**β-Functionalization of 5,15-Diazaporphyrins with Phosphorus, Oxygen, and Sulfur-Containing Substituents**

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**Abstract**

The β-functionalization of 5,15-diazaporphyrins (DAPs) with phosphoryl, phenoxy, sulfanyl, and sulfonyl groups was achieved by either cross-coupling or aromatic nucleophilic substitution reactions of β-bromo- and β,β′-dibromo-DAPs. The heteroatom-containing functional groups at the β-positions strongly affected the redox properties of the DAP π-systems.

**Keywords:** Diazaporphyrin | β-Functionalization | Cross-coupling reaction

**1. Introduction**

5,15-Diazaporphyrins (DAPs) have received increasing attention as potential sensitizers for use in photodynamic therapy1 and organic solar cells2 because they exhibit intrinsically high light absorption in the long-wavelength visible region and strong electron-accepting ability. These characteristic properties of DAPs result from the D2h symmetry of their π-systems; both the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of DAPs are energetically stabilized compared with those of porphyrins, and the HOMO-to-LUMO excitation of DAPs is symmetrically allowed.3,4 To further develop DAP-based photo-functional materials, it is necessary to reveal the structure–property relationships of various types of peripherally functionalized DAPs as well as to establish general methods for their syntheses.

In the last six years, DAPs substituted with aryl,5 heteroaryl,6 alkyl,5b alkynyl,2a,7 nitro,6 and amino1b,8 groups at the β-positions have been synthesized from β-unsubstituted DAPs 1M or β-bromo-DAPs 2M (Chart 1). The optical, electrochemical, and magnetic properties of these DAPs strongly depend on the nature of the β-substituents. For example, the strongly electron-donating aryl, heteroaryl, and amino substituents endow the entire π-systems with excited states that show strong charge-transfer character. However, no DAPs with phosporus (P)-, oxygen (O)-, or sulfur (S)-containing functional groups at the β-positions have been reported, and the intrinsic effects of these heteroatom substituents on the fundamental properties of the DAP π-system have not been comprehensively studied.

Herein, we report the first examples of β-phosphoryl-, β-phenoxy-, β-sulfanyl-, and β-sulfonyl-DAPs, which are prepared by either cross-coupling or aromatic nucleophilic substitution (SNAr) reactions of β-bromo-DAPs. During the screening of the reaction conditions, we unexpectedly found that direct and multiple sulfonfylation at the β-C–H bonds of β,β′-dibromo-DAPs with excess sulfinate ions occurs to afford 18π 3,7,13,17-tetrasulfonyl-DAPs together with 20π 3,7,13,17-tetrasulfonyl-5,15-dihydro-DAPs.

**2. Results and Discussion**

First, we introduced P-, O-, and S-containing functional groups onto the 3-position of the DAP ring by cross-coupling or SNAr reactions of 3-Br-DAPs5 2M (M = Ni, Cu, H2; Ar = 2,4,6-Me3C6H2) (Scheme 1). Palladium-catalyzed C–P cross-coupling reactions of 2M with diethyl phosphite and diphenylphosphine oxide in toluene afforded the corresponding 3-phosphoryl-DAPs 3M and 4Ni, respectively, whereas SNAr reactions of 2M with phenol and p-toluenesulfonic acid in benzene formed 3-phenyl-DAPs 5M and 3-(p-toluenesulfonyl)-DAP 6Ni, respectively. Furthermore, SNAr
reaction of 2M with sodium $p$-toluenesulinate (TolSO$_2$Na) in DMF proceeded at room temperature to afford 3-($p$-toluenesulfonyl)-DAPs 7M as the major products.

In attempts to synthesize $\beta,\beta'$-disulfonyl-DAPs from a mixture of 3,13- and 3,17-dibromo-DAPs 8M (M = Ni, Cu) and TolSO$_2$Na, we unexpectedly found that direct sulfonylation occurred at two $\beta$-C–H positions of 8M. That is, heating a DMF solution containing 8M and excess TolSO$_2$Na at 80 °C resulted in the formation of 3,7,13,17-tetrasulfonyl-DAP 9M and 3,7,13,17-tetrasulfonyl-5,15-dihydro-DAP 10M (Scheme 2). When 2Ni was used instead of 8Ni, 9Ni was obtained in very low yield. It is therefore likely that at least two $\beta$-sulfonyl groups are necessary to facilitate direct substitution at the $\beta$-C–H positions of the DAP ring. A plausible mechanism for this reaction is shown in Scheme S1. The sulfinate ion bound to the unsubstituted $\beta$-carbon of the $\beta,\beta'$-disulfonyl-DAP through nucleophilic addition, and then the resulting anionic intermediate was oxidized by atmospheric dioxygen or $\beta$-sulfonylated 18π DAP. Similar addition-oxidation/disproportionation reactions occurred sequentially to yield 9M and 10M. Unlike 5,15-dihydro-DAPs (H$_2$DAPs) 11M reported by Shinokubo and co-workers (Chart 1, M = Ni, H$_2$),$^{15}$ 10M showed resistance to aerobic oxidation, implying that the four sulfonyl groups sufficiently stabilize the 20π H$_2$DAP ring (vide infra).

The new DAPs were characterized by $^1$H NMR spectroscopy, infrared (IR) spectroscopy, and high-resolution mass spectrometry. The structure of 9Ni was further elucidated by X-ray crystallography (Figure S1). The relative orientation of the 3/7/13/17-sulfonyl groups in 9Ni was found to be up/down/down/up. In the $^1$H NMR spectra, the signals from the peripheral protons at the 2-position of 5M (M = Ni, H$_2$) and 6Ni were shifted upfield, whereas those from the same protons of 3M (M = Ni, H$_2$), 4Ni, and 7Ni were shifted downfield, compared with the peaks from the corresponding $\beta$-protons of 1M. These spectral features clearly reflect the resonance and inductive effects of the neighboring heteroatom-containing substituents.

In the $^1$H NMR spectra of 9Ni and 10Ni in CDCl$_3$, the pyrrolic $\beta$-protons were observed as singlet peaks at $\delta$ = 9.31 and 5.33 ppm, respectively (Figure 1). In terms of the magnetic criterion, 9Ni and 10Ni have aromaticity and antiaromaticity, respectively. The signals from the $\beta$- and N–H protons of 10Ni were appreciably shifted downfield ($\Delta \delta = +1.5$–2.1 ppm for $\beta$- and +2.5 ppm for N–H protons) compared with those of the corresponding protons of 11Ni. These downfield shifts are probably caused by not only the electron-withdrawing effects of the adjacent sulfonyl groups but also intramolecular hydrogen-bonding interactions between the $\beta$-S=O and $\beta$-C–H/meso-N–H groups. In the IR spectrum of 10Ni (KBr), the deformation vibration of the N–H group was detected at $\nu$ = 1602 cm$^{-1}$.

To elucidate the effects of the heteroatom-containing substituents on the optical and redox properties of the DAP $\pi$-system, UV–vis absorption spectra and cyclic voltammograms of 3M–7M were measured in CH$_2$Cl$_2$ (Figures 2 and S2–S6, Table 1). As shown in Figure 2b, the absorption spectra of 9Ni and 10Ni in CH$_2$Cl$_2$ exhibited intense bands with absorption maxima of 618 and 550 nm, respectively.$^{11}$ Based on time-dependent density functional theory calculations on models of these materials, these two intense bands were assigned to the HOMO-to-LUMO and HOMO-to-LUMO+1 excitations for 9Ni and 10Ni, respectively (for details, see the Supporting Information). The spectral features of 10Ni resembled those of 11Ni$^{5}$ and 20π 5,10,15,20-tetraaryl-DAP.
Table 1. Selected optical and electrochemical data in CH₂Cl₂

<table>
<thead>
<tr>
<th>DAP</th>
<th>λ&lt;sub&gt;max&lt;/sub&gt; (nm)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>E (V)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>∆E (V)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
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<tr>
<td>1N&lt;sup&gt;b&lt;/sup&gt;</td>
<td>571</td>
<td>+0.80, −1.40, −2.02</td>
<td>2.20</td>
</tr>
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<td>1Cu&lt;sup&gt;b&lt;/sup&gt;</td>
<td>577</td>
<td>+0.77, −1.37, −1.95</td>
<td>2.14</td>
</tr>
<tr>
<td>1H&lt;sub&gt;2&lt;/sub&gt;</td>
<td>627</td>
<td>+0.87, −1.26, −1.83</td>
<td>2.13</td>
</tr>
<tr>
<td>3Ni</td>
<td>581</td>
<td>+0.89, −1.27, −1.67</td>
<td>2.16</td>
</tr>
<tr>
<td>3Cu</td>
<td>587</td>
<td>+0.88, −1.23, −1.63</td>
<td>2.11</td>
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<tr>
<td>3H&lt;sub&gt;2&lt;/sub&gt;</td>
<td>629</td>
<td>+0.97, −1.12 −1.56</td>
<td>2.09</td>
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<tr>
<td>4Ni</td>
<td>583</td>
<td>+0.90, −1.28, −1.79</td>
<td>2.18</td>
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<td>5Ni</td>
<td>581</td>
<td>+0.74, −1.40, −1.89</td>
<td>2.14</td>
</tr>
<tr>
<td>5Cu</td>
<td>581</td>
<td>+0.74, −1.37, −1.81</td>
<td>2.11</td>
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<tr>
<td>5H&lt;sub&gt;2&lt;/sub&gt;</td>
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<td>+0.81, −1.26, −1.72</td>
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<td>6Ni</td>
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<td>+0.70, −1.35, −1.78</td>
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<td>7Ni</td>
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<tr>
<td>7Cu</td>
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<td>+0.96, −1.14, −1.62</td>
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<td>9Ni</td>
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<td>1.96</td>
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<tr>
<td>9Cu</td>
<td>623</td>
<td>+1.32, −0.60, −1.21</td>
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</tr>
<tr>
<td>10Ni</td>
<td>550</td>
<td>+0.24, +0.57, −1.32</td>
<td>1.56</td>
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<tr>
<td>10Cu</td>
<td>545</td>
<td>+0.23, +0.52, −1.28</td>
<td>1.51</td>
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</table>

<sup>a</sup> The longest absorption maxima. <sup>b</sup> Redox potentials vs. ferrocene/ferrocinium with Bu₄NPF₆. <sup>c</sup> Electrochemical HOMO−LUMO gaps. <sup>d</sup> Data from ref. 5a. <sup>e</sup> Data from ref. 10.

The first oxidation and reduction potentials of 9Ni were considerably shifted to the positive side (∆E = +0.52 and +0.76 V, respectively) compared with the corresponding potentials of 1Ni, indicating that both the HOMO and LUMO levels of the DAP π-system were markedly stabilized by the four β-sulfonyle groups. The electron-withdrawing β-sulfonyle groups play crucial roles in providing not only high electrophilicity to the 18τ DAP ring in the direct sulfonation reaction but also resistance to aerobic oxidation of the 20τ H₂DAP ring.

Finally, we examined the ability of freebases 3H<sub>2</sub> and 5H<sub>2</sub> to generate singlet oxygen (¹O₂). Irradiation of a toluene solution containing a DAP dye and 1,3-diaphenylisobenzofuran (DPBF; a ¹O₂ quencher) using a xenon lamp through a band-pass filter (λ<sub>max</sub> = 540 nm) caused the amount of DPBF to decrease, which was monitored by UV−vis absorption spectroscopy (for details, see the Supporting Information). The chemically determined quantum yields of ¹O₂ generation were 92%−95%, which are comparable to that reported for 3,7,13,17-tetramethyl-2,8,12,18-tetrahexyl-DAP (92%).

3. Conclusion

We established convenient methods to introduce P-, O-, and S-containing functional groups onto the β-positions of a DAP ring through cross-coupling or SonAr reactions. In addition, we found that the regioselective and multiple sulfonylations of β,β'−dibromo-DAPs with sodium sulfide proceeded to afford 3,7,13,17-tetrasulfonyle-DAPs in both 18τ and 20τ (5,15−NH) forms. In contrast to the extremely air-sensitive β-unsubstituted counterparts, the β-sulfonlated 20τ 5,15-dihydro-DAPs showed resistance to aerobic oxidation. The electron-withdrawing sulfonyle groups not only enhanced the electrophilicity of the 18τ DAP ring but also energetically stabilized the 20τ H₂DAP ring. Furthermore, the phosphoryl- and β-phenoxyl-DAPs effectively generated ¹O₂ under visible-light irradiation. These results confirm that incorporating P-, O-, and S-containing functional groups at the periphery of the DAP ring is a promising approach to finely tune the redox properties of DAP π-systems. The further development of DAP-based dyes substituted with heteroatom-containing functional groups is now in progress.

4. Experimental

Preparation of 4Ni. A mixture of 2Ni (49.9 mg, 0.729 mmol), Cs₂CO₃ (25.6 mg, 0.0786 mmol), diphenylphosphine oxide (18 mg, 0.089 mmol), Pd(dba)₂ (3.4 mg, 5 mol%), rac-BINAP (4.6 mg, 10 mol%), and toluene (10 mL) was refluxed for 12.5 h. The mixture was then concentrated under reduced pressure to leave a solid residue, which was subjected to silica-gel column chromatography using hexane and AcOEt as eluents. The reddish purple fraction (R<sub>f</sub> = 0.45 in hexane/AcOEt = 3/2) was concentrated under reduced pressure to afford 4Ni as a reddish purple solid (45.0 mg, 77%).

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Supporting Information

Experimental and computational details, spectroscopic data, X-ray crystallographic data, and ¹H NMR spectra are available in the Supporting Information on http://dx.doi.org/10.1246/bcsj.20180123.

References

11 It was difficult to completely suppress the aerobic oxidation of 10M in solution, so their spectra showed the weak absorption bands due to trace amounts of 9M.