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Synthesis and Characterization of Azobenzene-Confined Porphyrins

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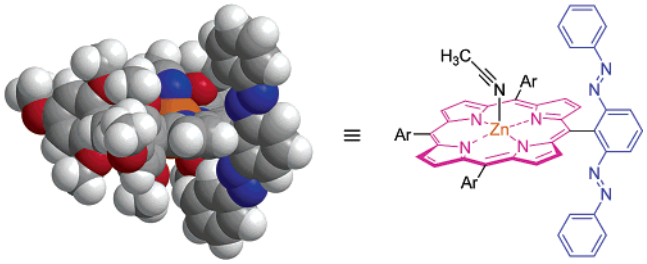
Received June 22, 2006



A versatile synthetic method has been developed to incorporate photochromic azobenzene moieties into tetraphenylporphyrin frameworks in an orthogonal fashion, positioning the phenylazo substituents above and below the plane of the macrocycle. Surprisingly, photoisomerization is completely suppressed in the resulting azobenzene-confined porphyrins.

The creation of stimulus-responsive molecules and materials capable of undergoing reversible property changes is of great interest for future technology. Light represents perhaps the most attractive external stimulus because it can be applied in a noninvasive fashion, i.e., without production of byproducts, and with exquisite control over time and location of exposure. In this context, photochromic molecules are of great interest since geometrical and electronic changes upon switching can be used to affect structure and function at the molecular level.[1] Arguably, catalysis is among the most attractive functions to photoswitch. However, reversible photomodulation of catalytic activity has thus far been poorly explored, and the few reported cases[2] suffer from a lack of generality and low on/off-ratios, i.e., small changes in activity. In search of a more general photoswitchable catalyst, we targeted photocontrol over the accessibility to metalloporphyrins,[3] which are ubiquitous in Nature[4] since they perform important binding, activation, and catalytic processes. Our design involves the direct incorporation of an azobenzene unit into the framework of a *meso*-tetraphenylporphyrin in such a way that two *o*-phenylazo substituents can occupy the space above and below the plane of the metalloporphyrin leading to an effective shielding of the catalytically active metal center (Figure 1). We expected that, upon irradiation, the large structural reorganization accompanying the *E*−*Z*-isomerization of the azobenzenes would open the pocket and dramatically increase access to the axial positions of the metal center, thereby enabling binding and catalysis to occur.[5] Here, we report the efficient synthesis as well as structural and photophysical characterization of a novel bisazobenzene-substituted porphyrin derivative.

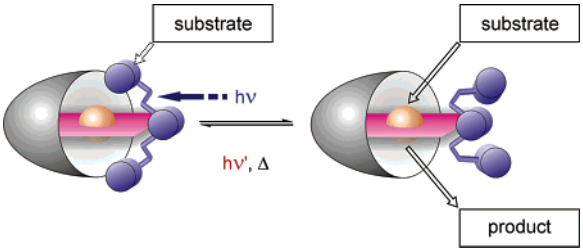


FIGURE 1. Concept of photomodulating axial accessibility and therefore catalytic activity in azobenzene-substituted metalloporphyrins.

Some examples of azobenzene-containing (metallo)porphyrins have been reported. However, they mostly carry the azobenzene unit either in the para position of the *meso*-phenyl group,[6] via a flexible linker,[7] or by axial coordination.[8] In the reported cases, either no or contradictory findings with regard to the photoisomerization have been given. To test our design concept, we targeted porphyrin **3** (Scheme 1), in which only two azobenzene units were introduced into the porphyrin skeleton via one *meso*-[2,6-bis(phenylazo)phenyl] group to limit the number of possible switching states, i.e., *E*,*E* vs *E*,*Z* vs *Z*,*Z*. The meta relationship prohibits electronic communication between the phenylazo substituents and ensures independent isomerization events.[9] The

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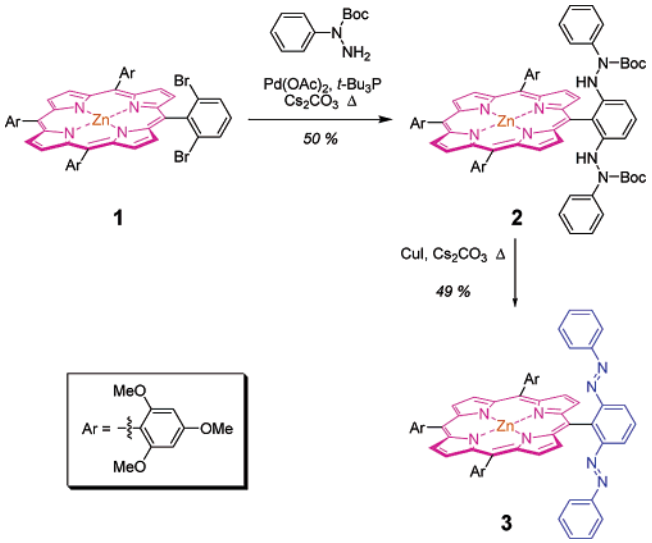
10.1021/jo0612877 CCC: $33.50
Published on Web 08/29/2006

SCHEME 1. Synthesis of Target Azoporphyrin



remaining three *meso* positions were occupied by spectator groups, i.e., 2,4,6-trimethoxyphenyl groups. The use of ortho-disubstituted *meso*-substituents is key to the design in order to ensure their orthogonal orientation with respect to the plane of the metalloporphyrin. It should be noted that accessibility could in principle be readily tuned by adjusting the size of the spectator substituents (Ar in Scheme 1) and by enlarging the phenylazo groups via substitution in the 4- or 3,5-positions.

Initial attempts to synthesize target porphyrin **3** from the corresponding 2,6-bis(phenylazo)benzaldehyde failed due to the illusive nature of *o*-formylazobenzenes.[10] Instead, porphyrin **3** could be accessed by starting from the nonsymmetric zinc 5-(2,6-dibromophenyl)-10,15,20-tris(2,4,6-trimethoxyphenyl)-porphyrin **1**, which was readily prepared via a mixed condensation[11] of 2,6-dibromobenzaldehyde and 2,4,6-trimethoxybenzaldehyde with its corresponding dipyrromethane[12] followed by oxidation of the formed porphyrinogen and zinc insertion. The sterically hindered aryl bromide functionalities in **1** were converted to the corresponding *tert*-butyloxycarbonyl-protected phenylhydrazides via a Pd-catalyzed cross-coupling reaction to yield **2**, which after subsequent deprotection/oxidation afforded the desired zinc porphyrin **3** in good yield (Scheme 1).[13] Importantly, this porphyrin postfunctionalization procedure allows in principle for the preparation of a large array of azobenzene-substituted porphyrin structures.

The structure of target **3** was unambiguously characterized by single-crystal X-ray analysis of its CH_3CN complex (Figure 2). Crystals were grown from acetonitrile and from acetonitrile/cyclohexane (reservoir) by the hanging drop method. The acetonitrile molecule is terminally bound to the zinc center, giving rise to a square pyramidal complex in which the zinc atom has moved out of the plane of the porphyrin ring by ca. 0.28(7) Å. The *meso*-[2,6-bis(phenylazo)phenyl] as well as all three *meso*-2,4,6-trimethoxyphenyl groups are oriented ap-

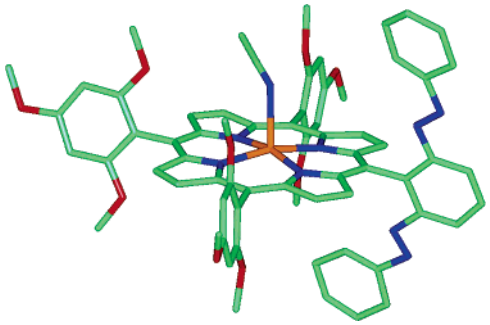


FIGURE 2. Structure of **3**(CH_3CN) crystallized from CH_3CN, showing the near-orthogonal arrangement of the *meso*-aryl substituents to the porphyrin ring. (Solute CH_3CN and disorder of one methoxy group are omitted for clarity. Zn: orange; C: green; N: blue; O: red.)

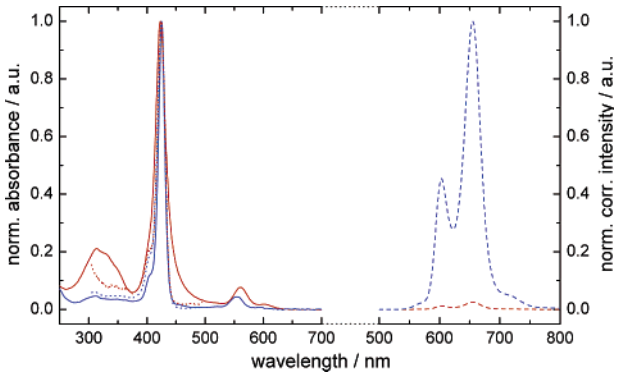


FIGURE 3. Absorbance (solid), excitation (λ_{em} = 590 nm, dotted), and emission (λ_{exc} = 424 nm, dashed) spectra of **2** (blue) and **3** (red) in CH_3CN.

proximately orthogonal to the plane of the porphyrin ring, presumably due to the presence of the ortho substituents, with plane angles in the range 75−90°. The absence of close contacts between the aryl substituents in the crystal suggests that the structure is representative of the system in solution. Indeed, inspection of the ^1H NMR spectrum in CD_3CN (see the Supporting Information) corroborates the crystal structure, most notably by revealing the loss of the planar symmetry due to acetonitrile ligation and exhibiting an unusual upfield shift ($\Delta\delta$ ~1 ppm with regard to non-porphyrin model compounds) of the terminal phenyl protons of the azobenzenes due to their specific location with regard to the ring current of the porphyrin macrocycle.

Inspection of the absorption spectrum of **3** (Figure 3) corroborates the presence of porphyrin and azobenzene chromophores. Comparison with **2**, displaying the negligible intrinsic porphyrin absorption in the UV, validates the possibility of selective excitation of the azobenzene moieties around 300−350 nm. However, irradiation of solutions of **3** under various conditions, i.e., various solvents (CH_3CN, CH_2Cl_2, THF[14]), excitation wavelengths (313 and 365 nm), and concentrations (10^{-5} − 10^{-7} M), led to no observable change in the UV/vis spectra. Clearly, photoisomerization of the azobenzene moiety does not occur in this system. Exchanging the central metal atom did not alter the photochemistry.

To understand this unexpected behavior and to qualitatively elucidate excitation energy migration in this multichromophore

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(14) Only in THF photochemistry was observed, giving rise to irreversible production of as yet unidentified photoproducts.

system, fluorescence emission and excitation spectra of **3** and the corresponding azobenzene-free model compound **2** were recorded (Figure 3). The excitation spectrum of **3** reveals significant participation of the azobenzene moieties in populating the emitting state and thereby points to efficient fluorescence resonance energy transfer (FRET) from the azobenzene moieties to the zinc porphyrin chromophore.[15] Interestingly, while **2** displays a fluorescence spectrum and quantum yield ($\Phi_f = 2 \times 10^{-3}$) typical for zinc porphyrins,[3] **3** shows a qualitatively similar emission spectrum yet with a greatly diminished intensity ($\Phi_f = 6 \times 10^{-6}$). Obviously, the presence of the azobenzene moieties leads to efficient fluorescence quenching, most likely due to photoinduced electron transfer (PET). Furthermore, it should be noted that **3** displays a rather broad Soret band (fwhm = 23 nm) as compared to **2** (fwhm = 13 nm), which indicates some sort of yet unexplained electronic interaction in the ground state.

These observations suggest that the dominant pathway for excitation energy migration in **3** is: initial FRET from the azobenzene donor to the zinc porphyrin acceptor, subsequent PET from the zinc porphyrin core to the azobenzene moiety, followed by final charge recombination to relax to the ground state. The efficient FRET process, preventing photoisomerization in the system, is strongly facilitated by the close distance and the significant spectral overlap[16] of the azobenzene donor and zinc porphyrin acceptor and most likely dominated by the Förster mechanism.[17] PET has been observed in a related system.[6b] Comparing our results with various other reports on azobenzene-appended porphyrins,[6−8] we believe that successful photoisomerization can only be achieved by moving the azobenzene photochrome further away[7] from the porphyrin moiety or by electronically decoupling both chromophores.[8] This finding is particularly important for the design of photoswitchable porphyrin-based catalysts such as proposed here as well as other molecular devices in which mechanical motion is powered by azobenzene photoisomerization.[18]

Experimental Section

Synthesis of Azoporphyrin 3. 5-(2,6-Dibromophenyl)-10,15,20-(2,4,6-trimethoxyphenyl)porphyrin $\mathbf{1}_{FB}$. Under an argon atmosphere, a flask was charged with 577 mg (2.94 mmol) of 2,4,6-trimethoxybenzaldehyde, 776 mg (2.94 mmol) of 2,6-dibromobenzaldehyde, and 1.84 g (5.88 mmol) of 2,4,6-trimethoxyphenyldipyrromethane[12] dissolved in 577 mL of chloroform, and argon was passed through the solution for 10 min. Subsequently, 0.25 mL (1.94 mmol) of $BF_3{\cdot}OEt_2$ was added, and the solution was stirred at room temperature for 1 h. Then, 2 g (8.82 mmol) of DDQ was added, and the reaction mixture was stirred overnight. The solvent was removed under reduced pressure. Purification by column chromatography ($CH_2Cl_2 \rightarrow$ 2 vol % EA in CH_2Cl_2) gave 141 mg of the product as a dark purple solid (5%): R_f (CH_2Cl_2/EA, 50/1) = 0.46; ^{1}H NMR ($CDCl_3$, 400 MHz, 27 °C) δ (ppm) = 8.74 (d, 2 H, ^3J = 4.5 Hz), 8.71 (s, 4 H, pyrrole-*H*), 8.50 (d, 2 H, ^3J = 4.5 Hz, pyrrole-*H*), 7.96 (d, 2 H, ^3J = 8.1 Hz, Ph-*m*-*H*), 7.45 (t, 1 H, ^3J = 8.1 Hz, Ph-*p*-*H*), 6.54 (s, 6 H, Ph-3,5-*H*), 4.07 (s, 9 H, Ph-OCH_3), 3.46 (s, 18H, Ph-OCH_3), −2.53 (s, 2H, N-*H*); MS (ESI) *m*/*z* = 1040 ([M + H]$^+$); HRMS (ESI) *m*/*z* = 1041.169917 (calcd 1041.170459 for $C_{53}H_{47}N_4O_9Br_2$).

Zinc 5-(2,6-Dibromophenyl)-10,15,20-(2,4,6-trimethoxyphenyl)porphyrin 1. A flask was charged with 152 mg (0.150 mmol) of $\mathbf{1}_{FB}$ dissolved in 80 mL of chloroform/methanol (1:1). Then, 167 mg (0.75 mmol) of zinc acetate dihydrate was added and the solution was stirred at 50 °C overnight, during which time a color change from wine red to pink was observed. The solvent was evaporated. The solution was washed with aq $NaHCO_3$ and water and dried over $MgSO_4$, and the solvent was removed in vacuo to yield 159 mg of a dark pink solid (95%): ^{1}H NMR ($CDCl_3$, 400 MHz, 27 °C) δ (ppm) = 8.78 (broad s, 6 H, pyrrole-*H*), 8.57 (broad s, 2 H, pyrrole-*H*), 7.98 (broad s, 2 H, 3,5-Ph-*H*), 7.43 (t, 1 H, ^3J = 8 Hz, 4-Ph-*H*), 6.56 (broad s, 6 H, 3,5-Ph-*H*), 4.08 (s, 9 H, 4-Ph-OCH_3), 3.50 (broad s, 18 H, 2,6-Ph-OCH_3); MS (ESI) *m*/*z* = 1103 ([M + H]$^+$), 1125 ([M + Na]$^+$), 1145 ([M + K]$^+$); HRMS (ESI) *m*/*z* = 1103.08360 (calcd 1103.083951 for $C_{53}H_{45}N_4O_9ZnBr_2$).

Zinc 5-(2,6-Bis(*N*-*tert*-butoxycarbonyl-*N*′-phenylhydrazino)-phenyl)-10,15,20-(2,4,6-trimethoxyphenyl)porphyrin 2. Under an argon atmosphere, a sealed tube was charged with 105 mg (0.095 mmol) of **1**, 75 mg (0.38 mmol) of 1-*tert*-butoxycarbonyl-1-phenylhydrazine,[19] 23 mg (0.114 mmol) of $Pd(OAc)_2$, 186 mg (0.57 mmol) of Cs_2CO_3, 0.23 mL (0.114 mmol) of tri-*tert*-butylphosphine solution (1 g in 10 mL toluene), and 4.5 mL of toluene. The mixture was stirred at room temperature for 30 min and was then heated to 110 °C for 5 h. After short filtration over Celite, using CH_2Cl_2 as the eluent, column chromatography (hexane/THF, 2/1) afforded 60 mg of the product as a purple solid (50%): R_f (THF/Hex, 2/1) = 0.56; ^{1}H NMR ($CDCl_3$, 300 MHz, 27 °C) δ (ppm) = 8.94 (s, 2 H, pyrrole-*H*), 8.82 (s, 6 H, pyrrole-*H*), 7.45 (t, 1 H, ^3J = 8.2 Hz, *p*-Ph-*H*), 7.23 (d, 4 H, Ph-*H*), 7.03 (t, 4 H, ^3J = 8.2 Hz, Ph-*H*), 6.85 (t, 2 H, ^3J = 7.2 Hz, Ph-*H*), 6.71 (d, 2 H, ^3J = 8.2 Hz, *m*-Ph-*H*), 6.55 (s, 2 H, Ph-*H*), 6.58 (s, 4 H, Ph-*H*), 4.11 (s, 6 H, Ph-OCH_3), 4.08 (s, 3 H, Ph-OCH_3), 3.49 (s, 12 H, Ph-OCH$_3$), 3.47 (s, 6 H, Ph-OCH_3), 1.29 (s, 18 H, Boc-*H*); MS (ESI) *m*/*z* = 1358 (M$^+$), 1381 ([M + Na]$^+$); HRMS (ESI) *m*/*z* = 1387.455675 (calcd 1381.455896 for $C_{75}H_{74}N_8O_{13}NaZn$).

Zinc 5-(2,6-Bis(phenylazo)phenyl)-10,15,20-(2,4,6-trimethoxyphenyl)porphyrin 3. Under an argon atmosphere, a flame-dried Schlenk tube was charged with 21 mg (0.016 mmol) of **2**, 27 mg (0.13 mmol) of CuI, 44 mg (0.13 mmol) of Cs_2CO_3, and 0.25 mL of dry DMF. The reaction mixture was heated at 140 °C for 4.5 h. Column chromatography (CH_2Cl_2/EA, 50/1) provided 9 mg of the product as a purple solid (49%): R_f (CH_2Cl_2/EA, 20/1) = 0.54; ^{1}H NMR (CD_3CN, 400 MHz, 27 °C) δ (ppm) = 8.64 (m, 4 H, Py-*H*) 8.58 (m, 4 H, Py-*H*), 8.20 (d, 2 H, ^3J = 8 Hz, Ph-*H*), 8.07 (t, 1 H, ^3J = 7.4 Hz, Ph-*H*), 6.91 (t, 2 H, ^3J = 7.3 Hz, Ph-*H*), 6.68 (m, 6 H, Ph-*H*), 6.59 (m, 8 H, Ph-*H*), 4.06 (s, 3 H, *p*-OCH_3), 4.01 (s, 6 H, *o*-OCH_3), 3.52 (s, 6 H, *p*-OCH_3), 3.40 (s, 12 H, o-OCH$_3$); MS (ESI) *m*/*z* = 1154 (M$^+$), 1177 ([M + Na]$^+$); HRMS (ESI): *m*/*z* = 1155.337316 (calcd 1155.337797 for $C_{65}H_{55}N_8O_9Zn$).

Crystal Structure Determination. Crystal data for **3**(CH_3CN): $[C_{67}H_{57}N_9O_9Zn]{\cdot}2.25[C_2H_3N]$, M = 1289.96, monoclinic, a = 16.481(2) Å, b = 27.466(4) Å, c = 14.888(2) Å, β = 103.509(6)°, U = 6553(2) Å^3, T = 100 K, space group $P2_1/c$ (No. 14), Z = 4, μ(Cu Kα) = 1.07 mm^{-1}, 19323 reflections measured, 2746 unique (R_{int} = 0.14), which were used in all calculations. Refinement on F_o^2. The final $R(F)$ = 0.0953 (1609 reflections $I > 2\sigma(I)$), w$R(F^2)$ = 0.2852 (all data). $\Delta\rho_{max/min}$ = 0.449/-0.359 eÅ^{-3}. A second crystal **3′**(CH_3CN) grown from acetonitrile/cyclohexane (reservoir) contained both solute acetonitrile and cyclohexane. Despite the slightly

(15) Due to experimental reasons, i.e., spectral overlap with the overtone band, low emission intensity, and residual porphyrin UV-absorption, the FRET efficiency could not be determined quantitatively.

(16) Although azobenzene is not fluorescent at room temperature, its emission spectrum has been determined; see: Fujino, T.; Arzhansev, S. Y.; Tahara, T. *J. Phys. Chem. A* **2001**, *105*, 8123−8129. The emission maximum is located around 390 nm, thereby exhibiting significant spectral overlap with the intense zinc porphyrin Soret band.

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different crystal environments the structures of the complex obtained under the two conditions are essentially similar (root-mean-square difference for non-H atoms: 0.2 Å).

Acknowledgment. We thank Professors Brent P. Krueger (Hope College), Gregory D. Scholes (University of Toronto), and Silvia E. Braslavsky (MPI for Bioinorganic Chemistry, Mülheim/Ruhr) for helpful discussions regarding energy and electron transfer. Generous support by the Sofja Kovalevskaja Program of the Alexander von Humboldt Foundation sponsored by the Federal Ministry of Education and Research and the Program for Investment in the Future (ZIP) of the German Government and the Max Planck Society (MPG) is gratefully acknowledged.

Supporting Information Available: General methods, crystallographic details, and copies of the ^{1}H NMR spectra including crystallographic information files (CIF) for **3**(CH_3CN) and **3′**(CH_3-CN). This material is available free of charge via the Internet at http://pubs.acs.org.

JO0612877