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Photooxidation of N-Confused Porphyrin: A Route to N-Confused Biliverdin Analogues

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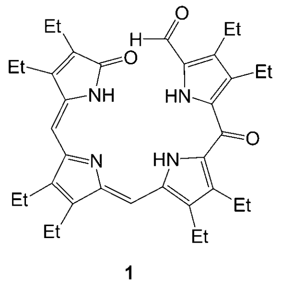
Carbaporphyrinoids have been recognized as a family of macrocyclic compounds used as a versatile platform for organometallic chemistry.[1] However, no linear analogue of these compounds capable of C−M bond formation has been reported so far.

Degradation of tetrapyrrolic macrocycles was widely investigated in the context of heme breakdown and the oxidative chlorophyll ring opening observed in vivo.[2] Model studies involved chemical oxidation with various reagents (e.g., Ce^{IV} or Tl^{III} salts),[3] as well as coupled oxidation of porphyrin complexes of redox-active metals.[4] The photooxidation process of metalloporphyrins leading to linear oligopyrrolic products was also studied.[5] Fuhrhop et al. established the structure of the final product **1** of magnesium octaethylporphyrin degradation.[6]

The mechanism of photooxidation of tetraphenylporphyrin complexes (TPP)M was investigated by several groups.[7] A proper structure (**2**) of the final product of this process was deduced from detailed NMR spectroscopic and mass spectrometric studies by Cavaleiro et al.[8]



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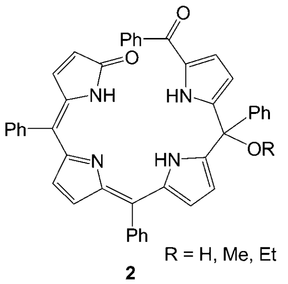

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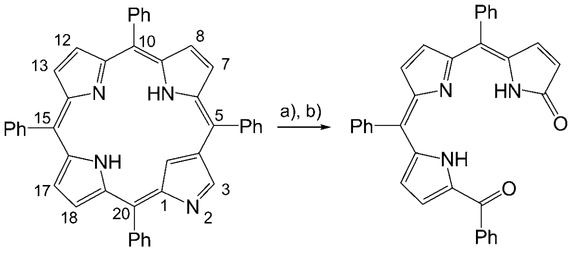
As compared to regular porphyrins, relative little study was devoted to the degradation of their N-confused isomers.[9] Initially, the frequently observed decomposition of these macrocycles during metallation process led Furuta et al. to investigate the nature of the degradation product.[10] They found that in the course of copper(II) insertion in the presence of air N-confused tetraphenylporphyrin **3** underwent an oxidative transformation. From the reaction mixture, copper(II) complex of a linear tripyrrole **4** was isolated in 34 % yield, and no other products were identified (Scheme 1).



3 **4**

Scheme 1. Degradation of the N-confused tetraphenylporphyrin. a) $Cu(OAc)_2$, O_2, toluene; b) H^+.

Further studies on the regioselectivity of the process showed that the N-confused pyrrole was cleaved together with the 5-aryl substituent, which proved the primary attack of dioxygen at the C(1)−C(20) bond.[10] This was in contrast to the findings of Pawlicki et al. who observed that the copper(II) complex of pyrrole-appended O-confused tetraaryloxaporphyrin reacted with dioxygen, yielding both possible tripyrrolic degradation products (resulting from attack on either the C(1)−C(20) or C(4)−C(5) bond) in 7:3 ratio, along with the product of oxygen atom insertion into a copper–carbon bond.[11]

Linear tetrapyrroles were also obtained through a rational synthetic approach.[12] Some of them were used as ligands,

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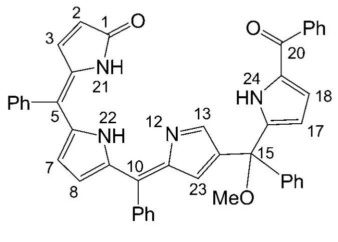
exhibiting interesting, and sometimes quite unpredictable, coordination chemistry.[13]

Herein, we present the first example of a linear tetrapyrrolic product obtained in the course of photoxidation of the N-confused tetraphenylporphyrin anion and its ability to accommodate two metal cations into the coordination core. When a solution of 2-aza-21-carba-5,10,15,20-tetraphenylporphyrin (**3**) in chloroform was photooxygenated for 5 h, only trace amounts of decomposition products could be detected in the ^{1}H NMR spectrum. Under these conditions, however, 5,10,15,20-tetraphenylporphyrin remains completely intact. It was previously shown that porphyrin dianions are more prone for dioxygen attack than porphyrins themselves due to increased electron density in the macrocycle.[6,8] We therefore decided to perform the photooxidation of N-confused porphyrin under basic conditions. Sodium methoxide dissolved in methanol was added to a solution of **3** in tetrahydrofuran and a stream of air was passed through the solution, which was irradiated with visible light. Its deep green color gradually turned brown and the ^{1}H NMR spectrum of reaction mixture taken after 1 h showed a large quantity of degradation products. After aqueous workup, chromatographic separation on a basic alumina column was performed. Elution with dichloromethane yielded the unreacted substrate, which was followed by fractions containing tripyrrolic products (tripyrrinone **4** and its isomer), and a red-violet band that was separated and evaporated to dryness, yielding compound **5**.



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The structure of product **5** was established by using NMR (^{1}H, ^{13}C) spectroscopy and mass spectrometry. The ^{1}H NMR spectrum of **5** is shown in Figure 1A. Seven resonances of equal intensity in the $\delta = 6–7$ ppm region can be attributed to 7 inequivalent pyrrolic protons of a linear N-confused tetrapyrrole. These peaks are accompanied by three broad signals in the low-field part of the spectrum ($\delta = 9.53$, 9.85, and 11.92 ppm) assigned to the inner NH protons. The resonance at $\delta = 3.19$ ppm, which is 3H in intensity, confirms the presence of the methoxy substituent in **5**. The remaining resonances can be found in the $\delta = 7–8$ ppm region. The overall picture resembles the spectrum obtained for compound **2** formed in the course of photooxidation of TPP dianion in the presence of methoxide.

The analysis of 2D NMR spectra (COSY, NOESY, HMQC, HMBC) allowed complete assignment and provided additional structural information. In particular, the H(13) signal was found at $\delta = 7.25$ ppm through its correlation with H(23) proton at $\delta = 6.44$ ppm ($J = 1.1$ Hz), confirming the presence of inverted pyrrole in compound **5**. Interestingly, this crucial fragment did not appear to be a terminal unit, as expected from the previous investigations on the oxidative degradation of confused porphyrins.[10,11] The C(15) resonance was found at $\delta = 79.4$ ppm in the ^{13}C NMR spectrum, as expected for an sp^3 carbon atom linked to the methoxy group. A specific contact found in the NOE map of H(23) and the methoxy substituent further confirmed the inversion of the N-confused pyrrole.

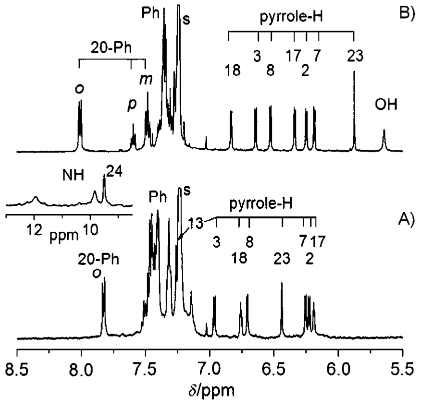
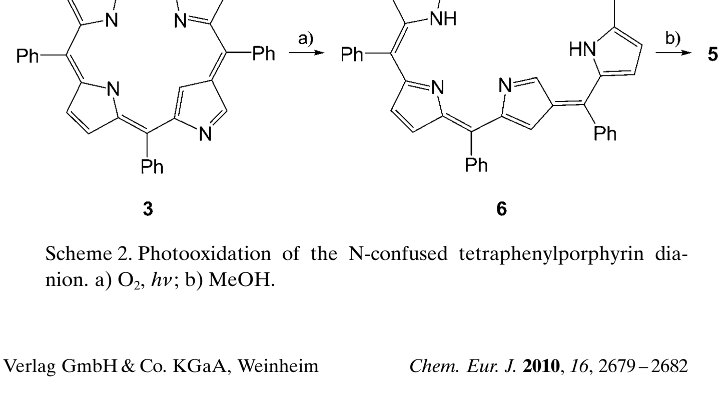


Figure 1. ^{1}H NMR spectra (500 MHz, CDCl$_3$, 300 K) of **5** (A) and palladium complex **7** (B). Assignments: pyrrole-H = pyrrole resonances; 20-Ph = signals of phenyl substituent on C(20); Ph = remaining phenyl signals; s = residual solvent peak. Inset in A shows the NH peaks of **5**.

In a full analogy to the photooxidation of the TPP dianion,[8] a mechanism can be proposed, including the cleavage of the C(α)–C(*meso*) bond by a dioxygen molecule, followed by an addition of methanol to the primary product **6** (Scheme 2). Although compound **6** has not been directly isolated, we found that it can be stabilized through coordination with palladium(II) (see below). Consequently, a structure similar to compound **2** was deduced for the final product **5**, albeit exhibiting the unique pyrrole with the N(12) and C(13) atoms located in the inner part of the molecule. Such an orientation of the N-confused ring was proposed by Smith et al. for one of the observed two isomers of β-octa-substituted N-confused biliverdin.[12a]

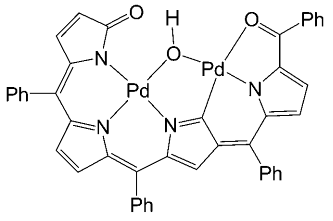


Scheme 2. Photooxidation of the N-confused tetraphenylporphyrin dianion. a) O$_2$, *hν*; b) MeOH.

The mass spectrum of **5** (ESI) exhibited a peak at m/z 647.24463 that corresponds to the proposed structure from which the *meso*-methoxy substituent was removed ($[M-\mathrm{OMe}]^+$).

The symmetry of the starting macrocycle (C_s) is lower than in the case of the TPP dianion. In principle, each one of eight inequivalent C(α)–C(*meso*) bonds can be broken, leading to eight possible open-chain isomeric products. Compound **5** results from cleavage of the C(10)–C(11) bond in the original macrocycle. At present we have determined that **5** is the principal tetrapyrrolic product of the photooxygenation of the N-confused porphyrin dianion. In fact the alleged regioselectivity could be explained by a limited stability of another cleavage products, as demonstrated by a tetrapyrrolic precursor(s) of compound **4**. Apparently these tetrapyrroles formed by bond cleavage at C(5) or C(20) *meso* positions are easily converted to a tripyrrinone **4** by one more molecule of dioxygen, which attacks another C_α–C_{meso} bond leading to the loss of an inverted pyrrole.[10] On the other hand, we found that when compound **5** was subjected to photooxidation conditions, decomposition was observed within 15 min. Therefore, the short reaction time is a prerequisite to isolate **5** among the photodegradation products of N-confused porphyrin. Control experiments showed that both light and oxygen are necessary for the observed reactivity.

Compound **5**, a biliverdin analogue with an inverted pyrrole, can be considered as a potential tetrapyrrolic ligand prearranged to place a carbon donor in the coordination core. Its quick reaction with palladium(II) acetate in methanol (10 min at room temperature) resulted in a blue solution, from which bimetallic complex **7** was isolated.



7

The ^{1}H NMR spectrum of compound **7** is shown in Figure 1B. Seven pyrrolic resonances ($\delta = 5.88$–6.83 ppm) are accompanied by phenyl signals ($\delta = 7.25$–8.00 ppm) and an exchangeable peak at $\delta = 5.64$ ppm, which was attributed to the –OH bridging group. Low-field NH signals, and H(13) are absent from this spectrum as a result of metal coordination. The disappearance of methoxy resonance, characteristic for compound **5**, indicates the ligand rearrangement upon coordination of palladium(II) ions. In the mass spectrum of **7**, the apparent molecular peak $[M+\mathrm{H}]^+$ was found at m/z 875.0325. This value and the characteristic isotopic pattern prove the presence of two palladium ions in compound **7**.

Single crystals of bimetallic complex were obtained by a slow diffusion of *n*-hexane into a solution of **7** in chloroform, and its structure was determined by X-ray crystallography (Figure 2). The complex **7**, which crystallized as the $\mathrm{CHCl_3}$ solvate, contains two palladium(II) ions coordinated by a trianion derived from compound **6** (formed from **5** by the loss of methanol). Six donating atoms are provided by the linear oligopyrrole: three nitrogen atoms of regular pyrroles, N(12) and C(13) of the inverted one, which serves as a bridging unit, and, additionally, the carbonyl oxygen atom from C(20). Two metal ions are also bridged by a hydroxyl anion. Their coordination geometry can be described as square planar, albeit with a marked distortion seen for Pd(2). This effect can be attributed to weak coordination of O(20), which results in a long Pd–O(20) bond (2.174(8) Å) and O(25)-Pd(2)-O(20) bond angle equal to 103.9(3)°. The overall structure of the coordinated tetrapyrrolic fragment is nearly planar, albeit with significant out-of-plane displacement of the terminal pyrrolone unit (Figure 2). Palladium–nitrogen bond lengths (Pd(1)–N(21) 2.020(10), Pd(1)–N(22) 2.010(10), Pd(1)–N(12) 2.012(9), Pd(2)–N(24) 1.967(9) Å) are in the range found in Pd$^{\mathrm{II}}$ complexes with linear oligopyrroles,[13f,14] whereas the Pd(2)–C(14) distance (1.903(12) Å) is among the shortest observed for coordinated pyrrole unit of N-confused porphyrins and expanded porphyrins.[15]

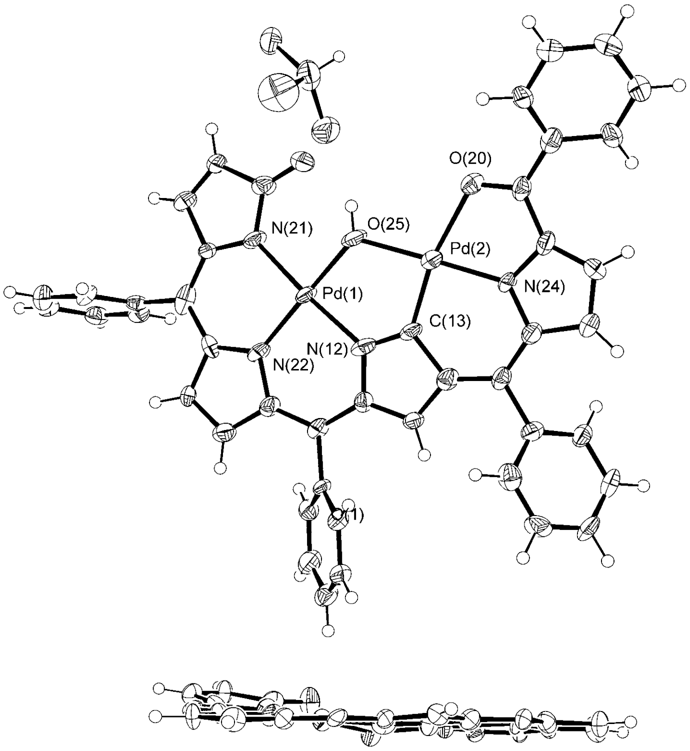


Figure 2. An ORTEP plot of the crystal structure of dipalladium complex **7**·$\mathrm{CHCl_3}$ (thermal elipsoids are drawn at the 30% probability level). Bottom: side view of the molecule ($\mathrm{CHCl_3}$ and phenyl substituents omitted).

Although binucleating linear tetrapyrroles have been described in the literature,[13d,e,16] complex **7** can be regarded as an unprecedented example of a tetrapyrrole coordinating two Pd^{II} ions. An identical metal-to-ligand stoichiometry was previously found in $Pd_4(OEB)_2$, in which, however, two palladium(II) octaethylbilindione (OEB) units were joined through a $(Pd^{I}_{2})^{2+}$ fragment.[17] The double coordination of inverted pyrrole is also a unique feature of structure **7**. Although pyrrole served as bridging unit in hexa- and heptaphyrin complexes, its coordination mode was different than that seen in **7**.[15d,18]

In conclusion, photooxidation of an N-confused porphyrin dianion provides a novel N-confused biliverdin analogue that can act as a binucleating ligand with two types of coordination surroundings: (NNNO) and (CNOO). This specific feature opens the route to the construction of heterobimetallic systems based on acyclic carbaporphyrin derivatives.

Acknowledgements

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Keywords: biliverdins · palladium · photooxidation · porphyrinoids

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