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## Directly linked hydroporphyrin dimers

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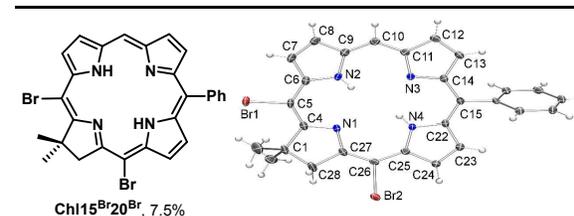
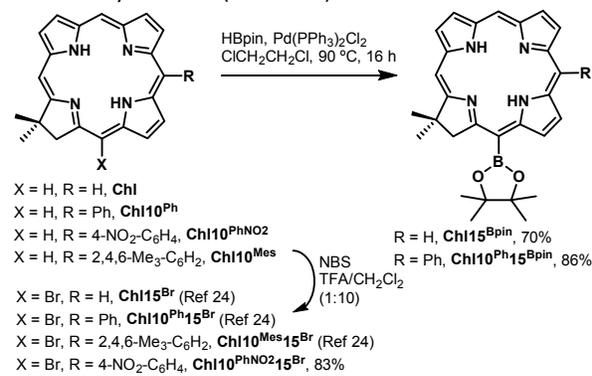
Directly linked porphyrin dimers and oligomers are used in photovoltaics,<sup>1,2</sup> in supramolecular chemistry<sup>3-5</sup> and molecular electronics,<sup>6,7</sup> and as models for photosynthetic light harvesting.<sup>8</sup> For several of these applications, architectures based on the strongly red-absorbing hydroporphyrins<sup>9</sup> (chlorins and bacteriochlorins) would be preferred to porphyrin-based ones. Here, we report the synthesis and characterisation of such directly linked chlorin dimers.

Porphyrin dimers are usually prepared by oxidative coupling using Ag(I),<sup>10</sup> DDQ/Sc(OTf)<sub>3</sub><sup>11</sup> and PIFA,<sup>12,13</sup> or electrochemical means,<sup>14,15</sup> affording varying amounts of higher oligomers in the process. These reactions were expected to be challenging for chlorins, as the partially reduced pyrrole makes the macrocycle asymmetric, and the above methods could yield multiple regioisomeric products. Furthermore, hydroporphyrins are easier to oxidise than porphyrins,<sup>16</sup> making them susceptible to side-reactions under strongly oxidising conditions. There is only one known example of a directly *meso-meso*-linked chlorin dimer, prepared by the treatment of Zn(II)-5,15-bis-*p*-tolylchlorin with PIFA.<sup>17</sup> In our hands, exposure of sparsely substituted chlorins (e.g. the Zn-chelate of **Chl10<sup>Mes</sup>**, Scheme 1) to these conditions resulted in extensive decomposition. Therefore, an alternative strategy was sought. Additionally, as peripheral substitution has a substantial impact on chlorin photophysics,<sup>18-20</sup> selective access to regioisomers was deemed imperative.

Metal-mediated reactions, e.g. Suzuki couplings<sup>21</sup> or reductive eliminations from peripheral transition metals<sup>22</sup> have been described for porphyrins, and are regioselective. We chose to forge the chlorin-chlorin link with Suzuki reaction, which enables the regioselective coupling of non-identical chlorins. The reaction is sufficiently mild to be compatible with sensitive tetrapyrroles. Synthetic chlorins with halogens in multiple positions are available (2, 3, 7, 8, 12, 13, 15),<sup>9</sup> thus this method is suitable for the synthesis of a large number of regioisomeric

Directly linked hydroporphyrin (chlorin) dimers were accessed regioselectively from bromochlorins. Versatile 15-borylated chlorins were prepared in excellent yield via Miyaura borylation. Suzuki coupling yielded *meso-meso*-linked homo- and heterodimers, and *meso-β*-linked dimers. The photophysical and electrochemical properties of the dimers are reported.

dimers. To minimise the possibility that additional substituents mask the properties arising from dimerisation, we used chlorins lacking peripheral substituents with the exception of the *gem*-dimethyl groups that lock-in the hydroporphyrin redox state.<sup>9,23</sup> Asymmetric dimers and a dimer with a reactive handle (a NO<sub>2</sub>-group) for further manipulation were prepared from 10-aryl-chlorins (Scheme 1).



Scheme 1.

Chlorins were selectively 15-brominated with NBS under acidic conditions (Scheme 1).<sup>24</sup> Small amounts (up to 14%) of the 15,20-dibrominated chlorins were also isolated. The assignment is based on literature precedent,<sup>24</sup> NMR-spectroscopy and X-ray crystallography (Scheme 1 and ESI). The formation of 15,20-dibromochlorins further confirms Lindsey's observation that acidic conditions selectively deactivate the β-positions against electrophilic attack.<sup>24</sup> Pd-catalysed borylation<sup>25,26</sup> with HBpin of **Chl15<sup>Br</sup>** and **Chl10<sup>Ph15Br</sup>** yielded **Chl15<sup>Bpin</sup>** and **Chl10<sup>Ph15Bpin</sup>** in excellent yield. B<sub>2</sub>pin<sub>2</sub> as the boron source did not give any borylated chlorin. The

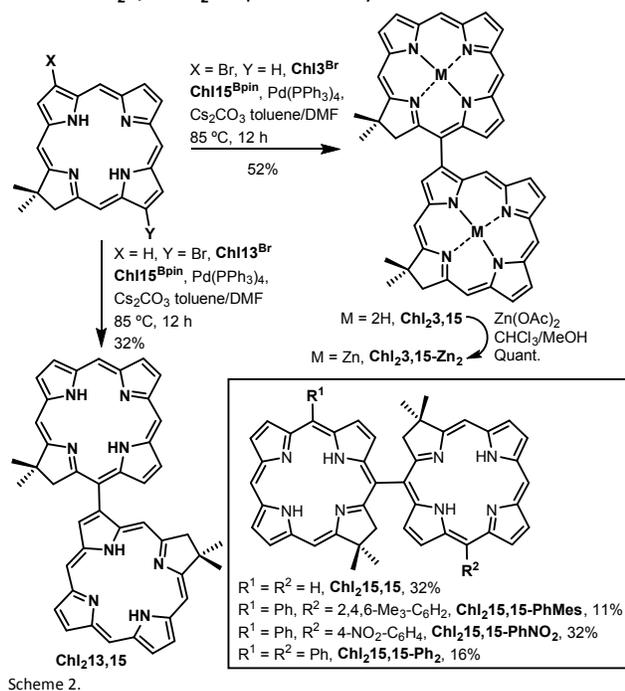
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reaction was scalable, and over 100 mg of **Chl10<sup>Ph</sup>15<sup>Bpin</sup>** was prepared in a single batch without erosion of the yield. Given the versatility of aryl boronic acids for the formation of C-C and C-heteroatom bonds,<sup>27-29</sup> we expect these compounds to become useful additions to the tetrapyrrole toolbox. Borylation of **Chl3<sup>Br</sup>** (Ref.<sup>30</sup>) and **Chl13<sup>Br</sup>** (Ref.<sup>31</sup>) were unsuccessful, and only dehalogenated **Chl** was returned. Hartwig borylation<sup>32</sup> of **Chl10<sup>Mes</sup>** was equally fruitless under a variety of conditions.

The Suzuki coupling of the  $\beta$ -Br-chlorins with **Chl15<sup>Bpin</sup>** proceeded smoothly to furnish **Chl2,3,15** and **Chl2,13,15** in 52% and 32% yield, respectively (Scheme 2). Attempts to perform the reaction on the Zn-chelate of **Chl3<sup>Br</sup>** did not afford a dimer. Treatment of **Chl2,3,15** with an excess of Zn(OAc)<sub>2</sub> gave bis-Zn-chelate **Chl2,3,15-Zn<sub>2</sub>** in quantitative yield.

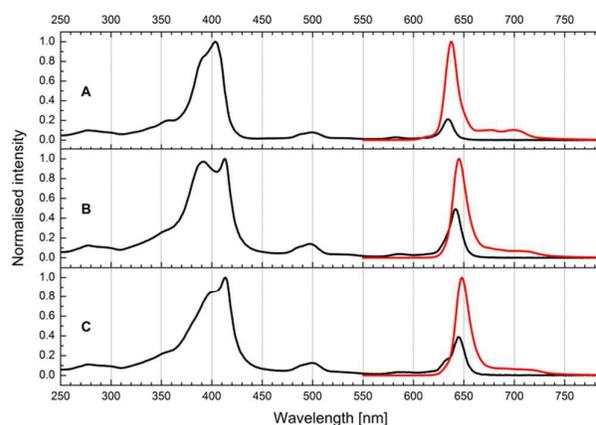


The synthesis of *meso-meso* linked dimers was more challenging, presumably due to the increased steric congestion around the new C-C-bond. After some optimisation, we found that the reaction proceeded at increased concentration; changing the Pd-source or the base so far has not resulted in improvements. This way unsubstituted **Chl2,15,15**, and diaryl **Chl2,15<sup>Ph</sup>,15<sup>Mes</sup>** and **Chl2,15<sup>Ph</sup>,15<sup>PhNO<sub>2</sub></sup>** could be synthesised, although yields remained modest. The major side-products were dehalogenated and deborylated chlorins, which were easily recovered from the reaction mixture. The homodimer **Chl2,15<sup>Ph</sup>,15<sup>Ph</sup>**, formed in the self-coupling of **Chl2,10<sup>Ph</sup>15<sup>Bpin</sup>**, was also isolated. The homo- and heterodimers were separable by standard silica gel column chromatography.

The <sup>1</sup>H NMR-spectra of the dimers were in accord with the proposed structures. Specifically, the chemical shifts of *CH<sub>3</sub>* and *CH<sub>2</sub>* of the *meso-meso* dimer **Chl2,15,15-H<sub>2</sub>** were at 1.82–1.85 ppm and 3.80–3.82 ppm, experiencing significant shielding compared to the protons in its monomeric analogue

**Chl15<sup>Ph</sup>** (2.06 and 4.84 ppm, respectively<sup>33</sup>) due to the ring current. For the  $\beta$ -*meso* dimers the effect was smaller, and more pronounced for the *meso*-functionalized chlorin than for the  $\beta$ -bound one.

Directly linked tetrapyrrole dimers are axially chiral. Enantiomer separation using chiral HPLC has been reported for *meso-meso*-linked porphyrin dimers.<sup>34</sup> We used variable temperature NMR to evaluate if the atropisomers of **Chl2,15,15** and **Chl2,3,15** interconvert upon heating. It was expected, and shown, that **Chl2,15,15** would have similar stability to its porphyrin analogues (Figures S1 and S2<sup>†</sup>). The  $\beta$ -*meso*-linked **Chl2,3,15** is less sterically hindered, and rotation around the C-C-bond might become possible at slightly elevated temperatures. However, the signals of the diastereotopic *CH<sub>2</sub>*-protons at  $\delta$  = 4.20 and 4.32 ppm (*J* = 17.6 Hz) did not coalesce upon heating the samples to 90 °C ( $\delta$  = 4.18 and 4.31 ppm, *J* = 17.6 Hz,  $\Delta\delta$  = –0.02 ppm for both signals). Only very small changes, readily explained by worsened shimming, were seen in signal quality in this temperature range. Thus, once separated, the enantiomers would resist racemisation. Furthermore, the lack of enantiomer interconversion at the coupling temperature suggests that the asymmetric synthesis of dimers may become possible. While not yet demonstrated for tetrapyrroles, axially chiral biaryls have been prepared enantioselectively via Suzuki reaction using chiral ligands.<sup>29</sup>



**Figure 1.** Normalised absorption and emission spectra of A) reference compound **Chl10<sup>Ph</sup>**, and dimers B) **Chl2,13,15** and C) **Chl2,15,15** in CH<sub>2</sub>Cl<sub>2</sub>. Emissions were recorded with Soret band excitation.

The absorption spectra of the dimers were recorded in CH<sub>2</sub>Cl<sub>2</sub> (Figure 1, Table 1). The UV-visible absorption spectra of the dimers were similar to those of monomeric chlorins, with small but significant differences. The Q-bands were red-shifted by ~8–10 nm compared to **Chl**, which is consistent with the effect of introducing one more aryl group in the 15-position. The Soret bands of the  $\beta$ -*meso* linked 3,15- and 13,15-dimers (**Chl2,3,15**, **Chl2,13,15**) were split (391/392 nm and 413 nm, respectively); interestingly, the split was smaller for **Chl2,15,15**. The ratio of B- and Q-bands is lower in the dimers than in the monomers (2.0–2.9 vs 2.4–5.6), and lower in the  $\beta$ -*meso* dimers (2.0–2.1) than in the *meso-meso* dimers (2.6–2.9). Metallation with Zn(II)- or Pd(II)-salts resulted in blue-shifted

Q-bands. The fluorescence quantum yields of the dimers were comparable to those of sparsely substituted chlorins (Table 1).

Chlorins are extensively used for photodynamic cancer therapy and photodynamic killing of bacteria. For all these applications, light-mediated singlet oxygen sensitisation via the chlorin triplet level is important. To investigate how dimerisation affects the triplet of the macrocycles, the Pd-chelates of **Chl<sub>2</sub>15,15** and model compound **Chl15<sup>Ph</sup>** (Ref<sup>35</sup>) were prepared by heating a mixture of the free-base macrocycle and a large excess of Pd(acac)<sub>2</sub> in pyridine in a microwave reactor.<sup>36</sup> The phosphorescence spectra of the Pd-complexes were recorded upon excitation at the Soret band at 77 K using time-resolved emission spectroscopy (Figures S3 and S4<sup>†</sup>). Phosphorescence emission was observed at 774 nm and 762 nm for **Chl<sub>2</sub>15,15-Pd<sub>2</sub>** and model **Chl15<sup>Ph</sup>-Pd**, indicating that the effect the dimerization has on the triplet is small. A triplet lifetime of 359 μs was measured for **Chl<sub>2</sub>15,15-Pd<sub>2</sub>**, slightly shorter than the 406 μs obtained for **Chl15<sup>Ph</sup>-Pd**.

Table 1. Photophysical properties of selected dimers and reference compounds.<sup>a</sup>

Compound	$\lambda_{\text{Soret}}, \lambda_{\text{Q}}$	$I_{\text{B}}/I_{\text{Q}}$	$\lambda_{\text{em}} (\lambda_{\text{exc}})$	$\Phi^{\text{c}}$
<b>Chl<sub>2</sub>3,15</b>	391, 413, 642	2.1	646	0.19
<b>Chl<sub>2</sub>13,15</b>	392, 413, 642	2.0	645	0.16
<b>Chl<sub>2</sub>15,15</b>	413, 645	2.6	648	0.255
<b>Chl<sub>2</sub>3,15-Zn<sub>2</sub></b>	401, 615	2.6	619	0.11
<b>Chl<sub>2</sub>15<sup>Ph</sup>,15<sup>Mes</sup></b>	410, 421, 648	2.6	652	0.39
<b>Chl<sub>2</sub>15<sup>Ph</sup>,15<sup>Ph</sup></b>	411, 421, 649	2.9	653	0.28
<b>Chl</b>	398, 636 <sup>d</sup>	2.4 <sup>d</sup>	636 <sup>d</sup>	0.19 <sup>d</sup>
<b>Chl15<sup>Ph</sup>-Pd<sup>b</sup></b>	391, 587	1.9	n.d.	n.d.
<b>Chl<sub>2</sub>15,15-Pd<sub>2</sub><sup>b</sup></b>	401, 601	1.5	n.d.	n.d.

<sup>a</sup> In CH<sub>2</sub>Cl<sub>2</sub>. <sup>b</sup> In THF. <sup>c</sup> Using meso-tetraphenylporphyrin in toluene as standard. <sup>d</sup> From reference<sup>33</sup>, measured in toluene.

Cyclic voltammetry showed that dimerisation had little effect on the first oxidation and reduction potentials, and thus the electrochemical HOMO-LUMO gap (Table 2 and Figures S5–S8<sup>†</sup>). Two reversible reduction and oxidation peaks were seen for free base dimers, as opposed to only one for **Chl15<sup>Ph</sup>**.

Table 2. Cyclic voltammetry data for chlorin dimers and the unsubstituted chlorin reference compound. Measured for 1 mM solutions of the analyte in CH<sub>2</sub>Cl<sub>2</sub> (0.1 M NBu<sub>4</sub>PF<sub>6</sub>), glassy C-electrode,  $v = 100$  mV/s. All potentials are given versus Fc<sup>+/0</sup>.

Compound	Reduction E <sub>pc</sub> [V]			Oxidation E <sub>pa</sub> [V]		
<b>Chl15<sup>Ph</sup></b>	-2.18	-1.73 <sup>f</sup>		0.40		1.00
<b>Chl<sub>2</sub>3,15-Zn<sub>2</sub></b>	-2.28	-2.02		0.22		1.11
<b>Chl<sub>2</sub>3,15-H<sub>2</sub></b>	-2.29	-1.77 <sup>f</sup>	-1.74 <sup>f</sup>	0.40	0.49	1.03
<b>Chl<sub>2</sub>15,15-H<sub>2</sub></b>	-2.24	-1.83 <sup>f</sup>	-1.70 <sup>f</sup>	0.43	0.55	1.09

<sup>f</sup> Peak is reversible, reported value corresponds to  $E_{1/2} = (E_{\text{pa}} + E_{\text{pc}})/2$ .

In conclusion, directly 3,15-, 13,15- and 15,15-linked chlorin homodimers and 15,15-linked heterodimers were synthesised regioselectively. The dimers had red-shifted absorption and emission spectra compared to monomeric chlorins. In addition to the substitution pattern and central metal, dimer properties were dependent on the position of the linker, with subtle differences noted even between the 3,15- and 13,15-isomers. Current efforts are directed towards the synthesis of  $\beta,\beta$ -

linked regioisomers, and the preparation of enantiomerically pure bis-chlorins.

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† See the Electronic Supporting Information.

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