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Synthesis of Mono- and Disubstituted Porphyrins: A- and 5,10-A_2-Type Systems

Claudia Ryppa,[a] Mathias O. Senge,*[b] Sabine S. Hatscher,[a] Erich Kleinpeter,[a] Philipp Wacker,[a] Uwe Schilde,[a] and Arno Wiehe[c]

Abstract: General syntheses have been developed for *meso*-substituted porphyrins with one or two substituents in the 5,10-positions and no β substituents. 5-Substituted porphyrins with only one *meso* substituent are easily prepared by an acid-catalyzed condensation of dipyrromethane, pyrrole-2-carbaldehyde, and an appropriate aldehyde using a "[2+1+1]" approach. Similarly, 5,10-disubstituted porphyrins are accessible by simple condensation of unsubstituted tripyrrane with pyrrole and various aldehydes using a "[3+1]" approach. The yields for these reactions are low to moderate and additional formation of either di- or monosubstituted porphyrins due to scrambling of the intermediates is observed. However, the reactions can be performed quite easily and the desired target compounds are easily removed due to large differences in solubility. A complementary and more selective synthesis involves the use of organolithium reagents for S_NAr reactions. Reaction of in situ generated porphyrin (porphine) with 1.1–8 equivalents of RLi gave the monosubstituted porphyrins, while reaction with 3–6 equivalents of RLi gave the 5,10-disubstituted porphyrins in yields ranging from 43 to 90%. These hitherto almost inaccessible compounds complete the series of different homologues of A-, 5,15-A_2-, 5,10-A_2-, A_3-, and A_4-type porphyrins and allow an investigation of the gradual influence of type, number, and regiochemical arrangement of substituents on the properties of *meso*-substituted porphyrins. They also present important starting materials for the synthesis of ABCD porphyrins and are potential synthons for supramolecular materials requiring specific substituent orientations.

Keywords: macrocycles · nitrogen heterocycles · nucleophilic addition · porphyrinoids · tetrapyrroles

Introduction

Porphyrin chemistry has undergone a renaissance in the last decade and its multifaceted applications and uses in nature are evidenced by the recent publication of 20 volumes of *The Porphyrin Handbook*.[1] Despite the many advances made in the synthesis and functionalization of porphyrins,[2] much less is known about the chemistry of the parent macrocycle porphyrin (porphine **1**) or derivatives thereof with only a few substituents. Indeed, most of the recent developments made with respect to chemical transformation and functional-group interconversions involving porphyrins have been made with the synthetically easily accessible 2,3,7,8,12,13,17,18-octaalkylporphyrins or 5,10,15,20-tetraarylporphyrins.[3] The latter are examples of so-called A_4-type porphyrins[4] and a typical compound is tetraphenylporphyrin (TPP, **10**; R = Ph), probably one of the most widely studied molecules in bioorganic and bioinorganic chemistry. Thus, many methods are available for chemical transformations involving the β position(s) of A_4 porphyrins.

On the other hand, there is increasing demand for unsymmetrically substituted porphyrins for applications in catalysis, optics, biomedicine, and biological studies. Notably, chiral or amphiphilic porphyrins are in high demand and progress on the application side is currently hampered due to the inaccessibility of such compounds in practical terms. Theoretically, almost any unsymmetric β-substituted porphyrin can be prepared by total synthesis.[5] However, these multistep syntheses are too cumbersome for large-scale synthesis or industrial use. Even more limited are the possibili-

[a] C. Ryppa, Dr. S. S. Hatscher, Prof. Dr. E. Kleinpeter, P. Wacker, Prof. Dr. U. Schilde
Institut für Chemie, Universität Potsdam
Karl Liebknecht Strasse 24–25, 14476 Golm (Germany)

[b] Prof. Dr. M. O. Senge
Department of Chemistry, Trinity College Dublin
Dublin 2 (Ireland)
Fax: (+353) 1-671-2826
E-mail: sengem@tcd.ie

[c] Dr. A. Wiehe
Biolitec AG, Winzerlaer Strasse 2a
07745 Jena (Germany)

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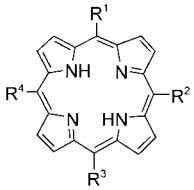
ties for *meso*-substituted, β-unsubstituted porphyrins. Total syntheses are yet only possible for selected types of substituents and still suffer from acid-catalyzed scrambling, again making this a futile endeavor in practical terms.[6] However, as mentioned, a broad range of methods for the β functionalization of *meso* substituents are available and strategies have emerged that put unsymmetrically *meso*-substituted porphyrins within reach. This involves use of either transition-metal-catalyzed coupling reactions[7] or of organometallic substitution reactions[8] for the modification of the *meso* positions and requires step-wise introduction of individual *meso* substituents in a regioselective manner,[8b] for example, through a sequence A-→AB-→ABC-→ABCD-type (**6**) porphyrin (Figure 1).



1	$R^1 = R^2 = R^3 = R^4 = H$	porphine
2	$R^2 = R^3 = R^4 = H$	A type
3	$R^3 = R^4 = H$	AB type (5,10)
4	$R^2 = R^4 = H$	AB type (5,15)
5	$R^4 = H$	ABC type
6		ABCD type
7	$R^1 = R^2$, $R^3 = R^4 = H$	A_2 type (5,10)
8	$R^1 = R^3$, $R^2 = R^4 = H$	A_2 type (5,15)
9	$R^1 = R^2 = R^3$, $R^4 = H$	A_3 type
10	$R^1 = R^2 = R^3 = R^4$	A_4 type

Figure 1. Different types of *meso*-substituted porphyrins.

However, several blank spots remain on the map of synthetic porphyrin chemistry. The most significant one of these is the synthesis of *meso*-substituted porphyrins with lower symmetry, that is, with fewer substituents than for example, TPP. Thus, while A_4-type porphyrins have been in use for a long time and 5,15-A_2-type porphyrins (**8**) have come of age,[9a] use of A_3- (**9**), 5,15-A_2B-,[9b,c] or 5,15-AB-type[9a] (**4**) porphyrins is just emerging, and A- (**2**), 5,10-A_2- (**7**), or -AB-type (**3**) porphyrins are almost unknown. In many of these cases the accessible porphyrins are routinely prepared from mixed condensation reactions, often requiring laborious purification methods resulting in low yields. Thus, there is a pressing need for simple syntheses of the latter to access the full range of ABCD porphyrins (**6**) by *meso* transformations.

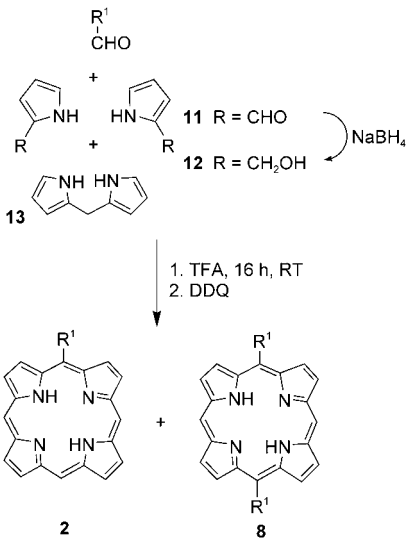
Herein we show that porphyrins of the A- (**2**) and A_2-type (**7**) can be prepared by either classical condensation reactions involving dipyrromethanes (**13**) or tripyrranes (**28**) or alternatively by S_NAr reactions of unsubstituted porphine **1**.[10] This opens the way for the first time for a synthesis of ABCD-type porphyrins by successive introduction of *meso* substituents. In addition, **2** and **7**, in conjunction with the other members of the ABCD- and A_n-type series, now allow an investigation of the gradual influence of type, number, and regiochemical arrangement of substituents on the properties of *meso*-substituted porphyrins.

Results and Discussion

Synthesis of A-type porphyrins by condensation reactions: Our previous work had shown that *meso* substitution with RLi is a facile method of introducing (additional) residues into the porphyrin.[8] Thus we envisaged the use of A-type porphyrins as starting materials for subsequent S_NAr reactions to yield, for example, AB-, then ABC-, and finally ABCD-type porphyrins. At that time no reliable method existed for either the large-scale preparation of porphine or the synthesis of mono-*meso*-substituted porphyrins (**2**). Indeed, only very few examples of 5-substituted porphyrins have been described in the literature. They were either obtained directly by functionalization of porphine or were isolated as byproducts from condensation reactions in yields of $\leq 1\%$. Examples are 5-*tert*-butylporphyrin (**14a**, 0.3%),[11] formylation (no yield),[12a] nitration,[12b] or bromination[12c] of porphine **1**, or condensation reactions of pyrrole (**27**)[13a] or dipyrromethane[13b] and the corresponding aldehyde. Due to the low yields their characterization is often incomplete.

Most porphyrins with D_2 or D_4 symmetry are synthesized by acid-catalyzed condensation reactions, using an aldehyde as the *meso*-building-block component and pyrrole or dipyrromethanes as a second component. Thus, monosubstituted porphyrin **2** should be accessible by condensation of an aldehyde with a bilane.[13b] However, unsubstituted bilane is difficult to prepare and highly unstable making it an unsuitable component for a simple synthesis. Looking for an alternative to bilane we focused on using pyrrole-2-carbaldehyde (**11**) as one building block. Hans Fischer, in one of the earliest syntheses, originally used the aldehyde for preparing porphine.[14] Use of two equivalents of aldehyde **11** together with one equivalent of the relatively stable dipyrromethane (**13**)[15] in a condensation reaction would then constitute an equivalent of the bilane. We anticipated that the deactivating effect of the formyl group in **11** would favor a reaction with **12** over self-condensation, as outlined in Scheme 1.

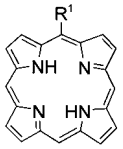
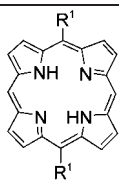
Initial test reactions with benzaldehyde using two equivalents of **11** and one of **13** were promising and gave the re-



Scheme 1. Synthesis of A-type porphyrins by condensation reactions (procedure A using **11** or procedure B using **12**).

spective monosubstituted 5-phenylporphyrin (**17a**) in a 7% yield (Table 1). Subsequent reactions with other aldehydes and attempts to optimize the conditions showed that this method can be used for the preparation of porphyrins with various types of *meso* substituents. These include simple alkyl and aryl residues, aryl halides useful for subsequent C–C coupling reactions (e.g., **18** or **19**), methoxyphenyl derivatives for the preparation of hydrophilic porphyrins (e.g., **22**–**24** after deprotection of the methyl ether),[16] **20** or **21** for in vivo ^{19}F NMR diagnostics, or compounds like **25** or **26** that can be used for the construction of superstructured systems (e.g., after conversion to the amines). The yields of the monosubstituted porphyrins vary between 2 and 16% if the reaction is performed under standard conditions (general procedure A in the Experimental Section). Although low, these yields are satisfactory given the low yields often observed for pyrrole condensation reactions and the inaccessibility of the target compounds by other means.

Table 1. Products and yields (% in relation to the aldehyde) for the condensation reaction A using **11**.

		 5-Mono- **a**[a]	 5,15-Di- **b**
14		7	–
15		11	7
16		2	15
17		7	5
18	Br	6	3
19	Cl	5	1
20	F, F	2	15
21	F, F	4	2
22	OMe	12	–
23	OMe	16	12
24	OMe, OMe	6	–
25	NO_2	3	6
26	NO_2	2	–

[a] Note, that in individual cases significantly higher yields are possible by modification of the reaction conditions or by using 2-hydroxymethylpyrrole (see text).

In many cases the 5,15-disubstituted porphyrins **8** (**b** in Table 1) are often observed as a second product. Their formation is due to acid-catalyzed scrambling reactions and individual rates of formation depend on the electronic structure of the intermediary porphyrinogens.[17] Nevertheless, the yields of mono- versus disubstituted product depend in practical terms more on their relative solubilities. The solubilities of the mono- and disubstituted compounds are quite different and in most cases the disubstituted porphyrin is much less soluble. Thus, the disubstituted (by)products are often simply retained on the column or can easily be removed by standard column chromatography. For example, for either the alkylporphyrins **14** or the dimethoxyphenylporphyrins **24** simple filtration through a short silica column is sufficient for purification.

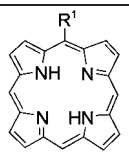
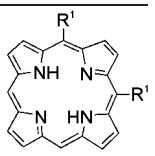
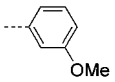
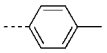
For individual compounds the possibility exists to significantly increase the yields. Utilizing a limiting amount of the aldehyde favors formation of the monosubstituted product. For example, reaction of **11** with **13** and 2-ethylbutanal in a molar ratio of 4:2:1, respectively, increased the yield of **15a** from 11 to 17% and lowered the yield of **15b** from 7 to 4%. The best overall yield was observed using a limiting amount of 3-methoxybenzaldehyde. Under these conditions the *m*-anisole aldehyde was completely converted into porphyrins to yield 34% of **23a** and 76% of **23b**. Another possibility is the alternative use of 2-hydroxymethylpyrrole (**12**)[18] instead of **11**. As hydroxymethylpyrrole should show a higher reactivity towards acid-catalyzed tetramerization,[18b] we prepared compound **12** by hydride reduction of **11**. Using **12** under standard conditions (general procedure B in the Experimental Section) resulted in an increase of the yields for **22a** and **24a** to 14 and 22%, respectively. Additionally, using a limited amount of the aldehyde as described above gave yields of 23 and 25% for **22a** and **23a**, respectively. Using four instead of two equivalents of **12** resulted in an increased yield of the disubstituted products. Contrary to the reactions with pyrrole-2-carbaldehyde (**11**), porphine **1** was obtained as a side product in yields of up to 14%. Unsubstituted porphyrin is difficult to remove from mixtures and together with the additional synthetic step and the more careful handling required for the less stable 2-hydroxymethylpyrrole, use of pyrrole-2-carbaldehyde is more efficient and recommended. Initial experiments using BF_3–etherate catalysis were not promising.

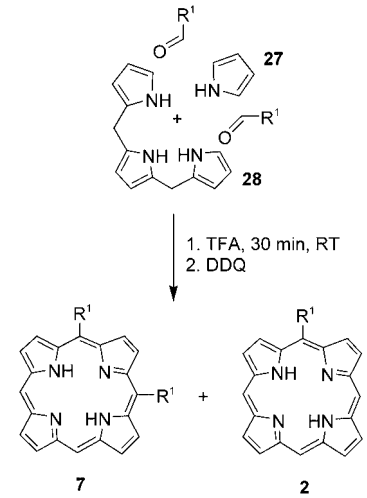
Synthesis of 5,10-A_2-type porphyrins by condensation reactions: The success of developing a practical condensation method for preparing monosubstituted porphyrins (**2**) prompted us to also try to establish a similar method for the preparation of 5,10-A_2-type porphyrins (**7**), which have remained rather elusive. Longo and Drach dinitrated porphine to yield 56% of a compound they speculated to be the 5,10-dinitro derivative,[12b] 5,10-bis[3,5-di(*tert*-butyl)phenyl]porphyrin has been prepared in small amounts (3% yield),[19a] and an N-confused 5,20-diphenylporphyrin has been described.[19b] The first rational synthesis was described in a recent report by Briñas and Brückner, who prepared 5,10-diphenylporphyrin (**17c**) in an elaborate synthesis involving the condensation of a substituted dipyrromethane dicarbinole (5 steps, 10–20% yield).[20]

Retrosynthetic analysis of **7** indicates that the simplest components for a condensation reaction would be a tripyrrane, a pyrrole, and two equivalents of aldehyde. So far unsubstituted tripyrrane has rarely been used;[19a,b] in most cases β-substituted tripyrranes were used for the preparation of porphyrins with both 5,10- and β substituents.[19c] We prepared tripyrrane **28** from pyrrole **27** and 2,5-bis(hydroxymethylpyrrole)[21a] by using a modified literature procedure.[21b] Reaction of tripyrrane **28** with pyrrole **27** under the conditions of a [3+1] condensation with trifluoroacetic acid (TFA) catalysis and benzaldehyde then gave the 5,10-diphenylporphyrin **17c** in a 6% yield (general procedure C in the Experimental Section). Variation of the aldehyde gave a variety of alkyl- (**15c**, **30c**, **31c**) or aryl-substituted (**17c**, **23c**, **29c**) A_2-type porphyrins **7** (**c** in Table 2) in yields of up to 11% (Scheme 2). Like the reaction shown in Scheme 1, scrambling occurred and resulted in the additional formation of the 5-monosubstituted porphyrins (**2**) as by-products (**a** in Table 2). Again, the yields are low but comparable to those of other condensation reactions.[2a] The mono- and disubstituted porphyrins are easily separated by column or flash chromatography and this method offers the first facile entry into the synthesis of this fundamental class of porphyrins.

Note that the reaction with pivalaldehyde gave solely the monosubstituted product **14a** in a 6% yield. This is most likely due to the steric bulk of the *tert*-butyl group. This group induces a high degree of ruffling in the porphyrin[11,22] and this effect is exacerbated if the steric strain is located in two neighboring quadrants of the macrocycle,[23] presumably leading to an instable intermediate.[24]

Table 2. Products and yields (% in relation to the aldehyde) for the condensation reaction B using **28**.

	R^1	 5-Mono- **a**	 5,10-Di- **c**
14		6	–
15		5	4
17		2	6
23		2	7
29		3	11
30		1	7
31		1	5

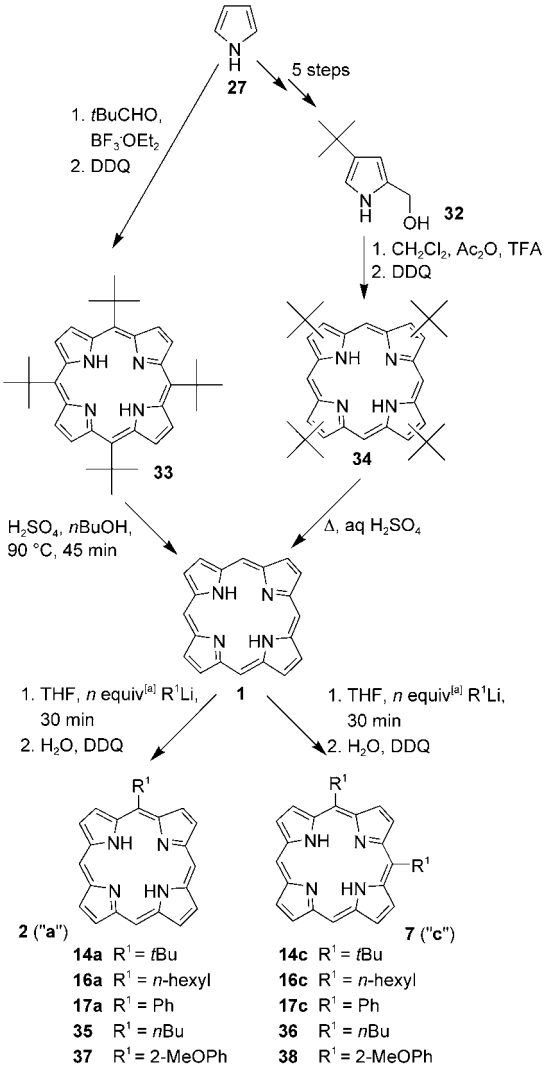


Scheme 2. Synthesis of 5,10-A_2-type porphyrins by condensation reactions (procedure C) using tripyrrane **28**.

Mono- and disubstitution of porphyrin by nucleophilic-substitution reactions: Although the described condensation reactions present a practical way of synthesizing 5- and 5,10-substituted porphyrins, reactions that proceed with conversion of ~90% of the starting material into a black, polymeric material are hardly satisfactory from an organic synthetic viewpoint. As stated in the introduction, *meso* substitution of porphyrins has been employed widely by us for the synthesis of various A_2B, A_2BC, or A_2B_2 porphyrins[8] and for ABCD-type derivatives of 2,3,7,8,12,13,17,18-octaethylporphyrin[8c] or tetrabenzoporphyrins.[8d] Thus, we reasoned that the direct transformation of unsubstituted porphine **1** should be possible, too. Until recently, such reactions were not possible due to the limited accessibility of this compound.[25]

A novel concept for the preparation of porphine **1** would be the acid-catalyzed thermal dealkylation of a suitable precursor porphyrin, akin to the classical reactions of *tert*-butyl-substituted benzenes.[26] Thus appropriate starting compounds would be either *meso*- or β-*tert*-butyl-substituted

porphyrins. During the course of our studies on the dealkylation of either **33** or **34**, Neya and Funasaki[27] showed that this is indeed possible and published a simple procedure for the de-*tert*-butylation of the easily accessible 5,10,15,20-tetra(*tert*-butyl)porphyrin (**33**)[22] that gives the target compound in high yield and good purity (Scheme 3).[27b] Similarly, β-*tert*-butylporphyrins can also be used for dealkylation although the steric strain in these molecules is smaller.[28a] For example, 2-*tert*-butyl-4-hydroxymethylpyrrole (**32**)[28b] or 2-dimethylaminomethyl-4-*tert*-butylpyrrole[28c] can be converted into a regioisomeric mixture of β-tetra(*tert*-butyl)porphyrins (**34**)[28d,e] and dealkylated in aqueous H_2SO_4.[28c,f]



Scheme 3. Synthesis of A-type or 5,10-A_2-type porphyrins by substitution of porphine (procedure D). [a] See text.

Having the desired porphine **1** in hand, we reacted it first with butyllithium under the standard reaction conditions used by us previously for other porphyrins (general procedure D in the Experimental Section).[8,9b] Treatment of **1** with three equivalents of *n*BuLi in THF at −70 °C followed by brief stirring at room temperature gave the 5,10-dibutylated porphyrin (**36**) in a quantitative yield. Analogous reactions with either hexyl- or phenyllithium required 6 equivalents to yield the disubstituted porphyrins **16c** and **17c** in 61 and 43 % yields, respectively. Similar to the observation made during condensation studies, the di-*tert*-butylated porphyrin **14c** could not be prepared by substitution reactions. Irrespective of the number of *t*BuLi equivalents used, the monosubstituted porphyrin **14a** was obtained as the sole product in low yield (4 %).

It became clear quickly that for unencumbered tetrapyrroles such as porphine **1** both mono- and disubstitution can occur.[8b] Thus, simple variation of the number of equivalents of the organolithium reagent used allows the facile preparation of either 5-mono- or 5,10-disubstituted porphyrins.[29] Indeed, reaction of **1** with 1.2–1.5 equivalents of RLi gave, for example, **16a** and **35** in yields of 48 % each. For the less reactive PhLi, 3 equivalents were necessary to obtain **17a** in a 17 % yield. Similarly, **37** could be prepared in a 17 % yield. This was the least reactive reagent as eight equivalents of in situ generated 2-methoxyphenyllithium (2-MeOPhLi) were required for monosubstitution. Further increases in the number of equivalents resulted in lower yields of **37** without any detectable formation of the 5,10-disubstituted porphyrin **38**.[30] In all of these cases either the mono- or disubstituted porphyrins were the sole product detected under the reaction conditions given. However, the latter reactions indicate that for less reactive RLi reagents a compromise has to be found between the necessity to use more equivalents and the need to prevent formation of the disubstituted product. For example, reaction of porphine **1** with 2 equivalents of PhLi gave no reaction at all, 3 equivalents gave 17 % of **17a**, 4 equivalents gave 25 % of **17a** and 20 % of **17b**, while 6 equivalents gave 43 % of **17b**. Alkyllithium reagents typically give much higher yields with the respective nickel(II) porphyrins.[8a] Thus, as long as nickel(II) can be tolerated in the context of the synthetic project, further improvements of the yields are possible.

Spectroscopic studies: The method just described offers a simple way to prepare the elusive 5,10-disubstituted porphyrins in good to excellent yields from an easily accessible symmetric porphyrin. Likewise, *meso*-monosubstituted porphyrins (**2**) can now be prepared in acceptable yields. Together with the known 5,15-A_2-, A_3-, and A_4-type porphyrins this finally offers the possibility to investigate the consequences of different numbers and regiochemical arrangements of individual *meso* substituents on the spectroscopic and structural properties of porphyrins.

Absorption spectra: One complete fundamental series of porphyrins that can now be studied is that of *meso*-phenyl-substituted porphyrins, thus closing the gap between unsubstituted porphine and the well-known tetraphenylporphyrin. The main absorption bands are gradually shifted bathochromically with increasing number of phenyl residues (Table 3). For example, **17a** exhibits the Soret band at 403 nm, the disubstituted porphyrins **17b** and **17c** at 406 nm,

Table 3. UV/Vis absorption spectra for *meso*-phenyl-substituted porphyrins in CH_2Cl_2.

	λ [nm]	
	Soret band	Q bands
5-phenylporphyrin (**17a**)	403	495, 526, 568, 622
5,15-diphenylporphyrin (**17b**)[32a]	406	502, 536, 574, 630
5,10-diphenylporphyrin (**17c**)	406	504, 534, 579, 630
5,10,15-triphenylporphyrin[9b]	412	508, 543, 584, 638
5,10,15,20-tetraphenylporphyrin[32b]	418	515, 549, 590, 645

while 5,10,15-triphenylporphyrin and 5,10,15,20-tetraphenylporphyrin have the strongest absorbing bands at 412 and 418 nm, respectively. Similar trends were observed for the Q bands and porphyrins with other substituents (not shown). Changes in absorption spectra can either be due to electronic or steric effects.[33] The present incremental redshift of both the Soret and Q bands in the series of phenylporphyrins appears to be mainly due to electronic effects. If steric effects were a main contributor, then the 5,15- and 5,10-disubstituted derivatives would differ in their spectra, the latter being potentially more distorted. This reasoning is born out by the fact that all 5,10- and 5,15-derivatives of porphyrins with linear alkyl chains described here have very similar absorption spectra with the main maxima around 406 and 634 nm. Steric effects become apparent only when inspecting derivatives with more bulky *meso* substituents.[22b] For example, on going from the mono-*n*-butyl derivative **35** to the 5,10-di(*n*-butyl) derivative **36** a shift from 399/621 to 406/633 nm occurs, while the relevant data for the *iso*-butyl derivatives **31a** and **31c** are 399/621 and 403/635 nm, respectively. For the 2-ethylpropyl derivatives with a -C(H)R_2 group in the *ipso* position a much larger shift from 399/621 (**15a**) to 412/644 nm (**15c**) occurs. Thus, electronic absorption spectroscopy is a simple means of determining the number of *meso* substituents present in a given series of *meso*-substituted porphyrins but not their regiochemical arrangement.

^{1}H NMR spectra: The regiochemical arrangement and substitution pattern is easily derived from the NMR spectra. Primarily, the ^{1}H signals of porphyrins depend on the distance and orientation of the protons with respect to the π electrons of the macrocyclic ring system with protons above or inside the ring being shielded and those outside the ring being deshielded.[34a] Due to this, the main ^{1}H signal groups are easily distinguished ($\delta H_\beta \sim 8$–9, $\delta H_{meso} \sim 10$, $\delta N{-}H < 0$ ppm). Due to the limited accessibility of the various A_n-type porphyrins, detailed NMR investigations on the influence of various substituents relied on the use of symmetric macrocycles such as tetraarylporphyrins.[34b] As discussed for the absorption spectra, the present syntheses now allow a comparative analysis of the NMR spectra of the changes occurring as a result of different numbers and regiochemical arrangements of *meso* substituents. If we consider the five *meso*-3-methoxyphenyl-substituted porphyrins (**23a**, **23b**, **23c**, 5,10,15-tris(3-methoxyphenyl)porphyrin, and 5,10,15,20-tetrakis(3-methoxyphenyl)porphyrin) the changes in symmetry[34b,c] are clearly reflected in the ^{1}H NMR spectra (Figure 2).

Porphyrins with four equal substituents such as 5,10,15,20-tetrakis(3-methoxyphenyl)porphyrin (D_4 symmetry) exhibit

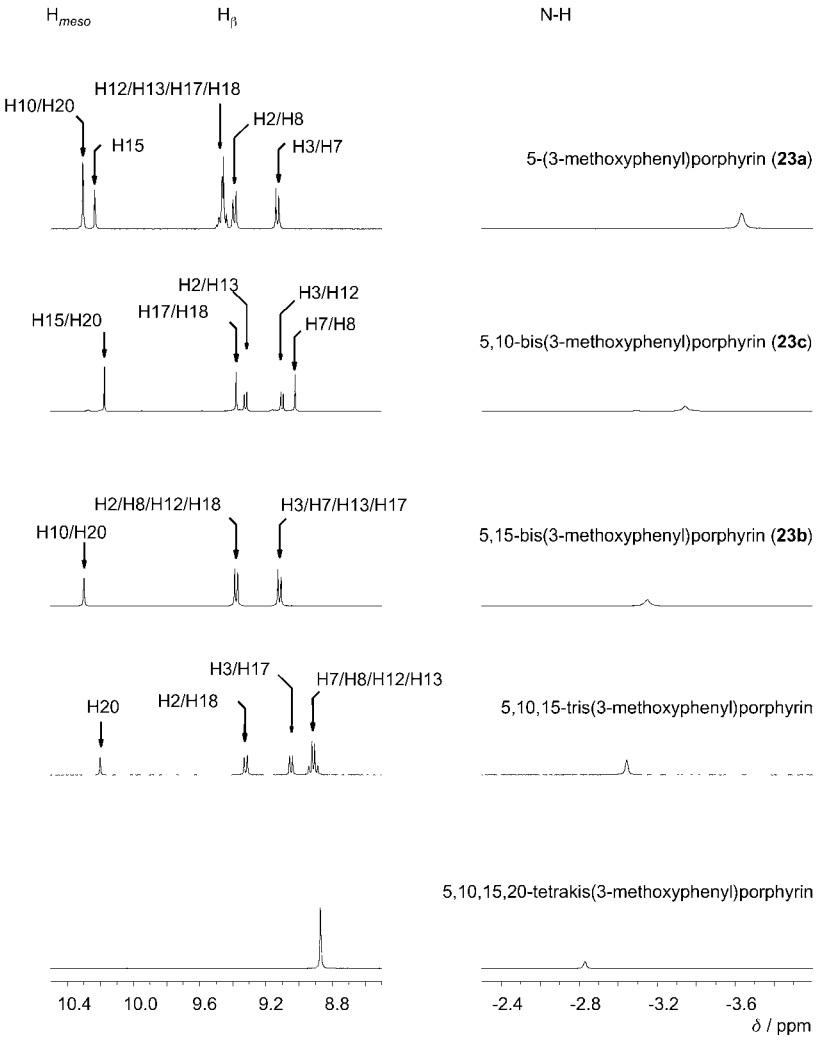


Figure 2. ^{1}H NMR spectra of *meso*-3-methoxyphenyl-substituted porphyrins in $CDCl_3$ at room temperature.

only one signal for the β protons at 8.87 ppm. The 5,15-disubstituted porphyrin **23b** (D_2 symmetry) shows two AB systems for the non-equivalent protons at 9.11 (H3/H7H13/H17) and 9.38 ppm (H2/H8H12/H18), respectively, and the two *meso* protons exhibit a singlet at 10.31 ppm. The 5,10,15-tris(3-methoxyphenyl)porphyrin, 5,10-bis(3-methoxyphenyl)porphyrin, and 5-(3-methoxyphenyl)porphyrin (C_2 symmetry) show characteristic splitting of the pyrrole protons along the C_2 axis. The triarylated porphyrin exhibits splitting of the AB signal for H2/H18 at 9.32 ppm and H3/H17 at 9.05 ppm. Due to the relative similarity in chemical environment of protons H7, H8, H12, and H13 they give a multiplet at 8.91 ppm, while a singlet at 10.20 ppm identifies the *meso* proton. The spectrum of **23c** exhibits two flanking singlets for H17/H18 at 9.38 ppm and H7/H8 at 9.02 ppm and two AB signals for H2/H13 at 9.32 ppm and H3/H12 at 9.10 ppm, while the two *meso* protons give a singlet at 10.17 ppm. The pattern of the β-pyrrole protons of the monoarylated porphyrin (**23a**) looks like a mirror image of that of the triarylated porphyrin. The pattern for **23a** is characterized by a multiplet for H12/H13/H17/H18 at 9.46 ppm and two AB signals at 9.39 and 9.13 ppm for H2/H8 and H3/H7, respectively, while the two *meso* protons (H10/H20) give a singlet at 10.31 ppm and H15 at 10.24 ppm. Depending on the degree of substitution, the N–H signals undergo low-field shifts with increasing number of *meso*-aryl residues. Similar spectral habits were found for a series of porphyrins with *meso*-2-methoxyphenyl, -phenyl, and -tolyl residues (not shown). Thus, the ^{1}H NMR spectra allow a simple and rapid identification of the number and arrangement of aryl substituents in the series of *meso*-substituted porphyrins.

The high-field shift of the β protons H3 and H7 in 5-aryl-substituted porphyrins with respect to other β protons results from the ring-current effect of the adjacent phenyl ring. An example for 5-aryl-substituted porphyrins can be demonstrated with 5-phenylporphyrin (Figure 3). A value of 64.8° was calculated for the torsion angle between the phenyl and porphyrin planes in the geometry optimized structure of this model compound. The ring-current effect of benzene was calculated elsewhere[35] and applied to 5-phenylporphyrin. The shaded area in Figure 3 gives the iso-chemical-shift surface (ICSS)[35] and represents a shielding of 0.4 ppm. H3 and H7 are located in this shielding region above and below the phenyl plane.

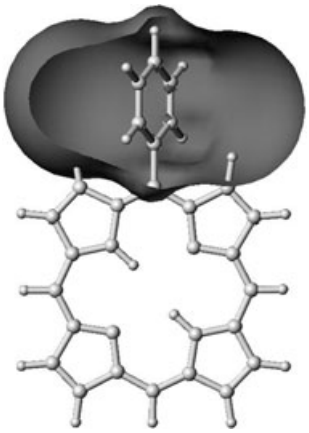


Figure 3. Iso-chemical-shift surface for the phenyl ring in 5-phenylporphyrin.

Likewise, porphyrins with alkyl substituents show a clear-cut dependence of the spectral composition on the symmetry of the porphyrin. For example, the series of hexylporphyrins shown in Figure 4 exhibits a similar shift of the NH proton signals from −2.67 (5,10,15,20-tetra(*n*-hexyl)porphyrin) to −3.56 ppm (**16a**). Considering the β protons of 5,10,15-tri(*n*-hexyl)porphyrin, the signals for H2/H18, H3/H17, H7/H13, and H8/H12 show a splitting in four AB systems at 9.23, 9.43, 9.47, and 9.53 ppm. The splitting of signals in the low-field region differs for **16c** and **16a** compared with aryl-substituted porphyrins. The chemical shift of the pyrrole protons (H7/H8) of **16c** does not differ enough from that of H3/H12. This results in a multiplet at 9.56 ppm by the overlap of a singlet and an AB signal. The pyrrole protons H2/H13/H17/H18 show similar behavior and give a multiplet at 9.29 ppm. For **16a**, an AB signal is found for H3/H7 at 9.63 ppm, an AB signal at 9.44 ppm for H2/H8, an AB signal for H12/H18 at 9.42 ppm, and an AB signal for H13/H17 at 9.38 ppm. For **16b**, two AB signals at 9.49 (H3/H7/H13/H17) and 9.33 ppm (H2/H8/H12/H18) are observed.

Structural studies: An ongoing focus in porphyrin chemistry is the inter-relationship between steric effects imposed by substituents and the physiochemical and biological properties of tetrapyrroles.[8c, 11, 22, 23, 33b] Most of the several hundred papers in this area[23a] have focused on symmetric porphyrins or on unsymmetric porphyrins carrying several types of substituents.[36] Only one study has addressed the question of the structural and conformational influence of the *tert*-butyl substituent on the porphyrin macrocycle of the nickel(II) complexes of **14a** and **14b**.[11] While being a landmark study, studying metal complexes has the inherent problem of measuring the influence of the central metal ion and the substituent effect at the same time. For example, nickel(II) induces a core contraction of the porphyrin resulting in ruffling (*ruf*) distortions.[37] The syntheses reported here will now allow detailed and comparative analyses of individual substituent types and arrangements on the macrocycle. As an initial result of these forthcoming studies we report here on the crystal structure of the free base 5-*tert*-butylporphyrin (**14a**; Figure 5). Visual inspection of the crystal structure reveals a "folded" macrocycle conformation with a localized influence of the *tert*-butyl substituents, clearly the deformation is more pronounced in the two quadrants involving the substituent than in the other quadrants. For example, the tilt angles of individual pyrrole rings against the 24-atom plane are 11.7, 14.3, 4.0, and 5.3° for pyrrole rings with N21, N22, N23, and N24, respectively. The compound crystallizes in the non-centrosymmetric space group $P2_12_12_1$ (no. 19) and the asymmetric nature of the conformation is especially evident when looking at the skeletal deviations given in Fig-

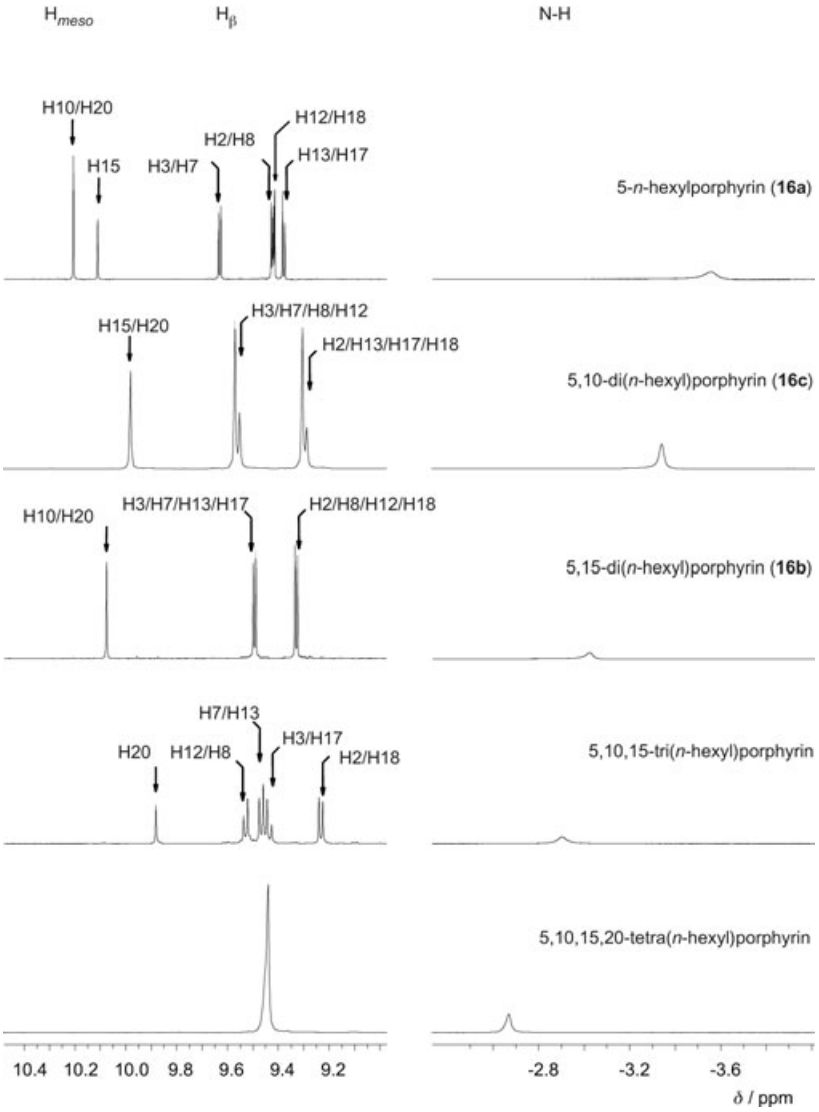


Figure 4. ^{1}H NMR spectra of *meso*-hexyl-substituted porphyrins in $CDCl_3$ at room temperature.

ure 5b. The *tert*-butyl group induces a local *ruf* distortion and the overall degree of nonplanarity is moderate, as evidenced by a deviation of 0.14 Å of the 24 macrocycle atoms from their least-squares plane. The crystal structure also provides evidence for some degree of in-plane distortion; the core elongation parameter (Ξ)[23a] is 0.25 Å.

A normal-coordinate structural decomposition analysis as developed by Shelnutt and co-workers[38] gives further details of the mix of distortion modes present in this porphyrin. This method classifies the distortions in terms of equivalent displacements along the normal coordinates. As shown in Figure 6, the main contributors to the out-of-plane distortions are *ruf* (B_{1u}), doming (A_{2u}), waving(x) (*wav*; E_{gx}), wav(y) (E_{gy}), and a minor contribution of saddling (B_{2u}) distortion. For the in-plane distortions the main contributor is *meso* stretching (*m-str*; B_{2g}). A comparison with the nickel complex[11] reveals significant differences. While minor differences in the observation and degree of *ruf* and *wav* deformations can be due to crystal packing effects, the nickel complex shows a significantly larger degree of *ruf* distortion (1.999 Å for B_{1u}) than the free base (0.678 Å for B_{1u}) and the degree of doming is larger in the latter (0.3086 Å for A_{2u} compared with 0.135 Å). For the in-plane distortions *m-str* is larger in the free base (−0.3756 Å vs −0.09 Å for B_{2g}) while the breathing contribution is smaller (0.081 Å vs −0.554 Å). Thus, the central metal exerts a significant influence on the overall conformation and the mix of individual distortion modes and so masks the steric influence of the individual *meso* substituents.

Conclusion

In conclusion, we have developed simple and straightforward methods that provide the first systematic access to synthesizing *meso*-monosubstituted and *meso*-5,10-disubstituted porphyrins *without* β substituents. For both types of porphyrins a condensation and a substitution method have been developed. It is most likely that the former methods will be more widely used, as they tolerate various aldehydes and the starting materials are easily available; nevertheless, yields are low and chromatographic separation of the byproducts is required. The substitution methods give the porphyrins in good to excellent yields but only a few organolithium compounds are commercially available requiring a more involved experimental setup. Both methods now allow a rational synthesis of the various porphyrins of the "alphabet soup" by stepwise introduction of additional *meso* substituents. For example, 5,10-AB-type porphrins (**3**) with electron-withdrawing and -releasing groups or related A_2B_2-type porphyrins would make a new approach available for the known push–pull porphyrins which can be used for nonlinear optics. Until now most push–pull porphyrins were based on 5,15-diphenylporphyrin (**17b**) with nitrophenyl "versus" aminophenyl, formyl, cyano groups, or covalently linked multiporphyrin arrays.[39a] Likewise, the now accessible 5,10-disubstitution pattern presents a convenient building block introducing an orthogonal (90°) substituent orientation.

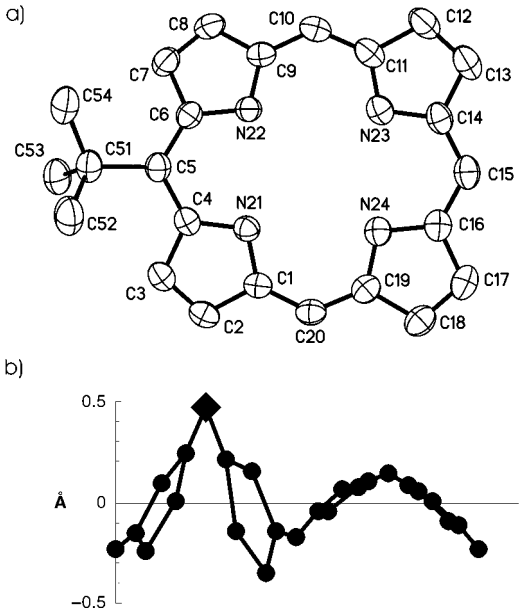


Figure 5. a) View of the molecular structure of **14a** in the crystal. Hydrogen atoms have been omitted for clarity; thermal ellipsoids give 50% occupancy. b) Skeletal deviation plot with respect to the plane of the 24 macrocycle atoms; ◆ denotes the *tert*-butyl-substituted *meso* carbon; *x* axis not to scale; sequence of pyrrole rings follows the IUPAC nomenclature from left to right (N21, N22, N23, N24).

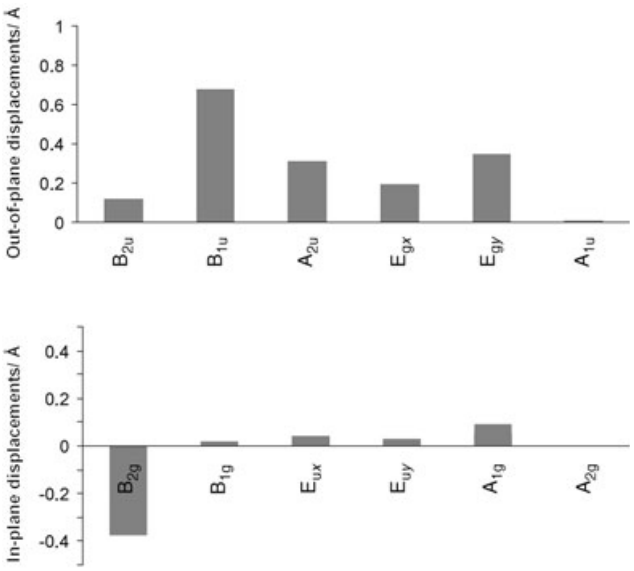


Figure 6. Graphical representation of the out-of-plane (above) and in-plane (below) displacements along the lowest-frequency coordinates that best simulate structure **14a**.

With appropriate functional groups this will be a valuable synthon in crystal engineering, supramolecular chemistry, or dynamic combinatorial libraries for which a "right angle" (↑→) orientation is required. Similarly, the 5-monosubstituted porphyrins can be considered a monodirectional synthon (↑). Additionally, they are important reference compounds for various applications.[39b,40] These two classes of *meso*-substituted porphyrin close the gap between porphyrin (porphine) and the well-studied 5,15-A_2- and A_4-type porphyrins. This has allowed initial studies on the systematic influence of the substituent pattern on the spectroscopic and physicochemical properties, as exemplified here with investigations of the UV-visible and ^{1}H NMR spectra. More detailed crystallographic investigations will be forthcoming once a complete series of structurally related porphyrins has been crystallized.

Experimental Section

General methods: All chemicals were of analytical grade and purified before use. Dichloromethane was dried over phosphorous pentoxide followed by distillation; THF was dried over sodium followed by distillation. The preparation of dipyrromethane (**13**),[41] 2-hydroxymethylpyrrole (**12**),[18a] tripyrrane (**28**),[21b] tetra(β-*tert*-butyl)porphyrin (**34**),[28d] and porphine (**1**)[27a] followed published procedures. All condensation reactions were performed under an argon atmosphere with the reaction flask shielded from ambient light. Silica gel 60 (Merck) was used for column chromatography. Analytical thin-layer chromatography (TLC) was carried out using silica gel 60 plates (fluorescence indicator F_{254}; Merck). Melting points are uncorrected and were measured with a Reichert Thermovar instrument. NMR spectra were recorded at frequencies of 250 (Bruker AM 270 instrument), 270 (Bruker AM 270 instrument), or 500 MHz (Bruker AMX 500). Chemical shifts are given in ppm and referenced to the TMS signal as internal standard. The assignment of the signals was confirmed by 2D spectra (COSY, HMBC, HMQC) except for those porphyrins with low solubility. See Figure 7 for the atom numbering and assignments used in the description of the NMR data. Electronic absorption spectra were recorded with a Specord S10 instrument (Zeiss) using CH_2Cl_2 as solvent. Mass spectra were recorded using a Varian MAT 711 or MAT 112 S mass spectrometer using the EI technique with a direct insertion probe and an excitation energy of 80 eV. FAB spectra were recorded with a CH-5 DF instrument from Varian. Elemental analyses were performed with a Perkin–Elmer 240 analyzer. Preparative HPLC was performed with columns (23×15 and 23×30 mm) filled with silica gel (Merck, Nucleosil 50, 5 μ) using a Knauer pump (Knauer MPLC Pump and Knauer HPLC Pump 64). The solvent flow rate was 64 mL min^{-1} (P=23 bar=23×10^5 Pa). UV detection (Knauer Variable Wavelength Monitor) was performed at 420 nm for the porphyrins. Analytical HPLC was performed using a Spectra Physics pump (SP 8810) and an analytical column (4×250 mm) filled with silica gel (Merck, Nucleosil 50, 5 μ). The solvent flow rate was 1 mL min^{-1}, with UV/Vis detection at 420 nm for the porphyrins. All yields are given with respect to the aldehyde used in the reactions.

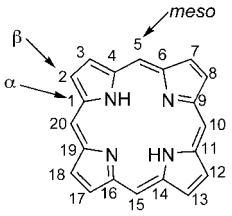


Figure 7. Porphyrin numbering and nomenclature used in the NMR assignments.

Calculations: The ab initio calculations were performed on SGI Origin 200 workstations using GAUSSIAN 98.[42] Geometry optimization was carried out using B3LYP[43]/6-31G** without constraints. The iso-

chemical-shift surface (ICSS) was calculated with the GIAO method[44] on the HF[45] theory level using the 6-31G* basis set.

2-Hydroxymethylpyrrole (12):[46] A three-necked flask (1 L) equipped with magnetic stirrer and bubble counter was charged with pyrrole-2-carbaldehyde (**11**: 10 g, 105 mmol) dissolved in THF (250 mL). Sodium borohydride was added (4 g, 106 mmol) resulting in warming of the reaction flask and gas evolution. The mixture was stirred for 1.5–2 h until the reaction was complete (TLC control, *n*-hexane/ethyl acetate 1:1) and then treated with water (250 mL). After the $NaBH_4$ in suspension was completely dissolved, the mixture was extracted with dichloromethane (4× 150 mL). The combined organic extracts were washed with water and dried over Na_2SO_4. The slightly milky solution should turn clear at this step. Triethylamine (ca. half-filled glass pipette) was added and the solution was concentrated with a rotary evaporator to yield a light-yellow oil. Again 1–2 drops of triethylamine were added. Final purification was achieved by round-flask distillation (5 mbar, 90 °C). The final product is a colorless, clear solution and *requires storage in the refrigerator*, otherwise polymerization occurs. Yield: 80–100 % (8.2–10.2 g, 7.2–9 mL).

General procedure A

Condensation method for A-type porphyrins using pyrrole-2-carbaldehyde: Dipyrromethane (**13**: 290 mg, 2.00 mmol), pyrrole-2-carbaldehyde (**11**: 380 mg, 4.00 mmol), and the corresponding aldehyde (2.00 mmol) were dissolved in dry dichloromethane (1 L) under argon. To this solution, TFA (70 μL, 0.9 mmol) was added, the reaction flask shielded from ambient light, and the mixture was stirred for 16 h in the dark. After this time, dichlorodicyanobenzoquinone (DDQ: 1.30 g, 5.73 mmol) suspended in CH_2Cl_2 (50 mL) was added and the mixture was stirred for another hour. The reaction was terminated by addition of triethylamine (1 mL), and concentrated in vacuo. Typically, the reaction mixture was concentrated to about 50 mL and filtered through a short silica-gel column, eluting with dichloromethane. The solution was concentrated in vacuo and the residue purified by column chromatography on silica gel.

General procedure B

Condensation method for A-type porphyrins using 2-hydroxymethylpyrrole: Dipyrromethane (**13**: 290 mg, 2.00 mmol), 2-hydroxymethylpyrrole (**12**: 349 μL, 4.00 mmol), and the corresponding aldehyde (2.00 mmol) were used. Further reaction conditions and workup are as described above for procedure A.

General procedure C

Condensation method for 5,10-A_2-type porphyrins: A three-necked flask was charged with a solution of tripyrrane (**28**: 0.46 g, 2.06 mmol), pyrrole (**27**: 0.14 mL, 2.06 mmol), and the corresponding aldehyde (4.12 mmol) in dry dichloromethane (1 L). The mixture was shielded from light and stirred under argon for 30 min. TFA (100 μL) was added and stirring was continued at RT for 16 h. This was followed by oxidation with DDQ (1.80 g, 7.93 mmol), stirring for 60 min, addition of triethylamine (1 mL), and concentration of the solution in vacuo.

General procedure D

S_NAr reaction method for A-type or 5,10-A_2-type porphyrins: A Schlenk flask was charged with porphine (20 mg, 0.06 mmol) dissolved in dry THF (30 mL) under an argon atmosphere. The solution was cooled to −70 °C for the alkyllithium or to 0 °C for the aryllithium reactions. After dropwise addition of the lithium reagent (for number of equivalents see individual procedures) over 15 min, the mixture was stirred for 30 min at RT. A mixture of THF/H_2O (5:1) was added and stirring continued for 15 min. For oxidation, 3.5 mL of a 0.1 M solution of DDQ in THF was added and the mixture was stirred for another 30 min. After filtration through a short silica-gel column, eluting with dichloromethane, the solution was concentrated in vacuo, and the residue purified by column chromatography on silica gel.

5-*tert*-Butylporphyrin (14a)[47]

Procedure A: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 2:1). After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (51 mg, 0.14 mmol, 7 %).

Procedure C: Reaction followed by standard workup yielded the title compound (45 mg, 0.12 mmol, 6 %).

Procedure D: A solution of *tert*-butyllithium (1.5 M, 0.06 mL, 0.09 mmol) in pentane was used for the reaction with porphine **1** yielding 1 mg of product (27 μmol, 4 %) after chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1).

R_f = 0.40 (CH_2Cl_2/*n*-hexane 2:1); m.p. 235 °C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.09 (s, 2H; 5,20-H_{meso}), 10.01 (s, 1H; 15-H_{meso}), 9.90 (AB, ^3J(H,H) = 5 Hz, 2H; 3,7-H_β), 9.33 (AB, ^3J(H,H) = 4 Hz, 2H; 12,18-H_β), 9.31 (AB, ^3J(H,H) = 4 Hz, 2H; 13,17-H_β), 9.23 (AB, ^3J(H,H) = 5 Hz, 2H; 2,8-H_β), 2.60 (s, 9H; CH_3), −2.69 ppm (br s, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 147.43, 146.63, 144.37, 142.52, 131.47, 130.70, 130.36, 130.28, 127.62, 104.33, 103.21, 41.14, 40.57 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 401 (5.15), 502 (3.96), 536 (3.51), 577 (3.53), 625 nm (2.78); MS (80 eV, EI, 350 °C): *m*/*z* (%): 366 (100) [M^+], 351 (94) [M^+-CH_3], 336 (10) [$M^+-C_2H_6$], 310 (32) [$C_{20}H_{14}N_4^+$], 183 (12) [M^{2+}], 175 (9) [$M^{2+}-CH_3$], 168 (8) [$M^{2+}-C_2H_6$], 155 (6) [$C_{20}H_{14}N_4^{2+}$]; HRMS: *m*/*z* calcd for $C_{24}H_{22}N_4$: 366.18445; found: 366.18634.

5-(1-Ethylpropyl)porphyrin (15a)

Procedure A: The crude reaction mixture was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). The first fraction contained the disubstituted porphyrin **15b** and the second fraction the monosubstituted porphyrin **15a**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (85 mg, 0.22 mmol, 11 %). Use of 2-ethylbutanal (1 mmol, 0.14 mL) in procedure A followed by standard workup gave 129 mg (0.34 mmol, 17 %) of the title compound **15a**, and compound **15b** as byproduct.

Procedure C: Yield 39 mg (5 %, 0.10 mmol); R_f = 0.45 (CH_2Cl_2/*n*-hexane 2:1); m.p. 281 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.27 (s, 2H; 10,20-H_{meso}), 10.11 (s, 1H; 15-H_{meso}), 9.84, 9.77 (AB, ^3J(H,H) = 4 Hz, 2H; 3,7-H_β), 9.44 (AB, ^3J(H,H) = 4 Hz, 4H; 2,8,12,18-H_β), 9.39 (AB, ^3J(H,H) = 4 Hz, 2H; 13,17-H_β), 5.14 (m, 1H; CH), 3.00, 2.84 (m, 4H; CH_2), 0.95 (t, ^3J(H,H) = 7 Hz, 6H; CH_3), −3.27, −3.48 ppm (each br s, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 148.72, 146.00, 146.88, 145.07, 144.76, 144.40, 142.98, 131.79, 131.55, 131.39, 130.67, 130.40, 129.04, 128.63, 123.42, 104.23, 103.90, 102.50, 50.06, 34.63, 13.83 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 399 (5.32), 497 (3.89), 526 (3.35), 569 (3.71), 621 nm (2.58); MS (80 eV, EI, 350 °C): *m*/*z* (%): 380 (79) [M^+], 352 (27) [$M^+-C_2H_4$], 351 (100) [$M^+-C_2H_5$], 350 (4) [$M^+-C_2H_6$], 336 (10) [$M^+-C_3H_8$], 335 (15) [$M^+-C_3H_9$], 324 (6) [$M^+-C_4H_8$], 190 (9) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{25}H_{24}N_4$: 380.20010; found: 380.20355.

5,15-Bis(1-ethylpropyl)porphyrin (15b)

Procedure A: Obtained during the synthesis of **15a**. After recrystallization from CH_2Cl_2/MeOH, the porphyrin was obtained as purple crystals (33 mg, 0.07 mmol, 7 %). Reaction using 2-ethylbutanal (1 mmol, 0.14 mL) and workup were as described above to yield the title compound (18 mg, 0.04 mmol, 4 %). R_f = 0.60 (CH_2Cl_2/*n*-hexane 1:1); m.p. > 330 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.21 (s, 2H; 10,20-H_{meso}), 9.68 (m, 4H; 3,7,13,17-H_β), 9.40 (m, 4H; 2, 8,12,18-H_β), 5.02 (m, 2H; CH), 2.96, 2.81 (m, 8H; CH_2), 0.93 (t, ^3J(H,H) = 7 Hz, 12H; CH_3), −2.46 ppm (br s, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25 °C): δ = 131.9, 128.6, 121.8, 104.3, 49.8, 34.6, 14.1 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 403 (4.81), 504 (3.98), 535 (3.40), 575 (3.48), 630 nm (2.97); MS (80 eV, EI): *m*/*z* (%): 450 (100) [M^+], 422 (31) [$M^+-C_2H_4$], 421 (99) [$M^+-C_2H_5$], 392 (5) [$M^+-2C_2H_5$], 377 (21) [$M^+-2C_2H_5-CH_3$], 225 (6) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{30}H_{34}N_4$: 450.27835; found: 450.27466.

5,10-Bis(1-ethylpropyl)porphyrin (15c)

Procedure C: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:3). The first fraction contained the disubstituted porphyrin **15c** and the second fraction the monosubstituted porphyrin **15a**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (40 mg, 0.09 mmol, 4 %). R_f = 0.68 (CH_2Cl_2/*n*-hexane 2:1); m.p. 254 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ = 9.98 (s, 2H; 15,20-H_{meso}), 9.55 (m, 4H; 3,7,8,12-H_β), 9.29 (m, 4H; 2,13,17,18-H_β), 4.99 (t, ^3J(H,H) = 8 Hz, 4H; $CH_2(CH_2)_4CH_3$), 2.55 (m, 4H; $CH_2CH_2(CH_2)_3CH_3$), 1.83 (m, 4H; $(CH_2)_2CH_2(CH_2)_2CH_3$), 1.53 (m,

4H; $(CH_2)_3CH_2CH_2CH_3$), 1.43 (m, 4H; $(CH_2)_4CH_2CH_3$), 0.96 (t, ^3J(H,H) = 7 Hz, 3H; $(CH_2)_5CH_3$), −3.37 ppm (brs, 2H; NH). ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 130.00, 103.00, 50.82, 35.00, 14.29 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 412 (5.08), 511 (4.00), 543 (3.52), 589 (3.49), 644 nm (3.29); MS (80 eV, EI): *m/z* (%): 450 (100) [M^+]; HRMS: *m/z* calcd for $C_{30}H_{34}N_4$: 450.27847; found: 450.27900.

5-*n*-Hexylporphyrin (16a)

Procedure A: The porphyrins were purified by using column chromatography on silica gel with *n*-hexane/ethyl acetate (5:1) as eluent. The first fraction contained the disubstituted porphyrin **16b** and the second fraction the monosubstituted porphyrin **16a**. After recrystallization from CH_2Cl_2/CH_3OH the title porphyrin was obtained as purple crystals (15 mg, 0.04 mmol, 2%).

Procedure D: A solution of 2.5 M *n*-hexyllithium in hexane (0.04 mL, 0.09 mmol) was added to the solution of porphyrin **1**. After purification by using column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1), porphyrin **16a** was obtained (13 mg, 0.03 mmol, 48%). R_f = 0.39 (*n*-hexane/ethyl acetate 5:1); m.p. 275 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.21 (s, 2H; 10,20-H$_{meso}$), 10.11 (s, 1H; 15-H$_{meso}$), 9.63 (AB, ^3J(H,H) = 5 Hz, 2H; 3,7-H$_\beta$), 9.44 (AB, ^3J(H,H) = 5 Hz, 2H; 2,8-H$_\beta$), 9.42 (AB, ^3J(H,H) = 5 Hz, 2H; 12,18-H$_\beta$), 9.38 (AB, ^3J(H,H) = 4 Hz, 2H; 13,17-H$_\beta$), 5.06 (t, ^3J(H,H) = 6 Hz, 2H; $CH_2(CH_2)_4CH_3$), 2.56 (m, 2H; $CH_2CH_2(CH_2)_3CH_3$), 1.82 (m, 2H; $CH_2CH_2CH_2(CH_2)_2CH_3$), 1.52 (m, 2H; $(CH_2)_3CH_2CH_2CH_3$), 1.40 (m, 2H; $(CH_2)_4CH_2CH_3$), 0.94 (t, ^3J(H,H) = 7 Hz, 3H; $(CH_2)_5CH_3$), −3.56 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = ~147, ~145, 131.77, 131.56, 130.77, 128.24, 120.18, 104.15, 102.73, 38.91, 35.16, 31.92, 30.30, 22.74, 14.14 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 401 (5.52), 496 (4.18), 525 (3.26), 570 (3.66), 622 nm (2.43); MS (70 eV, EI): *m/z* (%): 394 (24) [M^+], 365 (<1) [$M^+-C_2H_5$], 351 (<1) [$M^+-C_3H_7$], 337 (3) [$M^+-C_4H_9$], 323 (100) [$M^+-C_5H_{11}$], 197 (2) [M^{2+}], 162 (7) [(M−C_2H_5)$^{2+}$]; HRMS: *m/z* calcd for $C_{26}H_{26}N_4$: 394.2157; found: 394.2150.

5,15-Di(*n*-hexyl)porphyrin (16b)

Procedure A: Obtained during the synthesis of **16a**. After recrystallization from CH_2Cl_2/CH_3OH the title porphyrin was obtained as purple crystals (74 mg, 0.16 mmol, 15%). R_f = 0.55 (*n*-hexane/ethyl acetate 5:1); m.p. 133 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.08 (s, 2H; 10,20-H$_{meso}$), 9.49 (AB, ^3J(H,H) = 5 Hz, 4H; 3,7,13,17-H$_\beta$), 9.33 (AB, ^3J(H,H) = 5 Hz, 4H; 2,8,12,18-H$_\beta$), 4.92 (t, ^3J(H,H) = 8 Hz, 4H; $CH_2(CH_2)_4CH_3$), 2.53 (m, 4H; $CH_2CH_2(CH_2)_3CH_3$), 1.80 (m, 4H; $CH_2CH_2CH_2(CH_2)_2CH_3$), 1.53 (m, 4H; $(CH_2)_3CH_2CH_2CH_3$), 1.42 (m, 4H; $(CH_2)_4CH_2CH_3$), 0.97 (t, ^3J(H,H) = 7 Hz, 6H; $(CH_2)_5CH_3$), −3.03 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25 °C): δ = 147.35, 147.08, 131.73, 127.65, 118.70, 104.13, 38.56, 34.55, 31.91, 30.22, 22.73, 14.14 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = −405 (5.42), 504 (4.09), 535 (3.48), 578 (3.57), 633 nm (3.09); MS (80 eV, EI): *m/z* (%): 478 (100) [M^+], 407 (53) [$M^+-C_5H_{11}$], 336 (9) [$M^+-2C_5H_{11}$], 239 (5) [M^{2+}]; HRMS: *m/z* calcd for $C_{32}H_{38}N_4$: 478.30965; found: 478.30734.

5,10-Di(*n*-hexyl)porphyrin (16c)

Procedure D: A solution of 2.5 M *n*-hexyllithium (0.14 mL, 0.36 mmol) in hexane was added to porphyrin **1**. The title porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (18 mg, 0.04 mmol, 61%). M.p. 133 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ = 9.98 (s, 2H; 15,20-H$_{meso}$), 9.55 (m, 4H; 3,7,8,12-H$_\beta$), 9.29 (m, 4H; 2,13,17,18-H$_\beta$), 4.99 (t, ^3J(H,H) = 8 Hz, 4H; $CH_2(CH_2)_4CH_3$), 2.55 (m, 4H; $CH_2CH_2(CH_2)_3CH_3$), 1.83 (m, 4H; $(CH_2)_2CH_2(CH_2)_2CH_3$), 1.53 (m, 4H; $(CH_2)_3CH_2CH_2CH_3$), 1.43 (m, 4H; $(CH_2)_4CH_2CH_3$), 0.96 (t, ^3J(H,H) = 7 Hz, 3H; $(CH_2)_5CH_3$), −3.37 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$): δ = ~130, 119.76, 102.83, 38.96, 35.62, 31.90, 30.32, 22.76, 14.19 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 406 (6.31), 504 (5.17), 535 (4.39), 579 (4.65), 634 nm (4.17); MS (80 eV, EI, 180 °C): *m/z* (%): 478 (100) [M^+], 407 (53) [$M^+-C_5H_{11}$], 336 (9) [$M^+-C_{10}H_{22}$], 239 (5) [M^{2+}]; HRMS: *m/z* calcd for $C_{32}H_{38}N_4$: 478.30965; found: 478.30734.

5-Phenylporphyrin (17a)[40]

Procedure A: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). The first fraction contained the disubstituted porphyrin **17b** and the second fraction the monosubstituted porphyrin **17a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (50 mg, 0.13 mmol, 7%).

Procedure C: The yield was 2% (16 mg, 0.04 mmol).

Procedure D: A solution of 1.8 M phenyllithium in dibutyl ether (0.10 mL, 0.18 mmol) was added to porphine **1**. After standard workup, the product was obtained (4 mg, 0.01 mmol, 17%). R_f = 0.28 (CH_2Cl_2/*n*-hexane 1:1); m.p. 291 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.33 (s, 2H; 10,20-H$_{meso}$), 10.25 (s, 1H; 15-H$_{meso}$), 9.47 (m, 4H; 12,13,17,18-H$_\beta$), 9.40 (AB, ^3J(H,H) = 5 Hz, 2H; 2,8-H$_\beta$), 9.07 (AB, ^3J(H,H) = 5 Hz, 2H; 3,7-H$_\beta$), 8.27 (m, 2H; Ph$_{o\text{-H}}$), 7.80 (m, 3H; Ph$_{m\text{-H}}$, Ph$_{p\text{-H}}$), −3.61 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25 °C): δ = 141.77, 134.78, 131.73, 131.34, 131.25, 131.11, 127.73, 126.82, 119.54, 104.64, 103.53 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 403 (5.35), 495 (4.21), 526 (3.42), 568 (3.73), 622 nm (2.81); MS (70 eV, EI, 350 °C): *m/z* (%): 386 (100) [M^+], 193 (10) [M^{2+}]; HRMS: *m/z* calcd for $C_{26}H_{26}N_4$: 386.15315; found: 386.15564; elemental analysis calcd (%) for $C_{26}H_{18}N_4$ (386.46): C 80.81, H 4.69, N 14.50; found: C 80.56, H 4.40, N 14.35.

5,15-Diphenylporphyrin (17b)

Procedure A: Obtained during the synthesis of **17a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (23 mg, 0.05 mmol, 5%). Analytical data were as described in the literature.[32a]

5,10-Diphenylporphyrin (17c)

Procedure C: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:2). The first fraction contained the disubstituted porphyrin **17c** and the second fraction the monosubstituted porphyrin **17a**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (60 mg, 0.13 mmol, 6%).

Procedure D: A solution of 1.8 M phenyllithium in dibutyl ether (0.20 mL, 0.36 mmol) was added to porphine **1**. The reaction mixture was purified by column chromatography (CH_2Cl_2/*n*-hexane 1:1) to yield the product (12 mg, 0.01 mmol, 43%). Analytical data were as described in the literature.[20] M.p. 270 °C; MS (80 eV, EI): *m/z* (%): 462 (100) [M^+], 231 (14) [M^{2+}].

5-(4-Bromophenyl)porphyrin (18a)

Procedure A: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). The first fraction contained the disubstituted porphyrin **18b** and the second fraction the monosubstituted porphyrin **18a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (53 mg, 0.11 mmol, 6%). R_f = 0.48 (CH_2Cl_2/*n*-hexane 2:1); m.p. 294 °C; ^{1}H NMR (500 MHz, $CDCl_3$ 25 °C, TMS): δ = 10.32 (s, 2H; 10,20-H$_{meso}$), 10.25 (s, 1H; 15-H$_{meso}$), 9.48 (AB, ^3J(H,H) = 4 Hz, 2H; 12,18-H$_\beta$), 9.46 (AB, ^3J(H,H) = 4 Hz, 2H; 13,17-H$_\beta$), 9.41 (AB, ^3J(H,H) = 4 Hz, 2H; 2,8-H$_\beta$), 9.05 (AB, ^3J(H,H) = 4 Hz, 2H; 3,7-H$_\beta$), 8.12 (AB, ^3J(H,H) = 8 Hz, 2H; Ph$_{o\text{-H}}$), 7.94 (AB, ^3J(H,H) = 8 Hz, 2H; Ph$_{m\text{-H}}$), −3.66 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25 °C): δ = 140.81, 136.06, 131.84, 131.49, 131.26, 130.95, 130.03, 122.23, 117.83, 104.79, 103.80 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 401 (5.64), 496 (4.14), 526 (3.37), 568 (3.65), 622 nm (2.76); MS (80 eV, EI): *m/z* (%): 466 (99) [M^+], 464 (100) [M^+], 385 (6) [M^+−Br], 384 (7) [M^+−HBr], 233 (3) [M^{2+}], 232 (4) [M^{2+}]; HRMS: *m/z* calcd for $C_{26}H_{17}N_4Br$: 464.06366; found: 464.06634.

5,15-Bis(4-bromophenyl)porphyrin (18b)[48a,b]

Procedure A: Obtained during the synthesis of **18a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (18 mg, 0.03 mmol, 3%). R_f = 0.61 (CH_2Cl_2/*n*-hexane 1:1); m.p. >330 °C; ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ = 10.32 (s, 2H; 10,20-H$_{meso}$), 9.41 (brs, 4H; 3,7,13,17-H$_\beta$), 9.05 (brs, 4H; 2,8,12,18-H$_\beta$), 8.13 (m, 4H; Ph$_{o\text{-H}}$), 7.94 (m, 4H; Ph$_{m\text{-H}}$), −3.18 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 401 (5.58), 494 (4.22), 527 (3.43), 568 (3.71), 621 nm (2.67); MS (80 eV, EI): *m/z* (%): 620 (94) [M^+], 618 (45) [M^+], 539 (3) [M^+−Br], 538 (2) [M^+−HBr]; HRMS: *m/z* calcd for $C_{32}H_{20}N_4Br_2$: 618.00547; found: 618.00763.

5-(4-Chlorophenyl)porphyrin (19a)

Procedure A: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). The first fraction contained the disubstituted porphyrin **19b** and the second fraction the monosubstituted porphyrin **19a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (43 mg, 0.10 mmol, 5%). R_f=0.67 (CH_2Cl_2/*n*-hexane 1:1); m.p. 293°C; ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS): δ=10.31 (s, 2H; 10,20-H$_{meso}$), 10.23 (s, 1H; 15-H$_{meso}$), 9.47 (AB, ^3J(H,H)=4 Hz, 2H; 12,13-H$_\beta$), 9.44 (AB, ^3J(H,H)=4 Hz, 2H; 13,17-H$_\beta$), 9.40 (AB, ^3J(H,H)=4 Hz, 2H; 2,8-H$_\beta$), 9.04 (AB, ^3J(H,H)=4 Hz, 2H; 3,7-H$_\beta$), 8.17 (AB, ^3J(H,H)=8 Hz, 2H; Ph$_{o\text{-H}}$), 7.77 (AB, ^3J(H,H)=8 Hz, 2H; Ph$_{m\text{-H}}$), −3.67 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 254°C): δ=140.25, 135.71, 134.31, 131.81, 131.46, 131.23, 130.94, 127.09, 117.78, 104.77, 103.76 ppm; UV/Vis (CH_2Cl_2): λ_{max} (logε)=400 (5.49), 495 (3.91), 526 (3.06), 568 (3.39), 622 nm (2.24); MS (80 eV, EI): *m*/*z* (%): 422 (36) [M^+], 420 (100) [M^+], 385 (3) [M^+−Cl], 384 (4) [M^+−HCl], 211 (2) [M^{2+}], 210 (6) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{26}H_{17}N_4Cl$: 420.11417; found: 420.11721.

5,15-Bis(4-chlorophenyl)porphyrin (19b)

Procedure A: Obtained during the synthesis of **19a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (5 mg, 0.01 mmol, 1%). R_f=0.80 (CH_2Cl_2/*n*-hexane 1:1); m.p. >330°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ=10.32 (s, 2H; 10,20-H$_{meso}$), 9.40 (AB, ^3J(H,H)=4 Hz, 4H; 3,7,13,17-H$_\beta$), 9.04 (AB, ^3J(H,H)=4 Hz, 4H; 2,8,12,18-H$_\beta$) 8.19 (AB, ^3J(H,H)=8 Hz, 4H; Ph$_{o\text{-H}}$), 7.79 (AB, ^3J(H,H)=8 Hz, 4H; Ph$_{m\text{-H}}$), −3.18 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} (logε)=407 (4.87), 502 (3.75), 536 (3.29), 575 (3.24), 629 nm (2.70); MS (80 eV, EI): *m*/*z* (%): 532 (69) [M^+], 530 (100) [M^+], 495 (3) [M^+−Cl], 494 (3) [M^+−HCl], 266 (5) [M^{2+}], 265 (6) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{32}H_{20}N_4Cl_2$: 530.10650; found: 530.10547.

5-(2,6-Difluorophenyl)porphyrin (20a)

Procedure A: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). The first fraction contained the disubstituted porphyrin **20b** and the second fraction the monosubstituted porphyrin **20a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (19 mg, 0.04 mmol, 2%). R_f=0.51 (CH_2Cl_2/*n*-hexane 3:1); m.p. 303°C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS): δ=10.32 (s, 2H; 10,20-H$_{meso}$), 10.29 (s, 1H; 15-H$_{meso}$), 9.48 (m, 2H; 12,18-H$_\beta$), 9.47 (m, 2H; 13,17-H$_\beta$), 9.43 (AB, ^3J(H,H)=5 Hz, 2H; 2,8-H$_\beta$), 9.04 (AB, ^3J(H,H)=5 Hz, 2H; 3,7-H$_\beta$), 7.82 (m, 1H; Ph$_{p\text{-H}}$), 7.41 (m, 2H; Ph$_{m\text{-H}}$), −3.63 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25°C): δ=132.14, 131.63, 131.36, 130.88, 130.08, 111.33, 104.87, 104.60 ppm; UV/Vis (CH_2Cl_2): λ_{max} (logε)=399 (5.20), 493 (4.11), 524 (3.44), 567 (3.63), 620 nm (3.03); MS (80 eV, EI): *m*/*z* (%): 422 (100) [M^+], 211 (17) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{26}H_{16}N_4F_2$: 422.13430; found: 422.13653.

5,15-Bis(2,6-difluorophenyl)porphyrin (20b)

Procedure A: Obtained during the synthesis of **20a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (63 mg, 0.15 mmol, 15%). R_f=0.62 (CH_2Cl_2/*n*-hexane 2:1); m.p. >330°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ=10.31 (s, 2H; 10,20-H$_{meso}$), 9.41 (AB, ^3J(H,H)=5 Hz, 4H; 2,8,12,18-H$_\beta$), 9.03 (AB, ^3J(H,H)=5 Hz, 4H; 3,7,13,17-H$_\beta$), 7.81 (m, 2H; Ph$_{p\text{-H}}$), 7.41 (m, 4H; Ph$_{m\text{-H}}$), −3.19 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25°C): δ=162.49, 132.33, 130.96, 130.08, 118.44, 111.40, 105.67 ppm; UV/Vis (CH_2Cl_2): λ_{max} (logε)=403 (5.41), 498 (4.22), 530 (3.82), 572 (3.76), 626 nm (3.45); MS (80 eV, EI): *m*/*z* (%): 534 (100) [M^+], 267 (19) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{32}H_{18}N_4F_4$: 534.14676; found: 534.14532.

5-(3,5-Difluorophenyl)porphyrin (21a)

Procedure A: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 3:1). The first fraction contained the disubstituted porphyrin **21b** and the second fraction the monosubstituted porphyrin **21a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (30 mg, 0.07 mmol, 4%). R_f=0.22 (CH_2Cl_2/*n*-hexane 3:1); 324–326°C (decomp); ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS): δ=10.33 (s, 2H; 10,20-H$_{meso}$), 10.27 (s, 1H; 15-H$_{meso}$), 9.49 (AB, ^3J(H,H)=4 Hz, 2H; 12,18-H$_\beta$), 9.47 (AB, ^3J(H,H)=4 Hz, 2H; 13,17-H$_\beta$), 9.42 (AB, ^3J(H,H)=5 Hz, 2H; 2,8-H$_\beta$), 9.07 (AB, ^3J(H,H)=5 Hz, 2H; 3,7-H$_\beta$), 7.80 (m, 2H; Ph$_{o\text{-H}}$), 7.30 (m, 1H; Ph$_{p\text{-H}}$), −3.69 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25°C): δ=161.45, 132.26, 131.91, 131.40, 130.59, 118.05, 104.97, 104.19, 103.49 ppm; UV/Vis (CH_2Cl_2): λ_{max} (logε)=399 (4.96), 494 (4.12), 526 (3.44), 567 (3.67), 622 nm (3.07); MS (80 eV, EI): *m*/*z* (%): 422 (100) [M^+], 211 (8) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{26}H_{16}N_4F_2$: 422.13430; found: 422.13644.

5,15-Bis(3,5-difluorophenyl)porphyrin (21b)

Procedure A: Obtained during the synthesis of **21a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (12 mg, 0.02 mmol, 2%). R_f=0.34 (CH_2Cl_2/*n*-hexane 3:1); m.p. >330°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C): δ=10.35 (s, 2H; 10,20-H$_{meso}$), 9.43 (AB, ^3J(H,H)=4 Hz, 4H; 3,7,13,17-H$_\beta$), 9.07 (AB, ^3J(H,H)=4 Hz, 4H; 2,8,12,18-H$_\beta$), 7.80 (m, 2H; Ph$_{p\text{-H}}$), 6.82 (m, 4H; Ph$_{o\text{-H}}$), −3.24 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} (logε)=405 (5.03), 500 (3.82), 534 (3.30), 574 (3.32), 627 nm (2.82); MS (80 eV, EI): *m*/*z* (%): 534 (100) [M^+], 267 (20) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{32}H_{18}N_4F_4$: 534.14676; found: 534.1447.

5-(4-Methoxyphenyl)porphyrin (22a)

Procedure A: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 2:1). After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (99 mg, 0.24 mmol, 12%).

Procedure B: The title compound was obtained in a 14% yield (117 mg, 0.28 mmol). The use of 5-formylanisole (1 mmol) in procedure B gave **22a** (96 mg, 0.23 mmol, 23%). R_f=0.24 (CH_2Cl_2/*n*-hexane 2:1); m.p. 286°C; ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS): δ=10.29 (s, 2H; 10,20-H$_{meso}$), 10.21 (s, 1H; 15-H$_{meso}$), 9.46 (AB, ^3J(H,H)=4 Hz, 2H; 12,18-H$_\beta$), 9.44 (AB, ^3J(H,H)=4 Hz, 2H; 13,17-H$_\beta$), 9.39 (AB, ^3J(H,H)=5 Hz, 2H; 2,8-H$_\beta$), 9.11 (AB, ^3J(H,H)=5 Hz, 2H; 3,7-H$_\beta$), 8.16 (AB, ^3J(H,H)=9 Hz, 2H; Ph$_{o\text{-H}}$), 7.32 (AB, ^3J(H,H)=9 Hz, 2H; Ph$_{m\text{-H}}$), 4.11 (s, 3H; OCH$_3$), −3.60 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25°C): δ=159.49, 135.79, 134.05, ~131, 119.42, 112.39, 104.59, 103.36, 55.61 ppm; UV/Vis (CH_2Cl_2): λ_{max} (logε)=405 (5.13), 499 (4.11), 539 (3.60), 575 (3.64), 628 nm (3.12); MS (80 eV, EI): *m*/*z* (%): 416 (100) [M^+], 401 (4) [M^+−CH$_3$], 385 (1) [M^+−OCH$_3$], 208 (13) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{27}H_{20}N_4O$: 416.16371; found: 416.16522.

5-(3-Methoxyphenyl)porphyrin (23a)

Procedure A: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 3:1). The first fraction contained the monosubstituted porphyrin and the second fraction the disubstituted porphyrin. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (130 mg, 0.31 mmol, 16%). The use of 3-formylanisole (1 mmol) in procedure A gave the title compound (141 mg, 0.34 mmol, 34%), and compound **23b** as byproduct.

Procedure B: Reaction and standard workup gave compound **23a** (202 mg, 0.49 mmol, 24%), and **23b** as byproduct.

Procedure C: Yield 17 mg (0.04 mmol, 2%); R_f=0.26 (CH_2Cl_2/*n*-hexane 2:1), 0.66 (CH_2Cl_2/C_6H_{14} 3:1); m.p. 309°C; HPLC: (eluent: CH_2Cl_2, detection at 420 nm) t_R=3.87 min (97.1%), (same conditions but detection at 254 nm) t_R: 3.94 min (99.1%); ^{1}H NMR (270 MHz, $CDCl_3$, 25°C, TMS): δ=10.28 (s, 2H; 10,20-H$_{meso}$), 10.23 (s, 1H; 15-H$_{meso}$), 9.45 (m, 4H; 12,13,17,18-H$_\beta$), 9.36 (AB, ^3J(H,H)=5 Hz, 2H; 2,8-H$_\beta$), 9.01 (AB, ^3J(H,H)=5 Hz, 2H; 3,7-H$_\beta$), 8.04 (m, 1H; H$_{o\text{-Ph}}$), 7.81 (m, 1H; H$_{o\text{-Ph}}$), 7.70 (m, 1H; H$_{m\text{-Ph}}$), 7.51 (m, 1H; H$_{p\text{-Ph}}$), 4.01 (s, 3H; OCH$_3$), −3.60 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25°C): δ=158.64, 146.57, 145.61, 143.09, 131.71, 131.35, 131.27, 131.11, 127.89, 127.64, 120.83, 119.22, 113.53, 104.64, 103.58, 55.54 ppm; UV/Vis (CH_2Cl_2): λ_{max} (logε)=400 (5.47), 495 (4.21), 526 (3.39), 568 (3.74), 622 nm (2.82); MS (80 eV, EI): *m*/*z* (%): 416 (100) [M^+], 401 (6) [M^+−CH$_3$], 385 (3) [M^+−OCH$_3$], 208 (10) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{27}H_{20}N_4O$: 416.163711; found: 416.16632; elemental analysis calcd (%) for $C_{27}H_{20}N_4O$ (416.18): C 77.87, H 4.84, N 13.45; found: C 77.64, H 4.53, N 13.48.

5,15-Bis(3-methoxyphenyl)porphyrin (23b)[13,16,48a]

Procedure A: Obtained during the synthesis of **23a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (62 mg, 0.12 mmol, 12%). R_f=0.58 (CH_2Cl_2/*n*-hexane 3:1); m.p.

$>300\,°C$; ^1H NMR (270 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.31$ (s, 2H; 10,20-H_{meso}), 9.38 (AB, $^3J(H,H) = 5$ Hz, 4H; 2,8,12,18-H_β), 9.11 (AB, $^3J(H,H) = 5$ Hz, 4H; 3,7,13,17-H_β), 7.84 (m, 4H; $H_{o\text{-}Ph}$), 7.67 (m, 2H; $H_{m\text{-}Ph}$), 7.35 (m, 2H; $H_{p\text{-}Ph}$), 4.01 (s, 6H; OCH_3), −3.16 ppm (brs, 2H; NH); ^{13}C NMR (60 MHz, $CDCl_3$, 25 °C): $\delta = 158.29$, 153.64, 147.10, 145.30, 142.75, 131.58, 131.05, 127.92, 127.78, 120.82, 113.55, 105.26, 55.57 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 410 (5.57), 474 (3.77), 536 (3.88), 575 (3.84), 628 nm (3.56); MS (80 eV, EI): *m/z* (%): 522 (100) [M^+], 507 (2) [$M^+ - CH_3$], 491 (3) [$M^+ - OCH_3$], 261 (7) [M^{2+}]; HRMS: *m/z* calcd for $C_{34}H_{26}N_4O_2$: 522.20558; found: 522.20642.

5,10-Bis(3-methoxyphenyl)porphyrin (23c)

Procedure C: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 2:1). The first fraction contained the monosubstituted porphyrin **23a** and the second fraction the disubstituted porphyrin **23c**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (79 mg, 0.15 mmol, 7%). $R_f = 0.30$ (CH_2Cl_2/*n*-hexane 2:1); m.p. 304 °C; ^1H NMR (270 MHz, $CDCl_3$, 25 °C, TMS): $\delta =$ 10.17 (s, 2H; 15,20-H_{meso}), 9.38 (s, 2H; 17,18-H_β), 9.32 (AB, $^3J(H,H) =$ 5 Hz, 2H; 2,13-H_β), 9.10 (AB, $^3J(H,H) = 5$ Hz, 2H; 3,12-H_β), 9.02 (s, 2H; 7,8-H_β), 7.85 (m, 4H; $H_{o\text{-}Ph}$), 7.68 (m, 2H; $H_{m\text{-}Ph}$), 7.37 (m, 2H; $H_{p\text{-}Ph}$), 3.99 (s, 6H; OCH_3), −3.35 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): $\delta = 158.26$, 147.09, 145.28, 131.60, 131.06, 127.91, 127.78, 120.79, 113.51, 105.27, 55.54 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 406 (5.12), 502 (3.84), 536 (3.31), 575 (3.38), 628 nm (2.95); MS (80 eV, EI): *m/z* (%): 522 (100) [M^+], 416 (3) [$M^+ - C_7H_7O$]; HRMS: *m/z* calcd for $C_{34}H_{26}N_4O_2$: 522.20558; found: 522.20560.

5-(3,5-Dimethoxyphenyl)porphyrin (24a)

Procedure A: The porphyrin was purified by column chromatography on silica gel by using neat dichloromethane eluent. The first fraction was the desired porphyrin **24a**, followed by traces of 5,15-bis(3,5-dimethoxyphenyl)porphyrin **24b**.[48a,c] After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (50 mg, 0.11 mmol, 6%).

Procedure B: The yield of the title compound was 22% (0.44 mmol, 22%). $R_f = 0.37$ (CH_2Cl_2/*n*-hexane 3:1); m.p. $>340\,°C$, subl. $>315\,°C$; HPLC: (Nucleosil 50, 5µ, eluent: CH_2Cl_2, flow: 1 mL min^{-1}, detection at 420 nm) t_R: 5.17 min (99%), (same conditions but detection at 254 nm) t_R: 5.24 min (100.0%); ^1H NMR (270 MHz, $CDCl_3$, 25 °C, TMS): $\delta =$ 10.31 (s, 2H; 10,20-H_{meso}), 10.27 (s, 1H; 15-H_{meso}), 9.48 (m, 4H; 12,13,17,18-H_β), 9.40 (AB, $^3J(H,H) = 5$ Hz, 2H; 2,8-H_β), 9.17 (d, $^3J(H,H) = 5$ Hz, 2H; 3,7-H_β), 7.43 (m, 2H; $H_{o\text{-}Ph}$), 6.91 (m, 1H; $H_{p\text{-}Ph}$), 3.98 (s, 6H; OCH_3), −3.62 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 400 (5.49), 495 (4.22), 526 (3.40), 568 (3.73), 622 nm (2.85); MS (80 eV, EI): *m/z* (%):446 (100) [M^+], 431 (3) [$M^+ - CH_3$], 416 (4) [$M^+ - 2CH_3$], 223 (10) [M^{2+}]; HRMS: *m/z* calcd for $C_{28}H_{22}N_4O_2$: 446.174276; found: 446.17633.

5-(3-Nitrophenyl)porphyrin (25a)

Procedure A: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 2:1). The first fraction contained the disubstituted porphyrin **25b** and the second fraction the monosubstituted porphyrin **25a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (27 mg, 0.06 mmol, 3%). $R_f = 0.23$ (CH_2Cl_2/*n*-hexane 2:1); m.p. $>330\,°C$; ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.35$ (s, 2H; 10,20-H_{meso}), 10.29 (s, 1H; 15-H_{meso}), 9.50 (AB, $^3J(H,H) = 4$ Hz, 2H; 12,18-H_β), 9.48 (AB, $^3J(H,H) = 4$ Hz, 2H; 13,17-H_β), 9.43 (AB, $^3J(H,H) = 5$ Hz, 2H; 2,8-H_β), 9.12 (m, 1H; $Ph_{o\text{-}H}$), 8.95 (AB, $^3J(H,H) = 5$ Hz, 2H; 3,7-H_β), 8.70 (m, 1H; $Ph_{p\text{-}H}$), 8.56 (m, 1H; $Ph_{o\text{-}H}$), 7.97 (m, 1H; $Ph_{m\text{-}H}$), −3.67 ppm (brs, 2H; NH); ^{13}C NMR (63 MHz, $CDCl_3$, 25 °C): $\delta = 139.98$, 131.96, 131.52, 130.43, 128.49, 127.77, 122.88, 105.08, 104.31 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 401 (5.15), 495 (3.99), 526 (3.23), 567 (3.50), 622 nm (2.72); MS (80 eV, EI): *m/z* (%): 431 (100) [M^+], 385 (23) [$M^+ - NO_2$], 215 (3) [M^{2+}]; HRMS: *m/z* calcd for $C_{26}H_{17}N_5O_2$: 431.13822; found 431.13577.

5,15-Bis(3-nitrophenyl)porphyrin (25b)[48a,d]

Procedure A: Obtained during the synthesis of **25a**. After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (33 mg, 0.06 mmol, 6%). $R_f = 0.33$ (CH_2Cl_2/*n*-hexane 2:1); m.p. $>330\,°C$; ^1H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.39$ (s, 2H; 10,20-H_{meso}), 9.45 (AB, $^3J(H,H) = 4$ Hz, 4H; 2,8,12,18-H_β), 9.13 (m, 2H; 26,32-$Ph_{o\text{-}H}$), 8.98 (AB, $^3J(H,H) = 4$ Hz, 4H; 3,7,13,17-H_β), 8.70 (m, 2H; $Ph_{p\text{-}H}$), 8.59 (m, 2H; $Ph_{o\text{-}H}$), 8.00 (m, 2H; $Ph_{m\text{-}H}$), −3.19 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 408 (4.40), 501 (3.21), 535 (2.75), 574 (2.80), 628 nm (2.45); MS (80 eV, EI): *m/z* (%): 552 (16) [M^+], 431 (5) [$M^+ - C_6H_4NO_2$+H]; HRMS: *m/z* calcd for $C_{32}H_{20}N_6O_4$: 552.15460; found 552.15655.

5-(4-Nitrophenyl)porphyrin (26a)

Procedure A: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 2:1). After recrystallization from CH_2Cl_2/CH_3OH, the porphyrin was obtained as purple crystals (17 mg, 0.04 mmol, 2%). $R_f = 0.36$ (CH_2Cl_2/*n*-hexane 2:1); m.p. $>330\,°C$; compound too insoluble for NMR; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 401 (4.95), 496 (4.14), 530 (3.54), 568 (3.67), 624 nm (3.06); MS (80 eV, EI): *m/z* (%): 431 (100) [M^+], 385 (19) [$M^+ - NO_2$], 215 (3) [M^{2+}], 192 (3) [$M^{2+} - NO_2$]; HRMS: *m/z* calcd for $C_{26}H_{17}N_5O_2$: 431.13822; found: 431.13644.

5-*p*-Tolylporphyrin (29a)

Procedure C: Obtained during the synthesis of **29c**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (25 mg, 0.06 mmol, 3%). $R_f = 0.40$ (CH_2Cl_2/*n*-hexane 2:1); m.p. 280 °C; ^1H NMR (270 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.28$ (s, 2H; 10,20-H_{meso}), 10.19 (s, 1H; 15-H_{meso}), 9.43 (AB, $^3J(H,H) = 4$ Hz, 4H; 12,13,17,18-H_β), 9.38 (AB, $^3J(H,H) = 4$ Hz, 2H; 2,8-H_β), 9.12 (AB, $^3J(H,H) = 4$ Hz, 2H; 3,7-H_β), 8.14 (d, 2H; $^3J(H,H) = 8$ Hz, $H_{o\text{-}Ph}$), 7.59 (d, $^3J(H,H) = 8$ Hz, 2H; $H_{m\text{-}Ph}$), 2.74 (s, 3H; CH_3), −3.63 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 404 (5.26), 499 (4.11), 531 (3.32), 574 (3.60), 629 nm (2.81); MS (80 eV, EI): *m/z* (%): 400 (100) [M^+], 384 (7) [$M^+ - CH_2$]; HRMS: *m/z* calcd for $C_{27}H_{20}N_4$: 400.16880; found: 400.21536.

5,10-Di(*p*-tolyl)porphyrin (29c)

Procedure C: The porphyrins were purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:2). The first fraction contained the monosubstituted porphyrin **29a** and the second fraction the disubstituted porphyrin **29c**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (111 mg, 0.23 mmol, 11%). $R_f = 0.60$ (CH_2Cl_2/*n*-hexane 1:1); m.p. 270 °C; ^1H NMR (270 MHz, $CDCl_3$, 25 °C, TMS): $\delta =$ 10.19 (s, 2H; 15,20-H_{meso}), 9.41 (s, 2H; 17,18-H_β), 9.32 (AB, $^3J(H,H) =$ 5 Hz, 2H; 2,13-H_β), 9.05 (AB, $^3J(H,H) = 5$ Hz, 2H; 3,12-H_β), 8.95 (s, 2H; 7,8-H_β), 8.13 (d, 4H; $^3J(H,H) = 8$ Hz, $H_{o\text{-}Ph}$), 7.78 (d, $^3J(H,H) = 8$ Hz, 4H; $H_{m\text{-}Ph}$), 2.72 (s, 6H; CH_3), −3.35 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): $\delta = 139.20$, 137.37, 134.56, 131.04, 127.39, 120.19, 103.98, 21.50 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 405 (5.48), 502 (4.33), 531 (3.66), 575 (3.84), 625 nm (3.32); MS (80 eV, EI): *m/z* (%): 490 (15) [M^+], 400 (25) [$M^+ - C_6H_5$]; HRMS: *m/z* calcd for $C_{34}H_{26}N_4$: 490.21575; found: 490.21537.

5-Pentylporphyrin (30a)

Procedure C: Obtained during the synthesis of **30c**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (8 mg, 0.02 mmol, 1%). Alternatively, dipyrromethane **13** (0.34 g, 2.3 mmol) and 5-pentyldipyrromethane (0.5 g, 2.3 mmol) were dissolved in dichloromethane (1.2 L) and degassed for 10 min with argon. Trimethylorthoformiate (38 mL, 0.35 mol) was added, followed by dropwise addition of trichloroacetic acid (17.65 g, 108 mmol). After stirring for 4 h at RT the mixture was treated with pyridine (31.2 mL, 0.39 mol) and stirring was continued for 17 h. Subsequently, oxygen was bubbled through the solution for oxidation, followed by filtration, and chromatographic workup. Yield 1%; $R_f = 0.52$ (*n*-hexane/ethyl acetate 4:1); m.p. 275 °C; ^1H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.12$ (s, 2H; 10,20-H_{meso}), 10.11 (s, 2H; 15-H_{meso}), 9.65 (AB, $^3J(H,H) = 5$ Hz, 2H; 3,7-H_β), 9.41 (m, 4H; 2,8,12,18-H_β), 9.37 (AB, $^3J(H,H) = 5$ Hz, 2H; 13,17-H_β), 5.06 (t, $^3J(H,H) = 8$ Hz, 2H; $CH_2(CH_2)_3CH_3$), 2.56 (m, 2H; $CH_2CH_2(CH_2)_2CH_3$), 1.84 (m, 2H; $(CH_2)_2CH_2CH_2CH_3$), 1.74 (m, 2H; $(CH_2)_3CH_2CH_3$), 1.15 (t, $^3J(H,H) = 7$ Hz, 3H; $(CH_2)_4CH_3$), −3.57 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): $\delta = 131.83$, 131.62, 130.83, 128.30, 120.21, 104.21, 102.78, 38.64, 35.13, 31.71, 22.78, 14.14 ppm; UV/Vis (CH_2Cl_2): λ_{max} ($\log\varepsilon$) = 400 (5.33), 495 (4.12), 526 (3.25), 569 (3.62), 621 nm (2.53); MS (80 eV, EI, 250 °C): *m/z* (%): 390 (44) [M^+], 323 (100) [$M^+ - C_4H_9$]; HRMS: *m/z* calcd for $C_{25}H_{24}N_4$: 380.20010; found: 380.20008.

5,10-Dipentylporphyrin (30c)

Procedure C: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:3). The first fraction contained the disubstituted porphyrin **30c** and the second fraction the monosubstituted porphyrin **30a**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (63 mg, 0.14 mmol, 7%). R_f = 0.60 (CH_2Cl_2/*n*-hexane 2:1); m.p. 132°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ = 9.99 (s, 2H; 15,20-H_{meso}), 9.59 (brs, 4H; 3,7,8,12-H_β), 9.30 (brs, 4H; 2,13,17,18-H_β), 5.03 (t, ^3J(H,H) = 8 Hz, 4H; $CH_2(CH_2)_3CH_3$), 2.56 (tt, ^3J(H,H) = 8 Hz, ^3J(H,H) = 7 Hz, 4H; $CH_2CH_2(CH_2)_2CH_3$), 1.81 (tt, ^3J(H,H) = 7 Hz, ^3J(H,H) = 7 Hz, 4H; $(CH_2)_2CH_2CH_2CH_3$), 1.57 (tq, ^3J(H,H) = 7 Hz, ^3J(H,H) = 7 Hz, 4H; $(CH_2)_3CH_2CH_3$), 1.00 (t, ^3J(H,H) = 7 Hz, 6H; $(CH_2)_4CH_3$), −3.31 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25°C): δ = 130.99, 120.00, 102.88, 38.65, 35.60, 32.88, 22.78, 14.16 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 406 (5.40), 504 (4.12), 534 (3.39), 580 (3.60), 635 nm (3.16); MS (80 eV, EI, 350°C): *m*/*z* (%): 450 (98) [M^+], 393 (100) [$M^+-C_4H_9$], 336 (20) [$M^+-C_8H_{18}$], 225 (2) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{30}H_{34}N_4$: 450.27847; found: 450.27466.

5-*iso*-Butylporphyrin (31a)

Procedure C: Obtained during the synthesis of **31c**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (9 mg, 0.02 mmol, 1%). R_f = 0.50 (CH_2Cl_2/*n*-hexane 2:1); m.p. 270°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ = 10.28 (s, 2H; 10,20-H_{meso}), 10.12 (s, 2H; 15-H_{meso}), 9.82 (m, 2H; 3,7-H_β), 9.44 (m, 4H; 2,8,12,18-H_β), 9.39 (AB, ^3J(H,H) = 5 Hz, 2H; 13,17-H_β), 5.16 (m, 2H; CH_2), 2.93 (m, 1H; CH), 1.19 (m, 6H; CH_3), −3.30 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 399 (5.39), 496 (4.38), 526 (3.49), 569 (3.88), 621 nm (2.75); MS (80 eV, EI): *m*/*z* (%): 366 (46) [M^+], 323 (100) [$M^+-C_3H_7$]; HRMS: *m*/*z* calcd for $C_{24}H_{22}N_4$: 366.18445; found: 366.18450.

5,10-Di(*iso*-butyl)porphyrin (31c)

Procedure C: The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:3). The first fraction contained the disubstituted porphyrin **31c** and the second fraction the monosubstituted porphyrin **31a**. After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (44 mg, 0.10 mmol, 5%). R_f = 0.40 (CH_2Cl_2/*n*-hexane 1:1); m.p. 206°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ = 10.04 (s, 2H; 15,20-H_{meso}), 9.61 (s, 2H; 7,8-H_β), 9.60 (AB, ^3J(H,H) = 5 Hz, 2H; 3,12-H_β) 9.33 (m, 4H; 2,13,17,18-H_β), 4.95 (d, ^3J(H,H) = 7 Hz, 4H; CH_2), 2.84 (m, 2H; CH), 1.23 (d, ^3J(H,H) = 6 Hz, 12H; CH_3), −3.30 ppm (brs, 2H; NH); ^{13}C NMR (126 MHz, $CDCl_3$, 25°C): δ = 130.00, 118.84, 103.02, 43.92, 37.04, 23.39 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 403 (5.26), 505 (4.24), 534 (3.56), 579 (3.76), 635 nm (3.35); MS (80 eV, EI): *m*/*z* (%): 422 (85) [M^+], 379 (100) [$M^+-C_3H_7$]; HRMS: *m*/*z* calcd for $C_{28}H_{30}N_4$: 422.24705; found: 422.24710.

5-*n*-Butylporphyrin (35)

Procedure D: A solution of 2.5 M *n*-butyllithium in hexane (0.03 mL, 0.07 mmol) was added to the porphine **1** solution. The title porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (13 mg, 0.03 mmol, 48%). R_f = 0.44 (CH_2Cl_2/*n*-hexane 1:1); m.p. 232°C, ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ = 10.19 (s, 2H; 10,20-H_{meso}), 10.10 (s, 1H; 15-H_{meso}), 9.63 (AB, 2H; ^3J(H,H) = 5 Hz, 3,7-H_β), 9.41 (m, 4H; 2,8,12,18-H_β), 9.37 (AB, ^3J(H,H) = 5 Hz, 2H; 17,18-H_β), 5.06 (t, ^3J(H,H) = 8 Hz, 2H; $CH_2(CH_2)_2CH_3$), 2.56 (m, 2H; $CH_2CH_2CH_2CH_3$), 1.84 (m, 2H; $CH_2CH_2CH_2CH_3$), 1.15 (t, ^3J(H,H) = 7 Hz, 3H; $CH_2CH_2CH_2CH_3$), −3.57 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 399 (5.30), 496 (4.12), 526 (3.24), 569 (3.62), 621 nm (2.53); MS (80 eV, EI): *m*/*z* (%): 366 (59) [M^+], 323 (100) [$M^+-C_3H_7$]; HRMS: *m*/*z* calcd for $C_{24}H_{22}N_4$: 366.18445; found: 366.18449.

5,10-Di(*n*-butyl)porphyrin (36)

Procedure D: A solution of 2.5 M *n*-butyllithium in hexane (0.07 mL, 0.18 mmol) was added to porphine **1**. The title porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 1:1). After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (29 mg, 0.059 mmol, 99%). R_f = 0.55 (CH_2Cl_2/*n*-hexane 1:1); m.p. 140°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ = 9.97 (s, 2H; 15,20-H_{meso}), 9.55 (m, 4H; 3,7,8,12-H_β), 9.28 (m, 4H; 2,13,17,18-H_β), 5.01(t, ^3J(H,H) = 8 Hz, 2H; $CH_2CH_2CH_2CH_3$), 2.55 (m, 4H; $CH_2CH_2CH_2CH_3$), 1.86 (m, 4H; $CH_2CH_2CH_2CH_3$), 1.18 (t, ^3J(H,H) = 7 Hz, 6H; $CH_2CH_2CH_2CH_3$), −3.35 ppm (brs, 2H; NH); UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 406 (5.50), 503 (4.12), 534 (3.39), 580 (3.60), 633 nm (3.17); MS (80 eV, EI): *m*/*z* (%): 423 (100) [M^+], 211 (4.00) [M^{2+}]; HRMS: *m*/*z* calcd for $C_{28}H_{30}N_4$: 394.2157; found: 394.2150.

5-(2-Methoxyphenyl)porphyrin (37)

Procedure D: A Schlenk flask was charged with *o*-bromoanisole (59 μL, 0.48 mmol) dissolved in dry diethyl ether (15 mL) under an argon atmosphere. The solution was cooled to −78°C. After dropwise addition of *n*-butyllithium in hexane (2.5 M, 0.19 mL, 0.48 mmol) within 30 min, the solution was stirred for one hour at room temperature. A solution of porphine **1** in dry THF (40 mL) was rapidly added to the organolithium compound at room temperature. The solution was stirred for one hour at 50–60°C. The porphyrin was purified by column chromatography on silica gel (CH_2Cl_2/*n*-hexane 2:1). After recrystallization from CH_2Cl_2/CH_3OH, the product was obtained as purple crystals (5 mg, 0.01 mmol, 17%). R_f = 0.65 (CH_2Cl_2/*n*-hexane 2:1); m.p. 300°C; ^{1}H NMR (250 MHz, $CDCl_3$, 25°C, TMS): δ = 10.28 (s, 2H; 10,20-H_{meso}), 10.23 (s, 1H; 15-H_{meso}), 9.45 (m, 4H; 12,13,17,18-H_β), 9.36 (AB, ^3J(H,H) = 5 Hz, 2H; 2,8-H_β), 9.01 (AB, ^3J(H,H) = 5 Hz, 2H; 3,7-H_β), 7.70 (m, 1H; H-Ph_m), 7.51 (m, 1H; H-Ph_m), 3.60 (s, 3H; OCH_3), −3.60 ppm (brs, 1H; NH); UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 399 (5.32), 494 (4.18), 526 (3.34), 567 (3.68), 620 nm (2.70); MS (80 eV, EI): *m*/*z* (%): 416 (100) [M^+], 401 (12) [M^+-CH_3], 385 (4) [M^+-OCH_3]; HRMS: *m*/*z* calcd for $C_{27}H_{20}N_4$: 416.16371; found: 416.16369.

X-ray single-crystal structure determination of 14a: Growth and handling of crystals followed the concept developed by Hope.[49] Intensity data were collected at 210 K with a Stoe X-area system complete with 3-circle goniometer and CCD detector utilizing $Mo_{K\alpha}$ radiation (λ = 0.71073 Å). The intensities were corrected for Lorentz, polarization, and extinction effects. The structure was solved with Direct Methods using the SHELXTL PLUS program system[50a] and refined against $|F^2|$ with the program XL from SHELX-97 using all data.[50b] Non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were generally placed into geometrically calculated positions and refined using a ridging model. The N–H hydrogen atoms were refined as disordered over all four positions with occupancies of 50% each. CCDC-259220 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal data: $C_{24}H_{22}N_4$, M_r = 366.46, red block from CH_2Cl_2/CH_3OH, crystal size 0.4 × 0.3 × 0.25 mm, orthorhombic, $P2_12_12_1$, a = 9.9802(5), b = 12.2819(9), c = 15.4053(9) Å, V = 1888.3(2) Å^3, Z = 4, ρ_{calcd} = 1.289 Mg m^{-3}, $\mu(Mo_{K\alpha})$ = 0.078 mm^{-1}, transmission min/max = 0.962/0.985, θ_{max} = 29.54°, 18934 reflections collected, 5248 independent reflections, R_{int} = 0.0344, 3977 reflections with $I > 2.0\sigma(I)$, 257 parameters, $R1$ ($I > 2.0\sigma(I)$) = 0.0344, $R1$ (all data) = 0.0494, $wR2$ (all data) = 0.0781, S = 0.956, ρ_{max} = 0.153 e Å^{-3}.

Normal-coordinate structural decomposition: The theoretical background and development of this method has been described by Shelnutt and coworkers.[38] For calculations we used the NSD engine program version 2.0, as provided on the WWW under the URL http://jasheln.unm.edu/jasheln/content/nsd/NSDengine/nsd_index.htm.

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[27] a) S. Neya, N. Funasaki, *Tetrahedron Lett.* **2002**, *43*, 1057–1058; b) Besides the good yields (70–80%), an additional advantage of this method is the formation of porphine in high purity in solution. This greatly facilitates purification and subsequent use in other reactions. A constant disadvantage of older methods was not so much the formation of porphine in sufficient quantity but the separation of the target compound from the polymeric mixture of other products formed during condensation reactions. Impure porphine is almost impossible to dissolve. Isopropanol can be used instead of 1-butanol.

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[29] The strong regioselectivity of S_NAr reactions with porphyrins for the *meso* position neighboring a substituted position (5,10-orientation) has been shown by us before.[8b–d]

[30] The number of equivalents used in this reaction is an estimate as formation of 2-MeOPhLi gave a viscous material that was difficult to use quantitatively for the subsequent reaction. Use of 10 equivalents lowered the yield of **37** to 10% without formation of the 5,10-disubstituted porphyrin. The different number of equivalents re-

quired for reaction of, for example, *n*BuLi, hexyllithium, or PhLi, is a reflection of the nature of the aggregates formed in solution.[31]

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