

Simple and efficient method for synthesis of metallodeuteroporphyrin derivatives bearing symmetrical disulphide bond

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Abstract

A novel thiol-derivative porphyrin [2,7,12,18-tetramethyl-13,17-di(3-disulfidepropyl)porphyrin] bearing the symmetrical disulphide bond and its metal complexes have been successfully prepared by means of modification on naturally easily derived heme. The results are described by MS–MS and UV–vis spectroscopy.

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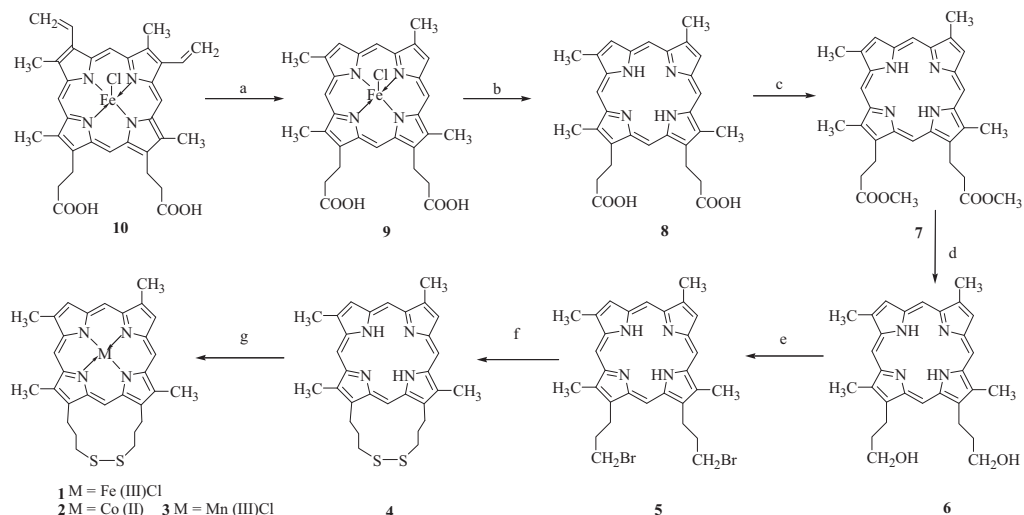
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Porphyrin is of particular interest because of its well known function in biological and biomimetic systems [1,2]. Metalloporphyrin containing the thiol or disulphide group is of the greatest motivation to apply in the fields of molecular technologies and biomimetic catalysis. It is well established that thiols and disulfides covalently linked to gold surfaces using a S–Au linkage [3,4]. And the thiol can coordinate the central metal ion of the porphyrin, resulting in multilayer formation as well as the blocking of the catalytic center [5]. However, the direct introduction of thiol or disulphide in the periphery of porphyrin has not been reported in the literature. Appending long alkanethiol chain to the periphery of a rigid tetrapyrrolic core has proved to be a general methodology for the synthesis of thiol-derivatized porphyrin [6,7]. On the other hand, Viana et al. prepared metalloporphyrin disulphide derivatives *via* link cystamine [8]. These approaches are inefficient route to synthesize thiol-derivatized porphyrin for improving the catalytic activity of porphyrin due to the chain length and space steric effect on the structure and photoelectrochemical properties of porphyrin. Multiple alkanethiol substituents around the porphyrin periphery constrain the porphyrin to lie parallel to the surface in self-assembled monolayers [9].

As the continuation of our work, we developed a facile method for the synthesis of 2,7,12,18-tetramethyl-13,17-di(3-disulfidepropyl)porphyrin (Scheme 1) as a precursor for direct introduction of disulphide bond in the periphery of porphyrin. The whole process was easily controlled and considered to be the most effective methodology from both experimental operation and economic effect perspectives. Furthermore, we have applied its metal complexes bearing markedly symmetrical disulfide bond to the field of self-assembled monolayers and they also have exhibited excellent catalytic activity as biomimetic catalysis in our laboratory.

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Scheme 1. Reagents and conditions: (a) $C_6H_6O_2$, $CH_3CH_2OCH_2CH_3$, $160\text{ }^\circ\text{C}$, 4 h; (b) $CH_3COOCO_3H/FeSO_4/HCl(aq)$, $100\text{ }^\circ\text{C}$ 2 h; (c) CH_3OH , H_2SO_4 , ultrasonic irradiation, 1 h; (d) $NaBH_4/LiCl$, THF, reflux, 6 h; (e) PBr_3 , CH_2Cl_2 , reflux, 4 h; (f) CH_3CH_2OH , H_2NCSNH_2 , reflux 8 h; (g) metal salts, DMF, reflux, 4 h.

1. Results and discussion

The target compounds were synthesized by a convenient seven-step procedure as outlined in Scheme 1, the compounds 6–10 have been reported in our primary study [10]. Treatment of 6 with PBr_3 in CH_2Cl_2 , stirred for 6 h at reflux gave 5. The compound 5 reacted with thiourea in the presence of the alkali in a mixed solvent of $CH_3CH_2OH/CHCl_3$ at reflux for 8 h afforded 4. Different solvents and alkalis were also screened for the synthesis of compound 4. The results are summarized in Table 1. It was found that $CH_3CH_2OH/CHCl_3$ was the best solvent in terms of yield. This phenomenon was due to the fact that the thiourea and porphyrin exhibit good solubility in CH_3CH_2OH and $CHCl_3$, respectively. The weak alkali Na_2CO_3 could effectively avoid the excessive hydrolysis of the intermediates product of the reaction of compound 4 with thiourea. Compound 4 reacted with different metal salts in DMF for 4 h to afford the corresponding metal complexes 1–3 in high yields of 89–92%, whose were fully characterized by mass spectrometric analysis and the detailed fragments were listed in Table 2.

Additionally, compounds 1–4 exhibited diverse absorption in the visible light region, the absorption spectra of 4 and its metal complexes 1–3 are shown in Fig. 1. Compared to the absorption band of the free-base porphyrin 4, which appears at 400, 497, 530, 565 and 619 nm, the metal complexes had taken an obvious change when a metal was inserted into the porphyrin. The absorption peaks of 1 were specially weak at 406 and 542 nm. Compound 2 has three obvious absorption peaks of 407, 535 and 575 nm. In contrast to Fe(III) and Co(II) complexes, the Mn(III) complex porphyrin 3 has the full absorption bands at about 457, 496, 532 and 619 nm when excited at its split absorption maximum of bands at 367 and 394 nm. The effects of the different metals on the absorption spectra can be observed in the expected shifts and disappearance of both Q and B bands. This phenomenon has been attributed to the $\pi \rightarrow \pi^*$ electronic transition from the HOMO to the LUMO of the ring of metalloporphyrin.

Table 1
The effect of solvent and alkali on the synthesis of compound 4.

Entries	Solvent		Alkali	Yield (%) ^a
1	$CHCl_3$	CH_3CH_2OH	NaOH	21
2	$CHCl_3$	CH_3CH_2OH	$NaHCO_3$	40
3	$CHCl_3$	CH_3CH_2OH	Na_2CO_3	80.8
4	$CHCl_3$	–	Na_2CO_3	30
5	–	CH_3CH_2OH	Na_2CO_3	50

^a Isolated yields.

Table 2
Melting point, yields and MS–MS analysis results of compounds 1–3.

Compounds	Metal salts	Mp (°C)	Yield (%) ^a	MS–MS <i>m/z</i> (%)
1	FeCl ₂	>250	89	565.89 (35 eV, 75) [M+H] ⁺ , 550.79 (5), 532.91 (20), 517.92 (35), 506.92 (45), 486.03 (25), 472.97 (100), 459.95 (95), 445.95 (35), 428.76 (5)
2	CoCl ₂ ·6H ₂ O	>250	92	568.92 (35 eV, 30) [M+H] ⁺ , 553.92 (10), 535.93 (20), 520.92 (25), 509.92 (45), 475.95 (95), 461.93 (100), 448.90 (50), 422.86 (5)
3	MnCl ₂ ·4H ₂ O	>250	91	564.93 (45 eV, 5) [M+H] ⁺ , 498.96 (30), 484.98 (15), 471.99 (100), 458.88 (50), 445.02 (25), 428.99 (3)

^a Isolated yields.

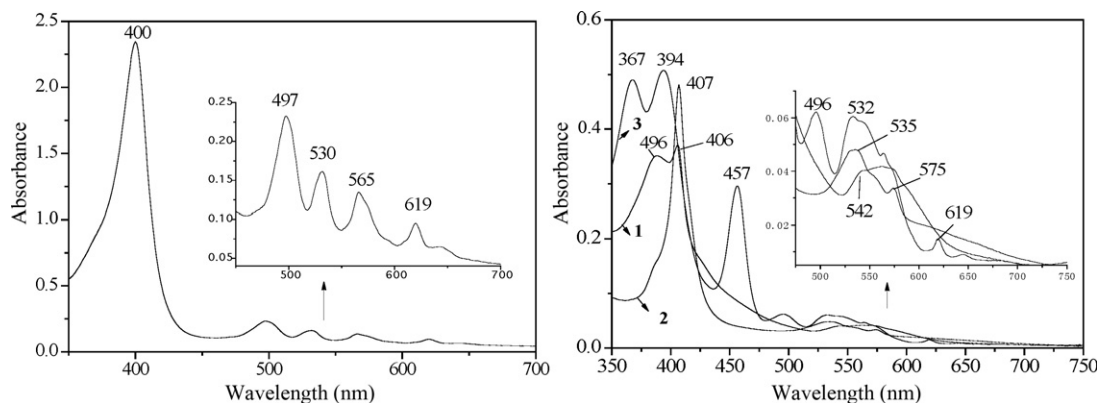


Fig. 1. UV–vis spectra of compounds 1–4 in CHCl₃.

In conclusion, we have demonstrated a convenient method for the first time syntheses of the three novel 2,7,12,18-tetramethyl-13,17-di(3-disulfidepropyl)porphyrin metal. Easy procedure, new aim compounds and high yields attained in almost short reaction times can be mentioned as advantages of this method. Currently, we are working on the investigation of catalytic activity of these novel compounds. Further details and application in modified electrodes, as catalysis for many important reactions will be presented in due course.

2. Experimental

Melting points were determined on a XT4 micro hot-stage apparatus and are uncorrected. IR spectra were obtained by a Perkin-Elmer 681 instrument with KBr optics. LC–MS/MS (ESI) mass spectra were recorded on a Finnigan TSQ Quantum ultra AM mass spectrometer. ¹H NMR was recorded on a Bruker 500 MHz spectrometers in CDCl₃ with tetramethylsilane (TMS) as an internal standard. Elemental analysis was conducted on an PE-2004 (Perkin-Elmer) elemental analyzer. The UV–vis spectra were measured by a Shimadzu UV-240 spectrophotometer.

Synthesis of 2,7,12,18-tetramethyl-13,17-di(3-bromicpropyl)porphyrin (5). A solution of compound 6 (0.4 g, 0.83 mmol) in 40 mL of dichloromethane was treated at 39 °C with 0.4 mL of PBr₃ in 5 mL of CH₂Cl₂ under the condition of stirring for 4 h. After completion, the reaction mixture was washed with water, extracted with CH₂Cl₂. The solution was concentrated and purified by silica gel chromatography (10:1, CH₂Cl₂/EtOAc) to give 0.41 g (82.8%) of 5 as clear. mp: >250 °C. ¹H NMR (500 MHz, CDCl₃): δ 3.86 (s, 2H), 2.85–2.88 (t, 4H, *J* = 11.5 Hz), 3.71–3.76 (s, 12H), 3.79–3.84 (t, 4H, *J* = 9.5 Hz), 4.29 (m, 4H), 9.12 (s, 2H), 10.08–10.24 (s, 4H); ESI⁺-MS (40 eV, *m/z*): 606.85 [M+H]⁺, 526.90 [M+H–HBr]⁺, 499.0 [M+H–CH₂CH₂–HBr]⁺, 485.96 [M+H–CH₂CH₂CH₂Br]⁺; Anal. Calcd. for C₂₈H₃₂N₄Br₂: C, 59.95; H, 4.86; N, 9.65. Found: C, 59.78; H, 4.74; N, 9.76.

Synthesis of 2,7,12,18-tetramethyl-13,17-di(3-disulfidepropyl)porphyrin (4). To a solution of thiourea (0.6 g, 7.9 mmol) in ethanol (50 mL) were added a solution of compound 5 (0.5 g, 0.83 mmol) in CHCl₃ (25 mL). The mixture was stirred magnetically under reflux condition for 8 h. The process of reaction was monitored by TLC until the compound 5 was consumed. Then, the saturated Na₂CO₃ solution was added to the mixture until the pH was 9.0.

After stirring at 80 °C for 30 min, the mixture was diluted with CH₂Cl₂ (60 mL) and then washed with H₂O (3 × 300 mL). The organic layers were decanted, combined, dried over NaSO₄, filtered and concentrated to yield the crude product, which was further purified by silica gel chromatography using CH₂Cl₂ as an eluent to provide the desired product in 79.8% (0.33 g) yield. mp: >250 °C. IR (KBr, cm⁻¹): 3463 (m), 2925 (m), 1739 (s), 1554 (m), 1224 (m), 887 (m), 848 (m), 788 (m); ¹H NMR (500 MHz, CDCl₃): δ 2.03 (s, 2H), 2.76 (t, 4H, *J* = 10.5 Hz), 3.07 (t, 4H, *J* = 12.5 Hz), 3.62–3.75 (s, 12H), 4.32–4.35 (m, 4H), 9.24 (s, 2H), 10.53 (s, 1H), 10.58–10.59 (s, 2H), 11.61 (s, H); ESI⁺-MS (25 eV, *m/z*): 512.92 [M+H]⁺, 447.05 [M+H-2HS]⁺, 420.09 [M+H-CH₂CH₂S-HS]⁺, 404.72 [M+H-CH₂CH₂S-HS-CH₃]⁺; Anal. Calcd. for C₃₀H₃₂N₄S₂: C, 70.27; H, 6.29; N, 10.93. Found: C, 70.37; H, 6.21; N, 11.23.

General procedure for the synthesis of 2,7,12,18-tetramethyl-13,17-di(3-disulfidepropyl)porphyrin metal. Compounds **1–3** were synthesized by the reaction of **4** (0.1 g, 0.19 mmol) with metal salts (2.0 mmol) in DMF (30 mL) under reflux for 4 h. After the completion of the reaction, the reaction was quenched with water (300 mL) and the mixture was extracted with CH₂Cl₂ (150 mL).

Acknowledgments

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