Synthesis and Functionalization of Double Picket Fence Porphyrins Starting from 4,6-Disubstituted Pyrimidine-5-carbaldehydes

S. Smeets, C. V. Asokan, F. Motmans, and W. Dehaen*

Department of Chemistry, Katholieke Universiteit Leuven, Celestijnenlaan 200F,B-3001 Heverlee, Belgium

wim.dehaen@chem.kuleuven.ac.be

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Introduction

The *ortho*-substituted and *ortho,ortho′*-disubstituted tetraarylporphyrins have been subject of intensive research. In general, sterically encumbered porphyrins have served as useful models for some aspects of the chemistry of hemoproteins.[1] The "picket fence",[2] "double picket fence", and "capped"[3] porphyrins have been studied as models for hemoproteins and as catalysts. *Ortho, ortho′*-substituted tetraarylporphyrins or "double picket fence" porphyrins have been used extensively in second-generation oxidation catalysts.[4] Membranes of picket-fence cobalt porphyrins have been studied as efficient oxygen carriers.[5] Ferric porphyrins bearing chiral binaphthalene moieties on both faces were used in enantioselective oxidation of sulfides and in asymmetric epoxidations.[6] These "twin coronet" porphyrins have been further modified to mimic the active center of heme enzymes such as cytochrome P-450.[7] Functionalization can be achieved with electrophiles on 5,10,15,20-tetrakis-(2,6-dihydroxyphenyl)porphyrin[8] and the analogous amino-substituted tetraarylporphyrins.[9] However, in general the synthesis of these porphyrins is not straightforward. For instance the condensation of 2,6-dinitrobenzaldehyde with pyrrole has been reported to give the octanitro precursor in only in 0.75% yield in the presence of TFA[10] while the use of $BF_3 \cdot Et_2O$ as catalyst gave 2−13% yield.[11] Better yields could be achieved using 2,6-dinitro-4-*tert*-butyl-benzaldehyde, where the *tert*-butyl group increased the solubility of the intermediates.[4] However, the latter aldehyde could only be obtained involving three steps in an overall yield of 41% starting from 4-*tert*-butyltoluene. The reduction toward the *ortho,ortho′*-amino-substituted porphyrins could be achieved in 60% yield. Condensation of 2,6-dimethoxybenzaldehyde with pyrrole yielded the octamethoxy precursor (12%).[12] This porphyrin was then demethylated using BBr_3 giving an overall yield of 9%.[8c] Nucleophilic substitution of the chlorine atoms of the readily available 5,10,15,20-tetrakis(2′,6′-dichlorophenyl)-porphyrin[13] is apparently not feasable. However, functionalization by electrophilic substitution at the meso aryl position could be achieved using 3- or 4-nitro-substituted 2,6-dichlorobenzaldehyde. The nitro group was reduced to amine which could then react further with electrophiles. It should be noted that tailed porphyrins bearing amido bonds are less stable than those having an ether linkage.[14]

Results and Discussion

In this paper we describe the synthesis of several double picket fence porphyrins using 4,6-disubstituted pyrimidine-5-carbaldehydes. The 4,6-dichloro-pyrimidine-5-carbaldehyde **1** can be considered as a heterocyclic analogue of 2,6-dichlorobenzaldehyde. The chlorine functionalities on the pyrimidine ring are highly activated toward nucleophilic substitution, allowing us to introduce substituents at the aldehyde as well as the porphyrin stage.[15]

The aldehyde **1** was prepared using the reported Vilsmeier conditions ($DMF/POCl_3$) for chloroformylation of 4,6-dihydroxypyrimidine.[16] Functionalization of the two chlorine atoms of aldehyde **1** was carried out with several substituted phenolates. Typically, the nucleo-

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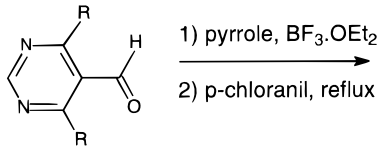
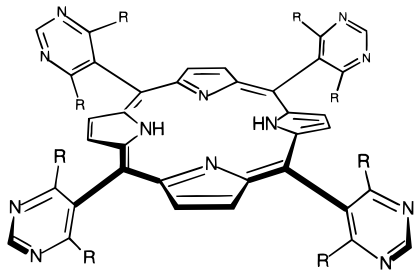
Scheme 1

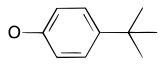
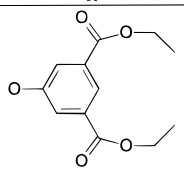
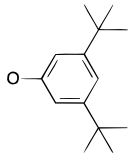
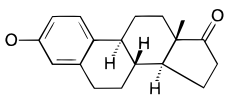
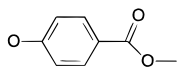


1a (R = Cl)
1b-g



2a (R = Cl)
2b-g

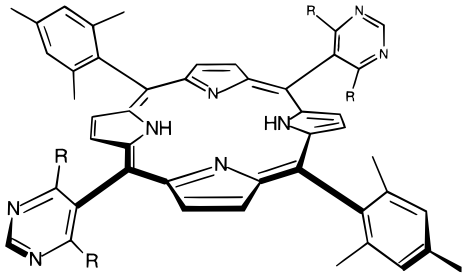
Table 1. Synthesis of Porphyrins 2b−g

R	Yield(%)	R	Yield(%)
	**2b** 40		**2e** 56
	**2c** 24		**2f** 30
	**2d** 54		**2g** 10

philic substitution of **1a** was carried out using 2.2 equiv of phenol and an excess K_2CO_3 (5-fold) under reflux in THF for 5 h. This yielded the 4,6-disubstituted pyrimidine-5-carbaldehydes **1b−g** in excellent yields.

These aldehydes were reacted with pyrrole under Lindsey conditions (Scheme 1).[17] The porphyrins **2b−e** were isolated in yields that ranged from good to excellent (24−59%) (Table 1). On introduction of a nitro group in *ortho*-position of phenol (aldehyde **1g**) the yield of the corresponding porphyrin decreased noticeably (6%). This relatively low yield is not only a consequence of the highly sterically hindered aldehyde but also of the low solubility of the corresponding intermediates in the reaction mixture (solvent: dichloromethane).

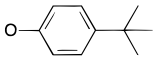
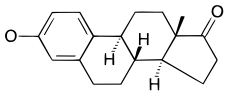
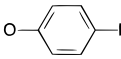
Working under more diluted conditions (3.4×10^{-3} M instead of 3.4×10^{-2} M) gave an increased yield of 10%. We were not able to isolate **2a**, the heterocyclic analogue of 5,10,15,20-tetrakis(2′,6′-dichlorophenyl)porphyrin using either Adler−Longo (refluxing propionic acid) or Lindsey conditions. Again, this may be a result of low solubility of the intermediates. On the other hand, the isolated yields after chromatographic separation and



3

Figure 1.

Table 2. Synthesis of Porphyrins 3a−e

R	Yield(%)	R	Yield(%)
Cl	**3a** 53		**3d** 90
OCH_3	**3b** 46		**3e** 75
	**3c** 60		

crystallization of double picket fence porphyrins **2d** (54%) and **2e** (59%) are among the highest ever obtained for a Rothemund porphyrin synthesis.

It might still be more effective to introduce the substituents directly at the porphyrin stage by substitution of the chlorine functions of the *meso*-(2,6-dichloropyrimidyl) substituents. Unfortunately, octachloro porphyrin **2a** is not available, as mentioned above. Mixed Rothemund condensations, as reported by us in a previous communication, give statistical mixtures of several pyrimidyl porphyrins which are difficult to separate. Therefore, a 5,15-bis(pyrimidyl)porphyrin **3a** was prepared by a McDonald condensation of mesityldipyrromethane[18] with aldehyde **2a**. In previous work we reported that the substitution of **3a** with methoxide gave an inseparable mixture of disubstituted atropoisomers. This reaction was carried out in THF at reflux for 72 h in the presence of K_2CO_3. We now carried out the substitution reaction in DMF using sodium methoxide. We were able to obtain the tetramethoxy-substituted porphyrin **3b**. Reaction of porphyrin **3a** with several phenols (see Figure 1) in the presence of potassium carbonate at 60°C in DMF resulted in the formation of four-picket porphyrins **3d** (60%), **3c** (90%), **3e** (75%) in high yields (Table 2). In case of expensive phenol starting materials (e.g., estrone), this method is clearly superior.

Conclusions

Double picket fence porphyrins which were highly sterically crowded could be prepared in high yields either from pyrimidine or porphyrin starting materials. Substituents are easily introduced on both faces of the porphyrins, which leads to three-dimensionally structured macromolecules. They have been developed as model compounds for oxygen-binding and oxygen-activat-

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ing heme proteins,[19] octopus porphyrins[20] that form monolayer assemblies, functional dendrimers[21] and donor−acceptor systems[22] of potential applications. Enantioselective catalysts can be designed by the introduction of chiral substituents close to the catalytic center of metalloporphyrins.[6,23] The three-dimensional architecture of such molecules would also make them valuable as host molecules for stereoselective molecular recognition.[24]

Experimental Section

General. Mass spectra were obtained on a Hewlett-Packard MS instrument nE 5989A in EI (250 °C), on a Micromass Quatro II in ESI (infusion of 50 ìl MeOH/CH_2Cl_2−NH_4OAc (0.1M in MeOH) with a Harvard pump, model 11), and on a Micromass Quatro II in APCI (250 μL of MeOH/CH_2Cl_2 using a Hewlett-Packard HP 1100 binary pump and infusion of 20−30 μL of MeOH/CH_2Cl_2−NH_4OAc (0.1M in MeOH) with a Harvard pump model 11).

General Procedure for the Synthesis of 4,6-Disubstituted Pyrimidine-5-carbaldehydes. To a well-stirred suspension of anhydrous potassium carbonate (1.52 g, 11 mmol) in THF (100 mL) the substituted phenol (4.4 mmol) was added, and the mixture was stirred with refluxing. After 0.5 h, 4,6-dichloropyrimidine-5-carbaldehyde **1a** (0.352 g, 2 mmol) was added, and the stirring and refluxing was continued for 5 h. The reaction mixture was cooled, and solvent was removed under vacuum. The residue was taken in dichloromethane (100 mL) and washed with water (3 × 30 mL). The organic layer was dried over magnesium sulfate and evaporated to give the crude product, which precipitated on addition of methanol. The resulting suspension was filtered to give the substituted pyrimidinecarbaldehydes **1b**−**g** as colorless solids. They were further purified by recrystallization (methylene chloride/hexane, 1:1).

4,6-Bis[4-(*tert*-butyl)phenoxy]pyrimidine-5-carbaldehyde (1b). Reaction of 4,6-dichloropyrimidine-5-carbaldehyde (0.352 g, 2 mmol) and 4-*tert*-butylphenol (0.660 g, 4.4 mmol) gave **1b** (0.735 g, 91%): mp 160−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (s, 18H), 7.12 (d, J = 8.7 Hz, 4H), 7.47 (d, J = 8.7 Hz, 4H), 8.45 (s, 1H), 10.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.42, 120.95, 126.65, 149.03, 149.77, 160.97, 170.23, 185.73; IR(KBr), ν = 2960, 2866, 1701, 1552, 1506, 1420 cm^{-1}; EI-MS 404 (M^+); Anal. Calcd for $C_{25}H_{28}N_2O_3$: C, 74.23; H, 6.98; N, 6.93. Found: C, 74.22; H, 7.06; N, 6.85.

4,6-Bis[3,5-di(*tert*-butyl)phenoxy]pyrimidine-5-carbaldehyde (1c). Reaction of 4,6-dichloropyrimidine-5-carbaldehyde (0.352 g, 2 mmol) and 3,5-di-*tert*-butylphenol (0.906 g, 4.4 mmol) gave **1c** (0.775 g, 96%): mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 36H), 7.01 (d, J = 1.6 Hz, 4H), 7.36 (s, 2H), 8.42 (s, 1H), 10.69 (s,1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.41, 115.90, 120.16, 151.87, 152.58, 161.18, 170.37, 186.08; IR (KBr), ν = 2945, 1701, 1569, 1413 cm^{-1}; EI-MS 516 (M^+); Anal. Calcd for $C_{33}H_{44}N_2O_3$ C, 76.71; H, 8.58; N, 5.42. Found: C, 76.76; H, 8.70; N, 5.10.

4,6-Bis(4-methoxycarbonylphenoxy)pyrimidine-5-carbaldehyde (1d). Reaction of 4,6-dichloropyrimidine-5-carbaldehyde (0.352 g, 2 mmol) and methyl 4-hydroxybenzoate (0.669 g, 4.4 mmol) gave **1d** (0.718 g, 88%): mp 223−224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (s, 6H), 7.27 (d, J = 6.8 Hz, 4H), 7.36 (s, 2H), 8.16 (d, J = 6.8 Hz, 4H), 8.38 (s, 1H), 10.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.25, 103.53, 121.79, 128.26, 131.46, 155.55, 160.67, 166.07, 169.66, 185.02; IR(KBr), 1735, 1702, 1583, 1552, 1441 cm^{-1}; APCI-MS 409 $(MH)^+$. Anal. Calcd for $C_{21}H_{16}N_2O_7$ C, 61.77; H, 3.95; N; 6.86. Found: C, 61.63; H, 3.95; N, 6.70.

4,6-Bis[3,5-bis(ethoxycarbonyl)phenoxy]pyrimidine-5-carbaldehyde (1e). Reaction of 4,6-dichloropyrimidine-5-carbaldehyde (0.352 g, 2 mmol) and diethyl isophthalate (1.05 g, 4.4 mmol) gave **1e** (1.115 g, 96%): mp 147−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, J = 7.2 Hz, 6H), 4.43 (q, J = 7.2 Hz, 4H), 8.06 (d, J = 1.48 Hz, 4H), 8.37 (s, 1H), 8.64 (t, J = 1.48 Hz, 2H), 10.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.26, 61.72, 103.43, 127.14, 128.35, 132.72, 151.93, 160.59, 164.73, 169.68, 184.82; IR(KBr) ν = 2976, 1740, 1721, 1700, 1553 cm^{-1}; EI-MS 580 (M^+). Anal. Calcd for $C_{29}H_{28}N_2O_{11}$ C, 60.00; H, 4.86; N, 4.83. Found: C, 60.01; H, 4.83; N, 4.66.

4,6-Bis[estra-17-oxo-1,3,5(10)-trien-3-oxy]pyrimidine-5-carbaldehyde (1f). Reaction of 4,6-dichloropyrimidine-5-carbaldehyde (0.352 g, 2 mmol) and estrone (1.190 g, 4.4 mmol) gave **1d** (0.953 g, 74%): mp >250 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 6H), 1.45−1.66 (m, 12H), 1.96−2.18 (m, 8H), 7.61 (t, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.90 (t, J = 8.0 Hz, 2H), 8.24 (d, J = 8.0 Hz, 2H), 8.43 (s, 1H), 10.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.43, 125.46, 125.84, 127.55, 135.82, 141.27, 144.43, 160.46, 168.61, 185.01; IR(KBr), ν = 2928, 2858, 1737, 1700, 1552, 1491 cm^{-1}; CI-MS 645 $(MH)^+$. Anal. Calcd for $C_{41}H_{44}N_2O_5$ C, 76.37; H, 6.88; N, 4.34. Found: C, 76.17; H, 6.81, N, 4.15.

4,6-Bis(2-nitrophenoxy)pyrimidine-5-carbaldehyde (1g). Reaction of 4,6-dichloropyrimidine-5-carbaldehyde (0.352 g, 2 mmol) and 2-nitrophenol (0.612 g, 4.4 mmol) gave **1g** (0.642 g, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (t, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.90 (t, J = 8.0 Hz, 2H), 8.24 (d, J = 8.0 Hz, 2H), 8.43 (s, 1H), 10.56 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.43, 125.46, 125.84, 127.55, 135.82, 141.27, 144.43, 160.46, 168.61, 185.01; IR(KBr), ν = 1703, 1568, 1530, 1506, 1343 cm^{-1}; CI-MS 383 $(MH)^+$. Anal. Calcd for $C_{17}H_{10}N_4O_7$ C, 53.41; H, 2.64; N, 14.66. Found: C, 53.48; H, 2.65; N, 14.60.

General Procedure for the Synthesis of Porphyrins 2b−g. A 0.05 M solution of pyrimidinecarbaldehyde **1b**−**g** and pyrrole (1 equiv) in dichloromethane was deoxygenated by purging with argon for 15 min. Boron trifluoride etherate (0.1 equiv) was added by syringe, and the solution was stirred under argon and protected from light for 2 h at 20 °C. *p*-Chloranil (1 equiv) was added, and the mixture was refluxed for 1 h. The solvent was removed, and the residue was chromatographed (silica gel; CH_2Cl_2). The obtained product was redissolved in dichloromethane and precipitated with MeOH yielding **2b**−**g** as purple solids.

5,10,15,20-Tetrakis[4,6-bis[4-(*tert*-butyl)phenoxy]pyrimidin-5-yl]porphyrin (2b) was obtained from aldehyde **1b** (0.650 g, 1.61 mmol) following the general procedure (0.300 g, 40%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.45 (s, 2H), 1.12 (72H, s), 6.93 (d, J = 8.8 Hz, 16H), 7.16 (d, J = 8.8 Hz, 16H), 8.91 (s, 4H), 9.15 (s, 8H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 422.1 (5.5978), 516.4 (4.2845), 549.3 (3.7736), 592.0 (3.8478), 646.9 (3.3078); APCI-MS 1807.9 (MH^+); Anal. Calcd for $C_{116}H_{118}N_{12}O_8$ C, 77.05; H, 6.58; N, 9.29. Found: C, 76.98; H, 6.65; N, 9.33.

5,10,15,20-Tetrakis[4,6-bis[3,5-bis(*tert*-butyl)phenoxy]-pyrimidin-5-yl]porphyrin (2c) was obtained from aldehyde **1c** (0.500 g, 0.97 mmol) following the general procedure (0.135 g, 24%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.45 (s, 2H), 1.12 (s,-144H), 6.80 (d, J = 1.6 Hz, 16H), 7.07 (d, J = 1.6 Hz, 16H), 8.88

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(s, 4H), 9.21 (s, 8H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 422.1 (5.5978), 516.4 (4.2845), 549.3 (3.7736), 592.0 (3.8478), 646.9 (3.3078); APCI-MS 2056.4 (MH^+); Anal. Calcd for $C_{148}H_{182}N_{12}O_8$ C, 78.76; H, 8.13; N, 7.45. Found: C, 78.60; H, 8.00; N, 7.43.

5,10,15,20-Tetrakis[4,6-bis(4-methoxycarbonylphenoxy)-pyrimidin-5-yl]porphyrin (2d) was obtained from aldehyde **1d** (0.500 g, 1.22 mmol) following the general procedure (0.303 g, 54%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.37 (s, 2H), 3.83 (s, 24H), 7.04 (d, J = 8.8 Hz, 16H), 7.89 (d, J = 8.8 Hz, 16H), 8.87 (s, 4H), 9.16 (s, 8H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 422.0 (5.6952), 518.1 (4.3272), 547.8 (3.5906), 591.6 (3.7848), 647.03 (2.2552); APCI-MS 1823.5 (MH^+). Anal. Calcd for $C_{100}H_{70}N_{12}O_{24}$ C, 65.86; H, 3.87; N, 9.22. Found: C, 65.46; H, 3.97; N, 8.97.

5,10,15,20-Tetrakis(4,6-bis(3,5-bis(ethoxycarbonyl)phenoxy)pyrimidin-5-yl)porphyrin (2e) was obtained from aldehyde **1e** (0.500 g, 0.86 mmol) following the general procedure (0.320 g, 59%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.29 (s, 2H), 1.25 (t, J = 7.2 Hz, 48H), 4.24 (q, J = 7.2 Hz, 32H), 7.87 (d, J = 1.4 Hz, 16H), 8.40 (t, J = 1.4 Hz, 8H), 8.84 (s, 4H), 9.28 (s, 8H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 421.3 (5.6727), 515.1 (4.3407), 545.9 (3.6300), 590.4 (3.8511), 645.0 (3.0256); ES-MS 2511.8 (MH^+); Anal. Calcd for $C_{132}H_{118}N_{12}O_{40}$ C, 63.10; H, 4.73; N, 6.69. Found: C, 63.02; H, 4.72; N, 6.54.

5,10,15,20-Tetrakis[4,6-bis[estra-17-oxo-1,3,5(10)-trien-3-oxy]-pyrimidin-5-yl]porphyrin (2f) was obtained from aldehyde **1f** (0.810 g, 1.26 mmol) following the general procedure (0.260 g, 30%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.54 (s, 2H), 0.68 (s, 24H), 1.05−1.60 (m, 48H), 1.65−2.45 (m, 56H), 2.50−265 (m, 16H), 6.65 (d, J = 2.3 Hz, 8H), 6.79 (dd, J = 8.5, 2.3 Hz, 8H), 7.03 (d, J = 8.4 Hz, 8H), 8.91 (s, 4H), 9.18 (s, 8H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 422.3 (5.8151), 516.8 (4.5928), 547.7 (4.1209), 593.0 (4.1673), 647.2 (3.8322); APCI-MS 2768.4 (MH^+). Anal. Calcd for $C_{180}H_{182}N_{12}O_{16}$ C, 78.06; H, 6.62; N, 6.07. Found: C, 78.05; H, 6.54; N, 6.19.

5,10,15,20-Tetrakis[4,6-bis(2-nitrophenoxy)pyrimidin-5-yl]porphyrin (2g) was obtained from aldehyde **1g** (0.500 g, 1.31 mmol) following the general procedure (0.035 g, 6.2%). Modification of this procedure using a 5×10^{-3} M solution yielded porphyrin **2g** (0.053 g) in 10% yield; ^{1}H NMR (400 MHz, DMSO) δ −2.71 (s, 2H), 7.40 (d, J = 5.8 Hz, 16H), 7.77 (t, J = 7.4 Hz, 8H), 8.02 (d, J = 8.0 Hz, 8H), 8.83 (s, 4H), 9.54 (s, 8H); UV−vis (THF): λ_{max} (log ϵ) 419.8 (4.4651), 513.2 (4.2741), 540.0 (4.0840), 590.2 (4.0905); ESI-MS 1718.3 (MH^+). Anal. Calcd for $C_{84}H_{46}N_{20}O_{24}$: C, 58.68; H, 2.70; N, 16.29. Found: C, 58.61; H, 2.79; N, 16.00.

5,15-Bis(4,6-dichloropyrimidin-5-yl)-10,20-bis(2,4,6-trimethylphenyl)porphyrin (3a). A solution of 2,4,6-trimethylphenyldipyrromethane (0.500 g, 1.89 mmol) and 4,6-dichloropyrimidine-5-carbaldehyde (0.337 g, 1.89 mmol) in dichloromethane (500 mL) was deoxygenated by purging with argon for 15 min. Boron trifluoride etherate (0.020 g, 0.19 mmol) was added by syringe, and the solution was stirred under argon and protected from light for 1 h at room temperature. *p*-Chloranil (0.454 g, 1.89 mmol) was added, and the mixture was refluxed for 1 h. The solvent was removed and the residue chromatographed (silica gel, dichloromethane) yielding porphyrin **3** as a purple solid (0.445 g, 53%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.50 (s, 2H), 1.86 (s, 12H), 2.63 (s, 6H), 7.29 (s, 4H), 8.59 (d, J = 4.8 Hz, 4H), 8.76 (d, J = 4.8 Hz, 4H), 9.26 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.45, 21.75, 108.97, 120.00, 127.96, 129.03, 131.88, 134.72, 137.28, 138.30, 139.35, 158.22, 164.06; UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 419.4 (5.8111), 514.6 (4.4410), 548.1 (3.8030), 591.2 (3.8255), 647.9 (3.5997); ESI-MS 839.2 (MH^+). Anal. Calcd for $C_{43}H_{34}N_{14}O_8$: C, 65.72; H, 4.08; N, 13.33. Found: C, 65.81; H, 4.11; N, 13.36.

General Procedure for Synthesis of Porphyrins 3c−e. To a solution of porphyrin **3a** (0.050 g, 0.06 mmol) and substituted phenol (4.4 equiv) in dry DMF (4 mL) was added K_2CO_3 (8.8 equiv). The mixture was stirred for 72 h at 60 °C under argon atmosphere. The solution was allowed to reach room temperature, and dichloromethane (20 mL) was added. The organic layer was washed three times with water (3 × 20 mL) and dried over $MgSO_4$. The solvent was removed and the residue purified by column chromatography (silica gel; dichloromethane/hexane 3/1). The obtained product was redissolved in dichloromethane and precipitated with MeOH yielding **3b−d** as purple solids.

5,15-Bis[4,6-di(4-bromophenoxy)pyrimidin-5-yl]-10,20-bis(2,4,6-trimethylphenyl]porphyrin (3c) was obtained from 4-bromophenol following the general procedure (0.074 g, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.43 (s, 2H), 1.86 (s, 12H), 2.64 (s, 6H), 6.87 (d, J = 8.9 Hz, 8H), 7.31 (s, 4H), 7.32 (d, J = 8.9 Hz, 8H), 8.78 (d, J = 4.7 Hz, 4H), 8.81 (s, 2H), 8.94 (d, J = 4.7 Hz, 4H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 419.1 (5.7318), 514.5 (4.3567), 548.1 (3.9324), 591.0 (3.8667), 646.6 (3.6673); APCI-MS 1383.0/1385.0/1387.0/1389.0/1391.0 (MH^+). Anal. Calcd for $C_{70}H_{50}Br_4N_8O_4$ C, 60.63; H, 3.63; N, 8.08. Found: C, 60.49; H, 3.74; N, 7.80.

5,15-Bis[4,6-bis[4-(*tert*-butyl)phenoxy]pyrimidin-5-yl]-10,20-bis(2,4,6-trimethylphenyl)porphyrin (3d) was obtained from 4-*tert*-butylphenol following the general procedure (0.050 g, 60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.45 (s, 2H), 1.16 (s, 36H), 1.88 (s, 12H), 2.65 (s, 6H), 6.90 (d, J = 8.8 Hz, 8H), 7.19 (d, J = 8.8 Hz, 8H), 7.31 (s, 4H), 8.76 (d, J = 4.7 Hz, 4H), 8.86 (s, 2H), 8.99 (d, J = 4.7 Hz, 4H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 419.2 (5.6847), 514.8 (4.3141), 548.4 (3.8706), 591.2 (3.8047), 646.9 (3.5729); APCI-MS 1295.7 (MH^+). Anal. Calcd for $C_{86}H_{86}N_8O_4$: C, 79.72; H, 6.69; N, 8.65. Found: C, 79.60; H, 6.79; N, 8.65.

5,10-Bis[4,6-bis[estra-17-oxo-1,3,5(10)-trien-3-oxy]pyrimidin-5-yl]-10,20- bis(2,4,6-trimethylphenyl)porphyrin (3e) was obtained from estrone following the general procedure (0.080 g, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.44 (s, 2H), 0.79 (s, 12H), 1.20−1.60 (m, 24H), 1.86 (s, 12H), 1.80−2.20 (m, 20H), 2.22−2.29 (m, 4H), 2.38−2.48 (m, 4H), 2.65 (s, 6H), 2.68−2.76 (m, 8H), 6.67 (d, J = 2.4 Hz, 4H), 6.79 (dd, J = 8.6, 2.4 Hz, 4H), 7.12 (d, J = 8.6 Hz, 4H), 7.31 (s, 4H), 8.77 (d, J = 4.7 Hz, 4H), 8.86 (s, 2H), 8.99 (d, J = 4.7 Hz, 4H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 419.5 (5.6662), 515.1 (4.3235), 548.2 (3.8699), 591.4 (3.8123), 647.1 (3.5959); APCI-MS 1777.2 (MH^+). Anal. Calcd for $C_{118}H_{118}N_8O_8$ C, 79.79; H, 6.70; N, 6.31. Found: C, 79.31; H, 6.70; N, 6.17.

5,15-Bis(4,6-dimethoxypyrimidin-5-yl)-10,20-bis(2,4,6-trimethylphenyl)porphyrin (3b). To a well-stirred suspension of sodium hydride (80%, 0.040 g, 1.3 mmol) in DMF (5 mL) under argon was added methanol (0.06 mL, 1.48 mmol), and the mixture was stirred for 15 min at room temperature. A solution of porphyrin **3a** (33.6 mg, 0.04 mmol) in DMF (5 mL) was added, and the mixture was stirred 60 °C for 40 h. The mixture was allowed to reach room temperature, water (30 mL) was added, and the mixture was extracted with dichloromethane (3 × 30 mL). The combined organics were washed with water (3 × 30 mL), dried over anhydrous magnesium sulfate, and evaporated under vacuum. The residue was chromatographed (silica gel/dichloromethane) to afford porphyrin **3e** which was recrystallized from dichloromethane/methanol (1:1) (0.015 g, 46%): ^{1}H NMR (400 MHz, $CDCl_3$) δ −2.51 (s, 2H), 1.85 (s, 12H), 2.62 (s, 6H); 3.82(s, 12H); 7.26 (s, 4H), 8.64 (d, J = 4.7 Hz, 4H), 8.67 (s, 2H), 8.91 (d, J = 4.7 Hz, 4H); UV−vis (CH_2Cl_2): λ_{max} (log ϵ) 417.8 (5.6202), 514.0 (4.2505), 546.8 (3.7227), 590.2 (3.7282), 645.6 (3.4422). APCI-MS 883 (MH^+). Anal. Calcd for $C_{50}H_{46}N_8O_4$: C, 72.97; H, 5.63; N, 13.62. Found: C, 72.85; H, 5.50; N, 13.60.

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