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## Rotaxanation as a sequestering template to preclude incidental metal insertion in complex oligochromophores

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The high yielding Cu<sup>I</sup>-mediated click reaction is an effective procedure for the preparation of oligoporphyrinoid conjugates. However, the Cu<sup>I</sup> catalyst leads to the adventitious and usually undesirable insertion of Cu ions into any non-metalated porphyrinoid centers during reaction. Here we report a “sacrificial rotaxane” strategy for the multifunctionalization of porphyrins with free base corroles without incidental copper insertion. This strategy can be considered a general method for implementing Cu<sup>I</sup>-mediated click reactions with metal cation sequestration to avoid detrimental effects caused by the presence of copper cations.

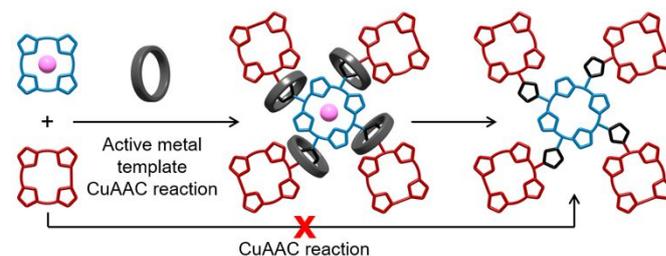
Porphyrinoids have been widely investigated as novel materials designed for various applications, e.g. multisite catalysts, mimics of biochemically important species (e.g., cytochrome c oxidase), sensors, molecular electronics and/or solar-energy conversion.<sup>1–13</sup> An intensively studied area of application involves the use of porphyrinoids as components of artificial photosynthetic system models<sup>14–29</sup> with corroles making up a significant class of compounds used for this purpose.<sup>30–35</sup>

We have previously contributed to this field with our work on corrole-porphyrin dendritic conjugates synthesized by using copper-mediated click reaction.<sup>34,35</sup> This reaction provides high yields for the multiple functionalization of the porphyrin core

with corrole units. However, these conjugates inevitably contain copper(I) corrole attached to a zinc porphyrin core as a result of the presence of copper cations in the reaction mixtures despite the preference, in many cases, that the final products contain non-metalated corrole moieties. On the other hand, functionalization involving freebase corroles can be synthetically tedious because of their relative instabilities. Stepwise syntheses completed to date include the construction of porphyrin core from formyl-substituted corrole precursors, which has been applied to construct porphyrin-freebase corrole conjugates.<sup>36–37</sup> Gross and coworkers have also successfully synthesized star-shaped all-free-base tetra-corrole dendrimers containing a core porphyrin unit.<sup>38</sup> Although the latter method provides access to conjugates lacking copper, similar to those that we envisioned here, the overall yields are low despite the synthesis of an effective formyl-corrole precursor.

In 2009, we described a reductive demetalation procedure<sup>39</sup> for the removal of copper cations from copper corroles, which permits selective metalation and demetalation of corrole-porphyrin units. This technique has been used as a general procedure for the protection of corroles by copper metalation during functionalization.<sup>40–41</sup> Elimination of copper cations from metalated corrole substituents offers a straightforward method for the preparation of free-base-corrole-only porphyrin conjugates. However, this is not always simple (*vide infra*).

In this report, we disclose a preparation of free-base-only conjugates containing or lacking rotaxanated interchromophore linking units using the high yielding copper-



Scheme 1: Synthetic strategy for fully free base oligocorrole-porphyrin conjugates using the sacrificial rotaxane template. Red = corrole, blue = porphyrin, pink = Zn(II), gray ring = BiPy macrocycle, black pentagon = 1,2,3-triazole

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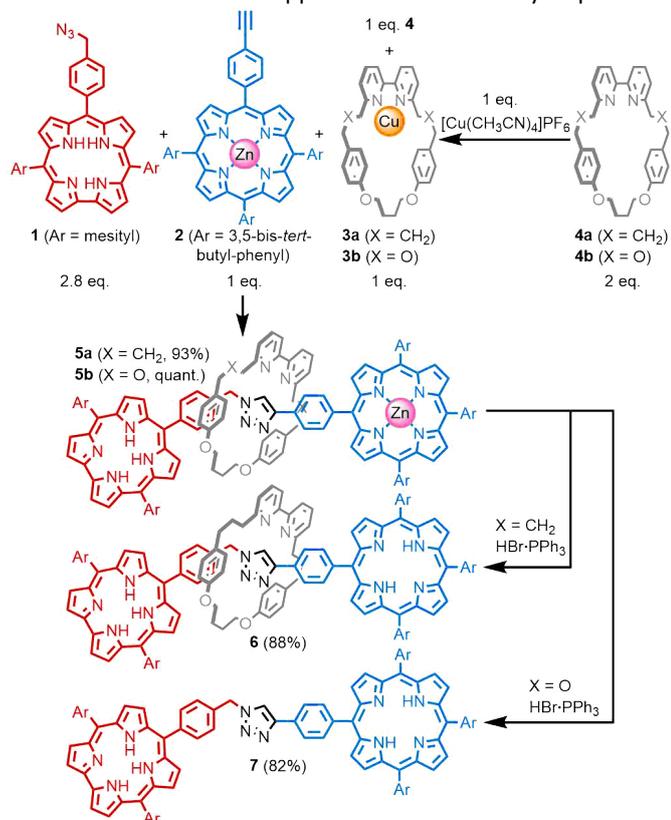
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mediated click reaction (Scheme 1). This synthetic route introduces the rotaxane unit as a sacrificial template.

Initially, we attempted the straightforward strategy of copper catalyzed click reaction<sup>42</sup> followed by reductive demetalation. Since the catalytic activity of the click reaction derives from Cu(I), CuI was employed as catalyst. The click reaction proceeded but a mixture of inseparable copper metalated and free base conjugates was obtained. Corrole moieties were obviously metalated by copper ions present during the click reaction. When CuSO<sub>4</sub> was used in the presence of ascorbic acid, copper metalated corrole-porphyrin diad could be observed using mass spectroscopy. Unfortunately, reductive demetalation of these conjugates also afforded inseparable mixtures of copper metalated and fully free base conjugates. Longer reaction times yielded mixtures of copper-metalated, free-base conjugates and tin metalated derivatives (from the tin chloride reductant: see SI). The pure free base corrole-porphyrin conjugate could not be obtained either by direct copper-mediated click reaction starting from non-metalated precursors or by reductive demetalation of the copper-corrole derivatives.

Previously, we described the high yielding synthesis of corrole-porphyrin rotaxanes.<sup>35</sup> High yields were obtained as a result of the more rapid complexation of Cu(I) into the macrocycles **4**.<sup>43</sup> Click reaction then only occurs at the macrocyclic cavity resulting in high yields. We hypothesized that the copper macrocyclic complex is sufficiently stable during the click reaction that free copper ions are effectively sequestered,



Scheme 2: Sacrificial rotaxane strategy toward fully freebase conjugates. Above: Click reaction mediated by copper macrocycle complexes **3** toward rotaxanated diads **5**. Below: Treatment with HBr•PPh<sub>3</sub> removed the Zn ion to give free base conjugates **6** and **7**, the latter through cleavage of ether-containing macrocycle.

thus precluding their complexation at corrole moieties. A mixture of bipyridinyl copper complexes **3** and one equimolar excess of uncomplexed bipyridine macrocycle **4a/b** were added to the mixture of equimolar zinc porphyrin **2** and an excess of corrole precursor **1** to afford interlocked free base corrole-porphyrin conjugates **5a/b** (Scheme 2). The excess of free bipyridine macrocycles present in the reaction mixture assures the sequestration of any copper ions released during the reaction thus preventing metalation of the corrole moieties.

Depending on the benzylic functional group of the bipyridinyl macrocycle **4**, fully free base interlocked and non-interlocked derivatives **6** and **7** were obtained upon demetalation with HBr•PPh<sub>3</sub>. Benzylic ether functional groups can be cleaved by HBr•PPh<sub>3</sub> during zinc demetalation, leading to the non-interlocked conjugate **7** while the interlocked derivative **6** was obtained when no benzylic ether function is present in the macrocycle.

This investigation was extended to larger conjugates containing two or four corrole units. When the sacrificial rotaxane strategy was applied, pure multi-corrole rotaxane derivatives were obtained in high yields: triad **8a/b**, **9** and pentad **10a/b** and **11** (Fig. 1, left). Overall yields of 57% and 54% for free base-only triad **9** and pentad **11**, respectively, were obtained starting from the respective click reactions.

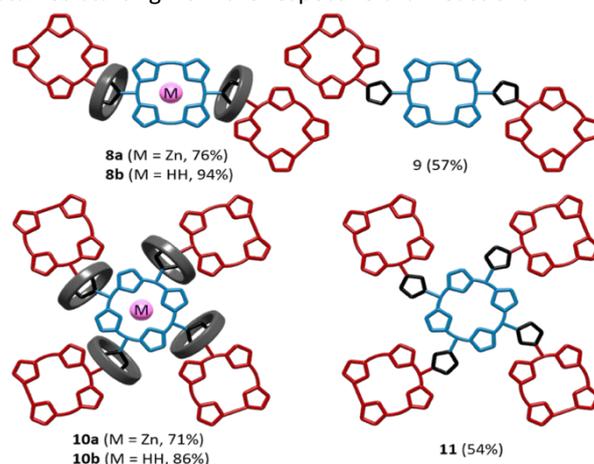
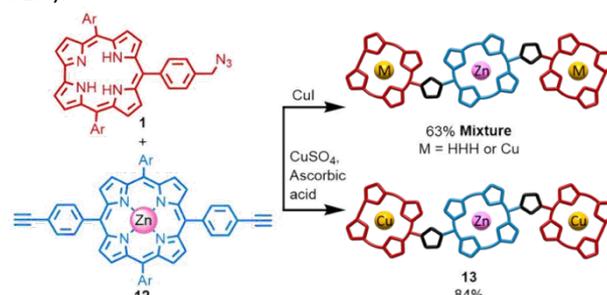


Figure 1: Triad **8a/b**, **9** and pentad **10a/b**, **11** containing freebase corrole and porphyrin moieties prepared by the sacrificial rotaxane strategy.

It should be noted that the formation of triazole linkers in the absence of the bipyridine macrocycle led, as expected, to metalation of the corrole moiety and reductive demetalation of these conjugates lead only to inseparable mixtures (Scheme 3, see ESI).



Scheme 3: Click reaction for synthesis of free base corrole zinc porphyrin conjugates using different copper catalysts. CuI catalyst gave partial copper metalation into corrole moiety while complete metalation with copper was observed using CuSO<sub>4</sub> and ascorbic acid.

The key reaction of this strategy toward exclusively free base conjugates is the copper macrocyclic complex mediated reaction where copper is not inserted into the corrole moieties. There are two critical questions regarding this step. First, is the formation of a mechanical bond required for inhibition of the corrole metalation to operate? Second, can the bipyridine macrocycle be replaced by other non-macrocyclic ligands? To address these questions, a more detailed NMR spectroscopic investigation was performed on the click reaction of free base corrole with phenyl acetylene in the presence of the copper bipyridine macrocyclic complex.

When equimolar amounts of phenyl acetylene and copper bipyridine macrocycle were added to the free base azido corrole solution in an NMR tube, reaction commenced almost instantaneously (5 minutes, Fig. 2 spectrum a). The phenyl-H doublet of the phenylacetylene copper complex **15** at 6.1 ppm (peak **a**) is reduced in intensity while a doublet (peak **b**) due to the intermediate **16** appears at 6.6 ppm (Fig. 2 spectra a and b). The resonance at 5.9 ppm due to benzylic protons of the free base corrole moieties of **16** (peak **c**) first increases in intensity up until the 120<sup>th</sup> minute (spectra a to e) and then reduces in intensity (spectra e to g). The benzylic protons of the copper metalated corrole unit of intermediate **17** (peak **d**) appear at 5.7 ppm after 60 minutes, that is, before the reaction was complete (spectra c to g). As the intensity of the peak **d** due to copper metalated intermediate **17** increases, peaks due to the copper free intermediate derivative **16** are reduced in intensity (spectra e to g). This indicates that free copper ions released during the

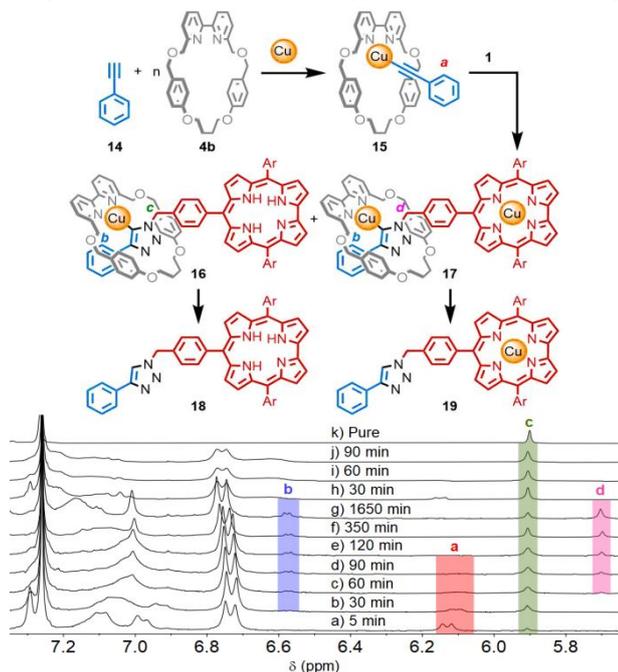


Figure 2: NMR study of the copper mediated click reaction of freebase corrole in  $\text{CDCl}_3$ . NMR spectrum of free base corrole **1**, phenyl acetylene **14** and one equivalent copper complex **3b** at a) 5 min, b) 30 min, c) 60 min, d) 90 min, e) 120 min, f) 350 min and g) 1650 min. Peak **c** at 5.9 ppm belongs to the benzylic protons of the freebase intermediate. Peak **d** at 5.7 ppm belongs to benzylic protons of the copper metalated intermediate. Spectra h to j show the reaction mixture with an excess of **3b** at 30 min, 60 min and 90 min respectively. k) Spectrum of pure free base product **18**.

reaction are complexed at the corrole moiety to form the stable copper corrole complex **17**.

To avoid copper cation insertion, two equivalents of phenylacetylene **14** were added to accelerate the reaction in the presence also of an excess of bipyridine macrocycle **4b**. The reaction was completed after 90 minutes (Fig. 2 spectrum j) and only the copper complexed product **16** could be detected (no benzylic proton peak **d** at 5.7 ppm in spectra h to j). Excess bipyridine macrocycle present in the reaction mixture preferentially sequesters any copper ions released during the reaction thus precluding copper insertion into the corrole macrocycle. Interestingly, the purified product has no  $^1\text{H-NMR}$  resonance peak **b** at 6.6 ppm (spectrum k), suggesting that the peak observed in the NMR study belongs to the intermediate **16** and **17** where copper is still complexed to the triazole and bipyridine units.<sup>44</sup>

Finally, the bipyridine macrocycle was substituted by using bipyridine, phenanthroline or tris(benzyltriazolyl)methyl amine as a ligand in the reaction. Mass spectroscopy and thin layer chromatography indicate that the click reaction occurred very slowly under these conditions and only copper metalation in corrole was observed after an extended reaction time. Bipyridine and phenanthroline form highly stable complexes with copper(I) ions as  $\text{CuL}_2$  complexes. These complexes are coordinatively saturated and sterically hindered making them inactive to mediate the click reaction. Similarly, tris(benzyltriazolyl)methyl amine forms a stable complex with copper(I). Thus, the click reaction is slowed down significantly, allowing the copper insertion into corrole moiety to happen. After days of reaction, copper insertion in both unreacted corrole precursor and corrole unit of the product was observed. The macrocyclic form of the bipyridine ligand is necessary for the corrole azide to undergo click reaction rapidly prior to the copper insertion.

## Conclusions

In summary, we report the use of an active template Cu-mediated azide–alkyne cycloaddition to synthesize free base corrole-porphyrin conjugates. The copper ion was pre-complexed in the bipyridine macrocycle and the reaction was carried out in the presence of an excess of macrocycles to avoid copper insertion in corrole. The choice of appropriate macrocycle permits successful benzylic ether cleavage to prepare non-interlocked free base corrole-porphyrin conjugates. By using this strategy, we have obtained both rotaxanated<sup>45</sup> and non-interlocked derivatives of diad, triad, and pentad corrole-porphyrin conjugates in their non-metalated form. These compounds are not accessible using conventional click reactions because of adventitious insertion of copper cations in the corrole moieties. This sacrificial rotaxane strategy is important to offer an alternative synthetic route to multi-functionalize free base corrole and porphyrin derivatives with high yields. The method avoids incidental copper insertion at corrole, obviates post-demetalation procedures, is useful for high yield multiple functionalization procedures, and the important bipyridine macrocycle reagent **3a** can be recovered following reaction completion. NMR study of the reaction revealed that the formation of a persistent mechanical bond is

not essential for the bipyridine macrocycle to exhibit their protective effect. The macrocyclic conformation of the bipyridine ligand is needed for this reaction to complete quickly before the copper insertion into corrole can take place. The photochemical studies to probe the excited state events of the prepared compounds are in progress.

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## Conflicts of interest

There are no conflicts to declare.

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- 45 The identity of the interlocked products was confirmed by NMR and MS. <sup>1</sup>H NMR confirmed that no macrocycle or axle were present in the isolated samples of rotaxanes 5, 6, 8 and 10. It should be noted that although ESI-MS confirmed the presence of the interlocked products, mass ions assigned to macrocycles 4 could also be observed. These are attributed to fragmentation of the axle, which is supported by the appearance of fragments corresponding to cleavage at the benzylic triazole unit. See ESI.