100 mL) were added. The organic layer was separated and washed with water (100 mL), sodium bicarbonate solution (5%, 100 mL), and water, dried over anhydrous sodium sulfate, filtered and the solvent completely removed. Crude TPPNH₂ was obtained as a dark purple-green solid and used without further purification. UV-Vis: (CH₂Cl₂) λ_{max} : 423, 523, 556, 594, 651, 667, 681 nm, in accordance with literature.³⁹ To the crude TPPNH₂ was added dry CH₂Cl₂ (30 mL), followed by Dess-Martin periodinane (DMP) (156 mg, 0.42 mmol). After stirring for 2.5 h in the dark, excess DMP (70 mg, 0.16 mmol) was added, and stirring in the dark was continued. After 12 h, 80 mL of 1 M HCl was added and stirring continued for one hour. The organic layer was separated and washed with water (2×100 mL), dried over Na₂SO₄, and filtered. The filtrate was evaporated to dryness and the residue was flash chromatographed through a column of silica gel using CH₂Cl₂:pentane (2:3) yielding porphyrin dione **8** as a dark blue solid (114 mg, 0.18 mmol, 32%). R_f = 0.47 (silica-CH₂Cl₂) ¹H NMR (500 MHz, 25 °C, CDCl₃): δ 8.75 (dm, J = 4.8 Hz, 2H), 8.60 (dm, J = 4.8 Hz, 2H), 8.56 (s, 2H), 8.14-8.11(m, 4H), 7.91-7.89 (m, 4H), 7.80-7.67 (m, 12H), -2.01 (br s, 2H). UV-Vis: (CH₂Cl₂) λ_{max} : 403, 475 nm. Spectroscopic data were in accordance with the literature.^{40b}

4.5. (2,3-Dioxo-5,10,15,20-tetrakisphenylchlorinato)zinc(II) (**9**)⁴¹

The porphyrin dione **8** was metallated quantitatively with Zn(II)acetate dihydrate following a literature procedure, and **9** was obtained as a green-bluish solid. UV-Vis: (CH₂Cl₂) λ_{max} : 416, 497 nm. ¹H NMR (500 MHz, 25 °C, CDCl₃): δ 8.54 (d, J = 4.7 Hz, 2H), 8.46 (s, 2H), 8.31 (d, J = 4.7 Hz, 2H), 8.04-8.02 (m, 4H), 7.80-7.88 (m, 4H), 7.62-7.81 (m, 12H). Spectroscopic data were in accordance with the literature.^{40b}

4.6. Free-base porphyrin-terminated diphenylglycoluril clip (**2**)

With care to maintain an argon atmosphere, molecular sieves, degassed THF/methanol/CH₂Cl₂ (1:1:1, 24 mL) and porphyrin dione **8** (114 mg, 0.18 mmol) were added to freshly prepared **6** (from 89 mg, 0.11 mmol of the tetranitro compound **5**). The solution was heated to reflux for 36 h, after which time it was cooled to r.t., filtered, and the precipitate was washed with CH₂Cl₂ (5×20 mL). The combined filtrate was washed with 1N NaOH solution, water and brine and dried over anhydrous Na₂SO₄, then filtered. The filtrate was evaporated to dryness and purified by column chromatography using 1:1 pentane:CH₂Cl₂ as eluent, followed by CH₂Cl₂, gradually adding ethyl acetate up to CH₂Cl₂:ethylacetate (8:2). Clip **2** was obtained as a dark purple solid (160 mg, mixture of tautomers). UV-Vis: (CH₂Cl₂) λ_{max} : 432, 527, 599, 652, 682. MS (MALDI-TOF), [M+H]⁺, m/z = 1895. Calculated for C₁₂₄H₈₆N₁₆O₆: m/z = 1894 (nominal MW), 1895 (100% peak). Clip **2** was directly metallated according to a literature procedure,⁴² producing clip **1** as a dark purple solid (39 mg, 0.019 mmol, 23%). For characterization, see 4.7. Zinc(II)porphyrin-terminated diphenylglycoluril clip (**1**).

4.7. Zinc(II)porphyrin-terminated diphenylglycoluril clip (**1**)

With care to maintain an argon atmosphere, molecular sieves, degassed THF/methanol/CH₂Cl₂ (1:1:1, 24 mL) and zinc-porphyrin dione **9** (360 mg, 0.51 mmol) were added to freshly prepared **6** (from 254 mg, 0.32 mmol of **5**). The solution was heated at reflux for 36 h, after which time it was cooled to r.t., filtered, and the precipitate washed with CH₂Cl₂ (5×20 mL). The combined filtrate was washed with 1M NaOH solution, water, brine, dried over anhydrous Na₂SO₄ and then filtered. The filtrate was evaporated to dryness and purified by sequential column chromatographies using CHCl₃:MeOH (100:1), 2% MeOH in toluene and 5% MeOH in toluene, followed by precipitation upon addition of n-pentane to a methanol solution. The precipitate was isolated by centrifugation, then dried under vacuum to obtain clip **1** as a dark purple solid (105 mg, 0.052 mmol, 20 %). UV-Vis: (CH₂Cl₂) λ_{max} : 271, 326, 436 (broad), 575, 619, 794. HRMS (CI): m/z calculated for C₁₂₄H₈₂N₁₆O₆Zn [M⁺]: 2018.5164, [M+H₂O]²⁺: 1027.2688 found: 1027.2689. ¹H NMR (500 MHz, 25 °C, toluene-*d*₈): δ 8.73 (d, J = 4.8 Hz, 4H, H-*e*), 8.70 (s, 4H, H-*d*), 8.47 (d, J = 4.8 Hz, 4H, H-*c*), 8.17 (dm, J = 6.9 Hz, 4H, H-ortho-*a*), 8.09 (dm, J = 6.9 Hz, 4H, H-ortho-*b*), 8.02 (dm, J = 6.9 Hz, 4H, H-ortho-*b*), 7.85-7.57 (m, 44H), 7.32-7.13 (m, 10H) 5.92 (d, J = 16.1 Hz, 4H, CH₂), 3.90 (d, J = 16.1 Hz, 4H, CH₂), 3.79 (s, 12H, OCH₃) ¹³C NMR (100.58 MHz, 40°C, CDCl₃): δ 157.4 (CO), 153.0 (-C(=O)CH₃), 149.8, 148.9, 142.8, 142.4, 140.8, 136.0 (CH-*d*), 134.1 (CH-ortho-*a+b*), 133.8 (CH-ortho-*b'*), 133.6 (CH-ortho-*a'*), 132.2 (CH-*c*), 131.5 (CH-*e* + -CCNNPh), 129.8, 129.0, 128.9, 128.8, 128.4, 128.2, 127.6, 127.4, 126.9, 126.6, 123.4, 117.3 (-CH₂CCCOCH₃), 63.8 (-OCH₃), 38.1 (CH₂).

4.8. 1,20-Diaminoeicosane dihydrochloride (**15**)

1,20-Eicosanedicarboxylic acid (4 g, 11.7 mmol) was dissolved in SOCl_2 (40 mL) and heated to reflux for 2.5 h until gas evolution had ceased completely. The solvent was evaporated and the solid residue redissolved in dioxane (20 mL). A NH_3 -solution (conc., in H_2O , 25 mL) was added upon which a white precipitate was formed (violent reaction, heat). The mixture was stirred for 1 h, filtered off and left to dry in air over night. The obtained white solid (3.75 g) was used as is, dissolved in hot dry THF and added to a suspension of LiAlH_4 (1 g, 30 mmol) in dry THF (30 mL) at r.t. The mixture was heated to reflux over night and then quenched with H_2O and filtered over a Büchner funnel. The product was obtained as a waxy white solid (3.67 g, 82 %). For storage the diamine was dissolved in hot EtOH and bubbled with HCl (g) to precipitate the dihydrochloric salt as a white solid (quant.), m.p. 200 °C (dec.) Calc. for $\text{C}_{20}\text{H}_{46}\text{Cl}_2\text{N}_2$: C, 62.4; H, 12.0; N, 7.3%. Found: C, 62.7; H, 12.0; N, 7.0%. ^1H NMR (500 MHz, 100 °C, $\text{CH}_3\text{COOH}-d_4$): δ 3.18 (dm, $J = 7.7$ Hz, 4H, H-1+H-20), 1.87-1.81 (m, 4H, H-2+H-19), 1.53-1.36 (m, 32H, H-3 – H-18). ^{13}C NMR (100.58 MHz, 100 °C, $\text{CH}_3\text{COOH}-d_4$): 42.4 (C-1+C-20), 31.4 (C-7 - C-14), 31.3 (C-6+C-15), 31.2 (C-5+C-16), 30.9 (C-4+C-17), 29.1 (C-2+C-19), 28.2 (C-3+C-18).

4.9. 1,20-Diaminoeicosane (**16**)⁴⁴

Amberlite IRA-400 resin (chloride form, Sigma-Aldrich, 0.5 cm³) was rinsed with H_2O (5 mL), NaOH (1M, 10 mL) and again with H_2O (5 mL) upon which a AgNO_3 -test for chloride was performed to verify complete conversion of the resin to the OH⁻ form. The converted resin was rinsed with MeOH (5 mL) and transferred into a 1 mL vial. 1,20-Diaminoeicosane dihydrochloride **15** (18 mg, 0.047 mmol) was dissolved in 0.5 mL MeOH and poured over the resin. The mixture was left to stir gently under argon atmosphere over night and then filtered through a glass wool plug. Evaporation of the solvent afforded the product as a pale yellow solid (14 mg, 0.044 mmol, 95 %). m.p. 84-85 °C (lit. 85 °C). ^1H NMR (500 MHz, 25 °C, CDCl_3): δ 2.67 (dm, $J = 6.9$ Hz, 4H, H-1+H-20), 1.46-1.39 (m, 4H, H-2+H-19), 1.33-1.20 (m, 32H, H-3 – H-18).

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References and notes

- (a) Hayashida, O.; Sebo L.; Rebek J. *J. Org. Chem.* **2002**, *67*, 8291; (b) Klärner, F. G.; Kahlert, B. *Acc. Chem. Res.* **2003**, *36*, 919; (c) Dignam, C. F.; Richards, C. J.; Zopf, J.J.; Wacker L. S.; Wenzel, T. *J. Org. Lett.* **2005**, *7*, 1773; (d) Rebek, J. *Nature* **2006**, *444*, 557; (e) Schramm, M. P.; Rebek, J. *Chem. Eur. J.* **2006**, *12*, 5924; (f) Ajami, D.; Iwasawa, T.; Rebek, J. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 8934; (g) Ajami D.; Rebek, J. *J. Am. Chem. Soc.* **2006**, *128*, 15038.
- (a) Crossley, M. J.; Thordarson, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 1709; (b) Reek, J. N. H.; Schenning, A. P. H. J.; Bosman, A. W.; Meijer, E. W.; Crossley, M. J. *Chem. Commun.* **1998**, 11; (c) Solladié, N.; Aziat F.; Bouatra, S.; Rein R. *J. Porphyrins Phthalocyanines* **2008**, *12*, 1250.
- (a) Crossley, M. J.; Mackay, L. G.; Try, A. C. *J. Chem. Soc., Chem. Commun.* **1995**, 1925; (b) Hayashi, T.; Nonoguchi M.; Aya T.; Ogoshi H. *Tetrahedron Lett.* **1997**, *38*, 1603; (c) Huang X., Rickman, B. H.; Borhan, B.; Berova, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1998**, *120*, 6185; (d) Yang, Q.; Olmsted, C.; Borhan, B. *Org. Lett.* **2002**, *4*, 3423. (e) Huang, X.; Nakanishi K.; Berova, N. *Chirality* **2000**, *12*, 237; (f) Huang, X.; Fujioka, N.; Pescitelli G.; Koehn, F. E.; Williamson, R. T.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2002**, *124*, 10320; (g) Borovkov, V. V. ; Hembury, G. A.; Inoue, Y. *Acc. Chem. Res.* **2004**, *37*, 449; (h) Berova, N.; Pescitelli, G.; Petrovica, A.G.; Pronic, G. *Chem. Commun.* **2009**, 5958; (i) Petrovic, A. G.; Vantomme, G.; Negrón-Abril, Y.; Lubian, E.; Saielli, G.; Menegazzo, I.; Cordero, R.; Proni, G.; Nakanishi, K.; Carofiglio, T.; Berova, N. *Chirality* **2011**, *23*, 808; (j) Tanasova, M.; Borhan, B. *Eur. J. Org. Chem.* **2012**, 3261.
- (a) Groves, J. T. *Nature* **1997**, *389*, 329; (b) Feiters, M. C.; Rowan, A. E.; Nolte, R. J. M. *Chem. Soc. Rev.* **2000**, *29*, 375.
- (a) Hunter, C. A.; Meah, N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5773. (b) Anderson, H. L.; Hunter, C. A.; Meah, N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5780; (c) Mizutani, T.; Wada, K.; Kitagawa, S. *J. Am. Chem. Soc.* **1999**, *121*, 11425; (d) Solladié, N.; Bouatra, S.; Merkas, S.; Rein, R.; Roeser, J. *J. Porphyrins Phthalocyanines* **2005**, *9*, 779.
- Danks, I. P.; Lane, T.G.; Sutherland, I. O.; Yap, M. *Tetrahedron* **1992**, *48*, 7679.

7. (a) Smeets, J. W. H.; Sijbesma, R. P.; van Dalen, L.; Spek, A. L.; Smeets, W. J. J.; Nolte, R. J. M. *J. Org. Chem.* **1989**, *54*, 3710; (b) Jansen, R. J.; de Gelder, R.; Rowan, A. E.; Scheeren, H. W.; Nolte, R. J. M. *J. Org. Chem.* **2001**, *66*, 2643; (c) Reek, J. N. H.; Elemans, J. A. A. W.; de Gelder, R.; Beurskens, P. T.; Rowan, A. E.; Nolte, R. J. M. *Tetrahedron* **2003**, *59*, 175; (d) Hardouin-Lerouge, M.; Hudhomme, P.; Sallé, M. *Chem. Soc. Rev.* **2011**, *40*, 30.
8. Polavarapu, P.; Melander, H.; Langer, V.; Gogoll, A.; Grennberg, H.; *New J. Chem.* **2008**, *32*, 643.
9. Gosling, P. A. Ph. D. Thesis, University of Nijmegen, (The Netherlands) **1996**.
10. (a) Promarak, V.; Burn, P. L. *J. Chem. Soc. Perkin Trans. I*, **2001**, 14; (b) Beavington, A.; Burn, P. L. *J. Chem. Soc. Perkin Trans. I*, **1999**, 583.
11. (a) Brückner, C.; Rettig, S. J.; Dolphin, D. *J. Org. Chem.* **1998**, *63*, 2094; (b) Daniell, H. W.; Williams, S. C.; Jenkins, H. A.; Brückner, C. *Tetrahedron Lett.* **2003**, *44*, 4045.
12. Plietker, B.; Niggemann, M.; Pollrich, A. *Org. Biomol. Chem.* **2004**, *2*, 1116.
13. (a) Sijbesma, R. P.; Wijmenga, S. S.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1992**, *114*, 9807; (b) Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *J. Supramol. Chem.* **2002**, *2*, 151.
14. (a) Dolenský, B.; Havlík, M.; Král, V. *Chem. Soc. Rev.* **2012**, *41*, 3839; (b) Uno, H.; Nakamoto, K.; Kuroki, K.; Fujimoto, A.; Ono, N. *Chem. Eur. J.* **2007**, *13*, 5773; (c) Uno, H.; Furukawa, M.; Fujimoto, A.; Uoyama, H.; Watanabe, H.; Okujima, T.; Yamada, H.; Mori, S.; Kuramoto, M.; Iwamura, T.; Hatae, N.; Tanid, F.; Komatsu, N. *J. Porphyrins Phthalocyanines* **2011**, *15*, 951; (d) Bogaschenko, T. Y.; Lyapunov, A. Y.; Kikot', L. S.; Mazepa, A. V.; Botoshansky, M. M.; Fonari, M. S.; Kirichenko, T. I. *Tetrahedron* **2012**, *68*, 4757; (e) Han, M.; Michel, R.; He, B.; Chen, Y.-S.; Stalke, D.; John, M.; Clever, G. H. *Angew. Chem. Int. Ed.* **2013**, *52*, 1319.
15. (a) Sijbesma, R. P.; Wijmenga, S. S.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1992**, *114*, 9807 (b) Magnus, P.; Morris, J. C.; Lynch, V. *Synthesis* **1997**, 506; (c) Kurebayashi, H.; Mine, T.; Harada, K.; Usui, S.; Okajima, T.; Fukazawa, Y. *Tetrahedron* **1998**, *54*, 13495; (d) Kurebayashi, H.; Sakaguchi, M.; Okajima, T.; Haino, T.; Usui, S.; Fukazawa, Y. *Tetrahedron Lett.* **1999**, *40*, 5545; (e) Kurebayashi, H.; Haino, T.; Usui, S.; Fukazawa, Y. *Tetrahedron* **2001**, *57*, 8667; (f) Elemans, J. A. A. W.; Rowan, A. E.; Nolte, R. J. M. *J. Supramol. Chem.* **2002**, *2*, 151; (g) Reek, J. N. H.; Elemans, J. A. A. W.; de Gelder, R.; Beurskens, P. T.; Rowan, A. E.; Nolte, R. J. M. *Tetrahedron* **2003**, *59*, 175.
16. (a) Lebedeva, N. Sh.; Vyugin, A. I.; Pavlycheva, N. A.; Parfennyuk, E. V.; Davydova, O. I. *Thermochim. Acta* **2002**, *390*, 179; (b) Camara-Campos, A.; Hunter, C. A.; Tomas, S. *PNAS* **2006**, *103*, 3034.
17. (a) Eaton S. S.; Eaton G. R. *Inorg. Chem.* **1978**, *17*, 1542; (b) Stolzenberg, A. M.; Haymond, G. S.; *Inorg. Chem.* **2002**, *41*, 300.
18. (a) Jimenez, H. R.; Julve, M.; Moratal, J. M.; Faus, J. J. *Chem. Soc., Chem. Commun.* **1987**, 910; (b) Jimenez, H. R.; Julve, M.; Faus, J. J. *Chem. Soc. Dalton Trans.* **1991**, 1945; (c) Chirvony, V. S.; van Hoek, A.; Galievsky, V. A.; Sazanovich, I. V.; Schaafsma, T. J.; Holten, D. *J. Phys. Chem. B* **2000**, *104*, 9909.
19. (a) Steinberg-Yfrach, G.; Liddell, P. A.; Hung, S.-C.; Moore, A. L.; Gust, D.; Moore, T. A. *Nature* **1997**, *385*, 239; (b) Flamigni, L.; Talarico, A. M.; Ventura, B.; Rein, R.; Solladié, N. *Chem. Eur. J.* **2006**, *7*, 701; (c) Palacios, R. E.; Kodis, G.; Gould, S. L.; de la Garza, L.; Brune, A.; Gust, D.; Moore, T. A.; Moore, A. L. *ChemPhysChem* **2005**, *6*, 2359.
20. (a) Weiss, J. J. *Incl. Phenom. Macrocycl. Chem.* **2001**, *40*, 1; (b) Barone, G.; Duca, D.; Silvestri, A.; Gomez-Paloma, L.; Riccio, R.; Bifulco, G.; *Chem. Eur. J.* **2002**, *8*, 3240; (c) Dambruoso, P.; Bassarello, C.; Bifulco, G.; Appendino, G.; Battaglia, A.; Fontana, G.; Gomez-Paloma, L. *Org. Lett.* **2005**, *7*, 983.
21. (a) Gust, D.; Moore, T. A.; Luttrull, D. K.; Seely, G. R.; Bittersmann, E.; Bensasson, R. V.; Rougée, M.; Land, E. J.; De Schryver, D. E.; Auweraer, M. V. *Photochem. Photobiol.* **1990**, *51*, 419; (b) Crossley, M. J.; Burn, P. L. *J. Chem. Soc., Chem. Commun.* **1991**, 1569; (c) Crossley, M. J.; Govenlock, L. J.; Prashar, J. J. *Chem. Soc., Chem. Commun.* **1995**, 2379. (d) Beavington, R.; Burn, P. L. *J. Chem. Soc., Perkin Trans. I*, **2000**, 605. (e) Satake, A.; Kobuke, Y. *Tetrahedron* **2005**, *61*, 13.
22. (a) Branda, T.; Cabritab, E. J.; Berger, S. *Prog. Nuc. Mag. Res. Sp.* **2005**, *46*, 159; (b) Gaynor, S. P.; Gunter, M. J.; Johnston, M. R.; Warrenner, R. N. *Org. Biomol. Chem.* **2006**, *4*, 2253; (c) Pastor, A.; Martínez-Viviente, E. *Coord. Chem. Rev.* **2008**, *252*, 2314; (d) Slovak, S.; Avram, L.; Cohen, Y.; *Angew. Chem. Int. Ed.* **2010**, *49*, 428.
23. Norrehed, S.; Johansson, H.; Grennberg, H.; Gogoll, A. *submitted*.
24. Augé S.; Schmit, P.-O.; Crutchfield, C. A.; Islam, M. T.; Harris D. J.; Durand, E.; Clemancey, M.; Quoineaud, A.-A.; Lancelin, J.-M.; Prigent, Y.; Taulelle, F.; Delsuc, M.-A. *J. Phys. Chem. B*, **2009**, *113*, 1914.
25. (a) Toronto, D.; Sarrazin, F.; Pecaut, J.; Marchon, J. C.; Shang, M. Y.; Scheidt, W. R. *Inorg. Chem.* **1998**, *37*, 526; (b) Proni, G.; Pescitelli, G.; Huang, X. F.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2003**, *125*, 12914; (c) Abraham, R. J.; Marsden, I. *Tetrahedron* **1992**, *48*, 7489; (d) Abraham, R. J.; Medforth, C. J. *Magn. Reson. Chem.* **1990**, *28*, 343.
26. Millen, D. J. in *Prog. Stereochem.* (Ed. P. B. D. de la Mare, W. Klyne), Butterworths, London **1962**, *3*, 138.
27. Li, X.; Burrell, C. E.; Staples, R. J.; Borhan, B. *J. Am. Chem. Soc.* **2012**, *134*, 9026.
28. Thordarsson, P. *Chem. Soc. Rev.* **2011**, *40*, 1305.
29. Mueller, L. *J. Magn. Reson.* **1987**, *72*, 191.
30. Davis, A. L.; Keeler, J.; Laue, E. D.; Moskau, D. *J. Magn. Reson.* **1992**, *98*, 207.

31. Hurd, R. E.; John, B. K. *J. Magn. Reson.* **1991**, *91*, 648.
32. Wagner, R.; Berger, S. *J. Magn. Reson. A*, **1996**, *123*, 119.
33. Bax, A.; Davis, D. G. *J. Magn. Reson.* **1985**, *63*, 207.
34. Braunschweiler, L.; Ernst, R. R. *J. Magn. Reson.* **1983**, *53*, 521.
35. (a) Morris, G. A.; Barjat, H. *Analytical spectroscopy library vol. 8*, Elsevier, **1997**, p. 209; (b) Gibbs, S. J.; Johnson, C. S. *J. Magn. Reson.* **1991**, *93*, 395.
36. Kato, H.; Saito, T.; Nabeshima, M.; Shimada, K.; Kinugasa, S. *J. Magn. Reson.* **2006**, *180*, 266.
37. Butzelaar, P. H. M., Ivorysoft **2006**.
38. (a) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, *32*, 476. (b) Lindsey, J. S.; Schreiman, I. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827. (c) Bäckvall, J.-E.; Hopkins, R. B.; Grennberg, H.; Mader, M. M.; Awasthi, A. K. *J. Am. Chem. Soc.* **1990**, *112*, 5160. (d) Li, F.; Yang, K.; Tyhonas, J. S.; MacCrum, K. A.; Lindsey, J. S. *Tetrahedron* **1997**, *53*, 12339.
39. Baldwin, J. E.; Crossley, M. J.; DeBernardis, J. *Tetrahedron* **1982**, *38*, 685.
40. (a) Brückner, C.; Rettig, S. J.; Dolphin, D. *J. Org. Chem.* **1998**, *63*, 2094. (b) Daniell, H. W.; Williams, S. C.; Jenkins, H. A.; Brückner, C. *Tetrahedron. Lett.* **2003**, *44*, 4045.
41. Monti, D.; Venanzi, M.; Mancini, G.; Marotti, F.; Monica, L. L.; Boschi, T. *Eur. J. Org. Chem.* **1999**, 1901.
42. (a) Munro, O. Q.; Shabalala, S. C.; Brown, N. J. *Inorg. Chem.* **2001**, *40*, 3303; (b) Rovira, C.; Kunc, K.; Hutter, J.; Parrinello, M. *Inorg. Chem.* **2001**, *40*, 11.
43. Power, N. P.; Dalgarno, S. J.; Atwood, J. L. *New J. Chem.* **2007**, *31*, 17.
44. Plateau, J.; Brouillet, G. Patent DE2133650 (A1), 1972. *Chem. Abstr.* **1972**, *76*, # 72000.