Studies on selective β/β' bromination of π -extended porphyrins and subsequent coupling reactions

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Abstract Monobromination of β , β' - π -extended porphyrins was found to selectively occur at the β or β' position of the porphyrins which is antipodal to the fused aromatic ring. Subsequent Sonogashira or Heck coupling of the resultant bromoporphyrin introduced a carboxylphenylethynyl group or an acrylic acid group to the π -extended porphyrin. The optimal reaction conditions were found for the Sonogashira and Heck coupling reaction. All of the coupling products have shown a broadening and red-shift of the Soret band and Q bands in the UV–Vis absorption spectra compared with the π -extended porphyrin starting materials and the original unmodified porphyrins.

Keywords Large π -aromatic · Porphyrin · Bromination · Selectivity · Sonogashira · Heck

Introduction

Porphyrin derivatives have been widely used in catalysis [1], photodynamic therapy [2], organic light-emitting diodes [3], and dye-sensitized solar cells (DSSCs) [4] due to their vital roles in natural photosynthetic system and strong absorption in the visible region, as well as the readily tunable optical, photophysical, and electrochemical properties by peripheral substitutions [5]. In recent years, intensive efforts have been directed at developing efficient porphyrin sensitizers used in DSSCs. A light-to-electric power-conversion efficiency (η) of over 12 % has been realized

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recently for porphyrin-based DSSCs [6], which is the highest η ever reported for DSSCs. However, it is believed that there is still room for further improvement of η for porphyrin-sensitized solar cells, since the strong Soret (400-450 nm) and moderate Q bands (550-600 nm) absorptions of porphyrins only cover a small part of the whole solar light spectrum. A strategy to increase the light-harvesting capabilities of porphyrins is to expand the porphyrin π -systems via aromatic ring fusion. For example, Imahori [7] has reported the construction of meso- and β -naphthalene-fused porphyrins, and aromatic β , β' edge-fused porphyrins; significant improvements of the light-harvesting capabilities by these π -extension strategies have been recorded. Most studies on the π -extended porphyrins reported to date involved porphyrin sensitizers with the fused aromatic ring also as the carboxyl linkage. However, the steric hindrance introduced by the fused aromatic ring may prohibit the efficient adsorption of sensitizers on the surface of the TiO_2 particles, which is detrimental to the conversion efficiency of the resultant DSSCs. Therefore, in an ongoing project on the synthesis of porphyrin-based sensitizers and their application in DSSCs, we decided to design a β , β' - π -extended porphyrin sensitizer with the fused ring and the carboxylic acid anchoring group on the opposite sites of porphyrin. Furthermore, the π -system can be further elongated via the unsaturated double or triple bond linkage. To realize this goal, a strategy involving bromination of the π -extended porphyrins and subsequent Pd(0)-mediated C-C coupling reaction such as Sonogashira or Heck coupling can be employed.

However, to the best of our knowledge, studies on the modification of the π -extended porphyrins [8, 9] are limited. In particular, the Sonogashira and Heck coupling of the selectively monobromo-substituted porphyrins with aromatic fused rings have not been reported. We have investigated the selective β or β' monobromination of the π -extended porphyrins, and the subsequent Sonogashira and Heck couplings, and here we want to report our preliminary results. A linear carboxylphenylethynyl group or a less linear acrylic acid group was introduced to the β or β' position of the porphyrin, which is antipodal to the fused aromatic ring. The UV–Vis absorption spectra of the coupling products, the π -extended porphyrins, and the original unmodified porphyrins were compared, which shows a broadened and red-shifted Soret band and Q bands in the UV–Vis absorption for the coupling products.

Results and discussion

It was determined that the π -extended porphyrin **1a** reported by Cavaleiro [10, 11] is a good compound with which to start our studies since it can be easily obtained by Diels–Alder reaction of Ni(II)-2-vinyl-5,10,15,20-tetraphenylporphyrin with 1,4naphthoquinone and subsequent demetallation. Ni(II)-2-vinyl-5,10,15,20-tetraphenylporphyrin was prepared according to a literature procedure [12, 13]. Interestingly, it was found that the Diels–Alder reaction also proceeded very well with the freebase and 1,4-naphthoquinone. The total yield is similar for these two approaches starting from 5,10,15,20-tetraphenylporphyrin. Furthermore, it was found that the reaction can also be applied to 2-vinyl-5,10,15,20-tetra- (4-tert-



Scheme 1 Synthesis of monobromo-substituted porphyrin 2

butylphenyl)porphyrin or its Ni(II) complex as shown in Scheme 1. The yield of **1d** starting from the Ni(II) complex of 2-vinyl porphyrin is 25 % and removal of the metal afforded compound **1b** quantitatively.

Bromination of the π -extended porphyrin **1** with 1.1 eq. *N*-bromosuccinimide (NBS) in refluxing chloroform afforded monobrominated porphyrin **2** as a mixture of two inseparable regioisomers in 50 % combined yield. Monobromination selectively occurred to the β or β' position of the porphyrin which is opposite to the fused aromatic ring.¹ It is believed that the metal-free porphyrin is required for the selective β bromination, which results from the bond-fixing entity of porphyrin caused by the β - β' -fused aromatic ring [14, 15]. In order to

¹ General procedure for bromination: Compound **1** (25.2 µmol) with *N*-bromosuccinimide (NBS) (4.5 mg, 25.2 µ mol) were dissolved in CHCl₃ (5 mL) and the resulting solution was refluxed for 1 h. After the reaction, the solvent was removed in vacuuo and the residue was then submitted to preparative TLC using DCM/PE as eluent. The two regioisomeric monobromo porphyrins were obtained as an inseparable mixture in CHCl₃ and the resulting solution was heated at reflux for 1 h. The resulting mixture was submitted to preparative TLC using dichloromethane (DCM)/petroleum (PE) as eluent, and we get a mixture of momobromination porphyrin. Compound **2b**: Column chromatography DCM:PE = 1:4–1:1, yield:46.5 %, UV/Vis (THF): $\lambda_{max}(nm)(\epsilon, 10^3 M^{-1} cm^{-1})$: 465 (144.5), 635 (12), 707 (8). ¹H NMR (400 MHz, CDCl₃) δ 9.92 (s, 1H), 9.71 (d, J = 4.7 Hz, 1H), 9.21 (s, 1H), 9.06 (d, J = 8.4 Hz, 1H), 8.91 (d, J = 4.7 Hz, 1H), 8.75–8.65 (m, 3H), 8.65–8.43 (m, 3H), 8.40 (d, J = 7.2 Hz, 1H), 8.10 (d, J = 6.8 Hz, 1H), 7.92 (s, 3H), 7.86–7.67 (m, 5H), 7.65–7.50 (m, 3H), 7.22 (d, J = 8.0 Hz, 1H), 1.74 (s, 9H), 1.62 (m, 18H), 1.57 (s, 9H), -1.07 (s, 1H), -1.24 (s, 1H). MALDI-TOF: m/z calcd for C₇₂H₆₃BrN₄O₂ (M⁺), 1,094.4134; found, 1,094.1184



Scheme 2 Sonogashira and Heck coupling reaction of bromo-substituted porphyrin 3

introduce a carboxylic group which can act as an anchorage in the later studies on the DSSC and further elongate the porphyrin π -system, we investigate the Sonogashira or Heck coupling reactions of the prepared monobromo-substituted π -extended porphyrins with methyl 4-ethynylbenzoate and methyl acrylate, respectively (Scheme 2).

We first examined the reaction of metal-free monobromo-substituted π -extended porphyrin **2a** or **2b** with methyl 4-ethynylbenzoate under standard Sonogashira coupling reaction conditions [16–18]. The reaction was carried out by using PdCl₂(Ph₃P)₂ as catalyst and CuI as co-catalyst in the presence of Et₃N in refluxing THF [19]. It was found by thin layer chromatography (TLC) analysis that a complex mixture resulted and no starting material remained. Furthermore, no major products can be isolated from the complex mixture. It was then decided to make a porphyrin metal complex. After metallation of the porphyrin with Zn(OAc)₂ 2H₂O, the resultant porphyrin complex **3a** was treated with methyl 4-ethynylbenzoate under the above-mentioned Sonogashira coupling reaction conditions. Trace amounts of coupling products were produced after 24 h and most of the starting materials were recovered. Interestingly, by changing PdCl₂(Ph₃P)₂ to Pd₂(dba)₃ and using AsPh₃ as ligand [20], in the absence of CuI, the coupling product **4a** was obtained in about 30 % yield. Base hydrolysis of 4 with KOH in the mixed solvent (THF/EtOH/H₂O = 4:4:1) furnished the carboxylic acid group

Entry	T(°C)	Catalyst (ligand)	Isolated yield (%)	Material recovered (%)
1	40	Pd ₂ (dba) ₃ (AsPh ₃)	8	90
2	60	Pd ₂ (dba) ₃ (AsPh ₃)	9	88
3	90	Pd ₂ (dba) ₃ (AsPh ₃)	54	36
4	120	Pd ₂ (dba) ₃ (AsPh ₃)	0	0
5	90	Pd(PPh ₃) ₄	47	44
6	90	$Pd(OAc)_2$ (PPh ₃)	82	Trace

Table 1 Heck coupling reaction of 3a with methyl acrylate

DMF was used as solvent and NEt3 as the base

in 5 as shown in Scheme 2.² Unfortunately, the two isomers in 5a or 5b are still inseparable at this stage.

To introduce a less linear double bond linkage, we next investigated the Heck coupling reaction of **3** with methyl acrylate [21–23]. On the basis of the results obtained from the above Sonogashira coupling reaction, the Heck coupling reaction was first examined by employing Pd₂(dba)₃ as catalyst, AsPh₃ as additional ligand, and NEt₃ as the base. In this reaction, DMF was used as the solvent. The studies began with the determination of the optimal temperature for the coupling reaction of **3a** as shown in Table 1 (entries 1–4). It was found that the best result was obtained at 90 °C; the coupling product **6a** was obtained in 54 % yield and 36 % starting material recovered.³ At low temperature, such as 40 and 60 °C, most starting materials were recovered and only trace amounts of the coupling product produced. At the optimal temperature, we examined the influence of the catalyst on the coupling reaction. Both Pd(0) and its precursor Pd(II) were evaluated in the presence of a proper base at 90 °C (Table 1, entries 5 and 6).⁴ The highest yield (82 %) of coupling product was achieved with air-stable Pd(OAc)₂ as pre-catalyst, PPh₃ as both

² General procedure for Sonogashira reaction: To a solution of **3** (30.0 μ mol) and methyl 4-ethynylbenzoate (48.0 mg, 0.3 mmol) in 10 ml dry THF was added Pd₂(dba)₃ (13.8 mg, 15 μ mol), AsPh₃(3.7 mg, 12.0 μ mol) in a glove box under N₂. NEt₃ (2 mL) was then added respectively via a syringe under N₂. After the resulting mixture was refluxed for 24 h under N₂, the solvent was removed in vacuo. The residue was submitted to preparative TLC using dichloromethane as eluent to provide the coupling product. Representative data: compound **4a** (9.1 mg, 30.0 % yield). UV/Vis (THF): $\lambda_{max}(nm)(\epsilon, 10^3 \text{ M}^{-1} \text{ cm}^{-1})$: 476 (171), 612 (14.7), 678.4 (11). ¹H NMR (400 MHz, DMSO-d6) δ 9.97 (s, 1H), 9.60 (d, *J* = 4.6 Hz, 0.66 H), 9.54 (d, *J* = 4.6 Hz, 0.33H), 9.43 (d, *J* = 8.4 Hz, 1H), 9.19–10 (m, 1H), 8.81 (d, *J* = 14.3 Hz, 1H), 8.75–8.49 (m, 5H), 8.40 (d, *J* = 7.3 Hz, 1H), 8.30 (d, *J* = 6.8 Hz, 1H), 8.18–8.05 (m, 2H), 8.04–7.53 (m, 15H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.35–7.26 (m, 1H), 7.25–7.16 (m, 1H), 3.91 (s, 3H). MALDI-TOF: m/z calcd for C₆₆H₃₆N₄O₄Zn (M⁺), 1,012.2028; found, 1,012.0293

³ General procedure for Heck reaction: A solution of **3** (11.9 μ mol), Pd(OAc)₂ (0.11 mg, 0.5 μ mol), PPh₃(0.83 mg, 2.7 μ mol), methyl acrylate (0.3 mmol) in 5 ml dry DMF and 2 ml NEt₃, and the resulting solution was heated for 12 h under the nitrogen atmosphere. Then, the solvent was evaporated to dryness. The resulting mixture was submitted to preparative TLC using dichloromethane as eluent to give the coupling product. Representative data: compound **6a** (9.1 mg, 82.0 % yield). UV/Vis (THF): λ_{max} (nm)(ε, 10³ M⁻¹ cm⁻¹): 474 (104.7), 612 (11), 692 (9). ¹H NMR (400 MHz, DMSO) δ 9.96 (s, 1H), 9.67–9.49 (m, 1H), 9.46–9.35 (m, 1H), 9.25–9.06 (m, 1H), 8.95–8.42 (m, 6H), 8.42–8.33 (m, 1H), 8.30 (d, *J* = 7.4 Hz, 1H), 8.17–7.42 (m, 16H), 7.32–7.18 (m, 2H), 6.36 (d, *J* = 16.0, 15.8 Hz, 1H), 3.88–3.63 (m, 3H). MALDI-TOF: m/z calcd for C₆₀H₃₄N₄O₄Zn (M⁺), 938.1872; found, 938.1633

⁴ See supplementary data for the detail



Fig. 1 Part of the ¹H-NMR spectrum of 1b

reducing agent and additional ligand, and NEt₃ as the base. With Pd(PPh₃)₄, the coupling product was produced in 47 % yield and 44 % starting material recovered, which is similar to the results obtained with $Pd_2(dba)_3$ (Table 1, entries 3 vs. 5). Base hydrolysis of **6** under the above-mentioned conditions yielded compound **7**.

The structure of monobromo-substituted π -extended porphyrin 2 was determined by analysis of ¹H-NMR spectra of the starting materials and products. Based on the studies reported by Cavaleiro, it is known that for 1b, similar to 1a (Fig. 1), β -pyrrolic protons H-18 and H-17 appear as two doublets at δ 9.74 and 8.95 ppm, respectively, with J value of 4.6 Hz. Pyrrolic protons H-8 and H-7 appear at δ 8.66 and 8.64 ppm, and each as a doublet with J value of 4.6 Hz. Protons H-12 and H-13 resonate at δ 8.84 ppm as a singlet. The ¹H-NMR spectrum of bromo-substituted porphyrin **2b** (Fig. 2) is very similar to that of starting porphyrin **1b**. Unfortunately, the signals for two regioisomers completely overlapped. Therefore, the ratio of the two isomers cannot be obtained at this stage. However, the structures of the bromo products can still be determined by comparing the ¹H-NMR spectrum of **1b** with that of **2b**. As shown in Fig. 1, β -pyrrolic protons H-17, H-18, H-8 and H-7 still appear as a doublet at δ 9.72, 8.91, and 8.73, 8.68 ppm. The coupling constants for two sets of doublets are 4.8 ($J_{H-18, H-17}$) and 4.8 Hz ($J_{H-8, H-7}$), respectively. Integration of the singlet at δ 8.70 ppm indicates that the signal is due to one proton resonance, which is assigned to β -pyrrolic proton H-12 or H-13. The other pyrrolic proton (H-12 or H-13) is substituted by bromine, which suggests that bromination occurred to the β position antipodal to the fused aromatic ring.

The structures of the coupling products **4** and **6** were characterized by ¹H-NMR spectrum [24], which also confirmed the presence of two regioisomers in compound **2**. For example, for the Sonogashira coupling product **4a**, the ratio of two isomers is 2:1 and calculated based on the integration of H-18 doublets at δ 9.60 and 9.54 ppm. For the two isomers of Heck coupling product **6a**, the H-18 doublets appear at δ 9.59 and 9.54 ppm, and the ratio of two isomers is calculated as 3:1 based on the integration. The presence of the methyl singlet due to the COOCH₃ group in **4** or **6** is diagnostic and confirms our assignment of the structures for the coupling products. The two methyl singlets in two isomers of **4a** completely overlap and appear at δ 3.91 ppm, whereas for **6a** two singlets resonate at δ 3.84 and 3.69 ppm.



Fig. 2 Part of the ¹H-NMR spectrum of 2b

It was also found that the coupling constants between two olefinic protons in two isomers of Heck coupling product **6a** are both 16.0 Hz, which indicates the stereo-chemistry of the introduced double bond is *trans*.

The UV–Vis spectra of 1, 5, 7, and **TPP** in THF were all obtained. Since the UV–Vis spectra of derivatives 1b, 5b and 7b are similar to the ones obtained for 1a, 5a and 7a, for the purposes of clarity, only the UV–Vis spectra of derivatives 1a, 5a and 7a are shown in Fig. 3. The hydrolyzed coupling products 5a and 7a have shown a broadened and a red-shift of the Soret band compared to the π -extended porphyrin 1a, and the original unmodified porphyrin **TPP**. The Soret bands of 5a



Fig. 3 UV-Vis spectra of 1a, 5a, 7a, and TPP in THF

and **7a** appear at 475 and 474 nm, whereas porphyrins **1a** and **TPP** possess a Soret band at 458 and 417 nm, respectively. The Q bands of **5a** and **7a** also red-shifted to the near infrared region (**5a** at 707 nm; **7a** at 695.5 nm) compared to those of **1a** and **TPP** as shown in the inset of Fig. 3. These results suggested that the lightharvesting capabilities of π -extended porphyrin **1a** were further enhanced by introducing a conjugated carboxylphenylethynyl group to the β position antipodal to the fused aromatic ring via Sonogashira coupling reaction. Therefore, compounds **5** and **7** can be potentially used as efficient dye-sensitizers in DSSCs.

However, interestingly, it was found that the molar extinction coefficients at the Soret bands for the π -extended porphyrins (1a, 5a and 7a) of the peaks reduced and are about 30 % of that for **TPP**. These results are consistent with those previously reported by Imahori [7].

Conclusions

In summary, we have developed a method for the preparation of π -extended porphyrin sensitizers with the fused aromatic ring and the carboxylic acid anchoring group on the opposite sites of porphyrins. The optimal reaction conditions were determined, which can be employed for the synthesis of various π -extended porphyrin sensitizers. The UV–Vis absorption spectra of the hydrolyzed coupling products show a broadened and red-shifted Soret band and Q bands compared with those of the starting π -extended porphyrins and the original unmodified porphyrins. The results suggest that the hydrolyzed coupling products can be potentially used in the fields of DSSC systems. Future studies will be focused on the performance of the solar cells sensitized by porphyrin **5** or **7**.

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