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Ambient Temperature Activation of Haloporphyrinic-Enediynes: Electronic Contributions to Bergman Cycloaromatization

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Porphyrins, by nature of their electronic and redox properties, are extremely versatile architectures that figure prominently in applications ranging from materials[1,2] to biomedicine.[3,4] Peripheral functionalization can enhance these existing properties or introduce new chemical behavior as in the generation of tetrapyrrole liquid crystals via incorporation of extended alkyl chains.[5] To this end, Smith et al. showed that an enediyne unit could be successfully formed by coupling two alkynes to a porphyrin skeleton at the β-pyrrole positions.[6] The resulting acyclic enediyne compounds undergo Bergman cyclization in solution to yield the corresponding picenoporphyrin derivatives at 190−280 °C. Within these specific constructs, large conformational changes to lower the enediyne activation barrier are difficult to introduce. However, recent theoretical studies have shown that alkyne termini functionalization, specifically electron-withdrawing halogen substitution, can have pronounced electronic effects on the barrier to Bergman cyclization.[7] We have applied this theoretical construct to the point of activating an acyclic enediyne unit fused to an aromatic system at ambient temperature without a catalyst.

Within this theme, we have synthesized the nickel(II) 2,3-bis-(haloethynyl)-5,10,15,20-tetraphenylporphyrins with −Br (**2a**) or −I (**2b**) at the alkyne termini position from the 2,3-diethynyl analogue (**1**). The cross coupling of nickel(II) 2,3-dibromo-5,10,-15,20-tetraphenylporphyrin with trimethyl(trimethylstannanylethynyl)-silane in the presence of a Pd^0 catalyst and subsequent deprotection with base under aqueous conditions yields the nickel(II) 2,3-diethynyl-5,10,15,20-tetraphenylporphyrin (**1**).[6,8] Subsequent reaction of **1** with *N*-bromo- or *N*-iodosuccinimide in dry acetone in the presence of $AgNO_3$ yields 2,3-bis(haloethynyl)-5,10,15,20-tetraphenylporphyrins in 70% (**2a**) and 68% (**2b**) yields (Scheme 1). All attempts to isolate the chloro-derivative resulted only in polymeric products.

The X-ray crystal structures of **2a**,**b** (Figure 1) show that the porphyrin backbone deviates significantly from planarity due to a Ni(II)-induced mixture of the classic ruffle and saddle distortions.[9] The former causes the pyrrole ring to twist relative to the idealized plane, permitting the alkynes at the β-carbons to point out of the normal plane of the macrocycle. As a consequence, the alkyne termini separations are significant (C27···C30, **2a**: 4.24 Å; **2b**: 4.32 Å), but typical of sterically unencumbered acyclic enediyne units of Ni(II) porphyrins.[8]

To assess the thermal reactivities of **2a** and **2b**, their thermal Bergman cyclization temperatures have been evaluated both in the solid state by differential scanning calorimetry (DSC) and in solution. Single, prominent exotherms are observed at 134 and 200 °C for **2a** and **2b**, respectively, indicating a substantial difference in the activation barriers to Bergman cyclization of these compounds. In solution, thermally activated Bergman cyclization of **2a** and **2b** leads to the generation of isolable picenoporphyrin products (Scheme 2). Thermolysis of **2a** at 190 °C for 6 h in chlorobenzene and 30-fold 1,4-cyclohexadiene (CHD) generates the

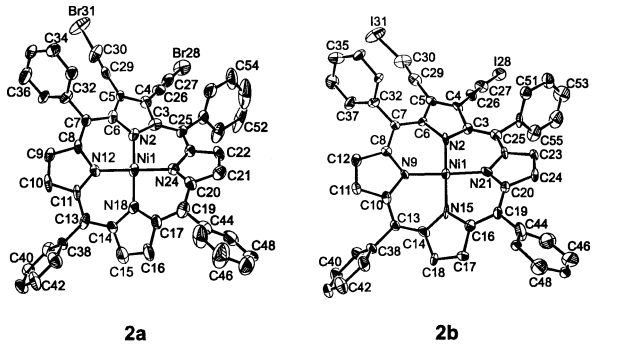
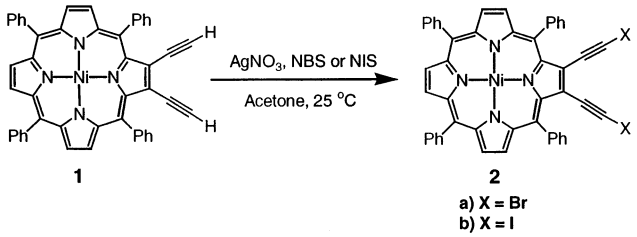
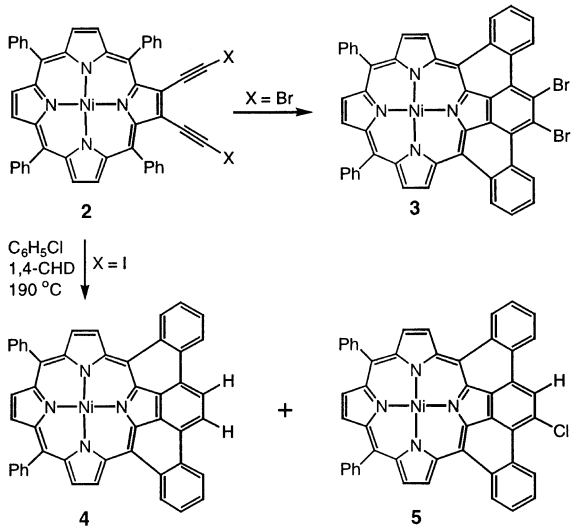


Figure 1. X-ray structures of **2a**,**b**. Thermal ellipsoids are illustrated at 50% probability.

Scheme 1. Preparation of Haloporphyrinic-Enediynes



Scheme 2. Cyclization of Haloporphyrinic-Enediynes



Bergman cyclized nickel(II) dibromopicenoporphyrin product (**3**) in 65% yield, which derives from diradical addition across the adjacent *meso*-phenyl substituents. Similarly, nickel(II) 2,3-bis-(iodoethynyl)-5,10,15,20-tetraphenylporphyrin, **2b**, cyclizes at 190 °C in chlorobenzene/CHD via high-temperature substitution of iodine by hydrogen (from CHD) or chlorine (from solvent) to afford a mixture of **4** (15%) and **5** (45%) (Scheme 2). The X-ray structures

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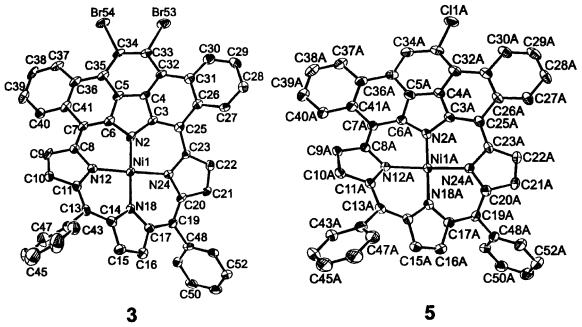

Figure 2. X-ray crystal structures of Bergman cyclized products **3** (from the ambient temperature reaction) and **5**. Thermal ellipsoids are illustrated at 50% probability.

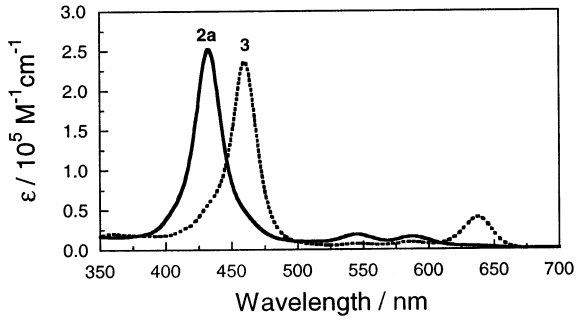

Figure 3. Electronic absorption spectra of **2a** (—) and **3** (- - -) in CH_2Cl_2.

of cyclized products **3** and **5** (Figure 2) reveal a Ni(II) porphyrin skeleton that displays a mixture of the traditional ruffle/saddle distortions fused to a planar piceno-unit at dihedral angles of 21° (for **3**) and 18° (for **5**) relative to the N12−Ni−N24 vector. The unusual structure is a consequence of carbon−carbon bond formation which locks the *meso*-phenyl groups into the plane of the newly formed 1,6-Bergman cyclized ring.

The electronic absorption spectrum of **2a** (Figure 3) reveals low-energy red-shifted Soret and Q-bands at $\lambda_{max} = 431$ ($\epsilon = 253\,700$ M^{-1} cm^{-1}), 544 ($\epsilon = 19\,300$ M^{-1} cm^{-1}), and 587 nm ($\epsilon = 16\,300$ M^{-1} cm^{-1}) due to extended conjugation through the alkynes. Bergman cyclization and radical addition to form **3** both extend the conjugation as well as accentuate the disparity in symmetry in the *x*,*y* plane, thereby shifting the Soret and one of the Q-bands to even lower energies ($\lambda_{max} = 459$, 636 nm, respectively). Substitution of halogen in **2a** versus **2b** leads to a <5 nm shift in the electronic spectrum, but ∼30 nm differences are observed across cyclized products **3**−**5** due mainly to asymmetric substitution in **5**.

Remarkably, formation of Bergman cyclized product **3** from acyclic enediyne starting material **2a** is not restricted to elevated temperatures. Ambient temperature incubation of **2a** in MeOH/$CHCl_3$ (1:3, 22 h) or chlorobenzene/CHD (3:1, 24 h) leads to generation of **3** in 15% and 22% isolated yields, respectively (Table 1). As we have shown,[8] the reaction coordinate for Bergman cyclization of porphyrinic-enediynes contains a significant barrier to the picenoporphyrin product, due to the need to oxidize/aromatize the hydro-intermediate[6] formed upon diradical addition to the *meso*-phenyl groups. Addition of 1.2 equiv of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in $CHCl_3$/MeOH dramatically accelerates the rate of reaction, producing **3** in 30% yield within 0.5 h.

Table 1. Reaction Conditions for Bergman Cyclization of **2a**

compd	reaction conditions	conversion[a]	**2a**[b]	**3**
2a	MeOH, $CHCl_3$, 25 °C, 22 h	40%	60%	15%
2a[c]	MeOH, $CHCl_3$, DDQ, 25 °C, 0.5 h	100%		30%
2a[d]	C_6H_5Cl, CHD, 25 °C, 24 h	60%	40%	22%
2a	MeOH, $CHCl_3$, 90 °C, 24 h	100%		45%
2a[d]	toluene, 115 °C, 6 h	100%		60%
2a[d]	C_6H_5Cl, IPA, 125 °C, 6 h	100%		30%
2a[d]	C_6H_5Cl, CHD, 150 °C, 6 h	100%		50%
2a	C_6H_5Cl, CHD, 190 °C, 6 h	100%		65%

[a] Conversion is based on the total consumption of **2a**. [b] Recovered starting material. [c] 1.2 equiv of DDQ was used. [d] The intermediate observed was oxidized to product **3** in the presence of DDQ in 10% MeOH/$CHCl_3$ at 25 °C.

Moreover, heating of **2a** in toluene at 115 °C for 6 h, or chlorobenzene in the presence of H-donors (e.g., 2-propanol (IPA)), leads to formation of the quasi-stable hydro-intermediate.[6] Cooling to room temperature and subsequent treatment of the intermediate with DDQ in 10% MeOH/$CHCl_3$ leads to complete conversion of the intermediate (based on NMR) to the picenoporphyrin product in 30−60% isolated yields (Table 1). In contrast to these results, **2b** is stable at ambient temperature and, upon heating under similar conditions, leads to only degradation products.

The origin of the ambient temperature activation of **2a** derives from the ability of electron-withdrawing functionalities at the alkyne termini to decrease the activation barrier to Bergman product. In this case, the reduction in the barrier for Br- relative to I- or H-substitution is remarkable and leads to a unique example of an uncatalyzed, ambient temperature Bergman cyclization of an acyclic enediyne fused to an aromatic system. These results contribute significantly to the broader theme of activation and control of diradical reactivity, which is important to future biomedical or materials applications.

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Supporting Information Available: Experimental procedures, characterizations, and crystallographic data for **2**−**5** (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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