Phthalocyanine Analogues

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18π-Electron Tautomeric Benziphthalocyanine: A Functional Near-Infrared Dye with Tunable Aromaticity**

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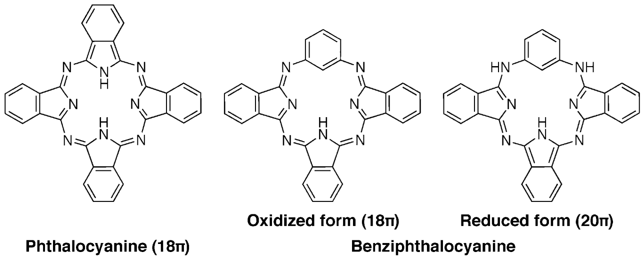
Abstract: *Dihydroxybenziphthalocyanine **1**, with bulky aryloxy groups, has been synthesized and characterized by X-ray crystallography, NMR and UV/Vis-NIR spectroscopy, and theoretical calculations. Macrocycle **1** is the first example of an aromatic benziphthalocyanine with an 18π-electron structure, and was found to exist as an equilibrium mixture of weakly aromatic and strongly aromatic tautomers. The aromaticity and near-IR absorption can be controlled by chemical modification at the reactive resorcinol moiety and by variation of the solvent.*

Phthalocyanines and their derivatives are an extremely important class of macrocycles and are utilized as key structural units and potent chromophores in many fields from material sciences to biology, for example as dyes and pigments for bioimaging, in photodynamic therapy, and in solar cells.[1] Hemiporphyrazines are a broad class of phthalocyanine derivatives in which 6π-electron aromatic rings replace two opposing isoindoline units.[2] Unlike 18π-electron aromatic phthalocyanines, most hemiporphyrazines do not display aromatic behavior. We recently synthesized a new type of hemiporphyrazine by incorporating two resorcinol moieties into the skeleton, and found that it could be oxidized to afford the first 18π-electron aromatic hemiporphyrazine.[3] Intriguingly, this hemiporphyrazine is a redox-switchable near-IR chromophore. Siri et al. recently used a similar strategy to prepare the first azacalixphyrin molecule with near-IR absorption.[4]

A phthalocyanine in which a single isoindoline is replaced with one benzene ring is known as benziphthalocyanine.[5] Although the first synthesis of benziphthalocyanine was achieved in 1957,[6] the electronic structure has not been established. There are two possible structural forms for benziphthalocyanine, an oxidized form (with an 18π-electron structure) and a reduced form (with a 20π-electron structure). Pioneering works by Ziegler and co-workers revealed that benziphthalocyanine with no peripheral substituents adopts exclusively the reduced 20π-electron form in the solid state.[7] Although benziporphyrins can adopt the oxidized form,[8] no 18π-electron aromatic form of benziphthalocyanines has been reported.



Recently, Ziegler and co-workers reported the synthesis and optical properties of dihydroxybenziphthalocyanine.[9] One redox-active resorcinol unit was incorporated into the skeleton, and the compound was found to have a 20π-electron nonaromatic structure in the solid state. This result, and our previously reported 18π-electron aromatic hemiporphyrazine containing two resorcinol units,[3] prompted speculation that the oxidized form would be formed by two-electron oxidation of the dihydroxybenziphthalocyanine.

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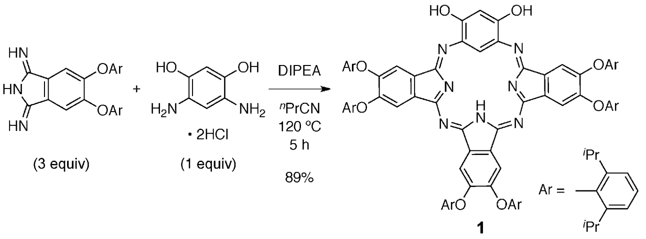
Herein, we report the synthesis and characterization of the first 18π-electron aromatic benziphthalocyanine. Given the absence of detailed NMR spectroscopic analysis and interpretation of dihydroxybenziphthalocyanine, we designed dihydroxybenziphthalocyanine with bulky aryloxy groups to increase the solubility. Surprisingly, under our experimental conditions, the peripherally substituted dihydroxybenziphthalocyanine **1** does not take the reduced form, instead taking exclusively the oxidized form. The 18π-electron benziphthalocyanine exists as two tautomers, one weakly aromatic and one strongly aromatic.

Scheme 1 shows the synthesis of **1**. The unsubstituted dihydroxybenziphthalocyanine was synthesized using a two-step method.[9] The desired macrocycle **1** was obtained in excellent yield in one step by mixing 3 equivalents of the 4,5-bis(2,6-diisopropylphenoxy)-1,3-diiminoisoindoline with 1 equivalent of 4,6-diaminoresorcinol dihydrochloride. Compound **1** is stable under ambient conditions, and is readily soluble in common organic solvents, such as chloroform, THF, ethyl acetate, hexane, toluene, and DMF.



Scheme 1. Synthesis of benziphthalocyanine **1**. DIPEA = *N,N*-diisopropylethylamine (Hünig's base).

Figure 1a shows the structure of **1** obtained by single-crystal X-ray diffraction analysis. The structure shows that benziphthalocyanine adopts the oxidized form and the resorcinol unit takes a quinone-like form, in which one resorcinol O–H proton transfers to the *meso*-nitrogen atom. There are two possible tautomers for the aromatic moiety of the 18π-electron benziphthalocyanine, a phenol form and a quinoidal form (see Figure 2a). The tetraazabenziporphyrin skeleton of **1** is planar, and the deviation from the averaged plane is within 0.14 Å. The C–N bond lengths in the macrocycle are similar to those in standard phthalocyanines.[1b] These bond lengths are significantly different from those of the unsubstituted dihydroxybenziphthalocyanine, in which two *meso* nitrogen atoms are protonated,[10] unambiguously demonstrating that **1** exists in the 18π-electron quinoidal form.

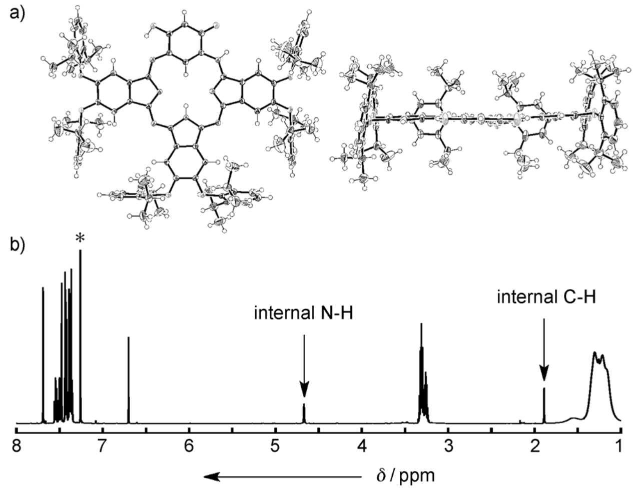


Figure 1. a) Single-crystal X-ray structure of **1**.[10] Thermal ellipsoids set at 50% probability. Solvent molecules have been omitted for clarity. b) ^{1}H NMR spectrum of **1** in CDCl$_3$ at room temperature. (*: residual CHCl$_3$ signal).

To investigate the structure in solution, the NMR spectrum of **1** in CDCl$_3$ was recorded.[10] The room temperature ^{1}H NMR spectrum of **1** is shown in Figure 1b. The NMR spectrum suggests that the structure is symmetric in nature, contrary to the unsymmetrical X-ray structure. This discrepancy may be explained by the possibility of fast exchange on the NMR timescale. Resonance signals for the external N–H or O–H protons were not detected at room temperature. The internal C–H and N–H protons were assigned to resonance signals in an upfield region of the spectrum, at $\delta = 1.89$ and 4.67 ppm, respectively, indicating the presence of a diatropic ring current in **1**. This result shows that **1** has phthalocyanine-like 18π-electron aromaticity. As signals for the internal N–H protons of octakis(2,6-diisopropylphenoxy)phthalocyanine are observed at $\delta = -0.84$ ppm,[11] the diatropic ring current effect of **1** is relatively weak.

To understand the origin of the weak diatropic ring current in **1**, nucleus-independent chemical shifts (NICS)[12] and ^{1}H chemical shifts of the two tautomers were calculated at the B3LYP/6-31+G(d) level (Figure 2a). In the quinoidal

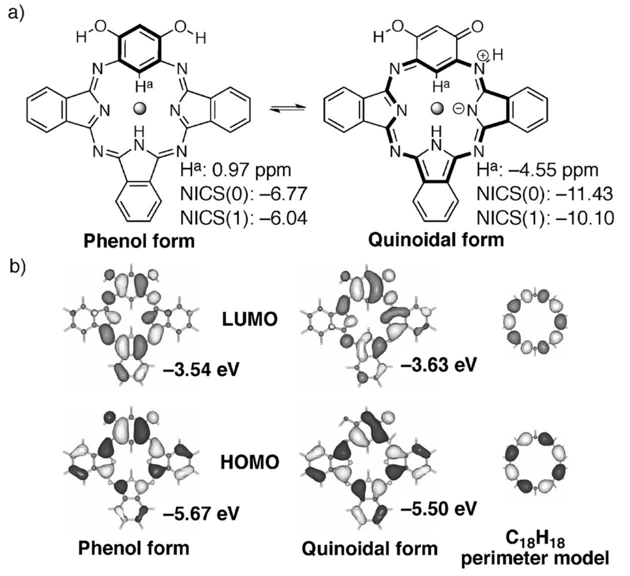


Figure 2. a) Calculated ^{1}H NMR chemical shifts and NICS for the optimized structure of the two oxidized forms of dihydroxybenziphthalocyanine at the B3LYP/6-31+G(d) level. b) Frontier molecular orbitals and energy levels of dihydroxybenziphthalocyanine. Isosurface plots for the molecular orbitals of the 18π-electron perimeter model are also shown.

form, the NICS(0) value and the chemical shift of the internal C–H proton (H^a) were estimated to be -11.43 and -4.55 ppm, respectively. This suggests a strongly aromatic character. In contrast, the phenol form, which has a cross-conjugated structure, has a weakly aromatic feature (NICS(0): -6.77 ppm; H^a: 0.97 ppm), in good agreement with the NMR measurement. The results of NICS(0) and NICS(1) calculations at other positions also suggested the different ring current effects.[10] Therefore, we consider that **1** exists in equilibrium between the phenol form (benzene system) and the quinoidal form (benzene-dearomatized system) in solution.[13] The quinoidal form was calculated to be slightly more stable than the phenol form by approximately 1 kcal mol^{-1}. Figure 2b shows molecular orbitals and energy levels for the two tautomers. The HOMO and LUMO of both forms were delocalized over the tetraazabenziporphyrin skeleton, and the nodal patterns of the frontier orbitals are similar to those of the 18π-electron perimeter model. The HOMO–LUMO energy gap of the quinoidal form was slightly smaller than that of the phenol form.

From the experimental results and computational analyses we conclude that peripherally substituted benziphthalocyanine **1** has an aromatic electron system. The 20π-electron-type of benziphthalocyanine was not observed. It was not possible to reduce the macrocycle of **1** using common reducing agents, such as $NaBH_4$ or hydrazine. Unexpectedly, there are two tautomers of 18π-electron benziphthalocyanine, the phenol form and the quinoidal form, which appear to exist in rapid equilibrium based on the preliminary NMR study and DFT calculations.

To obtain direct experimental evidence for the aromaticity of the phenol and quinoidal structures, a methylation reaction, in which ionizable external hydrogen atoms were replaced with methyl groups, was performed to capture the two tautomeric structures. Scheme 2 shows the methylation of **1** using MeI; various methylated derivatives were obtained.[10] Among the isolated methylation products, *O*-dimethylated compound **2** and *C*-dimethylated compound **3** exhibited significant changes in the 18π-electron aromaticity. The internal C–H proton of **2** has a resonance signal at $\delta = 5.78$ ppm, which suggests that its diatropic current is much weaker than that of **1**. The internal N–H proton resonance signal was not evident at room temperature. The diminished aromaticity of **2** is attributed to the fixed phenol form because of the two methyl groups on the resorcinol oxygen atoms. The chemical shift observed in **2** is comparable to that of dimethoxybenziporphyrin reported by Lash and co-workers.[14] The molecular structure of **2** was further confirmed by X-ray crystallographic analysis (Figure 3).[10] The tetraazabenziporphyrin skeleton was not planar because of the tilted dimethoxybenzene unit. Clear alternation of the bond lengths was observed in the skeleton. The calculations of NICS and ^{1}H chemical shifts using the X-ray geometry also suggested a significant decrease in aromaticity.[10] In contrast to **2**, compound **3** has two methyl groups on the central carbon atom. The methyl substituents break the benzene 6π-electron aromatic structure and force the macrocycle to take a fully conjugated 18π-electron structure, analogous to the quinoidal form of **1**. The internal C–H and N–H protons appeared at $\delta = -1.87$ and 0.53 ppm, respectively, which indicates a strong diatropic ring current effect. Other methylated compounds also showed changes in aromaticity.[10] These results strongly support the existence of the putative equilibrium of the phenol and quinoidal forms of **1**.

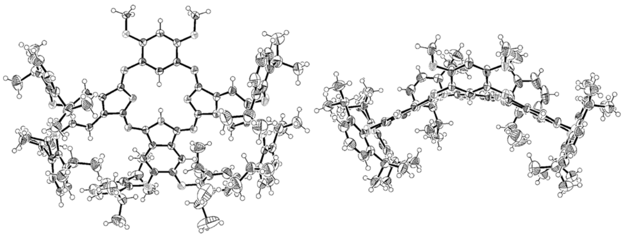
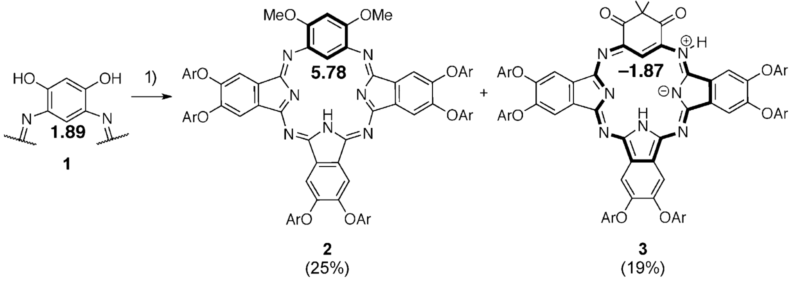


Figure 3. X-ray structure of **2**.[10] Thermal ellipsoids are set at 50% probability. Solvent molecules have been omitted for clarity.

Figure 4 shows the electronic absorption (from the UV to the near-IR region) and magnetic circular dichroism (MCD) spectra of *O*-dimethylated compound **2** and *C*-dimethylated compound **3**. It is evident that the peak position and extinction coefficient of the near-IR absorption bands depend strongly on the position of the methyl groups. In the case of *O*-dimethylated compound **2**, a weak and broad absorption band was observed in the $\lambda = 600$–700 nm region. The MCD intensity in this region was almost zero, showing that the electronic structure of **2** is significantly different to that of regular phthalocyanine derivatives.[15] In contrast, *C*-dimethylated compound **3** exhibited two intense absorption bands at $\lambda = 740$ and 648 nm. Since coupled Faraday *B* terms were observed for these bands in the MCD spectrum, the bands can be assigned to two split Q bands. Thus, these electronic transitions were attributed to π–π* transitions within porphyrinoids with an 18π-electron system.



Scheme 2. Structural characterization of compound **1** using a methylation reaction. Reagents and conditions: 1) MeI, K_2CO_3, DMF, room temperature, 28 h; measured chemical shifts (ppm) of internal C–H protons are shown in the macrocycles.

We measured the fluorescence spectra of **1**, **2**, and **3**.[10] Near-IR fluorescence was observed for **1** ($\lambda_{em} = 824$ nm; $\Phi_F = 0.011$) and **3** ($\lambda_{em} = 752$ nm; $\Phi_F = 0.0089$), whereas **2** did not exhibit detectable fluorescence.[10]

We then investigated whether the equilibrium could be disrupted intentionally to favor one of the tautomeric structures by application

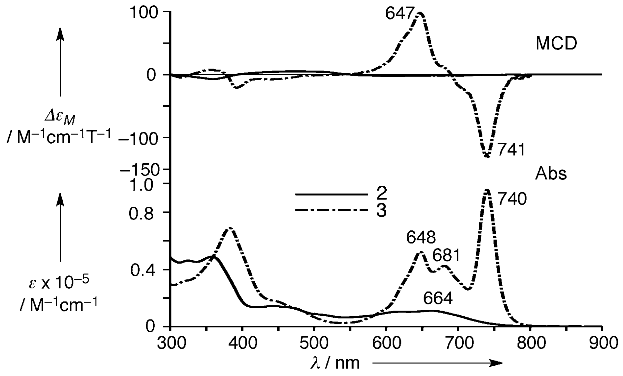
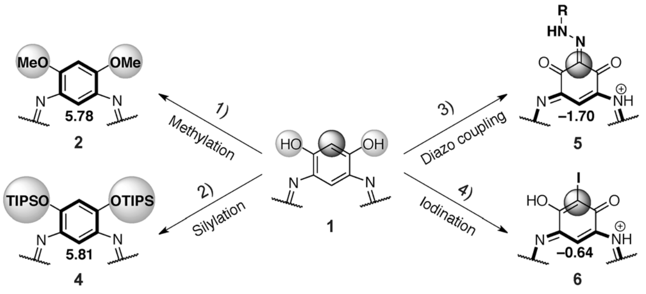


Figure 4. Top: MCD and bottom: electronic absorption spectra of **2** (solid line) and **3** (dashed line) in $CHCl_3$ at room temperature.

of external stimuli, for example, by chemical reaction at the resorcinol moiety or by changing solvents. The feasibility of site-selective chemical transformation to control aromaticity and to create functional chromophores was investigated (Scheme 3). The typical oxophilic Meerwein methylation and silylation reactions were selected. The oxygen atoms were selectively methylated in moderate yield using Meerwein's salt (trimethyloxonium tetrafluoroborate). On the other hand, triisopropylsilyl (TIPS) groups were introduced onto the oxygen atoms in 94% yield when **1** was treated with TIPSCl. The resonance signal for the internal C−H proton of **4** ($\delta = 5.81$ ppm) was almost the same as that of **2** (δ=5.78 ppm). Selective reaction at the carbon atom was demonstrated by a diazo coupling reaction which afforded **5** in moderate yield. As expected, the aromaticity of the product was as strong as that of *C*-dimethylated benziphthalocyanine **3**. Iodination with NIS (*N*-iodosuccinimide) at the carbon atom proceeded quantitatively within 15 minutes to form the iodo-substituted derivative **6**, which has the longest-wavelength absorption band ($\lambda = 831$ nm) among the derivatives examined.[10] The resonance signal for the internal C−H proton of **6** ($\delta = -0.64$ ppm) was at higher field compared with that of **1**.



Scheme 3. Selective functionalization of compound **1**. Reagents and conditions: 1) trimethyloxonium tetrafluoroborate, DIPEA, CH_2Cl_2, 0°C, 2 h, 35%; 2) TIPSCl, DIPEA, CH_2Cl_2, room temperature, 40 min, 94%; 3) 4-methoxybenzenediazonium tetrafluoroborate, DIPEA, DMF, 0°C, 30 min, 46%; 4) NIS, DIPEA, CH_2Cl_2, 0°C, 15 min, 99%; measured chemical shifts (ppm) of internal C−H protons are shown. NIS = *N*-iodosuccinimide.

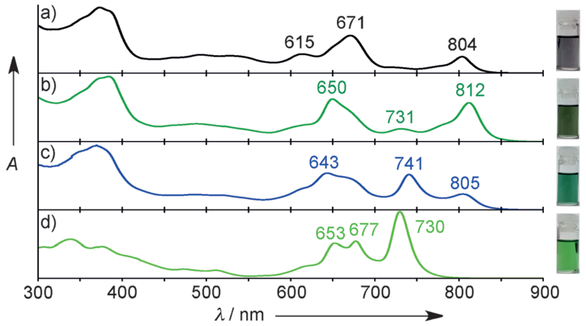


Figure 5. Electronic absorption spectra and photographs of **1** in toluene (a), $CHCl_3$ (b), EtOH (c), and DMF (d).

To study solvent effects on the tautomerism of the benziphthalocyanine, the electronic absorption spectra of dilute solutions (approximately 10^{-5} M) of **1** were measured. As seen in Figure 5, the position of the lowest-energy absorption maximum in the near-IR region varied significantly with the nature of the solvent ($\lambda = 812$ nm in $CHCl_3$; $\lambda = 730$ nm in DMF).[16] This solvatochromism can be attributed to the two tautomeric structures of **1**, since solvent effects are much weaker in regular phthalocyanines.[17]

In conclusion, the newly synthesized peripherally substituted dihydroxybenziphthalocyanine **1** is the first example of an aromatic benziphthalocyanine with an 18π-electron structure. Molecule **1** exists as a mixture of two tautomers, the weakly aromatic phenol form and the strongly aromatic quinoidal form. The electronic properties of the two tautomers were examined by fixing the structures with methyl groups. The nucleophilic resorcinol moiety reacts regioselectively with various electrophiles, providing a means to easily control the 18π-electron aromaticity and the near-IR absorption. Solvent effects can also be used to modulate the absorption of **1**. We believe that it will be possible to introduce various functional groups into this benziphthalocyanine, offering scope for the design of functional near-IR dyes. Further studies to create benziphthalocyanine-based near-IR dyes with ON/OFF switching functionality are underway, together with further spectroscopic and mechanistic investigations of this novel solvatochromic/tautomeric system.

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[16] Note, the spectral features of **1** in DMF were very similar to those of the unsubstituted dihydroxybenziphthalocyanine. This prompted us to reexamine the spectroscopic properties of the unsubstituted dihydroxybenziphthalocyanine (see Supporting Information). Our experimental results indicate that the intense visible/near-IR absorption bands observed for the unsubstituted dihydroxybenziphthalocyanine arise not from the 20π-electron reduced form, but rather from the 18π-electron oxidized form.

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