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SYNTHESIS OF DIARYL ETHER-LINKED PORPHYRIN DIMERS VIA ULLMANN COUPLING REACTION

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Abstract – Diaryl ether-linked porphyrin dimers were synthesized by CuI-catalyzed Ullmann coupling reaction between 5-(4-hydroxyphenyl)-10,15,20-triphenylporphyrin and 5-(4-iodophenyl)-10,15,20-triphenylporphyrin as well as their metalated derivatives.

Covalently linked porphyrin dimers and multi-porphyrinic molecules have been attracting continuous attention these years for their applications as biomimetic models of energy and electron transfers,¹ photonic materials,² and functional molecular devices.³ Efforts have been devoted to exploit a variety of covalent linkages for the connection of porphyrin components,⁴ because the overall properties of the porphyrin arrays strongly depend on the nature and position of the linker. The diaryl ether structural unit is an attractive linker which plays an important role in numerous synthetically challenging and biologically active chemicals.⁵ It also provides a rigid skeleton for specific orientation of connected components. However, in contrast to the large numbers of porphyrin dimers with ester and amide linkages, diaryl ether-linked porphyrin dimers have not been reported.

Copper-catalyzed Ullmann coupling between an aryl iodide or bromide and a phenol has been extensively used for the formation of diaryl ethers.⁶ Although recent progress has been made in efficient palladium-catalyzed functionalization of porphyrins,⁷ which usually involves the use of sophisticated phosphines as the ligands, copper catalysts still hold the advantage of availability and low cost. In the present study, porphyrins with *para*-hydroxyphenyl and *para*-iodophenyl substituents were employed for CuI-catalyzed Ullmann coupling, leading to a series of diaryl ether-linked porphyrin dimers. Figure 1 shows the structures of the starting porphyrins (**1**) and (**2**). Free base porphyrins (**1-Fb**) and (**2-Fb**) were prepared from 5-(4-aminophenyl)-10,15,20-triphenylporphyrin⁸ via routine diazotization conversions.⁹ Metalated porphyrin precursors shown in Figure 1 were obtained by the metalation¹⁰ of **1-Fb** and **2-Fb** accordingly.

remaining porphyrin substrates were found to convert to the copper chelates completely. Corresponding couplings of the nickel porphyrin (**2-Ni**) (Entry 3) and (**1-Ni**) (Entry 4) were found to give **3-NiOP** in relative low yields compared with those of the free base porphyrins.

Table 1 CuI-catalyzed Ullmann Coupling of Porphyrins with Phenol and Iodobenzene^a

Entry	Substrate 1	Substrate 2	Product	Yield(%) ^b
1	PhOH	2-Fb	3-CuOP	44
2	1-Fb	PhI	3-CuOP	40
3 ^c	PhOH	2-Ni	3-NiOP	37
4 ^c	1-Ni	PhI	3-NiOP	31

^a Reactions were carried out in dioxane (2 mL) under N₂ with CuI (0.1 mmol), Cs₂CO₃ (0.2 mmol), Me₂NCH₂CO₂H·HCl (0.05 mmol), Substrate 1 (0.05 mmol), Substrate 2 (0.05 mmol) at 100 °C for 20 h. ^b Isolated yield. ^c CuI (0.05 mmol).

On the basis of the above outcomes, the coupling reactions were carried out among porphyrins **1** and **2**. Each reaction was examined through its isolated yield of the porphyrin dimer. The results are summarized in Table 2. It was noted that coupling of free base porphyrins (**1-Fb**) and (**2-Fb**) gave **3-CuOCu** in the yield of 45%, whereas copper porphyrins (**1-Cu**) and (**2-Cu**) gave the same product in a lower yield of 31% (Entries 1 and 2). To make a close investigation, the coupling reactions were conducted for a short period of 3 h during which the copper insertion was found to be nearly complete with TLC detection. The coupling yields of the above two pairs of porphyrin substrates were 17% and 5%, respectively, indicating their differences in coupling reactivity existed mainly in the first 3 h of the reaction.

Table 2 CuI-catalyzed Ullmann Coupling of Porphyrin Substrates^a

Entry	Substrate 1	Substrate 2	Product	Yield(%) ^b
1 ^c	1-Fb	2-Fb	3-CuOCu	45 (17 ^c)
2	1-Cu	2-Cu	3-CuOCu	31 (5 ^c)
3	1-Zn	2-Zn	3-ZnOZn	16
4	1-Ni	2-Ni	3-NiONi	trace
5 ^d	1-Fb	2-Ni	3-NiOCu	15
6 ^d	1-Ni	2-Fb	3-NiOCu	21
7	1-Zn	2-Ni	3-NiOZn	10
8	1-Ni	2-Zn	3-NiOZn	12

^a Reactions were carried out in dioxane (2 mL) under N₂ with CuI (0.05 mmol), Me₂NCH₂CO₂H·HCl (0.1 mmol), Cs₂CO₃ (0.3 mmol), Substrate 1 (0.05 mmol), Substrate 2 (0.05 mmol) at 100 °C for 20 h. ^b Isolated yield. ^c CuI (0.15 mmol). ^d CuI (0.1 mmol). ^e for 3 h.

Zinc and nickel porphyrins (**1-Zn**), (**2-Zn**), (**1-Ni**), (**2-Ni**) were also employed for the coupling, affording the corresponding dimers (**3-ZnOZn**) and (**3-NiONi**) (Table 2, Entries 3 and 4). No scrambling of the metalated porphyrin sites was observed during the coupling reaction at 100 °C over days. In comparison to copper porphyrins, zinc and nickel porphyrins showed much lower reactivity toward the coupling

reaction. Especially for the coupling of **1-Ni** with **2-Ni**, only a trace of product was found due to extremely low conversion.

Among covalently linked porphyrin arrays, the preparation of mixed-metal porphyrin arrays has been a challenge for chemists.¹³ To expand our method, the coupling of porphyrins with different central metal ions was tested. Ni^{II}-Cu^{II} and Ni^{II}-Zn^{II} hybrid porphyrin dimers were obtained in yields of 10–20% (Table 2, entries 5-8). Figure 3 displays the UV-vis spectra of **3-NiOZn** and its component porphyrins (**1-Ni**) and (**1-Zn**). In comparison with its monomers, the dimer exhibited a red shift of 2–5 nm in the Soret band, and a broad absorption in the Q band which covers the Q bands of **1-Ni** and **1-Zn** at 529 and 548 nm, respectively. Similar features were observed for **3-NiOCu**. The absorption properties of the dimers were in accord with the out-of-plane structure of the diaryl ether unit which prevents efficient π -orbital overlap between porphyrin rings.

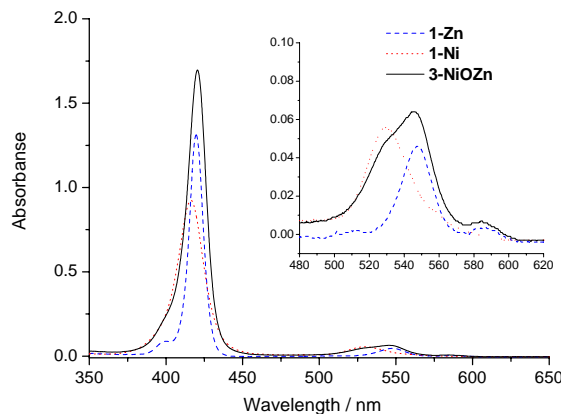


Figure 3 Absorption spectra of **1-Ni**, **1-Zn** and **3-NiOZn** in CHCl_3

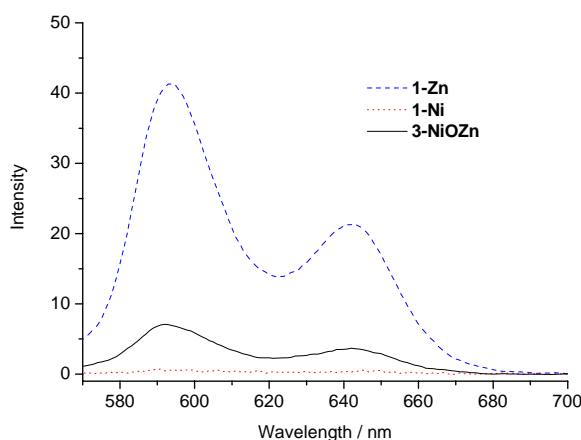


Figure 4 Fluorescence emission spectra of **1-Ni**, **1-Zn** and **3-NiOZn** in CHCl_3 at $2 \mu\text{M}$ with excitation at 548 nm

The structure of the hybrid porphyrin dimer was further confirmed by the emission spectrum. As shown in Figure 4, excitation of **1-Ni**, **1-Zn** and **3-NiOZn** in the same condition gave completely different

fluorescence emissions. The emission of **1-Ni** was extremely weak as reported,¹⁴ while **1-Zn** gave emission peaks at 594 and 642 nm. It can be found that the fluorescence intensity of **3-NiOZn** was only about 17% of that of **1-Zn**, indicating the inner Ni^{II}-porphyrin efficiently quenches the fluorescence of the inner Zn^{II}-porphyrin moiety. This result has been ascribed to the photoinduced intramolecular energy and/or electron transfer in porphyrin dimmers and arrays.^{13,15}

In summary, a facile synthesis of diaryl ether-linked porphyrin dimers, including mixed-metal porphyrin dimers, via a CuI-catalyzed Ullmann coupling reaction has been developed. The method is applicable to construct novel porphyrin arrays with metalated sites in a predictable manner.

EXPERIMENTAL

Dioxane was refluxed over sodium benzophenone and distilled under nitrogen. CuI, Cs₂CO₃ and Me₂NCH₂CO₂H·HCl were commercially available and used without further purification. 5-(4-hydroxyphenyl)-10,15,20-triphenylporphyrin (**1-Fb**) and 5-(4-iodinphenyl)-10,15,20-triphenylporphyrin (**2-Fb**) were prepared by routine diazotization conversions of 5-(4-aminophenyl)-10,15,20-triphenylporphyrin as described previously.⁹ Metalated porphyrins (**1-Zn**), (**2-Zn**), (**1-Ni**), (**2-Ni**), (**1-Cu**), and (**2-Cu**) were obtained from their corresponding free base porphyrins according to the method described in literature.¹⁰ Precoated silica gel plates (HGF254) were used for analytical TLC, and silica gel (G60, 200-300 mesh) were used for column chromatography. ¹H NMR spectra were measured on a Bruker ADVANCE DMX500 spectrometer with TMS as internal standard. UV-Vis spectra were recorded with an Analytikjena SPECORD 2000 spectrometer. ESI mass spectra were obtained on Bruker esquire 3000 Plus with Bruker Daltonics Data Analysis 3.0 instrument. Elemental analysis was performed at a Carlo Erba 1110 CHN Analyzer.

General procedures of the coupling reaction. All the coupling reactions were carried out with the detailed conditions noted in Table 1 and 2. A mixture of CuI, Cs₂CO₃, Me₂NCH₂CO₂H·HCl and two coupling substrates was stirred in dioxane under nitrogen atmosphere at 100 °C for 20 h. After cooling to room temperature, the mixture was diluted with ice water and then filtrated, the solid was dissolved in chloroform, washed with water for 3 times and concentrated to dryness. The crude product was purified by silica gel chromatography.

3-CuOP (Table 1, Entry 1). The general coupling reaction procedure was used to couple phenol (5mg, 0.05mmol) with **2-Fb** (37 mg, 0.05mmol), using CuI (20mg, 0.1mmol), Cs₂CO₃ (66mg, 0.2mmol), Me₂NCH₂CO₂H·HCl (7mg, 0.05mmol). The reaction was conducted in dioxane at 100 °C for 20 h. The title compound was isolated by silica gel chromatography (hexanes:CHCl₃ (v/v) = 5:2) as a red solid (17mg, 44%). mp > 300°C (decomp); UV-vis (CHCl₃, λ_{max}, nm): 540, 416; MS (ESI): *m/z* 767.3 [M]⁺; Anal. Calcd for C₅₀H₃₂N₄OCu: C 78.16, H 4.20, N 7.29. Found: C 78.24, H 4.21, N 7.26.

3-NiOP (Table 1, Entry 3). The general coupling reaction procedure was used to couple phenol (5mg, 0.05mmol) with **2-Ni** (40 mg, 0.05mmol), using CuI (10mg, 0.05mmol), Cs₂CO₃ (50mg, 0.15mmol), Me₂NCH₂CO₂H·HCl (7mg, 0.05mmol). The reaction was conducted in dioxane at 100 °C for 20 h. The title compound was isolated by silica gel chromatography (hexanes:CHCl₃ (v/v) = 5:2) as a red solid (14 mg, 37%). mp > 300°C (decomp); UV-vis (CHCl₃, λ_{max}, nm): 530, 416; ¹H NMR (CDCl₃) δ 8.82 (d, *J* = 4.90, 2H), 8.78 (d, *J* = 4.91, 2H), 8.76 (s, 4H), 8.03 (d, *J* = 6.44, 6H) 7.98 (d, *J* = 8.30, 2H), 7.69-7.72 (m, 9H), 7.49 (t, *J* = 8.03, 2H), 7.27-7.34 (m, 4H), 7.23-7.24 (m, 1H); MS (ESI): *m/z* 762.2 [M]⁺; Anal. Calcd for C₅₀H₃₂N₄ONi: C 78.65, H 4.22, N 7.34. Found: C 78.77, H 4.20, N 7.31.

3-CuOCu (Table 2, Entry 1). The general coupling reaction procedure was used to couple **2-Fb** (38mg, 0.05mmol), with **1-Fb** (32mg, 0.05mmol), using CuI (29mg, 0.15mmol), Cs₂CO₃ (100mg 0.3mmol), Me₂NCH₂CO₂H·HCl (14mg 0.1mmol). The reaction was conducted in dioxane at 100 °C for 20 h. The title compound was isolated by silica gel chromatography (hexanes:CHCl₃ (v/v) = 5:2) as a red solid (31mg, 45%). mp > 300°C (decomp); UV-vis (CHCl₃, λ_{max}, nm): 539, 417. MS (ESI): *m/z* 1364.3 [M]⁺; Anal. Calcd for C₈₈H₅₄N₈OCu₂: C 77.35, H 3.98, N 8.20. Found: C 77.51, H 4.00, N 8.18.

3-ZnOZn (Table 2, Entry 3). The general coupling reaction procedure was used to couple **2-Zn** (40 mg, 0.05mmol) with **1-Zn** (35mg, 0.05mmol), using CuI (10mg, 0.05mmol), Cs₂CO₃ (66mg, 0.2mmol), Me₂NCH₂CO₂H·HCl (14mg 0.1mmol). The reaction was conducted in dioxane at 100 °C for 20 h. The title compound was isolated by silica gel chromatography (hexanes:CHCl₃ (v/v) = 1:1) as a red solid (11mg, 16%). mp > 300°C (decomp); UV-vis (CHCl₃, λ_{max}, nm): 586, 548, 421; ¹H NMR (CDCl₃) δ 9.10 (d, *J* = 4.5, 4H), 9.00 (d, *J* = 4.5, 4H), 8.96 (s, 8H), 8.34 (d, *J* = 7.9, 4H), 8.24 (d, *J* = 5.15, 12H), 7.75 (d, *J* = 7.00, 22H); MS (ESI): *m/z* 1366.4 [M]⁺; Anal. Calcd for C₈₈H₅₄N₈OZn₂: C 77.14, H 3.97, N 8.18. Found: C 77.41, H 4.00, N 8.15.

3-NiOCu (Table 2, Entry 5). The general coupling reaction procedure was used to couple **2-Ni** (40 mg, 0.05mmol) with **1-Fb** (32mg, 0.05mmol), using CuI (20mg, 0.1mmol), Cs₂CO₃ (84mg, 0.25mmol), Me₂NCH₂CO₂H·HCl (14mg 0.1mmol). The reaction was conducted in dioxane at 100 °C for 20 h. The title compound was isolated by silica gel chromatography (hexanes:CHCl₃ (v/v) = 5:2) as a red solid (10mg, 15%). mp > 300°C (decomp); UV-vis (CHCl₃, λ_{max}, nm): 537, 417; MS (ESI): *m/z* 1359.4 [M]⁺; Anal. Calcd for C₈₈H₅₄N₈OCuNi: C 77.62, H 4.00, N 8.23. Found: C 77.75, H 3.98, N 8.21.

3-NiOZn (Table 2, Entry 7). The general coupling reaction procedure was used to couple **2-Ni** (40 mg, 0.05mmol) with **1-Zn** (35mg, 0.05mmol), using CuI (10mg, 0.05mmol), Cs₂CO₃ (66mg, 0.2mmol), Me₂NCH₂CO₂H·HCl (14mg 0.1mmol). The reaction was conducted in dioxane at 100 °C for 20 h. The title compound was isolated by silica gel chromatography (hexanes:CHCl₃ (v/v) = 2:1) as a red solid (7mg, 10%). mp > 300°C (decomp); UV-vis (CHCl₃, λ_{max}, nm): 585, 545, 420; ¹H NMR (CDCl₃) δ 9.10 (d, *J* = 4.44, 2H), 9.01 (d, *J* = 4.44, 2H), 8.97 (s, 4H), 8.91 (d, *J* = 4.86, 2H), 8.82 (d, *J* = 4.87, 2H), 8.77

(s, 4H), 8.33 (d, $J = 8.12$, 2H), 8.25 (s, 6H), 8.15 (d, $J = 8.17$, 2H), 8.04 (t, $J = 5.65$, 6H), 7.75-7.78 (m, 11H), 7.66-7.72 (m, 11H); MS (ESI): m/z 1360.4 $[M]^+$; Anal. Calcd for $C_{88}H_{54}N_8ONiZn$: C 77.52, H 3.99, N 8.22. Found: C 77.61, H 3.97, N 8.19.

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