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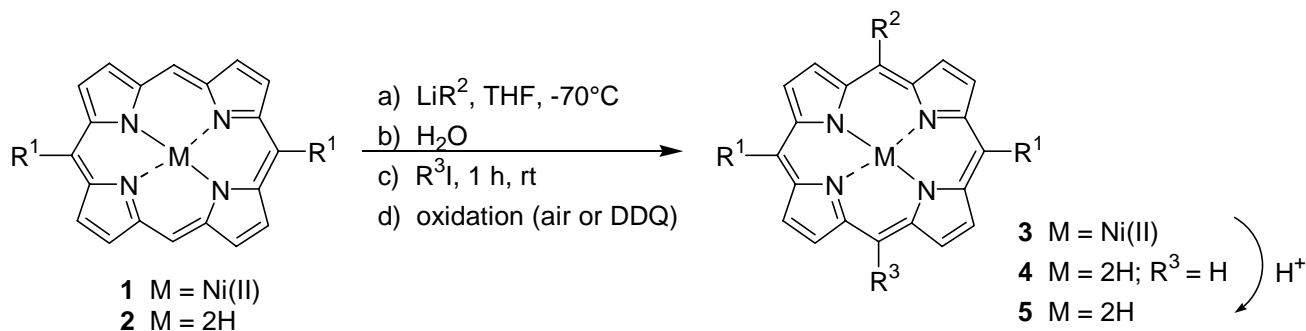
ONE-POT SYNTHESIS OF A<sub>2</sub>BC-TYPE FREE BASE PORPHYRINS

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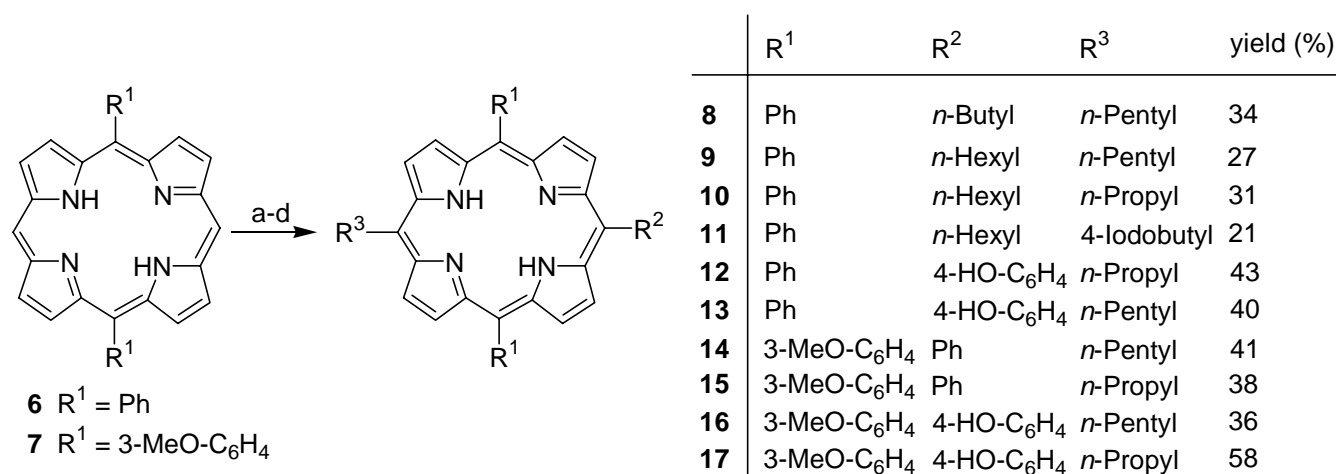
**Abstract** – Treatment of 5,15-diarylporphyrins with a combination of organolithium and alkyl iodide reagents followed by hydrolysis with water and oxidation with DDQ gives convenient access to A<sub>2</sub>BC-type meso-tetrasubstituted free base porphyrins in a one-pot synthesis. Key intermediates 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.<sup>1</sup> Next to total syntheses<sup>1</sup> substitution reactions offer good potential.<sup>2</sup> Earlier we had shown that S<sub>N</sub>Ar reactions of nickel(II)porphyrins (**1**) with organolithium reagents yield reactive intermediates<sup>3</sup>(Meisenheimer-type<sup>4</sup>porphodimethene anions) which can be trapped *in situ* with organic electrophiles to yield A<sub>2</sub>BC-type disubstituted nickel(II)porphyrins (**3**) in a one-pot reaction (Scheme 1).<sup>5</sup> 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.<sup>3b</sup> Thus, synthesis of A<sub>2</sub>BC-type free base porphyrins (**5**) *via* S<sub>N</sub>Ar reactions necessitated either two addition-oxidation sequences using two different LiR reagents<sup>3c</sup> or first preparation of **3** followed by demetallation; the latter typically requiring harsh reaction conditions (e.g., very strong acids or BBr<sub>3</sub>).<sup>6</sup>

Scheme 1. Standard reaction of Ni(II) and free base A<sub>2</sub> porphyrins with R<sup>2</sup>Li/R<sup>3</sup>I.

## RESULTS AND DISCUSSION

Using easily accessible 5,15-disubstituted porphyrins (**6,7**) as A<sub>2</sub>-type starting materials<sup>6,7</sup> 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.<sup>2e,8</sup> 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.<sup>3a</sup> Thus, it appeared feasible to achieve a disubstitution of free base porphyrins with both nucleophiles and electrophiles under thermodynamically controlled conditions.



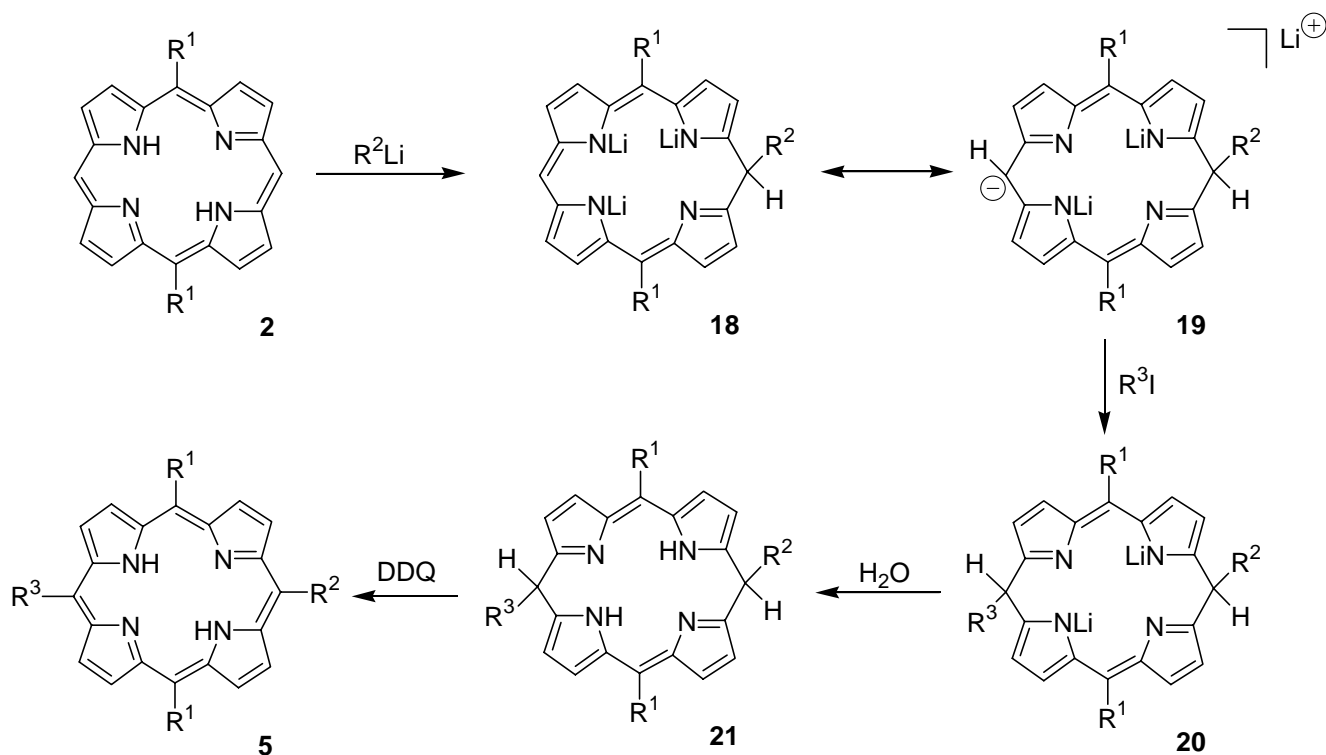
Scheme 2. Synthesis of A<sub>2</sub>BC-type porphyrins. a) LiR<sup>2</sup>, THF, -70°C; b) R<sup>3</sup>I, 12 h, 70°C; c) H<sub>2</sub>O; d) DDQ.

Indeed, reaction of the A<sub>2</sub>-type porphyrins **6** or **7** with various combinations of R<sup>2</sup>Li/R<sup>3</sup>I yielded the meso-tetrasubstituted A<sub>2</sub>BC-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 %).<sup>1</sup> 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<sup>9</sup> 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 alkyl iodides, 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  $70^\circ\text{C}$ ) after addition of  $R^3I$ , and c) addition of the  $R^3I$  prior to the hydrolysis step.

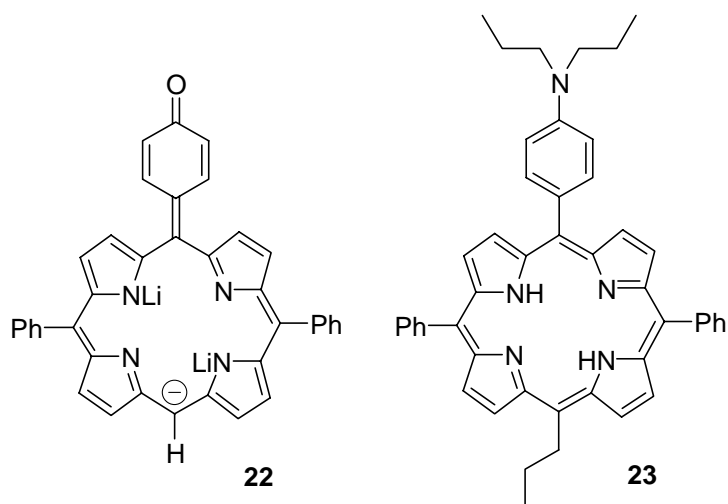
The sequence of our postulated mechanism involves addition of  $\text{LiR}^2$  to the free base porphyrin (**2**) to form the phlorin-type intermediate (**18**) (Scheme 3). Trapping of the mesomeric carbanionic complex (**19**) is then achieved by the alkyl iodide to form intermediate (**20**). Intermediate (**18**) is believed to have a planar conformation favoring a double bond character at position 20, facilitated by the putative sitting atop localization<sup>10</sup> of the two lithium ions with attached THF molecules.<sup>3a</sup> The more reactive nucleophilic form **19** requires a conformationally distorted  $\text{sp}^3$  hybridized meso-carbon atom which is facilitated by steric (*peri* interactions in the octaethylporphyrin series)<sup>11</sup> or metal (Ni-N bond contraction)<sup>12</sup> 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  $\text{A}_2\text{BC}$  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<sup>3,5,8</sup> 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  $\text{LiR}$  reagents. In line with observations for porphyrin  $\text{S}_{\text{N}}\text{Ar}$  monosubstitution reactions the yields are better with aryllithium reagents than alkyl lithium reagents.<sup>2e</sup> Using alkyl lithium/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<sup>13</sup> 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 a convenient entry into various hydrophilic and amphiphilic porphyrins significantly shortening the synthesis of related A<sub>2</sub>B- and A<sub>2</sub>BC-type porphyrins.<sup>6,14</sup> 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.

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-demetalation sequences.

## EXPERIMENTAL

General experimental conditions and instrumentations were as described before.<sup>2f</sup> The free base porphyrins (**6**)<sup>7b</sup> and (**7**)<sup>6</sup> 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  $-80\text{ }^{\circ}\text{C}$  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  $>300\text{ }^{\circ}\text{C}$ ;  $R_f=0.46$  (ethyl acetate/*n*-hexane, 1:6, v/v);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , TMS):  $\delta=-2.65$  (s, 2H,  $2\times\text{NH}$ ), 0.95 (t, 3H,  $J=7.5\text{ Hz}$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.11 (t, 3H,  $J=7.5$   $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.29 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.78 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 2.54 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 4.96 (t, 4H,  $J=7.8$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 7.73–7.79 (m, 6H, Ph-H), 8.18–8.21 (m, 4H, Ph-H), 8.85–8.87 (m, 4H,  $\beta$ -pyrrole-H), 9.41–9.43 (m, 4H,  $\beta$ -pyrrole-H); UV/VIS ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\log \epsilon$ )=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) [ $\text{M}^+$ ], 545 (60) [ $\text{M}^+-\text{C}_3\text{H}_7$ ], 531 (100) [ $\text{M}^+-\text{C}_4\text{H}_9$ ], 488 (52) [ $\text{M}^+-\text{C}_4\text{H}_9-\text{C}_3\text{H}_7$ ], 295 (40) [ $\text{M}^{++}$ ]; HRMS [ $\text{C}_{41}\text{H}_{40}\text{N}_4$ ]: calcd 588.3252, found 588.3235; Anal. Calcd for  $\text{C}_{41}\text{H}_{40}\text{N}_4$  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  $70\text{ }^{\circ}\text{C}$ , 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  $>300\text{ }^{\circ}\text{C}$ ;  $R_f=0.73$  (ethyl acetate/*n*-hexane, 1:4, v/v);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ , TMS):  $\delta=-2.66$  (s, 2H,  $2\times\text{NH}$ ), 0.92 (m, 6H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.27 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ) 1.54 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.82 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 2.51 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 4.99 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 7.75 (m, 6H, Ph-H), 8.18 (m, 4H, Ph-H), 8.85 (m, 4H,  $\beta$ -pyrrole-H), 9.43 (m, 4H,  $\beta$ -pyrrole-H);  $^{13}\text{C NMR}$  (60 MHz,  $\text{CDCl}_3$ ):  $\delta=13.68$ , 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 ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\log \epsilon$ )=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) [ $\text{M}^+$ ], 559 (14) [ $\text{M}^+-\text{C}_4\text{H}_9$ ], 545 (14) [ $\text{M}^+-\text{C}_5\text{H}_{11}$ ], 488 (20) [ $\text{M}^+-\text{C}_4\text{H}_9-\text{C}_5\text{H}_{11}$ ], 308 (10) [ $\text{M}^{++}$ ]; HRMS [ $\text{C}_{43}\text{H}_{44}\text{N}_4$ ]: calcd 616.3565, found 616.3547; Anal. Calcd for  $\text{C}_{43}\text{H}_{44}\text{N}_4$  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  $>300\text{ }^{\circ}\text{C}$ ;  $R_f=0.72$  (ethyl acetate/*n*-hexane, 1:4, v/v);  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ,

TMS):  $\delta$  = -2.66 (s, 2H, 2×NH), 0.92 (m, 6H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.28 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.52 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.82 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.51 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 4.99 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 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); <sup>13</sup>C NMR (60 MHz, CDCl<sub>3</sub>):  $\delta$  = 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<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\max}$  (log  $\epsilon$ ) = 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<sup>+</sup>], 559 (20) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>], 517 (50) [M<sup>+</sup>-C<sub>5</sub>H<sub>11</sub>], 488 (30) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>-C<sub>5</sub>H<sub>11</sub>], 294 (14) [M<sup>++</sup>]; HRMS [C<sub>41</sub>H<sub>40</sub>N<sub>4</sub>]: calcd 588.3252, found 588.3248; Anal. Calcd for C<sub>43</sub>H<sub>44</sub>N<sub>4</sub> 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<sub>f</sub> = 0.69 (ethyl acetate/*n*-hexane, 1:4, v/v); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = -2.15 (s, 2H, 2×NH),  $\delta$  = 0.91 (t, 3H,  $J$  = 7.2 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.26 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>I, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.33 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>I), 1.54 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.65 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>I), 1.88 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.66 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 4.24 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>I), 5.05 (t, 2H,  $J$  = 8.4 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 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); <sup>13</sup>C NMR (60 MHz, CDCl<sub>3</sub>):  $\delta$  = 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<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\max}$  (log  $\epsilon$ ) = 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<sup>+</sup>], 600 (12) [M<sup>+</sup>-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<sub>f</sub> = 0.81 (ethyl acetate/*n*-hexane, 1:4, v/v); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS):  $\delta$  = 1.32 (t, 3H,  $J$  = 7.2 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.62 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 5.01 (t, 2H,  $J$  = 7.5 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 6.83 (d, 2H,  $J$  = 7.5 Hz, Ph-H), 7.77 (m, 6H, Ph-H), 7.81 (s, 1H, OH), 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,

$\beta$ -pyrrole-H), 9.49 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H);  $^{13}\text{C}$  NMR (60 MHz,  $\text{CDCl}_3$ ):  $\delta=14.89, 31.65, 37.30, 113.52, 119.22, 119.52, 120.22, 126.59, 127.63, 134.49, 135.50, 142.44, 155.21$  ppm; UV/VIS ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\log \epsilon$ )=418 (5.05), 515 (3.70), 552 (3.40), 594 (3.02), 656 nm (3.52); MS (EI, 80 eV):  $m/z$  (%): 596 (18) [ $\text{M}^+$ ], 567 (70) [ $\text{M}^+-\text{C}_2\text{H}_5$ ], 299 (28) [ $\text{M}^{++}+\text{H}$ ]; HRMS [ $\text{C}_{41}\text{H}_{32}\text{N}_4\text{O}$ ]: calcd 596.2576, found 596.2562; Anal. Calcd for  $\text{C}_{41}\text{H}_{32}\text{N}_4\text{O}$  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);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS):  $\delta=0.98$  (t, 3H,  $J=7.2$  Hz,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.52 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.80 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 2.56 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 4.99 (t, 2H,  $J=7.5$  Hz,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 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,  $\beta$ -pyrrole-H), 8.93 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 9.48 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H);  $^{13}\text{C}$  NMR (60 MHz,  $\text{CDCl}_3$ ):  $\delta=13.69, 22.33, 29.27, 32.28, 38.11, 113.19, 115.32, 119.05, 120.13, 126.16, 127.21, 134.06, 135.16, 142.01, 154.88$  ppm; UV/VIS ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\log \epsilon$ )=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) [ $\text{M}^+$ ], 567 (68) [ $\text{M}^+-\text{C}_4\text{H}_9$ ], 312 (18) [ $\text{M}^{++}$ ]; HRMS [ $\text{C}_{43}\text{H}_{36}\text{N}_4\text{O}$ ]: calcd 624.2889, found 624.2867; Anal. Calcd for  $\text{C}_{43}\text{H}_{36}\text{N}_4\text{O}$  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);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS):  $\delta=-2.67$  (s, 2H,  $2\times\text{NH}$ ), 1.02 (t, 3H,  $J=7.2$  Hz,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.55 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.81 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 2.58 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 4.01 (s, 6H,  $2\times\text{OCH}_3$ ), 5.01 (t, 2H,  $J=8.1$  Hz,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 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,  $\beta$ -pyrrole-H), 8.87 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 8.98 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 9.48 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H);  $^{13}\text{C}$  NMR (60 MHz,  $\text{CDCl}_3$ ):  $\delta=13.69, 22.33, 32.28, 35.04, 38.11, 55.06, 113.08, 118.82, 120.01, 120.29, 126.27, 126.96, 134.08, 141.65, 143.33, 157.48$  ppm; UV/VIS ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\log \epsilon$ )=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);  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta=-2.71$  (s, 2H,  $2\times NH$ ), 1.34 (t, 3H,  $J=7.2$  Hz,  $CH_2CH_2CH_3$ ), 2.62 (m, 2H,  $CH_2CH_2CH_3$ ), 4.01 (s, 6H,  $2\times OCH_3$ ), 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,  $\beta$ -pyrrole-H), 8.99 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 9.49 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H);  $^{13}C$  NMR (60 MHz,  $CDCl_3$ ):  $\delta=15.36, 32.13, 37.76, 55.91, 113.93, 119.67, 120.82, 127.12, 128.04, 134.93, 142.48, 144.17, 158.31$  ppm; UV/VIS ( $CH_2Cl_2$ ):  $\lambda_{max}$  (log  $\epsilon$ )=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 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);  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta=0.99$  (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,  $2\times OCH_3$ ), 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, OH), 7.96 (d, 2H,  $J=7.5$  Hz, Ph-H), 8.82 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 8.88 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 9.01 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H), 9.49 (d, 2H,  $J=5.0$  Hz,  $\beta$ -pyrrole-H);  $^{13}C$  NMR (60 MHz,  $CDCl_3$ ):  $\delta=14.52, 23.17, 33.12, 35.88, 38.94, 55.92, 113.03, 114.03, 115.50, 117.48, 119.64, 121.03, 127.83, 129.17, 132.69, 134.82, 135.98, 144.19, 153.91, 155.69, 158.30$  ppm; UV/VIS ( $CH_2Cl_2$ ):  $\lambda_{max}$  (log  $\epsilon$ )=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); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS): δ=1.32 (t, 3H, *J*=7.2 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 2.60 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.98 (s, 6H, 2×OCH<sub>3</sub>), 5.03 (t, 2H, *J*=8.1 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 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, OH), 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); <sup>13</sup>C NMR (60 MHz, CDCl<sub>3</sub>): 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<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> (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<sup>+</sup>], 627 (8) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>]; HRMS [C<sub>43</sub>H<sub>36</sub>N<sub>4</sub>O<sub>3</sub>]: 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<sub>f</sub>=0.57 (ethyl acetate/*n*-hexane, 1:4, v/v); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS): δ=-2.64 (s, 2H, 2×NH), 1.11 (m, 6H, N(CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 1.33 (t, 2H, *J*=7.2 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.82 (m, 4H, N(CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 2.57 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 3.49 (m, 4H, N(CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>), 5.01 (t, 2H, *J*=8.1 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 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); <sup>13</sup>C NMR (60 MHz, CDCl<sub>3</sub>): 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<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> (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<sup>+</sup>-H], 664 (48) [M<sup>+</sup>-CH<sub>3</sub>], 650 (6) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>], 622 (5) [M<sup>+</sup>-C<sub>2</sub>H<sub>5</sub>-CH<sub>3</sub>-CH<sub>3</sub>+2H], 592 (6) [M<sup>+</sup>-3(C<sub>2</sub>H<sub>5</sub>)], 578 (44) [M<sup>+</sup>-H-N(CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>]; Anal. Calcd for C<sub>47</sub>H<sub>45</sub>N<sub>5</sub> 83.03, H 6.67, N 10.30. Found C 83.41, H 7.15, N 6.82.

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