Short Article

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

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Chart 1. DAP derivatives **1M**, **2M**, **8M**, and **11M**.

Scheme 1. Synthesis of β-functionalized DAPs **3M**–**7M**.

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.

1. Introduction

5,15-Diazaporphyrins (DAPs) have received increasing attention as potential sensitizers for use in photodynamic therapy[1] and organic solar cells[2] 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 D_{2h} 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 photofunctional 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,[8] and amino[1b,8] groups at the β-positions have b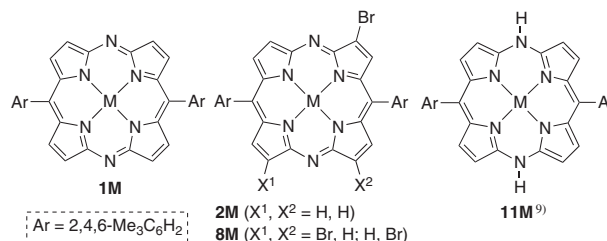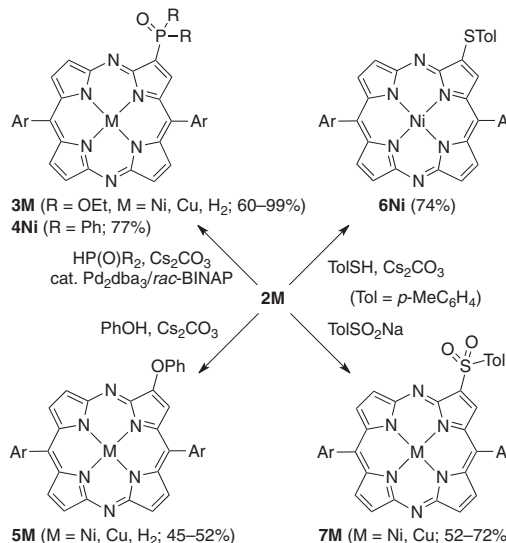een synthesized from β-unsubstituted DAPs **1M** or β-bromo-DAPs **2M** (Chart 1). The optical, electrochemical, and magnetic properties of these DAPs strongly depend on the nature of the β-substituents. For example, the strongly electron-donating aryl, heteroaryl, and amino substituents endow the entire π-systems with excited states that show strong charge-transfer character. However, no DAPs with phosphorus (*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 (S$_N$Ar) reactions of β-bromo-DAPs. During the screening of the reaction conditions, we unexpectedly found that direct and multiple sulfonylation 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 S$_N$Ar reactions of 3-Br-DAPs[7] **2M** (M = Ni, Cu, H$_2$; Ar = 2,4,6-Me$_3$C$_6$H$_2$) (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 S$_N$Ar reactions of **2M** with phenol and *p*-toluenethiol in the presence of cesium carbonate in *N*,*N*-dimethylformamide (DMF) gave 3-phenoxy-DAPs **5M** and 3-(*p*-toluenesulfanyl)-DAP **6Ni**, respectively. Furthermore, S$_N$Ar
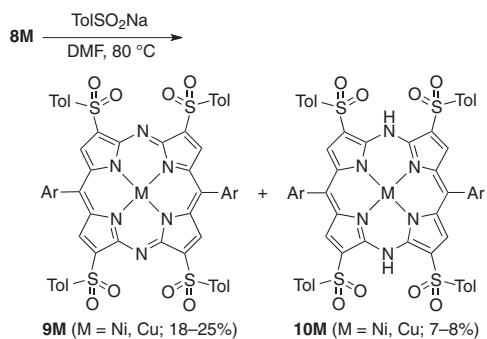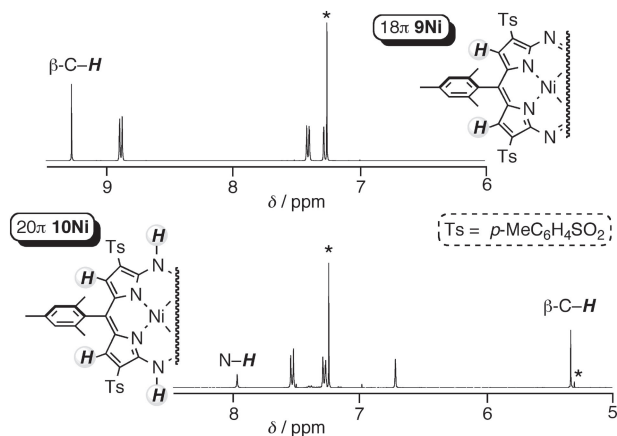
**Scheme 2.** Synthesis of tetrasulfonyl-DAPs **9M** and **10M**.

Figure 1. ^{1}H NMR spectra of **9Ni** (6–9.5 ppm) and **10Ni** (5–8.5 ppm) in CDCl$_3$. Asterisks indicate residual solvent peaks.

Figure 2. UV–vis absorption spectra of (a) **1Ni** and **4–7Ni** and (b) **9Ni** and **10Ni** in CH$_2$Cl$_2$.

reaction of **2M** with sodium p-toluenesulfinate (TolSO$_2$Na) in DMF proceeded at room temperature to afford 3-(p-toluenesulfonyl)-DAPs **7M** as the major products.

In attempts to synthesize β,β'-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 β-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 β-sulfonyl groups are necessary to facilitate direct substitution at the β-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 β-carbon of the β,β'-disulfonyl-DAP through nucleophilic addition, and then the resulting anionic intermediate was oxidized by atmospheric dioxygen or β-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$_2$),[9] **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 β-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 β-protons were observed as singlet peaks at δ = 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 β- and N–H protons of **10Ni** were appreciably shifted downfield ($\Delta\delta$ = +1.5–2.1 ppm for β, +2.5 ppm for N–H protons) compared with those of the corresponding protons of **11Ni**.[9] 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 β-S=O and β-C–H/*meso*-N–H groups. In the IR spectrum of **10Ni** (KBr), the deformation vibration of the N–H group was detected at ν = 1602 cm^{-1}.
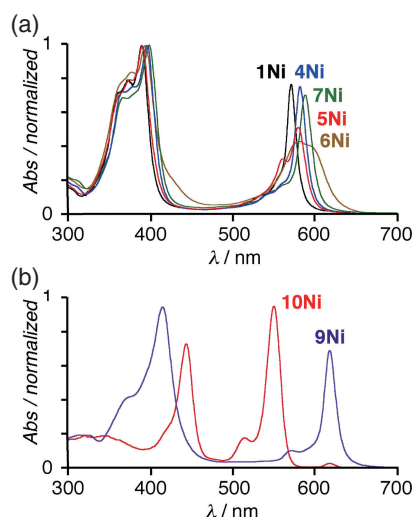
To elucidate the effects of the heteroatom-containing substituents on the optical and redox properties of the DAP π-system, UV–vis absorption spectra and cyclic voltammograms of **3M**–**7M** were measured in CH$_2$Cl$_2$ (Figures 2 and S2–S6, Table 1). As shown in Figure 2a, the Q bands of the 3-substituted DAPs were slightly red-shifted compared with those of **1M**.[5a,10] The redox potentials of **3M**, **4Ni**, and **7M** were shifted to the positive side, whereas those of **5M** and **6Ni** were slightly shifted to the negative side, compared with those of **1M**. These potential shifts reflect the electron-withdrawing (**3**, **4**, and **7**) and electron-donating (**5** and **6**) effects of the corresponding β-substituents. The HOMO–LUMO gaps of **3M**–**7M** determined from cyclic voltammetry were appreciably smaller than those of **1M** and consistent with the HOMO–LUMO gaps deduced from their absorption spectra. 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**[9] and 20π 5,10,15,20-tetraaryl-DAP

Table 1. Selected optical and electrochemical data in CH_2Cl_2

DAP	λ_{max} (nm)[a]	E (V)[b]	ΔE (V)[c]
1Ni[d]	571	+0.80, −1.40, −2.02	2.20
1Cu[d]	577	+0.77, −1.37, −1.95	2.14
1H$_2$[e]	627	+0.87, −1.26, −1.83	2.13
3Ni	581	+0.89, −1.27, −1.67	2.16
3Cu	587	+0.88, −1.23, −1.63	2.11
3H$_2$	629	+0.97, −1.12 −1.56	2.09
4Ni	583	+0.90, −1.28, −1.79	2.18
5Ni	581	+0.74, −1.40, −1.89	2.14
5Cu	581	+0.74, −1.37, −1.81	2.11
5H$_2$	631	+0.81, −1.26, −1.72	2.07
6Ni	582	+0.70, −1.35, −1.78	2.05
7Ni	589	+0.98, −1.15, −1.65	2.13
7Cu	595	+0.96, −1.14, −1.62	2.10
9Ni	618	+1.32, −0.64, −1.23	1.96
9Cu	623	+1.32, −0.60, −1.21	1.92
10Ni	550	+0.24, +0.57, −1.32	1.56
10Cu	545	+0.23, +0.52, −1.28	1.51

a) The longest absorption maxima. b) Redox potentials vs. ferrocene/ferrocenium with Bu_4NPF_6. c) Electrochemical HOMO–LUMO gaps. d) Data from ref. 5a. e) Data from ref. 10.

derivatives.[12] The first oxidation and reduction potentials of **9Ni** were considerably shifted to the positive side ($\Delta E = +0.52$ 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-sulfonyl groups. The electron-withdrawing β-sulfonyl groups play crucial roles in providing not only high electrophilicity to the 18π DAP ring in the direct sulfonylation reaction but also resistance to aerobic oxidation of the 20π H$_2$DAP ring.

Finally, we examined the ability of freebases **3H$_2$** and **5H$_2$** to generate singlet oxygen ($^1O_2$). Irradiation of a toluene solution containing a DAP dye and 1,3-diphenylisobenzofuran (DPBF; a $^1O_2$ quencher) using a xenon lamp through a band-pass filter ($\lambda_{ex} = 540$ 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 $^1O_2$ generation were 92%–95%, which are comparable to that reported for 3,7,13,17-tetramethyl-2,8,12,18-tetrahexyl-DAP (92%).[1a]

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 S_NAr reactions. In addition, we found that the regioselective and multiple sulfonylations of β,β′-dibromo-DAPs with sodium sulfinate proceeded to afford 3,7,13,17-tetra-sulfonyl-DAPs in both 18π and 20π (5,15-NH) forms. In contrast to the extremely air-sensitive β-unsubstituted counterparts, the β-sulfonylated 20π 5,15-dihydro-DAPs showed resistance to aerobic oxidation. The electron-withdrawing sulfonyl groups not only enhanced the electrophilicity of the 18π DAP ring but also energetically stabilized the 20π H$_2$DAP ring. Furthermore, the β-phosphoryl- and β-phenoxy-DAPs effectively generated $^1O_2$ 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), Cs_2CO_3 (25.6 mg, 0.0786 mmol), diphenylphosphine oxide (18 mg, 0.089 mmol), Pd_2dba_3 (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 on silica-gel column chromatography using hexane and AcOEt as eluents. The reddish purple fraction ($R_f = 0.45$ in hexane/AcOEt = 3/2) was concentrated under reduced pressure to afford **4Ni** as a reddish purple solid (45.0 mg, 77%).

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.

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