Porphyrinoids

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Facile Peripheral Functionalization of Porphyrins by Pd-Catalyzed [3+2] Annulation with Alkynes[**]

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The electronic nature of a porphyrin ring is susceptible to modifications through the introduction of fused π-conjugated segments at the periphery.[1] This feature has been employed as a strategy for the creation of a variety of conjugated porphyrin systems that exhibit unique optical and electrochemical properties and which are expected to have applications in various types of functional materials. However, the introduction of such fused π systems on porphyrins often requires laborious multistep synthesis and suffers from frustratingly low yields. It is clear that novel and direct transformations of porphyrins are needed for further development of this area.[2]

A few transition-metal-catalyzed cross-coupling reactions, such as the Sonogashira and Suzuki–Miyaura reactions, have been successfully applied to porphyrins.[3] However, application of modern transition-metal-catalyzed reactions to porphyrin synthesis is still limited. We envisaged that a carbon–carbon bond-forming reaction of meso-bromoporphyrins with alkynes by carbopalladation[4] would be useful in generating a new molecular entity. We report herein an efficient way to incorporate a fused cyclopentadiene moiety into porphyrins such that the porphyrin π system is significantly perturbed. The wide scope of this procedure offers us rapid access to a diverse range of functionalized porphyrins. In addition, this cross-annulative coupling reaction allows a modular approach to a fascinating π system, namely, 7,8-dehydropurpurin.[5–7]

A mixture of 5-bromo-10,20-bis(3,5-di-*tert*-butylphenyl)porphyrinnickel(II) (**1**; $\mathrm{M}=\mathrm{Ni}$) and diphenylacetylene (1.2 equiv) in 1,4-dioxane was heated at reflux in the presence of a catalytic amount of $\mathrm{Pd(OAc)_2/Ph_3P}$ and $\mathrm{K_2CO_3}$. We found

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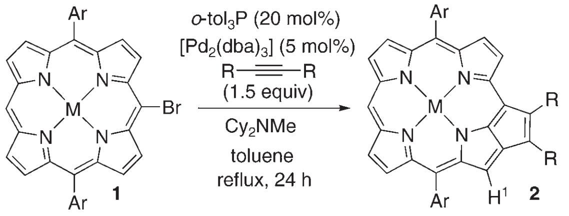


Scheme 1. Pd-catalyzed [3+2] annulation of porphyrin with alkynes. Cy = cyclohexyl, dba = *trans*,*trans*-dibenzylideneacetone, tol = tolyl.

Table 1: Pd-catalyzed [3+2] annulation of porphyrin with alkynes.[a]

Entry	R	M	Product	Yield (%)
1	Ph	Ni	**2a** (M = Ni)	78
2	4-CF$_3$(C$_6$H$_4$)	Ni	**2b** (M = Ni)	81
3	4-MeO(C$_6$H$_4$)	Ni	**2c** (M = Ni)	78
4	2-thienyl	Ni	**2d** (M = Ni)	82
5	*n*Pr	Ni	**2e** (M = Ni)	85
6	Ph	Cu	**2a** (M = Cu)	87
7	*n*Pr	Cu	**2e** (M = Cu)	86
8	Ph	Zn	**2a** (M = Zn)	79
9	4-CF$_3$(C$_6$H$_4$)	Zn	**2b** (M = Zn)	78
10[b]	4-MeO(C$_6$H$_4$)	Zn	**2f** (M = Zn)	69

[a] Reaction conditions: [Pd$_2$(dba)$_3$] (1.5 μmmol), *o*-tol$_3$P (6.0 μmmol), meso-bromoporphyrin (30 μmmol), alkyne (45 μmmol), Cy$_2$NMe (0.15 mmol), toluene (1.5 mL), reflux, and 16–24 h. Ar = 3,5-di-*tert*-butylphenyl. [b] Ar = 3,5-dioctyloxyphenyl.

that dehydropurpurin **2a** (M = Ni, R = Ph) was formed in 10% yield along with the debrominated porphyrin (Scheme 1). The parent mass ion peak of **2a** (M = Ni) was observed at m/z 918.4136 (calcd for $[C_{62}H_{60}N_4Ni]^+ = 918.4166$ $[M]^+$) in its high-resolution electrospray-ionization time-of-flight (HRESI-TOF) mass spectrum. ^{1}H NMR and H-H COSY spectra of **2a** (M = Ni) showed the presence of seven pyrrolic β protons: six doublets and one singlet ($\delta = 7.36$ ppm) appear, and the singlet can be assigned as H^1 (see the Supporting Information). After extensive optimization, the catalyst system comprising [Pd$_2$(dba)$_3$]/tris(*o*-tolyl)phosphine and dicyclohexylmethylamine in toluene delivered **2a** (M = Ni) in 78% yield. The reaction proceeded cleanly without by-products, other than the debrominated porphyrin, and none of the simple addition product without cyclization was detected in the reaction mixture.

The annulation reaction with various alkynes is summarized in Table 1. This process was found to have a wide scope in regard to the metal ions at the center of the porphyrin ring and the alkynyl substituents. The reaction provided the desired products in good to excellent yields with aromatic and aliphatic alkynes. Zinc and copper porphyrins **1** (M = Zn and Cu) also underwent this annulation reaction with excellent yields.

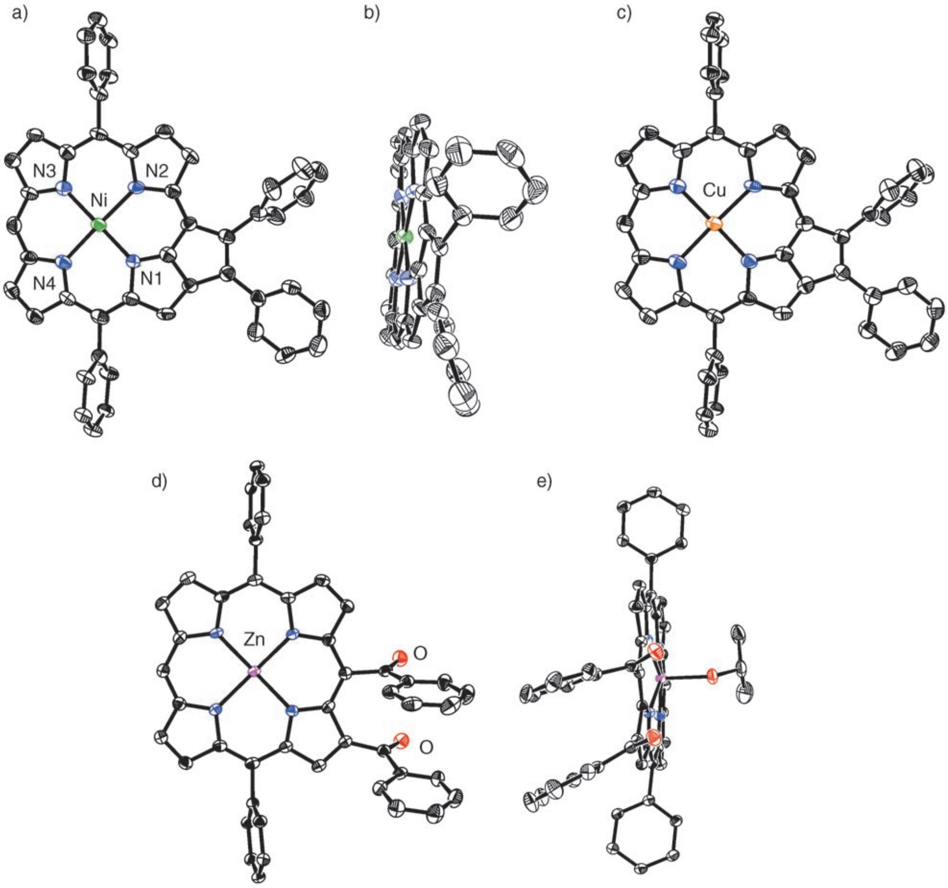
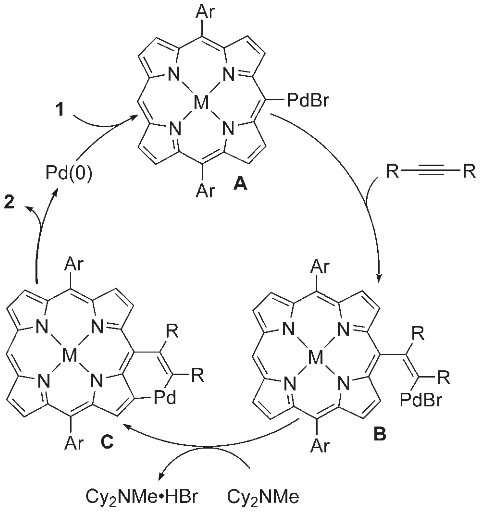


Figure 1. X-ray structures of **2a** (M = Ni and Cu) and **3**·*i*PrOH. a) Top view and b) side view of **2a** (M = Ni), and c) top view of **2a** (M = Cu); d) top view and e) side view of **3**. The thermal ellipsoids are at the 50% probability level. Hydrogen atoms and *tert*-butyl groups are omitted for clarity.

X-ray crystallographic analyses unambiguously elucidated the structures of **2a** (M = Ni or Cu), and showed the presence of a fused five-membered ring (Figure 1).[8] The porphyrin framework of the nickel derivative is almost flat but slightly ruffled with small deviations (< 0.2 Å) from the mean plane. Annulation with a diphenylethene moiety results in contraction of the inner cavity, which leads to a better fit of the small nickel(II) ion. The Ni–N1 bond (1.904 Å) is shorter than the other Ni–N bonds (1.942–2.002 Å). Interestingly, one of the phenyl groups on the diphenylethene moiety is nearly perpendicular (72.8°) to the cyclopentadiene ring, but the other one is nearly coplanar (32.0°), which may permit its effective conjugation with the porphyrinic π network. The C–C double bond is relatively long at 1.374 Å, which indicates that this bond participates in the aromatic conjugated system. The copper derivative exhibits a similar structure.

Scheme 2 shows a plausible catalytic cycle. Oxidative addition of Pd^0 to the C−Br bond of **1** triggers the formation of porphyrinylpalladium **A**. Subsequent carbopalladation of **A** at the C−C triple bond provides alkenylpalladium species **B**, which is then converted into palladacycle **C** by intramolecular activation of the C−H bond. Reductive elimination eventually furnishes cyclized porphyrin **2** and regenerates the Pd^0 species. An intramolecular Heck-type reaction (carbopalladation–elimination sequence) of **B** is another possible pathway, but this involves unfavorable anti-β-hydride elimination.



Scheme 2. A plausible mechanism for the Pd-catalyzed [3+2] anulation.

The UV/Vis absorption spectra of **2a** (M = Ni and Cu) and **2e** (M = Ni; Figure 2a) exhibit substantially different shapes from those of typical porphyrins. Split Soret bands indicate the electronic structure has been significantly altered. In fact, DFT calculations elucidate significant development of frontier orbitals in the five-membered ring along with a much smaller gap between the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO; see the Supporting Information). Cyclic voltammetry studies showed a small separation between the first oxidation and the first reduction potential ($\Delta E = 1.66$ V) for **2a** (M = Ni) relative to that of 5,15-bis(3,5-di-*tert*-butylphenyl)porphyrinnickel(II) ($\Delta E = 2.29$ V). Incorporation of π orbitals from the C−C double bond resulted in a breaking of the symmetry of the porphyrin π system and expansion of the porphyrinic π network, as evident from the absorption spectra, which differ significantly from the typical spectra of porphyrins. Characteristically, the absorption spectra reach into the near infrared region.

During the measurement of the absorption spectra we encountered an interesting phenomenon with **2a** (M = Zn). The absorption spectrum of **2a** (M = Zn) in $CHCl_3$ was completely different from that of the typical porphyrin-like shape after exposure of the solution to air under room light for 3 h (Figure 2b). This process was found to be quantitative conversion of **2a** (M = Zn) into meso,β-dibenzoylporphyrin **3** by oxidation of the outer C−C double bond. The assignment of **3** was based on HRESI-TOF mass and ^{13}C NMR spectra, the latter of which indicated the presence of two carbonyl groups in **3**. Final elucidation of the structure was accomplished by X-ray crystallographic analysis of crystals of **3** grown by vapor diffusion of isopropyl alcohol into a chloroform solution (Figure 1 d e).[9] The porphyrin framework of **3** is perfectly flat, without any distortion. The two benzoyl groups are positioned close to each other and this accounts for the temperature-dependent ^1H NMR spectra of **3** (see the Supporting Information). The strain induced by a bicyclo[3.3.0]octane skeleton would increase the reactivity of **2** toward oxidation. Contrasting photochemical stabilities of **2a** (M = Ni and Cu) suggested the involvement of singlet oxygen in this conversion.

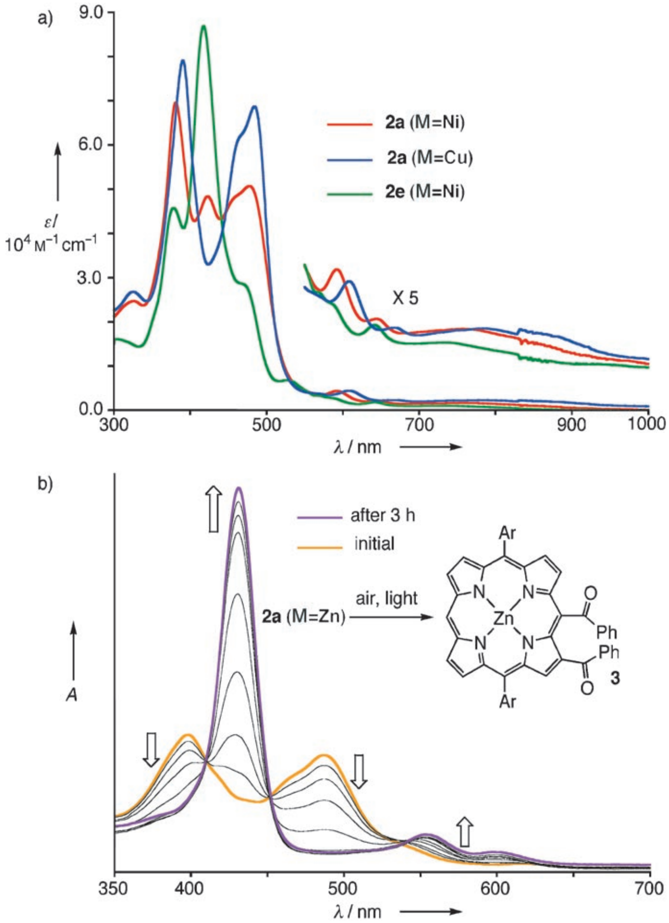


Figure 2. a) UV/Vis absorption spectra of **2a** (M = Ni and Cu), and **2e** (M = Ni) in $CHCl_3$. b) Change in the UV/Vis absorption spectra of **2a** (M = Zn) in $CHCl_3$ under ambient conditions.

In conclusion, the palladium-catalyzed coupling reaction of meso-bromoporphyrins with a variety of internal alkynes efficiently provides peripherally cyclopentadiene-fused porphyrins by a rational one-step synthetic protocol. Incorporation of the C−C double bond alters both the electronic and chemical properties of porphyrins. This efficient and direct functionalization indicates the prospect of using transition-metal-catalyzed reactions in porphyrin chemistry. Investigations on the application of this strategy to multiporphyrinic compounds and elucidation of the mechanism of oxidative cleavage of **2a** (M = Zn) are currently in progress.

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[8] Crystal data of **2a** (M = Ni): $C_{68}H_{64}Cl_2N_4Ni$, $M_r = 1066.84$, monoclinic, space group Cc (no. 9), $a = 35.997(12)$, $b = 5.8843(15)$, $c = 26.293(8)$ Å, $\beta = 96.469(12)°$, $V = 5534(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.280\,g\,cm^{-3}$, $T = 90(2)$ K, 10185 measured reflections, 7628 unique reflections, $R = 0.0971$, $R_w = 0.2832$ (all data), GOF = 1.041 ($I > 2.0\sigma(I)$). Crystal data of **2a** (M = Cu): $C_{68}H_{64}Cl_2N_4Cu$, $M_r = 1071.67$, monoclinic, space group Cc (no. 9), $a = 35.996(13)$, $b = 5.847(2)$, $c = 26.325(9)$ Å, $\beta = 96.380(13)°$, $V = 5506(3)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.293\,g\,cm^{-3}$, $T = 123.1$ K, 11657 measured reflections, 8262 unique reflections, $R = 0.0774$, $R_w = 0.2285$ (all data), GOF = 1.056 ($I > 2.0\sigma(I)$). CCDC-619420 (**2a** (M = Ni)), CCDC-619421 (**2a** (M = Cu)), and CCDC-619419 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[9] Crystal data of **3**: $C_{71}H_{84}O_5N_4Zn$, $M_r = 1138.85$, triclinic, space group $P\bar{1}$ (no. 2), $a = 11.688(3)$, $b = 15.783(4)$, $c = 19.429(6)$ Å, $\alpha = 112.513(10)$, $\beta = 95.172(11)$, $\gamma = 104.909(8)°$, $V = 3127.3(14)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.209\,g\,cm^{-3}$, $T = 123(2)$ K, 30667 measured reflections, 14114 unique reflections, $R = 0.0601$, $R_w = 0.1708$ (all data), GOF = 1.033 ($I > 2.0\sigma(I)$).