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Synthesis of β-Functionalized Porphyrins via Palladium-Catalyzed Carbon−Heteroatom Bond Formations: Expedient Entry into β-Chiral Porphyrins

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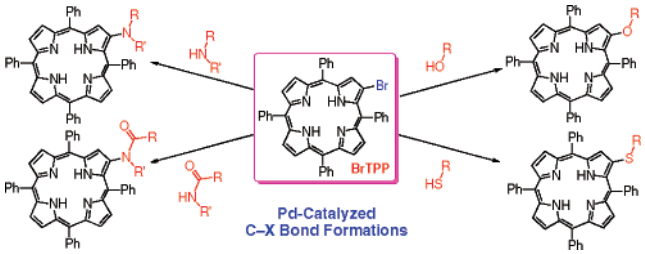

A procedure was developed for the preparation of β-monobromo-tetraphenylporphyrin (BrTPP) in a greatly improved yield from the selective bromination of tetraphenylporphyrin (TPP) by NBS. BrTPP was successfully employed as a versatile synthon for convenient synthesis of a wide range of β-monofunctionalized porphyrins with various heteroatom functionalities via palladium-mediated carbon−heteroatom bond formations. Examples include β-amino, -amido, -oxo, and -mercaptoporphyrins from reactions with amines, amides, alcohols, and thiols, respectively. Applying the synthetic approach to chiral amides, β-chiral porphyrins were effectively constructed.

Introduction

Chiral porphyrins have been employed for various important applications such as asymmetric catalysis, chiral recognition/sensing, and enzymatic mimicry.[1] Among different approaches for chiral porphyrin synthesis,[2] covalent attachment of proper chiral units to a preformed porphyrin synthon via peripheral functional groups is considered to be the most general method with chirality economy.[1,2] The most widely used porphyrin synthon is *meso*-tetrakis(2-aminophenyl)porphyrin.[3] Other significant examples include *meso*-tetrakis(2,6-diaminophenyl)-porphyrin,[4] *meso*-tetrakis(2,6-dihydroxyphenyl)porphyrin,[5] and *meso*-tetrakis(2,6-dicarboxyphenyl)porphyrin.[6] Chiral acids, amines, and alcohols have been successfully attached to these porphyrin synthons through multiple amide or ester bond formations.[1,2] Despite these advances, there remains a need to develop alternative synthons that allow versatile and effective assembly of chiral porphyrins with enhanced generality and practicality.

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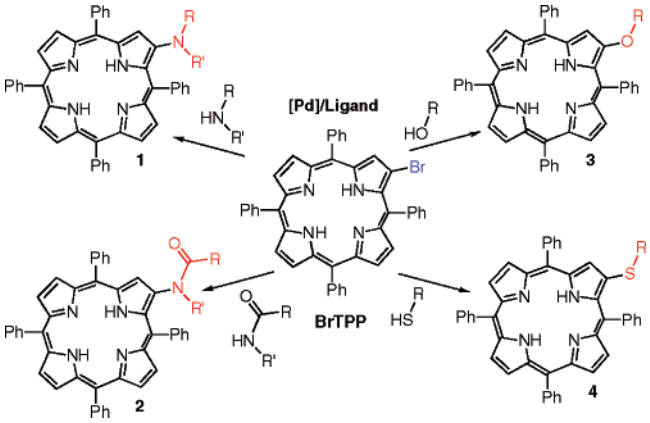
Utilizing metal-catalyzed carbon−heteroatom bond formations,[7] we[8] and others[9] have established a powerful new strategy for general and efficient synthesis of heteroatom-substituted porphyrins from catalytic reactions of halogenated porphyrins with soft, non-organometallic nucleophiles. In principle, these catalytic reactions can be performed in high yields under mild conditions and are suitable for a wide variety of amines, amides, alcohols, thiols, selenols, and phosphines, resulting in the formation of a diverse family of functionalized porphyrins.[8,9] Since various chiral amines, amides, alcohols, and thiols are readily available, we envisioned the new synthetic strategy[8,9] rendering halogenated porphyrins, especially brominated porphyrins, a new class of synthons for construction of chiral porphyrins. For example, we demonstrated previously that 5,-10-bis(2′,6′-dibromophenyl)porphyrins are versatile synthons for modular preparation of *ortho*-chiral porphyrins via Pd-catalyzed amidation reactions with chiral amides.[8f] For various chiral amide building blocks, the quadruple carbon−nitrogen bond formation reactions were accomplished under mild conditions, constructing a family of D_2-symmetric *ortho*-chiral porphyrins in high yields.[8f] Recently, *meso*-dibromoporphyrins were shown to be useful synthons for general syntheses of *meso*-chiral porphyrins from reactions with chiral nucleophiles via Pd-catalyzed etheration and amidation.[8g] This synthesis could be carried out under mild conditions and typically gave high yields. It was employed for various combinations of porphyrin precursors and chiral alcohols as well as amides, leading to the formation of a series of novel *meso*-chiral porphyrins.[8g]

As a part of our current research program of developing catalytic carbene[8f,8g,10] and nitrene[11] transfer processes by metalloporphyrins, we showed that cobalt(II) complexes of both *ortho*-[8f,10g,10h] and *meso*-[8g] chiral porphyrins are active catalysts for asymmetric cyclopropanation but exhibited different diastereoselectivity and enantioselectivity. To further examine the correlation between porphyrin structure and catalytic reactivity

SCHEME 1. Palladium-Catalyzed Carbon−Heteroatom Bond Formation Reactions of β-Bromo-Tetraphenylporphyrin



in the cobalt(II) porphyrin-based asymmetric cyclopropanation system, we have a need to access β-chiral porphyrins. To this end, we set to expand the Pd-mediated carbon−heteroatom bond formation strategy to include β-bromoporphyrins.[12] We report herein that a wide range of β-functionalized porphyrins,[13] including those containing amino, amido, oxo, and mercapto substituents, were effectively prepared from catalytic reactions of β-bromo-tetraphenylporphyrin (BrTPP) with various amines, amides, alcohols, and thiols, respectively (Scheme 1). Consequently, β-chiral porphyrins could be conveniently accessed by using readily available chiral building blocks such as chiral amides. In this paper, we also describe a new procedure for the preparation of BrTPP in a greatly improved yield.

Results and Discussion

The original selective bromination procedure developed by Callot[14] has been successfully applied for synthesis of BrTPP

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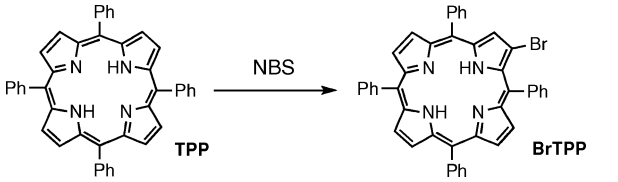
TABLE 1. Synthesis of β-Bromo-tetraphenylporphyrin via Selective Bromination of TPP with NBS[a]



entry	solvent	equiv[b]	add[c]	py[d]	TPP[e]	Br_nTPP[e]	BrTPP[e]	yield[f]
1[g]	CH_3CN	1.0	−	−	++++++++	−	−	−[i]
2[g]	THF	1.0	−	−	++++++++	−	−	−[i]
3[g]	DMF	1.0	−	−	++++++	+	+	−[i]
4[g]	MeC_6H_5	1.0	−	−	++++++	+	+	−[i]
5[g]	ClC_6H_5	1.0	−	−	++++++	+	+	−[i]
6[g]	$CHCl_3$	1.0	−	−	++++	+	+++	−[i]
7[h]	$CHCl_3$	1.0	−	−	++++	+	+++	−[i]
8	$CHCl_3$	1.0	−	−	++++	+	+++	−[i]
9	$CHCl_3$	0.8	−	−	+++++	+	++	20%
10	$CHCl_3$	1.5	−	−	+++	+	++++	−[i]
11	$CHCl_3$	3.0	−	−	+++	++	+++	−[i]
12	$CHCl_3$	2.0	+	−	+++	+	++++	−[i]
13	$CHCl_3$	2.0	+	+	++	+	+++++	78%
14	$CHCl_3$	3.0	+	−	+++	+	++++	−[i]
15	$CHCl_3$	3.0	+	+	++	+	+++++	64%[j]
16	$CHCl_3$	5.0	+	−	+++	++	+++	33%

[a] Reactions were carried out at 60 °C for 3−4 h with [TPP] = 0.4 mM. [b] Equivalents of NBS. [c] With (+) or without (−) slow addition of predissolved NBS. [d] With (+) or without (−) the presence of pyridine. [e] The distribution of TPP, its mono-brominated (BrTPP), and multi-brominated (Br_nTPP) products was estimated by TLC. [f] Yields represent isolated yields in >95% purity as determined by ^1H NMR. [g] Carried out at 23 °C with [TPP] = 2.0 mM. [h] Carried out at 60 °C with [TPP] = 2.0 mM. [i] No isolation was attempted. [j] Carried out in large scale for 8 h; see Supporting Information for details.

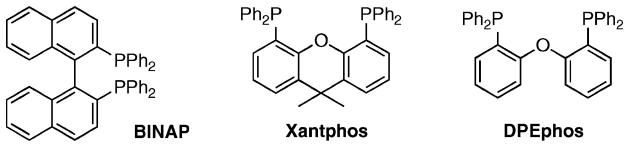
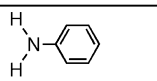
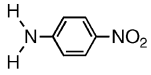
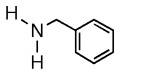
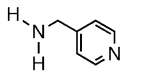
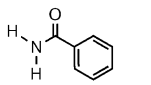
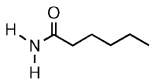
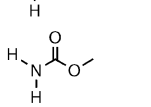
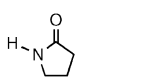
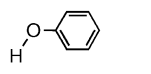
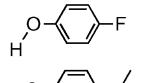
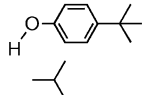
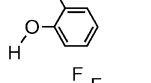
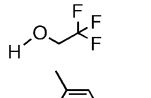
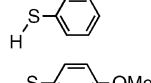
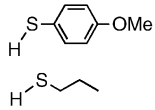


FIGURE 1. Structures of chelating diphosphine ligands.

and related β-monobromoporphyrins.[15] The yields ranged from 30 to 47%, often requiring preinsertion of metal ion for yield improvement.[14,15] At the outset of this project, we decided to systematically investigate selective bromination of TPP by NBS with an expectation to improve the yield of BrTPP formation (Table 1). Among the solvents tested, $CHCl_3$ gave the best result, as the highest BrTPP percentage was observed in the product distribution (Table 1, entries 1−6). Change in reaction temperature and/or TPP concentration had no observable effect on the product distribution in $CHCl_3$ (Table 1, entries 6−8). Alteration in NBS equivalents, however, had a large influence on the outcome. Although both substoichiometric amount of (Table 1, entry 9) and over excess (Table 1, entry 11) NBS gave lower yields, 1.5 equiv of NBS appeared to maximize the formation of BrTPP (Table 1, entry 10) as a balanced decrease of both unreacted TPP and multibromination products was reached. It was found that slow addition of predissolved NBS allowed the use of higher equivalents of NBS to enhance the reaction rate without deterioration in yield (Table 1, entries 12 and 14). But additional increase in the NBS equivalents led to a poorer yield (Table 1, entry 16). In combination with slow addition of NBS, using pyridine as an additive resulted in a significant improvement of BrTPP yield. For example, BrTPP was isolated in 78 and 64% yields under the conditions when 2.0 and 3.0 equiv of NBS were used, respectively (Table 1, entries 13 and 15).

With the greatly improved yield, BrTPP could be accessed in gram scale. This allowed us to employ BrTPP as a viable precursor to synthesize β-functionalized porphyrins via Pd-catalyzed carbon−heteroatom bond formations (Scheme 1). On the basis of our previous results with *meso*- and *ortho*-

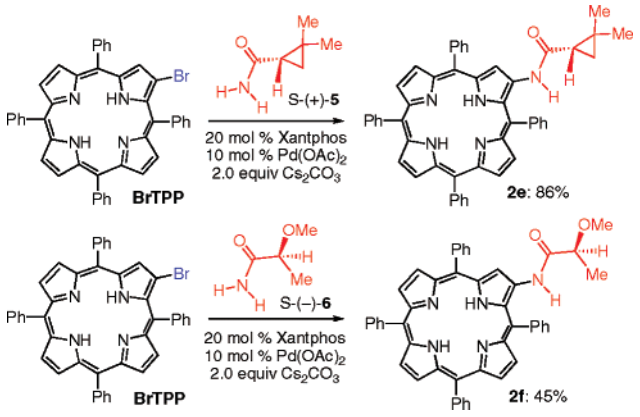
TABLE 2. Synthesis of β-Heteroatom-Substituted Porphyrins 1−4 via Palladium-Catalyzed C−N/C−O/C−S Bond Formations of BrTPP with Amines, Amides, Alcohols, and Thiols[a]

entry	amine/amide alchohol/thiol	P-ligand Pd-comp	time	product yield[b]
1		BINAP $Pd(OAc)_2$	24 h	**1a** 48%
2[c]		BINAP $Pd(OAc)_2$	24 h	**1b** 75%
3[c]		BINAP $Pd(OAc)_2$	5 h	**1c** 46%
4[c]		BINAP $Pd(OAc)_2$	24 h	**1d** 71%
5		Xantphos $Pd(OAc)_2$	24 h	**2a** 65%
6		Xantphos $Pd_2(dba)_3$	28 h	**2b** 76%
7[c]		Xantphos $Pd(OAc)_2$	5 h	**2c** 45%
8		Xantphos $Pd_2(dba)_3$	24 h	**2d** 71%
9[d]		DPEphos $Pd_2(dba)_3$	24 h	**3a** 66%
10[c,d]		DPEphos $Pd_2(dba)_3$	26 h	**3b** 65%
11[d]		DPEphos $Pd_2(dba)_3$	24 h	**3c** 77%
12[d]		DPEphos $Pd_2(dba)_3$	26 h	**3d** 79%
13[d]		DPEphos $Pd_2(dba)_3$	40 h	**3e** 71%
14[c,d]		BINAP $Pd_2(dba)_3$	40 h	**4a** 35%
15[d]		BINAP $Pd_2(dba)_3$	28 h	**4b** 24%
16[d]		BINAP $Pd_2(dba)_3$	28 h	**4c** 32%

[a] Reactions were carried out at 100 °C under N_2 in THF with 1.0 equiv of BrTPP; 4.0 equiv of amine, amide, alcohol, or thiol; 10 mol % [Pd]; and 20 mol % P-ligand in the presence of 2.0 equiv of Cs_2CO_3. Concentration: 0.01 mmol BrTPP/mL THF. [b] Yields represent isolated yields in >95% purity as determined by ^1H NMR. [c] Cs_2CO_3 (4.0 equiv) was used. [d] Carried out in toluene.

(15) For selected examples, see: (a) Tse, M. K.; Zhou, Z.-Y.; Mak, T. C. W.; Chan, K. S. *Tetrahedron* **2000**, *56*, 7779. (b) Fletcher, J. T.; Therien, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 4298. (c) Shen, D.-M.; Liu, C.; Chen, Q.-Y. *Chem. Commun.* **2005**, 4982.

SCHEME 2. Synthesis of β-Chiral Porphyrins via Palladium-Catalyzed Amidation of BrTPP with Chiral Amides



bromoporphyrins,[8] three chelating diphosphine ligands BINAP, Xantphos, and DPEphos (Figure 1), in combination with Pd(OAc)$_2$ or Pd$_2$(dba)$_3$, were evaluated as potential catalysts for carbon−heteroatom bond formation reactions of BrTPP with amines, amides, alcohols, and thiols (Table 2). The combination of BINAP and Pd(OAc)$_2$ could effectively catalyze amination reactions of BrTPP with different amines such as aniline, substituted aniline, benzylamine, and pyridine-containing amine, forming the corresponding β-aminoporphyrins in 46−75% yields (Table 2, entries 1−4). Using Xantphos/Pd$_2$(dba)$_3$ as the catalyst, amidation of BrTPP was also successfully achieved with both aromatic and aliphatic amides (Table 2, entries 5−6). The amidation system could be applied to carbamates such as methyl carbamate and cyclic amides such as pyrrolidinone as well (Table 2, entries 7−8).

In addition to C−N bond formation, catalytic C−O bond formation reactions of BrTPP could be also accomplished. For example, both aromatic and aliphatic alcohols were effectively coupled with BrTPP employing Xantphos/Pd$_2$(dba)$_3$ as the catalyst, forming the desired β-oxoporphyrins in good yields (Table 2, entries 9−13). Similarly, C−S bond formation between BrTPP and different thiols could be carried out to produce β-arylsulfanyl- and alkylsulfanyl-substituted porphyrins when BINAP and Pd$_2$(dba)$_3$ were used, albeit in lower yields (Table 2, entries 14−16).

With the establishment of BrTPP as a viable precursor for Pd-catalyzed carbon−heteroatom bond formations, a straightforward access to different β-chiral porphyrins became achievable by using readily available chiral amines, amides, alcohols, and thiols. As a demonstration of its utility, BrTPP was successfully coupled with commercially available chiral amides S-(+)-**5** and S-(−)-**6** to provide β-chiral porphyrins **2e** and **2f** in 86 and 45% yields, respectively (Scheme 2).

Conclusions

In summary, a new procedure has been established to prepare BrTPP in greatly improved yield from direct bromomination of TPP by NBS. We have shown that BrTPP can be employed as a versatile synthon for convenient synthesis of β-monofunctionalized porphyrins containing various heteroatom functionalities via Pd-catalyzed carbon−heteroatom bond formations. Using readily available chiral building blocks, the synthetic approach allows expedient entry into different β-chiral porphyrins that could find potential applications in areas such as asymmetric catalysis.

Experimental Section

General Considerations. All reactions were carried out under a nitrogen atmosphere in oven-dried glassware following standard Schlenk techniques. Toluene and tetrahydrofuran were distilled under nitrogen from sodium benzophenone ketyl. ^{1}H and ^{13}C NMR spectra were obtained at ambient temperatures on either a Varian 300 MHz or a Bruker 250 MHz instrument. All amines, alcohols, amides, and thiols were purchased from commercial sources and used without further purification. Palladium(II) acetate, tris(dibenzylideneacetone)dipalladium(0), bis(2-diphenylphosphinophenyl)ether (DPEphos), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (Xantphos), (±)BINAP, and cesium carbonate were purchased commercially. All ligands, palladium precursors and bases were stored in desiccators filled with anhydrous calcium sulfate, and weighed in the air. β-Bromotetraphenylporphyrin was prepared according to the method described below.

Synthesis of β-Bromo-5,10,15,20-tetraphenylporphyrin.[14] To a three neck round-bottom flask charged with 5,10,15,20-tetraphenylporphyrin (61.4 mg, 0.10 mmol) and chloroform (60 mL) was added 1 mL pyridine. After refluxing for 5 min, a solution of *N*-bromosuccinamide (35.6 mg, 0.20 mmol, dissolved in 60 mL chloroform) was added dropwise over 3−4 h into the flask. The solution was refluxed for an additional 30 min, quenched with acetone (30 mL), and concentrated by rotary evaporator to dryness. The residue was purified via gravity column chromatography (silica gel, toluene: cyclohexane (v/v) = 1:1). The title compound was obtained as purple solid (54.3 mg, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.81−8.90 (m, 5H), 8.76 (m, 2H), 8.20 (m, 6H), 8.09 (d, J = 6.6 Hz, 2H), 7.71−7.76 (m, 12H), −2.84 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.0, 141.7, 140.8, 138.0, 134.6, 134.5, 134.4, 134.3, 133.8, 129.6, 128.8, 128.2, 127.9, 127.5, 126.9, 126.8, 126.7, 126.6, 120.7, 120.3, 119.9, 119.6. UV−vis, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 421 (5.55), 517 (4.27), 552 (3.72), 593 (3.70), 648 (3.67). HRMS-EI ([M]$^+$): Calcd for $C_{44}H_{29}BrN_4$, 692.1576; found, 692.1544, with an isotope distribution pattern that is the same as the calculated one.

General Procedures for Synthesis of β-Substituted Porphyrins. An oven-dried Schlenk tube equipped with a stirring bar was degassed on vacuum line and purged with nitrogen. The tube was then charged with palladium precursor (10 mol %); phosphine ligand (20 mol %); β-bromoporphyrin (0.050 mmol); amine, amides, alcohols, or thiols (if it is solid, 4.0 equiv); and base (2.0−4.0 equiv). The tube was capped with a Teflon screwcap, evacuated and backfilled with nitrogen. After the Teflon screwcap was replaced with a rubber septum, solvent (3 mL) and amine, amides, alcohols, or thiols (if it is liquid, 4.0 equiv) were added via syringe successively, followed by additional solvent (2 mL) to wash down possible reactants on the tube wall. The tube was purged with nitrogen (1−2 min) and the septum was then replaced with the Teflon screwcap and sealed. The reaction mixture was heated in an oil bath with stirring and monitored by TLC. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate, washed with water (×3), and concentrated to dryness. The solid residue was purified by flash chromatography.

2-Phenylamino-5,10,15,20-tetraphenylporphyrin (1a, Table 2, Entry 1). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with aniline (18 μL, 0.20 mmol), using Pd(OAc)$_2$ (1.1 mg 0.0050 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 3:2) as a purple brown solid (17.0 mg, 48% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.73−8.82 (m, 5H), 8.56 (d, J = 4.8 Hz, 1H), 8.30 (s, 1H), 8.19−8.22 (m, 8H), 7.83−7.91 (m, 3H), 7.71−7.75

(m, 9H), 7.29 (t, J = 7.8 Hz, 2H), 7.02 (d, J = 8.1 Hz, 2H), 6.94 (t, J = 7.2 Hz, 1H), 6.61 (s, 1H), −2.56 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.8, 142.2, 141.9, 140.8, 134.5, 134.4, 134.2, 133.1, 129.3, 129.1, 128.5, 127.7, 127.6, 126.8, 126.7, 126.6, 121.5, 121.1, 119.7, 116.7, 116.3. UV−vis, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 409 (6.09), 446 (5.55), 529 (5.07), 571 (4.81), 601 (4.79), 657 (4.58). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{50}H_{36}N_5$, 706.2965; found, 706.2948, with an isotope distribution pattern that is the same as the calculated one.

2-(4′-Nitrophenyl)amino-5,10,15,20-tetraphenylporphyrin (1b, Table 2, Entry 2). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 4-nitroaniline (27.5 mg, 0.20 mmol), using $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.20 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride) as a purple solid (28.0 mg, 75% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.87 (d, J = 5.4 Hz, 1H), 8.83 (m, 2H), 8.75 (s, 2H), 8.64 (d, J = 5.4 Hz, 1H), 8.45 (s, 1H), 8.15−8.21 (m, 8H), 8.13 (d, J = 9.0 Hz, 2H), 7.81−7.92 (m, 3H), 7.73−7.77 (m, 9H), 6.86 (d, J = 9.0 Hz, 2H), 6.81 (s, 1H), −2.72 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.3, 142.3, 142.0, 141.7, 140.8, 134.5, 134.4, 134.2, 133.0, 129.2, 128.6, 128.0, 127.8, 126.9, 126.8, 126.7, 126.1, 121.3, 120.4, 116.5, 114.2. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 414 (5.12), 459 (4.81), 525 (4.35), 566 (4.07), 597 (3.95), 652 (3.37). HRMS-EI ($[M]^+$): Calcd for $C_{50}H_{34}N_6O_2$, 750.2743; found, 750.2732, with an isotope distribution pattern that is the same as the calculated one.

2-Benzylamino-5,10,15,20-tetraphenylporphyrin (1c, Table 2, Entry 3). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with benzylamine (22 μL, 0.20 mmol), using $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.20 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 5 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: ethyl acetate (v/v) = 9:1) as a purple solid (16.5 mg, 46% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.70−8.76 (m, 4H), 8.65 (d, J = 4.2 Hz, 1H), 8.44 (d, J = 4.5 Hz, 1H), 8.10−8.19 (m, 6H), 8.06 (d, J = 6.6 Hz, 2H), 7.56−7.73 (m, 11H), 7.48 (s, 1H), 7.31−7.34 (m, 3H), 7.19−7.24 (m, 3H), 4.62 (s, 1H), 4.45 (d, J = 4.2 Hz, 2H), −2.58 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.1, 142.4, 142.2, 140.8, 138.0, 134.5, 134.3, 134.2, 132.6, 131.0, 128.7, 128.4, 128.2, 127.8, 127.6, 127.5, 127.4, 126.8, 126.7, 126.5, 119.3, 50.48. UV−vis, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 406 (5.47), 425 (5.27), 440 (5.18), 527 (5.27), 567 (5.18), 602 (4.06), 656 (4.11). HRMS-EI ($[M]^+$): Calcd for $C_{51}H_{37}N_5$, 719.3049; found, 719.3047, with an isotope distribution pattern that is the same as the calculated one.

2-(Pyridin-4′-yl)methylamino-5,10,15,20-tetraphenylporphyrin (1d, Table 2, Entry 4). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 4-(aminomethyl)pyridine (21 μL, 0.20 mmol), using $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.20 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: ethyl acetate (v/v) = 9:1) as a purple solid (25.5 mg, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.77 (d, J = 4.8 Hz, 1H), 8.71−8.74 (m, 3H), 8.66 (d, J = 4.5 Hz, 1H), 8.56 (dd, J = 1.5, 4.8 Hz, 2H), 8.47 (d, J = 4.8 Hz, 1H), 8.17−8.19 (m, 4H), 8.09−8.13 (m, 3H), 8.07 (d, J = 4.8 Hz, 1H), 7.67−7.75 (m, 12H), 7.39 (s, 1H), 7.14 (dd, J = 1.5, 4.2 Hz, 2H), 4.66 (t, J = 5.1 Hz, 1H), 4.47 (d, J = 5.1 Hz, 2H), −2.64 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.9, 140.9, 134.5, 134.3, 134.1, 132.7, 128.9, 128.4, 127.7, 127.4, 126.8, 126.7, 126.6, 122.5. UV−vis, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 406 (5.40), 430 (5.21), 525 (4.49), 598 (4.18), 653 (4.16). HRMS-EI ($[M]^+$): Calcd for $C_{50}H_{36}N_6$, 720.3001; found, 720.3000, with an isotope distribution pattern that is the same as the calculated one.

2-Benzamido-5,10,15,20-tetraphenylporphyrin (2a, Table 2, Entry 5). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with benzamide (24.2 mg, 0.20 mmol), using $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and Xantphos (5.7 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 8:2) as a purple solid (24.0 mg, 65% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.61 (s, 1H), 9.11 (s, 1H), 8.77−8.88 (m, 5H), 8.44 (d, J = 4.8 Hz, 1H), 8.28−8.30 (m, 2H), 8.18−8.26 (m, 6H), 7.72−7.84 (m, 12H), 7.54 (t, J = 6.9 Hz, 1H), 7.35−7.44 (m, 4H), −2.76 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 142.3, 142.1, 141.8, 140.8, 134.6, 134.4, 134.3, 134.2, 133.8, 131.8, 130.3, 129.4, 128.6, 128.3, 127.9, 127.8, 127.0, 126.9, 126.8, 126.6, 121.1, 120.4, 120.0, 116.1. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 421 (5.34), 518 (4.30), 553 (3.82), 592 (3.86), 648 (3.58). HRMS-EI ($[M]^+$): Calcd for $C_{51}H_{35}N_5O$, 733.2842; found, 733.2854, with an isotope distribution pattern that is the same as the calculated one.

2-Hexanamido-5,10,15,20-tetraphenylporphyrin (2b, Table 2, Entry 6). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with hexanamide (23.0 mg, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and Xantphos (5.8 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 27.5 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 6:4) as a purple solid (27.5 mg, 76% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.36 (s, 1H), 8.79−8.85 (m, 5H), 8.59 (d, J = 4.8 Hz, 1H), 8.17−8.24 (m, 8H), 7.83−7.93 (m, 4H), 7.70−7.76 (m, 9H), 1.97 (t, J = 7.2 Hz, 2H), 1.62 (q, J = 7.5 Hz, 2H), 1.34 (m, 4H), 0.94 (t, J = 7.2 Hz, 3H), −2.82 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 142.2, 142.1, 141.8, 140.8, 134.5, 134.4, 134.3, 133.3, 129.3, 128.3, 127.8, 127.7, 126.8, 126.7, 126.6, 121.0, 120.4, 119.8, 116.1, 37.7, 31.5, 25.1, 22.4, 14.0. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 421 (5.47), 517 (4.40), 551 (3.88), 591 (3.94), 646 (3.69). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{50}H_{42}N_5O$, 728.3384; found, 728.3393, with an isotope distribution pattern that is the same as the calculated one.

2-Methoxycarbonylamino-5,10,15,20-tetraphenylporphyrin (2c, Table 2, Entry 7). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with methyl carbamate (15.0 mg, 0.20 mmol), using $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and Xantphos (5.8 mg, 0.010 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.20 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 5 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride) as a purple solid (15.5 mg, 45% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.05 (s, 1H), 8.77−8.84 (m, 5H), 8.59 (d, J = 4.8 Hz, 1H), 8.15−8.20 (m, 7H), 7.81−7.90 (m, 3H), 7.72−7.75 (m, 9H), 7.25 (s, 1H), 7.14 (s, 1H), 3.74 (s, 3H), −2.84 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.6, 134.4, 134.3, 133.0, 129.4, 128.3, 127.7, 126.8, 126.7, 126.5, 52.7. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 420 (5.56), 517 (4.50), 551 (4.00), 592 (4.07), 646 (3.84). HRMS-EI ($[M]^+$): Calcd for $C_{46}H_{33}N_5O_2$, 687.2634; found, 687.2636, with an isotope distribution pattern that is the same as the calculated one.

2-(*N*-2′-Pyrrolidinone-yl)-5,10,15,20-tetraphenylporphyrin (2d, Table 2, Entry 8). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 2-pyrrolidinone (15 μL, 0.20 mmol), $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and Xantphos (5.8 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in THF (5 mL) at 80 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: ethyl acetate (v/v) = 9.5:0.5) as a purple solid (24.6 mg, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.75−8.85 (m, 5H), 8.66 (s, 1H), 8.60 (d, J = 4.8 Hz, 1H), 8.16−8.21 (m, 7H), 7.67−7.78 (m, 13H), 3.76 (s, 2H), 1.8−2.2 (m, 4H), −2.78 (s, 2H). ^{13}C NMR (75 MHz,

$CDCl_3$): δ 175.7, 142.1, 142.0, 141.8, 140.9, 134.6, 127.7, 126.8, 126.7, 126.2, 120.4, 118.6, 52.7, 30.9, 18.0. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 420 (5.69), 516 (4.38), 552 (3.92), 593 (3.84), 647 (3.75). HRMS-EI ($[M]^+$): Calcd for $C_{48}H_{35}N_5O$, 697.2842; found, 697.2833, with an isotope distribution pattern that is the same as the calculated one.

2-Phenoxy-5,10,15,20-tetraphenylporphyrin (3a, Table 2, Entry 9). The general procedure was used to couple β-bromo-5,-10,15,20-tetraphenylporphyrin (34.7 mg, 0.05 mmol) with phenol (19.0 mg, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and DPEphos (5.4 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 1:1) as a brown solid (23.3 mg, 66% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.88 (d, J = 4.8 Hz, 1H), 8.81−8.83 (m, 3H), 8.79 (s, 1H), 8.73 (d, J = 4.8 Hz, 1H), 8.17−8.23 (m, 6H), 8.15 (s, 1H), 7.99 (d, J = 8.1 Hz, 2H), 7.67−7.76 (m, 9H), 7.48−7.58 (m, 3H), 7.20 (t, J = 7.5 Hz, 2H), 7.02 (t, J = 7.8 Hz, 1H), 6.90 (d, J = 8.7 Hz, 2H), −2.81 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.1, 142.2, 142.1, 142.0, 141.0, 134.6, 134.5, 134.4, 133.1, 129.2, 127.7, 127.3, 126.72, 126.70, 126.6, 126.3, 122.7, 120.8, 120.2, 119.4, 118.5, 117.0. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 419 (5.28), 515 (4.09), 549 (3.55), 590 (3.55), 645 (3.25). HRMS-EI ($[M]^+$): Calcd for $C_{50}H_{34}N_4O$, 706.2733; found, 706.2725, with an isotope distribution pattern that is the same as the calculated one.

2-(4′-Fluorophenoxy)-5,10,15,20-tetraphenylporphyrin (3b, Table 2, Entry 10). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 4-fluorophenol (22.4 mg, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and DPEphos (5.4 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 26 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 1:1) as a brown solid (23.5 mg, 65% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.72−8.89 (m, 6H), 8.14−8.21 (m, 6H), 8.06 (s, 1H), 8.00 (d, J = 8.7 Hz, 2H), 7.68−7.75 (m, 9H), 7.56 (m, 3H), 6.87−6.89 (m, 4H), −2.82 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.0, 156.8, 142.2, 142.1, 141.9, 141.0, 134.6, 134.5, 134.3, 133.1, 127.7, 127.4, 126.7, 126.6, 126.4, 120.8, 120.2, 118.4, 118.2, 115.9, 115.6. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 420 (5.69), 515 (4.57), 549 (4.18), 591 (4.18), 645 (4.01). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{50}H_{34}FN_4O$, 725.2711; found, 725.2704, with an isotope distribution pattern that is the same as the calculated one.

2-(4′-*tert*-Butylphenoxy)-5,10,15,20-tetraphenylporphyrin (3c, Table 2, Entry 11). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 4-*t*-butylphenol (30.4 mg, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and DPEphos (5.4 mg, 0.010 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.20 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 8:2) as a brown solid (29.5 mg, 77% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.87 (t, J = 4.8 Hz, 1H), 8.80−8.83 (m, 3H), 8.79 (s, 1H), 8.72 (d, J = 4.8 Hz, 1H), 8.17−8.24 (m, 6H), 8.16 (s, 1H), 7.99−8.02 (m, 2H), 7.67−7.79 (m, 9H), 7.50−7.60 (m, 3H), 7.22 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 9.0 Hz, 2H), 1.29 (s, 9H), −2.80 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.6, 145.6, 142.3, 142.2, 142.0, 141.1, 134.6, 134.5, 134.4, 133.1, 129.6, 127.7, 127.6, 127.3, 126.7, 126.6, 126.5, 126.3, 126.0, 120.8, 120.1, 119.3, 118.5, 116.5, 31.5. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 419 (5.60), 515 (4.45), 549 (3.92), 590 (3.93), 645 (3.66). HRMS-EI ($[M]^+$): Calcd for $C_{54}H_{42}N_4O$, 762.3359; found, 762.3356, with an isotope distribution pattern that is the same as the calculated one.

2-(2′-Isopropanylphenoxy)-5,10,15,20-tetraphenylporphyrin (3d, Table 2, Entry 12). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 2-isopropylphenol (27 μL, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and DPEphos (5.4 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 26 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 8:2) as a brown solid (29.5 mg, 79% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.86 (t, J = 4.8 Hz, 2H), 8.79 (m, 3H), 8.72 (d, J = 4.8 Hz, 1H), 8.20−8.23 (m, 4H), 8.09−8.12 (m, 4H), 7.69−7.75 (m, 7H), 7.62−7.65 (3H), 7.55−7.57 (m, 3H), 7.29−7.32 (m, 1H), 7.10−7.19 (m, 3H), 3.15 (heptet, J = 7.2 Hz, 1H), 1.13 (d, J = 7.2 Hz, 6H), −2.80 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.8, 142.2, 142.1, 142.0, 141.4, 139.7, 134.6, 134.5, 134.3, 133.0, 129.5, 127.7, 127.6, 127.3, 126.7, 126.6, 126.4, 124.3, 120.9, 120.1, 118.9, 118.4, 112.4, 31.6, 26.4, 23.2. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 420 (5.47), 515 (4.32), 549 (3.76), 590 (3.79), 645 (3.45). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{53}H_{41}N_4O$, 749.3275; found, 749.3270, with an isotope distribution pattern that is the same as the calculated one.

2-(α,α,α-Trifluoroethoxy)-5,10,15,20-tetraphenylporphyrin (3e, Table 2, Entry 13). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with α,α,α-trifluoroethanol (15 μL, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and DPEphos (5.4 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 40 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 8:2) as a brown solid (25.2 mg, 71% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.88 (d, J = 5.1 Hz, 1H), 8.84 (d, J = 5.4 Hz, 1H), 8.79 (d, J = 4.5 Hz, 1H), 8.72−8.75 (m, 3H), 8.16−8.21 (m, 6H), 8.01 (dd, J = 7.5, 1.5 Hz, 2H), 7.65−7.79 (m, 13H), 4.55 (q, J = 7.8 Hz, 2H), −2.90 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.4, 142.1, 141.9, 140.9, 134.5, 134.4, 134.1, 132.8, 127.8, 127.7, 127.5, 126.8, 126.7, 126.6, 121.1, 120.2, 118.5, 118.4, 107.8, 68.4, 67.9. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 419 (5.55), 514 (4.36), 548 (3.88), 588 (3.86), 643 (3.45). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{46}H_{32}F_3N_4O$, 713.2523; found, 713.2500, with an isotope distribution pattern that is the same as the calculated one.

2-(*o*-Tolylsulfanyl)-5,10,15,20-tetraphenylporphyrin (4a, Table 2, Entry 14). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 2-methylbenzenethiol (24 μL, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (65.2 mg, 0.20 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 40 h. The title compound was isolated by flash chromatography (silica gel, toluene: cyclohexane (v/v) = 1:1) as a brown solid (13.0 mg, 35% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.76−8.84 (m, 5H), 8.69 (d, J = 4.8 Hz, 1H), 8.17−8.20 (m, 4H), 8.07 (d, J = 6.6 Hz, 2H), 8.00 (d, J = 6.6 Hz, 2H), 7.92 (s, 1H), 7.70−7.79 (m, 9H), 7.53−7.61 (m, 3H), 7.32 (d, J = 7.5 Hz, 1H), 7.18−7.23 (m, 2H), 7.04 (m, 1H), 2.27 (s, 3H), −2.72 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.2, 141.9, 141.8, 140.9, 134.6, 134.5, 134.4, 134.0, 133.6, 130.6, 128.5, 128.2, 127.7, 127.4, 127.3, 126.7, 126.6, 126.5, 126.4, 20.3. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ε): 421 (5.40), 521 (4.43), 555 (3.98), 595 (4.01), 651 (3.82). HRMS-EI ($[M]^+$): Calcd for $C_{51}H_{36}N_4S$, 736.2661; found, 736.2673, with an isotope distribution pattern that is the same as the calculated one.

2-(4′-Methoxyphenylsulfanyl)-5,10,15,20-tetraphenylporphyrin (4b, Table 2, Entry 15). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 4-methoxybenzenethiol (25 μL, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 28 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 8:2) as a brown solid (9.0 mg, 24% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.76−8.83 (m, 5H), 8.66 (d, J = 4.8 Hz, 1H), 8.17−8.20 (m, 4H), 8.11 (d, J = 7.2 Hz, 2H),

7.99 (d, J = 7.2 Hz, 2H), 7.72−7.79 (m, 10H), 7.53−7.61 (m, 3H), 7.48 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 3.85 (s, 3H), −2.76 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.0, 142.2, 142.0, 141.9, 140.7, 135.9, 134.6, 134.5, 134.4, 134.1, 129.9, 128.7, 127.7, 127.5, 127.3, 126.7, 126.6, 126.3, 120.8, 119.8, 119.5, 118.2, 114.9, 55.4. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 413 (5.44), 521 (4.51), 556 (4.06), 595 (4.10), 651 (3.91). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{51}H_{37}N_4OS$, 753.2683; found, 753.2649, with an isotope distribution pattern that is the same as the calculated one.

2-Propylsulfanyl-5,10,15,20-tetraphenylporphyrin (4c, Table 2, Entry 16). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with 1-propanethiol (18 μL, 0.20 mmol), using $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol) and (±)BINAP (6.2 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in toluene (5 mL) at 100 °C for 28 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 8:2) as a brown solid (11.0 mg, 32% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.75−8.87 (m, 5H), 8.64 (d, J = 5.4 Hz, 1H), 8.31 (s, 1H), 8.18−8.22 (m, 6H), 8.03−8.06 (m, 2H), 7.70−7.82 (m, 12H), 3.05 (t, J = 7.5 Hz, 2H), 1.78 (m, 2H), 1.01 (t, J = 7.5 Hz, 3H), −2.73 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.5, 142.2, 141.9, 140.8, 134.5, 134.4, 134.3, 134.0, 128.6, 127.7, 127.5, 126.7, 126.66, 126.61, 120.9, 119.8, 119.3, 117.6, 36.7, 21.3, 13.7. UV-*vis*, CH_2Cl_2, λ_{max}, nm, (Log ϵ): 412 (5.29), 521 (4.34), 555 (3.77), 595 (3.84), 651 (3.49). HRMS-MALDI ($[M+H]^+$): Calcd for $C_{47}H_{37}N_4S$, 689.2733; found, 689.2760, with an isotope distribution pattern that is the same as the calculated one.

(S)-(+)-2,2-Dimethyl-cyclopropanecarboxylic Acid (5,10,15,-20-Tetraphenyl-porphyrin-2-yl)-amide (2e, Scheme 2). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with (S)-(+)-2,2-dimethyl-cyclopropanecarboxamide (22.6 mg, 0.20 mmol), $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and Xantphos (5.8 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 6:4) as a purple solid (31.1 mg, 86% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.31 (bs, 1H), 8.75−8.84 (m, 5H), 8.60 (d, J = 4.9 Hz, 1H), 8.24−8.28 (m, 2H), 8.14−8.21 (m, 6H), 7.99 (bs, 1H), 7.70−7.91 (m, 3H), 7.71−7.76 (m, 9H), 1.20 (s, 3H), 1.19 (s, 3H), 0.78−0.84 (m, 3H), −2.82 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 142.2, 142.1, 141.8, 140.9, 134.5, 134.4, 134.3, 133.4, 133.2, 129.2, 128.4, 128.2, 127.8, 127.7, 126.8, 126.7, 126.6, 121.0, 120.3, 119.7, 116.0, 30.22, 27.05, 22.86, 20.50, 18.78. UV-*vis*, $CHCl_3$, λ_{max}, nm, (Log ϵ): 421 (5.60), 518 (4.57), 552 (3.92), 591 (4.01), 646 (3.66). HRMS-EI ($[M]^+$): Calcd for $C_{50}H_{39}N_5O$, 725.3155; found, 725.3137, with an isotope distribution pattern that is the same as the calculated one.

(S)-(−)-2-Methoxy-*N*-(5,10,15,20-tetraphenyl-porphyrin-2-yl)-propionamide (2f, Scheme 2). The general procedure was used to couple β-bromo-5,10,15,20-tetraphenylporphyrin (34.7 mg, 0.050 mmol) with (S)-(−)-2-methoxypropionamide (20.6 mg, 0.20 mmol), $Pd(OAc)_2$ (1.1 mg, 0.0050 mmol) and Xantphos (5.8 mg, 0.010 mmol) in the presence of Cs_2CO_3 (37.6 mg, 0.10 mmol). The reaction was conducted in THF (5 mL) at 100 °C for 24 h. The title compound was isolated by flash chromatography (silica gel, methylene chloride: hexanes (v/v) = 6:4) as a purple solid (16.1 mg, 45% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.49 (bs, 1H), 9.08 (bs, 1H), 8.78−8.86 (m, 5H), 8.48 (d, J = 4.9 Hz, 1H), 8.16−8.25 (m, 8H), 7.81−7.88 (m, 3H), 7.71−7.76 (m, 9H), 3.79 (q, J = 6.7 Hz, 1H), 3.27 (s, 3H), 1.36 (d, J = 6.7 Hz, 3H), −2.79 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.3, 142.3, 142.1, 141.8, 140.3, 134.5, 134.4, 134.3, 133.5, 133.1, 129.5, 128.2, 128.1, 127.8, 127.7, 126.7, 126.6, 120.9, 120.2, 119.8, 116.8, 78.36, 57.23, 17.94. UV-*vis*, $CHCl_3$, λ_{max}, nm, (Log ϵ): 421 (5.69), 518 (4.36), 552 (3.82), 592 (3.88), 647 (3.55). HRMS-EI ($[M]^+$): Calcd for $C_{48}H_{37}N_5O_2$, 715.2947; found, 715.2950, with an isotope distribution pattern that is the same as the calculated one.

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Supporting Information Available: Detailed experimental procedure for a large scale synthesis of BrTPP and NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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