Pergamon

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Bioorganic & Medicinal Chemistry 11 (2003) 2695–2707

BIOORGANIC & MEDICINAL CHEMISTRY

Superoxide Dismutase Mimetics. Part 2: Synthesis and Structure–Activity Relationship of Glyoxylate- and Glyoxamide-Derived Metalloporphyrins

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Received 14 August 2002; accepted 4 April 2003

Abstract—Novel glyoxylate- and glyoxamide-derived metalloporphyrins **26–58** were synthesized and evaluated as potential superoxide dismutase (SOD) mimetics. Relative to previously studied MnTBAP analogues, the glyoxylate-derived metalloporphyrins **32**, **39**, and **54** and glyoxamide-derived metalloporphyrin **49**, exhibited enhanced activity in the SOD assay and the majority of the analogues in the current series showed enhanced inhibition of lipid peroxidation and catalase activity.

Introduction

Superoxide radicals ($O_2^{\cdot-}$) have been implicated in the pathogenesis of disease processes including inflammation diseases, cancer and neurological disorders.[1–4] By catalyzing the intra- and extracellular conversion of $O_2^{\cdot-}$ to H_2O_2 plus O_2, superoxide dismutases (SODs) represent the first line of defense against the harmful effects of superoxide radicals that participate in the initiation of lipid peroxidation. Lipid peroxidation is a naturally occurring reaction between polyunsaturated fatty acids and reactive oxygen species. The resulting degradation products, such as small aldehyde fragments, are thought to be associated with a number of disease processes.[5]

Several studies,[6] including ours, are geared toward the development of metalloporphyrin-based antioxidants with SOD activity. More recently, we reported the study of MnTBAP analogues as SOD mimetics.[7] The compounds studied were ester and amide analogues of MnTBAP that have molecular masses close to or over 1000 amu. In an effort to improve the physical, pharmacological, and biological properties of our previously reported SOD mimetics,[7] we set out to design and synthesize metalloporphyrin analogues with significantly reduced molecular weights. We hypothesized that removal of the bridging phenyl group, by placing the carboxylic acid or carboxylate group directly at the *meso* position of the porphyrin ring, using glyoxylic acid derivatives as precursors, would satisfy these objectives.

To date, glyoxylate esters have been utilized in ene[8] and cycloaddition[9] reactions, and as precursors to *N*-aryl iminoesters,[10] enamines,[11] bromo(acyloxy)acetate esters,[12] α-hydroxycyanoacetate esters,[13] and 5,6-dihydro-2*H*-1,3-oxazines.[14] Benzyl and *tert*-butyl glyoxylate have been shown to condense with pyrrole in the presence of $ZnCl_2$ to provide hydroxyester-substituted pyrroles.[15] Collman and co-workers[16] described the preparation of 5,15-diethylcarboxylate-substituted porphyrins through acetal esters. We report herein the preparation of novel metalloporphyrins **26–58** that were derived from glyoxylic acid derivatives and the results of our biological assays designed to determine their potential as catalytic antioxidants with SOD activity.

Results and Discussion

Chemistry

Methyl (**1a**) and ethyl (**1b**) glyoxylate were prepared according to the procedure described by Hook.[17]

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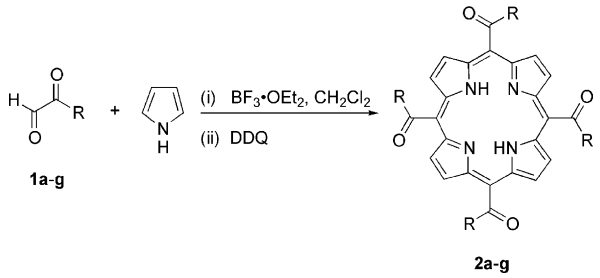
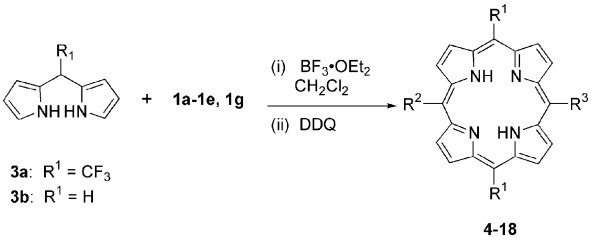
doi:10.1016/S0968-0896(03)00272-4

Table 1. Glyoxylic acid-derived symmetrical tetra-*meso*-porphyrin **2a–2g**

Reactant	Product	R	% Yield
1a	**2a**	$-OCH_3$	6.1
1b	**2b**	$-OCH_2CH_3$	6
1c	**2c**	$-OCH_2CF_3$	3.4
1d	**2d**	$-O(CH_2)_2CH_3$	7
1e	**2e**	$-O(CH_2)_3CH_3$	11
1f	**2f**	$-O(CH_2)_5CH_3$	15
1g	**2g**	$-N(CH_3)_2$	1.7



Scheme 1.



Scheme 2.

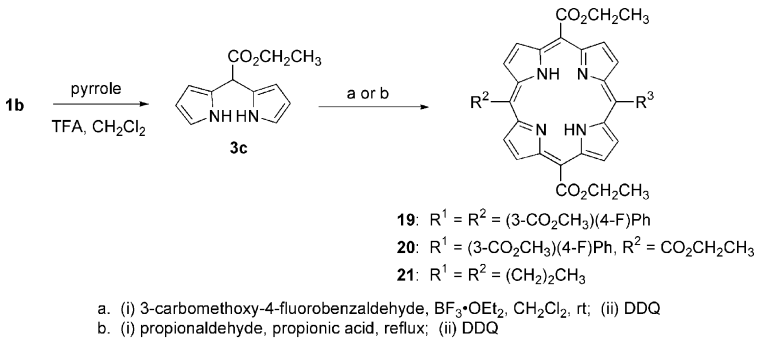
Glyoxylates **1c–f** were prepared by oxidative cleavage of the corresponding tartrates[18] with periodic acid dihydrate.[19] The resulting glyoxylate esters **1a–f** were immediately subjected to $BF_3{\cdot}OEt_2$-catalyzed condensation with pyrrole followed by oxidation with DDQ (Scheme 1) to afford the symmetrical tetra-*meso*-porphyrins **2a–f** in 6–15% yield (Table 1). The procedure is also amenable to the preparation of *meso* amide porphyrin analogues: the porphyrin **2g** was isolated from the condensation of pyrrole with glyoxamide **1g**, that was derived from its corresponding tartramide by periodic cleavage.

Having demonstrated the application of glyoxylic acid derivatives **1a–g** as porphyrin precursors, we next directed our attention to the reaction of glyoxylic acid derivatives with representative dipyrromethanes. Dipyrromethanes are known precursors to *trans*-substituted porphyrins;[20] however, one drawback for utilizing dipyrromethanes in porphyrin synthesis is their propensity to undergo acidolysis under the reaction conditions, resulting in the formation of multiple scrambled *meso*-substituted porphyrin products. The trifluoromethyl-substituted dipyrromethane[21] **3a** was reported to be more resistant to scrambling than other known dipyrromethanes. Therefore, the reaction of **3a** with glyoxylate esters (**1a** and **1d**) was attempted first (Scheme 2) to provide only the *trans*-substituted products **4** and **5**, respectively (Table 2). When the reaction of glyoxylate esters with known dipyrromethane **3b**[22] was evaluated, the desired *trans* porphyrins (i.e., **6**, **9**, **11**, **13**, and **15**) in addition to acidolysis products (i.e., **7**, **8**, **10**, **12**, **14**, **16**, and **18**) were obtained.

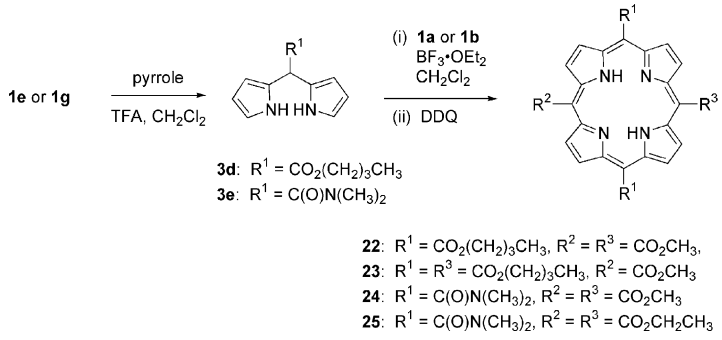
We next investigated the preparation of dipyrromethane **3c** and its utility in porphyrin synthesis. Dipyrromethane

Table 2. Reaction of glyoxylic acid derivatives with dipyrromethanes

Reactants		Product(s)	R^1	R^2	R^3	% Yield
3a	**1a**	**4**	CF_3	CO_2CH_3	CO_2CH_3	30
3a	**1d**	**5**	CF_3	$CO_2(CH_2)_2CH_3$	$CO_2(CH_2)_2CH_3$	3.7
3b	**1a**	**6**	H	CO_2CH_3	CO_2CH_3	1.4
		7	H	CO_2CH_3	H	0.5
		8	H	H	H	Trace
3b	**1b**	**9**	H	$CO_2CH_2CH_3$	$CO_2CH_2CH_3$	7
		10	H	$CO_2CH_2CH_3$	H	<1
		8	H	H	H	0.5
3b	**1c**	**11**	H	$CO_2CH_2CF_3$	$CO_2CH_2CF_3$	1.2
		12	H	$CO_2CH_2CF_3$	H	0.7
		8	H	H	H	Trace
3b	**1d**	**13**	H	$CO_2(CH_2)_2CH_3$	$CO_2(CH_2)_2CH_3$	2.9
		14	H	$CO_2(CH_2)_2CH_3$	H	1.2
		8	H	H	H	Trace
3b	**1e**	**15**	H	$CO_2(CH_2)_3CH_3$	$CO_2(CH_2)_3CH_3$	7.0
		16	H	$CO_2(CH_2)_3CH_3$	H	1.3
3b	**1g**	**17**	H	$C(O)N(CH_3)_2$	$C(O)N(CH_3)_2$	0.9
		18	H	$C(O)N(CH_3)_2$	H	0.2
3c	**8**	**19**	$CO_2CH_2CH_3$	(3-CO_2CH_3)(4-F)Ph	(3-CO_2CH_3)(4-F)Ph	3.3
		20	$CO_2CH_2CH_3$	(3-CO_2CH_3)(4-F)Ph	$CO_2CH_2CH_3$	5.2
3c	**9**	**21**	$CO_2CH_2CH_3$	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	10
3d	**1a**	**22**	$CO_2(CH_2)_3CH_3$	CO_2CH_3	CO_2CH_3	2.8
		23	$CO_2(CH_2)_3CH_3$	CO_2CH_3	$CO_2(CH_2)_3CH_3$	0.7
3e	**1a**	**24**	$C(O)N(CH_3)_2$	CO_2CH_3	CO_2CH_3	1.7
3e	**1b**	**25**	$C(O)N(CH_3)_2$	$CO_2CH_2CH_3$	$CO_2CH_2CH_3$	1



Scheme 3.

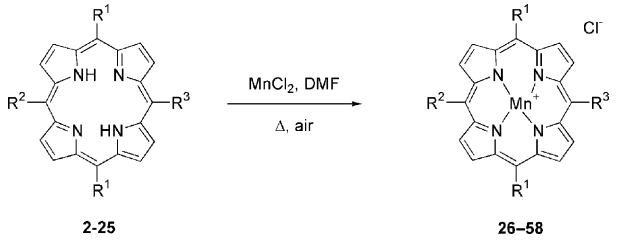


Scheme 4.

3c, obtained from the reaction of ethyl glyoxylate (**1b**) with pyrrole under TFA catalysis, was condenxsed with 3-carbomethoxy-4-fluorobenzaldehyde[23] to provide the desired *trans* porphyrin **19** and acidolysis product **20** (Scheme 3, Table 2). Our desire to prepare a representative porphyrin bearing an alkyl group at the *meso* position led us to attempt the condensation of dipyrromethane **3c** with propionaldehyde, first, under BF_3 catalysis. However, no desired product **21** was isolated. When the condensation was performed in refluxing propionic acid,[24] *trans* porphyrin product **21** was successfully isolated. The preceding examples demonstrated the utility of glyoxylate ester-derived dipyrromethanes, such as **3c**, in porphyrin synthesis.

The synthesis of a representative mixed carboxylate porphyrin was realized when methyl glyoxylate (**1a**) was condensed with dipyrromethane **3d** to provide *trans*-substituted porphyrin **22** and acidolysis product porphyrin **23** (Scheme 4). To explore the utility of an amide-substituted dipyrromethane as a precursor to porphyrins, we synthesized dipyrromethane **3e** then condensed it with methyl and ethyl glyoxylate to provide only the *trans*-substituted products **24** and **25**, respectively (Scheme 4, Table 2).[25]

Isolated porphyrins **4**–**25** were metalated with $MnCl_2$ in DMF (Scheme 5) to provide metalloporphyrins **26**–**58** (Table 3). In some cases, byproducts, due to partial hydrolysis and/or decarboxylation during metalation, were isolated. The metalated porphyrin derivatives were then assayed for biological activity.



Scheme 5.

Biology

Reactive oxygen species (superoxide, hydrogen peroxide, lipid peroxides and hydroxyl radicals) are important mediators of biomacromolecule oxidation, such as proteins, lipids, sugars, and DNA.[26] These oxidized macromolecules that are thought to contribute to organ dysfunction and inflammation associated with many common disease states such as stroke,[3c] cancer[3d] and diabete.[3e] The body possesses powerful antioxidant defenses, both enzymatic (superoxide dismutase, catalase, glutathione peroxidase) and non-enzymatic (glutathione, vitamin E, ascorbate, urate), to limit the deleterious actions of reactive oxygen species under normal conditions, but these defenses can be consumed or overwhelmed under pathological states. A number of animal models of human disease can be attenuated by the over-expression of endogenous antioxidant defenses.[1c,27a,27b] Reactive oxygen species are thus a logical pharmacological target in disease states associated with excessive inflammation and oxidative stress. A number

Table 3. Metallation of glyoxylic acid-derived porphyrins

Reactant	Product	R^1	R^2	R^3	% Yield	FAB MS *m/z*
2a	**26**	CO_2CH_3	CO_2CH_3	CO_2CH_3	59	595
	27	CO_2CH_3	CO_2H	CO_2CH_3	< 5	581
2b	**228**	$CO_2CH_2CH_3$	$CO_2CH_2CH_3$	$CO_2CH_2CH_3$	84	651
	29	$CO_2CH_2CH_3$	CO_2H	$CO_2CH_2CH_3$	< 5	623
	30	$CO_2CH_2CH_3$	H	$CO_2CH_2CH_3$	< 5	579
2c	**31**	$CO_2CH_2CF_3$	$CO_2CH_2CF_3$	$CO_2CH_2CF_3$	58	867
2d	**32**	$CO_2(CH_2)_2CH_3$	$CO_2(CH_2)_2CH_3$	$CO_2(CH_2)_2CH_3$	88	707
2e	**33**	$CO_2(CH_2)_3CH_3$	$CO_2(CH_2)_3CH_3$	$CO_2(CH_2)_3CH_3$	43	763
	34	$CO_2(CH_2)_3CH_3$	CO_2H	$CO_2(CH_2)_3CH_3$	2.7	707
2f	**35**	$CO_2(CH_2)_5CH_3$	$CO_2(CH_2)_5CH_3$	$CO_2(CH_2)_5CH_3$	98	875
2g	**36**	$C(O)N(CH_3)_2$	$C(O)N(CH_3)_2$	$C(O)N(CH_3)_2$	27	647
4	**37**	CF_3	CO_2CH_3	CO_2CH_3	88	615
	38	CF_3	CO_2H	CO_2CH_3	12	601
5	**39**	CF_3	$CO_2(CH_2)_2CH_3$	$CO_2(CH_2)_2CH_3$	87	671
6	**40**	H	CO_2CH_3	CO_2CH_3	34	479
7	**41**	H	CO_2CH_3	H	14	421
9	**42**	H	$CO_2CH_2CH_3$	$CO_2CH_2CH_3$	19	507
11	**43**	H	$CO_2CH_2CF_3$	$CO_2CH_2CF_3$	72	615
12	**44**	H	$CO_2CH_2CF_3$	H	92	489
13	**45**	H	$CO_2(CH_2)_2CH_3$	$CO_2(CH_2)_2CH_3$	98	535
14	**46**	H	$CO_2(CH_2)_2CH_3$	H	74	449
15	**47**	H	$CO_2(CH_2)_3CH_3$	$CO_2(CH_2)_3CH_3$	43	563
16	**48**	H	$CO_2(CH_2)_3CH_3$	H	44	463
17	**49**	H	$C(O)N(CH_3)_2$	$C(O)N(CH_3)_2$	23	505
18	**50**	H	$C(O)N(CH_3)_2$	H	43	434
19	**51**	$CO_2CH_2CH_3$	(3-CO_2CH_3)(4-F)Ph	(3-CO_2CH_3)(4-F)Ph	73	811
20	**52**	$CO_2CH_2CH_3$	(3-CO_2CH_3)(4-F)Ph	$CO_2CH_2CH_3$	82	731
21	**53**	$CO_2CH_2CH_3$	$(CH_2)_2CH_3$	$(CH_2)_2CH_3$	24	563
22	**54**	$CO_2(CH_2)_3CH_3$	CO_2CH_3	CO_2CH_3	39	679
	55	$CO_2(CH_2)_3CH_3$	CO_2CH_3	CO_2H	12	665
23	**56**	$CO_2(CH_2)_3CH_3$	CO_2CH_3	$CO_2(CH_2)_3CH_3$	27	721
24	**57**	CO_2CH_3	$C(O)N(CH_3)_2$	$C(O)N(CH_3)_2$	21	621
25	**58**	$CO_2CH_2CH_3$	$C(O)N(CH_3)_2$	$C(O)N(CH_3)_2$	29	649

of metal containing antioxidants with SOD activity have been pursued for development with this intent.[28]

Porphyrin analogues **26–58** were assayed for SOD, catalase and/or peroxidase activity. Superoxide dismutase activity was measured by cytochrome c reductase previously described by McCord and Fridovich.[29] Catalase activity was monitored by measuring oxygen evolution with a Clark-type electrode in the presence of 1 mM H_2O_2[6d,30] and the ability of mimetics to inhibit lipid peroxidation (TBARS, IC_{50} μM) was assessed as previously described.[31] Iron and ascorbate were used to initiate lipid peroxidation in tissue homogenates and the formation of thiobarbituric acid reactive species (TBARS) was measured.[32,33]

The biological activity data are shown in Table 4. Relative to our previously studied MnTBAP analogues,[7] porphyrin **55** exhibited similar activity and porphyrins **32**, **39**, **49**, and **54** exhibited enhanced activity in the SOD assay. Those porphyrin analogues derived from dipyrromethane **3b** and glyoxylate esters **1a–f** (i.e., compounds **40–48**) generally interfered with the SOD assay, whereas the corresponding analogues derived from the dipyrromethane **3b** and glyoxamide **1g** (i.e., compounds **49** and **50**) exhibited SOD activity.

All the compounds except for compound **35** exhibited enhanced lipid peroxidation activity as indicated by improved IC_{50} values in the TBARS assay compared to the MnTBAP analogues in our previous studies.[7] In the current report, the porphyrins bearing two unsubstituted *meso* positions (compounds **40**, **43**, **45**, **47** and **49**) showed from 2- to 5-fold enhancement in the TBARS assay relative to the corresponding monosubstituted compounds (**41**, **44**, **46**, **48**, and **50**, respectively).

Many of the porphyrin derivatives in Table 4 exhibited a more significant catalase activity relative to our previously studied MnTBAP analogues. In this series, most of the porphyrins bearing two unsubstituted *meso* position (compounds **40**, **43**, **45**, and **49**) showed significant catalase activity relative to their corresponding tetra *meso*-substituted compounds (**26**, **31**, **32** and **36**, respectively). There was no significant difference in the catalase activity of the tetra *meso*-substituted compounds (**26**, **31**, **32** and **36**) relative to the corresponding monosubstituted compounds (**41**, **44**, **46**, and **50**, respectively).

Recent studies have shown that an early glycolate analogue, **28** (AEOL-11201), was effective in attenuating an acetic acid-induced colitis in rats.[34] Rats were treated with AEOL-11201 (5 mg/kg, ip daily for 5 days) and this regimen significantly decreased the severity of diarrhea and the severity of macroscopic and histological changes in the colon.

Table 4. In vitro biological activity data for porphyrins **26–58**

Product	SOD activity[a] (SOD unit/mg)	TBARS[b] (IC_{50} μM)	Catalase[c] (min^{-1})
MnTBAP	41 ($n=3$)[d]	45[d]	0.81 ($n=3$)
26	NA[e]	0.725 ($n=2$)	0.125 ($n=2$)
27	NA	0.259[f]	0.62
28	5.62 ($n=5$)	3.35 ($n=2$)	0.884 ($n=5$)
29	2.3 (est)	1.3	NA
30	NA	0.1	1.85
31	3.4	15	1.59
32	129.5 ($n=2$)	6.65 ($n=2$)	0.4 ($n=2$)
33	Interferes[f]	8.2	0.93
34	Red cyt c[g]	17	—
35	Red cyt c	306	0.22
36	4.5	30	0.16
37	NA	8.2 ($n=2$)	0.525 ($n=2$)
38	4.3 (est)	16	0.62
39	98	4	—
40	Interferes	8.5	0.08
41	Interferes	15	0.22
42	Interferes	9.7	—
43	Interferes	4.7	0.33
44	0.6 (est)	12	0.33
45	Red cyt c	8.4	0.04
46	Interferes	17	0.39
47	Interferes	4.4	0.93
48	Interferes	26	—
49	70.4	15.5	0.12
50	1.7	39	0.17
51	19	1.2	1.56
52	6.5	0.91	0.54
53	Red cyt c	14.7	0.54
54	67.4	7.1	0.17
38b55	41.9 (est)	2.6	Bleached[h]
56	—	8.6	1.09
57	0.7 (est)	2.1	0.06
58	5.6	1.5	—

[a]Units of superoxide dismutase (SOD) activity defined as the amount of compound that inhibits 50% reduction of cytochrome c.
[b]The concentration of compound that inhibits iron/ascorbate-mediated brain homogenate lipid peroxidation by 50%.
[c]Pseudo first order rate constant for H_2O_2 decay.
[d]Results from ref 7.
[e]NA, not active.
[f]Interferes with cytochrome c assay by unknown mechanism.
[g]Compound directly reduces cytochrome c.
[h]Compound is not stable under assay conditions.

Conclusion

We have shown that glyoxylic esters **1a–f** and glyoxamide **1g** are useful precursors in the synthesis of novel low molecular weight metalloporphyrins **26–58**.

This study also demonstrated that the removal of the bridging phenyl group (i.e., in MnTBAP series[7]) by direct attachment of the carboxylate groups at the porphyrin meso positions resulted in analogues with enhanced activities. Relative to previously studied MnTBAP analogues, four compounds in this series, 5,10,15,20-tetrakis(*n*-butylcarbonyl)-, 5,15-bis(*n*-butylcarbonyl)-10,20-bis(trifluoromethyl)-, 5,15-bis(dimethylamido)-, and [5,15-bis(*n*-butoxycarbonyl)-10,20-bis(methoxycarbonyl)-porphyrinato]manganese(III) analogues, showed improved activity in the SOD assay. The majority of compounds in this study showed enhanced efficacy in the TBARS assay and showed enhanced catalase activity relative to MnTBAP and other MnTBAP analogues[7] previously studied. These compounds are now under active investigation for their therapeutic potential in animal models of disease that involved excessive inflammation and oxidative stress.

Experimental

Proton and carbon NMR spectra were obtained on a Bruker AC 300 spectrometer at 300 and 75 MHz, respectively. Proton spectra were referenced to tetramethylsilane as an internal standard, and the carbon spectra were referenced to $CDCl_3$ or DMSO-d_6 (purchased from Cambridge Isotope Laboratories). All carbon spectra were proton decoupled. The IR spectrometer used was a single beam Perkin–Elmer Spectrum 1000 FT-IR. All IR spectra obtained were prepared in a pressed disc of KBr. All IR spectra obtained were acquired with a total of four accumulations at a resolution of 4.00 cm^{-1}. Melting points were obtained on a Mel-Temp II apparatus and are uncorrected. CI Mass spectra were obtained on a Shimadzu QP-5000 Mass Spectrometer and FAB mass spectral analyses were performed by M-Scan of West Chester, PA, USA. Elemental analyses were performed by Quantitative Technologies, Inc. of Whitehouse, NJ, USA. HLPC analyses were obtained using a Microsorb C18 Column with UV detection at 230 nm (unless otherwise specified). HPLC grade methylene chloride and anhydrous DMF and ethyl ether were used.

2,2,2-Trifluoroethyl glyoxylate (1c). *d*-Tartaric acid (25 g, 0.17 mol), 2,2,2-trifluoroethanol (200 mL), and concentrated H_2SO_4 (59 mL) were heated at reflux for 1 day. The solution was cooled to room temperature then partitioned between H_2O and CH_2Cl_2. The organic layer was washed consecutively with aqueous saturated $NaHCO_3$, H_2O, and brine, then dried (Na_2SO_4), filtered, and the solvent removed in vacuo. Recrystallization from hexanes/ether provided di-(2,2,2-trifluoroethyl) tartrate (17.3 g, 33%) as white crystals: mp 77–79 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.13 (br s, 2H), 4.59–4.74 (m, 6H); CI MS *m*/*z* 315 $[C_8H_{10}F_6O_6+H]^+$.

A solution of di-(2,2,2-trifluoroethyl) tartrate (1 g, 3.2 mmol) in ether (25 mL) was magnetically stirred at 0 °C under N_2 as periodic acid dihydrate (0.72 g, 3.2 mmol) was added in portions (3 × 0.24 g) over the course of 1 h. The solution was stirred for an additional 4 h then decanted from the solid precipitate, dried (Na_2SO_4), filtered, and the solvent removed in vacuo to provide crude **1c** (0.85 g, 86%) which was immediately used without further purification and characterization. The glyoxylic esters and glyoxamide readily polymerized making their characterization difficult. When there was a need for these glyoxylic acid derivatives, they were usually prepared fresh and used immediately and without purification.[18,19]

***n*-Propyl glyoxylate (1d).** *d*-Tartaric acid (2.56 g, 17.0 mmol), *n*-propanol (30 mL), and concentrated H_2SO_4 (6 mL) were heated at reflux for 3 days. The solution was cooled to room temperature then partitioned between H_2O and CH_2Cl_2. The organic layer was

washed consecutively with aqueous saturated $NaHCO_3$, H_2O, and brine, then dried (Na_2SO_4), filtered, and the solvent removed in vacuo to provide crude di-*n*-propyl tartrate (2.6 g, 65%) that was used without further purification: ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (t, 6H), 1.68–1.79 (m, 2H), 3.22 (d, 2H), 4.15–4.29 (m, 4H), 4.55 (d, 2H); CI MS *m*/*z* 235 $[C_{10}H_{18}O_6+H]^+$.

A solution of di-*n*-propyl tartrate (0.73 g, 3.1 mmol) in ether (10 mL) was magnetically stirred at 0 °C under dry N_2, as periodic acid dihydrate (0.711 g, 3.12 mmol) was added. The resulting solution was stirred for 1 h. Anhydrous Na_2SO_4 was added and the resulting milky solution was filtered. The solvent was evaporated in vacuo to provide **1d** (0.670 g; 93%) as an oil: CI MS *m*/*z* 117 $[C_5H_8O_3+H]^+$.[18,19]

***n*-Butyl glyoxylate (1e).** *d*-Tartaric acid, (25 g, 0.17 mol), *n*-butanol (200 mL), and concentrated H_2SO_4 (59 mL) were heated at reflux overnight. The solution was cooled to room temperature then partitioned between H_2O and CH_2Cl_2. The organic layer was washed consecutively with aqueous saturated $NaHCO_3$, H_2O, and brine, then dried (Na_2SO_4), filtered, and the solvent removed in vacuo. Kugelrohr distillation (bp 100–105 °C, 0.06 mm Hg) provided di-*n*-butyl tartrate as an oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, 6H), 1.30–1.48 (m, 4H), 1.60–1.74 (m, 4H), 3.15–3.28 (m, 2H), 4.16–4.30 (m, 4H), 4.54 (d, 2H).

A solution of di-*n*-butyl tartrate (5 g, 19 mmol) in ether (150 mL) was magnetically stirred at 0 °C under dry N_2, as periodic acid dihydrate (4.35 g, 19 mmol) was added over 1 h in portions (3 × 1.45 g). The resulting solution was stirred for 4 h, decanted from the solid precipitate, dried (Na_2SO_4), filtered, and the solvent was evaporated in vacuo to provide **1e** (4.72 g, 96%) as an oil. The crude mixture was immediately used without further purification and characterization.[18,19]

***n*-Hexyl glyoxylate (1f).** *d*-Tartaric acid (15 g, 0.10 mol), *n*-hexanol (150 mL), and concentrated H_2SO_4 (35 mL) were heated at reflux overnight. The solution was cooled to room temperature then partitioned between H_2O and CH_2Cl_2. The organic layer was washed consecutively with aqueous saturated $NaHCO_3$, H_2O, and brine, then dried (Na_2SO_4), filtered, and the solvent removed in vacuo. Purification by column chromatography on silica gel (4:1 hexanes/ether) provided di-*n*-hexyl tartrate (7.88 g, 25%) as an oil: ^1H NMR (300 MHz, $CDCl_3$) δ 0.85–0.95 (m, 6H), 1.28–1.40 (m, 12H), 1.67–1.73 (m, 4H), 3.15 (d, 2H), 4.25 (m, 4H), 4.55 (d, 2H); CI MS *m*/*z* 319 $(C_{16}H_{30}O_6+H)^+$.

A solution of di-*n*-hexyl tartrate (7.88 g, 25 mmol) in ether (150 mL) was magnetically stirred at 0 °C under dry N_2, as periodic acid dihydrate (5.64 g, 25 mmol) was added in portions (3 × 1.88 g) over 1 h. The resulting solution was stirred for 2.5 h, decanted from the solid precipitate, dried (Na_2SO_4), filtered and the solvent was evaporated in vacuo to provide crude **1f**. The crude mixture was immediately used without further purification and characterization.[18,19]

***N,N*-Dimethyl glyoxamide (1g).** A solution of (+)-*N,N,N′,N′*-tetramethyl-L-tartaric acid diamide (2.00 g, 9.79 mmol) in CH_2Cl_2 (60 mL) was magnetically stirred at 0 °C under dry N_2, as periodic acid dihydrate (2.79 g, 12.2 mmol) was added. The resulting solution was stirred for 4.5 h, decanted from the solid precipitate, dried (Na_2SO_4), filtered, and the solvent was evaporated in vacuo to provide crude **1g** (1.84 g, 93%) as an oil and was immediately used without further purification: CI MS *m*/*z* 102 $[C_4H_7NO_2+H]^+$.

5,10,15,20-Tetrakis(methoxycarbonyl)porphyrin (2a). In a foil covered, 22-L three-neck round-bottomed flask equipped with a mechanical stirrer and a N_2 inlet was added sequentially, freshly distilled methyl glyoxylate (**1a**, 16.5 g, 187 mmol), CH_2Cl_2 (19 L), and pyrrole (13.0 mL, 194 mmol). The reaction mixture was stirred for 5–10 min then $BF_3{\cdot}OEt_2$ (2.30 mL, 18.7 mmol) was added dropwise. The reaction was monitored by the formation of a Soret band through UV–vis spectrometry: small aliquots of the reaction mixture were drawn, oxidized with DDQ, and the solution analyzed by UV–vis spectrometry. After a stirring period of 1.25 h at room temperature, DDQ (31.9 g, 140 mmol) was added. The reaction mixture was stirred for an additional 2.25 h at room temperature, then clay (Clarion 550, 25 g) was added and the suspension was stirred for 2.5 h. Filtration of the reaction mixture through Celite provided, after evaporation of solvents, a crude solid mixture that was adsorbed onto silica gel (15 g). Purification by column chromatography on silica gel (CH_2Cl_2 as eluent) provided porphyrin **2a** (1.55 g, 6.1%) as a purple solid: UV–vis λ_{max}, nm: 404.5; ^1H NMR (300 MHz, $CDCl_3$) δ 9.48 (s, 4H), 4.60 (s, 12H), −3.42 (s, 2H).

5,10,15,20-Tetrakis(ethoxycarbonyl)porphyrin (2b). Following the procedure for the preparation of **2a** and using freshly distilled ethyl glyoxylate (**1b**, 19.3 g, 189 mmol), the porphyrin **2b** (1.7 g; 6%) was isolated after purification by column chromatography on silica gel (elution with CH_2Cl_2) as a purple solid: mp 260–265 °C; UV–vis λ_{max}, nm (ε): 409 (2.34×10^5); ^1H NMR (300 MHz, $CDCl_3$) δ 9.52 (s, 8H), 5.11 (q, $J=7.2$ Hz, 8H), 1.81 (t, $J=7.2$ Hz, 12H), −3.33 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 145.3, 131.6, 112.4, 63.7, 15.0; FAB MS *m*/*z* 599 $[C_{32}H_{30}N_4O_8+H]^+$. Anal. calcd for $C_{32}H_{30}N_4O_8$: C, 64.21; H, 5.05; N, 9.36. Found: C, 64.00; H, 5.18; N, 9.19.

5,10,15,20 - Tetrakis(2,2,2 - trifluoroethoxycarbonyl)porphyrin (2c). Following the procedure for the preparation of **2a** and using freshly prepared 2,2,2-trifluoroethyl glyoxylate (**1c**, 0.85 g, 5.4 mmol), the porphyrin **2c** (37 mg, 3.4%) was isolated after purification by column chromatography on silica gel (gradient elution with 50–66% CH_2Cl_2/hexanes) as a purple solid: ^1H NMR (300 MHz, $CDCl_3$) δ 9.51 (s, 8H), 5.54 (q, 8H), −3.49 (s, 2H).

5,10,15,20 - Tetrakis(propoxycarbonyl)porphyrin (2d). Following the procedure for the preparation of **2a** and using freshly prepared *n*-propyl glyoxylate (**1d**, 1.31 g,

11.3 mmol), the porphyrin **2d** (130 mg, 7%) was isolated after purification by column chromatography on silica gel (gradient elution with 66–100% CH_2Cl_2/hexanes) as a purple solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (s, 8H), 5.02 (t, J = 6.5 Hz, 8H), 2.13–2.22 (m, 8H), 1.29 (t, J = 7.8 Hz, 12H), −3.31 (s, 2H).

5,10,15,20-Tetrakis(butoxycarbonyl)porphyrin (2e). Following the procedure for the preparation of **2a** and using freshly prepared *n*-butyl glyoxylate (**1e**, 2.5 g, 19 mmol), the porphyrin **2e** (0.36 g; 11%) was isolated after purification by column chromatography on silica gel (gradient elution with 50–100% CH_2Cl_2/hexanes) as a dark violet solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (s, 8H), 5.06 (t, J = 6.7 Hz, 8H), 2.14 (q, J = 7.3 Hz, 8H), 1.68–1.73 (m, 8H), 1.12 (t, J = 7.3 Hz, 12H), −3.32 (s, 2H).

5,10,15,20-Tetrakis(*n*-hexyloxycarbonyl)porphyrin (2f). Following the procedure for the preparation of **2a** and using freshly prepared *n*-hexyl glyoxylate **1f** (4.0 g, 26 mmol), the porphyrin **2f** (810 mg, 15%) was isolated after purification by column chromatography on silica gel (gradient elution with 50–70% CH_2Cl_2/hexanes) as a dark violet solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (s, 8H), 5.05 (t, 8H), 2.10–2.20 (m, 8H), 1.62–1.71 (m, 8H), 1.35–1.50 (m, 16H), 0.95 (t, 12H), −3.31 (s, 2H).

5,10,15,20-Tetrakis(dimethylamido)porphyrin (2g). Following the procedure for the preparation of **2a** and using freshly prepared glyoxamide **1g** (1.82 g, 18.0 mmol), the porphyrin **2g** (80 mg, 3%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–2% MeOH/CH_2Cl_2) as a solid mixture of atropisomers: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.27 (s, 8H), 3.80 (s, 12H), 2.71–2.91 (m, 12H), −3.18 to −3.10 (three s, 2H, atropisomers); FAB MS m/z 595 $[C_{32}H_{34}N_8O_4 + H]^+$.

***meso*-(Ethoxycarbonyl)dipyrromethane (3c).** In a round-bottom flask equipped with a magnetic stir bar and N_2 inlet was placed freshly prepared ethyl glyoxylate (**1b**, 12.6 g, 123 mmol), pyrrole (102 mL, 1.48 mol), and CH_2Cl_2 (700 mL). Trifluoroacetic acid (3.8 mL, 49 mmol) was then added. The resulting dark solution was stirred overnight at room temperature, diluted with CH_2Cl_2, then washed with H_2O, saturated aqueous $NaHCO_3$, H_2O, and brine. The organic layer was dried (Na_2SO_4), filtered and the solvent removed in vacuo. The crude product was repeatedly purified by column chromatography on silica gel (elution with 50% CH_2Cl_2/hexanes) then recrystallized from CH_2Cl_2/hexanes to provide **3c** (9.39 g; 35%) as white crystals: mp 70–75 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (br s, 2H), 6.70–6.75 (m, 2H), 6.14–6.17 (m, 2H), 6.06–6.10 (m, 2H), 5.10 (s, 1H), 4.24 (q, J = 7.3 Hz, 2H), 1.31 (t, J = 7.3 Hz, 3H).

***meso*-(*N,N*-Dimethylamido)dipyrromethane (3e).** Following the procedure for the preparation of **3c** and using freshly prepared *N,N*-dimethyl glyoxamide (**1g**, 2.0 g, 20 mmol), the dipyrromethane **3e** (1.24 g; 31%) was isolated after purification by column chromatography on silica gel (gradient elution with 40% CH_2Cl_2/hexanes to 3% MeOH/CH_2Cl_2) as a light brown solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.30 (br s, 2H), 6.50–6.55 (m, 2H), 6.06–6.10 (m, 2H), 6.01–6.14 (m, 2H), 5.41 (s, 1H), 3.18 (s, 3H), 2.99 (s, 3H); CI MS m/z 217 $[C_{12}H_{15}N_3O]^+$.

***meso*-(*n*-Butoxycarbonyl)dipyrromethane (3f).** Following the procedure for the preparation of **3c** and using freshly prepared *n*-butyl glyoxylate (**1d**, 3.85 g, 29.6 mmol), the dipyrromethane **3f** (1.04 g, 14%) was isolated after purification by column chromatography on silica gel (elution with 1:1 hexanes/CH_2Cl_2) as a tan solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (br s, 2H), 6.72–6.75 (m, 2H), 6.14–6.18 (m, 2H), 6.08 (br s, 2H), 5.12 (s, 1H), 4.18 (t, 2H), 1.60–1.70 (m, 2H), 1.31–1.53 (m, 2H), 0.95 (t, 3H).

5,15-Bis(methoxycarbonyl)-10,20-bis(trifluoromethyl)porphyrin (4). In a foil covered, 500-mL three-neck round-bottomed flask equipped with a magnetic stirrer and a N_2 inlet was added consecutively, freshly distilled methyl glyoxylate (**1a**, 244 mg, 2.77 mmol), dipyrromethane **3a** (590 mg, 2.75 mmol), and CH_2Cl_2 (280 mL). The reaction mixture was stirred for 5–10 min then $BF_3{\cdot}OEt_2$ (112 μL, 0.9 mmol) was added. After a stirring period of 2 h at room temperature, DDQ (945 mg, 4.1 mmol) was added in the mixture and stirring was continued for an additional 2 h at room temperature. The solvent was removed in vacuo and the residue was adsorbed onto silica gel (3.8 g). Purification by column chromatography on silica gel (elution with CH_2Cl_2) to provide porphyrin **4** (390 mg, 30%) as a solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (m, 4H), 9.44 (d, J = 5.1 Hz, 4H), 4.60 (s, 6H), −2.96 (s, 2H).

5,15-Bis(*n*-propoxycarbonyl)-10,20-bis(trifluoromethyl)-porphyrin (5). Following the procedure for the preparation of **4**, and using freshly prepared *n*-propyl glyoxylate (**1d**, 154 mg, 1.3 mmol), and dipyrromethane **3a** (283 mg, 1.3 mmol), the porphyrin **5** (15 mg, 3.7%) was isolated after purification by column chromatography on silica gel (elution with 50% CH_2Cl_2/hexanes) as a purple solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68–9.79 (m, 4H), 9.46 (d, 4H), 5.04 (t, 4H), 2.15–2.25 (m, 4H), 1.30 (t, 6H), −2.94 (s, 2H).

5,15-bis(Methoxycarbonyl)porphyrin (6) and 5-(methoxycarbonyl)porphyrin (7). Following the procedure for the preparation of **4**, and using freshly distilled methyl glyoxylate (**1a**, 1.76 g, 20 mmol) and dipyrromethane **3b** (2.92 g, 20 mmol), the porphyrins **6** (61 mg, 1.4%), **7** (30 mg, 0.7%), and **8** (trace) were isolated after purification by column chromatography on silica gel (gradient elution with 33% hexanes/CH_2Cl_2 to 100% CH_2Cl_2). For porphyrin **6**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.40 (s, 2H), 9.70 (d, 2H), 9.50 (d, 4H), 4.65 (s, 6H), −3.21 (s, 2H). For porphyrin **7**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.49 (s, 2H), 10.34 (s, 1H), 9.70 (d, 2H), 9.52 (d, 2H), 9.48 (s, 2H), 4.65 (s, 3H), −3.60 (s, 2H).

5,15-Bis(ethoxycarbonyl)porphyrin (9) and 5-(ethoxycarbonyl)porphyrin (10). Following the procedure for

the preparation of **4**, and using commercially available ethyl glyoxylate (**1b**, 50% in toluene; 310 mg, 1.5 mol) and dipyrromethane **3b**, the porphyrins **9** (22 mg, 7%), **10** (10 mg, 2%), and **7** (3 mg, 0.5%) were isolated after purification by column chromatography on silica gel (gradient elution with 50–75% CH_2Cl_2/hexanes). For porphyrin **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.39 (s, 2H), 9.71 (d, 4H), 9.48 (d, 4H), 5.15 (q, 4H), 1.90 (t, 6H), −3.23 (s, 2H). For porphyrin **10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.31 (s, 2H), 10.26 (s, 1H), 9.69 (d, J = 4.7 Hz, 2H), 9.47 (d, J = 4.7 Hz, 2H), 9.40–9.45 (m, 4H), 5.14 (q, J = 6.9 Hz, 2H), 1.87 (t, J = 6.9 Hz), −3.74 (s, 2H); FAB MS m/z 382 $[C_{23}H_{18}N_4O_2]^+$.

5,15-Bis(2,2,2-trifluoroethoxycarbonyl)porphyrin (11) and 5-(2,2,2-trifluoroethoxycarbonyl)porphyrin (12). Following the procedure for the preparation of **4**, and using freshly prepared 2,2,2-trifluoroethyl glyoxylate (**1c**, 1.6 g, 9.6 mmol) and dipyrromethane **3b** (1.41 g, 9.6 mmol), the porphyrins **11** (54 mg, 1.2%), **12** (38 mg, 0.7%), and **8** (trace) were isolated after purification by column chromatography on silica gel (gradient elution with 50–80% CH_2Cl_2/hexanes). For porphyrin **11**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.42 (s, 2H), 9.70 (d, 4H), 9.50 (d, J = 4.8 Hz, 4H), 5.44 (q, J = 8.4 Hz, 4H), −3.11 (s, 2H). For porphyrin **12**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.35 (s, 2H), 10.30 (s, 1H), 9.70 (d, 2H), 9.51 (d, 2H), 9.43–9.49 (m, 4H), 5.43 (q, 2H), −3.58 (s, 2H).

5,15-Bis(*n*-propoxycarbonyl)porphyrin (13) and 5-(*n*-propoxycarbonyl)porphyrin (14). Following the procedure for the preparation of **4**, and using freshly prepared *n*-propyl glyoxylate (**1d**, 0.5 g, 4.3 mmol) and dipyrromethane **3b** (0.63 g, 4.3 mmol), the porphyrins **13** (30 mg, 2.9%), **14** (10 mg, 1.2%), and **8** (trace) were isolated after purification by column chromatography on silica gel (gradient elution with 50–80% CH_2Cl_2/hexanes). For porphyrin **13**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.38 (s, 2H), 9.69 (d, J = 4.8 Hz, 4H), 9.47 (d, J = 4.8 Hz, 4H), 5.03 (t, J = 7.1 Hz, 4H), 2.20–2.27 (m, 4H), 1.31 (t, J = 1.3 Hz, 6H), −3.33 (s, 2H). For porphyrin **14**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.36 (s, 2H), 10.33 (s, 1H), 9.70 (d, J = 4.8 Hz, 2H), 9.51 (d, J = 4.8 Hz, 4H), 9.48 (d, J = 4.8 Hz, 2H), 5.04 (t, J = 6.7 Hz, 2H), 2.22–2.28 (m, 2H), 1.31 (t, J = 7.3 Hz, 3H), −3.62 (s, 2H).

5,15-Bis(*n*-butoxycarbonyl)porphyrin (15). Following the procedure for the preparation of **4**, and using freshly prepared *n*-butyl glyoxylate (**1e**, 1.0 g, 7.7 mmol) and dipyrromethane **3b** (1.12 g, 7.7 mmol), porphyrins **15** (137 mg, 7%) and **16** (15 mg, 1.3%) were isolated after purification by column chromatography on silica gel (gradient elution with 50–66% CH_2Cl_2/hexanes) as purple solids. For porphyrin **15**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.19 (s, 2H), 9.58 (d, 4H), 9.37 (d, 4H), 5.07 (t, 4H), 2.13–2.27 (m, 4H), 1.69–1.81 (m, 4H), 1.16 (t, 6H), −3.71 (s, 2H). Porphyrin **18** was not characterized and was used directly in the preparation of **48**.

5,15-Bis(dimethylamido)porphyrin (17) and 5-(dimethylamido)porphyrin (18). Following the procedure for the preparation of **4**, and using freshly prepared amide **1g** (2.07 g, 20.5 mmol) and dipyrromethane **3b** (3.00 g, 20.5 mmol), the porphyrins **17** (40 mg, 0.9%), **18** (11 mg, 0.2%), and **8** (trace) were isolated after purification by column chromatography on silica gel (gradient elution with 0–5% CH_3OH/CH_2Cl_2). For porphyrin **17**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.26 (s, 1H), 10.23 (s, 1H), 9.33–9.42 (m, 8H), 3.81 (s, 6H), 2.80 (s, 3H), 2.73 (s, 3H), −3.48 (s, 1H), −3.58 (s, 1H). For porphyrin **18**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.25 (s, 2H), 10.22 (s, 1H), 9.43 (d, J = 7.3 Hz, 2H), 9.42 (s, 4H), 9.34 (d, J = 4.2 Hz, 2H), 3.78 (s, 3H), 2.72 (s, 3H), −3.85 (s, 2H).

5,15-Bis(ethoxycarbonyl)-10,20-bis(4-fluoro-3-methoxyphenylcarbonyl)porphyrin (19) and 5,10,15-tris(ethoxycarbonyl)-20-(4-fluoro-3-methoxyphenylcarbonyl)porphyrin (20). Following the procedure for the preparation of **4**, methyl 6-fluoro-3-formylbenzoate[22] (650 mg, 3.56 mmol), and dipyrromethane **3c** (778 mg, 3.56 mmol), the porphyrins **19** (44 mg, 3.3%) and **20** (42 mg, 5.2%) were isolated after purification by column chromatography on silica gel (elution with CH_2Cl_2). For porphyrin **19**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.47 (d, J = 4.8 Hz, 4H), 8.89 (d, J = 4.8 Hz, 4H), 8.78 (dd, J = 6.2, 1.9 Hz, 2H), 8.32–8.36 (m, 2H), 7.6 (dd, J = 9.4, 9.2 Hz, 2H), 5.09 (q, J = 7.2 Hz, 4H), 4.10 (s, 6H), 1.79 (t, J = 7.2 Hz, 6H), −3.08 (s, 2H). For porphyrin **20**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 4H), 9.43 (d, J = 4.8 Hz, 2H), 8.89 (d, J = 4.8 Hz, 2H), 8.75 (dd, J = 6.0, 2.1 Hz, 1H), 8.29–8.32 (m, 1H), 7.6 (dd, J = 9.2, 9.1 Hz, 1H), 5.13 (q, J = 7.2 Hz, 6H), 4.01 (s, 3H), 1.83 (t, J = 7.2 Hz, 9H), −3.13 (s, 2H).

5,15-Bis(ethoxycarbonyl)-10,20-bis(ethyl)porphyrin (21). In a foil-covered round-bottomed flask equipped with an air condenser, dipyrromethane **3c** (150 mg, 0.687 mmol) was stirred in propionic acid (5 mL), H_2O (0.2 mL), and pyridine (17 μL) at 90 °C for 5 min. Propionaldehyde (25 μL, 0.34 mmol) was added and the reaction mixture was stirred for 40 min. Another portion of propionaldehyde (10 μL, 0.14 mmol) was added to the reaction mixture, stirred for 2 h and diluted with CH_2Cl_2 (15 mL). The organic phase was washed with H_2O (10 mL), 0.05 N NaOH (2 × 10 mL), and H_2O (10 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (250 mL) and DDQ (108 mg, 0.48 mmol) was added. After stirring overnight, the sample was adsorbed onto silica gel (4 g). Purification by column chromatography on silica gel (gradient elution with 50–100% CH_2Cl_2/hexanes) provided porphyrin **21** (12 mg, 10%) as a purple solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (d, J = 4.5 Hz, 4H), 9.44 (d, J = 4.5 Hz, 4H), 5.11–4.99 (m, 8H), 2.13 (t, J = 7.3 Hz, 6H), 1.81 (t, J = 7.0 Hz, 6H); FAB MS m/z 511 $[C_{30}H_{30}N_4O_4 + H]^+$.

5,15-Bis(*n*-butoxycarbonyl)-10,20-bis(methoxycarbonyl)-porphyrin (22) and 5-methoxycarbonyl-10,15,20-tris-(*n*-butoxycarbonyl)porphyrin (23). Following the procedure for the preparation of **4** and using freshly distilled methyl glyoxylate (**1a**, 376 mg, 4.27 mmol) and dipyrromethane **3d** (1.04 g, 4.23 mmol), the porphyrins **22** (75 mg, 2.8%) and **23** (20 mg, 0.7%) were isolated after purification by column chromatography. For porphyrin **22**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.49 (s, 8H), 5.05 (t,

$J = 6.7$ Hz, 4H), 4.59 (s, 6H), 2.11–2.16 (m, 4H), 1.67–1.72 (m, 4H), 1.11 (t, $J = 7.5$ Hz, 6H), −3.41 (s, 2H). For porphyrin **23**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (s, 8H), 5.05 (t, $J = 6.7$ Hz, 6H), 4.60 (s, 3H), 2.10–2.14 (m, 6H), 1.67–1.74 (m, 6H), 1.11 (t, $J = 7.4$ Hz, 9H), −3.34 (s, 2H).

5,15-Bis(dimethylamido)-10,20-bis(methoxycarbonyl)porphyrin (24). Following the procedure for the preparation of **4** and using freshly distilled methyl glyoxylate (370 mg, 4.21 mmol) and dipyrromethane **1g** (915 mg, 4.21 mmol), the porphyrin **24** (40 mg, 1.7%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–10% CH_3OH/CH_2Cl_2) as a dark violet solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (d, $J = 4.9$ Hz, 4H), 9.30 (d, $J = 4.9$ Hz, 4H), 4.60 (s, 6H), 3.81 (s, 6H), 2.71, 2.78 (two s, 6H), −3.12 (s, 2H); FAB MS m/z 569 $[C_{30}H_{28}N_6O_6 + H]^+$.[25]

5,15-Bis(dimethylamido)-10,20-bis(ethoxycarbonyl)porphyrin (25). Following the procedure for the preparation of **4** and using ethyl glyoxylate (**1b**, 50% in toluene, 470 mg, 2.30 mmol) and dipyrromethane **1g** (500 mg, 2.30 mmol), the porphyrin **25** (7 mg, 1%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–3% CH_3OH/CH_2Cl_2) as a dark violet solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (d, 4H), 9.30 (d, 4H), 5.11 (q, 4H), 3.80 (s, 6H), 2.70–2.90 (m, 6H), 1.82 (t, 6H), −3.14 (s, 2H); FAB MS m/z 597 $[C_{32}H_{32}N_6O_6 + H]^+$.[25]

[5,10,15,20 - Tetrakis(methoxycarbonyl)porphyrinato]-manganese(III) chloride (26) and [5-carboxy-10,15,20-tris(methoxycarbonyl)porphyrinato]manganese(III) chloride (27). A solution of **2a** (1.11 g, 2.0 mmol) and $MnCl_2$ (1.3 g, 10.3 mmol) in DMF (100 mL) was heated at 145 °C for 1–1.5 h then exposed to a stream of air. The reaction mixture was heated for an additional 2–3 h. The reaction mixture was allowed to cool to room temperature overnight under a stream of air. Evaporation of the DMF provided a solid mixture that was adsorbed onto silica gel (3.5 g). Purification by column chromatography on silica gel (gradient elution with 0–10% $MeOH/CH_2Cl_2$) provided porphyrin **26** (760 mg, 59%) and porphyrin **27** (<5%) as black solids. For porphyrin **26**: mp >300 °C; UV–vis λ_{max}, nm (ε): 455.5 (8.8×10^4); IR (KBr) 2952, 1724, 1543, 1435, 1339, 1252, 1079, 1010, 900, 803, 800 cm^{-1}; FAB MS m/z 595 $[C_{28}H_{20}MnN_4O_8]^+$. Anal. calcd for $C_{28}H_{20}ClMnN_4O_8$: C, 53.31; H, 3.20; N, 8.88. Found: C, 53.05; H, 3.08; N, 8.92. For porphyrin **27**: mp >300 °C; UV–vis λ_{max}, nm (ε): 459.5 (8.5×10^4); IR (KBr) 2952, 1720, 1560, 1438, 1384, 1255, 1204, 1080, 1011, 803, 780 cm^{-1}; FAB MS m/z 581 $[C_{27}H_{18}MnN_4O_8]^+$.

[5,10,15,20-Tetrakis(ethoxycarbonyl)porphyrinato]manganese(III) chloride (28), [5-carboxy-10,15,20-tris(ethoxycarbonyl)porphyrinato]manganese(III) chloride (29), and [5,10,15-tris(ethoxycarbonyl)porphyrinato]manganese(III) chloride (30). Following the procedure for the preparation of **26** and using **2b** (4.43 g, 7.4 mmol), $MnCl_2$ (4.67 g, 37.1 mmol), and DMF (500 mL), the porphyrins **28** (4.3 g; 84%), **29** (<5%), and **30** (<5%) were isolated after purification by column chromatography on silica gel (gradient elution with 0–7% $MeOH/CH_2Cl_2$) as black solids. For porphyrin **28**: mp >300 °C; UV–vis λ_{max}, nm (ε): 456 (1.08×10^5); IR (KBr) 2972, 1720, 1542, 1448, 1368, 1248, 1204, 1078, 1011, 798 cm^{-1}; FAB MS m/z 651 $[C_{32}H_{28}MnN_4O_8]^+$. Anal. calcd for $C_{32}H_{28}ClMnN_4O_8$: C, 55.95; H, 4.11; N, 8.16. Found: C, 55.70; H, 4.23; N, 7.96. For porphyrin **29**: mp >300 °C; UV–vis λ_{max}, nm (ε): 460.5 (7.8×10^4); IR (KBr) 2925, 1720, 1630, 1447, 1367, 1249, 1204, 1079, 1011, 835, 799 cm^{-1}; FAB MS m/z 623 $[C_{30}H_{24}MnN_4O_8]^+$. For porphyrin **30**: mp >300 °C; UV–vis λ_{max}, nm (ε): 454.5 (1.14×10^5); IR (KBr) 1981, 1719, 1245, 1162, 1076, 1006, 797 cm^{-1}; FAB MS m/z 579 $[C_{29}H_{24}MnN_4O_6]^+$.

[5,10,15,20 - Tetrakis(2,2,2 - trifluoroethoxycarbonyl)porphyrinato]manganese(III) chloride (31). Following the procedure for the preparation of **26** and using porphyrin **2c** (36 mg, 0.043 mmol), $MnCl_2$ (27 mg, 0.21 mmol), and DMF (10 mL), the porphyrin **31** (23 mg, 58%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–3% $MeOH/CH_2Cl_2$) as a dark brown solid: UV–vis λ_{max}, nm (ε): 453.5 (7.30×10^4); IR (KBr) 2931, 1744, 1175, 1082, 801 cm^{-1}; FAB MS m/z 867 $[C_{32}H_{16}F_{12}MnN_4O_8]^+$.

[5,10,15,20 - Tetrakis(*n* - propoxycarbonyl)porphyrinato]-manganese(III) chloride (32). Following the procedure for the preparation of **26** and using porphyrin **2d** (170 mg, 0.260 mmol), $MnCl_2$ (167 mg, 1.32 mmol), and DMF (30 mL), the porphyrin **32** (170 mg, 88%) was isolated after purification by column chromatography on silica gel (elution with 2.5% $MeOH/CH_2Cl_2$) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 456.0 (1.35×10^5); IR (KBr) 2968, 1720, 1542, 1458, 1245, 1204, 1079, 1010, 924, 804 cm^{-1}; FAB MS m/z 707 $[C_{36}H_{36}MnN_4O_8]^+$.

[5,10,15,20 - Tetrakis(*n* - butoxycarbonyl)porphyrinato]-manganese(III) chloride (33) and [5-carboxy-10,15,20-tris(*n*-butoxycarbonyl)porphyrinato]manganese(III) chloride (34). Following the procedure for the preparation of **26** and using porphyrin **2e** (355 mg, 0.50 mmol), $MnCl_2$ (318 mg, 2.53 mmol), and DMF (50 mL), the porphyrins **33** (170 mg, 43%) and **34** (10 mg, 2.7%) were isolated after purification by column chromatography on silica gel (gradient elution with 0–5% $MeOH/CH_2Cl_2$) as black solids. For porphyrin **33**: mp 200–210 °C; UV–vis λ_{max}, nm (ε): 456.0 (1.4×10^5); IR (KBr) 2960, 2873, 1721, 1543, 1459, 1384, 1339, 1249, 1204, 1079, 1010, 800 cm^{-1}; FAB MS m/z 763 $[C_{40}H_{44}MnN_4O_8]^+$. For porphyrin **34**: mp 200–205 °C; UV–vis λ_{max}, nm (ε): 459.5 (7.2×10^4); IR (KBr) 2960, 1720, 1560, 1459, 1249, 1204, 1080, 1011, 799 cm^{-1}; FAB MS m/z 707 $[C_{36}H_{36}MnN_4O_8]^+$.

[5,10,15,20-Tetrakis(*n*-hexyloxycarbonyl)porphyrinato]-manganese(III) chloride (35). Following the procedure for the preparation of **26** and using porphyrin **2f** (200 mg, 0. 43 mmol), $MnCl_2$ (152.3 mg, 1.21 mmol), and DMF (200 mL), the porphyrin **35** (218 mg, 98%)

was isolated after purification by column chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 456.0 (1.6×10^5); IR (KBr) 2931, 1720, 1543, 1459, 1248, 1204, 1081, 1010, 800 cm^{-1}; FAB MS *m/z* 875 $[C_{48}H_{60}MnN_4O_8]^+$.

[5,10,15,20 - Tetrakis(dimethylamido)porphyrinato]manganese(III) chloride (36). Following the procedure for the preparation of **26** and using porphyrin **2g** (80 mg, 0.14 mmol) $MnCl_2$ (270 g, 2.15 mmol), and DMF (35 mL), the porphyrin **36** (25 mg, 27%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–10% MeOH/CH_2Cl_2) as a dark brown solid: UV–vis λ_{max}, nm: 462.0; IR (KBr) 2927, 1624, 1497, 1452, 1406, 1188, 1071, 1012, 799, 699 cm^{-1}; FAB MS *m/z* 647 $[C_{32}H_{32}MnN_8O_4]^+$.

[5,15-Bis(methoxycarbonyl) - 10,20 - bis(trifluoromethyl)-porphyrinato]manganese(III) chloride (37) and [5,15-bis(-trifluoromethyl) - 10 - carboxy - 20 - (methoxycarbonyl) porphyrinato]manganese(III) chloride (38). Following the procedure for the preparation of **26** and using porphyrin **4** (115 mg, 0.20 mmol), $MnCl_2$ (130 mg, 1.0 mmol), and DMF (30 mL), the porphyrins **37** (117 mg, 88%) and **38** (15 mg, 12%) were isolated after purification by column chromatography on silica gel (gradient elution with 3–10% MeOH/CH_2Cl_2) as black solids. For porphyrin **37**: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 450 (9.90×10^4); IR (KBr) 2926, 1734, 1541, 1436, 1259, 1159, 1127, 1081, 1041, 800 cm^{-1}; FAB MS *m/z* 615 $[C_{26}H_{14}F_6MnN_4O_4]^+$. For porphyrin **38**: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 455 (3.06×10^4); IR (KBr) 2926, 1728, 1586, 1257, 1157, 1123, 1084, 1041, 799 cm^{-1}; FAB MS *m/z* 601 $[C_{25}H_{12}F_6MnN_4O_4]^+$.

[5,15-Bis(*n*-propoxycarbonyl)-10,20-bis(trifluoromethyl)-porphyrinato]manganese(III) chloride (39). Following the procedure for the preparation of **26** and using porphyrin **5** (15 mg, 0.02 mmol), $MnCl_2$ (28 mg, 0.22 mmol), and DMF (10 mL), the porphyrin **39** (15 mg, 87%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–2.5% MeOH/CH_2Cl_2) as a black solid: UV–vis λ_{max}, nm (ε): 450.5 (1.10×10^5); IR (KBr) 2921, 1720, 1542, 1259, 1127, 1081, 1042, 800 cm^{-1}; FAB MS *m/z* 671 $[C_{30}H_{22}F_6MnN_4O_4]^+$.

[5,15 - Bis(methoxycarbonyl)porphyrinato]manganese(III) chloride (40). Following the procedure for the preparation of **26** and using porphyrin **6** (61 mg, 0.142 mmol), $MnCl_2$ (90 mg, 0.71 mmol), and DMF (70 mL), the porphyrin **40** (25 mg, 34%) was isolated after purification by column chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 452.0 (4.40×10^4); IR (KBr) 2921, 1697, 1437, 1384, 1317, 1272, 1156, 1076, 1005, 897, 797 cm^{-1}; FAB MS *m/z* 479 $[C_{24}H_{16}MnN_4O_4]^+$.

[5-(Methoxycarbonyl)porphyrinato]manganese(III) chloride (41). Following the procedure for the preparation of **26** and using porphyrin **7** (30 mg, 0.081 mmol), $MnCl_2$ (51 mg, 0.41 mmol), and DMF (30 mL), the porphyrin **41** (5 mg, 14%) was isolated after purification by column chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 451.5 (3.90×10^4); FAB MS *m/z* 421 $[C_{22}H_{14}MnN_4O_2]^+$.

[5,15 - Bis(ethoxycarbonyl)porphyrinato]manganese(III) chloride (42). Following the procedure for the preparation of **26** and using porphyrin **9** (22 mg, 0.058 mmol), $MnCl_2$ (55 mg, 0.44 mmol), and DMF (8 mL), the porphyrin **42** (6 mg, 19%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–7% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 452.5 (2.48×10^4); IR (KBr) 2921, 1717, 1259, 1151, 1074, 698 cm^{-1}; FAB MS *m/z* 507 $[C_{26}H_{20}MnN_4O_4]^+$.

[5,15 - Bis(2,2,2 - trifluoroethoxycarbonyl)porphyrinato]-manganese(III) chloride (43). Following the procedure for the preparation of **26** and using porphyrin **11** (54 mg, 0.1 mmol), $MnCl_2$ (63 mg, 0.5 mmol), and DMF (60 mL), the porphyrin **43** (45 mg, 72%) was isolated after purification by column chromatography on silica gel (gradient elution with 5–7.5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 451.0 (8.0×10^4); IR (KBr) 2921, 1736, 1286, 1227, 1178, 1151, 1077, 1001, 794 cm^{-1}; FAB MS *m/z* 615 $[C_{26}H_{14}F_6MnN_4O_4]^+$.

[5 - (2,2,2 - Trifluoroethoxycarbonyl)porphyrinato]manganese(III) chloride (44). Following the procedure for the preparation of **26** and using porphyrin **12** (38 mg, 0.09 mmol), $MnCl_2$ (58 mg, 0.46 mmol), and DMF (40 mL), the porphyrin **44** (42 mg, 92%) was isolated after purification by column chromatography on silica gel (gradient elution with 5–7.5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 451.0 (3.90×10^4); IR (KBr) 2931, 1736, 1618, 1287, 1153, 1086, 1004 cm^{-1}; FAB MS *m/z* 489 $[C_{23}H_{13}F_3MnN_4O_4]^+$.

[5,15-Bis(*n*-propoxycarbonyl)porphyrinato]manganese(III) chloride (45). Following the procedure for the preparation of **26** and using porphyrin **13** (30 mg, 0.062 mmol), $MnCl_2$ (39 mg, 0.27 mmol), and DMF (25 mL), the porphyrin **45** (35 mg, 98%) was isolated after purification by column chromatography (gradient elution with 5–7.5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 452.5 (6.10×10^4); IR (KBr) 2968, 1711, 1536, 1458, 1384, 1262, 1236, 1156, 1075, 1001, 922 cm^{-1}; FAB MS *m/z* 535 $[C_{28}H_{24}MnN_4O_4]^+$.

[5-(*n*-Propoxycarbonyl)porphyrinato]manganese(III) chloride (46). Following the procedure for the preparation of **26** and using porphyrin **14** (10 mg, 0.025 mmol), $MnCl_2$ (22 mg, 0.17 mmol), and DMF (20 mL), the porphyrin **46** (9 mg, 74%) was isolated after purification by column chromatography on silica gel (gradient elution with 5–7.5% MeOH/CH_2Cl_2) as a black solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm (ε): 451.5 (3.7×10^4); IR (KBr) 2921, 1719, 1384, 1259, 1154, 1084, 1003 cm^{-1}; FAB MS *m/z* 449 $[C_{24}H_{18}MnN_4O_2]^+$.

[5,15-Bis(*n*-butoxycarbonyl)porphyrinato]manganese(III) chloride (47). Following the procedure for the preparation of **26** and using porphyrin **15** (137 mg, 0.27 mmol), $MnCl_2$ (170 mg, 1.3 mmol), and DMF (110 mL), the porphyrin **47** (65 mg, 43%) was isolated after purification by column chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 563 (8.4×10^4); IR (KBr) 2959, 1717, 1537, 1458, 1384, 1260, 1234, 1073, 1001, 794 cm^{-1}; FAB MS *m/z* 563 $[C_{30}H_{28}MnN_4O_4]^+$.

[5-(*n*-Butoxycarbonyl)porphyrinato]manganese(III) chloride (48). Following the procedure for the preparation of **26** and using porphyrin **16** (15 mg, 0.037 mmol), $MnCl_2$ (18 mg, 0.15 mmol), and DMF (15 mL), the porphyrin **48** (8 mg, 44%) was isolated after purification by column chromatography on silica gel (gradient elution with 2.5–5% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 452.0 (5.6×10^4); IR (KBr) 2921, 1718, 1384, 1257, 1154, 1084, 1003 cm^{-1}; FAB MS *m/z* 463 $[C_{25}H_{20}MnN_4O_2]^+$.

[5,15 - Bis(dimethylamido)porphyrinato]manganese(III) chloride (49). Following the procedure for the preparation of **26** and using porphyrin **17** (40 mg, 0.088 mmol), $MnCl_2$ (195 mg, 1.55 mmol), and DMF (18 mL), the porphyrin **49** (11 mg, 23%) was isolated after purification by column chromatography on silica gel (gradient elution with 2–8% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 455.5 (3.03×10^4); IR (KBr) 2926, 1611, 1498, 1074, 1006, 697 cm^{-1}; FAB MS *m/z* 505 $[C_{26}H_{22}MnN_6O_2]^+$.

[5-(Dimethylamido)porphyrinato]manganese(III) chloride (50). Following the procedure for the preparation of **26** and using porphyrin **18** (11 mg, 0.029 mmol), $MnCl_2$ (2 × 73 mg, 0.58 mmol), and DMF (10 mL), the porphyrin **50** (6 mg, 43%) was isolated after purification by column chromatography on silica gel (7% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 453.0 (2.17×10^4); IR (KBr) 2925, 1637, 1508, 1005, 698 cm^{-1}; FAB MS *m/z* 434 $[C_{23}H_{17}MnN_5O]^+$.

[5,15-Bis(ethoxycarbonyl)-10,20-bis(4-fluoro-3-methoxyphenylcarbonyl)porphyrinato]manganese(III) chloride (51). Following the procedure for the preparation of **26** and using porphyrin **19** (44 mg, 0.06 mmol), $MnCl_2$ (42 mg, 0.33 mmol), and DMF (25 mL), the porphyrin **51** (36 mg, 73%) was isolated after purification by column chromatography on silica gel (gradient elution with 2.5–4% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 460.5 (1.58×10^5); IR (KBr) 2921, 1720, 1492, 1430, 1303, 1246, 1277, 1011, 800, 698 cm^{-1}; FAB MS *m/z* 811 $[C_{42}H_{30}F_2MnN_4O_8]^+$.

[5,10,15-Tris(ethoxycarbonyl)-20-(4-fluoro-3-methoxyphenylcarbonyl)porphyrinato]manganese(III) chloride (52). Following the procedure for the preparation of **26** and using porphyrin **20** (42 mg, 0.06 mmol), $MnCl_2$ (100 mg, 0.79 mmol), and DMF (25 mL), the porphyrin **52** (34 mg, 72%) was isolated after purification by column chromatography on silica gel (gradient elution with 2.5–5% MeOH/CH_2Cl_2) as a black: mp 200–205 °C; UV–vis λ_{max}, nm (ε): 458.0 (1.18×10^5); IR (KBr) 2921 1720, 1542, 1369, 1249, 1203, 1078, 1011, 800, 698 cm^{-1}; FAB MS *m/z* 731 $[C_{37}H_{29}FMnN_4O_8]^+$.

[5,15-Bis(ethoxycarbonyl)-10,20-bis(ethyl)porphyrinato]-manganese(III) chloride (53). Following the procedure for the preparation of **26** and using porphyrin **21** (12 mg, 0.025 mmol), $MnCl_2$ (23 mg, 0.19 mmol), and DMF (4 mL), the porphyrin **53** (3.5 mg, 24%) was isolated after purification by column chromatography on silica gel (gradient elution with 0–6% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 462.5 (3.43×10^4); IR (KBr) 2926, 1708, 1542, 1459, 1250, 1200, 1078 cm^{-1}; FAB MS *m/z* 563 $[C_{30}H_{28}MnN_4O_4]^+$.

[5,15-Bis(*n*-butoxycarbonyl)-10,20-bis(methoxycarbonyl)-porphyrinato]manganese(III) chloride (54) and [10,20-bis(*n*-butoxycarbonyl)-5-carboxy-15-(methoxycarbonyl)-porphyrinato]manganese(III) chloride (55). Following the procedure for the preparation of **26** and using porphyrin **22** (75 mg, 0.12 mmol), $MnCl_2$ (163 mg, 1.30 mmol), and DMF (35 mL), the porphyrins **54** (33 mg, 39%), and **55** (10 mg, 12%) were isolated after purification by column chromatography on silica gel (gradient elution with 0–7.5% MeOH/CH_2Cl_2) as black solids. For porphyrin **54**: mp 200–205 °C; UV–vis λ_{max}, nm (ε): 456.0 (9.50×10^4); IR (KBr) 2958, 1724, 1450, 1250, 1205, 1079, 1011, 802 cm^{-1}; FAB MS *m/z* 679 $[C_{34}H_{32}MnN_4O_8]^+$. For porphyrin **55**: mp >300 °C; UV–vis λ_{max}, nm (ε): 460.0 (8.20×10^4); IR (KBr) 2960, 1720, 1560, 1352, 1250, 1204, 1080, 1011, 800, 698 cm^{-1}; FAB MS *m/z* 665 $[C_{33}H_{30}MnN_4O_8]^+$.

[5-Methoxycarbonyl-10,15,20-tris(*n*-butoxycarbonyl)porphyrinato]manganese(III) chloride (56). Following the procedure for the preparation of **26** and using porphyrin **23** (20 mg, 0.03 mmol), $MnCl_2$ (28 mg, 0.22 mmol), and DMF (25 mL), the porphyrin **56** (6 mg, 27%) was isolated after purification by column chromatography on silica gel (gradient elution with 2–7.5% MeOH/CH_2Cl_2) as a black solid: mp 180–185 °C; UV–vis λ_{max}, nm (ε): 456.0 (7.10×10^4); IR (KBr) 2960, 1721, 1542, 1458, 1250, 1205, 1080, 1011, 801 cm^{-1}; FAB MS *m/z* 721 $[C_{37}H_{38}MnN_4O_8]^+$.

[5,15 - Bis(dimethylamido) - 10,20 - bis(methoxycarbonyl)-porphyrinato]manganese(III) chloride (57). Following the procedure for the preparation of **26** and using porphyrin **24** (41 mg, 0.072 mmol), $MnCl_2$ (181 mg, 1.44 mmol), and DMF (18 mL), the porphyrin **57** (10 mg, 21%) was isolated after purification by column chromatography on silica gel (gradient elution with 5–20% MeOH/CH_2Cl_2) as a black solid: mp >300 °C; UV–vis λ_{max}, nm (ε): 458.5 (3.33×10^4); FAB MS *m/z* 621 $[C_{30}H_{26}MnN_6O_6]^+$.

[5,15-Bis(dimethylamido)-10,20-bis(ethoxycarbonyl)porphyrinato]manganese(III) chloride (58). Following the procedure for the preparation of **26** and using porphyrin **25** (7.0 mg, 0.012 mmol), $MnCl_2$ (15 mg, 0.12 mmol), and DMF (6 mL), the porphyrin **58** (2.3 mg, 29%) was isolated after purification by column

chromatography on silica gel (10% MeOH/CH_2Cl_2) as a dark brown solid: mp $>300\,^{\circ}C$; UV–vis λ_{max}, nm: 458.5; IR (KBr) 1916, 1720, 1618, 1542, 1492, 1452, 1257, 1206, 1081, 1011, 801, 698 cm^{-1}; FAB MS m/z 649 $[C_{32}H_{30}MnN_6O_6]^+$.

SOD assay

Superoxide dismutase activity was measured by cytochrome c reduction as previously described.[29,35] Briefly, reactions were performed in buffer containing 50 mM potassium phosphate and 0.1 mM EDTA at pH 7.8. The addition of EDTA allows one to examine only complexes that tightly ligate the metal. Cytochrome c was titrated to give a final concentration of 10 uM of the oxidized form. Xanthine was added to give a final concentration of 50 μM. Xanthine oxidase (~2 nM) was titrated to generate superoxide flux that reduces cytochrome c at a rate of 0.025 abs/min at 550 nm. The amount of metalloporphyrin that inhibited this rate of cytochrome c reduction by one-half was defined as 1 SOD unit of activity. Possible interferences in the SOD assay were examined by checking the direct reduction of cytochrome c by the metalloporphyrin and possible inhibition of xanthine oxidase by monitoring urate production at 234 nm. A number of compounds still interfered with the SOD assay through unknown mechanisms.

Catalase assay

The dismutation of hydrogen peroxide was measured by following the formation of oxygen with a Clark-type electrode as previously described.[6d] Reactions were performed in degassed buffer containing 50 mM potassium phosphate and 0.1 mM EDTA at pH 7.8. Pseudo first order rate constants were obtained from plotting the decay of 1 mM hydrogen peroxide at four concentrations of metalloporphyrin (k_{app}, min^{-1}). Some of the metalloporphyrins were not stable in the presence of 1 mM hydrogen peroxide and were excluded from the assay.

Lipid peroxidation assay

The ability of metalloporphyrins to inhibit lipid peroxidation was assessed as previously described.[31] Iron and ascorbate were used to initiate lipid peroxidation in rat brain homogenates and the formation of thiobarbituric acid reactive species (TBARS) was measured as an index of lipid peroxidation.[32,33] Potency of the metalloporphyrins was determined as their concentration that inhibited 50% of the iron/ascorbate-initiated TBARS formation (IC_{50}, μM). Blanks were run to determine if any of the metalloporphyrins tested reacted with thiobarbituric acid and all samples were corrected for color absorption due to the metalloporphyrins.

References and Notes

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