A study on the oxidation of 2-hydroxyporphyrins to porphyrin-α-diones

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Porphyrin-α-diones have been used for the preparation of extended rigidly oriented porphyrin systems. Copper 2, free-base 3, and zinc 4 2-hydroxyporphyrins have been prepared by an improved method and treated with a range of oxidants to form the corresponding porphyrin-α-diones, 5, 6, and 7 in yields of up to 94%. We have found that the free-base 2-hydroxyporphyrin 3 was easily oxidised and usually gave the best yields of porphyrin-α-dione. In this study the most effective general oxidant was determined to be the Dess–Martin periodinane which oxidised all three 2-hydroxyporphyrins to their respective porphyrin-α-diones in good yields.

Introduction

In recent years there has been a strong interest in developing extended porphyrin arrays.[1–7] Many of these studies have involved porphyrins linked through their *meso*-positions.[3–7] However, there have been a number of reports of porphyrin and porphyrin–non-porphyrin arrays which have been linked through the β-pyrrolic positions.[1,2,7–9] The starting porphyrins for these latter routes contain a porphyrin-α-dione which was originally prepared by a five step synthesis from a copper chelated porphyrin.[10] The final steps in this reported synthetic pathway involve the photo-oxidation of a 2-amino-5,10,15,20-tetraphenylporphyrin followed by hydrolysis of the resultant keto imine to the dione. The main difficulty of this route is in scaling up the photolysis reaction. Apart from this route there have been two other methods reported for the preparation of porphyrin-α-diones, in low to fair yields, and these involve the oxidation of 2-hydroxyporphyrins by either selenium dioxide or photo-oxidation.[2,11] As part of our studies on functionalising porphyrins we were interested in exploring a range of reagents capable of the oxidation of the free-base and metallo 2-hydroxyporphyrins to the corresponding porphyrin-α-diones. For this investigation we chose the copper 2, free-base 3, and zinc 4 2-hydroxy-5,10,15,20-tetrakis(3′,5′-di-*tert*-butylphenyl)-porphyrins as our substrates to determine the utility of each of the oxidants. The 3,5-di-*tert*-butylphenyl substituents were chosen to impart good solubility to the porphyrins.

Results and discussion

The starting point of this investigation was the copper 2-nitroporphyrin 1 which was prepared from 5,10,15,20-tetra-kis(3′,5′-di-*tert*-butylphenyl)porphyrin following a literature procedure.[10] The hydroxyation to form the copper 2-hydroxy-porphyrin involves an S_NAr reaction of the benzaldoximate anion with 1 using dimethyl sulfoxide as the solvent.[2,11,12] The problem with this reaction is that a number of porphyrins, including 1, are only poorly soluble in dimethyl sulfoxide. This obviously hinders the reaction and limits the scale on which the reaction can be easily carried out.[11] Therefore, porphyrin hydroxyations in dimethyl sulfoxide are usually carried out at high temperature and low concentrations of substrate. In an attempt to address the problem of substrate solubility for 1, the reaction was attempted using tetrahydrofuran as the solvent. This proved unsuccessful and under these conditions we observed no hydroxyation, and 1 was recovered in a 91% yield. However, we have found that by using tetrahydrofuran as a co-solvent with dimethyl sulfoxide it was possible to carry out
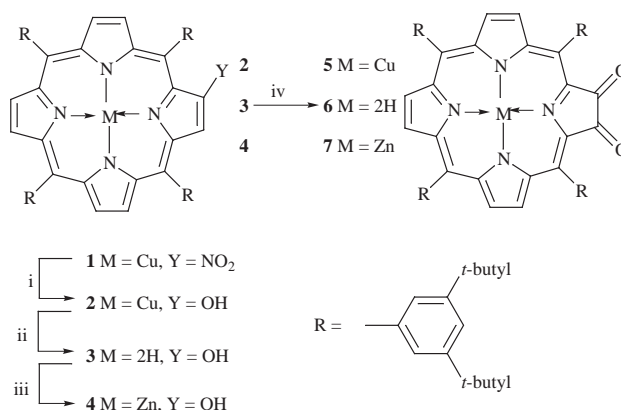
Scheme 1 *Reagents and conditions*: i, sodium benzaldoximate, DMSO–THF, Δ, 1 h, N_2; ii, H_2SO_4, DCM, rt; iii, $Zn(OAc)_2 \cdot 2H_2O$, DCM–MeOH, Δ; iv, oxidations

the conversion on larger scales using higher concentrations of 1 and form copper 2-hydroxyporphyrin 2 in yields of up to 92% (Scheme 1). The free-base 2-hydroxyporphyrin 3 was formed by demetallation of 2 using concentrated sulfuric acid in 95% yield. Care had to be taken when forming and purifying 3 as it is unstable to photo-oxidation, especially on silica. A similar instability was reported for 2-hydroxy-5,10,15,20-tetraphenylporphyrin.[13] Finally, the zinc chelated 2-hydroxy-porphyrin 4 was formed in quantitative yield by treatment of 3 with zinc acetate dihydrate in a dichloromethane–methanol mixture heated at reflux.

The 2-hydroxyporphyrins 2, 3 and 4 can exist in their enol (phenol) and keto tautomeric forms.[13] Infrared analysis of dry samples of copper 2-hydroxyporphyrin 2 and zinc 2-hydroxyporphyrin 4 indicated that these 2-hydroxyporphyrins were in their enol (phenol) form with absorptions in the hydroxy region. In the case of zinc 2-hydroxyporphyrin 4 this was confirmed by ^{1}H NMR spectroscopy which showed a signal at 6.2 ppm corresponding to the hydroxy proton. The ^{1}H NMR spectrum of a dry sample of free-base 2-hydroxyporphyrin 3 showed it to be predominantly in the enol (phenol) form with a signal for the hydroxy proton at 6.2 ppm. In addition, there were also signals associated with a small amount of the keto tautomer. The infrared spectrum of 3 showed absorptions at 3485 cm^{-1} for the hydroxy group and 1727 cm^{-1} for the carbonyl group. We followed the keto–enol tautomerism of 3 in solution by ^{1}H NMR spectroscopy, and found that the ratio of keto to enol tautomers increased over time. In our work we observed up to approximately 15% of the keto tautomer. The ^{1}H NMR

spectrum of the keto–enol mixture showed three broad signals for the NH protons and signals at 4.6 and 6.2 ppm corresponding to the methylene protons at C(3) and the hydroxy proton respectively. The same keto–enol (phenol) tautomerism has been reported earlier for 2-hydroxy-5,10,15,20-tetraphenylporphyrins.[13]

As the 2-hydroxyporphyrins can exist in both keto and enol (phenol) forms our choice of oxidants was based on methods for oxidising phenols to quinones as well as oxidation of a methylene α to a carbonyl. The results of our study are summarised in Table 1. The oxidants we studied fall into three classes; oxygen, metal oxides, and organic. Each experiment was carried out at room temperature with the oxidant added to a dichloromethane solution of the 2-hydroxyporphyrin.

Our initial oxidation experiment arose from the observation that purification of the free-base hydroxyporphyrin 3 on silica gel under laboratory lighting gave the dione 6 rather than 3. Both copper and free-base 2-hydroxyporphyrins have been photo-oxidised to give the corresponding dione in low to medium yield.[11] In the case of the copper 2-hydroxyporphyrin Rose Bengal was required to photosensitise the reaction. Under controlled conditions we found that photo-oxidation of the 2-hydroxyporphyrins over silica under normal laboratory lighting could occur slowly. Under these conditions the free-base 2-hydroxyporphyrin 3 could be oxidised in an excellent yield of 94% after 5 days. In contrast, the copper 2-hydroxyporphyrin 2 was, as expected, relatively stable to these conditions [11] with the zinc 2-hydroxyporphyrin 4 being intermediate in reactivity. We believe that the oxidation involves singlet oxygen and requires the 2-hydroxyporphyrins to undergo keto–enol tautomerism, with the silica acting as a mild acid catalyst (Scheme 2).
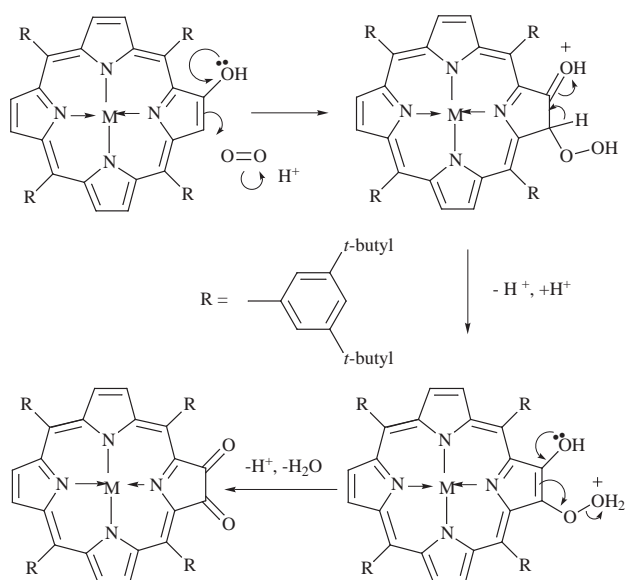
Scheme 2 Proposed mechanism for silica catalysed oxygen oxidation of 2-hydroxyporphyrins

This would mean that failure to react under these conditions would be due to the 2-hydroxyporphyrin not acting as a singlet oxygen photosensitiser and/or not being able to undergo facile keto–enol tautomerism. Both zinc and free-base *meso*-tetraphenylporphyrins are good singlet oxygen sensitisers.[14] Therefore, as the free-base 2-hydroxyporphyrin is more efficiently oxidised than the zinc 2-hydroxporphyrin, it follows that the ability to undergo keto–enol tautomerism is important for this oxidation to proceed. Although good yields of the free-base dione 6 were achievable, this route was clearly not suitable for large scale preparations.

The metal oxides investigated were chromium trioxide [15] and lead dioxide [16] which have both been shown to oxidise phenols to quinones. In the case of lead dioxide the *para*-quinones were

Table 1 Oxidations of **2**, **3** and **4**

Reagent	Equivalents	2 Yield (%)		3 Yield (%)		4 Yield (%)	
		2	**5**	**3**	**6**	**4**	**7**
Silica, *hv*, O2	—	85	10	—	94	45	28
CrO3 in acetic acid	1	54	20	—	84	—	54
CrO3 in acetic acid	2	4	43	—	63	—	53
PbO2 in acetic acid	2	—	4	—		—	
		8	(29%)	**9**	(25%)	**10**	(11%)
DDQ	1	—	65	—	30	—	32
DMP	unknown	—	76	—	79	—	57

formed.[16] We considered that chromium trioxide oxidation could also be an analogous reaction to the reported oxidations of hydroxyporphyrins with selenium dioxide and therefore the free-base 2-hydroxyporphyrin 3 should be oxidised more easily than the metallo 2-hydroxyporphyrins.[2,11] This was indeed the case and we found that when one equivalent of chromium trioxide was used the free-base 2-hydroxyporphyrin 3 was oxidised quickly and cleanly to give 6 in an excellent 84% yield. Zinc 2-hydroxyporphyrin 4 was also rapidly oxidised and gave zinc dione 7 in a fair yield. Once again the oxidation of copper 2-hydroxyporphyrin 2 was slowest and required more than one equivalent of chromium trioxide to consume nearly all the starting material. When two equivalents of chromium trioxide were used most of the copper 2-hydroxyporphyrin 2 was consumed. However, the yield of copper dione 5 was low which we presume is due to the oxidation of the dione formed in the reaction. In all the reactions there was competition between oxidation of the starting 2-hydroxyporphyrin and the formed dione.

Oxidation of the 2-hydroxyporphyrins with lead oxide in acetic acid to give the diones was essentially unsuccessful. Although oxidation occurred in each case the corresponding, '*ortho*', 2,2-diacetoxy-3-oxoporphyrins **8**, **9**, and **10** were the

8 M = Cu
9 M = 2H
10 M = Zn
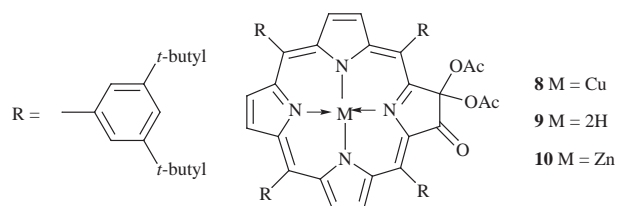
Bis-acetate-keto intermediates from PbO2 oxidation

main products which were isolated in the poor yields of 29, 25, and 11% respectively. Similar intermediates have been described in the oxidations of simple phenols with lead oxide.[16] It is interesting to note that in this reaction two diacetoxyoxoporphyrins can be formed, the isolated 2,2-diacetoxy-3-oxoporphyrins and the less sterically crowded, '*para*', 2,2-diacetoxy-12-oxoporphyrins which were not found. In principle, the 2,2-diacetoxy-3-oxoporphyrins could be hydrolysed through to the diones but as the yields of **8**, **9**, and **10** were low and unoptimised this was not investigated.

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and the Dess–Martin periodinane were the two organic oxidants investigated. Oxidation with DDQ was only partially successful and although oxidation occurred rapidly the yields were only fair and unreliable with the best yield in this case achieved for the oxidation of the copper 2-hydroxyporphyrin 2 to the copper dione 5. Both the free-base and zinc 2-hydroxyporphyrins were oxidised with DDQ but gave only poor yields of the respective diones.

Our choice of the Dess–Martin periodinane [1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one; DMP] as an oxidant

was based on a report which showed that it can oxidise 1,3-dicarbonyls to tricarbonyls.[17] It has been postulated that the oxidation occurs through the enol form of the dicarbonyl and we therefore considered that it should oxidise the free-base 2-hydroxyporphyrin **3** easily. We had difficulty in preparing pure DMP, however, we found that although the material produced by the method of Ireland and Lui[18] was not particularly soluble in dichloromethane it still contained active oxidant. As it was not possible to determine the level of active oxidant the oxidations were usually carried out by adding aliquots of crude DMP and following the extent of the reaction by thin-layer chromatography. Under these mild conditions we found that the free-base 2-hydroxyporphyrin **3** could be oxidised to the dione **6** in good yield. In addition, we were surprised to find that DMP could also oxidise the copper and zinc 2-hydroxyporphyrins to their respective diones also in good yields.

Conclusion

We have successfully developed an improved method for the hydroxylation of a lipophilic copper 2-nitroporphyrin which has enabled us to prepare good quantities of 2-hydroxyporphyrins. We have found that the copper, zinc, and free-base hydroxyporphyrins can be oxidised to give the corresponding diones using a variety of reagents. In most cases we found that the metal chelated 2-hydroxyporphyrins were harder to oxidise than the free-base 2-hydroxyporphyrin with the latter normally also giving the best yields of dione. Of the two metal chelated 2-hydroxyporphyrins the zinc 2-hydroxyporphyrin was more easily oxidised. We have also found that the Dess–Martin periodinane is the most general oxidant and can oxidise metal chelated and free-base 2-hydroxyporphyrins to their corresponding diones in good yields under mild conditions.

Experimental

General methods

^{1}H NMR Spectra were recorded on Varian Gemini 200 (200 MHz) and Bruker AM-500 (500 MHz) spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) and are referenced to the residual solvent peak. Coupling constants J are given in Hz. Infrared spectra were recorded using KBr disks with a Perkin-Elmer Paragon 1000 infrared spectrometer. UV–visible spectra were recorded on a Perkin-Elmer Lambda 14P UV–visible spectrometer. It should be noted that the 2,2-diacetoxy-3-oxoporphyrins, **8**, **9**, and **10**, were single compounds by thin-layer chromatography but were not analytically pure. Therefore, the extinction coefficients for these compounds only give the relative intensities of the absorption peaks. Fast atom bombardment (FAB) mass spectra (m/z) were recorded on a VG Autospec spectrometer. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. All solvents for recrystallization were distilled before use. Dimethyl sulfoxide was dried over calcium hydride and freshly distilled before use. Tetrahydrofuran was dried over sodium wire and freshly distilled before use. Light petroleum refers to the fraction of boiling point 60–80 °C and ether refers to diethyl ether. Thin-layer chromatography was performed on glass microplates coated with silica GF_{254}, or with Merck aluminium plates coated with silica gel 60 F_{254}. Column chromatography was performed using either the flash chromatography technique or gravity feed chromatography in the dark, with ACROS Organics silica gel, 0.035–0.07 mm. Where solvent mixtures are used, the proportions are given by volume.

[2-Hydroxy-5,10,15,20-tetrakis(3′,5′-di-*tert*-butylphenyl)-porphinato]copper(II) 2

Dry, freshly distilled dimethyl sulfoxide (140 cm³) was transferred by cannula to a flask containing sodium hydride (60% suspension in oil, 239 mg, 5.98 mmol) and the mixture was

stirred under nitrogen at 75 °C for 30 min. The mixture was transferred by cannula to a flask containing benzaldoxime (797 mg, 6.58 mmol) and the resultant yellow mixture was immediately transferred by cannula to a flask containing a refluxing solution of **1** (700 mg, 0.598 mmol) in dry tetrahydrofuran (140 cm³). The reaction mixture was heated at reflux in the dark for 1 h, then cooled in an ice-bath and diluted with ether (200 cm³). The organic layer was washed with water (6 × 200 cm³), dried over anhydrous sodium sulfate, filtered and the solvent removed. The residue was purified by chromatography over silica using dichloromethane–light petroleum (1:4) as eluent to yield **2** (627 mg, 92%) mp >300 °C; ν_{max}/cm⁻¹ 3486 (OH); λ_{max}(CHCl₃)/nm [log(ε/dm³ mol⁻¹ cm⁻¹)] 419 [5.54], 541 [4.26], and 581 [3.70]; m/z (high resolution) (FAB) calc. for $C_{76}H_{92}N_4OCu$: 1139.6567; found: 1139.6542 (M⁺).

2-Hydroxy-5,10,15,20-tetrakis(3′,5′-di-*tert*-butylphenyl)-porphyrin 3

Sulfuric acid (98%, 2 cm³) was added dropwise to a vigorously stirred solution of **2** (1.067 g, 0.925 mmol) in dichloromethane (100 cm³). The reaction mixture was stirred in the dark for 5 min and then diluted with cold water (100 cm³). The organic layer was separated and washed with water (100 cm³), aqueous sodium hydrogen carbonate solution (5%, 100 cm³), water (100 cm³), and brine (100 cm³), dried over anhydrous sodium sulfate, and filtered through a plug of silica using dichloromethane as eluent. The solvent was removed to leave **3** as a purple microcrystalline solid (945 mg, 95%). A sample for analysis was recrystallised from a dichloromethane–methanol mixture. It should be noted that there was some keto-tautomer in the dried sample; mp >300 °C; ν_{max}/cm⁻¹ 3485 (OH), 3315 (NH), 1727 (C=O); λ_{max}(CHCl₃)/nm [log(ε/dm³ mol⁻¹ cm⁻¹)] 421 [5.56], 517 [4.28], 552 [3.86], 591 [3.76], and 647 [3.68]; δ_H(500 MHz; CDCl₃) **enol** −2.83 (2 H, br s, NH), 1.52–1.53 (72 H, m, *t*-butyl H), 6.16 (1 H, br s, OH), 7.77 [1 H, dd, $J_{2′,4′} = J_{6′,4′} = 2$, C(4′)H], 7.79 [2 H, m, C(4′)H], 7.93 [1 H, dd, $J_{2′,4′} = J_{6′,4′} = 2$, C(4′)H], 8.04 [2 H, d, $J_{4′,2′} = J_{4′,6′} = 2$, C(2′)H and C(6′)H], 8.08 [4 H, $J_{4′,2′} = J_{4′,6′} = 2$, C(2′)H and C(6′)H], 8.10 [2 H, d, $J_{4′,2′} = J_{4′,6′} = 2$, C(2′)H and C(6′)H], 8.63 (1 H, 1/2 ABq, $J_{AB} = 5$, pyrrolic H), 8.83 (1 H, 1/2 ABq, $J_{AB} = 5$, pyrrolic H), and 8.86–8.92 (4 H, pyrrolic H): **NB** C(3)H was not observed; m/z (high resolution) (FAB) calc. for $C_{76}H_{94}N_4O$: 1078.7428; found: 1078.7426 (M⁺).

[2-Hydroxy-5,10,15,20-tetrakis(3′,5′-di-*tert*-butylphenyl)-porphinato]zinc(II) 4

A solution of **3** (448 mg, 0.415 mmol) and zinc acetate dihydrate (273 mg, 1.24 mmol) in dichloromethane (80 cm³) and methanol (8 cm³) was heated at reflux in the dark for 65 minutes, and the solvent completely removed. The residue was passed through a plug of silica gel using dichloromethane as eluent to yield **4** as a purple solid (474 mg, 100%). A sample for analysis was recrystallised from a dichloromethane–methanol mixture; mp >300 °C; ν_{max}/cm⁻¹ 3484 (OH); λ_{max}(CH₂Cl₂)/nm [log(ε/dm³ mol⁻¹ cm⁻¹)] 423 [5.49], 514 [3.41], 550 [4.16], and 590 [3.66]; δ_H(500 MHz; CDCl₃) 1.52–1.53 (72 H, *t*-butyl H), 6.20 (1 H, s, OH), 7.77 [1 H, dd, $J_{2′,4′} = J_{6′,4′} = 2$, C(4′)H], 7.79 [2 H, dd, $J_{2′,4′} = J_{6′,4′} = 2$, C(4′)H], 7.94 [1 H, dd $J_{2′,4′} = J_{6′,4′} = 2$, C(4′)H], 8.05 [2 H, d $J_{4′,2′} = J_{4′,6′} = 2$, C(2′)H and C(6′)H], 8.10 [4 H, m, C(2′)H and C(6′)H], 8.11 [2 H, d, $J_{4′,2′} = J_{4′,6′} = 2$, C(2′)H and C(6′)H], 8.15 [1 H, s, C(3)H], 8.71 (1 H, 1/2 ABq, $J_{AB} = 5$, pyrrolic H), 8.93 (1 H, 1/2 ABq, $J_{AB} = 5$, pyrrolic H), 8.97–9.01 (4 H, pyrrolic H); m/z (high resolution) (FAB) calc. for $C_{76}H_{92}N_4OZn$: 1140.6563; found: 1140.6572 (M⁺).

1,1,1-Triacetoxy-1,1-dihydro-1,2-benzodioxol-3(1*H*)-one (the Dess–Martin periodinane)[18]

1-Hydroxy-1,2-benzodioxol-3(1*H*)-one[19] (2.71 g) was added to a mixture of acetic anhydride (10.8 cm³, 114 mmol) and

toluene-*p*-sulfonic acid monohydrate (22 mg, 12 mmol). The mixture was heated at 80–90 °C for 2 h to give a pale yellow solution. The solution was cooled in an ice-bath to give a white precipitate which was collected by filtration, washed with ether (3 × 30 ml), and air-dried at the pump to leave the Dess–Martin periodinane as a white powder (2.9 g).

Oxidation by O₂/*hν* on silica

Copper dione 5. A mixture of **2** (20 mg, 0.018 mmol) and silica (400 mg) in dichloromethane (5 cm³) was stirred in ambient light at room temperature for 5 days. The solvent was completely removed and the residue purified by chromatography over silica using dichloromethane–light petroleum (2:3) as eluent to yield recovered **2** (17 mg, 85%) and **5** (2 mg, 10%) which co-chromatographed with and had an identical infrared spectrum to a sample prepared by a reported procedure;[20] v_{max}/cm⁻¹ 1728 (C=O).

Free-base dione 6. A mixture of **3** (20 mg, 0.019 mmol) and silica (400 mg) in dichloromethane (5 cm³) was stirred in ambient light at room temperature for 5 days. The solvent was completely removed and the residue purified by chromatography over silica using dichloromethane–light petroleum (2:3) as eluent to yield **6** (19 mg, 94%) which co-chromatographed with and had an identical ¹H NMR spectrum to a sample prepared by a reported procedure;[20] δ_H(200 MHz; CDCl₃) −1.93 (2 H, s, NH), 1.49 and 1.52 (72 H, 2 × s, *t*-butyl H), 7.74–7.80 (8 H, m, phenyl H), 8.01 [4 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 8.63 (4 H, m, pyrrolic H), and 8.81 (2 H, 1/2 ABq, pyrrolic H).

Zinc dione 7. A mixture of **4** (46 mg, 0.041 mmol) and silica (400 mg) in dichloromethane (10 cm³) was stirred in ambient light at room temperature for 5 days. The reaction mixture was filtered and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:1) as eluent to yield **4** (21 mg, 45%) and **7** (13 mg, 28%) which co-chromatographed with and had an identical ¹H NMR spectrum to a sample prepared by a reported procedure;[20] δ_H(200 MHz, CDCl₃) 1.46 and 1.49 (72 H, 2 × s, *t*-butyl H), 7.64 [4 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 7.70 [2 H, dd, $J_{2',4'} = J_{6',4'} = 2$, C(4′)H], 7.75 [2 H, dd, $J_{2',4'} = J_{6',4'} = 2$, C(4′)H], 7.92 [4 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 8.34 and 8.60 [4 H, ABq, $J_{AB} = 5$, C(2)H, C(3)H, C(12)H, and C(13)H], 8.52 [2 H, s, C(7)H and C(8)H].

Oxidation by chromium trioxide

Copper dione 5. A solution of **2** (50 mg, 0.044 mmol) in dichloromethane (10 cm³) was treated with a solution of chromium trioxide in 70% acetic acid (66 mᴍ, 1.33 cm³, 0.088 mmol) in the dark at room temperature for 18.8 h. The solution was washed with water (20 cm³), aqueous sodium hydrogen carbonate (5%, 50 cm³), and water (20 cm³), dried over anhydrous sodium sulfate, filtered, and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:3) as eluent to yield **5** (22 mg, 43%) and recovered **2** (2 mg, 4%).

Free-base dione 6. A solution of **3** (50 mg, 0.047 mmol) in dichloromethane (10 cm³) was treated with a solution of chromium trioxide in 70% acetic acid (64 mᴍ, 0.73 cm³, 0.047 mmol) in the dark at room temperature for 1 h. Dichloromethane (10 cm³) was added and the solution was washed with water (20 cm³), aqueous sodium hydrogen carbonate solution (5%, 50 cm³), and water (20 cm³), dried over anhydrous sodium sulfate, filtered, and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:3) as eluent to yield **6** (43 mg, 84%).

Zinc dione 7. A solution of the **4** (46 mg, 0.040 mmol) in dichloromethane (10 cm³) was treated with a solution of chromium trioxide in 70% acetic acid (64 mᴍ, 0.63 cm³, 0.040 mmol) in the dark at room temperature for 19 h. The solution was washed with water (20 cm³), aqueous sodium hydrogen carbon-

ate solution (5%, 50 cm³), and water (20 cm³), dried over anhydrous sodium sulfate, filtered, and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:1) as eluent to yield **7** (25 mg, 54%).

Oxidation by lead dioxide

[2,2-Diacetoxy-3-oxo-5,10,15,20-tetrakis(3′,5′-di-*tert*-butyl-phenyl)chlorinato]copper(II) 8. A solution of **2** (50 mg, 0.044 mmol) and lead dioxide (42 mg, 0.18 mmol) in dichloromethane (5 cm³) and acetic acid (5 cm³) was stirred in the dark at room temperature for 0.5 h. The solution was washed with water (25 cm³), aqueous sodium hydrogen carbonate solution (5%, 50 cm³), and water (25 cm³), dried over anhydrous sodium sulfate, filtered, and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:3) as eluent to yield copper dione **5** (2 mg, 4%) and **8** (16 mg, 29%), mp >250 °C; v_{max}/cm⁻¹ 1766 (C=O), and 1750 (C=O); λ_{max}(CH₂Cl₂)/nm [log(ε/dm³ mol⁻¹ cm⁻¹)] 435 [5.22], 531 [3.61], 578 sh [3.84], and 624 [4.33]; *m/z* (high resolution) (FAB) calc. for C₈₀H₉₆N₄O₅Cu: 1257.6659; found: 1257.6679 (M⁺).

2,2-Diacetoxy-3-oxo-5,10,15,20-tetrakis(3′,5′-di-*tert*-butyl-phenyl)chlorin 9. A solution of **3** (50 mg, 0.046 mmol) and lead dioxide (44 mg, 0.19 mmol) in dichloromethane (5 cm³) and acetic acid (5 cm³) was stirred in the dark at room temperature for 0.4 h. The solution was washed with water (25 cm³), aqueous sodium hydrogen carbonate solution (5%, 50 cm³), and water (25 cm³), dried over anhydrous sodium sulfate, filtered, and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:3) as eluent to yield **9** (14 mg, 25%), mp >250 °C; v_{max}/cm⁻¹ 3357 (NH), 1767 (C=O), and 1753 (C=O); λ_{max}(CH₂Cl₂)/nm [log(ε/dm³ mol⁻¹ cm⁻¹)] 424 [5.20], 437 [5.16], 534 [4.09], 566 [4.12], 601 [3.95], and 654 [3.92]; δ_H(500 MHz; CDCl₃) −2.13 and −2.04 (2 H, 2 × s, NH), 1.50–1.53 (72 H, *t*-butyl H), 1.96 (6 H, s, OAc), 7.71 [1 H, dd, $J_{2',4'} = J_{6',4'} = 2$, C(4′)H], 7.76–7.80 (5 H, m, phenyl H), 7.93 [2 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 7.99 [2 H, d, $J_{4',2'} = J_{4',6'} = 1.78$, C(2′)H and C(6′)H], 8.02 [2 H, d, $J_{4',2'} = J_{4',6'} = 1.78$, C(2′)H and C(6′)H], 8.18 (1 H, 1/2 br ABq, $J_{AB} = 5$ pyrrolic H), 8.59 and 8.63 [2 H, ABq, $J_{AB} = 4.57$, C(12)H and C(13)H], 8.71 (2 H, br m, pyrrolic H), and 8.79 (1 H, 1/2 br ABq, $J_{AB} = 5$ pyrrolic H); *m/z* (high resolution) (FAB) calc. for C₈₀H₉₈N₄O₅: 1194.7537; found: 1194.7506 (M⁺).

[2,2-Diacetoxy-3-oxo-5,10,15,20-tetrakis(3′,5′-di-*tert*-butyl-phenyl)chlorinato]zinc(II) 10. A solution of **4** (49 mg, 0.043 mmol) and lead dioxide (41 mg, 0.17 mmol) in dichloromethane (5 cm³) and acetic acid (5 cm³) was stirred in the dark at room temperature for 0.7 h. The solution was washed with water (25 cm³), aqueous sodium hydrogen carbonate solution (5%, 50 cm³), and water (25 cm³), dried over anhydrous sodium sulfate, filtered, and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (2:1) as eluent to yield **10** (6 mg, 11%), mp >250 °C; v_{max}/cm⁻¹ 1758 (C=O) and 1748 (C=O); λ_{max}(CH₂Cl₂)/nm [log(ε/dm³ mol⁻¹ cm⁻¹)] 437 [5.06], 538 [3.68], 579 [3.87], and 627 [4.35]; δ_H(500 MHz; CDCl₃) 1.46–1.50 (72 H, *t*-butyl H), 1.97 (6 H, s, OAc), 7.65 [1 H, dd, $J_{2',4'} = J_{6',4'} = 2$, C(4′)H], 7.68 [2 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 7.71 [1 H, dd, $J_{2',4'} = J_{6',4'} = 2$, C(4′)H], 7.74 [2 H, dd, $J_{2',4'} = J_{6',4'} = 2$, C(4′)H], 7.84 [2 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 7.94 [2 H, d, $J_{4',2'} = J_{4',6'} = 2$, C(2′)H and C(6′)H], 7.97 [2 H, d, $J_{4',2'} = J_{4',6'} = 1.78$, C(2′)H and C(6′)H], and 7.95, 8.54, 8.56, 8.58, 8.59 and 8.67 (6 H, 3 × ABq, pyrrolic H); *m/z* (high resolution) (FAB) calc. for C₈₀H₉₆N₄O₅Zn: 1257.6750; found: 1257.6773 (MH⁺).

Oxidation by DDQ

Copper dione 5. DDQ (7.0 mg, 0.031 mmol) was added to a

stirred solution of **2** (35 mg, 0.031 mmol) in dichloromethane (10 cm³) in the dark and after 3 min the solvent was completely removed. The residue was purified by chromatography on silica gel using dichloromethane–light petroleum (2:3) as eluent to yield **5** (23 mg, 65%).

Free-base dione 6. DDQ (7.0 mg, 0.031 mmol) was added to a stirred solution of **3** (30 mg, 0.028 mmol) in dichloromethane (10 cm³) at room temperature. The mixture was stirred in the dark for 20 min at which stage thin-layer chromatography (dichloromethane–light petroleum; 2:3) showed that no **3** remained. The solvent was completely removed and the residue was purified by chromatography on silica gel using dichloromethane–light petroleum (2:3) as eluent to yield **6** (9 mg, 30%).

Zinc dione 7. A solution of **4** (51 mg, 0.044 mmol) and DDQ (10 mg, 0.044 mmol) in dichloromethane (5 cm³) was stirred for 2 minutes at room temperature and then filtered through a plug of silica gel with dichloromethane as the eluent. The filtrate was collected and the solvent completely removed. The residue was purified by chromatography on silica gel using dichloromethane–light petroleum (2:3 to 2:1) as eluent to yield **7** (17 mg, 32%).

Oxidation by Dess–Martin periodinane

Copper dione 5. Small aliquots of Dess–Martin periodinane (65 mg) were added to a stirred solution of **2** (30 mg, 0.026 mmol) in dichloromethane (10 cm³) at room temperature in the dark. Addition was continued until thin-layer chromatography (dichloromethane–light petroleum; 2:3) showed that no **2** remained. After 1.5 h the reaction mixture was filtered through a plug of silica and the solvent completely removed. The residue was purified by chromatography on silica gel using dichloromethane–light petroleum (2:3) as eluent to yield **5** (23 mg, 76%).

Free-base dione 6. Dess–Martin periodinane (120 mg, 0.28 mmol) was added in four aliquots over 0.5 h to a solution of the **3** (51 mg, 0.047 mmol) in dichloromethane (10 cm³). The reaction mixture was stirred at room temperature in the dark for a further 1.3 h until thin-layer chromatography (dichloromethane–light petroleum; 2:3) showed that no **3** remained. The mixture was filtered through a plug of silica gel with dichloromethane as the eluent and the filtrate collected. The solvent was completely removed and the residue was purified by chromatography on silica gel using dichloromethane–light petroleum (2:3) as eluent to yield **6** (40 mg, 79%).

Zinc dione 7. Dess–Martin periodinane (52 mg, 0.12 mmol) was added to a solution of **4** (46 mg, 0.041 mmol) in dichloro-

methane (10 cm³). The reaction mixture was stirred at room temperature in the dark for 0.5 h and then filtered through a plug of silica gel with dichloromethane as the eluent. The filtrate was collected and the solvent completely removed. The residue was purified by chromatography on silica gel with dichloromethane–light petroleum (1:1) as eluent to yield **7** (26 mg, 57%).

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