

The First Versatile Synthetic Approach to Cofacial Bis-Porphyrins with Calixarene Spacers

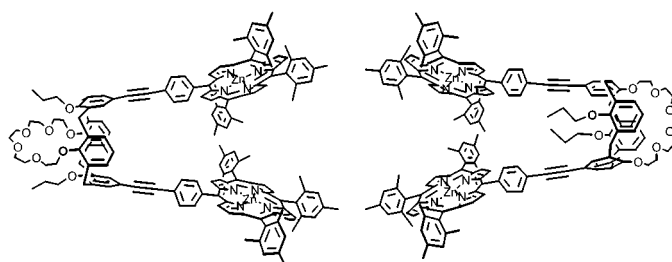
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ABSTRACT



A versatile stepwise synthetic approach to cofacial bis-porphyrin species with calix[4]arene spacers has been designed. The three examples described demonstrate that the method allows selection, in a tailor-made fashion, of the calix[4]arene conformation, the type of functionalization of the calixarene rims, and the anchoring point of the chromophores on the calix[4]arene spacer.

Due to their involvement in photosynthetic processes^{1,2} and in electrocatalytic tetraelectronic reduction of molecular nitrogen and oxygen,^{3,4} cofacial porphyrins have been investigated since the beginning of the 1980s. The synthesis of cofacial porphyrins has always been a challenge,⁵ and

variation of the interporphyrinic distance implied the revisiting of syntheses leading to the cofacial porphyrin species.⁶ Conformational control of the spatial arrangement of flexible porphyrin dimers and trimers has been achieved via a diarylurea linkage⁷ or via sodium complexation within a polyether link.⁸ Binaphthyl crown ethers have also been used as flexible spacers in bis-porphyrin species, leading to interesting chirality transfer processes.⁹

The advantages of calixarene platforms as spacers have been demonstrated by the first through-space interaction

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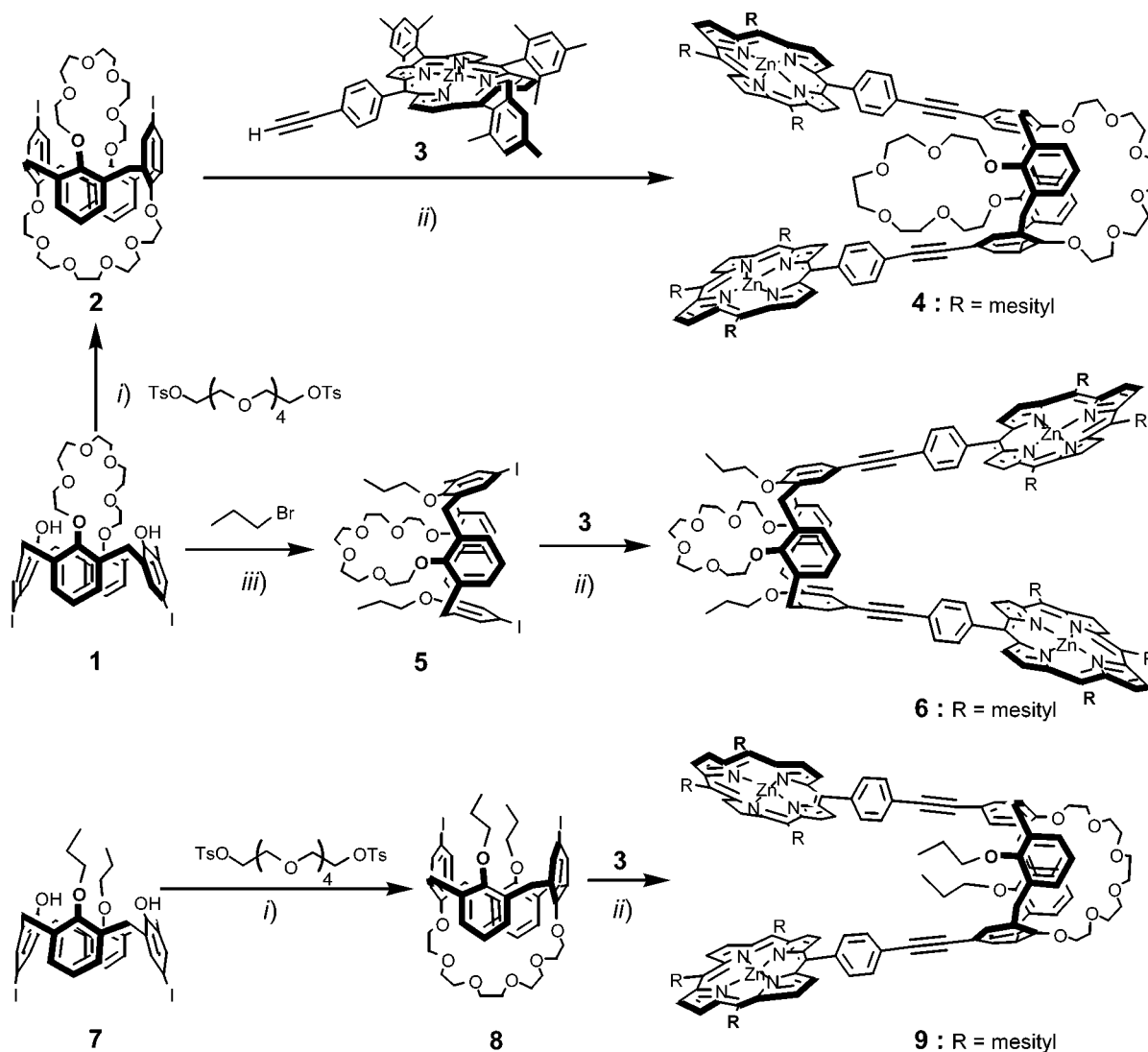
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Scheme 1^a

^a Reaction conditions: (i) Cs_2CO_3 , CH_3CN , reflux; afforded **2** (65%) and **8** (60%). (ii) 10% $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, CuI , NEt_3 , 323 K; afforded **4** (35%), **6** (45%), **9** (40%). (iii) NaI (cat.), NaH , DMF , 298 K; afforded **5** (75%).

between two chromophores observed for a calixarene platform bearing two heteroquinones.¹⁰ Recent publications have also emphasized the potential use of porphyrin-calixarene assemblies in either the control and selection of axial coordinates on metalloporphyrins¹¹ or the enhancement of noncovalent interactions between porphyrins and substrates complexed by the calixarenes.^{12,13} On the basis of numerous reports on the complexing properties of calixcrown derivatives,¹⁴ these species were selected as spacers for the

targeted bis-porphyrins, such species being of interest in molecular recognition processes.^{15,16} A versatile approach based on tailor-made conformations of calixarenes has been designed.

As depicted in Scheme 1, diiodinated calixarenes **1** and **7** have been obtained via selective halogenation of crown[6]-

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calix[4]arene and dipropoxy-calix[4]arene, respectively.¹⁷ Further dialkylation of these materials under appropriate reaction conditions afforded spacers **2**, **5**, or **8**, locked in either 1,3-alternate or cone conformations. At this stage, the versatility of the approach should be emphasized. As shown by the synthesis of precursors **2**, **5**, and **8**, choosing appropriate alkylation conditions allows the respective behavior of the spacers to be selected. Preventing the interconversion between calixarene conformations requires etherification of the phenolic oxygens with, at the smallest, *n*-propyl chains. Thus, conformational isomers **5** and **8** cannot interconvert, even upon heating, and will generate the corresponding conformational isomers of bis-porphyrin species. Thus, the conformation of the spacer, as well as the type of functionalization introduced via etherification, is fully controllable. Depending on when the iodination step is performed, the anchoring point of the chromophore can be chosen as well. Indeed, methylation, iodination, and demethylation sequences can be performed to allow tailor-made introduction of binding groups onto the lower rim of a diiodo calix[4]arene in a cone conformation. Connection of the chromophores is quite straightforward and proceeds via coupling of 5-(*p*-iodophenyl)-10,15,20-trimesityl-porphinatozinc, prepared as described by Lindsey,¹⁸ with trimethylsilyl acetylene in the presence of Pd(PPh₃)₂Cl₂ and triethylamine as both the solvent and the base, to yield porphyrin **3** (Scheme 1) in 75% yield after removal of the trimethylsilyl protection. Finally, coupling of **3** with the calix[4]arene derivatives **2**, **5**, and **8** proceeded under similar, unoptimized coupling conditions to afford three calix[4]arene bis-porphyrin conjugates **4**, **6**, and **9** in yields ranging from 35 to 45%.

Comparison between bis-porphyrins **4** and **6** provides information concerning the influence of the steric bulk on the inner rim of the 1,3-alternate calixarene on the respective arrangement of the chromophores, while comparison of **6** and **9** provides information concerning the effect of the calixarene conformation (cone or 1,3-alternate). In general, excitonic coupling between cofacial porphyrins induces a hypsochromic shift and broadening of the absorption bands, both effects increasing as the distance between the chromophores decreases. In compounds **4**, **6**, and **9**, the mesityl meso substituents forbid strong excitonic coupling between the two porphyrins. Thus, except for bis-porphyrin **6**, absorption maxima do not differ from those observed for isolated chromophores. However, as shown in Figure 1, the ratio of the mid-height bandwidth to the absorbance of the Soret band increases considerably. In cofacial structure **4**, obvious steric interactions of the spacers with the inner polyethylenoxy chain prevent any shortening of the distance between the two chromophores, and the absorbance of **4** is similar to that of **3** at twice the concentration.

In **9**, and **6**, the chromophores are able to develop a weak excitonic coupling as the steric bulk separating them decreases, from a closed macrocycle to an open dipropyl

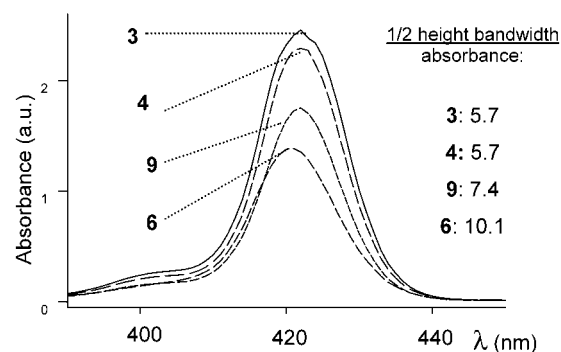


Figure 1. Comparison of Soret bands of cofacial species **4**, **6**, and **9** with that of reference **3**. [*c*] = 2.5×10^{-6} M for **4**, **6**, and **9**; [*c*] = 5×10^{-6} M for **3** in CH₂Cl₂.

substitution in **9**, and a conformationally more flexible cone spacer in **6**. For the latter, a 2 nm blue shift of the absorption maxima is concurrent with the significant shape change of the Soret band. Further characterization of these bis-porphyrins confirms these topographic changes.

In a first analysis, ¹H NMR characterization of the species shows a global superimposition of the three calixarene spectra with the spectrum of the reference porphyrin **3**, but a closer examination of the spectra displayed in Figure 2 (left) shows small high-field shifts for β-pyrrolic protons and for protons located on the *meso*-phenyl. Together with changes in the multiplicity of the signals, these displacements are consistent with an accentuated cofacial arrangement of the tetrapyrrolic macrocycles, and the amplitude of the shielding correlates with the diminution of the steric bulk between the two porphyrins. The ¹H NMR spectrum of **4** shows a great similitude with that of isolated **3**, with nearly identical chemical shifts for the porphyrinic and mesityl protons. Direct interporphyrinic correlations cannot be observed by ROESY and COSY experiments due to the magnetic equivalence of the groups of protons located on both porphyrin rings (see Supporting Information). In the case of **4**, two correlations, depicted in Figure 2, provide indirect confirmation of the cofacial character of the tetrapyrrolic macrocycles. The spectra of **6** and **9** show that when the inner polyether chain of **4** is replaced by an open dipropyl substitution in **9**, a slight shielding of the porphyrinic protons suggests a shortening of the interporphyrinic distance. This shielding becomes significant in the case of the cone conformer **6**, as a maximum displacement of 0.15 ppm is observed for protons H_a and H_b and 0.11 ppm for proton H_c.

¹H NMR also shows that, in the case of **6**, the pattern of peaks observed for the polyethylenoxy chain is quite different in **6** than in the precursor **5**. The calixarene appears to act as a hinge between the functionalized lower rim and the bis-porphyrinic arrangement on the upper rim.

The cofacial preorganization of the porphyrins is adequate for the formation of inclusion complexes with bidentate ligands such as 4,4'-diazabicyclo[2,2,2]octane (Dabco),

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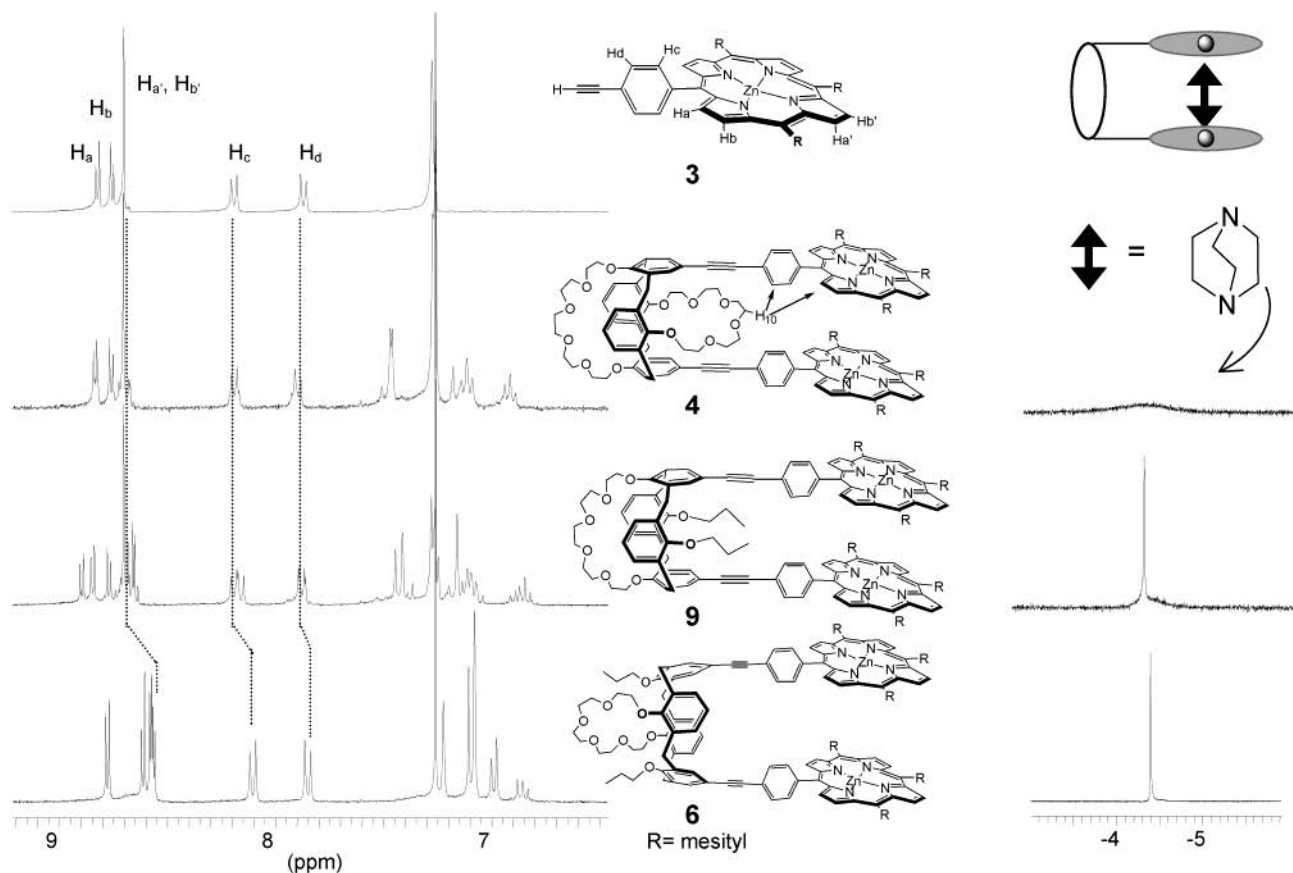


Figure 2. Chemical shift displacements observed for ligands **4**, **6**, and **9** compared with that of porphyrin precursor **3** (CDCl₃, 300 MHz). NOESY (CD₂Cl₂, 500 MHz) correlations observed in **4** are indicated by arrows (left). Dabco signal for 1:1 mixtures of **4**, **9**, and **6** with 4,4'-diazabicyclo[2,2,2]octane (right).

whose singlet appears around -5 ppm when inserted between porphyrins. Receptors **4**, **6**, and **9** display very different behaviors in the presence of Dabco (Figure 2, right), with **4** allowing a fast exchange between bound and free substrates, while **6** and **9** provide a well-resolved singlet for the Dabco bidentate. Further studies of diamine complexation as well as cation complexation by the calixarene spacers are currently under progress.

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Supporting Information Available: Full characterization (¹H NMR, CHN analysis, FAB⁺ mass spectrometry, UV-vis absorption, NOESY) for bis-porphyrins **4**, **6**, and **9**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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