

New Enzyme Models of Chloroperoxidase: Improved Stability and Catalytic Efficiency of Iron Porphyrinates Containing a Thiolato Ligand

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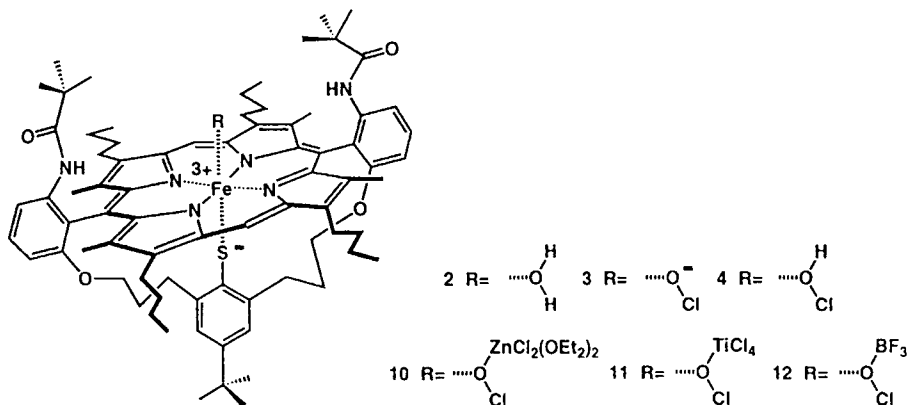
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The heme-thiolate protein chloroperoxidase (CPO) catalyzes the chlorination of activated C–H bonds. A reaction mechanism is proposed for this enzymatic transformation (*Scheme 1*), and a new iron(III) porphyrinate complex **13** is synthesized containing pentafluorophenyl groups at two *meso*-positions and a thiophenolato ligand coordinating to the Fe-atom (*Schemes 2* and *3*). Due to the presence of the electron-withdrawing substituents, the catalyst **13** is appreciably resistant to oxidants (HOCl) and chlorinates, e.g., monochlorodimedone (**5**), with turnover numbers up to 1530. The redox potential of **13**, $E_0 = -134$ mV, and the *Soret* band (λ_{max} 448 nm) of the CO adduct of the reduced state of **13** are close to the corresponding values of the enzyme CPO.

Introduction. – The heme-thiolate proteins comprise a large number of different enzymes, such as chloroperoxidase (CPO) [1], cytochrome P450 [2], and nitric-oxide synthase [3]. The inherent reactivity of these enzymes is attributed to an (protoporphyrinato IX) iron(III) complex located in the active site, which is bound to the protein by H-bridges of the two propanoate side chains of the heme, and, most significantly, by a thiolato ligand coordinated to the Fe-center. This ligand is delivered by a cysteine residue in a highly conserved area of all heme-thiolate proteins and is located at the face of the porphyrin opposite to the substrate and O-binding site. Due to its electron-donating character, the thiolato ligand plays an important role in the reactivity of the prosthetic heme group [4], and triggers the redox potential of these enzymes [5].

CPO, first isolated from the mold *Caldariomyces fumago* [6], is the most versatile of the heme-thiolate enzymes catalyzing the chlorination of activated C–H bonds employing H_2O_2 and Cl^- at pH 2.7, and reactions reminiscent of peroxidases, catalase, and cytochrome P450 [1]. Except for the participation of ‘compound I’ (**1**) [7], the high-valent oxoiron intermediate of the catalytic cycle of cytochrome P450 [8], the reaction mechanism of chlorinations catalyzed by CPO was not elucidated. It was suggested that ‘compound I’ (**1**) oxidizes Cl^- and releases HOCl into solution which, in turn, reacts with activated substrates RH in a nonenzymatic way [9]. A lack of stereospecificity in the halogenation reactions catalyzed by CPO [10] was seemingly in agreement with the participation of an ‘enzyme-free’ halogenating species. In contrast, however, the CPO-catalyzed addition of HOBr (KBr, H_2O_2 , pH 2.7) to steroid derivatives [11] or a highly substituted glycal [12] occurred stereospecifically. Despite numerous investigations of the enzyme [13], the identification of significant reactive intermediates remained elusive.

Recently, we reported the synthesis of **2**, a new enzyme model of CPO. It was shown that this thiolato-coordinating iron(III) porphyrinate forms stable ^-OCl and HOCl adducts, **3** and **4**, respectively, under strictly defined conditions [14], and it was further demonstrated that only **4** is catalytically active to chlorinate monochlorodimedone (**5**), the substrate of the standard assay of CPO [15], yielding dichlorodimedone (**6**).



It is important to note that **3**, and subsequently **4**, was produced from **2** by two independent reaction pathways, namely using (benzyl)(triethyl)ammonium hypochlorite [14], or H₂O₂ together with (benzyl)(triethyl)ammonium chloride. In particular, the latter, enzyme-like conditions suggested that **3** and **4** are kinetically competent analogues of intermediates of the catalytic cycle of the enzyme CPO. Consequently, the spectroscopic parameters of the active-site analogues **3** and **4** were employed to search for these until then elusive intermediates of CPO's reaction sequence.

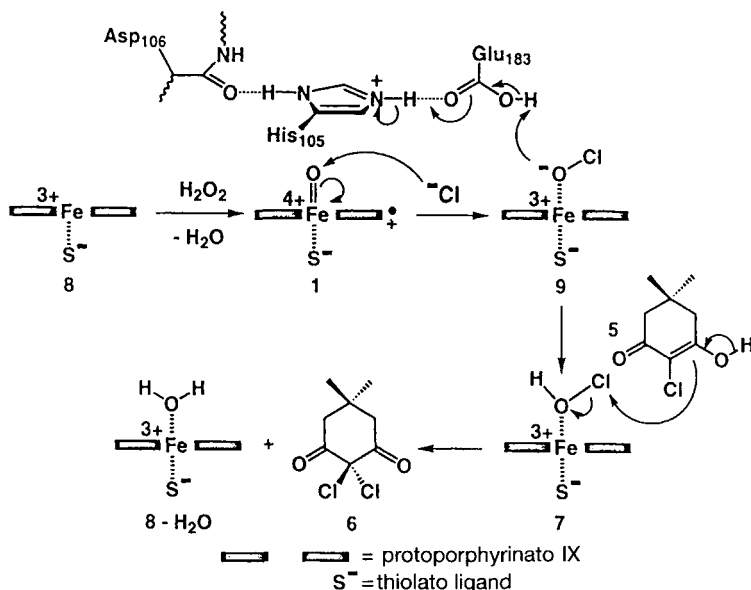
UV/VIS Spectroscopy of CPO from *Caldariomyces fumago* in the presence of NaOCl in a pH range of 3–9 revealed that, only at pH 4.4, a new compound was detected [16]. This complex was identified as the HOCl adduct **7** of the active-site's iron(III) porphyrinate due to its split *Soret* band (λ_{\max} 376 and 434 nm) corresponding to the model complex **4** (λ_{\max} 390 and 412 nm) (see *Scheme 1*).

The recently published X-ray crystal-structure analysis of CPO's resting state **8** from *Caldariomyces fumago* led to the identification of three amino-acid residues Glu¹⁸³, His¹⁰⁵, and Asp¹⁰⁶ above the porphyrin face opposite to the thiolato coordination site [17]. It seems very plausible that these amino acids participate in catalysis as a proton-delivery system *i*) by assisting the H₂O₂ cleavage, leading to 'compound I' (**1**) and *ii*) by protonation of the adduct **9** (see *Scheme 1*). Thus, we assumed that the ⁻OCl adduct **9** would be observable only if the proton supply is inactivated. This was accomplished by covalent modification of His¹⁰⁵ using diethyl pyrocarbonate [18], which blocks the catalytic activity of CPO completely [19].

In fact, using the 'CPO derivative', the ⁻OCl adduct **9** of the heme thiolate cofactor was detected exhibiting a single *Soret* band (λ_{\max} 406 nm) [16] close to the absorption of the corresponding complex **3** derived from the enzyme model **2**.

Iron(III) porphyrinates **2–3** served as a decisive guide to trace intermediates of the catalytic cycle of CPO. These complexes have, however, a certain limitation concerning stability and turnover when used in catalytic chlorinations, in particular when the proton in **4** was replaced by *Lewis* acids (see **10–12**). We wish to report here on the synthesis, stability, and catalytic reactivity of a new tetraarylporphyrinate **13** as an improved active-site analogue of CPO.

Scheme 1. Mechanism of the Chlorination of Monochlorodimedone (5) Catalyzed by Chloroperoxidase. The essential proton for the chlorination is provided by a proton-supply system containing Glu¹⁸³ and His¹⁰⁵



Results and Discussion. – X-Ray crystal-structure determinations of chloroperoxidase [17] and of different forms of cytochrome P450 [20] revealed that the thiolato ligand is H-bonded to two peptide amide groups shifting the redox potential of the heme group of, e.g., CPO to $E_0 = -140$ mV at pH 6.9 [21]. New porphyrinate models prepared by Nakamura and co-workers aimed to mimic this situation using noncovalently attached thiophenolato ligands, which provide amide protons as H-bond donors to the S-atom [22]. It was shown that the redox potential changes from $E_0 = -680$ mV of the corresponding porphyrinate without NH–S⁻ H-bonding to $E_0 = -350$ mV for the iron porphyrinate that has two NH–S⁻ bonds. This anodic shift is a consequence of the reduced charge density at the thiolato ligand and is in agreement with our results using 4-nitrobenzenethiolato ligands [23].

In principle, however, a positive change of the redox potential of iron (metal) porphyrinates, concomitant stabilization of the iron(II) oxidation state and increased electrophilicity of the corresponding oxoiron(IV) state ('compound I'), can be achieved attaching electron-withdrawing substituents in the periphery of the porphyrinato ligand in the so-called β -pyrrole positions or at the Ph groups of tetraphenylporphyrinato ligands. There is ample precedence for the latter approach in drug-metabolism studies [24] and, more general, in oxidation of alkenes [25]. Concerning a CPO model, a less basic porphyrinato ligand is expected to be more reactive with respect to the Cl⁺ release from the HOCl bound to the Fe-center.

The design of iron(III) porphyrinate **13** takes into account structural increments important to the heme-thiolate proteins such as the thiolato ligand tightly coordinating to the Fe-center. Regarding the synthesis and stability of the complex, the porphyrinate **13** is *face-protected* against μ -oxo-dimer formations by both the bridge carrying the

proximal thiophenolato ligand, and two pivalamido (= (2,2-dimethyl-1-oxopropyl)-amino) residues [26] on the distal site. All four *meso*-positions are aryl-substituted to prevent oxidative degradation at these most vulnerable C-atoms of the porphyrinates. Last but not least, two opposite phenyl groups are F-substituted to lower the electron-donating character of the porphyrin macrocycle.

The synthesis of the porphyrinate **13** started with the condensation of the *N*-(2-formylphenyl)pivalamide **14** [27] with 2 equiv. of 1*H*-pyrrole (**15**) under acid catalysis (*Scheme 2*) [28]. The resulting dihydrodipyrryn derivative **16** was condensed with 2,3,4,5,6-pentafluorobenzaldehyde (**17**) in the presence of CF₃COOH [28]. The mixture of porphyrins and chlorins was oxidized with DDQ (4,5-dichloro-3,6-dioxocyclohexa-1,4-diene-1,2-dicarbonitrile) [29], and subsequently Zn^{II} was inserted to facilitate the chromatographic purification of the desired porphyrin in the form of its Zn^{II} complex [4][29]. Thus, **18** was obtained as separable mixture of α,α - (shown in *Scheme 2*) and α,β -atropisomers in 9% overall yield from **16** (α,α : both pivalamido moieties on the same side of the macrocycle reference plane). An alternative route using **17** led, *via* **19**, also to **18**, however, with less satisfactory yields.

Removal of the zinc ion from porphyrinate **18** with conc. HCl solution [30] yielded **20**, and cleavage of the methyl aryl ether with AlCl₃ in ethanethiol [31] furnished the porphyrin **21**.

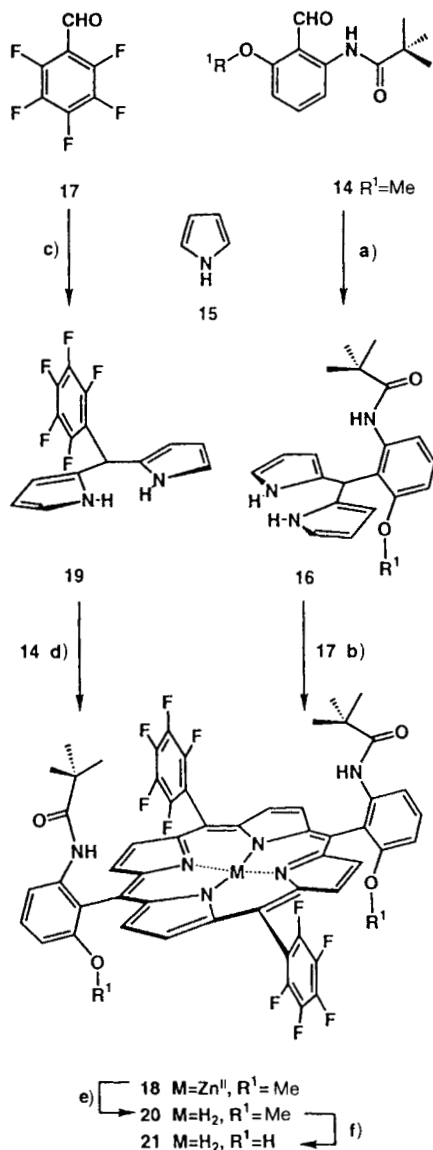
The mixture of α,α - and α,β -porphyrin **21** was condensed [4] with the dimesylate **22** [32] under isomerizing conditions at 65° to yield the bridged, but still *S*-protected porphyrin **23** (see *Scheme 3*). Subsequent removal of the protecting group at the thiophenol moiety [4][32] gave the porphyrin **24**, and Fe insertion [33] completed the preparation of **13**.

The complex **13** is a high-spin ($g = 6.318$, $g = 2.019$) iron(III) porphyrinate displaying a *Soret* band in UV/VIS spectrum at λ_{\max} 420 nm. In comparison to the porphyrinate **2** [14], the *Soret* band of **13** is red-shifted by 12 nm due to the presence of the electron-withdrawing pentafluorophenyl residues. The ¹H-NMR spectrum of **13** showed one broad characteristic downfield-shifted signal of the β -pyrrole protons (82 ppm). On treatment with 30% HBr in CH₂Cl₂ [4], the thiolato ligand of **13** could be protonated yielding **13** · HBr with a *Soret* band at λ_{\max} 452 nm. Reduction of **13** with NaBH₄ in THF quantitatively provided the corresponding Fe^{II} complex **25** with λ_{\max} 426 nm, which, on addition of CO, furnished **26** displaying the expected bathochromic shift to λ_{\max} 448 nm, characteristic of a heme-thiolate system.

Cyclic voltammetry of the active-site analog **2** revealed a redox potential $E_0 = -630$ mV (*vs.* SCE); this value is well within the range determined for other iron porphyrinates carrying a thiolate ligand [4][23][32]. The electron-withdrawing effect of the two pentafluorophenyl groups in porphyrinate **13** shifts the potential anodically to $E_0 = -134$ mV (*Fig. 1*). CPO itself displays a redox potential of -140 mV at pH 6.9 and $+150$ mV at pH 2.7 [21], the pH optimum of CPO for chlorination reactions.

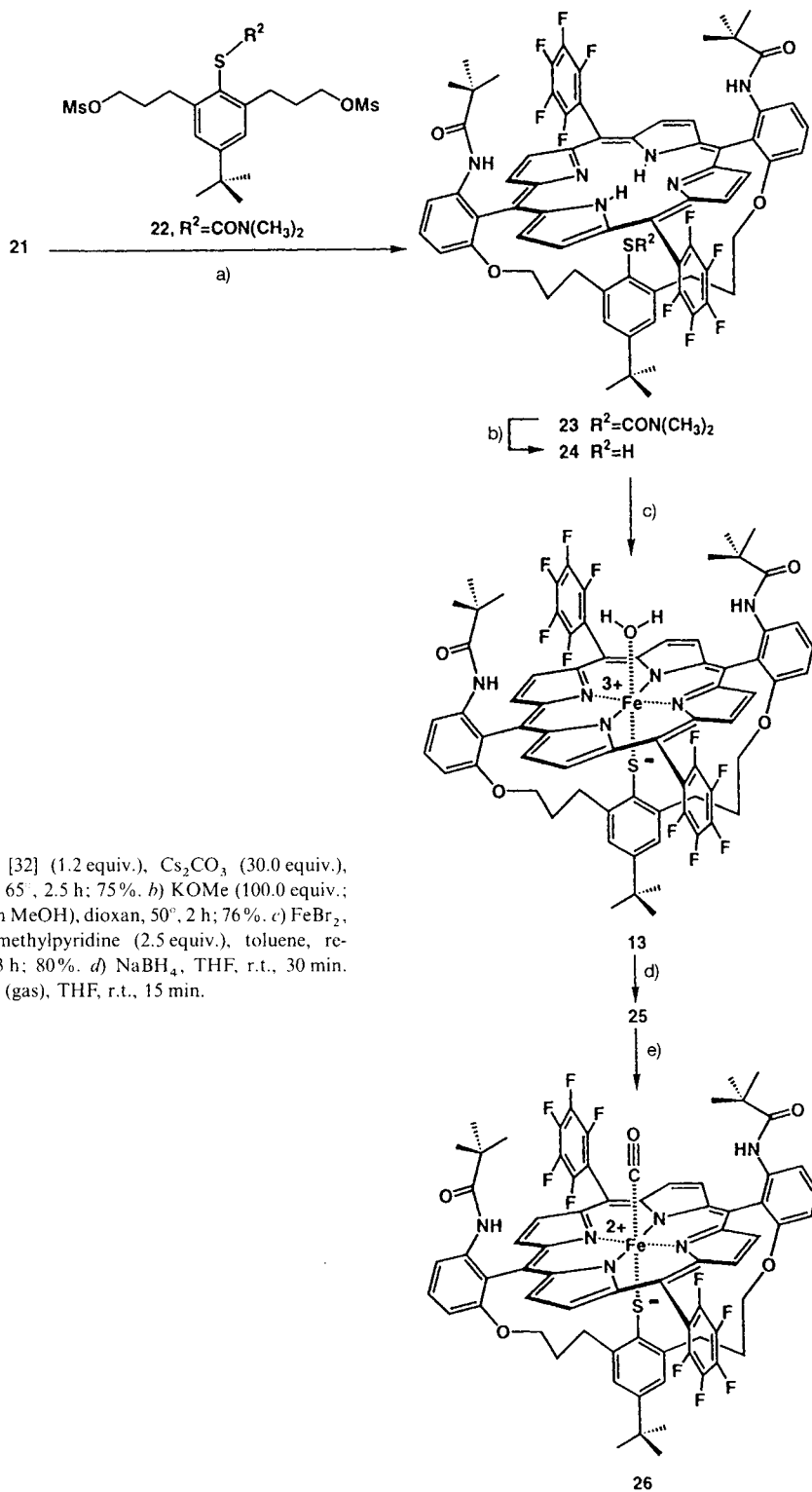
Thus, regarding spectroscopy and electrochemistry, the complex **13** is a suitable model to mimic different features of heme-thiolate proteins. Concerning chemical reactivity and stability, it was important to investigate whether **13** is resistant to degradation in the presence of strong oxidants. Thus, **13** was treated with (benzyl)(triethyl)ammonium hypochlorite [14] or H₂O₂, and the change of absorbance of its *Soret* band at 420 nm was

Scheme 2. Synthesis of 21



a) CF_3COOH (0.1 equiv.), CH_2Cl_2 , r.t., 3 h; 75%. b) 1) 17 (1.0 equiv.), CF_3COOH (1.0 equiv.), CH_2Cl_2 , r.t., 20 min; 2) DDQ (2.0 equiv.), $\text{CH}_2\text{Cl}_2/\text{THF}$ 10:1, reflux, 2 h; 3) $\text{Zn}(\text{OAc})_2$ (5.0 equiv.), $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 5:1, reflux, 2 h; 9%. c) CF_3COOH (0.1 equiv.), CH_2Cl_2 , r.t., 3 h; 91%. d) 1) 14 [27] (1.0 equiv.), CF_3COOH (1.0 equiv.), CH_2Cl_2 , r.t., 15 min; 2) DDQ (2.0 equiv.), $\text{CH}_2\text{Cl}_2/\text{THF}$ 10:1, reflux, 2 h; 3) $\text{Zn}(\text{OAc})_2$ (5 equiv.), $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 5:1, reflux, 2 h; 6%. e) Conc. HCl soln., CH_2Cl_2 , r.t., 15 min; 95%. f) AlCl_3 (78.0 equiv.), $\text{CH}_2\text{Cl}_2/\text{EtSH}$ 3:2, r.t., 15 h; 98%.

Scheme 3. Synthesis of 13



a) **22** [32] (1.2 equiv.), Cs_2CO_3 (30.0 equiv.), DMF, 65°, 2.5 h; 75%. b) KOMe (100.0 equiv.; 3.5M in MeOH), dioxan, 50°, 2 h; 76%. c) FeBr_2 , 2,6-dimethylpyridine (2.5 equiv.), toluene, reflux, 3 h; 80%. d) NaBH_4 , THF, r.t., 30 min. e) CO (gas), THF, r.t., 15 min.

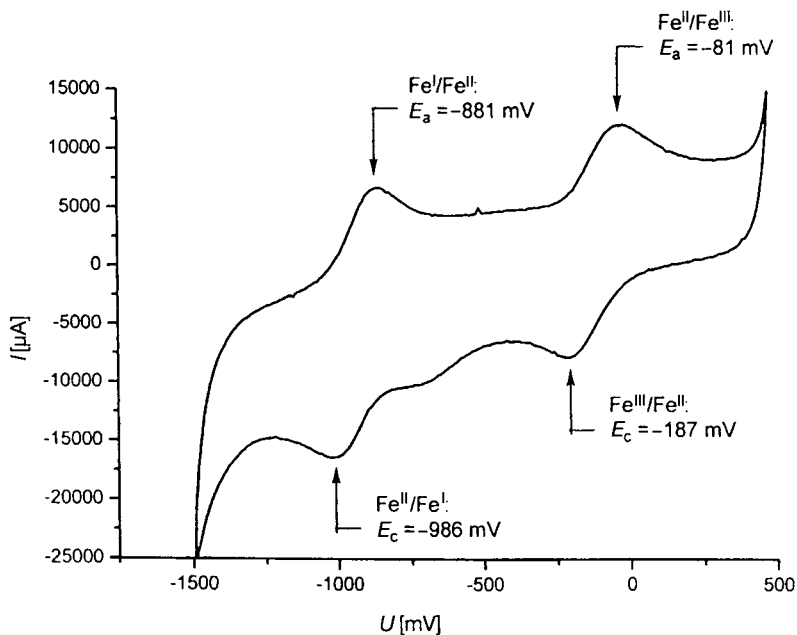


Fig. 1. Cyclic voltammetry of the iron porphyrinate **13** (3.0 mM in 0.1M LiClO₄ in DMF (saturated with LiBr); 400 mV/s; E_a : anodic potential; E_c : cathodic potential; potentials are given vs. SCE)

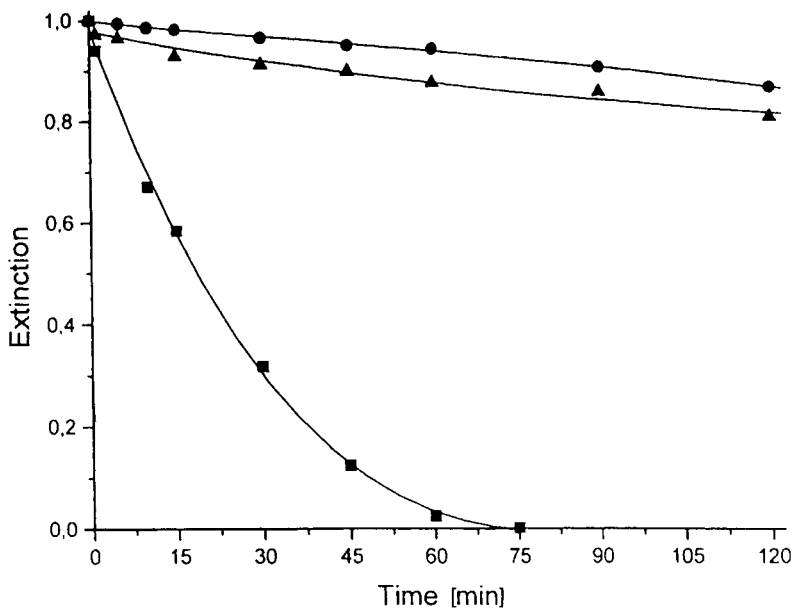


Fig. 2. Change of absorbance of the iron(III) porphyrinates **2** and **13** in the presence of (benzyl)(triethyl)ammonium hypochlorite (BTAH) [14]. ■: **4** (λ_{\max} 390 nm) + 80 equiv. of BTAH and AcOH; ●: **13** (λ_{\max} 420 nm) + 80 equiv. of BTAH and AcOH; ▲: **13** (λ_{\max} 420 nm) + 1500 equiv. of BTAH and AcOH.

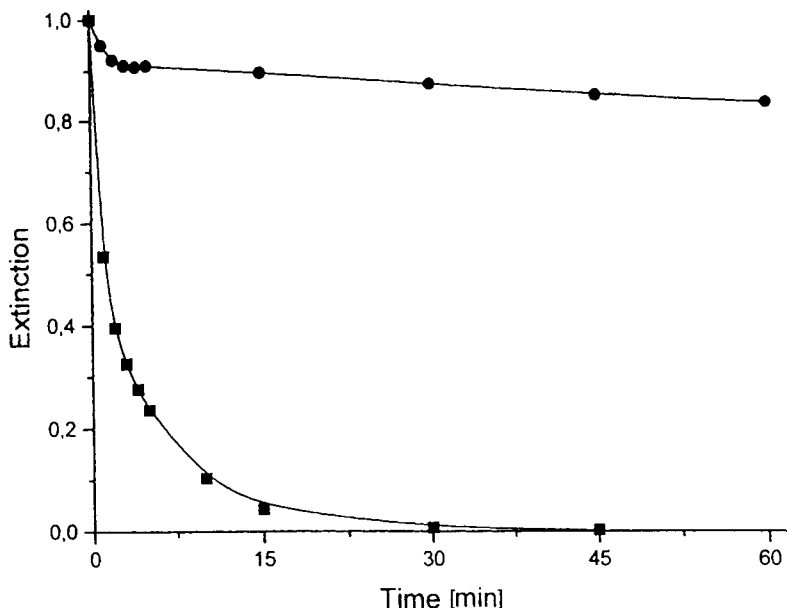


Fig. 3. Change of absorbance of the iron(III) porphyrinates **2** and **13** in the presence of H_2O_2 . ■: **2** (λ_{max} 398 nm) + 230 equiv. of H_2O_2 ; ●: **13** (λ_{max} 420 nm) + 230 equiv. of H_2O_2 .

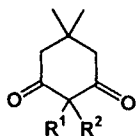
used as a measure of degradation and compared with the corresponding absorbance behavior of complex **4** (Soret band at 390 nm). As shown in Figs. 2 and 3, the catalyst **13** retained ca. 85% of its activity, whereas the iron porphyrinates **2** and **4**, respectively, are completely oxidized within 1 h.

Brominations and chlorinations of activated C–H bonds of the substrates **5**, **27–30**, and **32** using various catalysts derived from **13** are reported in Tables 1–3. One can see that only very low concentrations of the catalyst, such as 0.05–0.09 mol-%, are required to approach a turnover number of 1030 (bromination of **5**; see Table 1, Entry 4), 1530 (chlorination of **5**; see Table 2, Entry 4), and 970 (chlorination of anisole (**27**); Table 3, Entry 4).

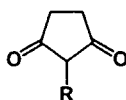
These experiments reveal that employing Lewis acids as co-catalysts is advantageous, because Cl^+ donation to the substrate is facilitated, and turnovers become significantly higher. Even substrates like cyclohexanone (**28**) and toluene (**29**), which are not highly activated, are chlorinated using **13** and $BF_3 \cdot OEt_2$ with turnover numbers of 50 (Table 2,

Table 1. Catalytic Halogenation of Monochlorodimedone (**5**) Using H_2O_2/Cl^- or H_2O_2/Br^- to Yield Dichlorodimedone (**6**) or Bromochlorodimedone (**31**), Respectively

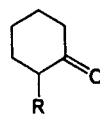
Entry	Catalyst	[mol-%]	Reagents	Turnover number	Product	Yield [%]
1 [14]	2	0.7	H_2O_2 , $(BnEt_3N)Cl$, AcOH	20	6	81
2	2	0.7	H_2O_2 , $(Bu_4N)Br$, AcOH	100	31	73
3	13	0.09	H_2O_2 , $(BnEt_3N)Cl$, AcOH	270	6	68
4	13	0.09	H_2O_2 , $(Bu_4N)Br$, AcOH	1030	31	86



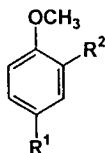
- 30 $R^1 = H, R^2 = H$
 5 $R^1 = Cl, R^2 = H$
 31 $R^1 = Br, R^2 = H$
 6 $R^1 = Cl, R^2 = Cl$



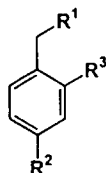
- 32 $R = H$
 33 $R = Cl$



- 28 $R = H$
 34 $R = Cl$



- 27 $R^1 = H, R^2 = H$
 35 $R^1 = Cl, R^2 = H$
 36 $R^1 = H, R^2 = Cl$



- 29 $R^1 = H, R^2 = H, R^3 = H$
 37 $R^1 = Cl, R^2 = H, R^3 = H$
 38 $R^1 = H, R^2 = Cl, R^3 = H$
 39 $R^1 = H, R^2 = H, R^3 = Cl$

Table 2. Catalytic Chlorination of the Ketones **5**, **28**, **30**, and **32** with Various Iron(III) Porphyrinate Adducts

Entry	Substrate	Catalyst	[mol-%]	Reagents ^{a)}	Turnover number	Product	Yield [%]
1 [14]	5	2	1.3	BTAH, AcOH	37	6	52
2	5	13	0.07	BTAH, AcOH	420	6	71
3 [14]	5	2	0.7	BTAH, $ZnCl_2 \cdot (OEt_2)_x$	97	6	83
4	5	13	0.05	BTAH, $ZnCl_2 \cdot (OEt_2)_x$	1530	6	55
5 [14]	5	2	0.7	BTAH, $BF_3 \cdot OEt_2$	87	6	87
6	5	13	0.05	BTAH, $BF_3 \cdot OEt_2$	1260	6	73
7	30	2	1.0	BTAH, AcOH	b)		
8	30	13	0.38	BTAH, AcOH	30	5 6	53 –
9	30	2	1.0	BTAH, $ZnCl_2 \cdot (OEt_2)_x$	37	5 6	74 20
10	30	13	0.43	BTAH, $ZnCl_2 \cdot (OEt_2)_x$	130	5 6	40 14
11	30	2	1.0	BTAH, $BF_3 \cdot OEt_2$	10	5 6	95 c)
12	30	13	0.22	BTAH, $BF_3 \cdot OEt_2$	250	5 6	150 50
13	32	2	0.7	BTAH, $BF_3 \cdot OEt_2$	b)		
14	32	13	0.60	BTAH, $BF_3 \cdot OEt_2$	50	33	74
15	28	2	0.7	BTAH, $BF_3 \cdot OEt_2$	b)		
16	28	13	0.44	BTAH, $BF_3 \cdot OEt_2$	50	34	51

^{a)} BTAH: (benzyl)(triethyl)ammonium hypochlorite [14]. ^{b)} No reaction. ^{c)} Not detectable.

Table 3. Catalytic Chlorination of Anisole (**27**) and Toluene (**29**) Using Various Iron(III) Porphyrin Adducts

Entry	Substrate	Catalyst	[mol-%]	Reagents ^{a)}	Turnover number	Product	Yield [%]
1 [14]	27	2	10.4	BTAH, TiCl ₄	103	35 36	50 38
2	27	13	0.08	BTAH, TiCl ₄	930	35 36	35 29
3 [14]	27	2	0.4	BTAH, BF ₃ ·OEt ₂	134	35 36	57 9
4	27	13	0.05	BTAH, BF ₃ ·OEt ₂	970	35	52
5	29	2	0.5	BTAH, BF ₃ ·OEt ₂ ^{b)}			
6	29	13	0.29	BTAH, BF ₃ ·OEt ₂	50	37 38 39	38 14 11

^{a)} BTAH = (Benzyl)(triethyl)ammonium hypochlorite. ^{b)} No reaction.

Entry 16, and Table 3, Entry 6). With porphyrinate **2** as catalyst, no conversion of **28** and **29** was detectable (Table 2, Entry 15, and Table 3, Entry 5).

The synthetic *face-protected* tetraarylporphyrinate **13** is a new active-site analogue of chloroperoxidase which perfectly mimics the electron-deficient character of the heme-thiolate cofactor of CPO. Clearly, **13** is more stable than **2** in the presence of strong oxidants, e.g., H₂O₂ or ⁻OCl, and shows an appreciable reactivity towards monochlorodimedone (**5**) and anisole (**27**), substrates commonly used for the enzyme CPO. Finally, turnover numbers accomplished with derivatives of **13** surpass those achieved with corresponding adducts of **2** by a factor of 10.

Experimental Part

General. All reactions were performed in freshly distilled solvents under Ar. The insertion of the iron(III) into the porphyrin ligand was carried out in a 'glove box' with distilled solvents which had been degassed prior to use. M.p.: Mettler FP52 apparatus; uncorrected. TLC: 0.2-mm Merck silica gel 60 F₂₅₄ plates. Flash chromatography (FC): Merck 60 silica gel (40–63 μm). UV/VIS Spectra: Hewlett-Packard 8452A diode-array spectrophotometer. IR Spectra: Perkin-Elmer FTIR 1600; $\tilde{\nu}$ in cm⁻¹. NMR Spectra: Varian Gemini (300 MHz) or Bruker AC-250 (250 MHz) spectrometer; at r.t.; δ in ppm downfield rel. to Me₄Si as internal standard (¹H) or (trifluoromethyl)benzene as external standard (¹⁹F); C-atom numbering according to [4]; because of high coupling constants, the δ values of C-atoms connected to F-atoms are not reported in ¹³C-NMR spectra. EPR Spectra: Bruker-ESP-300 spectrometer with a TE₁₀₂ cavity. Cyclic voltammetry: Amel-443 polarograph; 3 mm porphyrinate in 0.1M LiClO₄ in dry and degassed DMF; to prevent ligand exchange, the soln. was saturated with LiBr. EI-MS: Varian-MAT-112S spectrometer; ionization potential of 70 eV; *m/z* (rel. %). LDI-TOF- or MALDI-TOF-MS (α -cyano-4-hydroxycinnamic acid as matrix): Voyager-Vestec-Biospectrometry workstation. Elemental analysis: Perkin-Elmer-240 analyzer.

N-{3-Methoxy-2-[di(1H-pyrrol-2-yl)methyl]phenyl}-2,2-dimethylpropanamide (**16**). To a soln. of the N-(3-methoxy-2-formylphenyl)propanamide (**14**) [27] (2.00 g, 8.50 mmol) in 1H-pyrrole (**15**; 47.2 ml, 45.62 g, 0.68 mol), CF₃COOH (65.0 μl, 97.0 mg, 0.85 mmol) was added. The mixture was stirred under Ar at r.t. for 3 h in the dark, neutralized with sat. aq. NaHCO₃ soln. (100 ml), and extracted with CH₂Cl₂ (3 × 30 ml). The combined org. extracts were dried (Na₂SO₄) and evaporated. Purification by FC (CH₂Cl₂ + 1% Et₃N) gave 2.25 g (75%) of **16**. Yellow solid. M.p. 52–58°. TLC (CH₂Cl₂ + 1% Et₃N): R_f 0.32. UV/VIS (CH₂Cl₂): 286 (100). IR (KBr): 3360s, 3100m, 2960s, 2870m, 2840m, 1670s, 1590s, 1560m, 1510s, 1470s, 1430s, 1370m, 1330m, 1280s, 1250s, 1170s, 1120s, 1080s, 1030s, 970m, 950m, 890m, 850m, 810m, 770s, 720s, 560m, 500m, 460w. ¹H-NMR (300 MHz, CDCl₃): 8.32 (br., 2 NH (pyr)); 7.37 (*d*, *J* = 8.0, H–C(6')); 7.28 (*t*, *J* = 8.0, H–C(5')); 6.81 (*d*, H–C(4')); 6.65 (*d*, *J* = 3.0, 2 H–C(3) (pyr)); 6.24 (br., 1 CONH); 6.16 (*t*, *J* = 3.0, 2 H–C(4) (pyr)); 6.06 (*t*, *J* = 2.7, 2 H–C(5) (pyr)); 3.77

(s, MeO–C(3')); 1.58 (s, CH–C(2'')); 0.97 (s, Me₃C(2)). ¹³C-NMR (75 MHz, CDCl₃): 178.0 (NHCO); 157.7; 130.2; 128.5; 119.4; 117.1; 117.0; 109.0; 108.9; 108.7; 106.1; 56.4 (MeO); 39.3 (Me₃C); 33.1 (CH–C(2'')); 27.0 (Me₃C). EI-MS: 353 (5), 352 (23), 351 (62, M⁺), 350 (8), 294 (5), 280 (5), 268 (5), 267 (30), 266 (100), 251 (7), 250 (10), 249 (7), 235 (9), 227 (7), 223 (5), 222 (6), 211 (5), 199 (8), 185 (5), 184 (7), 145 (9), 144 (8), 91 (5), 80 (9), 57 (20), 41 (11). Anal. calc. for C₂₁H₂₅N₃O₂ (351.48): C 71.77, H 7.17, N 11.96, O 9.11; found: C 71.60, H 7.38, N 11.78, O 8.92.

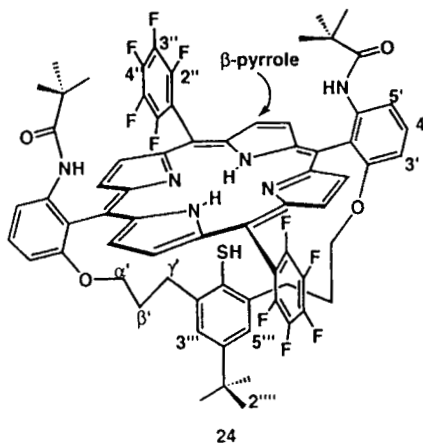
{N,N'-[10,20-Bis(2,3,4,5,6-pentafluorophenyl)-21H,23H-porphyrin-5,15-diyl-κN²¹,κN²²,κN²³,κN²⁴]bis(6-methoxy-2,1-phenylene)}bis[2,2-dimethylpropanamidato](2-)-zinc(II) (**18**). To a soln. of **16** (2.25 g, 6.41 mmol) and **17** (1.28 g, 6.41 mmol) in dry CH₂Cl₂ (180 ml), CF₃COOH (0.49 ml, 0.73 g, 6.41 mmol) was added. The mixture was stirred for 20 min at r.t. and quenched with sat. aq. NaHCO₃ soln. (150 ml). The aq. phase was extracted with CH₂Cl₂ (2 × 50 ml), and the combined org. phase dried (Na₂SO₄) and evaporated. To a soln. of the residue in CH₂Cl₂ (100 ml), a soln. of DDQ (2.91 g, 12.83 mmol) in THF (50 ml) was added. The mixture was stirred for 2 h under reflux and then evaporated. The residue in CH₂Cl₂ was filtered through silica gel and the filtrate evaporated. To a soln. of the residue in CH₂Cl₂ (200 ml), a soln. of Zn(OAc)₂ (5.88 g, 32.1 mmol) in MeOH (40 ml) was added. The mixture was stirred for 2 h under reflux and quenched with sat. aq. NaHCO₃ soln. The org. layer was filtered through *Celite* and evaporated. FC of the residue (hexane/AcOEt 4:1) yielded 288 mg (9%) of **18** as an atropisomer mixture which was separated by FC.

The same procedure was used for the synthesis of **18** starting with **19** (100 mg, 0.32 mmol) and **14** [27] (75 mg, 0.32 mmol), using the same dilutions and same mol-equiv. as described above: 103 mg (6%) of **18** as an atropisomer mixture. The two isolated compounds were assigned to the atropisomers according to *Stäubli et al.* [4].

Data of α,β-18: Red-pink solid. M.p. > 250°. TLC (hexane/AcOEt 1:1 + 1% Et₃N): R_f 0.65. UV/VIS (CH₂Cl₂): 418 (100), 546 (6). IR (KBr): 3430s, 2930m, 1690m, 1650m, 1590s, 1520s, 1500s, 1470s, 1430s, 1390s, 1260s, 1180s, 1080m, 1040m, 990s, 940m, 840w, 800m, 760m, 650m, 580w, 520w, 420w. ¹H-NMR (300 MHz, CDCl₃)¹⁾: 8.98 (d, J = 4.7, 4 H–C(β) (pyr)); 8.86 (d, 4 H–C(β) (pyr)); 8.40 (d, J = 8.4, 2 H–C(5')); 7.83 (t, J = 8.4, 2 H–C(4')); 7.18 (d, 2 H–C(3')); 6.89 (s, 2 CONH); 3.60 (s, 2 MeO–C(2'')); 0.00 (s, 2 *t*-Bu). ¹³C-NMR (75 MHz, CDCl₃)¹⁾: 176.3 (CONH); 159.3; 151.1; 149.9; 140.1; 132.8 (C(β) (pyr)); 131.5 (C(β) (pyr)); 130.8 (C(4')); 128.8; 120.3; 114.1 (C(5')); 112.3; 106.8 (C(3')); 56.1 (MeO); 26.3 (Me₃C); 1.1 (Me₃C). ¹⁹F-NMR (282 MHz, CDCl₃)¹⁾: –4.1 (dd, J = 23.9, 7.9, F–C(2''), F–C(6'')); –19.1 (t, J = 20.5, F–C(4'')); –28.7 (m, F–C(3''), F–C(5'')). LDI-TOF-MS: 1115 ([M – 3]⁺, [C₅₆H₄₂F₁₀N₆O₄Zn – 3]⁺; calc. 1115.40).

Data of α,α-18: Red-pink solid. M.p. > 250°. TLC (hexane/AcOEt 1:1 + 1% Et₃N): R_f 0.60. UV/VIS (CH₂Cl₂): 420 (100), 548 (6). IR (Br): 3430s, 2930m, 1650m, 1520s, 1470s, 1430m, 1400m, 1340w, 1260s, 1180m, 1080m, 1040m, 990s, 940m, 840w, 760m, 710w, 650m, 580w, 520w, 410w. ¹H-NMR (300 MHz, CDCl₃)¹⁾: 8.90 (d, J = 4.7, 4 H–C(β) (pyr)); 8.85 (d, 4 H–C(β) (pyr)); 8.37 (d, J = 8.4, 2 H–C(5')); 7.81 (t, J = 8.4, 2 H–C(4')); 7.13 (d, 2 H–C(3')); 7.03 (s, 2 CONH); 3.48 (s, 2 MeO–C(2'')); 0.06 (s, 2 *t*-Bu). ¹³C-NMR (75 MHz, CDCl₃)¹⁾: 176.3 (CONH); 159.4; 151.1; 149.9; 140.1; 132.9 (C(β) (pyr)); 131.4 (C(β) (pyr)); 130.8 (C(4')); 128.8; 120.3; 114.1

¹⁾ For numbering, cf. **24**.



(C(5')); 112.3; 107.0 (C(3')); 56.0 (MeO); 26.3 (Me₃C); 1.1 (Me₃C). ¹⁹F-NMR (282 MHz, CDCl₃)¹: –3.9 (*dd*, *J* = 23.8, 8.0, F–C(2''), F–C(6'')); –18.9 (*t*, *J* = 20.5, F–C(4'')); –28.5 (*m*, F–C(3''), F–C(5'')). LDI-TOF-MS: 1116 ([*M* – 2]⁺, [C₅₆H₄₂F₁₀N₆Zn – 2]⁺; calc. 1116.40).

2,2'-[2,3,4,5,6-Pentafluorophenyl)methylene]bis[1*H*-pyrrole] (**19**). To a soln. of **17** (0.50 g, 2.55 mmol) in 1*H*-pyrrole (**15**) (14.2 ml, 13.7 g, 0.204 mol), CF₃COOH (19.5 μl, 97.0 mg, 0.85 mmol) was added. The mixture was stirred for 3 h under Ar at r.t. in the dark, neutralized with sat. aq. NaHCO₃ soln. (20 ml), and extracted with CH₂Cl₂ (3 × 10 ml). The combined org. extract was dried (Na₂SO₄) and evaporated. Purification by FC (CH₂Cl₂ + 1% Et₃N) gave 721 mg (91%) of **19**. Grey solid. M.p. 76–79°. TLC (CH₂Cl₂ + 1% Et₃N): R_f 0.34. UV/VIS (CH₂Cl₂): 246 (100). IR (KBr): 3360w, 3100w, 2970w, 1660m, 1500s, 1420m, 1320m, 1260w, 1180w, 1120s, 1030m, 980s, 930m, 880w, 710m, 730s, 630w, 560m. ¹H-NMR (300 MHz, CDCl₃): 8.12 (br., 2 NH); 6.82 (*dd*, *J* = 4.4, 2.2, H–C(3)); 6.72 (*dd*, *J* = 6.0, 2.7, H–C(3'')); 6.26 (*dd*, *J* = 2.2, H–C(4)); 6.16 (*dd*, *J* = 2.7, H–C(4'')); 6.02 (br., H–C(5)); 5.89 (br., H–C(5'')); 5.80 (*s*, C₆F₆CH). ¹³C-NMR (75 MHz, CDCl₃): 118.1; 117.7; 108.7; 108.2 (C(1)); 107.6. ¹⁹F-NMR (282 MHz, CDCl₃): –8.3 (*d*, *J* = 17.1, F–C(2''), F–C(6'')); –22.5 (*t*, *J* = 21.1, F–C(4'')); –28.0 (*m*, F–C(3''), F–C(5'')). EI-MS: 313 (28), 312 (100, *M*⁺), 311 (42), 296 (8), 292 (7), 291 (18), 285 (6), 284 (16), 283 (9), 264 (6), 263 (5), 247 (12), 246 (52), 245 (18), 244 (8), 237 (6), 226 (17), 225 (6), 218 (7), 193 (6), 192 (8), 173 (7), 169 (10), 167 (5), 156 (11), 146 (17), 145 (22), 144 (7), 143 (15), 123 (7), 119 (10), 117 (14), 116 (5), 104 (5), 95 (7), 92 (86), 91 (9), 89 (5), 78 (11), 73 (79), 72 (85), 68 (5), 67 (42), 65 (6), 63 (5), 52 (86), 51 (8), 41 (10), 40 (8), 39 (18), 38 (7). Anal. calc. for C₁₅H₉F₅N₂ (312.25): C 57.70, H 2.91, N 8.97; found: C 57.88, H 3.04, N 9.12.

N,N'-[10,20-Bis(2,3,4,5,6-pentafluorophenyl)-21*H*,23*H*-porphyrin-5,15-diyl]bis(6-methoxy-2,1-phenylene)}-bis[2,2-dimethylpropanamide] (**20**). To a soln. of **18** (mixture of atropisomers; 279 mg, 0.25 mmol) in CH₂Cl₂ (200 ml), conc. HCl soln. (20 ml) was added at 0°. The mixture was stirred vigorously for 15 min. After separation, the org. layer was neutralized with sat. aq. NaHCO₃ soln. (200 ml), dried (Na₂SO₄), and evaporated. FC (hexane/AcOEt 3:1 + 1% Et₃N) yielded 228 mg (95%) of **20** as a non-separable mixture of both atropisomers. Violet solid. M.p. > 250°. TLC (hexane/AcOEt 1:1 + 1% Et₃N): R_f 0.62. UV/VIS (CH₂Cl₂): 412 (100), 510 (14), 542 (3), 586 (5). IR (KBr): 3430s, 2960m, 2930m, 1690s, 1650m, 1590s, 1520s, 1500s, 1470s, 1430s, 1400m, 1340m, 1290m, 1260s, 1160m, 1080s, 1040m, 990s, 950w, 920m, 870w, 800m, 780w, 760m, 650w, 570w. ¹H-NMR (300 MHz, CDCl₃)¹: 8.89 (*d*, *J* = 4.6, 4 H–C(β) (pyr)); 8.78 (*d*, 4 H–C(β) (pyr)); 8.39 (*d*, *J* = 8.4, H–C(5'')); 8.36 (*d*, *J* = 8.4, H–C(5'')); 7.85 (*t*, *J* = 8.4, H–C(4'')); 7.82 (*t*, *J* = 8.4, H–C(4'')); 7.18 (*d*, H–C(3'')); 7.16 (*d*, H–C(3'')); 6.96 (*s*, CONH); 6.85 (*s*, CONH); 3.60 (*s*, MeO–C(2'')); 3.51 (*s*, MeO–C(2'')); 0.08 (*s*, *t*-Bu); 0.04 (*s*, *t*-Bu); –2.67 (br., 2 NH (pyr)). ¹³C-NMR (75 MHz, CDCl₃)¹: 176.4 (CONH); 159.4; 140.0 (C(β) (pyr)); 139.7 (C(β)); 132.7; 132.2; 132.1; 132.0; 131.8; 131.3; 130.8; 130.7 (C(4'')); 130.6; 130.5; 130.4; 119.9; 119.6; 116.0; 114.3; 114.2 (C(5'')); 111.8; 111.7; 106.8 (C(3'')); 102.4; 56.0 (MeO); 26.3 (Me₃C); 1.01 (Me₃C). ¹⁹F-NMR (282 MHz, CDCl₃)¹: –3.9 (*dd*, *J* = 23.6, 7.8, F–C(2''), F–C(6'')); –18.7 (*t*, *J* = 21.0, F–C(4'')); –28.4 (*m*, F–C(3''), F–C(5'')). LDI-TOF-MS: 1055 (*M*⁺, C₅₆H₄₄F₁₀N₆O₄⁺; calc. 1055.03).

N,N'-[10,20-Bis(2,3,4,5,6-pentafluorophenyl)-21*H*,23*H*-porphyrin-5,15-diyl] (6-hydroxy-2,1-phenylene)}-bis[2,2-dimethylpropanamide] (**21**). To a soln. of **20** (mixture of atropisomers; 228 mg, 0.22 mmol) in dry CH₂Cl₂ (30 ml) and dry EtSH (20 ml), AlCl₃ (2.19 g, 16.4 mmol) was added. The mixture was stirred for 24 h and neutralized with sat. aq. NaHCO₃ soln. (100 ml). The aq. layer was extracted with CH₂Cl₂ (3 × 20 ml), and the combined org. extract dried (Na₂SO₄) and evaporated. FC (CH₂Cl₂/MeOH 96:4) yielded 220 mg (97%) of **21**. The atropisomers were separated by FC.

Data of α,β-**21**: Violet solid. M.p. > 250°. TLC (CH₂Cl₂/MeOH 95:5 + 1% Et₃N): R_f 0.34. UV/VIS (CH₂Cl₂): 416 (100), 510 (8), 584 (5), 652 (1). IR (KBr): 3430s, 2960m, 1690s, 1600m, 1520s, 1500s, 1460s, 1400m, 1340m, 1260m, 1150m, 1030m, 990m, 920m, 800m, 780m, 760m, 730m, 570w. ¹H-NMR (300 MHz, CDCl₃)¹: 9.00 (*d*, *J* = 4.9, 4 H–C(β) (pyr)); 8.85 (*d*, 4 H–C(β) (pyr)); 8.30 (*d*, *J* = 8.3, 2 H–C(5'')); 7.75 (*t*, *J* = 8.3, 2 H–C(4'')); 7.16 (*d*, 2 H–C(3'')); 6.80 (*s*, 2 CONH); 5.29 (br., 2 OH–C(2'')); 0.06 (*s*, 2 *t*-Bu); –2.74 (br., 2 NH (pyr)). ¹³C-NMR (75 MHz, CDCl₃)¹: 176.5 (CONH); 155.9 (C(β) (pyr)); 148.0; 144.7; 139.4; 139.2 (C(β) (pyr)); 135.8; 132.2 (C(4'')); 132.0; 131.7; 131.3; 131.1; 130.7; 118.3; 115.5; 114.1; 112.1 (C(5'')); 110.1 (C(3'')); 102.8; 87.3; 26.2 (Me₃C); 14.2 (Me₃C). ¹⁹F-NMR (282 MHz, CDCl₃)¹: –4.2 (*dd*, *J* = 23.4, 7.3, F–C(2''), F–C(6'')); –18.2 (*t*, *J* = 20.9, F–C(4'')); –28.2 (*m*, F–C(3''), F–C(5'')). LDI-TOF-MS: 1024 ([*M* – 3]⁺, [C₅₄H₄₀F₁₀N₆O₄ – 3]⁺; calc. 1023.97).

Data of α,α-**21**: Violet solid. M.p. > 250°. TLC (CH₂Cl₂/MeOH 95:5 + 1% Et₃N): R_f 0.30. UV/VIS (CH₂Cl₂): 416 (100), 50 (8), 584 (4), 656 (4). IR (KBr): 3420s, 2960m, 1690s, 1600m, 1470s, 1390m, 1260m, 1150m, 1040m, 980m, 920m, 750m, 570w. ¹H-NMR (300 MHz, CDCl₃)¹: 9.00 (*d*, *J* = 5.0, 4 H–C(β) (pyr)); 8.84 (*d*, 4 H–C(β) (pyr)); 8.27 (*d*, *J* = 8.3, 2 H–C(5'')); 7.75 (*t*, *J* = 8.3, 2 H–C(4'')); 7.23 (*d*, 2 H–C(3'')); 6.84 (*s*, 2 CONH); 5.29 (br., 2 HO–C(2'')); 0.07 (*s*, 2 *t*-Bu); –2.74 (br., 2 NH (pyr)). ¹³C-NMR (75 MHz, CDCl₃)¹:

176.5 (CONH); 155.9 (C(β) (pyr)); 148.0; 144.7; 139.4; 139.2 (C(β) (pyr)); 135.8; 132.2 (C(4')); 132.0; 131.7; 131.3; 131.1; 130.7; 118.3; 155.5; 114.1; 112.1 (C(5')); 110.1 (C(3')); 102.8; 87.3; 26.2 (Me₃C); 142 (Me₃C). ¹⁹F-NMR (282 MHz, CDCl₃)¹: –5.0 (*dd*, *J* = 20.8, 5.8, F–C(2''), F–C(6'')); –17.8 (*t*, *J* = 23.2, F–C(4'')); –27.7 (*m*, F–C(3''), F–C(5'')). LDI-TOF-MS: 1025 ([*M* – 2]⁺, [C₅₄H₄₀F₁₀N₆O₄ – 2]⁺; calc. 1024.97).

N,N'-{10,20-Bis(2,3,4,5,6-pentafluorophenyl)-5,15-[[1,2]benzenoxypropano{[2]{{dimethylamino}carbonyl}thio}[5]{{1,1-dimethylethyl}[1,3]benzenoxy[1,2]benzeno}-21H,23H-porphyrin-30,47-diy]bis[2,2-dimethylpropanamide]} (23). To a soln. of **21** (mixture of atropisomers; 127 mg, 0.12 mmol) in dry DMF (50 ml), Cs₂CO₃ (1.21 g, 3.71 mmol) was added. The mixture was stirred for 30 min at 65° under Ar. A soln. of **22** [32] (76 mg, 0.15 mmol) in dry DMF (30 ml) was added during 90 min at 65° using an infusion pump. The mixture was stirred for 30 min at 65°, quenched with 10% aq. HCl soln. (50 ml), and extracted with CH₂Cl₂ (3 × 50 ml). The combined org. extracts were dried (Na₂SO₄) and evaporated. Purification by FC (CH₂Cl₂/MeOH 97:3) yielded 125 mg (75%) of **23**. Violet solid. M.p. > 250°. TLC (CH₂Cl₂/MeOH 95:5): R_f 0.23. UV/VIS (CH₂Cl₂): 420 (100), 512 (10), 588 (4), 654 (3). IR (KBr): 3430s, 2960m, 1660s, 1580m, 1490s, 1350s, 1260m, 1170s, 1100s, 980s, 920s, 800m, 760m, 730m, 530m. ¹H-NMR (300 MHz, CDCl₃)¹: 8.91–8.86 (*m*, 8 H–C(β) (pyr), 2 H–C(5')); 7.99 (*s*, H–C(3''), H–C(5'')); 7.71 (*t*, *J* = 9.0, 2 H–C(4'')); 7.53 (*d*, 2 H–C(3'')); 7.26 (*s*, 2 CONH); 3.76–3.51 (*m*, 4 H–C(α')); 2.94 (br., MeN); 2.87 (br., MeN); 2.34–2.29 (*m*, 4 H–C(β')); 2.31 (*s*, 9 H–C(2''')); 2.04–1.67 (*m*, 4 H–C(β')); 0.07 (*s*, 2 *t*-Bu); –2.68 (br., 2 NH (pyr)). ¹⁹F-NMR (282 MHz, CDCl₃)¹: –5.9 (*m*, F–C(2''), F–C(6'')); –18.2 (*m*, F–C(4'')); –28.2 (*m*, F–C(3''), F–C(5'')). MALDI-TOF-MS: 1343 ([*M* – 1]⁺, [C₇₃H₆₇F₁₀N₇O₅S – 1]⁺; calc. 1343.49).

N,N'-{10,20-Bis(2,3,4,5,6-pentafluorophenyl)-5,15-[[1,2]benzenoxypropano{[5]{{1,1-dimethylethyl}[2]mercapto[1,3]benzenoxy[1,2]benzeno}-21H,23H-porphyrin-30,47-diy]bis[2,2-dimethylpropanamide]} (24). To a soln. of **23** (125 mg, 0.093 mol) in degassed dry dioxane (125 ml), 3.5M KOMe in MeOH (2.66 ml, 9.3 mmol) was added. The green soln. was stirred at 50° under Ar, quenched with sat. aq. NH₄Cl soln., and extracted with CH₂Cl₂ (3 × 50 ml). The combined org. extracts were dried (Na₂SO₄) and evaporated. FC (CH₂Cl₂/MeOH 97:3) yielded 91 mg (76%) of **24**. Violet solid. M.p. > 250°. TLC (CH₂Cl₂/MeOH 95:5): R_f 0.21. UV/VIS (CH₂Cl₂): 420 (100), 514 (8), 588 (2), 654 (3). IR (KBr): 3430s, 2930s, 2850m, 1670m, 1580m, 1540w, 1460s, 1400m, 1260m, 1080m, 990m, 920m, 800w, 760w, 570w, 400m. ¹H-NMR (300 MHz, CDCl₃)¹: 8.96–8.88 (*m*, 8 H–C(β) (pyr)); 8.33–8.30 (*m*, 2 H–C(5'')); 7.78–7.75 (*m*, 2 H–C(4'')); 7.24–7.22 (*m*, 2 H–C(3'')); 7.01–6.81 (*m*, 2 CONH, H–C(3''), H–C(5'')); 4.42–4.30 (*m*, 4 H–C(α')); 1.34–1.18 (*m*, 4 H–C(β')); 1.25 (*s*, 9 H–C(2''')); 0.91–0.84 (*m*, 4 H–C(γ')); 0.06 (*s*, 2 *t*-Bu); –2.69 (br., 2 NH (pyr)). ¹⁹F-NMR (282 MHz, CDCl₃)¹: –5.8 (*m*, F–C(2''), F–C(6'')); –18.3 (*m*, F–C(4'')); –29.2 (*m*, F–C(3''), F–C(5'')). MALDI-TOF-MS: 1273 (*M*⁺, C₇₀H₆₂F₁₀N₆O₄S⁺; calc. 1273.41).

Aqua[*N,N'*-{10,20-bis(2,3,4,5,6-pentafluorophenyl)-5,15-[[1,2]benzenoxypropano{[5]{{1,1-dimethylethyl}[2]{{mercapto- κ S}}[1,3]benzenoxy[1,2]benzeno}-21H,23H-porphyrin-30,47-diy]- κ N²¹, κ N²², κ N²³, κ N²⁴}-bis[2,2-dimethylpropanamide]}(3-)}iron(III)] (13). To a soln. of **24** (91 mg, 0.071 mmol) in refluxing toluene (30 ml), 2,6-dimethylpyridine (0.5 ml) was added. The soln. was saturated with FeBr₂. The mixture was stirred 2 h under reflux, filtered through *Celite*, and evaporated. FC yielded 76 mg (80%) of **13**. Brown solid. M.p. > 250°. R_f 0.21 (CH₂Cl₂/MeOH 95:5). UV/VIS (CH₂Cl₂): 420 (100), 510 (11), 580 (7), 656 (3). ¹H-NMR (250 MHz, (D₈)toluene)¹: 82.0 (br., 8 H–C(β) (pyr)); 11.5 (br., H–C(3''), H–C(5'')); 8.4 (br.); 8.1 (br., 2 H–C(3'), 2 H–C(5'')); 7.5 (br., 2 H–C(4'')); 7.2 (br., 4 H–C(γ')); 6.7 (br., 2 CONH); 4.3 (br., 9 H–C(2''')); 4.1 (br., 4 H–C(β')); 3.0 (br., 4 H–C(α')); –0.2 (br., 2 *t*-Bu). MALDI-TOF-MS: 1345 ([*M* + H₂O]⁺), 1324 (*M*⁺, C₇₀H₅₇F₁₀FeN₆O₄S⁺; calc. 1324.21). EPR (toluene, 100 K, 20 mW): 6.318, 2.019.

Reaction of 13 with HBr. To a UV/VIS soln. of **13** in CH₂Cl₂ with an extinction between 1 and 2, 50 μ l of 30% HBr in AcOH were added. The soln. was stirred for 2 h at r.t. under Ar: corresponding bromoiron(III) complex **13**·HBr. Violet soln. UV/VIS (CH₂Cl₂): 452 (100), 516 (29), 588 (13), 644 (15).

Preparation of Complexes 25 and 26. A UV/VIS soln. of **13** in dry THF with an extinction between 1 and 2 was saturated with NaBH₄. The suspension was stirred for 30 min at r.t. under Ar to yield the corresponding aquaferrate(1–) **25**. Through the soln. CO gas was bubbled for 15 min at r.t. to yield the corresponding carbonylferrate(1–).

Data of 25: Red soln. UV/VIS (THF): 366 (sh, 65), 426 (100), 486 (19), 538 (17), 656 (4).

Data of 26: Bright-red soln. UV/VIS (CH₂Cl₂; difference spectrum to that of **25**): 448.

Chlorination Experiments: General Procedure. (Benzyl)(triethyl)ammonium chloride (200 mg, 0.44 mmol) was dissolved in CH₂Cl₂ (200 ml) and stirred with in the presence of conc. aq. NaOCl soln. (*Sigma*, 5% Cl; 3.2 ml) for 30 min. The org. layer was dried (Na₂SO₄) and directly used for the chlorination experiments. The substrate (**5**: 100 mg, 0.573 mmol; **27**: 40 mg, 0.370 mmol; **28**: 20 mg, 0.204 mmol; **29**: 20 mg, 0.217 mmol; **30**: 20 mg, 0.143 mmol; **32**: 20 mg, 0.204 mmol) was dissolved in CH₂Cl₂ (5 ml). The iron(III) porphyrinate **13** (for equiv.

amount, see *Tables 1–3*) and AcOH (1.2 equiv. rel. to substrate), or Lewis acid ($\text{ZnCl}_2 \cdot (\text{OEt}_2)_x$; 0.1 equiv.; SnCl_4 ; 0.1 equiv.; TiCl_4 ; 0.1 equiv.; $\text{BF}_3 \cdot \text{OEt}_2$; 0.02 equiv.). were added. Using an infusion pump, a freshly prepared (35 mM) soln. of (benzyl)(triethyl)ammonium hypochlorite (or a mixture of (benzyl)(triethyl)ammonium chloride and H_2O_2) [14] in CH_2Cl_2 (1.2 equiv. rel. to substrate) was added during 15 min. The soln. was concentrated *in vacuo* at r.t. to 1 ml. In case of **5**, **30**, and **32**, the products were purified by FC (hexan/AcOEt/AcOH 20:20:1) and analyzed by $^1\text{H-NMR}$ and by EI-MS. In case of **27–29**, the soln. was filtered through silica gel (CH_2Cl_2) and analyzed by $^1\text{H-NMR}$ (**27**) or GC/MS using standard curves (**28** and **29**). All experiments were repeated in the absence of the iron(III) porphyrinate **13** under otherwise identical conditions. Substrates **5**, **28–30**, and **32** were recovered unchanged in all cases; in contrast, **27** was chlorinated in the presence of Lewis acids. Accordingly, the corresponding values (*Table 3*) are corrected for these 'background reactions'.

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