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ONE–POT SYNTHESIS OF A_2BC–TYPE FREE BASE PORPHYRINS

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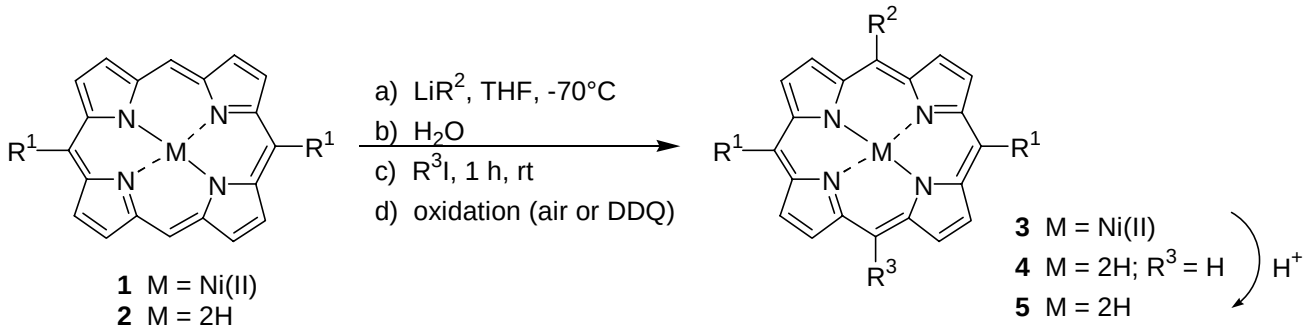
Abstract – Treatment of 5,15-diarylporphyrins with a combination of organolithium and alkyl iodide reagents followed by hydrolysis with water and oxidation with DDQ gives convenient access to A_2BC−type meso-tetrasubstituted free base porphyrins in a one-pot synthesis. Key intermediates are mesomeric phlorin− and porphodimethene−type anions, the latter one being able to react with electrophiles under thermodynamic control.

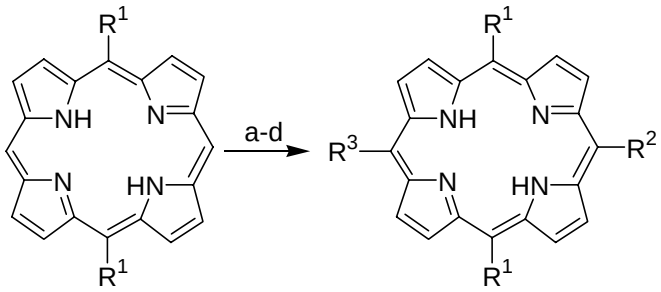
The synthesis of unsymmetrically meso-substituted porphyrins, e.g., the so-called ABCD–type porphyrins remains a challenging topic in porphyrin chemistry.[1] Next to total syntheses[1] substitution reactions offer good potential.[2] Earlier we had shown that S_NAr reactions of nickel(II)porphyrins (**1**) with organolithium reagents yield reactive intermediates[3](Meisenheimer–type[4]porphodimethene anions) which can be trapped *in situ* with organic electrophiles to yield A_2BC–type disubstituted nickel(II)porphyrins (**3**) in a one-pot reaction (Scheme 1).[5] Similar conditions applied to the free base porphyrins (**2**) resulted only in mono-substitution (**4**) and mechanistic studies indicated a phlorin anion to be the key intermediate of this reaction.[3b] Thus, synthesis of A_2BC–type free base porphyrins (**5**) *via* S_NAr reactions necessitated either two addition-oxidation sequences using two different LiR reagents[3c] or first preparation of **3** followed by demetallation; the latter typically requiring harsh reaction conditions (e.g., very strong acids or BBr_3).[6]



Scheme 1. Standard reaction of Ni(II) and free base A_2 porphyrins with R^2Li/R^3I.

RESULTS AND DISCUSSION

Using easily accessible 5,15-disubstituted porphyrins (**6**,**7**) as A_2–type starting materials[6,7] we attempted to achieve a one-pot two-step disubstitution of free base porphyrins. In earlier work using 2,3,7,8,12,13,17,18-octaethylporphyrin derivatives we found that thermodynamic control of the reaction with RLi results in the predominant formation of oxidation–resistant porphodimethenes.[2e,8] This requires the intermediary formation of a porphodimethene anion capable of reaction with electrophiles, while kinetic control of the reaction appeared to proceed via a nonnucleophilic phlorin.[3a] Thus, it appeared feasible to achieve a disubstitution of free base porphyrins with both nucleophiles and electrophiles under thermodynamically controlled conditions.



6 R^1 = Ph
7 R^1 = 3-MeO-C_6H_4

	R^1	R^2	R^3	yield (%)
8	Ph	*n*-Butyl	*n*-Pentyl	34
9	Ph	*n*-Hexyl	*n*-Pentyl	27
10	Ph	*n*-Hexyl	*n*-Propyl	31
11	Ph	*n*-Hexyl	4-Iodobutyl	21
12	Ph	4-HO-C_6H_4	*n*-Propyl	43
13	Ph	4-HO-C_6H_4	*n*-Pentyl	40
14	3-MeO-C_6H_4	Ph	*n*-Pentyl	41
15	3-MeO-C_6H_4	Ph	*n*-Propyl	38
16	3-MeO-C_6H_4	4-HO-C_6H_4	*n*-Pentyl	36
17	3-MeO-C_6H_4	4-HO-C_6H_4	*n*-Propyl	58

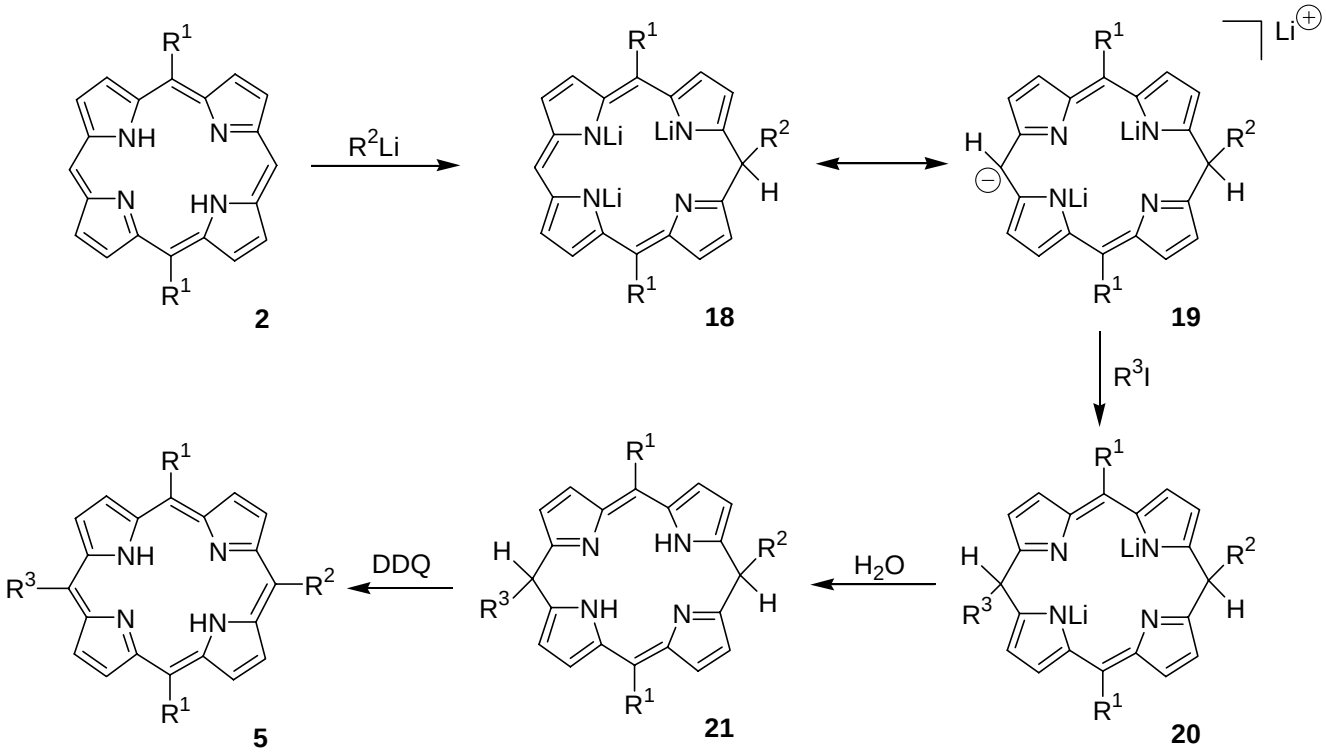
Scheme 2. Synthesis of A_2BC–type porphyrins. a) LiR^2, THF, –70°C; b) R^3I, 12 h, 70°C; c) H_2O; d) DDQ.

Indeed, reaction of the A_2–type porphyrins **6** or **7** with various combinations of R^2Li/R^3I yielded the meso-tetrasubstituted A_2BC–type free base porphyrins (**8**-**17**) under optimized reaction conditions (Scheme 2). The yields are low to moderate in the range of 20 to 60 %. Nevertheless, this is superior when compared to the yields for related porphyrins derived from mixed condensations or multi-step syntheses (typically ranging from 5-20 %).[1] In general, three to four equivalents of organolithium reagents were used and more than ten equivalents of alkyl iodides. In most cases minor amounts of starting material or meso-trisubstituted porphyrins were recovered. 1,3-Diiodobutane gave the lowest yield (21 % for **11**) besides formation of the meso-trisubstituted porphyrin and the starting material.

The overall reaction of RLi with the free base porphyrins is a nucleophilic substitution like the Ziegler alkylation[9] and proceeds via initial reaction of organic nucleophile with a meso carbon yielding an anionic species. This is hydrolyzed to a dihydroporphyrin or can be used as an *in situ* nucleophile for the reaction with alkyliodides, allowing the introducing of two different substituents in a one-pot reaction. Subsequent hydrolysis with water and oxidation with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) yields the meso-substituted porphyrins. Key features of the optimized conditions were: a) using excess

R^3I reagent (10-15 equivalents), b) prolonged reaction times under heating (12-24 h at 70°C) after addition of R^3I, and c) addition of the R^3I prior to the hydrolysis step.

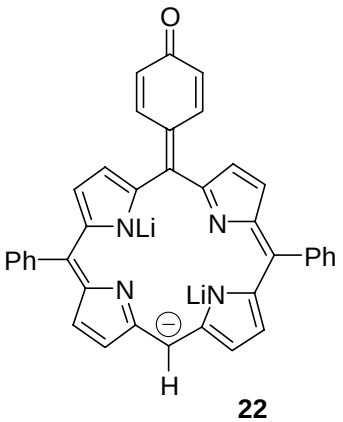
The sequence of our postulated mechanism involves addition of LiR^2 to the free base porphyrin (**2**) to form the phlorin–type intermediate (**18)** (Scheme 3). Trapping of the mesomeric carbanionic complex (**19**) is then achieved by the alkyliodide to form intermediate (**20**). Intermediate (**18**) is believed to have a planar conformation favoring a double bond character at position 20, facilitated by the putative sitting atop localization[10] of the two lithium ions with attached THF molecules.[3a] The more reactive nucleophilic form **19** requires a conformationally distorted sp^3 hybridized meso-carbon atom which is facilitated by steric (*peri* interactions in the octaethylporphyrin series)[11] or metal (Ni-N bond contraction)[12] effects. Presumably, thermal removal of the THF ligands aids in the formation of a conformationally more distorted form with a higher nucleophilic character of meso position 20. Subsequent hydrolysis with water to obtain compound (**21**) followed by oxidation with DDQ then yields the A_2BC porphyrin (**5**).



Scheme 3. Putative reaction mechanism.

The lower yields of the free base porphyrins (**2**) compared to the nickel(II) or octaethylporphyrin derivatives described earlier[3,5,8] reflect the lesser degree of conformational distortion and thus weaker nucleophilic character of **19**. The necessity to effectively stabilize the porphodimethene anion is also reflected in the different yields derived from reaction with various LiR reagents. In line with observations for porphyrin S_NAr monosubstitution reactions the yields are better with aryllithium reagents than alkyllithium reagents.[2e] Using alkyllithium/alkyl iodide combinations the yields are low to moderate

while use of phenyllithium as the attacking nucleophile gives yields of about 40 % (e.g., for **12** and **13**). The best yields were obtained using *p*-hydroxyphenyllithium while use of *m*-hydroxyphenyllithium resulted in only small amounts of product (not shown). An explanation of the difference in the behavior between the *m*- and *p*-hydroxyphenyl derivatives lies in the formation of **22** for the latter. This quinoid form[13] favors a localization of the negative charge at the meso position opposite to the one attacked by the *p*-hydroxyphenyllithium. The lithiated hydroxyphenyl group also offers an convenient entry into various hydrophilic and amphiphilic porphyrins significantly shortening the synthesis of related A_2B– and A_2BC–type porphyrins.[6,14] Likewise, *p*-aminophenyllithium proved to be a convenient reagent. Reaction of **6** with *p*-aminophenyllithium/propyl iodide resulted in the formation of porphyrin (**23**) in 36 % yield. Here, four substituents were introduced in a one-pot reaction. First, the *p*-aminophenyl residue was introduced as a nucleophile, followed by trapping of the electrophilic propyl group accompanied by concomitant dialkylation of the intermediary dilithiated amino group on the phenyl residue.



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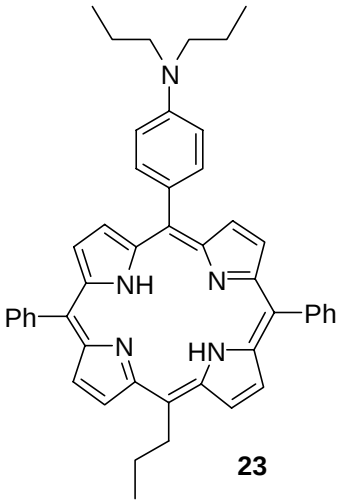

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In conclusion, the present methodology complements already established reactions for the preparation of meso-substituted porphyrins by providing access to meso-disubstituted free base porphyrins in a one-pot procedure while circumventing the use of activated metal complexes or the need for metallation-demetallation sequences.

EXPERIMENTAL

General experimental conditions and instrumentations were as described before.[2f] The free base porphyrins (**6**)[7b] and (**7**)[6] were prepared according to literature procedures.

General procedure. A vigorously stirred solution of the organolithium reagent was mixed with a solution of the free base porphyrin in dry THF under an argon atmosphere. The mixture changed color from deep purple to brown within 30 min. After 1 h the solution was treated with the alkyl iodide and stirred for 12 h under heating to 70 °C. Subsequently, a mixture of 2 mL of water in 3 mL of THF was added for hydrolysis. After stirring of the mixture for 20 min, a solution of 10 equivalents of DDQ in THF was added and the reaction mixture was stirred for another 1 h at rt. Subsequently, the mixture was filtered through silica gel (Machery & Nagel) and the organic solvent was removed followed by column chromatography on silica gel and recrystallization from methylene chloride/methanol.

5-Butyl-15-pentyl-10,20-diphenylporphyrin (8). *n*-Butyllithium (0.4 mL of 2.5 M solution in hexane, 1 mmol) was slowly added under an argon atmosphere to a 100 mL Schlenk flask charged with a solution of 5,15-diphenylporphyrin (**6**) (200 mg, 0.46 mmol) in 40 mL of dry THF at –80 °C under an argon atmosphere. After 15 min the solution was treated with 0.1 mL (0.6 mmol) of *n*-pentyl iodide and stirred for 12 h. Further reaction as described in the general procedure and chromatography eluting with ethyl acetate/*n*-hexane (1:4, v/v) yielded the title compound (87 mg, 34 %) as purple crystals, mp >300 °C; R_f=0.46 (ethyl acetate/*n*-hexane, 1:6, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=–2.65 (s, 2H, 2×N*H*), 0.95 (t, 3H, *J*=7.5 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.11 (t, 3H, *J*=7.5 $CH_2CH_2CH_2CH_3$), 1.29 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.78 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 2.54 (m, 4H, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 4.96 (t, 4H, *J*=7.8, $CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_3$), 7.73–7.79 (m, 6H, Ph-H), 8.18–8.21 (m, 4H, Ph-H), 8.85−8.87 (m, 4H, β-pyrrole-H), 9.41−9.43 (m, 4H, β-pyrrole-H); UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (4.96), 438 (3.76), 486 (3.65), 516 (3.73), 552 (3.55), 595 (3.43), 650 nm (3.43); MS (EI, 80 eV): *m/z* (%): 588 (80) [M^+], 545 (60) [$M^+-C_3H_7$], 531 (100) [$M^+-C_4H_9$], 488 (52) [$M^+-C_4H_9-C_3H_7$], 295 (40) [M^{++}]; HRMS [$C_{41}H_{40}N_4$]: calcd 588.3252, found 588.3235; Anal. Calcd for $C_{41}H_{40}N_4$ C 83.64, H 6.85, N 9.52. Found C 83.88, H 6.93, N 9.73.

5-Hexyl-15-pentyl-10,20-diphenylporphyrin (9). *n*-Hexyllithium (1 mL of a 2.5 M solution in hexane) was reacted with **6** (100 mg, 0.23 mmol) in 40 mL of dry THF as described for **8**. Treatment with 0.8 mL (6.1 mmol) of *n*-pentyl iodide and stirring for 24 h at 70 °C, followed by standard workup and chromatography eluting with ethyl acetate/*n*-hexane (1:4, v/v) yielded the title compound (37 mg, 27 %) as purple crystals. mp >300 °C; R_f=0.73 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=−2.66 (s, 2H, 2×N*H*), 0.92 (m, 6H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.27 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.54 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.82 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.51 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.99 (m, 4H, $CH_2CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.75 (m, 6H, Ph-H), 8.18 (m, 4H, Ph-H), 8.85 (m, 4H, β-pyrrole-H), 9.43 (m, 4H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=13.68, 22.01, 22.27, 29.27, 29.78, 31.47, 32.25, 34.82, 35.20, 37.93, 39.94, 118.45, 119.35, 126.09, 127.05, 134.00, 142.27 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (4.94), 486 (3.14), 516 (2.88), 558 (3.23), 594 (3.18), 651 nm (3.30); MS (EI, 80 eV): *m/z* (%): 616 (7) [M^+], 559 (14) [$M^+-C_4H_9$], 545 (14) [$M^+-C_5H_{11}$], 488 (20) [$M^+-C_4H_9-C_5H_{11}$], 308 (10) [M^{++}]; HRMS [$C_{43}H_{44}N_4$]: calcd 616.3565, found 616.3547; Anal. Calcd for $C_{43}H_{44}N_4$ C 83.73, H 7.19, N 9.08. Found C 83.59, H 7.05, N 9.33.

5-Hexyl-10,20-diphenyl-15-propylporphyrin (10). Reaction of 5,15-diphenylporphyrin (**6**) (100 mg, 0.23 mmol) as described for **9** but using with 0.8 mL (8.1 mmol) of propyl iodide followed by chromatography eluting with ethyl acetate/*n*-hexane (1:6, v/v) gave the title compound (40 mg, 31 %) as purple crystals. mp >300 °C; R_f=0.72 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$,

TMS): δ=−2.66 (s, 2H, 2×N*H*), 0.92 (m, 6H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.28 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$) 1.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.82 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.51 (m, 4H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.99 (m, 4H, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.78 (m, 6H, Ph-H), 8.19 (m, 4H, Ph-H), 8.87 (m, 4H, β-pyrrole-H), 9.41 (m, 4H, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=14.55, 15.32, 23.12, 29.79, 30.11, 30.63, 32.32, 37.59, 39.10, 119.32, 119.86, 120.26, 126.95, 128.01, 134.85, 143.12, 143.87, 145.82 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (4.99), 486 (2,86), 516 (3.46), 551 (2.94), 594 (2.46), 656 nm (3.25); MS (EI, 80 eV): *m/z* (%): 588 (16) [M^+], 559 (20) [$M^+-C_2H_5$], 517 (50) [$M^+-C_5H_{11}$], 488 (30) [$M^+-C_2H_5-C_5H_{11}$], 294 (14) [M^{++}]; HRMS [$C_{41}H_{40}N_4$]: calcd 588.3252, found 588.3248; Anal. Calcd for $C_{43}H_{44}N_4$ C 83.59, H 7.05, N 9.33. Found C 83.09, H 6.88, N 9.58.

5-Hexyl-15-(4-iodobutyl)-10,20-diphenylporphyrin (11). Reaction and workup of 5,15-diphenylporphyrin (**6**) (120 mg, 0.26 mmol) as described for **9** but using 0.2 mL (0.6 mmol) of 1,4-diiodobutane and stirring for 12 h yielded the title compound (33 mg, 21 %) as purple crystals. mp >300 °C; R_f=0.69 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=−2.15 (s, 2H, 2×N*H*), δ=0.91 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.26 (m, 4H, $CH_2CH_2CH_2CH_2I$, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.33 (m, 2H, $CH_2CH_2CH_2CH_2I$), 1.54 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 1.65 (m, 2H, $CH_2CH_2CH_2CH_2I$), 1.88 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 2.66 (m, 2H, $CH_2CH_2CH_2CH_2CH_2CH_3$), 4.24 (m, 2H, $CH_2CH_2CH_2CH_2I$), 5.05 (t, 2H, *J*=8.4 Hz, $CH_2CH_2CH_2CH_2CH_2CH_3$), 7.66 (m, 6H, Ph-H), 8.02 (d, 2H, *J*=5.0 Hz, β-pyrrole-H) 8.22 (m, 4H, Ph-H), 8.53 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.97 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.58 (d, 2H, *J*=5.0 Hz, β-pyrrole-H)); ^{13}C NMR (60 MHz, $CDCl_3$): δ=10.96, 14.04, 14.16, 22.74, 28.92, 29.69, 30.36, 31.21, 31.96, 38.74, 116.68, 120.41, 126.54, 134.36, 142.22, 145.44, 149.38, 152.38, 156.23 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (5.12), 486 (3.73), 515 (3.81), 552 (3.46), 596 (3.35), 650 nm (2.98); MS (EI, 80 eV): *m/z* (%): 728 (16) [M^+], 600 (12) [M^+-H-I].

5-(4-Hydroxyphenyl)-10,20-diphenyl-15-propylporphyrin (12). *n*-Butyllithium (3 mL of a 2.5 M solution in hexane, 7.5 mmol) was added under an argon atmosphere to a 100 mL Schlenk flask charged with a solution of *p*-bromophenol (0.7 g, 4 mmol) in 10 mL of dry ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for 18 h at room temperature. Reaction with 5,15-diphenylporphyrin (**6**) (100 mg, 0.23 mmol) in 40 mL of dry THF and 0.7 mL (7.1 mmol) of propyl iodide followed by chromatography eluting with ethyl acetate/*n*-hexane (1:5, v/v) gave (56 mg, 43 %) of purple crystals of **12**. mp >300 °C; R_f=0.81 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=1.32 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_3$), 2.62 (m, 2H, $CH_2CH_2CH_3$), 5.01 (t, 2H, *J*=7.5 Hz, $CH_2CH_2CH_3$), 6.83 (d, 2H, *J*=7.5 Hz, Ph-H), 7.77 (m, 6H, Ph-H), 7.81 (s, 1H, O*H*), 7.96 (d, 2H, *J*=7.5 Hz, Ph-H), 8.24 (m, 4H, Ph-H), 8.85 (m, 4H, β-pyrrole-H), 8.98 (d, 2H, *J*=5.0 Hz,

β-pyrrole-H), 9.49 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=14.89, 31.65, 37.30, 113.52, 119.22, 119.52, 120.22, 126.59, 127.63, 134.49, 135.50, 142.44, 155.21 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=418 (5.05), 515 (3.70), 552 (3.40), 594 (3.02), 656 nm (3.52); MS (EI, 80 eV): *m/z* (%): 596 (18) [M^+], 567 (70) [$M^+-C_2H_5$], 299 (28) [M^{++}+H]; HRMS [$C_{41}H_{32}N_4O$]: calcd 596.2576, found 596.2562; Anal. Calcd for $C_{41}H_{32}N_4O$ C 82.52, H 5.41, N 9.39. Found C 82.88, H 5.35, N 9.63.

5-(4-Hydroxyphenyl)-15-pentyl-10,20-diphenylporphyrin (13). Preparation as described for **12** using 150 mg (0.35 mmol) 5,15-diphenylporphyrin (**6**), 0.8 mL (6.1 mmol) of *n*-pentyl iodide and stirring for 12 h at 70 °C. Chromatography eluting with ethyl acetate/*n*-hexane (1:4, v/v) yielded the title compound (81 mg, 40 %) as purple crystals, mp >300 °C; R_f=0.66 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.98 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.52 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 1.80 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 2.56 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 4.99 (t, 2H, *J*=7.5 Hz, $CH_2CH_2CH_2CH_2CH_3$), 7.03 (d, 2H, *J*=7.5 Hz, Ph-H), 7.75 (s, 1H, OH), 7.78 (m, 6H, Ph-H), 8.01 (d, 2H, *J*=7.5 Hz, Ph-H), 8.24 (m, 4H, Ph-H), 8.81 (m, 4H, β-pyrrole-H), 8.93 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.48 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=13.69, 22.33, 29.27, 32.28, 38.11, 113.19, 115.32, 119.05, 120.13, 126.16, 127.21, 134.06, 135.16, 142.01, 154.88 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=416 (5.01), 486 (3.77), 516 (3.85), 548 (3.72), 596 (3.59), 655 nm (3.86); MS (EI, 80 eV): *m/z* (%): 624 (19) [M^+], 567 (68) [$M^+-C_4H_9$], 312 (18) [M^{++}]; HRMS [$C_{43}H_{36}N_4O$]: calcd 624.2889, found 624.2867; Anal. Calcd for $C_{43}H_{36}N_4O$ C 82.66, H 5.81, N 8.97. Found C 82.91, H 5.71, N 9.13.

5,15-Bis(3-methoxyphenyl)-10-pentyl-20-phenylporphyrin (14). Phenyllithium (2 mL of a 1.8 M solution in hexane, 0.06 mmol) was slowly added (*ca*. 1 h) under an argon atmosphere to a 100 mL Schlenk flask charged with a solution of 5,15-bis(3-methoxyphenyl)porphyrin (**7**) (200 mg, 0.38 mmol) in 40 mL of dry THF. The mixture was heated to 50 °C and stirred for 30 min. After 1 h the solution was treated with 0.8 mL (6.1 mmol) of *n*-pentyl iodide and stirred for 20 h at 70 °C. Standard workup and chromatography eluting with ethyl acetate/*n*-hexane (1:2, v/v) yielded the title compound (105 mg, 41 %) as purple crystals. mp >300 °C; R_f=0.76 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=−2.67 (s, 2H, 2×NH), 1.02 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.55 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 1.81 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 2.58 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 4.01 (s, 6H, 2×OCH_3), 5.01 (t, 2H, *J*=8.1 Hz, $CH_2CH_2CH_2CH_2CH_3$), 7.38 (m, 2H, Ph-H), 7.63−7.85 (m, 9H, Ph-H), 8.21 (m, 2H, Ph-H), 8.83 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.87 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.98 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.48 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=13.69, 22.33, 32.28, 35.04, 38.11, 55.06, 113.08, 118.82, 120.01, 120.29, 126.27, 126.96, 134.08, 141.65, 143.33, 157.48 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (5.05), 486 (3.35), 514 (3.71), 550

(3.35), 592 (3.02), 656 nm (3.32); MS (EI, 80 eV): *m/z* (%):653 (3) [M^+-CH_3], 334 (10) [M^{++}]; HRMS [$C_{45}H_{40}N_4O_2$]: calcd 668.3151, found 668.3122.

5,15-Bis(3-methoxyphenyl)-10-phenyl-20-propylporphyrin (15). Reaction and workup of free base **7** (150 mg, 0.285 mmol) as described for **14** but using 0.7 mL (7.1 mmol) of propyl iodide. Chromatography eluting with ethyl acetate/*n*-hexane (1:4, v/v) yielded the title compound (71 mg, 38 %) as purple crystals, mp >300 °C; R_f=0.73 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=−2.71 (s, 2H, 2×N*H*), 1.34 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_3$), 2.62 (m, 2H, $CH_2CH_2CH_3$), 4.01 (s, 6H, 2×OCH_3), 5.03 (t, 2H, *J*=8.1 Hz, $CH_2CH_2CH_3$), 7.37 (m, 4H, Ph-H), 7.77 (m, 6H, Ph-H), 8.22 (m, 3H, Ph-H), 8.82 (m, 4H, β-pyrrole-H), 8.99 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.49 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=15.36, 32.13, 37.76, 55.91, 113.93, 119.67, 120.82, 127.12, 128.04, 134.93, 142.48, 144.17, 158.31 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (5.03), 486 (3.65), 513 (3.86), 558 (3.53), 592 (3.44), 656 nm (3.55); MS (EI, 80 eV): *m/z* (%): 640 (10) [M^+], 613 (12) [$M^+-C_2H_5$+2H]; HRMS [$C_{43}H_{36}N_4O_2$]: calcd 640.2838, found 640.2849; Anal. Calcd for $C_{43}H_{36}N_4O_2$ C 80.60, H 5.66, N 9.13. Found C 80.74, H 5.93, N 8.99.

5-(4-Hydroxyphenyl)-10,20-bis(3-methoxyphenyl)-15-pentylporphyrin (16). Preparation as described for **13** using 2 mL of a 2.5 M solution of *n*-butyllithium in hexane (5 mmol), 0.43 g (2.5 mol) of *p*-bromophenol in 10 mL of dry ether, and a solution of 5,15-bis(3-methoxyphenyl)porphyrin (**7**) (100 mg, 0.19 mmol) in 40 mL of dry THF. Chromatography and elution with with ethyl acetate/*n*-hexane (1:2, v/v) yielded the title compound (48 mg, 36 %) as purple crystals, mp >300 °C; R_f=0.55 (ethyl acetate/*n*-hexane, 1:1, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=0.99 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_2CH_2CH_3$), 1.31 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 1.75 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 2.60 (m, 2H, $CH_2CH_2CH_2CH_2CH_3$), 4.01 (s, 6H, 2×OCH_3), 5.03 (t, 2H, *J*=8.1 Hz, $CH_2CH_2CH_2CH_2CH_3$), 6.64 (d, 2H, *J*=7.5 Hz, Ph-H), 6.95−7.04 (m, 2H, Ph-H), 7.35−7.38 (m, 2H, Ph-H), 7.63−7.86 (m, 4H, Ph-H), 7.82 (s, 1H, O*H*), 7.96 (d, 2H, *J*=7.5 Hz, Ph-H), 8.82 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.88 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.01 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.49 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=14.52, 23.17, 33.12, 35.88, 38.94, 55.92, 113.03, 114.03, 115.50, 117.48, 119.64, 121.03, 127.83, 129.17, 132.69, 134.82, 135.98, 144.19, 153.91, 155.69, 158.30 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=418 (5.05), 448 (4.12), 515 (3.87), 595 (3.71), 650 nm (3.64); MS (EI, 80 eV): *m/z* (%): 684 (8) [M^+], 627 (10) [$M^+-C_4H_9$], 342 (11) [M^{++}]; HRMS [$C_{45}H_{40}N_4O_3$]: calcd 684.3100, found 684.3085.

5-(4-Hydroxyphenyl)-10,20-bis(3-methoxyphenyl)-15-propylporphyrin (17). Preparation as described for **16** using 150 mg 5,15-bis(3-methoxyphenyl)porphyrin (**7**) (0.28 mmol) in 40 mL of dry THF, 0.7 mL (7.1 mmol) of propyl iodide and stirring for 12 h at 70 °C. Chromatography and elution with ethyl acetate/*n*-hexane (1:5, v/v) gave **17** (110 mg, 58 %) as purple crystals. mp >300 °C; R_f=0.57 (ethyl

acetate/*n*-hexane, 1:3, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=1.32 (t, 3H, *J*=7.2 Hz, $CH_2CH_2CH_3$), 2.60 (m, 2H, $CH_2CH_2CH_3$), 3.98 (s, 6H, 2×OCH_3), 5.03 (t, 2H, *J*=8.1 Hz, $CH_2CH_2CH_3$), 7.35 (d, 2H, *J*=7.5 Hz, Ph-H), 7.63 (m, 2H, Ph-H), 7.69 (m, 2H, Ph-H), 7.84 (m, 4H, Ph-H), 7.89 (s, 1H, O*H*), 7.94 (d, 2H, *J*=7.5 Hz, Ph-H), 8.82 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.88 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.01 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.49 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=14.89, 31.65, 37.27, 55.47, 113.49, 114.95, 119.23, 120.48, 127.41, 127.67, 134.02, 135.46, 143.75, 155.34, 157.86 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=418 (4.99), 485 (3.71), 515 (3.82), 551 (3.63), 594 (3.39), 656 nm (3.59); MS (EI, 80 eV): *m/z* (%): 656 (4) [M^+], 627 (8) [$M^+-C_2H_5$]; HRMS [$C_{43}H_{36}N_4O_3$]: calcd 656.2787, found 656.2766.

5-[4-(Dipropylamino)phenyl]-10,20-diphenyl-15-propylporphyrin (23). *n*-Butyllithium (2 mL of a 2.5 M solution in hexane, 5 mmol) was added under an argon atmosphere to a 100 mL Schlenk flask charged with a solution of *p*-bromoaniline (0.5g, 2.5 mmol) in 10 mL of dry ether at 0 °C. After addition of *n*-butyllithium the cold bath was removed and stirring was continued for another 2 h at room temperature. Reaction with 5,15-diphenylporphyrin (**6**) (100 mg, 0.22 mmol) and 1 mL (1.04 mmol) of propyl iodide as described in the general procedure, followed by chromatography eluting with ethyl acetate/*n*-hexane (1:5, v/v) yielded the title compound (53 mg, 36 %) as purple crystals. mp >300 °C; R_f=0.57 (ethyl acetate/*n*-hexane, 1:4, v/v); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ=−2.64 (s, 2H, 2×N*H*), 1.11 (m, 6H, $N(CH_2CH_2CH_3)_2$, 1.33 (t, 2H, *J*=7.2 Hz, $CH_2CH_2CH_3$), 1.82 (m, 4H, $N(CH_2CH_2CH_3)_2$), 2.57 (m, 2H, $CH_2CH_2CH_3$), 3.49 (m, 4H, $N(CH_2CH_2CH_3)_2$), 5.01 (t, 2H, *J*=8.1 Hz, $CH_2CH_2CH_3$), 7.02 (d, 2H, *J*=7.5 Hz, Ph-H), 7.77 (m, 6H, Ph-H), 8.03 (d, 2H, *J*=7.5 Hz, Ph-H), 8.21 (m, 4H, Ph-H), 8.77 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.89 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 8.96 (d, 2H, *J*=5.0 Hz, β-pyrrole-H), 9.46 (d, 2H, *J*=5.0 Hz, β-pyrrole-H); ^{13}C NMR (60 MHz, $CDCl_3$): δ=13.69, 20.09, 29.26, 31.19, 36.83, 39.70, 109.58, 118.81, 121.51, 126.12, 127.11, 134.10, 135.61, 142.24 ppm; UV/VIS (CH_2Cl_2): λ_{max} (log ε)=417 (5.15), 517 (4.21), 558 (3.75), 594 (3.16), 652 nm (3.73); MS (EI, 80 eV): *m/z* (%): 678 (36) [M^+-H], 664 (48) [M^+-CH_3], 650 (6) [$M^+-C_2H_5$], 622 (5) [$M^+-C_2H_5-CH_3-CH_3+2H$], 592 (6) [$M^+-3(C_2H_5)$], 578 (44) [$M^+-H-N(CH_2CH_2CH_3)_2$]; Anal. Calcd for $C_{47}H_{45}N_5$ C 83.03, H 6.67, N 10.30. Found C 83.41, H 7.15, N 6.82.

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