meso-Oxidation of Porphyrins: Convenient Iron(III)-Mediated Synthesis of Dioxoporphyrins

Dong-Mei Shen, Chao Liu, Xiao-Guang Chen, Qing-Yun Chen*

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, P. R. of China Fax +86(21)64166128; E-mail: chenqy@mail.sioc.ac.cn

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Abstract: Iron(III)-mediated *meso*-oxidation reactions of 5,15-diarylporphyrins resulted in a variety of dioxoporphyrins in high yields. In the case of *meso*-amino-substituted diarylporphyrins, a variety of products was produced.

Key words: FeCl₃·6H₂O, oxidation, dioxoporphyrin

Dioxoporphyrins are a class of special electron-deficient porphyrins. The oxo functionality interrupts the macrocycle conjugation and divides the porphyrin nucleus into two separate dipyrromethane units.¹ Their metal complexes show great affinity for many basic and popular ligands, which render them valuable templates for the applications in supramolecular chemistry.² However, there are only a few reports on their preparations, which might be ascribed to their synthetic difficulty. To our best knowledge, the main synthetic method was the thallium trifluoroacetate mediated oxidation of porphyrins developed by Smith and his co-workers.^{1d} Although dioxoporphyrins could be produced in good yields by this method, the use of highly toxic and expensive thallium trifluoroacetate limits its application. Here we would like to present a convenient and practical iron(III)-mediated synthesis of dioxoporphyrins.

Our interests recently focused on the redox reactions of porphyrins.³ In an attempt to utilize FeCl₃·6H₂O as an oxidant to promote the oxidative coupling of (5,15-diphenylporphyrinato)zinc(II) (Zn1a) in DMF at 130 °C, we were surprised not to obtain the expected oxidative coupling products, but an interesting dioxoporphyrin Zn2a. Encouraged by these results, we decided to investigate the reaction conditions in detail. As shown in Table 1, the equivalents of FeCl₃·6H₂O used had a significant effect on the product yield (Table 1, entries 1-3). The use of 10 equivalents facilitated the oxidation reaction, permitting the formation of **Zn2a** in high yield in shorter reaction time (Table 1, entry 3). Higher reaction temperatures were favorable for the formation of Zn2a because both the conversion and yield decreased dramatically when the reactions were performed at lower temperatures (Table 1, entries 4 and 5). The central metal ions of the porphyrin macrocycle also played an important role in the reaction.

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Using nickel(II) 5,15-diphenylporphyrin complex **Ni1** as the starting porphyrin under similar conditions resulted in lower conversion and yield (Table 1, entry 6). Serious degradation of porphyrins took place in the case of free base 5,15-diphenylporphyrin **H**₂**1** (Table 1, entry 7). The selection of solvents was also critical for the success of the reaction and DMF proved to be the best one (Table 1, entries 3, 8–10). All these studies revealed that the oxidation reaction was successfully done in the presence of 10 equivalents of FeCl₃·6H₂O in DMF at 130 °C.⁴ It should be noted that the presence of a small amount of H₂O (coming from FeCl₃·6H₂O or moisture in DMF) was very important since the reaction did not proceed under extremely

Table 1Iron(III)-Mediated Oxidation of 5,15-DiphenylporphyrinsM1a (M = Zn, Ni, or 2 H) under Various Conditions^a



Entry	М	[Fe]/ M1a	Solvent	Temp (°C)	Conversion Yield (%) (%) ^b	
1	Zn	1	DMF	130	0	0
2	Zn	5	DMF	130	67	55
3	Zn	10	DMF	130	100	85°
4	Zn	10	DMF	60	45	30
5	Zn	10	DMF	20	0	0
6	Ni	10	DMF	130	15	10
7	2 H	10	DMF	130	100	0^d
8	Zn	10	toluene	110	0	0
9	Zn	10	THF	80	0	0
10	Zn	10	CHCl ₃	60	0	0

 $^{\rm a}$ Reactions were carried out in DMF (10 mL) with M1a (50 mg, 1.0 equiv) for 24 h.

^b Isolated yields.

^c Reaction time: 5 h.

^d Degradation of porphyrin was observed.

 Table 2
 Iron(III)-Mediated Oxidation Reactions of Zn1 under Optimized Conditions^a



 a Reactions were carried out in DMF (10 mL) with M2a (50 mg, 1.0 equiv) and FeCl_3·6H_2O (10 equiv) at 130 °C.

^b Isolated yields.

dry conditions, which was advantageous for the operation and workup.

Under the optimized conditions, various (5,15-diarylporphyrinato)zinc(II) (**Zn1**) with different substituents at the *meso*-phenyl group were successfully applied to the oxidation reaction, providing good yields of the dioxoporphyrins **Zn2** (Table 2). As expected, the reactivity of substrates with an electron-donating group at the *meso*phenyl group was somewhat higher than that with an electron-withdrawing group. The dioxoporphyrins **Zn2** were easily demetalated by HCl to afford the free base dioxoporphyrins H_22 in high yields (Scheme 1). Nickel(II) ion insertion under routine conditions led to the corresponding nickel(II) dioxoporphyrin complexes **Ni2**. All products were unambiguously characterized by their ¹H NMR, MS spectrometry, UV/vis spectroscopy, HRMS, or ele-



Figure 1 Two views of the X-ray crystal structure of (5,15-dioxoporphyrinato)Ni(II) Ni2a-2MeOH.

mental analysis, as well as X-ray crystallography for **Ni2a**. The X-ray crystallographic diffraction analysis of **Ni2a** showed that the macrocycle was planar with two methanol molecules coordinated to the central nickel(II) ion (Figure 1), which revealed the electron-deficient character of dioxoporphyrins.⁴

To further understand the effect of the *meso*-substituents on the Fe(III)-mediated oxidation reaction, we attempted to carry out the reactions on a variety of *meso*-substituted diphenylporphyrins. Considering that electron-donating groups facilitate the oxidation reaction, various *meso*amino-substituted diphenylporphyrins were subjected to the reactions. Interestingly, different *meso*-amino substituents gave rise to distinct results, indicating the diversity and complexity of the oxidation reaction. For example, when *meso*-amino-substituted porphyrin **Ni3**⁵ was examined in the reaction, the intriguing head-to-tail dimer **Ni4**⁵ was obtained in high yield. Nevertheless, utilizing *meso*-



Scheme 1 Demetalation of Zn2 and nickel insertion reactions of H₂2

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Scheme 2 Iron(III)-mediated oxidation reactions of various meso-amino-substituted porphyrins

amino-substituted porphyrin $\mathbf{Zn5}^5$ as the starting porphyrin afforded a fascinating azoporphyrin $\mathbf{Zn6}^5$ in good yield (Scheme 2). In the case of *meso-N,N'*-dimethylamino-substituted porphyrin **Ni7**,⁶ oxidative coupling occurred. Using *meso*-hexahydropyridine-substituted porphyrin **Ni9**⁶ as a substrate resulted in *meso*-chlorination. To our surprise, while the oxidation reaction was conducted on nickel(II) 5-bromo-15-hexahydropyridinyl-10,20-diphenylporphyrin complex **Ni11**,⁶ dioxoporphyrin **Ni2a** was obtained in excellent yield.

In summary, dioxoporphyrins were conveniently synthesized by Fe(III)-mediated *meso*-oxidation of various 5,15diarylporphyrins in good yields. The *meso*-substituents of the starting porphyrins play an important role in the oxidation reaction and different *meso*-substituents gave rise to distinct oxidation products. Due to the convenience and efficiency of the reaction, this method will allow quick access to various dioxoporphyrin, which might find a number of applications. Detailed studies and explanations on the mechanism are in progress.

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References and Notes

- (a) Fuhrhop, J.-H. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier Scientific Publications: Amsterdam, **1975**, 593–623. (b) Inhoffen, H. H.; Fuhrhop, J.-H.; von der Haar, F. *Liebigs Ann. Chem.* **1966**, 700, 92.
 (c) Fuhrhop, J.-H. *J. Chem. Soc., Chem. Commun.* **1970**, 781. (d) Barnett, G. H.; Evans, B.; Smith, K. M. *Tetrahedron* **1975**, *31*, 2711.
- (2) (a) Watson, Z. C.; Bampos, N.; Sanders, J. K. M. New J. Chem. 1998, 1135. (b) Marty, M.; Watson, Z. C.; Twyman, L. J.; Nakash, M.; Sanders, J. K. M. Chem. Commun. 1998, 2265. (c) McCallien, D. W. J.; Sanders, J. K. M. J. Am. Chem. Soc. 1995, 117, 6611.
- (3) (a) Shen, D.-M.; Liu, C.; Chen, X.-G.; Chen, Q.-Y. J. Org. Chem. 2009, 74, 206. (b) Liu, C.; Shen, D.-M.; Chen, Q.-Y. J. Am. Chem. Soc. 2007, 129, 5814. (c) Jin, L.-M.; Chen, L.; Yin, J.-J.; Guo, C.-C.; Chen, Q.-Y. Eur. J. Org. Chem. 2005, 3994. (d) Jin, L.-M.; Yin, J.-J.; Chen, L.; Guo, C.-C.; Chen, Q.-Y. Synlett 2005, 2893.
- (4) Typical Procedure for the Fe(III)-Mediated Synthesis of Dioxoporphyrins Zn2

A mixture of **Zn1a** (100 mg, 0.19 mmol, 1.0 equiv) and FeCl₃·6H₂O (513 mg, 10 equiv) was stirred in DMF (20 mL) in air at 130 °C for 5 h. After cooling to r.t., the reaction mixture was diluted with CH₂Cl₂ (20 mL) and washed with H₂O three times. The organic layer was passed through dry SiO₂ and evaporated to dryness. The resulting solid was crystallized from CH₂Cl₂–MeOH or purified by flash column chromatography (SiO₂, 300–400 mesh, PE–EtOAC 4:1) to produce the desired dioxoporphyrin **Zn2a** (90 mg, 85% yield).

Characterization Data for Selected Representative Compounds

Dioxoporphyrin Zn2a

¹H NMR (300 MHz, acetone-d₆): δ = 6.28–6.31 (m, 4 H, β-H), 6.87–6.90 (m, 4 H, β-H), 7.33 (d, *J* = 3.6 Hz, 4 H, PhH), 7.40–7.42 (m, 6 H, PhH). MS (MALDI): *m/z* = 555.1 [M + H⁺]. UV/vis (CH₂Cl₂): λ_{max} (%) = 403 (13.0), 450 (6.7), 509 (2.6), 546 (5.6), 708 (1.0) nm. Anal. Calcd for C₃₂H₁₈N₄O₂Zn·2MeOH: C, 65.86; H, 4.23; N, 9.04. Found: C, 65.14; H, 4.07; N, 8.86.

Dioxoporphyrin H₂2a

¹H NMR (300 MHz, CDCl₃): δ = 6.51 (br s, 4 H, β-H), 7.17 (d, *J* = 4.2 Hz, 4 H, β-H), 7.42–7.53 (m, 10 H, PhH), 14.02 (s, 2 H, NH). MS (MALDI): *m/z* = 493.2 [M + H⁺]. UV/vis (CH₂Cl₂): λ_{max} (%) = 408 (3.1), 472 (1.0), 499 (1.2) nm. Anal. Calcd for C₃₂H₂₀N₄O₂·0.5EtOH: C, 76.88; H, 4.50; N, 10.87. Found: C, 76.37; H, 4.31; N, 10.45.

Dioxoporphyrin Ni2a

¹H NMR (300 MHz, CDCl₃): $\delta = 6.20$ (d, J = 4.2 Hz, 4 H, β -H), 6.45 (d, J = 4.5 Hz, 4 H, β -H), 7.45 (s, 10 H, PhH). MS (MALDI): $m/z = 549.1 [M + H^+]$. UV/vis (CH₂Cl₂): λ_{max} (%) = 358 (14.4), 445 (35.4), 524 (8.1), 660 (1.0) nm. Anal. Calcd for C₃₂H₁₈N₄O₂Ni: C, 68.85; H, 3.43; N, 10.04. Found: C, 68.63; H, 3.49; N, 9.67. Crystal data: C₃₄H₂₆NiO₄, M = 613.30, triclinic, space group P-1, a = 7.6032 (11), b = 8.6684 (12), c = 11.3434 (16) Å, a = 94.136 (2), $\beta = 100.890 (2), \gamma = 108.289 (2)^{\circ}, V = 690.11 (17) \text{ Å}^3,$ T = 293 (2) K, Z = 1, $D_c = 1.476$ g/cm⁻³, 4091 reflections measured, 2937 unique which were used in all calculations. R(int) = 0.0734; $R_1 = 0.0465$. The final $wR(F^2)$ was 0.0465 (all data). CCDC 711638 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif.

- (5) Esdaile, L. J.; Jensen, P.; McMurtrie, J. C.; Arnold, D. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2136.
- (6) Liu, C.; Shen, D.-M.; Chen, Q.-Y. J. Org. Chem. 2007, 72, 2732.