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PAPER

Naphthalene-fused metallo-porphyrins–synthesis and spectroscopy†

Jan P. Lewtak,[a] Dorota Gryko,[a] Duoduo Bao,‡[a] Ernest Sebai,[b] Olena Vakuliuk,[b] Mateusz Ścigaj[a] and Daniel T. Gryko*[a,b]

Oxidative aromatic coupling of *meso*-substituted porphyrins bearing one electron-rich naphthalene unit has been studied in detail. After thorough optimization of oxidant, naphthalene-fused porphyrins were prepared in high yield without contamination from chlorinated side-products using $Fe(ClO_4)_3 \cdot 2H_2O$. Copper and nickel complexes were successfully transformed into π-expanded porphyrins in 40–83% yield.

Porphyrins and other porphyrinoids, by nature of their electronic and redox properties, are extremely versatile architectures that figure prominently in applications ranging from materials[1] to biomedicine.[2] The relationship between the structure of porphyrinoids and their spectroscopic and photophysical properties is a complex and deeply intriguing issue.[3] Among other changes, π-expansion of a porphyrin chromophore usually leads to a certain bathochromic shift in its absorption (and hence emission) spectrum. The magnitude of this alteration depends more on the type of conjugation than on the actual number of double or triple bonds added. The subtle nature of this relationship can be exemplified by Osuka's expanded porphyrin which, in spite of possessing an extra double bond, displays hipsochromic shift.[4] The vast diversity of π-expanded porphyrinoids[5] attracts attention not only because of the theoretical issues involved, but also because of the opportunities to explore their linear and non-linear properties in technology and medicine.[6] Among various synthetic strategies, a breakthrough approach was demonstrated in 1997 by Osuka *et al.* Porphyrins that are unsubstituted at the *meso* positions were firstly oxidized to form a *meso-meso* link[7] and then treated with $DDQ/Sc(OTf)_3$ to form two additional bridges between the β positions. This structural change caused an extension of the conjugated π-system and a concomitant strong bathochromic absorption shift.[8,9]

An elegant example of such a multiplied effect is shown in the so-called *meso-meso*, β-β, β-β triply linked 'porphyrin tapes' (10 nm molecular size), which display absorption at 2850 nm.[10] In principle, any aromatic unit located at the *meso*-position of a

porphyrin and possessing high electron density should be able to form analogous products *via* oxidative aromatic coupling which was proved by seminal contribution by Anderson *et al.*[11] This concept was also successfully realized for such units as azulene,[12a] BODIPY,[12b] and pyrene.[13] Very recently, elaborated examples of oxidative coupling were presented by Wu, Wang and Thompson.[14] The attachment of simpler units using oxidative aromatic coupling is a less explored subject. An alternative approaches based on acylation[14f,g] and direct arylation[14h] were also presented.

We were intrigued by the question of what kind of changes can be introduced by fusion of the porphyrin core with the most fundamental two-ring aromatic unit–naphthalene. Naphthalene-fused porphyrins have been prepared sporadically in the past. In 2005 Cammidge and co-workers unexpectedly found that direct aromatic coupling occurs when a porphyrin bearing one naphthalene unit at the *meso*-position and a triflate group at position 8 is exposed to typical Suzuki reaction conditions. A fused porphyrin lacking any substituents on the naphthalene moiety was isolated in 14% yield.[15] Shortly afterwards, Imahori and co-workers revealed that Ni-porphyrin bearing a naphthalene unit at the *meso*-position (and possessing an additional ester group) undergoes oxidative aromatic coupling in the presence of $FeCl_3$ to give fused-porphyrin in 16% yield.[16a] Scott and co-workers proposed an alternative route based on rearrangement of cyclic bis-dipyrrines.[16b]

Naphthalene-fused porphyrinoids are simple systems that allow us to study the chemical, spectroscopic, and photophysical effects of this type of π-expansion. We were also intrigued by the relation between the output of oxidative aromatic coupling reactions and the nature of the oxidizing agent and the central metal cation.
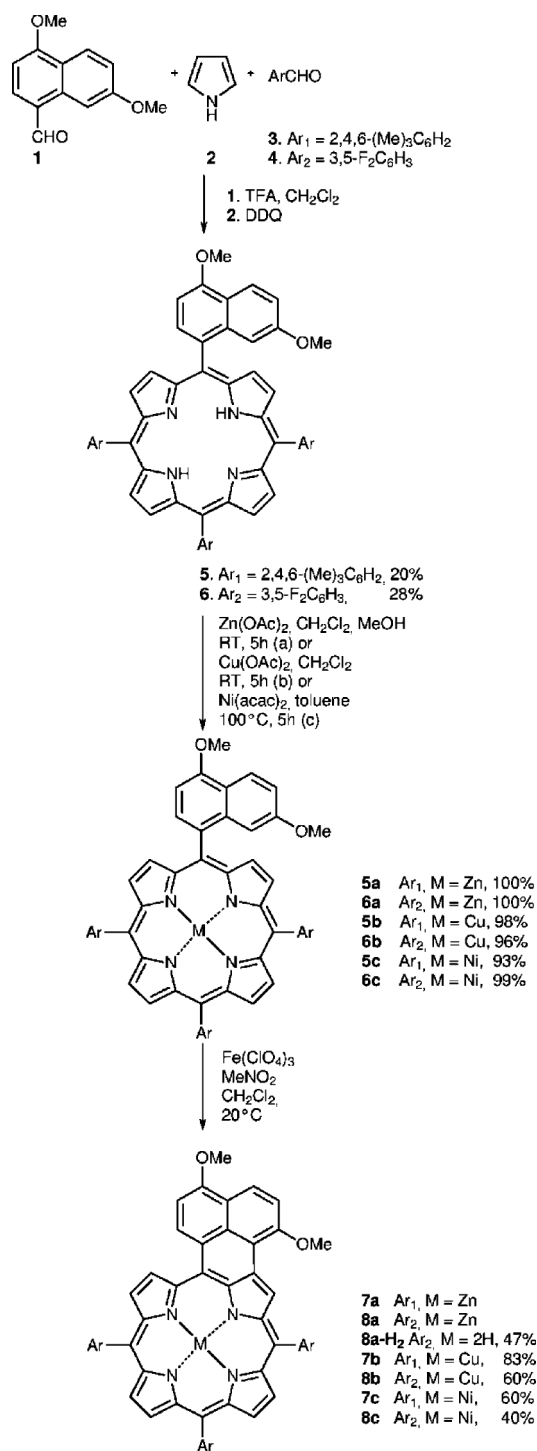
Previous studies (most notably by Osuka and Anderson)[7–11] and general knowledge of aromatic oxidative coupling[17] both indicate that the planned concept can only be realized if the naphthalene porphyrin bears an electron-donating substituent at a suitable position (Scheme 1). Macrocycles of this type could in principle be synthesized either *via* Suzuki coupling starting from *meso*-bromo porphyrins or from the corresponding aldehydes *via* mixed condensation. The second route is more straightforward

[a]Institute of Organic Chemistry Polish Academy of Sciences, Kasprzaka 44/52 01-224, Warsaw, Poland. E-mail: dtgryko@icho.edu.pl; Fax: +48 22 632 66 81; Tel: +48 22 343 20 37

[b]Warsaw University of Technology, Noakowskiego 3, 00-664, Warsaw, Poland; Fax: +48 22 628 27 41; Tel: +48 22 343 30 63

† Electronic supplementary information (ESI) available: Experimental details, ^{1}H NMR spectra of compounds **5**, **5a**, **5c**, **6**, **6a**, **6c**, **7c**, **8a-H2**, **8c** and ^{13}C NMR spectra of compounds **5**, **5c**, **6**, **6a**, **6c**, **8c** data in PDF format. See DOI: 10.1039/c1ob06281f

‡ On the leave from University of California Riverside.

Scheme 1

pyrrole (**2**) and mesitaldehyde (**3**) under Lindsey's[18] conditions for sterically hindered aldehydes gave the desired A₃B-porphyrin **5** in 20% yield (Scheme 1). This porphyrin was subsequently metallated under standard conditions resulting in zinc, copper and nickel complexes **5a–c** in excellent yields. Zinc porphyrin **5a**, when subjected to standard Scholl conditions (FeCl₃/CH₃NO₂, substrate/CH₂Cl₂), gave on TLC a distinct green spot representing probably fused complex **7a**.

Chromatography of that porphyrin revealed its instability, and in spite of many attempts its purification could not be achieved. In light of this result we replaced the moderately electron-rich mesityl unit with an electron-neutral 3,5-difluorophenyl. An analogous mixed condensation performed under Lindsey's[19] conditions gave A₃B-porphyrin **6** in 28% yield (Scheme 1). After transformation into the zinc complex **6a** and subsequent treatment under FeCl₃/CH₃NO₂ conditions free-base porphyrin **8a-H₂** was obtained in 47% yield as green solid, which turned out to be the product of oxidative aromatic coupling followed by demetalation.

Since zinc complexes proved to be unstable in the presence of a Lewis acid (FeCl₃), subsequent research focused on copper(II) and nickel(II) complexes, which are significantly more robust. Complexes **5b**, **5c**, **6b**, and **6c** were synthesized using the standard procedure (Scheme 1). Not only porphyrins with mesityl units (**5**, **5a**, **5b** and **5c**) but also these bearing 3,5-difluorophenyl substituents (**6**, **6a**, **6b** and **6c**) possessed good solubility. We were delighted to see that all four compounds underwent intramolecular oxidative ring closure with FeCl₃ to give **7b**, **7c**,**8b**, and **8c** in 50%, 77%, 86%, 72% yields, respectively, and no demetalation was observed. Unfortunately, fused products were contaminated with mono-chlorinated by-products, which were clearly visible by FD/MS as well as by elemental analysis. The chlorination of electron-rich aromatic compounds using FeCl₃ was reported for the first time by Niementowski.[20] This serious problem was mentioned before by Osuka[21] and Anderson.[11] Since separation of these side-products from the desired fused porphyrins is basically impossible, efforts were directed toward suppressing chlorination. We have chosen porphyrin **5c** as a model, and oxidative aromatic coupling was performed on this compound using various conditions (Table 1).

Replacement of FeCl₃ with the standard procedure for preparation of *meso-meso*, *β-β*, *β-β* triple-fused porphyrins (*i.e.* DDQ/Sc(OTf)₃) led to drastically lower yields (Table 1, entries 4–6). The use of copper(II)[22] or molybdenum(V) salts resulted in no desired product (Table 1. Entries 7–8).

Osuka *et al.* reported that addition of silver triflate suppresses formation of chlorinated fused porphyrins.[21] When applied to our compounds, this procedure still resulted in chlorinated impurities. (Table 1, entry 2). A survey of other oxidation methods suggested that iron perchlorate dihydrate may offer a solution to this problem—indeed, pure **7c** was obtained in satisfactory yield. In spite of running >20 reactions with iron(III) perchlorate hydrate we never experienced any problems, however this compound may be explosive in large quantities.

The detailed analysis revealed that this product is free of any chlorinated side-products. The reaction with Fe(ClO₄)₃·2H₂O gave compounds **7b**, **7c**, **8b** and **8c** in 83%, 60%, 60%, and 40% yields, respectively (Scheme 1).

Purification and characterization of **7b**, **7c**, **8b** and **8c** proved to be challenging due to their low solubility and tendency to

for the preparation of A₃B-porphyrins. We have therefore chosen the readily available 4,7-dimethoxy-1-naphthaldehyde (**1**) as a precursor, which possesses high electron density at the required position 8 due to the suitably positioned methoxy groups. Mesitaldehyde (**3**) was chosen as the second coupling partner since its presence in porphyrin molecules ensures their high solubility. This aspect is of paramount importance as the products are expected to possess a larger π-electron system, which will substantially decrease their solubility. A mixed condensation of aldehyde **1**,

Table 1 Results of oxidation of porphyrin **5c** into **7c**

Entry	Oxidizing reagent	Solvent	$T/°C$	Time (h)	Yield of **7c** (%)
1	FeCl$_3$	MeNO$_2$/DCM	RT	0.5	86[a]
2	FeCl$_3$/AgOTf	MeNO$_2$/DCM	RT	0.5	80[a]
3	PIFA/BF$_3$·OEt$_2$	Toluene	110	5	46
4	DDQ, Sc(OTf)$_3$	Toluene	110	72	12.5
5	DDQ, Sc(OTf)$_3$	Xylenes	140	72	20
6	DDQ, Sc(OTf)$_3$	1,2-Dichlorobenzene	170	72	dec.
7	CuCl$_2$,O$_2$/[iPrMgCl·LiCl+TMP]	THF	50	48	0
8	molybdenum 2-ethylhexanoate	DCM	RT	48	0
9	Fe(acac)$_3$	DCM	RT	48	0
10	K$_3$[Fe(CN)$_6$]	THF/18-crown-6	RT	48	0
11	Cu(ClO$_4$)$_2$	DCM	RT	48	0
12	Mn(CH$_3$COO)$_3$	DCM	RT	48	14
13	Fe(ClO$_4$)$_3$·2H$_2$O	MeNO$_2$/DCM	RT	0.33	60
14	Fe(OTf)$_3$	MeNO$_2$/DCM	RT	0.5	42

[a] Product contaminated with chlorinated porphyrins.

aggregate. The traces of some solvents could not be removed from these complexes, even after prolonged drying in 80 °C.
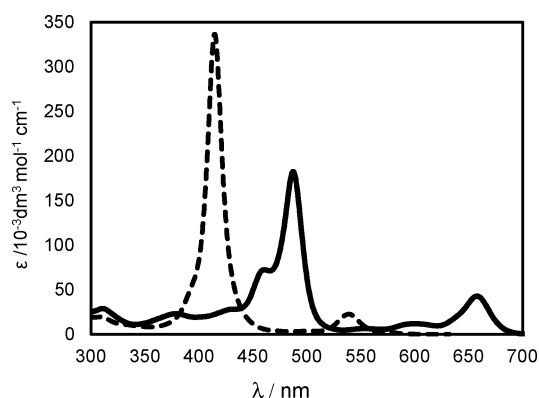
All fused porphyrins have distinct deep green color. The bathochromic shift that resulted from attaching the dimethoxy-naphthalene unit at positions 1 and 3 is ~60–70 nm for the Soret bands and ~100–130 nm for the Q-bands, depending on the type of complex (Fig. 1–3). For nickel complexes red-shift of Q-bands is higher than for corresponding copper complexes. For both copper and nickel fused-complexes the least energy Q-band are more significantly intense than in case of their non-fused counterparts. In accord with previous findings of Imahori[16a] *et al.* we observed that molar absorptivity at the Soret band of fused porphyrins is lower than that of non-fused porphyrin complexes. At the same time broadening of both the Soret band and the Q-bands is observed. The free-base fused-porphyrin **8a-H$_2$** produces the most complex absorption spectrum (Fig. 3): not only does it possess five well resolved peaks (with additional shoulders), but the lowest energy Q-band has intense ($\varepsilon = 27000$) absorption at 701 nm with a shoulder up to 750 nm. **8a-H$_2$** also displays fluorescence in the near-infrared region ($\lambda_{max} = 710$ and 760 nm, $\Phi_{fl} = 10\%$).
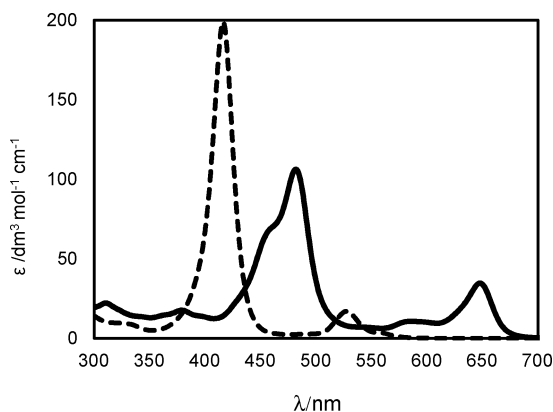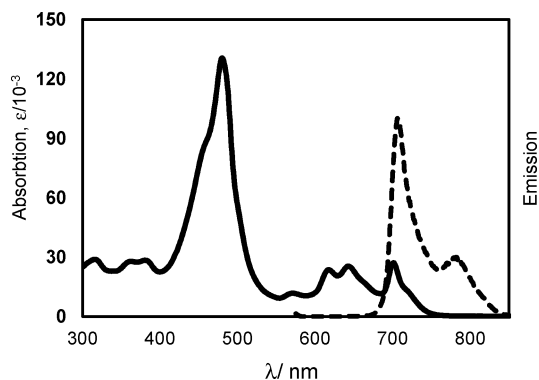

Fig. 1 Absorption of **5c** (dotted line) and **7c** (solid line).

Fig. 2 Absorption of **6b** (dotted line) and **8b** (solid line).

Fig. 3 Absorption (solid line) and normalized fluorescence (dotted line) of porphyrin **8a-H$_2$** in CH$_2$Cl$_2$.

Replacing the commonly used FeCl$_3$ with readily available Fe(ClO$_4$)$_3$ as an oxidizing reagent was an effective strategy for preventing chlorinated by-products, and thus opens new horizons in oxidative aromatic coupling of porphyrins and other electron-rich aromatic compounds. Oxidation of a Zn-coordinated porphyrin resulted in demetalation of the complex, while replacement of zinc by copper and nickel allowed stable fused porphyrin complexes to be synthesized. The fusion of a small naphthalene unit with a porphyrin causes a ~100 nm red shift in the absorption spectrum. Free-base π-expanded porphyrins display relatively

Conclusions

In conclusion, fused electron-rich naphthalene-porphyrins have been synthesized *via* intramolecular oxidative aromatic coupling.

strong emission in the NIR region, which we plan to utilize in the design of new fluorescence probes.

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