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Synthesis of *meso*-Extended Tetraarylporphyrins

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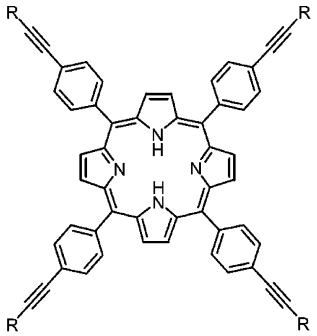

R = pyridine, pyrimidine, benzonitrile

The synthesis of five new *meso*-tetraarylporphyrins having pyridine, pyrimidine, or nitrile groups extending tetragonally via alkynyl linkages from the *para* positions is described. The radial extension is nearly double that of common porphyrins such as tetra-*p*-pyridylporphyrin. Practical quantities can be produced by Pd-coupling protocols when traditional methods fail. Applications of these extended porphyrins in the area of porous metal-organic frameworks are anticipated.

Introduction

An active area of contemporary chemistry is the assembly of new materials using porphyrin building blocks. Particularly intriguing are the possibilities with porous metal-organic frameworks (MOFs), sometimes called "artificial zeolites". In seminal work in the early 1990s, Robson combined the tetragonal shape propagation properties of tetraarylporphyrins with metal-directed coordinate bond formation to produce porous framework solids whose voids were filled with exchangeable solvent molecules.[1] In the past decade or so, a variety of infinite framework, lamellar, and ribbon structures have been discovered using tetraarylporphyrins that contain peripheral groups capable of forming metal−ligand coordinate bonds in a divergent manner,[1−13] and a number of reviews on this topic are now available.[14−18] The control of pore size and the maintenance of structural integrity after solvent removal from the pores are two of the critical issues that must be addressed before practical applications can result.[19−22] More robust structures can be produced using bridging ligands with metalloporphyrins[5] or fullerenes as supramolecular pillars[11] but typically at the expense of pore size.

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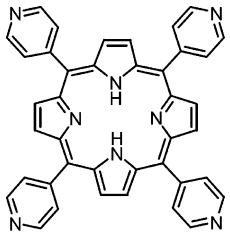
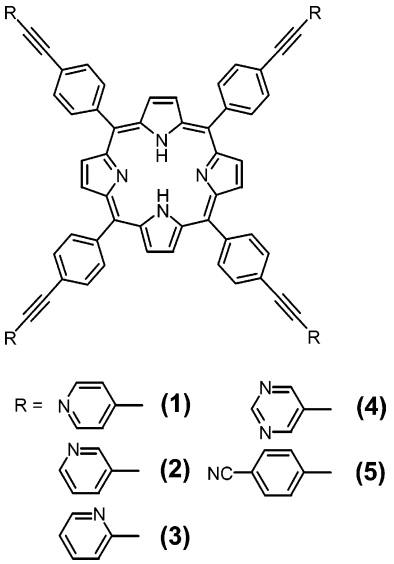
For the most part, work in this area has been restricted to a few easily synthesized or commercially available tetraarylporphyrins, such as 5,10,15,20-tetrakis(4-cyanophenyl)porphyrin or 5,10,15,20-tetrakis(4-pyridyl)porphyrin:



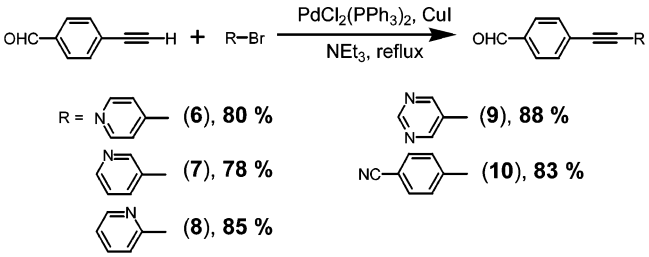
With the possibility of metal-organic frameworks with larger pore sizes in mind, we have synthesized analogues of these popular porphyrins having radial extensions of N-donor groups designed to bind metal ions.



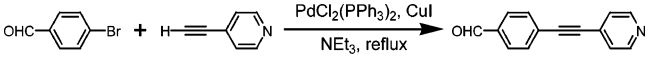
Alkynyl linkages from the *para* positions of the *meso*-aryl groups maintain a rigid propagation of tetragonal shape. A related *meta*-alkynyl derivative has recently been used to prepare a bisporphyrin box.[23]

The most commonly employed method for making a symmetrical tetraarylporphyrin continues to be the Rothemund synthesis from a benzaldehyde[24] using Adler and Longo's modification.[25] Many porphyrins are also amenable to Lindsey conditions.[26] However, there are significant problems when benzaldehydes bearing heterocyclic moieties are used. Adler−Longo conditions typically give low yields, and Lindsey conditions can fail all together. This has been attributed to the poor solubility of intermediates in the acidified solvent.[27] In this paper, we explore these limitations with alkynyl-linked benzaldehydes containing basic groups and then improve the methodology by employing palladium cross-coupling reactions on a preformed tetra(*p*-bromophenyl)porphyrin.

SCHEME 1



SCHEME 2



Palladium cross-coupling methodologies are playing an increasingly important role in porphyrin synthesis.[28−31] Excellent protocols have been developed for Suzuki,[32] Stille,[33] Negishi,[34] and Sonogashira conditions involving porphyrin coupling partners. The simplicity of the experimental procedure, the wide availability of acetylenes, advances in the catalyst formulation,[35] and the efficiency of coupling all contribute to the popularity of the Sonogashira reaction in porphyrin chemistry. It is these factors that prompted us to explore its utility in the current study.

Results and Discussion

Preparation of Alkynyl Benzaldehydes. The benzaldehydes **6**, **7**,[36] **8**,[37] **9**, and **10** were each produced in good yield (78−88%) by the Sonogashira reaction of 4-ethynylbenzaldehyde with the appropriate bromide (Scheme 1). Compound **6** was also produced from the reverse coupling partners in equally good yield (80%) (Scheme 2).

Compounds **6**−**9** were isolated as colored solids which, when necessary, could be purified by sublimation to colorless compounds, albeit with some product loss due to decomposition. Compound **10** could not be sublimed but could be recrystallized to analytical purity, despite the retention of a golden color.

Preparations of Porphyrins under Adler−Longo Conditions. Compounds **6**−**8** were reacted with pyrrole under Adler−Longo conditions for 20 min (Scheme 3). From these reactions,

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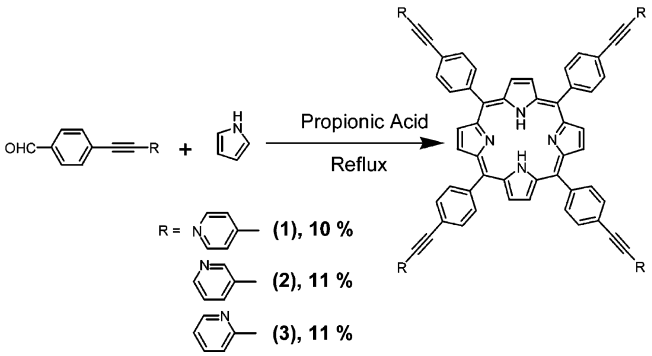
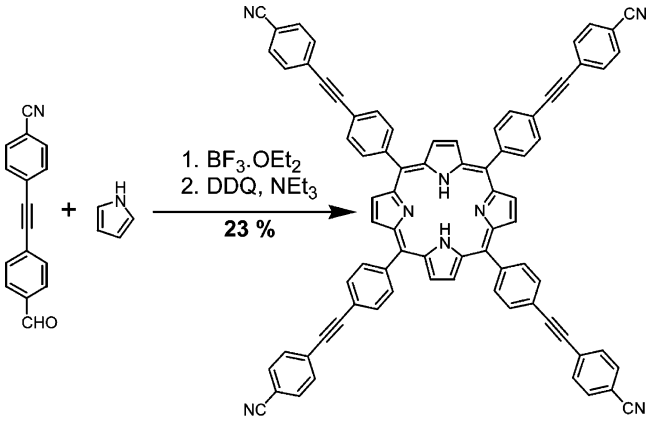
SCHEME 3



SCHEME 4

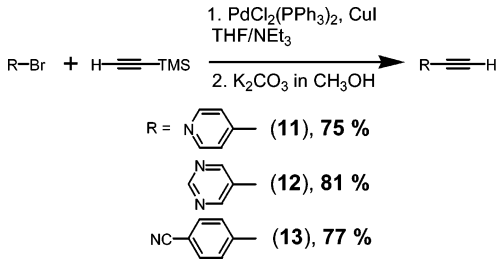


the corresponding porphyrins **1**−**3** were isolated in better than expected yields of ca. 11% after chromatographic purification. We found it beneficial to use aldehydes purified by sublimation in these reactions because then the porphyrin purification process was facilitated.

The reactions of **9** and **10** resulted in the precipitation of much solid during the porphyrin-forming reactions, presumably from decomposition. Porphyrins could be isolated after chromatography of each reaction mixture, but they always contained a stubborn impurity, resistant to separation by chromatography or recrystallization. Due to the low yield of these reactions (ca. 2%) and the problem of purification, this method was abandoned for **4** and **5**.

Preparation of Porphyrins Using Lindsey Conditions. Reactions of benzaldehydes **9** and **10** were attempted using Lindsey conditions. Upon addition of $BF_3{\cdot}OEt_2$ to the reaction mixture of **9** and pyrrole in chloroform, an immediate precipitate developed and no porphyrin was formed. We attribute this to complexation of BF_3 with the heterocyclic base, like that encountered with other unprotected pyrimidines.[38] In a separate reaction with a Brønsted acid in place of the Lewis acid, the addition of trifluoroacetic acid to the reaction mixture did not lead to the formation of any porphyrin at room temperature, even after 6 h. In contrast, the addition of $BF_3{\cdot}OEt_2$ to a mixture of **10** and pyrrole in chloroform led smoothly to the formation of porphyrin **5** after DDQ oxidation (Scheme 4). A pure product was isolated in 23% yield after chromatography and crystallization, providing a quite satisfactory preparation of this new, extended porphyrin.

SCHEME 5



Having identified the limits of porphyrin-forming reactions using Adler−Longo and Lindsey conditions, we turned our attention toward the use of cross-coupling protocols with a preformed porphyrin. This takes advantage of a higher-yielding porphyrin synthesis but demands high efficiency in the subsequent 4-fold coupling reaction. Successful 4-fold couplings have been reported[39] but not with N-heterocycles.

Preparation of the Alkynes. Following the excellent procedure detailed by Thorand and Krause,[40] we coupled 4-bromopyridine, 5-bromopyrimidine, and 4-bromobenzonitrile with trimethylsilylacetylene in THF/triethylamine (Scheme 5). Standard methods were used for deprotection of the silylethers,[41] and compounds **11**,[42] **12**, and **13**[43,44] were isolated as colorless solids in good yields (75−81%).

Preparation of Porphyrins by Cross-Coupling with Alkynes. Our strategy was to use the easily prepared 5,10,15,20-tetrakis-(4-bromophenyl)porphyrin and couple it to the alkyne in the final step. This makes best use of the alkyne and also reduces the amount of Pd catalyst needed compared to the earlier procedures (Scheme 1). To the best of our knowledge, there is only one example of 4-fold coupling of an alkyne to 5,10,15,-20-tetrakis(4-bromophenyl)porphyrin. Chan and co-workers[39] used trimethylsilylacetylene and $PdCl_2(PPh_3)_2$ in triethylamine to produce the 4-fold coupled product in 78% yield. These conditions, however, gave no coupled product with our alkynes. We conducted a survey of conditions using three commonly employed solvents and two common catalysts (see Supporting Information for details) and found success when using conditions similar to those reported for the synthesis of tetravinylated porphyrins via the Heck reaction,[45] namely, a Pd(0) reagent in DMF solvent at elevated temperature. Our procedure bears similarity to the recently reported Heck (Cu-free Sonogashira) alkynylation reaction of porphyrins[46] and to a 4-fold coupling reaction using a *meso*-tetrakis(ethynyl)porphyrin.[47]

Each of the alkynes **11**−**13** was reacted with 5,10,15,20-tetrakis(4-bromophenyl)porphyrin under the conditions outlined

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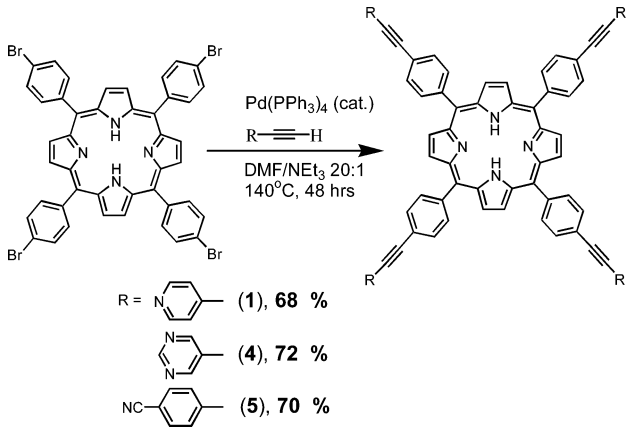
SCHEME 6



in Scheme 6, and the 4-fold alkynylated compounds **1**, **4**, and **5** were isolated in ca. 70% yields.

Stoichiometry was important because excess alkyne led to lower yields, and MALDI mass spectrometry indicated higher than 4-fold levels of alkyne incorporation. Excess alkyne incorporation has been seen in the Sonogashira reaction of other porphyrin substrates.[48] Reaction time was also important because, given enough time, the alkynyl linkages become hydrogenated to vinyl linkages.

Conclusions

We have shown that acceptable yields of extended pyridine-containing porphyrins **1**−**3** can be obtained under Adler−Longo conditions. Lindsey conditions with BF_3 catalysis are incompatible with N-heterocyclic groups, but less basic cyano substituents are tolerated, allowing a good synthesis of porphyrin **5** to proceed. This finding is useful because subsequent derivatization chemistry of the cyano groups is possible.

More flexible, however, is the palladium-catalyzed route to extended porphyrins. This method did not display the functional group incompatibility problems of Adler−Longo or Lindsey conditions, allowing extended porphyrins to be synthesized on a gram scale with operational simplicity. The yield on the last step is particularly good, making efficient use of the materials and the palladium catalyst.

The potential of tetraarylporphyrins with extended *meso*-substituents can now be explored in studies of metal-organic frameworks.

Experimental Section

General Procedure for Aldehyde Synthesis by Pd-Catalyzed Coupling. A flask was charged with 4-ethynylbenzaldehyde (1 equiv), the requisite arylbromide (1 equiv), $PdCl_2(PPh_3)_2$ (1−2 mol %), and dry Et_3N. The mixture was stirred magnetically for 10 min with Ar bubbled through the solution before CuI (2−4 mol %) was added and a reflux condenser attached and the mixture heated to reflux with stirring under Ar for 2 h. Following removal of Et_3N by rotary evaporation, $CHCl_3$ was added and the solution was filtered, washed with 15% aq K_2CO_3, H_2O, and brine, dried ($MgSO_4$ or Na_2SO_4), and the $CHCl_3$ removed. Compounds were treated by passing through a plug of silica gel or by the addition of EtOH and sonication/trituration before sublimation (<0.2 mm, heat gun), whereupon colorless solids were obtained.

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4-(4-Pyridinyl)benzaldehyde (6). The general procedure with 4-ethynylbenzaldehyde (3.40 g, 26.1 mmol), 4-bromopyridine hydrochloride (5.26 g, 27.1 mmol), $PdCl_2(PPh_3)_2$ (0.38 g, 2 mol %), Et_3N (100 mL), and CuI (0.20 g, 4 mol %) was followed. Silica gel treatment and sublimation gave pure **6** (4.34 g, 80%). Compound **6** was also produced in the same manner from 4-ethynylpyridine (1.51 g, 14.6 mmol), 4-bromobenzaldehyde (2.47 g, 13.4 mmol), $PdCl_2(PPh_3)_2$ (88 mg, 1 mol %), and CuI (69 mg, 2.5 mol %) in Et_3N (50 mL). Yield 2.22 g, 80%: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, 2H, J_{HH} = 4.6 Hz), 7.69 (d, 2H, J_{HH} = 8.2 Hz) 7.88 (d, 2H, J_{HH} = 6.7 Hz), 8.62 (d, 2H, J_{HH} = 4.6 Hz), 10.02 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 90.75, 93.20, 126.16, 128.82, 130.25, 131.24, 133.05, 136.73, 150.56, 191.88; *m*/*z* calcd for $C_{14}H_9N_1O_1$ 207.06933, found 207.06841. Anal. Calcd for $C_{14}H_9N_1O_1$: C, 81.14; H, 4.38; N, 6.76. Found: C, 81.38; H, 4.65; N, 6.61.

4-(3-Pyridinyl)benzaldehyde (7). The general procedure from 4-ethynylbenzaldehyde (1.14 g, 8.8 mmol), 3-bromopyridine (1.45 g, 9.2 mmol), $PdCl_2(PPh_3)_2$ (120 mg, 2 mol %), and CuI (70 mg, 4 mol %) in Et_3N (35 mL) was followed. EtOH (ca. 1 mL) was added to the solid and the mixture sonicated/triturated before filtering off a yellow-orange powder (1.42 g, 78%). Purification by sublimation gives a colorless solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (t, 1H, J_{HH} = 4.1 Hz), 7.67 (d, 2H, J_{HH} = 8.2 Hz), 7.81 (d, 1H, J_{HH} = 8.2 Hz), 7.86 (d, 2H, J_{HH} = 8.2 Hz), 8.57 (d, 1H, J_{HH} = 5.1 Hz), 8.77 (s, 1H), 10.00 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 89.68, 91.52, 119.65, 123.07, 128.61, 129.55, 132.15, 135.75, 138.53, 149.12, 152.29, 191.24; *m*/*z* calcd for $C_{14}H_9N_1O_1$ 207.06841, found 207.06795. Anal. Calcd for $C_{14}H_9N_1O_1$: C, 81.14; H, 4.38; N, 6.76. Found: C, 81.16; H, 4.48; N, 6.51.

4-(2-Pyridinyl)benzaldehyde (8). The general procedure from 4-ethynylbenzaldehyde (1.16 g, 8.9 mmol), 2-bromopyridine (1.43 g, 9.1 mmol), $PdCl_2(PPh_3)_2$ (120 mg, 2 mol %), and CuI (70 mg, 4 mol %) in Et_3N (35 mL) was followed. EtOH (ca. 1 mL) was added to the solid and the mixture sonicated/triturated before filtering off a tan powder (1.58 g, 85%). Purification by sublimation gives a colorless solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (t, 1H, J_{HH} = 5.1 Hz), 7.56 (d, 1H, J_{HH} = 8.2 Hz), 7.71 (t, 1H, J_{HH} = 7.7 Hz), 7.74 (d, 2H, J_{HH} = 8.2 Hz), 7.87 (d, 2H, J_{HH} = 6.2 Hz), 8.64 (d, 1H, J_{HH} = 4.6 Hz), 10.02 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 87.93, 91.98, 123.32, 127.42, 128.38, 129.51, 132.51, 135.89, 136.32, 142.67, 150.17, 191.31; *m*/*z* calcd for $C_{14}H_9N_1O_1$ 207.06841, found 207.06879. Anal. Calcd for $C_{14}H_9N_1O_1$: C, 81.14; H, 4.38; N, 6.76. Found: C, 81.10; H, 4.47; N, 6.77.

4-(5-Pyrimidinyl)benzaldehyde (9). The general procedure from 4-ethynylbenzaldehyde (3.14 g, 24.1 mmol), 5-bromopyrimidine (3.92 g, 24.7 mmol), $PdCl_2(PPh_3)_2$ (0.20 g, 1.2 mol %), and CuI (0.12 g, 2.6 mol %) in Et_3N (100 mL) was followed. Silica gel treatment and sublimation gave pure **9** (4.40 g, 88%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, 2H, J_{HH} = 6.7 Hz), 7.90 (d, 2H, J_{HH} = 8.2 Hz), 8.88 (s, 2H), 9.18 (s, 1H), 10.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.50, 95.70, 119.89, 128.44, 130.30, 132.98, 136.87, 157.86, 159.42, 191.85; *m*/*z* calcd for $C_{13}H_8N_2O_1$ 207.05584, found 207.05579. Anal. Calcd for $C_{13}H_8N_2O_1$: C, 74.94; H, 3.87; N, 13.45. Found: C, 75.26; H, 3.70; N, 13.15.

4-(4-Cyanophenyl)benzaldehyde (10). The general procedure from 4-ethynylbenzaldehyde (2.76 g, 21.2 mmol), 4-bromobenzonitrile (3.86 g, 21.2 mmol), $PdCl_2(PPh_3)_2$ (0.30 g, 2 mol %), PPh_3 (0.11 g, 2 mol %), and CuI (0.16 g, 4 mol %) in Et_3N (85 mL) was followed. EtOH (ca. 1−2 mL) was added and the mixture sonicated/triturated before filtering off a solid that was crystallized by layering hexane (4−5 volumes) onto a solution of the title compound dissolved in the minimum of hot $CHCl_3$ (4.05 g, 83%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (m, 4H), 7.69 (d, 2H, J_{HH} = 8.2 Hz), 7.90 (d, 2H, J_{HH} = 8.7 Hz), 10.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 91.15, 92.39, 112.17, 118.25, 127.32, 128.29, 129.57, 132.08, 132.21, 132.28, 135.96, 191.20; *m*/*z* calcd for $C_{16}H_9N_1O_1$ 231.06841, found 231.06878. Anal. Calcd for $C_{16}H_9N_1O_1$: C, 83.10; H, 3.92; N, 6.06. Found: C, 83.05; H, 3.67; N, 5.95.

General Procedure for Porphyrins by Rothemund Synthesis. Aldehydes **1**−**3** (1 equiv) and pyrrole (1 equiv) were placed in a flask, and propionic acid was added and the mixture refluxed for 20 min. In the case of easily identified crystalline products, filtration was used. Alternatively, the solvent was removed under reduced pressure and the residue taken up in $CHCl_3$ and loaded onto an Al_2O_3 column and eluted with $CHCl_3$. In all cases, chromatography on silica gel eluting with $CHCl_3$−alcohol mixtures was used, and crystalline products were obtained by layering MeOH onto concentrated $CHCl_3$ solutions.

5,10,15,20-Tetrakis(4-(4-pyridinylethynyl)phenyl)porphyrin (1). The general procedure from **6** (1.00 g, 4.8 mmol), pyrrole (0.32 g, 4.8 mmol), and propionic acid (20 mL) was followed. The crystallized solid was collected on a frit, washed with hot water (3 × 10 mL) and then ethanol (3 × 5 mL), chromatographed on silica gel (2 × 20 cm, $CHCl_3$−MeOH, 95:5) for purification, and recrystallized giving beautiful, shiny purple needles (120 mg, 10%): ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.78 (br s, 2NH), 7.54 (d, 8H, J_{HH} = 6.1 Hz), 7.98 (d, 8H, J_{HH} = 8.6 Hz), 8.25 (d, 8H, J_{HH} = 8.0 Hz), 8.70 (d, 8H, J_{HH} = 5.5 Hz), 8.89 (s, 8H); UV−vis λ_{nm} (log ϵ) 424 (5.43), 519 (4.09), 555 (3.91), 592 (3.59), 649 (3.53); MALDI mass spectrum *m*/*z* calcd for $C_{72}H_{43}N_8$ 1019.3605, found 1019.3602. Anal. Calcd for $C_{72}H_{42}N_8$: C, 84.85; H, 4.15; N, 11.00. Found: C, 84.64; H, 4.13; N, 10.99.

5,10,15,20-Tetrakis(4-(3-pyridinylethynyl)phenyl)porphyrin (2). The general procedure from **7** (1.00 g, 4.8 mmol), pyrrole (0.32 g, 4.8 mmol), and propionic acid (20 mL) was followed. After the Al_2O_3 (8 × 10 cm, $CHCl_3$) and silica gel chromatography (4 × 30 cm, $CHCl_3$−EtOH, 97.5:2.5), crystallization gave shiny purple needles (131 mg, 11%): ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.76 (br s, 2NH), 7.37 (m, 4H, J_{HH} = 8.2 Hz), 7.96 (m, 12H), 8.26 (d, 8H, J_{HH} = 6.2 Hz), 8.64 (d, 4H, J_{HH} = 4.9 Hz), 8.90 (s, 8H), 8.94 (s, 4H); UV−vis λ_{nm} (log ϵ) 425 (5.76), 519 (4.36), 555 (4.19), 592 (3.87), 649 (3.83); MALDI mass spectrum *m*/*z* calcd for $C_{72}H_{43}N_8$ 1019.3605, found 1019.3627. Anal. Calcd for $C_{72}H_{42}N_8$: C, 84.85; H, 4.15; N, 11.00. Found: C, 85.32; H, 4.33; N, 10.33.

5,10,15,20-Tetrakis(4-(2-pyridinylethynyl)phenyl)porphyrin (3). The general procedure from **7** (1.00 g, 4.8 mmol), pyrrole (0.32 g, 4.8 mmol), and propionic acid (20 mL) was followed. After the Al_2O_3 (8 × 10 cm, $CHCl_3$) and silica gel chromatography (4 × 30 cm, $CHCl_3$−EtOH, 97:3), crystallization gave shiny purple needles (126 mg, 10.5%): ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.79 (br s, 2NH), 7.33 (t, 4H, J_{HH} = 6.0 Hz), 7.69 (d, 4H, J_{HH} = 7.7 Hz), 7.78 (t, 4H, J_{HH} = 7.5 Hz), 8.02 (d, 8H, J_{HH} = 7.9 Hz), 8.24 (d, 8H, J_{HH} = 7.9 Hz), 8.72 (d, 4H, J_{HH} = 4.6 Hz), 8.90 (s, 8H); UV−vis λ_{nm} (log ϵ) 424 (5.79), 518 (4.37), 554 (4.21), 593 (3.87), 648 (3.84); MALDI mass spectrum *m*/*z* calcd for $C_{72}H_{43}N_8$ 1019.3605, found 1019.3578. Anal. Calcd for $C_{72}H_{42}N_8$: C, 84.85; H, 4.15; N, 11.00. Found: C, 82.07; H, 3.68; N, 9.00.

5,10,15,20-Tetrakis(4-(4-cyanophenylethynyl)phenyl)porphyrin (5). To a two-necked flask charged with **10** (0.50 g, 2.16 mmol) and a stir bar was attached a reflux condenser fitted with an Ar gas supply and a suba-seal. After three evacuation−refill cycles, dry, oxygen-free $CHCl_3$ (200 mL) and pyrrole (0.15 mL, 2.16 mmol) were admitted through the seal. After stirring a few minutes, BF_3·OEt_2 (0.27 mL, 2.16 mmol) was added via syringe and the mixture stirred for 1 h at rt. DDQ (0.45 g 1.98 mmol) and Et_3N (1.5 mL) were then added, and the mixture was refluxed 1 h. After removing ca. 3/4 of the solvent by rotary evaporation, the reaction mixture was loaded directly onto an Al_2O_3 column (8 × 15 cm, $CHCl_3$) and a single fraction collected. The volume was reduced by rotary evaporation until near saturation, and the solution was loaded onto silica gel (4 × 30 cm, $CHCl_3$) and the fraction following a small head band was collected and crystallized by layering methanol onto a concentrated $CHCl_3$ solution to gave a purple solid (140 mg, 23%): ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.78 (br s, 2NH), 7.74 (m, 16H), 7.96 (d, 8H, J_{HH} = 7.9 Hz), 7.25 (d, 8H, J_{HH} = 7.9 Hz), 8.88 (s, 8H); UV−vis λ_{nm} (log ϵ) 425 (5.62), 519 (4.23), 555 (4.07), 592 (3.74), 648 (3.68); MALDI mass spectrum *m*/*z* calcd for $C_{80}H_{43}N_8$ 1115.3605, found 1115.3527. Anal. Calcd for $C_{80}H_{42}N_8$: C, 86.15; H, 3.80; N, 10.05. Found: C, 86.18; H, 3.91; N, 10.32.

General Procedure for Synthesis of Terminal Alkynes by Sonogashira Reaction. A modified Schlenk flask was charged with requisite arylbromide (1 equiv), PPh_3 (2.5 mol %), $PdCl_2(PPh_3)_2$ (3−5 mol %), and a stir bar and evacuated−refilled three times with Ar. THF (to give ca. 0.5 M solution), Et_3N (1.5 equiv [2.25 equiv in the case of **11**]), and trimethylsilylacetylene (1.5 equiv) were added by syringe, and the mixture was stirred for 15 min under Ar before CuI (2−2.5 mol %) was added and the Teflon screw valve closed and the reaction stirred at rt. After reaction, THF was removed under reduced pressure, hexane added, and the mixture filtered over Celite. The filtrate was washed with H_2O and the hexane removed. The residual solid was dissolved in MeOH (to give ca. 0.5 M solution), K_2CO_3 (0.1 g/10 mmol) added, and the mixture stirred at rt for 1.5 h. The reactions were worked up by removal of some MeOH by rotary evaporation, dilution with H_2O, extraction with Et_2O (4×), drying ($MgSO_4$ or Na_2SO_4), and removal of solvent. The residues were purified by chromatography on silica gel or sublimation (<0.5 mm, heat gun) to give a colorless solids.

4-Ethynylpyridine (11). Following the general procedure from 4-bromopyridine hydrochloride (1.80 g, 9.25 mmol), PPh_3 (40 mg, 2.5 mol %), $PdCl_2(PPh_3)_2$ (250 mg, 3 mol %), Et_3N (3.0 mL, 21.5 mmol), trimethylsilylacetylene (1.10 g, 11.2 mmol), and CuI (37 mg, 1.7 mol %) in THF (20 mL) for 8 h gave a dark solid after work up. MeOH/K_2CO_3 treatment and subsequent workup gave a dark residue that was purified by passing through a plug of silica gel (CH_2Cl_2) and then sublimation (0.72 g, 75%). NMR data were consistent with those reported.[40]

5-Ethynylpyrimidine (12). Following the general procedure from 5-bromopyrimidine (5.10 g, 32.1 mmol), Ph_3P (0.21 g, 0.80 mmol), $PdCl_2(PPh_3)_2$ (1.10 g, 5 mol %), Et_3N (4.86 g, 48.1 mmol), trimethylsilylacetylene (4.72 g, 48.1 mmol), and CuI (0.12 g, 2 mol %) in THF (60 mL) for 16 h gave a golden solid following workup. The residue after MeOH/K_2CO_3 treatment and workup was purified by sublimation (2.70 g, 81%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.40 (s, 1H), 8.80 (s, 2H), 9.15 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.40, 119.89, 157.23, 159.29; *m*/*z* calcd for $C_6H_4N_2$ 104.03694, found 104.03745. Anal. Calcd for $C_6H_4N_2$: C, 69.22; H, 3.87; N, 26.91. Found: C, 68.89; H, 3.63; N, 27.00.

4-Ethynylbenzonitrile (13). Following the general procedure from 4-bromobenzonitrile (4.97 g, 27.3 mmol), PPh_3 (0.17 g, 2.5 mol %), $PdCl_2(PPh_3)_2$ (0.96 g, 5 mol %), Et_3N (4.23 g, 41.8 mmol), trimethylsilylacetylene (4.05 g, 41.2 mmol), and CuI (0.17 g, 2.5 mol %) in THF (60 mL) for 16 h at rt gave a yellow solid after workup. The residue after MeOH/K_2CO_3 treatment and workup was purified by column chromatography on silica gel eluting with CH_2Cl_2−hexanes (1:3, R_f 0.2) to give **13** as a colorless solid (2.67 g, 77%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.30 (s, 1H), 7.61 (d, 2H), 7.56 (d, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 81.49, 81.84, 112.36, 118.19, 126.99, 131.99, 132.65; *m*/*z* calcd for $C_9H_5N_1$ 127.04220, found 127.04172. Anal. Calcd for $C_9H_5N_1$: C, 85.02; H, 3.96; N, 11.02. Found: C, 85.01; H, 3.89; N, 11.09.

General Procedure for Porphyrin Synthesis by Pd-Catalyzed Coupling. A modified Schlenk tube was charged with 5,10,15,-20-tetrakis(4-bromophenyl)porphyrin (ca. 100 mg, 0.11 mmol), the desired alkyne (4.5−5 equiv), $Pd(PPh_3)_4$ (10 mol %), dry Et_3N (1 mL), dry DMF (20 mL), and a magnetic stir bar. The mixture was degassed by three freeze−pump−thaw cycles before being back-filled with Ar and closing the Teflon screw valve. The contents of the tube were stirred and heated at 140 °C for 48 h. After cooling, the solvents were removed under reduced pressure to dryness, and the purple solid was taken up in $CHCl_3$ (ca. 30 mL) and sonicated before filtering through Celite. After removal of solvent, the residue was redissolved in the minimum of hot $CHCl_3$, and methanol was then layered onto the solution; the crystals that formed were collected by filtration and washed with methanol and hexane.

5,10,15,20-Tetrakis(4-(4-pyridinylethynyl)phenyl)porphyrin (1). 5,10,15,20-Tetrakis(4-bromophenyl)porphyrin (108.3 mg, 0.116 mmol), 4-ethynylpyridine (60.7 mg, 0.589 mmol), $Pd(PPh_3)_4$ (11.3 mg, 10 mol %). Yield 80.2 mg, 68%.

5,10,15,20-Tetrakis(4-(5-pyrimidinylethynyl)phenyl)porphyrin (4). 5,10,15,20-Tetrakis(4-bromophenyl)porphyrin (108.7 mg, 0.117 mmol), 5-ethynylpyrimidine (56.8 mg, 0.546 mmol), $Pd(PPh_3)_4$ (13.5 mg, 10 mol %). Yield 85.6 mg, 72%: ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.78 (br s, 2NH), 7.98 (d, 8H, J_{HH} = 7.9 Hz), 8.27 (d, 8H, J_{HH} = 7.9 Hz), 8.89 (s, 8H), 9.02 (s, 8H), 9.24 (s, 4H); UV−vis λ_{nm} (log ϵ) 425 (5.62), 519 (4.23), 555 (4.07), 592 (3.74), 648 (3.68). Anal. Calcd for $C_{68}H_{38}N_{12}\cdot 0.5H_2O$: C, 79.13; H, 3.81; N, 16.28. Found: C, 79.01; H, 4.11; N, 15.93.

5,10,15,20-Tetrakis(4-(4-cyanophenylethynyl)phenyl)porphyrin (5). 5,10,15,20-Tetrakis(4-bromophenyl)porphyrin (101.7 mg, 0.109 mmol), 4-ethynylbenzonitrile (64.2 mg, 0.505 mmol), $Pd(PPh_3)_4$ (12.9 mg, 10 mol %). Yield 84.1 mg, 70%.

Procedure for Large-Scale Porphyrin Synthesis by Pd-Catalyzed Coupling. 5,10,15,20-Tetrakis(4-(5-pyrimidinylethynyl)phenyl)porphyrin (5). To a single-necked round-bottomed flask were placed reagent grade DMF (200 mL) and reagent grade triethylamine (20 mL). Ar was bubbled through the magnetically stirred solution with a fritted bubbler for 1 h before 5,10,15,20-tetrakis(4-bromophenyl)porphyrin (1.03 g, 1.11 mmol), 5-ethynylpyrimidine (0.53 g, 5.10 mmol), and $Pd(PPh_3)_4$ (121 mg, 10 mol %) were added under a flow of Ar and a reflux condenser attached. The contents were heated at 130 °C with stirring for 60 h under Ar. The same general procedure as above was followed for the isolation and purification (0.77 g, 59%).

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Supporting Information Available: Further experimental procedures, ^{1}H NMR spectra for compounds **1**−**13**, ^{13}C NMR spectra for compounds **6**−**10**, **12**, **13**, mass spectra for compounds **1**−**9**, **11**−**13**, UV−visible spectra for compounds **1**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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