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Synthesis of *meso*-Extended Tetraaryl Porphyrins

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Abstract

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.

Keywords

Porphyrins; heterocycles; Sonagashira reaction; palladium cross-coupling; Rothemund synthesis; metal-organic frameworks

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 last 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 metalloporphyrins⁵ or fullerenes as supramolecular pillars¹¹ but typically at the expense of pore size.

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 bis-porphyrin box.²³

The most commonly employed method for making a symmetrical tetraarylporphyrin continues to be the Rothemund synthesis from a benzaldehyde²⁴ 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. Alder-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 pre-formed tetra(*p*-bromophenyl)porphyrin.

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 Sonagashira 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 Sonagashira 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 Sonagashira 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 twenty minutes (Scheme 3). From these reactions 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 BF₃·OEt₂ 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 BF₃ 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 six hours. In contrast, the addition of BF₃·OEt₂ 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.

Having identified the limits of porphyrin-forming reactions using Adler-Longo and Lindsey conditions, we turned our attention towards the use of cross-coupling protocols with a pre-formed porphyrin. This takes advantage of a higher-yielding porphyrin synthesis but demands high efficiency in the subsequent four-fold coupling reaction. Successful four-fold couplings have been reported³⁹ but not with N-heterocycles.

Preparation of the alkynes

Following with the excellent procedure detailed by Thorand and Krause,⁴⁰ 4-bromopyridine, 5-bromopyrimidine and 4-bromobenzonitrile were coupled with trimethylsilylacetylene in

THF/triethylamine (Scheme 5). Standard methods were used for deprotection of the silylethers⁴¹ 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 four-fold coupling of an alkyne to 5,10,15,20-tetrakis(4-bromophenyl)porphyrin. Chan and co-workers³⁹ used trimethylsilylacetylene and PdCl₂(PPh₃)₂ in triethylamine to produce the four-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 tetra-vinylated 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 porphyrins⁴⁶ and to a four-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 in Scheme 6 and the four-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 four-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 BF₃ 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 is charged with 4-ethynylbenzaldehyde (1 equiv), the requisite arylbromide (1 equiv), PdCl₂(PPh₃)₂ (1–2 mol%), and dry Et₃N. The mixture is 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 Et₃N by rotary evaporation, CHCl₃ was added and the solution was filtered, washed with 15% aq. K₂CO₃, H₂O, brine, dried (MgSO₄ or Na₂SO₄) and the CHCl₃ 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 colourless solids were obtained.

4-(4-pyridinyl)benzaldehyde (6)—Following the general procedure with 4-ethynylbenzaldehyde (3.40 g, 26.1 mmol), 4-bromopyridine hydrochloride (5.26 g, 27.1 mmol), PdCl₂(PPh₃)₂ (0.38 g, 2 mol%), Et₃N (100 mL) and CuI (0.20 g, 4 mol%). 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), PdCl₂(PPh₃)₂ (88 mg, 1 mol%) and CuI (69 mg, 2.5 mol%) in Et₃N (50 mL) (2.22 g, 80 %). ¹H NMR (300 MHz, CDCl₃) 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). ¹³C NMR (75 MHz, CDCl₃) δ: 90.75, 93.20, 126.16, 128.82, 130.25, 131.24, 133.05, 136.73, 150.56, 191.88. *m/z* Calcd C₁₄H₉N₁O₁ 207.06933; Found 207.06841. Anal.: Found: C, 81.38; H, 4.65; N, 6.61; Calcd for C₁₄H₉N₁O₁: C, 81.14; H, 4.38; N, 6.76.

4-(3-pyridinyl)benzaldehyde (7)—Following the general procedure from 4-ethynylbenzaldehyde (1.14 g, 8.8 mmol), 3-bromopyridine (1.45 g, 9.2 mmol), PdCl₂(PPh₃)₂ (120 mg, 2 mol%) and CuI (70 mg, 4 mol%) in Et₃N (35 mL). EtOH (ca. 1 mL) was added to the solid and the mixture sonicated/trituated before filtering off a yellow-orange powder (1.42 g, 78%). Purification by sublimation gives a colorless solid. ¹H NMR (300 MHz, CDCl₃) 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). ¹³C NMR (75 MHz, CDCl₃) 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 C₁₄H₉N₁O₁ 207.06841; Found 207.06795. Anal.: Found: C, 81.16; H, 4.48; N, 6.51; Calcd for C₁₄H₉N₁O₁: C, 81.14; H, 4.38; N, 6.76.

4-(2-pyridinyl)benzaldehyde (8)—Following the general procedure from 4-ethynylbenzaldehyde (1.16 g, 8.9 mmol), 2-bromopyridine (1.43 g, 9.1 mmol), PdCl₂(PPh₃)₂ (120 mg, 2 mol%) and CuI (70 mg, 4 mol%) in Et₃N (35 mL). EtOH (ca. 1 mL) was added to the solid and the mixture sonicated/trituated before filtering off a tan powder (1.58 g, 85%). Purification by sublimation gives a colorless solid. ¹H NMR (300 MHz, CDCl₃) 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). ¹³C NMR (75 MHz, CDCl₃) 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 C₁₄H₉N₁O₁ 207.06841; Found 207.06879. Anal.: Found: C, 81.10; H, 4.47; N, 6.77; Calcd for C₁₄H₉N₁O₁: C, 81.14; H, 4.38; N, 6.76.

4-(5-Pyrimidinyl)benzaldehyde (9)—Following the general procedure from 4-ethynylbenzaldehyde (3.14 g, 24.1 mmol), 5-bromopyrimidine (3.92 g, 24.7 mmol), PdCl₂(PPh₃)₂ (0.20 g, 1.2 mol%) and CuI (0.12 g, 2.6 mol%) in Et₃N (100 mL). Silica gel treatment and sublimation gave pure **9** (4.40 g, 88%). ¹H NMR (300 MHz, CDCl₃) 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). ¹³C NMR (75 MHz, CDCl₃) δ: 86.50, 95.70, 119.89, 128.44, 130.30, 132.98, 136.87, 157.86, 159.42, 191.85. *m/z* Calcd C₁₃H₈N₂O₁ 207.05584; Found 207.05579. Anal.: Found: C, 75.26; H, 3.70; N, 13.15; Calcd for C₁₃H₈N₂O₁: C, 74.94; H, 3.87; N, 13.45.

4-(4-cyanophenyl)benzaldehyde (10)—Following the general procedure from 4-ethynylbenzaldehyde (2.76 g, 21.2 mmol), 4-bromobenzonitrile (3.86 g, 21.2 mmol), PdCl₂(PPh₃)₂ (0.30 g, 2 mol%), PPh₃ (0.11 g, 2 mol%) and CuI (0.16 g, 4 mol%) in Et₃N (85 mL). EtOH (ca. 1–2 mL) was added and the mixture sonicated/trituated 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%). ^1H 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 $\text{C}_{16}\text{H}_9\text{N}_1\text{O}_1$ 231.06841; Found 231.06878. Anal.: Found: C, 83.05; H, 3.67; N, 5.95: Calcd for $\text{C}_{16}\text{H}_9\text{N}_1\text{O}_1$: C, 83.10; H, 3.92; N, 6.06.

General Procedure for porphyrins by Rothmund synthesis

Aldehydes **1–3** (1 equiv) and pyrrole (1 equiv) were placed in a flask and propionic acid added and the mixture refluxed for 20 min. In the case of easily identified crystalline product 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)—Following the general procedure from **6** (1.00 g, 4.8 mmol), pyrrole (0.32 g, 4.8 mmol) and propionic acid (20 mL). The crystallized solid was collected on a frit and washed with hot water (3×10 mL) and then ethanol (3×5 mL) and chromatographed on silica gel (2×20 cm, CHCl_3 –MeOH, 95–5) for purification and recrystallized giving beautiful, shiny purple needles (120 mg, 10%). ^1H NMR (300 MHz, CDCl_3) δ : –2.78, (s(br) 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: Calcd m/z $\text{C}_{72}\text{H}_{43}\text{N}_8$ 1019.3605; Found 1019.3602. Anal.: Found: C, 84.64; H, 4.13; N, 10.99: Calcd for $\text{C}_{72}\text{H}_{42}\text{N}_8$: C, 84.85; H, 4.15; N, 11.00.

5,10,15,20-tetrakis(4-(3-pyridinylethynyl)phenyl)porphyrin (2)—Following the general procedure from **7** (1.00 g, 4.8 mmol), pyrrole (0.32 g, 4.8 mmol) and propionic acid (20 mL). 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 %). ^1H NMR (300 MHz, CDCl_3) δ : –2.76 (s(br) 2NH); 7.37 (m 4H [J_{HH} 8.2]); 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: Calcd m/z $\text{C}_{72}\text{H}_{43}\text{N}_8$ 1019.3605; Found 1019.3627. Anal.: Found: C, 85.32; H, 4.33; N, 10.33: Calcd for $\text{C}_{72}\text{H}_{42}\text{N}_8$: C, 84.85; H, 4.15; N, 11.00.

5,10,15,20-tetrakis(4-(2-pyridinylethynyl)phenyl)porphyrin (3)—Following the general procedure from **7** (1.00 g, 4.8 mmol), pyrrole (0.32 g, 4.8 mmol) and propionic acid (20 mL). 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 %). ^1H NMR (300 MHz, CDCl_3) δ : –2.79, (s(br) 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: Calcd m/z $\text{C}_{72}\text{H}_{43}\text{N}_8$ 1019.3605; Found 1019.3578. Anal.: Found: C, 82.07; H, 3.68; N, 9.00: Calcd for $\text{C}_{72}\text{H}_{42}\text{N}_8$: C, 84.85; H, 4.15; N, 11.00.

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 $\text{BF}_3 \cdot \text{OEt}_2$ (0.27 mL, 2.16 mmol) was added via syringe and the mixture stirred for 1 h at r.t. DDQ (0.45 g 1.98 mmol) and Et_3N (1.5 mL) were then added and the mixture refluxed 1 h. After removing ca. $\frac{3}{4}$ of the solvent by rotary evaporation the reaction

mixture was loaded directly onto an Al₂O₃ column (8 × 15 cm, CHCl₃) and a single fraction collected. The volume was reduced by rotary evaporation until near saturation and the solution loaded onto silica gel (4 × 30 cm, CHCl₃) and the fraction following a small head band was collected and crystallized by layering methanol onto a concentrated CHCl₃ solution to give a purple solid (140 mg, 23 %). ¹H NMR (300 MHz, CDCl₃) δ: -2.78, (s(br) 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: Calcd *m/z* C₈₀H₄₃N₈ 1115.3605; Found 1115.3527. Anal.: Found: C, 86.18; H, 3.91; N, 10.32; Calcd for C₈₀H₄₂N₈: C, 86.15; H, 3.80; N, 10.05.

General Procedure for synthesis of terminal alkynes by Sonagashira reaction

A modified Schlenk flask was charged with requisite arylbromide (1 equiv), PPh₃ (2.5 mol%), PdCl₂(PPh₃)₂ (3–5 mol%) and a stir bar and evacuated-refilled three times with Ar. THF (to give ca. 0.5 M soln), Et₃N (1.5 equiv [2.25 equiv in the case of **11**]) and trimethylsilylacetylene (1.5 equiv) were added by syringe and the mixture 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 r.t. After reaction THF was removed under reduced pressure and hexane added and the mixture filtered over Celite. The filtrate was washed with H₂O and the hexane removed. The residual solid was dissolved in MeOH (to give ca. 0.5 M soln) and K₂CO₃ (0.1 g per 10 mmol) added and the mixture stirred at r.t. for 1.5 h. The reactions were worked up by removal of some MeOH by rotary evaporation, dilution with H₂O, extraction with Et₂O (4x), drying (MgSO₄ or Na₂SO₄) 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), PPh₃ (40 mg, 2.5 mol%), PdCl₂(PPh₃)₂ (250 mg, 3 mol %), Et₃N (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/K₂CO₃ treatment and subsequent work up gave a dark residue that was purified by passing through a plug of silica gel (CH₂Cl₂) 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), Ph₃P (0.21 g, 0.80 mmol), PdCl₂(PPh₃)₂ (1.10 g, 5 mol%), Et₃N (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 work up. The residue after MeOH/K₂CO₃ treatment and work up was purified by sublimation (2.70 g, 81 %). ¹H NMR (300 MHz, CDCl₃) δ: 3.40, (s 1H); 8.80, (s 2H); 9.15, (s 1H). ¹³C NMR (75 MHz, CDCl₃) δ: 84.40, 119.89, 157.23, 159.29. *m/z* Calcd C₆H₄N₂ 104.03694; Found 104.03745. Anal.: Found: C, 68.89; H, 3.63; N, 27.00; Calcd for C₆H₄N₂: C, 69.22; H, 3.87; N, 26.91.

4-Ethynylbenzonitrile (13)—Following the general procedure from 4-bromobenzonitrile (4.97 g, 27.3 mmol), PPh₃ (0.17 g, 2.5 mol %), PdCl₂(PPh₃)₂ (0.96 g, 5 mol%), Et₃N (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 r.t. gave a yellow solid after work up. The residue after MeOH/K₂CO₃ treatment and work up was purified by column chromatography on silica gel eluting with CH₂Cl₂–hexanes (1–3, R_f 0.2) (2.67 g, 77 %). ¹H NMR (300 MHz, CDCl₃) δ: 3.30, (s 1H); 7.61, (d 2H); 7.56, (d 2H). ¹³C NMR (75 MHz, CDCl₃) δ: 81.49, 81.84, 112.36, 118.19, 126.99, 131.99, 132.65. *m/z* Calcd C₉H₅N₁ 127.04220; Found 127.04172. Anal.: Found: C, 85.01; H, 3.89; N, 11.09; Calcd for C₉H₅N₁: C, 85.02; H, 3.96; N, 11.02.

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. 100mg, 0.11 mmol), the desired alkyne (4.5–5 equiv.), Pd(PPh₃)₄ (10 mol%), dry Et₃N (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 CHCl₃ (ca. 30 mL) and sonicated before filtering through Celite. After removal of solvent the residue was redissolved in the minimum of hot CHCl₃ 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(PPh₃)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(PPh₃)₄ (13.5 mg, 10 mol%). Yield (85.6 mg, 72 %). ¹H NMR (300 MHz, CDCl₃) δ: -2.78, (s(br) 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.: Found: C, 79.01; H, 4.11; N, 15.93; Calcd for C₆₈H₃₈N₁₂·0.5H₂O: C, 79.13; H, 3.81; N, 16.28.

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(PPh₃)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)—In a single necked round bottomed flask was 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(PPh₃)₄ (121 mg, 10 mol%) were added under 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 %).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Scheme 1.

Scheme 2.

Scheme 3.

Scheme 4.

Scheme 5.

Scheme 6.