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Rigid, Cross-Conjugated Macrocycles: A Cyclic Alternative to 4,4′-Bipyridines in Supramolecular Chemistry

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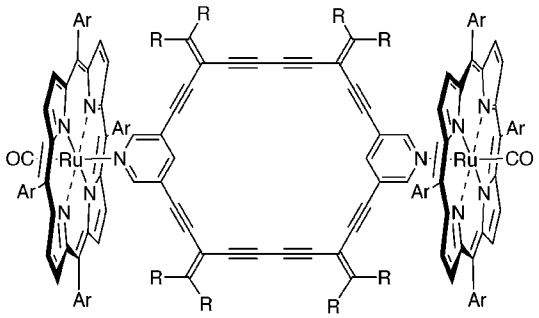
ABSTRACT



The synthesis of two fully conjugated, rigid macrocyclic analogues to 4,4′-bipyridine is described. The use of these macrocycles in self-assembly processes is demonstrated by axial coordination to metalloporphyrins, and one system (R = Me) has been characterized by single-crystal X-ray crystallography.

The rigidity and directed coordinative ability of bipyridines and related molecules make them among the most ubiquitous constituents of supramolecular assemblies.[1−5] This is particularly true of 4,4′-bipyridines, which have been widely used for the realization of discrete, highly ordered nanostructures based on transition metal coordination.[6]

Shape-persistent conjugated macrocycles can also provide a versatile basis for the realization of well-defined materials with tubular, rigid structures and desirable properties.[7] Complementing the rigid framework of these macrocycles is the fact that their physical attributes can be readily manipulated by the covalent incorporation of functional groups. For example, coordinative functionality, namely the nitrogen of pyridine(s), directed toward the interior of macrocycles has been used in the design of artificial receptors.[8]

We envisioned that the strategic placement of pyridine(s) within a macrocyclic framework with nitrogen directed away

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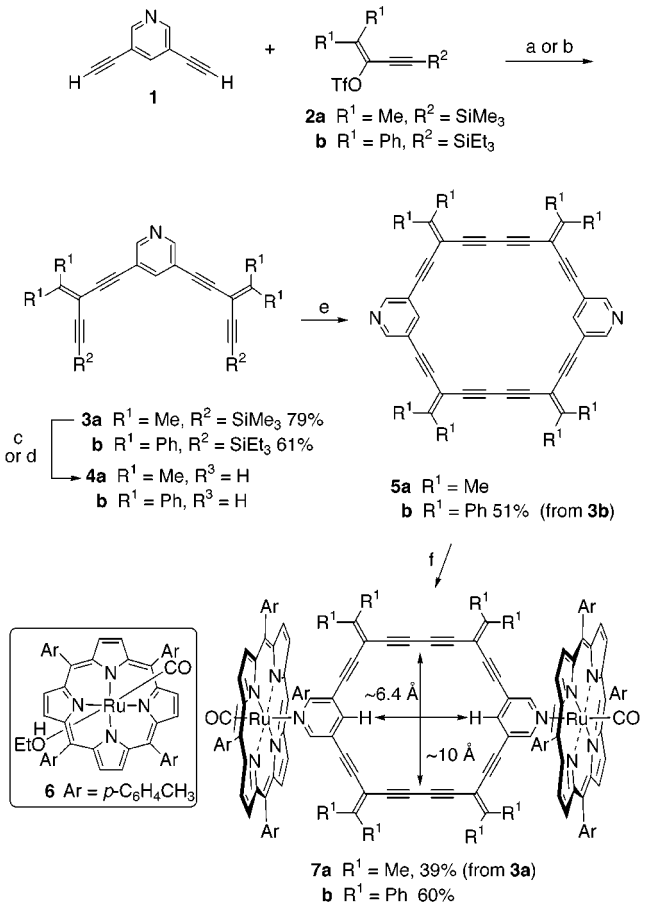
from the cyclic core would combine the desirable attributes of both conjugated macrocycles and self-assembly. Thus, a fully conjugated macrocycle based on 3,5-diethynylpyridyl subunits was designed. It was predicted that these building blocks (e.g., **5a**,**b**) would readily function as macrocyclic analogues to 4,4′-bipyridines for creation of highly ordered assemblies via metal coordination.

We report herein the realization of these two unprecedented macrocycles, **5a**,**b**, based on a cross-conjugated enyne framework. The rigid skeleton and directed orientation of the pyridyl nitrogens in **5a** and **5b** ensure predictable assembly into well-defined supramolecular scaffolds. This concept is demonstrated for **5a** and **5b** by axial coordination to metalloporphyrins to give **7a** and **7b**.[9] These particular targets attracted our attention due to the widespread interest in two- and three-dimensional porphyrinic arrays, in addition to the well-established photophysical properties of porphyrins.[10] X-ray crystallographic analysis for **7a** confirms the ability of these macrocycles to afford highly ordered crystalline materials.

The synthesis of macrocycles **5a**,**b** and supramolecular assemblies **7a**,**b** is outlined in Scheme 1. Our efforts began with the palladium-catalyzed cross-coupling of dimethyl substituted vinyl triflate **2a**[11] with 3,5-diethynylpyridine **1**[12] to give **3a** in 79% yield.[13] Protodesilylation of **3a** with methanolic K_2CO_3 gave the deprotected tetrayne **4a**, which was carried on to an oxidative acetylenic coupling following aqueous workup. The coupling of **4a** in CH_2Cl_2, utilizing CuI and TMEDA in the presence of oxygen,[14] afforded a mixture of **5a** and linear oligomers that together showed very limited solubility in organic solvents.

As a result, purification of **5a** by chromatography was impractical. Selective extraction of the product **5a** from

Scheme 1



[a] (a) $Pd(PPh_3)_4$, CuI, Et_2NH, THF, rt; (b) $Pd(PPH_3)_4$, CuI, Et_2NH, THF, 55 °C; (c) K_2CO_3, wet MeOH/THF, rt; (d) TBAF, THF, rt; (e) CuI, TMEDA, O_2, CH_2Cl_2, rt; (f) **6** (2 equiv), CH_2Cl_2, rt.

byproducts proved equally frustrating, requiring unworkable amounts of solvent. To circumvent the problems associated with the separation of **5a** from oligomeric impurities, the combined mixture was treated with 2 equiv (based on **3a**) of porphyrin **6** in CH_2Cl_2. The self-assembly reaction of **5a** and **6** was monitored by TLC, which clearly showed rapid formation of the desired assembly **7a**. The more limited solubility of linear oligomers assured that porphyrin coordination occurs almost exclusively with macrocycle **5a**. Following porphyrin complexation, the solubility of the product, **7a**, was greatly improved relative to **5a**, and it was easily purified by column chromatography on neutral alumina. Subsequent crystallization from CH_2Cl_2 gave **7a** as a deep burgundy solid in 39% yield from **3a**. It is worth noting that the majority (>90%) of the uncoordinated porphyrin **6** could be reclaimed by simply flushing the column with an $EtOH/CH_2Cl_2$ mixture following the isolation of **7a**. The limited solubility of **5a** demanded a structural change to the macrocyclic framework that would facilitate handling and purification. We thus redesigned the synthetic sequence described above to use vinyl triflate **2b**, incorporating diphenyl vinylidene substitution that was expected to increase solubility.[15]

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(13) The purity and structure of all new compounds (except **5a**) were confirmed by ^1H and ^{13}C NMR, IR, and MS. Selected synthetic and characterization details are provided as Supporting Information.

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Palladium-catalyzed coupling of **1** and **2b** gave **3b** in 61% yield. Removal of the triethylsilyl groups by treatment with TBAF afforded deprotected **4b**, which was carried on directly to the next step, following workup. Oxidative homocoupling of **4b** successfully effected formation of macrocycle **5b**, which was isolated in 51% yield (based on **3b**) by crystallization from CH_2Cl_2. Macrocycle **5b** is a bright yellow, highly fluorescent solid. It is quite stable to heat, light, air, and moisture, and it can be stored indefinitely under refrigeration without appreciable decomposition.

Self-assembly of **5b** with 2 equiv of porphyrin **6** was brought about in CH_2Cl_2, and concentration of the reaction solution afforded the pure assembly **7b** as a burgundy solid in 60% yield. Attempts to crystallize the readily soluble complex **7b** from, for example, CH_2Cl_2 by the addition of hexanes resulted only in selective precipitation of the less soluble macrocycle **5b** and indicated that the axial coordination within **7b** was considerably less robust than that observed for **7a**. The increased steric demands of the vinylidene phenyl moieties likely account for this behavior. On the basis of NMR analysis for both **7a** and **7b**, however, there is little doubt that the solution-state equilibrium in CD_2Cl_2 favors **7b**. Specifically, the pyridyl protons at C1/C5 and C3 for the uncomplexed macrocycle **5b** resonate at 8.13 and 7.83 ppm, respectively.[16] For both complexes **7a** and **7b**, these protons are found upfield as a result of diamagnetic anisotropy of the porphyrin, and they resonate at ca. 1.1 and 6.1 ppm, respectively.[17]

Single crystals of **7a** suitable for X-ray crystallographic analysis were obtained from a crude reaction mixture (CH_2Cl_2) that still contained excess porphyrin **6**.[18] The complex **7a** cocrystallized with 1 equiv of **6** that is sandwiched between layers of the macrocyclic assembly. The tolyl groups of two offset porphyrin cocrystallites occupy the majority of the macrocyclic cavities. An ORTEP of **7a** is shown in Figure 1 and confirms the internal dimensions of the macrocycle circumscribed by the enyne framework, giving a cavity of 0.64 by 1.0 nm.[19]

When the crystal packing for **7a** is viewed along the *b*-axis (Figure 1, bottom), stacking of the macrocycles in the solid state can be seen. There is a relatively large separation of layers of the macrocyclic assemblies of approximately 9 Å to accommodate the cocrystallized porphyrin molecules.

Large crystals of both **7a** and **7b** can also be grown from

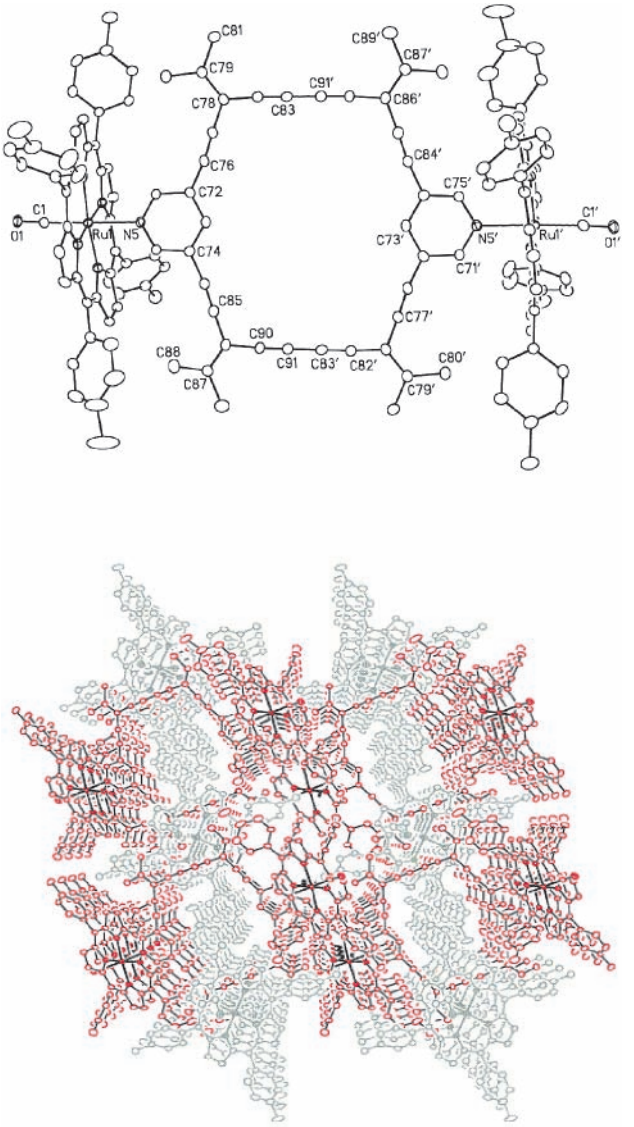

Figure 1. Top: ORTEP drawing of supramolecular complex **7a**. Bottom: a view down the crystallographic *b*-axis, showing order within the crystal lattice (cocrystallite porphyrin shown in gray).

CH_2Cl_2 solutions in the absence of excess porphyrin. In all cases to date, however, X-ray analysis of these crystals has been thwarted by rapid desolvation of these samples.

In conclusion, we have realized the first examples of a novel class of cross-conjugated macrocycles that function as macrocyclic analogues of 4,4′-bipyridines. The directed pyridyl functionality of these building blocks readily allows for their predictable self-assembly into highly ordered systems, which has been demonstrated by axial coordination of the macrocycles to metalloporphyrins.

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(15) The incorporation of the triethylsilyl alkyne protecting group was necessary for a more effective synthesis of **2b**.

(16) gHMQC analysis of **7a** and **7a** was used to unambiguously assign the pyridyl protons. See Supporting Information for details.

(17) Restricted rotation of the tolyl groups of the porphyrin moiety is observed for metalloporphyrin **6**, as well as for assemblies **7a**/**7b**, and is evidenced by the splitting of nonequivalent protons in the respective ^{1}H NMR spectra. The difference in chemical shifts for these protons for **6** and **7a/7b** also supports the assignment of a solution state equilibrium that favors **7a** and **7b**. The ^{1}H spectrum of **6** is provided as Supporting Information for comparison.

(18) Compound **7a** ($C_{140}H_{102}N_{10}O_2Ru_2 \cdot C_{51}H_{42}N_4O_2Ru$; $M_r = 3002.41$) crystallized in the triclinic space group $P\bar{1}$ with $a = 16.1421(11)$ Å, $b = 17.1025(11)$ Å, $c = 17.5359(12)$ Å; $\alpha = 90.3641(14)°$, $\beta = 100.8011(13)°$, $\gamma = 114.5012(14)°$; $V = 4308.0(5)$ Å^3, $Z = 1$; $R = 0.089$ (10363 reflections with $F_o^2 \geq 2\sigma(F_o^2)$), $R_w = 0.29$ for 960 variables and 17506 unique reflections with $F_o^2 \geq -3\sigma(F_o^2)$).

(19) For a discussion of channel structures, see: Moore, J. S. *Nature* **1995**, *374*, 495−496.

Supporting Information Available: Synthetic and characterization details for all new compounds, ^{1}H and ^{13}C NMR spectra for compounds **5a**, **6** (^{1}H spectrum), **7a**,**b**, gHMQC spectra for **7a**,**b**, X-ray crystallographic details for **7a**, and the ESI MS spectrum for **7a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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