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Porphyrins bearing halogens at the *meso*-phenyl and β-pyrrolic[†] positions: synthesis and spectral properties[‡]

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Summary — The synthesis of symmetrical porphyrins chlorinated at both *ortho* positions of the *meso*-aryl substituents, and the chlorination and bromination of the β-pyrrole positions is reported. The β-chlorination of *meso*-tetraphenylporphyrin via its nickel(II) complex is also described. In addition, we communicate the first perchlorination of tetramesitylporphyrin, where halogen substitution occurred at the β-pyrrolic positions as well as at *both* the vacant *meta* positions of the trimethylphenyl groups. The iron complexes of these various polyhalogenated porphyrins are also described, since they are robust and efficient catalysts in oxidation reactions.

bromination / chlorination / metalloporphyrin / tetrakis(2,6-dichlorophenyl) porphyrin / heme / iron porphyrin / oxidation catalyst

Résumé — Porphyrines portant des halogènes substitués sur des *méso*-phényls ainsi qu'en position β-pyrrolique. *La synthèse de porphyrines chlorées à chacune des positions* ortho *des substituants aromatiques* méso *ainsi que les chloration et bromation des positions β des pyrroles sont décrites. La β-chloration des* méso-*tétraphénylporphyrine via ses complexes du nickel(II) est aussi exposée. Nous décrivons également la première perchloration de la tétramésitylporphyrine, dans laquelle la substitution par l'halogène se fait en positions β-pyrrolique ainsi qu'à chacune des positions* méta *vacantes des groupes triméthylphényl. Les complexes du fer de ces diverses porphyrines halogénées sont aussi décrits; ils sont stables et se révèlent des catalyseurs efficaces dans les réactions d'oxydation.*

bromation / chloration / métalloporphyrine / tétrakis(2,6-dichlorophényl)porphyrine / hème / fer-porphyrine / catalyseur d'oxidation

Introduction

Since our first report of *meso*-tetrakis-(2,6-dichlorophenyl)porphyrin [1], interest has grown steadily over the years regarding high-valent polyhalogenated metalloporphyrins as catalysts in oxidative reactions of organic substrates [1–10]. Despite significant advances made during the past ten years, preparation of suitable porphyrin derivatives that are sufficiently stable towards oxidative degradation, in the presence of strong oxygen donors, still remains a major challenge. It is known that the enhanced stability and efficiency of these metalloporphyrin catalysts are due to their stereochemical features and to the presence of electron-withdrawing halogen substituents [3–6, 8]. When directly substituted on the porphyrin macrocycle, these electronegative groups cause large anodic shifts, thus altering their redox properties to a substantial extent [11–13].

In addition the bulky groups around the periphery of the porphyrins cause distortion of the 'normally flat' porphyrin. The distortion of the porphyrins into saddle-shaped conformations and the effects this has on the redox properties of these systems is an area of research that is being actively pursued by Prof Weiss and his colleagues [14, 15].

Porphyrin derivatives with halogens substituted either on the *meso*-aryl groups [1, 16, 17], ('type A') or at the β-pyrrole positions [6, 11, 18–21] ('type B'), as well as at both sites [11, 22–24] ('type C') have been reported in the literature. We describe here in detail the synthesis of polychlorinated and polybrominated porphyrins which are of the *meso*-tetraphenylporphyrin (TPP) type, carrying up to 28 atoms of chlorine, and/or

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[†] The term β-pyrrolic is used to indicate the 2,3,7,8,12,13,17,18 positions of the porphyrin macrocycle.

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eight atoms of bromine at the β-pyrrolic positions. Preparation of their corresponding metal complexes are also described and relevant spectral properties are discussed.

For the syntheses reported here, four symmetrical porphyrins were used as precursors: *meso*-tetraphenylporphyrin (H_2TPP, **1a**) (prepared by the procedure of Adler and coworkers [25, 26]), *meso*-tetrakis-(2,6-dichlorophenyl)- and -(pentachlorophenyl)-porphyrin (H_2TPPCl_8, **3a** and H_2TPPCl_{20}, **7a**) (made from a modified [1, 27] Hill [28]/Rothemund [29] procedure and/or from Lindsey's electron transport chain method [30, 31]), and *meso*-tetrakis(2,4,6-trimethylphenyl) porphyrin (H_2TMP, **9a**) (prepared by the Lindsey [30-34, 44] methods). These free base porphyrins, after insertion of the appropriate metal, were then halogenated.

Results and discussion

In previous studies, β-polybromination of *meso*-tetraphenylporphyrin derivatives with *N*-bromosuccinimide (NBS) led to several brominated products [21–23, 35], but the analogous chlorination reactions using *N*-chlorosuccinimide (NCS) gave either mono- or disubstituted products [36] or, as observed in this work, led to the destruction of the macrocycle. It was also found that attempts to polychlorinate H_2TPPCl_8 (**3a**) or its Zn(III) or Fe(III) complexes (**3b**, **3c**) with excess NCS failed, no reaction being observed even after heating for 5 h at 140 °C [11]. We also observed that chlorination of **1a** using SO_2Cl_2 in the presence of $AlCl_3$ resulted in the destruction of the porphyrin. In this study we describe the synthesis of several polychlorinated *meso*-tetraphenylporphyrin derivatives where primarily chlorine gas is used as the halogenating agent in the presence of anhydrous $FeCl_3$. By this method the hemin complexes *meso*-tetrakis-(2,6-dichlorophenyl)porphinato-iron(III)chloride (**3c**, $Fe(TPPCl_8)Cl$), *meso*-tetrakis(pentachlorophenyl)-porphinato-iron(III)chloride (**7c**, $Fe(TPPCl_{20})Cl$) and *meso*-tetrakis(2,4,6-trimethylphenyl)porphinato-iron(III) chloride (**9c**, Fe(TMP)Cl), which are derived from their corresponding free base porphyrins **3a**, **7a** and **9a**, were successfully chlorinated.

Except in the case of the hemin derivative of *meso*-tetramesitylporphyrin, the principle chlorination sites in all compounds are the β-pyrrolic positions of the macrocycle, and not the phenyl substituents. In contrast, attempted β-chlorination of the Fe(III) complex of *meso*-tetraphenylporphyrin (**1d**, Fe(TPP)Cl) with Cl_2 gas and $FeCl_3$ in *o*-dichlorobenzene (ODCB) resulted in complete destruction of the macrocycle. A similar result was seen when **1d** or its free base **1a** was reacted with NCS in ODCB for 15 h at 80–100 °C. In addition, the reaction of CuTPP (**1c**) with NCS in the same solvent at 140 °C for 15 h led to the partial destruction of the complex.

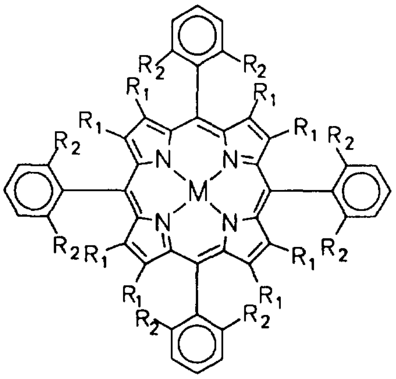
We also attempted the β-chlorination of Zn(TPP) (**1e**) with NCS in ODCB. The reaction was initiated at 80 °C with 12 equiv NCS, after which the temperature was increased to 140 °C over 2 h; after 3.5 h reaction, another 12 equiv of NCS was added. Although a progressive bathochromic shift of the Soret band was observed (suggesting slow β-chlorination), the UV-vis spectrum indicated complete decomposition after 5 h. In a subsequent attempt, the porphyrin was heated directly at 140 °C, then 11 equiv of NCS was added; the Soret band shifted to 444 nm after 7 h. After cooling, the complex was demetallated with trifluoroacetic acid (TFA). However the UV-vis spectrum of the neutralized product indicated only partial chlorination of the macrocycle. When chlorination was attempted in refluxing CCl_4 with 12 equiv of NCS, no noticeable reaction occurred even after 5 h. Nevertheless in a recent study, the chlorination of **1e** with NCS has been achieved in refluxing $CHCl_3$, with only a 10% yield, but the reactants were irradiated with a 1 kW tungsten daylight lamp [24], which indicates a free-radical, rather than an ionic mechanism.

However, Ni(TPP) (**1b**) reacted with NCS at 140 °C for 1.5 h in ODCB to give the β-chlorinated derivative $Ni(TPP\beta Cl_8)$ (**2b**) in good yield (78%). The red shift of the Soret band from 414 to 440 nm upon halogenation indicates chlorination of the eight β-pyrrole positions [11], in addition a 28 nm shift of the β-band (from 526 to 554 nm) was observed. The ^1H NMR spectrum of the complex also confirmed that chlorination took place only on the β-pyrrolic positions. Interestingly, as observed for **1d**, the reaction of **1b** with Cl_2 gas/$FeCl_3$ in ODCB resulted in the destruction of the porphyrin macrocycle.

In concentrated sulfuric acid, **2b** is demetallated to its free base **2a** (90% yield); it can be converted to the corresponding hemin $Fe(TPP\beta Cl_8)Cl$ (**2c**) with an 85% yield by the standard $FeCl_2{\cdot}4H_2O$/DMF procedure [37, 38] (scheme 1, protocol 1 in the *Experimental section*).

The analogous β-brominated copper complex $Cu(TPP\beta Br_8)$ (**5b**) had already been prepared by reacting **1c** with liquid Br_2 in $CHCl_3/CCl_4$ (v/v, 1:1), and after demetallation in perchloric acid the free base **5a** was converted to several metallated derivatives, although no iron insertion was reported [19]. In that preparation, the use of perchloric acid for demetallation of the copper complex was found to be unsatisfactory. Therefore we used an alternative procedure to prepare the free base as well as its hemin derivative **5c**; a smooth demetallation occurred when a biphasic mixture of the copper complex in toluene/conc H_2SO_4 (v/v, 1:1) was stirred at room temperature for 1 h, leading to the free base **5a** in 86% yield (scheme 2, protocol 2 in *Experimental section*).

In contrast, β-bromination of H_2TPPCl_8 (**3a**) was carried out via its Zn complex **3b** with NBS in CCl_4, affording the expected $Zn(TPPCl_8\beta Br_8)$ (**4b**), which was converted to its free base **4a** using TFA in CH_2Cl_2 (scheme 1). The detailed procedure and UV-visible spectral characteristics have already been published by Traylor and Tsuchiya [22, 23]. This work was challenged by Rocha Gonsalves and coworkers [24] who failed to obtain the β-brominated derivative using CCl_4 as solvent, as described. But an erratum [23] to his communication was published later by Traylor, mentioning that "the bromination must be carried out under scrupulous anhydrous conditions". Nevertheless, Rocha Gonsalves and coworkers did achieve β-bromination



1a $R_1=R_2=H$, M=2H
1b $R_1=R_2=H$, M=Ni
1c $R_1=R_2=H$, M=Cu
1d $R_1=R_2=H$, M=FeCl
1e $R_1=R_2=H$, M=Zn
2a $R_1=Cl$, $R_2=H$, M=2H
2b $R_1=Cl$, $R_2=H$, M=Ni
2c $R_1=Cl$, $R_2=H$, M=FeCl
3a $R_1=H$, $R_2=Cl$, M=2H
3b $R_1=H$, $R_2=Cl$, M=Zn
3c $R_1=H$, $R_2=Cl$, M=FeCl
4a $R_1=Br$, $R_2=Cl$, M=2H
4b $R_1=Br$, $R_2=Cl$, M=Zn
4c $R_1=Br$, $R_2=Cl$, M=FeCl

$$\mathbf{1b} \xrightarrow{\text{NCS}} \mathbf{2b} \xrightarrow{H_2SO_4} \mathbf{2a} \xrightarrow{FeCl_3} \mathbf{2c}$$

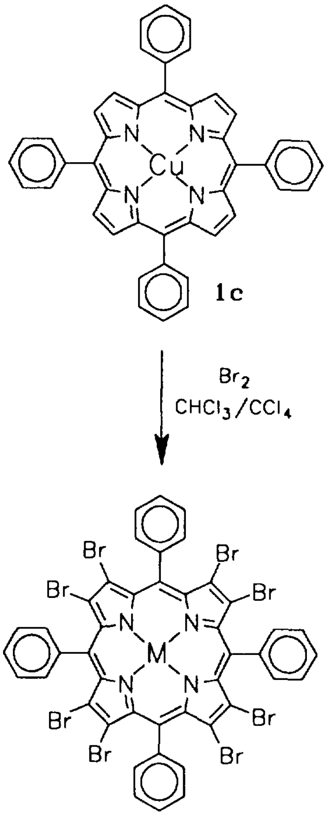
$$\mathbf{3b} \xrightarrow{\text{NBS}} \mathbf{4b} \xrightarrow{\text{TFA}} \mathbf{4a} \xrightarrow{FeCl_3} \mathbf{4c}$$

Scheme 1. β-Halogenation using *N*-halogenosuccinimides.

of Zn($TPPCl_8$) using tetrachloroethene [24] instead of CCl_4. Ellis and Lyons have also reported [35] this reaction using Traylor's conditions, but they obtained the tetrabrominated derivative Zn($TPPCl_8\beta Br_4$).

Attempts to insert iron into the β-brominated compounds **5a** and **4a** by the standard $FeCl_2{\cdot}4H_2O$/DMF procedure [37, 38] resulted in extensive decomposition of the porphyrins. These free bases were eventually converted to the corresponding hemins **5c** and **4c** by treating a refluxing toluene/AcOH (v/v, 3:1) solution of the porphyrin with anhydrous $FeCl_3$/NaOAc [39] (w/w, 3:1), which gave yields of 45 and 42% respectively (see protocols 2 and 4 in the *Experimental section*).

meso-Tetrakis(2,6-dichlorophenyl)porphyrin (**3a**) had been prepared earlier by Kim and coworkers [40], using a modification of the original Adler's condensation [25], where 2,6-dichlorobenzaldehyde, glacial acetic acid and pyrrole were refluxed in a benzene solution for 3 h, affording a poor yield of only 0.7%. We have synthesized **3a** from its zinc complex **3b** prepared by a modified [1, 27] Hill [28]/Rothemund [29] method (protocol 3 in *Experimental section*). As an alternative to performing the reaction in a stainless steel autoclave, which required heating in pyridine at 175 °C for 48 h, our simplified procedure uses a Soxhlet extractor with a thimble loaded with a drying agent (such as anhydrous Na_2SO_4), which removes water formed in the reaction. In addition, pyridine was replaced by 2,6-dimethylpyridine. In a previous communication [1], Traylor and coworkers used 2,4,6-trimethylpyridine, but our alternative solvent presents the advantage of a lower boiling point (144 °C instead of 172 °C) and hence it can be removed on a rotary evaporator; this substitution of 2,4,6-trimethylpyridine did not noticeably affect the yield of the isolated porphyrin **3b**. Stirring in $CHCl_3$/TFA (v/v, 30:1) for 1 h afforded the impure free base **3a** (87% yield) which was rendered chlorin-free [29, 41–43] by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (**3a**, 95% yield). The overall yield based on pyrrole is about 4%.



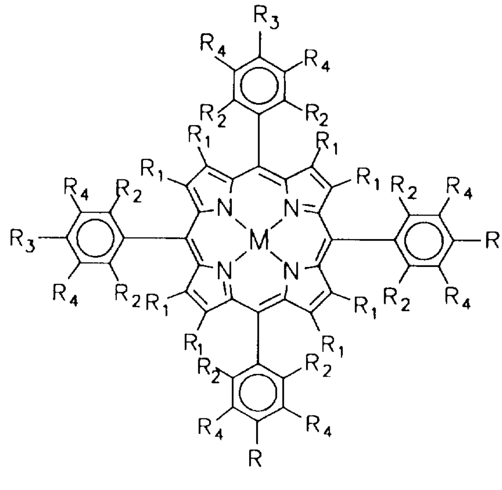
5a M=2H
5b M=Cu
5c M=FeCl

$$\mathbf{5b} \xrightarrow{H_2SO_4} \mathbf{5a} \xrightarrow{FeCl_3} \mathbf{5c}$$

Scheme 2. β-Bromination using molecular bromine.

Moreover, although the method of Lindsey [32–34, 44] has been used recently to prepare **3a** in higher yields [16, 20] (from 10 to 30% depending on the reaction conditions), the volume of solvent involved is impractical where large scale preparations (several grams) are required; consequently the Hill/Rothemund method remained (until recently) the method of choice in these scaled-up preparations. However, the recently published [30] 'electron transport chain' method (where *meso*-porphyrins are prepared at room temperature and at high concentration) shed new light on porphyrin synthesis and prompted us to apply this new approach to the large scale preparation of **3a**, using the 'two-step aerobic synthesis', where the reaction vessel is charged with ethanol-stabilized chloroform, tetrachloro-1,4-benzoquinone (TCQ), phthalocyanine-iron(II) (FePc), 2,6-dichlorobenzaldehyde and pyrrole. The mixture is degassed, before adding boron trifluoride etherate ($BF_3{\cdot}Et_2O$) as catalyst (1st step), then stirred at room temperature for 30–45 min after which it is oxidized by air for 90–120 min (2nd step). The processing and purification are simplified, and the reaction can be performed at a concentration similar to that of the original Adler's method, allowing gram-scale preparations (>8 g/L (11.3%)). The detailed procedure is described elsewhere [31].

Prior to β-chlorination, the free base **3a** was converted to the corresponding hemin **3c** by the standard $FeCl_2{\cdot}4H_2O$/DMF procedure [37, 38] in near quantitative yield. Chlorination was carried out in ODCB at 140 °C in the presence of anhydrous $FeCl_3$, by bubbling Cl_2 gas for 5 min, with continuous stirring and heating [11, 27]. The reaction, monitored by UV-vis spectroscopy, was stopped after 30 min: the double Soret, initially at 370/420 nm, shifted to 396/444 nm upon completion of the chlorination of the eight β-pyrrolic positions. The β-chlorinated derivative Fe(TPPCl$_8$βCl$_8$)Cl (**6b**) was isolated in good yield (88%), and characterized by UV-vis and mass spectroscopy and its elemental analysis indicated a high degree of purity. A small sample (9%) of the corresponding free base H$_2$TPPCl$_8$βCl$_8$ (**6a**), formed during the chlorination process in the highly acidic reaction medium, was recovered during the chromatography of the crude product (scheme 3; protocol 5 in *Experimental section*). In this chlorination method, we observed that an insufficient quantity of $FeCl_3$ decreases the reaction rate, and leads to a higher yield of demetallated β-chlorinated material.



3c $R_1=R_3=R_4=H$, $R_2=Cl$, $M=FeCl$
6a $R_1=R_2=Cl$, $R_3=R_4=H$, $M=2H$
6b $R_1=R_2=Cl$, $R_3=R_4=H$, $M=FeCl$
7a $R_1=H$, $R_2=R_3=R_4=Cl$, $M=2H$
7b $R_1=H$, $R_2=R_3=R_4=Cl$, $M=Zn$
7c $R_1=H$, $R_2=R_3=R_4=Cl$, $M=FeCl$
8a $R_1=R_2=R_3=R_4=Cl$, $M=2H$
8b $R_1=R_2=R_3=R_4=Cl$, $M=FeCl$
9a $R_1=R_4=H$, $R_2=R_3=CH_3$, $M=2H$
9b $R_1=R_4=H$, $R_2=R_3=CH_3$, $M=Zn$
9c $R_1=R_4=H$, $R_2=R_3=CH_3$, $M=FeCl$
10 $R_1=R_4=Cl$, $R_2=R_3=CH_3$, $M=FeCl$

$$\mathbf{3c} \xrightarrow{Cl_2/FeCl_3} \mathbf{6b} \xrightarrow{H^+} \mathbf{6a}$$

$$\mathbf{7c} \xrightarrow{Cl_2/FeCl_3} \mathbf{8b} \xrightarrow{H^+} \mathbf{8a}$$

$$\mathbf{9c} \xrightarrow{Cl_2/FeCl_3} \mathbf{10}$$

Scheme 3. β-Chlorination using molecular chlorine/$FeCl_3$.

The use of ODCB as solvent presents several difficulties: toxicity and high boiling point (180 °C), and hence a relatively complicated work-up. In addition, ODCB is partially chlorinated during the reaction process, leading to tetra- and pentachlorobenzenes which are not readily removed and affect the subsequent chromatography. Therefore chlorination of **3c** with Cl_2 gas was also attempted in acetic acid, a lower boiling and less toxic solvent. This preliminary experiment (see protocol 5 in the *Experimental section*) gave the β-chlorinated product **6b** with a reduced yield (45%). The MS spectrum of this product showed the expected patterns, although the peaks centered at $m/z = 1\,184$ were significantly higher in intensity relatively to the base peak MS = 1 220 (by a factor of ~ 3) than that observed for the same product synthesized using ODCB as solvent. This suggests that the isolated compound is probably contaminated by some β-heptachlorinated by-product.

Recently, Chorghade, Dolphin and coworkers [31] developed improved procedures for the perhalogenation of the porphyrin ring of *meso*-tetrakis(2,6-dichlorophenyl)porphyrin (**3a**). Both β-bromination and β-chlorination were performed via the zinc complex **3b** in CH_3OH following the work of Meunier and coworkers [6]. β-Bromination was carried out at reflux using NBS or *N*-bromoacetamide (NBA), or at room tem-

Table I. Optical absorption data of 'type A' porphyrins[a].

	Compound		*Soret*		*Q-IV*	*Q-III*	β	*Q-II*	α	*Q-I*
1a	H_2TPP^{29} (in benzene)		419 (478)	485 (3)	515 (19)	548 (8)		592 (5)		647 (3)
3a	$H_2TPPCl_8^{31}$	400sh (86)	417 (393)	479 (3)	512 (22)	540 (3)		587 (7)		643 (0.4)
3b	$Zn(TPPCl_8)^{31}$	400 (45)	420 (371)		512 (2)		550 (21)		584 (2)	
3c	$Fe(TPPCl_8)Cl$	365 (58)	417 (124)		508 (15)			578 (5)		643 (5)
7a	H_2TPPCl_{20}	402sh (104)	420 (395)	482sh (4)	514 (25)	544sh (4)		590 (8)		646 (1)
	(TFA added)	414sh (0.24)	434 (1.00)		506sh (0.01)	542 (0.02)	576 (0.09)		626 (0.04)	
7c	$Fe(TPPCl_{20})Cl$	355 (54)	420 (103)		510 (15)			576 (7)		638 (6)

[a] In CH_2Cl_2.

perature using molecular bromine, and β-chlorination was carried out at reflux using NCS or at 0–5 °C using molecular chlorine.

The hemin complex $Fe(TPPCl_{20})Cl$ (**7c**) prepared in this study was obtained via the zinc derivative **7b**, which was synthesized with a 2.9% yield by the Hill [1, 28] method, although in our preparation the reflux was continued for 48 h instead of 3 h (protocol 6 in *Experimental section*). As for **3b** above, treatment with TFA (10% in CH_2Cl_2) afforded the impure free base H_2TPPCl_{20} (**7a**), which was subsequently oxidized by DDQ [29, 41–43] to give **7a** (93% yield), then converted to its corresponding hemin **7c** with a 76% yield [37, 38]. The chlorination of **7c** was again carried out with Cl_2 gas under similar experimental conditions to those reported [11, 27] above for **3c**. As expected, the Soret band, initially at 420 nm, red-shifted to 444 nm upon completion of the reaction. The β-chlorinated derivative $Fe(TPPCl_{20}\beta Cl_8)Cl$ (**8b**) was isolated in 70% yield and analyzed by UV-vis and mass spectroscopy. A small quantity of free base **8a** (UV-vis: 446, 544, 576 sh, 630 nm) was recovered during the chromatography, as already observed for the β-chlorination of **3c** (scheme 3; protocol 7 in the *Experimental section*).

An alternative procedure for the synthesis of the free base **7a** had been reported previously by Longo [17] and coworkers. These authors used an acid-catalyzed condensation of pentachlorobenzaldehyde and pyrrole in a benzene solution of monochloracetic acid where the yield, before isolation of the porphyrin, was indicated as "7% spectrophotometric". However as the isolated yield was not communicated, we are unable to evaluate the efficiency of this method in comparison to our procedure.

The chlorination of Zn(TMP) (**9b**) with NCS has been reported recently [6]. This reaction gave a product formulated as $Zn(TMPCl_4\beta Cl_8)$, where chlorination had occurred at the eight β-pyrrolic positions and additionally at *one* meta position on each mesityl group. However in our study, when the analogous hemin derivative Fe(TMP)Cl (**9c**) was halogenated using $Cl_2/FeCl_3$, further chlorination of the remaining four *meta* positions took place, leading to $Fe(TMPCl_8\beta Cl_8)Cl$ (**10**) with a 38% yield (scheme 3; protocol 8 in the *Experimental section*). The mass spectrum of the compound with the main peaks centered at $m/z = 1\,388$ (base) and 1 423 (M^+) is in agreement with computer-simulated isotope patterns [45] for the formula $C_{56}H_{36}N_4Cl_{16}Fe$ (without axial ligands) and $C_{56}H_{36}N_4Cl_{17}Fe$ for the hemin chloride.

The iron complex **9c** was prepared from its free base H_2TMP (**9a**) in a manner similar to the other hemins discussed in this study [37, 38, 46, 47]. The free base [6, 32, 44] was synthesized using the Lindsey [32–34] method and obtained in 25% yield. We also prepared **9a** using the newer Lindsey's electron transport chain method, at a concentration three times higher [31] than described originally by Lindsey [30]. In this case, the yield was reduced only slightly (12.1%) compared to 15.7% when the reaction was carried out at 0.1 M concentration. This shows that the reaction is more productive when performed at a concentration similar to that of the original Adler's method [25] (see protocol 8 in the *Experimental section*).

It would have been interesting to synthesize porphyrins of type **C** such as the hemins **6b** and **8b**, via a type **B** complex, thus avoiding the difficult and costly preparation of type **A** porphyrins (**3a**, **7a**). Unfortunately, our attempt to chlorinate the phenyl positions of $Ni(TPP\beta Cl_8)$ (**2b**) using the $Cl_2/FeCl_3$ method (in ODCB) failed, resulting in the destruction of the macrocycle.

For all the β-halogenated porphyrins, a bathochromic shift for the Soret band has been observed in their UV-vis spectra; the shift is approximately 3 to 3.5 nm per added chlorine atom [11] and 4.5 to 6.5 nm per additional bromine atom [19, 22–23]. For easy comparison, UV-vis data of the halogenated porphyrins, as well as their non-halogenated precursors, are conveniently presented in tables I–III ("types A, B and C" porphyrins respectively).

It is clear from halogenations of the various metallated TPP derivatives that the centrally coordinated

Table II. Optical absorption data of 'type B' porphyrins[a].

	Compound		*Soret*		*Q-IV*	*Q-III*	*β*	*Q-II*	*α*	*Q-I*
1b	Ni(TPP)[57] (in benzene)		416 (233)	490 (3)			529 (17)		560sh (n/a)	
1c	Cu(TPP)[57] (in benzene)		417 (447)	505 (4)			540 (20)		580sh (2)	
1d	Fe(TPP)Cl[58] (in $CHCl_3$)	380 (59)	417 (110)		511 (13)			577 (3)	658 (3)	690 (3)
2a	$H_2TPP\beta Cl_8$ (TFA added)		452 482			552		602		720 736
2b	$Ni(TPP\beta Cl_8)$		440 (226)				554 (18)		584sh (7)	
2c	$Fe(TPP\beta Cl_8)Cl$	404 (66)	448 (70)		526 (12)			560 (9)		770 (3)
5a	$H_2TPP\beta Br_8$[19]	370 (33)	469 (204)			569 (9)		626 (13)		743 (7)
5b	$CuTPP\beta Br_8$[19]	365 (28)	466 (132)				581 (18)		625sh (n/a)	
5c	$Fe(TPP\beta Br_8)Cl$	416 (49)	458 (58)		532 (12)			576 (8)		

[a] In CH_2Cl_2.

Table III. Optical absorption data of 'type C' porphyrins[a].

	Compound		*Soret*		*Q-IV*	*Q-III*	*β*	*Q-II*	*α*	*Q-I*
4a	$H_2TPPCl_8\beta Br_8$[22,23]		462 (1)			557 (0.07)		598 (0.03)		603sh (n/a)
4b	$ZnTPPCl_8\beta Br_8$[22,23]		468 (1)				602 (0.06)		660sh (n/a)	
4c	$Fe(TPPCl_8\beta Br_8)Cl$	402 (0.86)	454 (1.00)		514sh (0.26)			572 (0.19)		
6a	$H_2TPPCl_8\beta Cl_8$		446 (176)			542 (16)		580sh (5)		630 (4)
6b	$Fe(TPPCl_8\beta Cl_8)Cl$	396 (56)	444 (60)		504 (11)			560 (8)		708 (3)
8a	$H_2TPPCl_{20}\beta Cl_8$		446 (n/a)			544 (n/a)		576sh (n/a)		630 (n/a)
8b	$Fe(TPPCl_{20}\beta Cl_8)Cl$ (in $CHCl_3$)	396 (66)	444 (76)					560sh (10)		
9a	H_2TMP[32,b]	403sh	418 (427)	480sh (1)	514 (16)	547 (4)		590 (5)		647 (3)
9c	Fe(TMP)Cl[56] (in toluene)	370 (54)	420 (128)		508 (14)			572 (5)	656 (3)	594 (4)
10	$Fe(TMPCl_8\beta Cl_8)Cl$	396 (0.86)	446 (1.00)		528sh (0.22)			560sh (0.17)		

[a] In CH_2Cl_2. [b] In CH_2Cl_2/ethanol 3:1.

metal exerts an important influence on the peripheral electrophilic substitution reaction at the β-pyrrolic sites. In an earlier study [48], the site of nitration on a series of metalloporphyrins was found to be dependent on the coordinated metal ion with Cu(II), Ni(II) and Pd(II) complexes been nitrated specifically on the β-pyrrolic positions while Mg(II), Zn(II), ClFe(III) and Co(II) complexes also gave products nitrated at the *meso* positions when not substituted by phenyl groups.

Some halogenated and perhalogenated iron and manganese porphyrins have also been sulfonated previously to obtain sterically protected water-soluble complexes

[27, 49] which are found to be suitable catalysts in the modeling of the lignin-degrading enzyme ligninase [50–52].

Conclusion

We have shown that the halogenation of porphyrin derivatives can be achieved using primarily two methods, the choice of which depends on the porphyrin being halogenated: (a) the '*N*-halogenosuccinimide method', for the β-bromination of Zn(TPPCl$_8$) (**3b**), and for the β-chlorination of Ni(TPP) (**1b**) (scheme 1), and (b) the 'molecular halogen method', for the β-chlorination of Fe(TPPCl$_8$)Cl (**3c**), Fe(TPPCl$_{20}$)Cl (**7c**) and Fe(TMP)Cl (**9c**) (scheme 3), the latter being chlorinated on the remaining vacant positions of the phenyl rings as well.

Experimental section

Instrumental analysis

UV-vis spectra were recorded in CH_2Cl_2 unless otherwise specified, either on Hewlett-Packard 8452A or on Cary 17D spectrophotometers; λ_{max} are given in nm and extinction coefficients ε in mol^{-1} mL cm^{-1}. Mass spectra were obtained on a Kratos MS 50 spectrometer for low resolution mass spectrometry (LRMS) (EI, 70 eV) and an AEI MS 9 spectrometer (FAB); the peak values are followed by their intensity, given as a percentage of the most intense peak observed in the spectrum. The observed mass spectral data of the respective compounds were matched with computer-simulated isotope patterns [45]. NMR spectra were obtained at 300 and 400 MHz on Varian XL-300 and Bruker WH-400 spectrometers. Chromatographic separations were performed using columns (Merck 60, 230–400 mesh (unless otherwise stated) silica gel, or Fischer neutral alumina, Brockman activity I, 80–200 mesh). Reactions were followed by thin-layer chromatography (TLC) using Merck 60 F$_{254}$ silica gel plates (0.2 mm thickness).

In general, the products were purified further by chromatography followed by recrystallization and overnight drying under vacuum, before obtaining spectral data and microanalysis.

Materials and methods

Boron trifluoride etherate ($BF_3 \cdot Et_2O$) was distilled according to Zweifel [53]; pentene-stabilized [34] chloroform was distilled from K_2CO_3; pentachlorobenzaldehyde was prepared by treatment of the Grignard derivative of hexachlorobenzene with DMF [54, 55]; pyrrole was refluxed for 1 h under argon with CaH_2, then distilled under atmospheric pressure; 2,4,6-trimethylbenzaldehyde was used as received; 2,4,6-trimethylpyridine was distilled under reduced pressure from $MgSO_4$; anhydrous zinc acetate was prepared by drying the commercial salt in a Schlenk tube under high vacuum at 120 °C for 4 h, then overnight at room temperature.

Protocol 1

- meso-*Tetraphenyl-β-octachloroporphinato-nickel(II)* **2b**

The nickel complex **1b** [38] (671 mg; 1.0 mmol) was dissolved in ODCB (75 mL) and placed in a 125 mL three-necked round-bottomed flask (RBF); NCS (1.6 g; 12.0 mmol) was added and the solution heated to 140 °C [11]. The reaction, monitored by UV-vis (Soret band shifts from 414 to 440, while in the visible region the spectrum changed from 526, 616 to 554, 582sh), was complete in 90 min. The solvent was removed in vacuo, the residue dissolved in $CHCl_3$ (60 mL) (a better solvent than CH_2Cl_2) and chromatographed on alumina (300 g), using $CHCl_3$. The product eluted cleanly as a reddish-yellow solution and was crystallized by concentration to 50 mL followed by addition of methanol. The crystals were collected by filtration, rinsed with methanol and dried, affording 736 mg (0.78 mmol, yield = 77.8%) of **2b**.

UV-vis: λ_{max} (ε): 440 (226), 554 (18), 584 sh (7).

LRMS: The shape of the cluster of peaks in this region corresponds to the complex containing one Ni and eight chlorine atoms [45].

EI HRMS m/z calculated for $^{58}NiC_{44}H_{20}N_4{}^{35}Cl_8$, 941.8550; found: 941.8555.

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.88 (8H, dd, H *ortho* phenyl, J = 6.3 and 1.3 Hz), 7.66 (12H, m, H *meta* and *para* phenyl).

^{13}C NMR (75.4 MHz, $CDCl_3$) δ (ppm): 140.30 (α), 135.55 (*ipso*), 134.45 (β), 133.83 (*o*), 129.34 (*p*), 128.01 (*m*), 119.04 (*meso*).

Anal calc (found) for $C_{44}H_{20}N_4Cl_8Ni$: C, 55.81 (55.75); H, 2.13 (2.17); N, 5.92 (5.92); Cl, 29.95 (29.79).

- meso-*Tetraphenyl-β-octachloroporphyrin* **2a**

A solution of **2b** (209 mg; 0.22 mmol) in CH_2Cl_2 (70 mL) was stirred with conc sulfuric acid (50 mL) at room temperature. Within 5 min, a shiny green solid separated from the green-brown emulsion. After a further 15 min of stirring, the mixture was poured onto ice (500 g) and CH_2Cl_2 (300 mL) was added to dissolve the solids. The dichroic organic layer (yellow-green) was separated while the aqueous one was extracted once with CH_2Cl_2/TFA (100 mL/3 mL). The combined organic phase was washed with saturated aqueous $NaHCO_3$, then twice with water, and dried over Na_2SO_4. The compound was crystallized after concentration and addition of methanol, affording 176 mg (0.20 mmol, yield = 89.5%) of **2a**.

UV-vis: λ_{max}: (green solution) 452, 552, 602, 720; (TFA added, yellow solution): 482, 736.

LRMS: 890 (M^+).

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.43 (8H, d, H *ortho* phenyl, J = 6.4 Hz), 7.96 (12H, m, H *meta* and *para* phenyl); NH was not be detected.

^{13}C NMR (75.4 MHz, 10% w/w TFA/$CDCl_3$) δ (ppm): 141.72 (α), 137.26 (*o*), 134.10 (*ipso*), 132.54 (*p*), 129.63 (*m*), 128.99 (β), 121.78 (*meso*).

- meso-*Tetraphenyl-β-octachloroporphinato-iron(III) chloride* **2c**

The free base **2a** (123 mg; 0.14 mmol), $FeCl_2 \cdot 4H_2O$ (500 mg; 2.52 mmol) and DMF (100 mL) were deoxygenated and refluxed under argon [37, 38] in a 250 mL RBF. The progress of the reaction was monitored by UV-vis, an aliquot being diluted in CH_2Cl_2 (the free base exhibits a Soret at 452, which is shifted to 446 nm upon completion of the reaction); metal insertion was complete in 1 h. Heating was discontinued and the solution was stirred *open to the air* and allowed to cool at room temperature. After removing solid $FeCl_3$ by filtration, the solution was concentrated in vacuo to approximately 60 mL, and 5 N HCl (120 mL) was added; the hemin precipitated out as a brown solid. After filtration, it was thoroughly washed with water and dried in a vacuum desiccator.

This product was purified by chromatography on silica (20 g). Some uncharacterized compounds were separated with CH_2Cl_2 as eluent, then the hemin was eluted using

5% CH_3OH in CH_2Cl_2 (v/v). This was evaporated to dryness, redissolved in CH_2Cl_2, treated once with an equal volume of 2 N HCl [37, 56], washed with water until neutral and dried over Na_2SO_4. The hemin was recrystallized from CH_2Cl_2/hexane, affording 96 mg (0.10 mmol, 71.0% yield) of **2c**.

UV-vis: λ_{max} (ε): 404 (66), 448 (70), 526 (12), 560 (9), 770 (3).

LRMS: 944 (M^+ - Cl).

Anal calc (found) for $C_{44}H_{20}N_4Cl_9Fe$: C, 53.95 (54.36); H, 2.06 (2.23); N, 5.72 (5.55); Cl, 32.57 (32.25).

Protocol 2

- meso-*Tetraphenyl-β-octabromoporphyrin* **5a**

The copper complex **5b** [19] (128 mg; 9.79 × 10^{-5} mol) was dissolved in toluene (30 mL), and concentrated sulfuric acid (30 mL) was added. The heterogeneous mixture was stirred at room temperature for 1 h then poured onto crushed ice, extracted with toluene, washed once with a saturated aqueous solution of $NaHCO_3$, then three times with water, and finally dried over Na_2SO_4. The free base **5a** was crystallized from CH_2Cl_2/MeOH (108 mg; 8.67 × 10^{-5} mol) (yield = 85.5%).

Spectral characteristics were identical to those previously published [19].

- meso-*Tetraphenyl-β-octabromoporphinato-iron(III) chloride* **5c**

The free base **5a** (63 mg; 5.06 × 10^{-5} mol) was dissolved in toluene (50 mL), while anhydrous $FeCl_3$ (10 mg, 6.16 × 10^{-5} mol) and NaOAc (3 mg) were dissolved in glacial acetic acid [39] (20 mL); the two solutions were added together in a 125 mL RBF and the mixture was refluxed (color turns from green to brown). The progress of the reaction was monitored by UV-vis spectroscopy; after 30 min, the Soret band had shifted to 416/458 nm. Heating was discontinued after 1 h and the solution was washed three times with water then dried over Na_2SO_4. The hemin was purified by chromatography on silica (15 g). Elution with toluene removed a small amount of an uncharacterized green product, then the iron complex was eluted with 2% CH_3OH/CH_2Cl_2. After evaporation to dryness and redissolution in toluene, the compound was treated with 2 N HCl [37, 56] washed with water until neutral, and dried over Na_2SO_4. Attempts to precipitate the product failed, and hence it was lyophilized from a benzene solution, affording 30 mg (2.25 × 10^{-5} mol) of **5c** (yield = 44.5%).

UV-vis: λ_{max} (ε): 416 (49), 458 (58), 532 (12), 576 (8).

LRMS: (peak of maximum intensity within each isotopic cluster) 660 (1.7), 740 (1.3), 820 (1.4), 900 (0.8), 980 (0.3), 1058 (0.1), 1140 (0.2), 1220 (0.7), 1300 (base, 1.5) [45].

Protocol 3

- meso-*Tetrakis(2,6-dichlorophenyl)porphyrin* **3a**

The detailed procedures for the modified Hill/Rothemund method (isolation of the crude zinc complex **3b**, demetallation (**3a**) and oxidation of the chlorin impurity), as well as for the electron transport chain method, are described elsewhere [31].

Protocol 4

- meso-*Tetrakis(2,6-dichlorophenyl)-β-octabromoporphinato-iron(III) chloride* **4c**

The free base **4a** [22, 23] (10 mg; 6.57 × 10^{-6} mol) was metallated in toluene/AcOH (8 mL/2 mL) by anhydrous $FeCl_3$/NaOAc (2.7 mg/0.8 mg) under similar reaction conditions [39] to that of **5a**. However, the reflux was prolonged overnight: the principal UV-vis bands shifted from 462, 558 to 454, 576 nm. After work-up and chromatography, lyophilization afforded 4.4 mg (2.73 × 10^{-6} mol) of **4c** (yield = 41.6%).

UV-vis: λ_{max} (rel int): 402 (0.86), 454 (1), 514 sh (0.26), 572 (0.19).

No MS spectrum could be obtained.

Protocol 5

- meso-*Tetrakis(2,6-dichlorophenyl)porphinato-iron(III) chloride* **3c**

The free base **3a** (1.22 g; 1.37 mmol), $FeCl_2 \cdot 4H_2O$ (2.73 g; 13.7 mmol), and DMF (400 mL) were degassed and refluxed under argon [37, 38] in a 1 L RBF. The progress of the reaction was monitored by UV-vis in CH_2Cl_2. The single sharp absorption at 417 changed to a split Soret at 360/417 while in the visible region the spectrum changed from 512, 587 to 508, 578, 643 nm. Metal insertion was complete in 3 h. Heating was discontinued and the solution was stirred *open to the air* and allowed to cool at room temperature. After removing solid $FeCl_3$ by filtration, the solution was concentrated in vacuo to approximately 250 mL, and 5 N HCl (750 mL) was added; the hemin precipitated out as a brown solid from a clear yellow solution. After filtration, it was thoroughly washed with water and dried in a vacuum desiccator.

This product was redissolved in $CHCl_3$ (150 mL) (the complex is significantly more soluble in chloroform than in dichloromethane) and purified by chromatography on silica (130 g; 5 × 17 cm). A trace of unreacted free base **3a** was eluted using CH_2Cl_2; it was followed by a trace of bluish-purple ring-opened by-product which was eluted using 2% CH_3OH in CH_2Cl_2 (v/v). The hemin was then eluted by increasing the concentration of CH_3OH to 5%. After evaporation to dryness, the complex was redissolved in $CHCl_3$ (150 mL), treated once with an equal volume of 5 N HCl [37, 56], washed with water until neutral, and dried over $MgSO_4$. The hemin **3c** was recrystallized from $CHCl_3$/hexane; a first crop of 1.30 g (1.33 mmol, yield = 96.8%) of shiny purple crystals was obtained; a second crop of 22 mg (2.25 × 10^{-5} mol, yield = 1.6%) was also recovered.

UV-vis: λ_{max} (ε): 365 (58), 417 (124), 508 (15), 578 (5), 643 (5); (in hexane): 344, 419, 501, 565, 630.

LRMS: 944 (100), 979 (M^+, 6).

^1H NMR (CD_2Cl_2, 400 MHz, 300 K) δ (ppm): 79.20 (8H, br s, H pyrrole), 13.90 (4H, s, H *meta* phenyl), 12.68 (4H, s, H *meta* phenyl), 8.27 (4H, s, H *para* phenyl).

Anal calc (found) for $C_{44}H_{20}N_4Cl_9Fe$: C, 53.95 (53.26); H, 2.06 (2.10); N, 5.72 (5.60); Cl, 32.57 (32.40).

- meso-*Tetrakis(2,6-dichlorophenyl)-β-octachloroporphinato-iron(III) chloride* **6b**

■ *ODCB as solvent*

The iron complex **3c** (286 mg; 0.29 mmol) was dissolved in ODCB (35 mL) and introduced with anhydrous $FeCl_3$ (1.6 g; 9.9 mmol) into a 125 mL RBF equipped with a reflux condenser surmounted by a drying tube. The reaction mixture was stirred and heated to 140 °C on a preheated oil-bath (the reaction flask should be brought up to this temperature as quickly as possible). Cl_2 gas was then bubbled for 5 min through a septum, using a long stainless steel needle. Stirring was continued and the progress of the reaction was followed by UV-vis spectroscopy: the split Soret shifted to 396/444 nm upon completion of the reaction (30 min). The reaction mixture was worked up immediately to avoid an increase in the amount of demetallated porphyrin and the solvent removed in vacuo. The residue was diluted with CH_2Cl_2, washed with water until neutral, dried over $MgSO_4$ and chromatographed on silica (75 g). CH_2Cl_2 was initially used to remove some uncharacterized by-product followed by β-chlorinated free base **6a** (see details below), then 5% $MeOH/CH_2Cl_2$ caused the elution of the iron complex **6b**. Concentrated HCl (1 mL) was added (the UV-vis spectrum of the eluted iron porphyrin might show a broad absorption band centered around 420 nm, a shoulder around 480 nm and a weak band around 600 nm, due to the exchange of the axial chloride ligand [37, 56]: treating with HCl reverses this process), and the hemin was crystallized by evaporation of CH_2Cl_2. The crystals were washed with MeOH, rinsed with pentane and dried at 75 °C, affording 323 mg (0.26 mmol, yield = 88.0%).

UV-vis: λ_{max} (ε): 396 (56), 444 (60), 504 (11), 560 (8), 708 (3).

LRMS: 1 220 (base, 100), 1 254 (M^+, 9) [45].

Anal calc (found) for $C_{44}H_{12}N_4Cl_{17}Fe$: C, 42.11 (42.04); H, 0.96 (1.10); N, 4.46 (4.35); Cl, 48.02 (47.80).

■ *Acetic acid as solvent*

To a 125 mL RBF was added **3c** (107 mg; 0.11 mmol), acetic acid (50 mL) and anhydrous $FeCl_3$ (600 mg). The mixture was stirred and heated to reflux, then chlorine gas was bubbled through for 8 min. After refluxing for 45 min the UV-vis spectrum showed the Soret band shifted at 442 nm. Heating was discontinued, CH_2Cl_2 (50 mL) was added, and the mixture was washed with water until neutral, dried over Na_2SO_4 and chromatographed on silica (30 g). CH_2Cl_2 was initially used to remove a fraction which was possibly a mixture of free base and β-halogenated iron complex, then 5% $MeOH/CH_2Cl_2$ was used. A fraction displaying the expected UV-vis spectrum [λ_{max} (rel int): 396 (0.91), 442 (1)], was collected and crystallized as described above, affording 61 mg (0.05 mmol) of **6b** (yield = 44.6%).

The MS spectrum showed the expected patterns, although the peaks centered at m/z = 1 184 were observed with a relative intensity significantly higher (25, based on 100 for MS = 1 220) than that observed with the experiment using ODCB as solvent (9). See comments in the discussion above.

• meso-*Tetrakis(2,6-dichlorophenyl)-β-octachloroporphyrin* **6a**

Some free base **6a** was recovered from the chromatography of the crude product obtained after β-chlorination of **3c** (using method with ODCB as solvent) and was crystallized from a $CH_2Cl_2/MeOH$ solution by addition of hexane, affording 30 mg (2.57×10^{-5} mol) of **6a** (yield = 8.8%).

UV-vis: λ_{max} (ε): 446 (176), 542 (16), 580sh (5), 630 (4), 696 (1).

LRMS (detected as Cu complex, from the spectrometer's probe): 1 227.

^1H NMR (10% TFA/CD_2Cl_2 v/v) δ (ppm): 7.86 (12H, m).

^{13}C NMR (10% $TFA/CDCl_3$, 300 MHz, decoupled spectrum) δ (ppm): 140.70 (α), 139.63 (*o*), 134.04 (*p*), 132.34 (β), 129.06 (*m*), 114.04 (*meso*); *ipso* peak was not detected.

Protocol 6

• meso-*Tetrakis(pentachlorophenyl)porphyrin* **7a**

■ *Isolation of the crude zinc complex* **7b**

Pentachlorobenzaldehyde (7.5 g; 27 mmol), anhydrous zinc acetate (1.5 g; 8.2 mmol), 2,4,6-trimethylpyridine (75 mL) and pyrrole (1.9 mL; 27 mmol) were placed in a 250 mL RBF surmounted by a reflux condenser. The mixture was heated to reflux, and when the solution had turned deep-orange (after about 45 min to 1 h) the condenser was removed, allowing evaporation of water formed as droplets in the reaction. The condenser was replaced about 5 min later and the reflux continued for 48 h. After evaporating the solvent in vacuo, the resulting tarry residue was triturated with a mixture of toluene (150 mL) and methanol (50 mL), and allowed to stand in the refrigerator overnight. The zinc complex was isolated as fine purple crystals which were filtered and washed with 25 mL of *cold* toluene/methanol (75:25) and finally with CH_3OH, affording 265 mg (0.19 mmol, yield = 2.9%) of **7b**.

■ *Demetallation*

The crude zinc complex **7b** was dissolved in TFA in CH_2Cl_2 (1:10) and the mixture was stirred for 3 h. The progress of the reaction was monitored by UV-vis spectroscopy [$H_4TPPCl_{20}^{2+}$: 432 (Soret), 576, 632 (principal bands)]. The crude product was poured onto crushed ice, stirred for 10 min and the organic layer was treated with saturated aqueous $NaHCO_3$, washed twice with water, and dried over Na_2SO_4. The free base **7a** (contaminated with chlorin) was crystallized by addition of methanol followed by partial evaporation of CH_2Cl_2; crystals were washed with CH_3OH and dried.

■ *Oxidation of the chlorin impurity [29, 41–43]*

The impure free base **7a** (175 mg; 0.13 mmol) was dissolved in *pentene-stabilized* $CHCl_3$ (180 mL) and the solution was heated to reflux in a 500 mL RBF. A solution of DDQ (1.2 g) in dry benzene (60 mL) was added dropwise and the reflux continued. The reaction was monitored by UV-vis; after 45 h the relative intensity of $\lambda_{660}/\lambda_{590}$ decreased to 0.41 from 1.41, and to 0.28 after 3 days. The reaction mixture was passed through 70 g of alumina, using CH_2Cl_2 as eluent. After evaporation of the eluate to dryness, the compound was recrystallized by addition of hexane (preferable to CH_3OH) to a concentrated CH_2Cl_2 solution, affording 162 mg (0.12 mmol, yield = 92.6%) of **7a**.

UV-vis: λ_{max} (ε): 402 sh (104), 420 (395), 482 sh (4), 514 (25), 544 sh (4), 590 (8), 646 (1); (in CH_2Cl_2/1 drop TFA): 414 sh (0.24), 434 (1), 506 sh (0.01), 542 (0.02), 576 (0.09), 626 (0.04).

^{13}C NMR (10% $TFA/CDCl_3$, 300 MHz, decoupled spectrum) δ (ppm): 145.05 (α), 137.77 (*ipso*), 136.54 (*o*), 135.68 (*p*), 133.65 (*m*), 129.25 (β), 116.67 (*meso*).

Protocol 7

• meso-*Tetrakis(pentachlorophenyl)porphinatoiron(III) chloride* **7c**

The free base **7a** (162 mg; 0.12 mmol) was metallated with $FeCl_2 \cdot 4H_2O$ (1.5 g; 7.55 mmol) in DMF (600 mL) in a manner similar to that of **3a** [37, 38]. However, the reaction was slow and the metallating agent was added in three parts: at the beginning of the reaction, then at 2 h intervals. The single absorption at 420, inflected at 402, changed to a split Soret at 364/420 while in the visible region the spectrum changed from 512, 587 to 508, 578, 643 nm. Heating was discontinued after 6 h and the solution was stirred overnight under argon. After chromatography and crystallization from CH_2Cl_2/hexane, the hemin **7c** was obtained in 76.5% yield (132 mg; 0.09 mmol).

UV-vis: λ_{max} (ε): 355 (54), 420 (103), 510 (15), 576 (7), 638 (6).

LRMS: 1 392 (M^+) [45].

• meso-*Tetrakis(pentachlorophenyl)-β-octachloroporphinato-iron(III) chloride* **8b**

The hemin **7c** (90 mg; 6.46×10^{-5} mol) was chlorinated in ODCB (15 mL) with anhydrous $FeCl_3$ (385 mg) in a manner similar to that for **3c**. However, Cl_2 gas was first bubbled for 6 min, and the Soret band shifted to 442 nm after 50 min; then Cl_2 gas was bubbled again (3 min) and the solution stirred for an additional 20 min at 140 °C. The work-up in this preparation was carried out using $CHCl_3$, the solubility of **8b** being significantly higher than in CH_2Cl_2. After chromatography (60 g SiO_2, similar elution conditions) and HCl treatment [37, 56], the perchlorohemin was crystallized (two crops) from $CHCl_3$/hexane (spectroscopic grade chloroform stabilized by non-polar hydrocarbon was used), affording 54 mg (3.24×10^{-5} mol, yield = 50.1%) of **8b**. The filtrate, after evaporation to dryness, yielded 23 mg (1.38×10^{-5} mol, yield = 21.3%) of **8b**.

UV-vis: λ_{max} (ε, in $CHCl_3$): 396 (66), 444 (76), 560 sh (10).

LRMS: 1 634 ($M^+ + 1 - Cl$) [45].

EI HRMS m/z calculated for $FeC_{44}N_4^{35}Cl_{22}^{37}Cl_7$, 1668.0233; found: 1668.0220.

Protocol 8

• meso-*Tetrakis(2,4,6-trimethylphenyl)porphyrin* **9a**

Ethanol-stabilized chloroform [34] (150 mL) was placed in a 250 mL RBF and deoxygenated under a slow stream of nitrogen (20 min bubbling) through a septum, using a stainless steel needle. TCQ (0.46 g, 1.87 mmol) and FePc (1.07 g, 1.87 mmol) were added with stirring, and the solution was deoxygenated again for 8 min. Mesitaldehyde (7.5 mL, 50 mmol, 0.31 M) and pyrrole (3.5 mL, 50 mmol, 0.31 M) were then added.

After a further 8 min deoxygenation, pure freshly distilled $BF_3 \cdot Et_2O$ (2.5 mL, 21 mmol, 0.13 M) was added using an air-free syringe. The solution was stirred for a further 45 min with nitrogen bubbling. At this point the nitrogen was switched to oxygen and bubbling was continued for 2 h. At the end of this time, the acid catalyst was quenched with 3 mL water and the mixture was taken to dryness on a rotary evaporator and dried under a high vacuum. The solid residue was dissolved in CH_2Cl_2/hexanes 1:1 (v/v) (60 mL) and the resulting solution was introduced onto the top of an alumina column (4 × 28 cm) prepared with the same solvent mixture. The column was eluted with this solvent. The porphyrin moved ahead, pure at first, then contaminated with some impurities at the end of elution. The combined eluates were evaporated to dryness and the residue (1.68 g) redissolved in the above-mentioned solvent mixture (100 mL). The mixture was chromatographed on silica (4 × 32 cm); the porphyrin was readily separated as a fast moving red band, using the same solvent mixture. The product, crystallized by evaporating CH_2Cl_2, was rinsed with hexane and dried in oven, affording 1.18 g (1.51 mmol) of **9a** (yield = 12.1%). Spectral characteristics were identical to those previously published [6, 29, 32].

• meso-*Tetrakis(3,5-dichloro-2,4,6-trimethylphenyl)-β-octachloroporphinato-iron(III) chloride* **10**

The hemin **9c** [46, 47] (102 mg; 0.12 mol) and anhydrous $FeCl_3$ (688 mg; 4.24 mmol) were placed in a 50 mL RBF equipped with a reflux condenser surmounted by a drying tube, and ODCB (16 mL) was added. The mixture was stirred and rapidly heated to 140 °C in a pre-heated oil bath, and Cl_2 gas was bubbled through for 5 min. The progress of the reaction was monitored by UV-vis spectroscopy (Soret shifted from 420 to 446 nm). Heating was discontinued after 40 min, and the solvent was removed in vacuo; the residue was dissolved in CH_2Cl_2 (100 mL) and the solution washed three times with water, then dried over Na_2SO_4. The complex was twice purified by chromatography on silica (50 g), treated with 5 N HCl [37, 56] then with water, and dried over Na_2SO_4. Addition of hexane to the concentrated CH_2Cl_2 solution did not crystallize the porphyrin but removed a trace of non-porphyrinic impurity. The filtered solution was evaporated to dryness, the product redissolved in benzene and lyophilized, affording 63 mg (4.43×10^{-5} mol) of **10** (yield = 37.9%).

UV-vis: λ_{max} (rel int): 396 (0.86), 446 (1), 528 sh (0.22), 560 sh (0.17).

LRMS: 1 423 (M^+).

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References

1 Traylor PS, Dolphin D, Traylor TG, *J Chem Soc, Chem Commun* (1984) 279-280

2 Collman JP, Zhang X, Lee VJ, Uffelman ES, Brauman JI, *Science* (1993) 261, 1404-1411

3 Meunier B, *Chem Rev* (1992) 92, 1411-1456

4 Battioni P, Bartoli JF, Mansuy D, Byun YS, Traylor TG, *J Chem Soc, Chem Commun* (1992) 1051-1053

5 Traylor TG, Hill KW, Fann W, Tsuchiya S, Dunlop BE, *J Am Chem Soc* (1992) 114, 1308-1312

6 Hoffmann P, Robert A, Meunier B, *Bull Soc Chim Fr* (1992) 129, 85-97

7 Nakano T, Traylor TG, Dolphin D, *Can J Chem* (1990) 68, 1504-1506

8 Ellis Jr PE, Lyons JE, *Catal Lett* (1989) 3, 389-398

9 Renaud JP, Battioni P, Bartoli JF, Mansuy D, *J Chem Soc, Chem Commun* (1985) 888-889

10 Dolphin D, Traylor T, Xie LY, in preparation

11 Wijesekera T, Matsumoto A, Dolphin D, Lexa D, *Angew Chem Int Ed Engl* (1990) 29, 1028-1030

12 Donohoe RJ, Atamian M, Bocian DF, *J Am Chem Soc* (1987) 109, 5593-5599

13 Kadish KM, Boisselier-Cocolios B, Simonet B, Chang D, Ledon H, Cocolios P, *Inorg Chem* (1985) 24, 2148-2156

14 Ochsenbein P, Ayougou K, Mandon D, Fischer J, Weiss R, Austin RN, Jayaraj K, Gold A, Terner J, Fajer J, *Angew Chem Int Ed Engl* (1994) 33, 348-350

15 Ochsenbein P, Mandon P, Fischer J, Weiss R, Austin R, Jayaraj K, Gold A, Terner J, Bill E, Müther M, Trautwein AX, *Angew Chem Int Ed Engl* (1993) 32, 1437-1439

16 Turk H, Ford WT, *J Org Chem* (1991) 56, 1253-1260

17 Longo FR, Finarelli MG, Kim JB, *J Heterocycl Chem* (1969) 6, 927-931

18 Brigaud O, Battioni P, Mansuy D, *New J Chem* (1992) 16, 1031-1038

19 Bhyrappa P, Krishnan V, *Inorg Chem* (1991) 30, 239-245

20 van der Made AW, Hoppenbrouwer EJH, Nolte RJM, Drenth W, *Recl Trav Chim Pays-Bas* (1988) 107, 15-16

21 Callot HJ, *Bull Soc Chim Fr* (1974) 1492-1496

22 Traylor TG, Tsuchiya S, *Inorg Chem* (1987) 26, 1338-1339

23 Traylor TG, Tsuchiya S, *Inorg Chem* (1988) 27, 4520

24 Rocha Gonsalves AMd, Johnstone RAW, Pereira MM, Shaw J, Sobral AJFdN, *Tetrahedron Lett* (1991) 32, 1355-1358

25 Adler AD, Longo FR, Finarelli JD, Goldmacher J, Assour J, Korsakoff L, *J Org Chem* (1967) 32, 476

26 Wu D, Xu G, Qu, S, Xue R, Gu C, Zhang F, *Thermochim Acta* (1989) 154, 233-245

27 Dolphin DH, Nakano T, Maione TE, Kirk TK, Farrell RL, Wijesekera TP, *Int Patent No* (1988) 88/07 988

28 Hill CL, Williamson MM, *J Chem Soc, Chem Commun* (1985) 1228-1229

29 Badger GM, Jones RA, Laslett RL, *Aust J Chem* (1964) 17, 1028-1035

30 Lindsey JS, MacCrum KA, Tyhonas JS, Chuang Y-Y, *J Org Chem* (1994) 59, 579-587

31 Chorghade MS, Dolphin D, Dupré D, Hill DR, Lee EC, Wijesekera TP, *Synthesis*, in press

32 Wagner RW, Lawrence DS, Lindsey JS, *Tetrahedron Lett* (1987) 28, 3069-3070

33 Lindsey JS, Schreiman IC, Hsu HC, Kearney PC, Marguerettaz AM, *J Org Chem* (1987) 52, 827-836

34 Lindsey JS, Wagner RW, *J Org Chem* (1989) 54, 828-836

35 Ellis Jr PE, Lyons JE, *Coord Chem Rev* (1990) 105, 181-193

36 Giraudeau A, Callot HJ, Jordan J, Ezhar I, Gross M, *J Am Chem Soc* (1979) 101, 3857-3862

37 Kobayashi H, Higushi T, Kaizu Y, Osada H, Aoki M, *Bull Chem Soc Jpn* (1975) 48, 3137-3141

38 Adler AD, Longo FR, Kampas F, Kim J, *J Inorg Nucl Chem* (1970) 32, 2443-2445

39 Buchler JW, *Porphyrins and Metalloporphyrins*; KM Smith Ed; Elsevier, Amsterdam, 1975, pp 157-278

40 Kim JB, Leonard JJ, Longo FR, *J Am Chem Soc* (1972) 94, 3986-3992

41 Barnett GH, Hudson MF, Smith KM, *J Chem Soc, Perkin I* (1975) 1401-1403

42 Rousseau K, Dolphin D, *Tetrahedron Lett* (1974) 4251-4254

43 Barnett GH, Hudson MF, Smith KM, *Tetrahedron Lett* (1973) 2887-2888

44 Kihn-Botulinski M, Meunier B, *Inorg Chem* (1988) 27, 209-210

45 Arnold LJ, *J Chem Educ* (1992) 69, 811

46 Robert A, Loock B, Momenteau M, Meunier B, *Inorg Chem* (1991) 30, 706-711

47 Groves JT, Nemo TE, *J Am Chem Soc* (1983) 105, 6243-6248

48 Catalano MM, Crossley MJ, Harding MM, King LG, *J Chem Soc, Chem Commun* (1984) 1535-1536

49 Hoffmann P, Labat G, Robert A, Meunier B, *Tetrahedron Lett* (1990) 31, 1991-1994

50 Dolphin D, Nakano T, Maione TE, Kirk TK, Farrell R, *Dégradation de la lignine par voie enzymatique et microbienne*, INRA, Paris, 1987, pp 157-162

51 Skerker PS, Farrell RL, Dolphin D, Cui F, Wijesekera T, *Biotechnology in Pulp and Paper Manufacture*, TK Kirk, HM Chang, Eds; Butterworth-Heinemann, Boston, 1990, pp 203-210

52 Labat G, Meunier B, *J Org Chem* (1989) 54, 5008-5011

53 Zweifel G, Brown HC, *Org Reactions* (1963) 13, 28-29

54 Pearson DE, Cowan D, *Org Synth Coll Vol* (1973) 5, 890-893

55 Polniaszek RP, Belmont SE, Alvarez R, *J Org Chem* (1990) 55, 215-223

56 Cheng R-J, Latos-Grazynski L, Balch AL, *Inorg Chem* (1982) 21, 2412-2418

57 Thomas DW, Martell AE, *Arch Biochem Biophys* (1958) 76, 286-294

58 Fleischer EB, Palmer JM, Srivastava TS, Chatterjee A, *J Am Chem Soc* (1971) 93, 3162-3165