

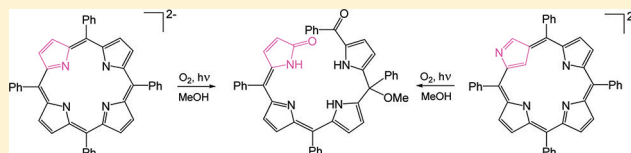
# Common Origin, Common Fate: Regular Porphyrin and N-Confused Porphyrin Yield an Identical Tetrapyrrolic Degradation Product

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Supporting Information

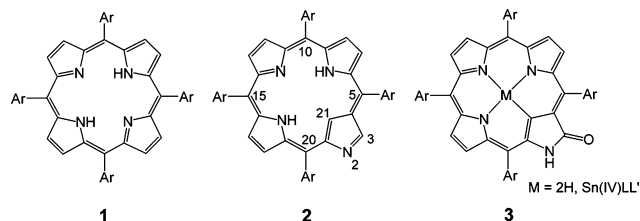
**ABSTRACT:** The formation of an identical linear tetrapyrrole observed in the course of photooxidation of *meso*-tetraarylporphyrin and its N-confused isomer can be explained as a result of 1,2- and 1,3-dioxygen addition, respectively, as substantiated by DFT calculations.



## INTRODUCTION

Since the discovery in 1994 that the acid-catalyzed Rothmund condensation of pyrrole and aryl aldehyde yields both regular tetraarylporphyrin (**1**, Chart 1) and its N-confused isomer **2**,<sup>1</sup> the

Chart 1

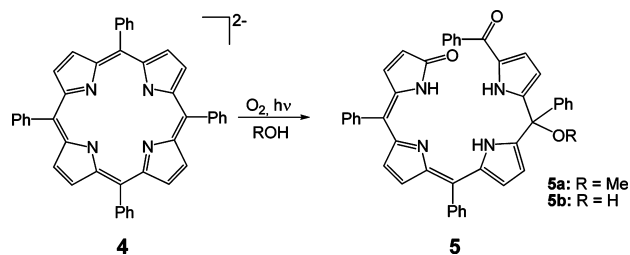


chemistry of the latter macrocycle has developed considerably.<sup>2</sup> In particular, the specific reactivity of the 3-carbon of N-confused pyrrole has been exemplified by the formation of 3-oxo-2-aza-21-carbachlorin derivatives **3**, containing a lactam functionality,<sup>3</sup> synthesis of a 3,3'-linked dimer,<sup>4</sup> substitution with pyrrole,<sup>5</sup> and fusion of pyrrole rings preceded by halogenation of 21- and 3-carbon atoms.<sup>6</sup>

The oxidative degradation of tetrapyrrolic macrocycles was extensively investigated in the context of heme and chlorophyll catabolism.<sup>7</sup> The studies on mechanisms of dioxygen and/or light-driven ring-opening reactions of porphyrins and their complexes are also of special importance because they are widely used as oxidation catalysts and photosensitizers.<sup>8,9</sup> Photooxidation of zinc, magnesium, cadmium, and thallium(I) complexes of tetraphenylporphyrin as well as the porphyrin dianion (TPP<sup>2-</sup>, **4**) was previously examined; the final product **5** bearing an -OR substituent in the 15-position results from dioxygen attack on the C<sub>meso</sub>-C<sub>β</sub> bond, followed by the addition of water or alcohol (Scheme 1).<sup>10</sup> As proved by isotope labeling studies, both carbonyl oxygen atoms are derived from a single molecule of O<sub>2</sub>.<sup>10b,c</sup> An analogous mechanism of ring-opening, based on 1,2-cycloaddition of dioxygen, was suggested for other tetrapyrroles, such as octaethylporphyrin,<sup>11</sup> and corroles.<sup>12</sup>

Recently, we have shown that photooxidation of the dianion of N-confused tetraphenylporphyrin led to a mixture of

Scheme 1



degradation products, from which a linear N-confused tetrapyrrole could be isolated. Upon metalation with palladium (II), this compound converts into an N-confused biliverdin analogue that can act as a binucleating ligand with two types of coordination surroundings: (NNNO) and (CNOO).<sup>13</sup> In this contribution, we concentrate on further exploration of photooxidation products, which led to the identification of the unexpected but mechanistically very significant tetrapyrrolic compound **5a**, typically formed in the course of TPP<sup>2-</sup> degradation. Thus, we have shown that both 1,2-dioxygen addition (common) and 1,3-dioxygen addition (unprecedented for porphyrinoids) are of importance in N-confused porphyrin cleavage.

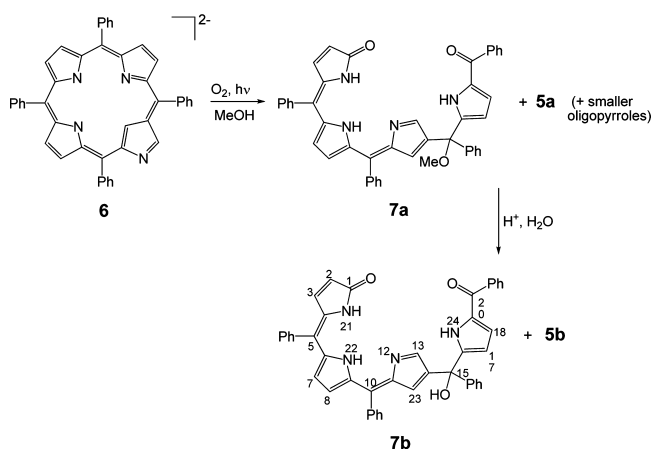
## RESULTS AND DISCUSSION

**Degradation of NCTPP<sup>2-</sup>.** N-confused tetraphenylporphyrin dianion (NCTPP<sup>2-</sup>, **6**) was photooxidized under standard conditions as described previously.<sup>13</sup> Originally, after chromatographic purification, **5a** was present in the fraction containing its N-confused analog **7a** (the amount of **5a** was estimated from <sup>1</sup>H NMR spectrum as 20–30% of **7a**) and was treated as an impurity, which could be removed by recrystallization. The effective chromatographic separation of the two tetrapyrroles required their conversion into hydroxylated analogues **5b** and **7b**, which exhibited more distinct R<sub>f</sub> values (Scheme 2).<sup>14</sup>

Received: July 21, 2011

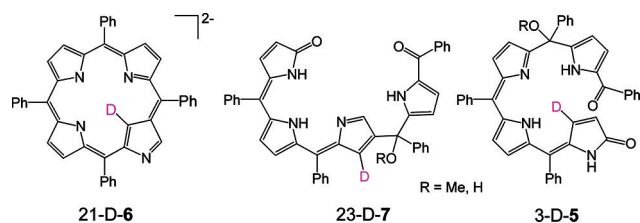
Published: October 26, 2011

## Scheme 2

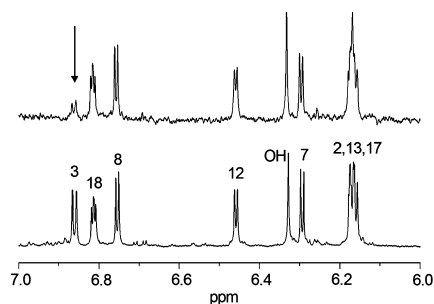


The starting NCTPP<sup>2-</sup> contained no traces of the TPP<sup>2-</sup> dianion as carefully proved by the <sup>1</sup>H NMR spectrum. Thus, compound **5a** was formed from the oxidation of N-confused porphyrin dianion **6**. However, to establish the undeniable origin of product **5a** and to give insight into the reaction mechanism, a selectively deuterated substrate, 21,22,24-D<sub>3</sub>-**2**, was prepared (<sup>1</sup>H NMR revealed ca. 80% deuteration of 21-C),<sup>1a</sup> and the corresponding dianion 21-D-**6** was subjected to a photooxidation procedure under the conditions used previously for **6**. The tetrapyrrolic degradation products were then converted into -OH derivatives (23-D-**7b** and 3-D-**5b**, Chart 2) and

## Chart 2



separated. Under the conditions of their preparation, the deuterium label was not exchanged as demonstrated by mass spectrometry.<sup>15</sup> The examination of <sup>1</sup>H NMR spectra allowed us to establish the fate of N-confused pyrrole. In particular, the analysis of the 6–7 ppm region of compound 3-D-**5b** (Figure 1)



**Figure 1.** Parts of <sup>1</sup>H NMR spectra of **5b** (lower trace) and deuterated 3-D-**5b** obtained from 21-D-**2**. Resonance assignments taken from ref 10d.

showed that a signal attributed to the 3-position exhibited a lowered intensity as compared to the rest of the pyrrolic

resonances because of the deuteration of the particular carbon atom. This observation served as an additional proof that compound **5a** was not formed from trace TPP<sup>2-</sup> (which would not be regioselectively pyrrole-deuterated under the conditions used for preparation of 21-D-**2**). The newly observed degradation product must then originate from dianion of N-confused porphyrin and is formed by an attachment of oxygen atoms to the 3- and 5-positions (1,3-cycloaddition) instead of the expected breaking of the C<sub>4</sub>–C<sub>5</sub> bond. Therefore, a mechanism different from those previously proposed for the degradation of tetrapyrrolic macrocycles should be responsible for the observed phenomenon.<sup>10–12</sup> One should remember, however, that the formation of compound **7** requires 1,2-cycloaddition to the C<sub>10</sub>–C<sub>11</sub> bond. Thus, two different mechanisms operating in one molecule could be detected.

In a control experiment, photooxidation of TPP dianion was performed under identical conditions. No traces of degradation product coming from dioxygen attachment to 3,5-carbons could be detected. Apparently, the presence of inverted pyrrole in dianion **3** seems to be a prerequisite of this kind of reactivity.

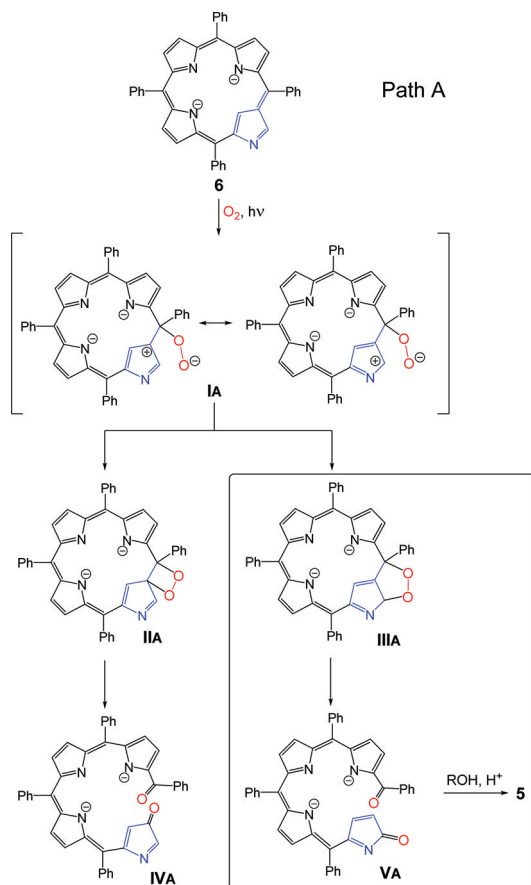
**DFT Studies.** DFT calculations were performed to substantiate the formation of unexpected degradation products. We limited the theoretical analysis to the reaction pathways leading from **6** to the identified tetrapyrrolic compounds. The proposed mechanism included the previous observations concerning the origin of carbonyl oxygen atoms.<sup>10b,c</sup>

Thus, two main paths resulting from dioxygen attack on C<sub>5</sub> (path A) or C<sub>10</sub> (path B) of dianion **6** were considered. The analysis of calculated electron density distribution and the coefficients of frontier molecular orbitals of starting NCTPP<sup>2-</sup> dianion showed no significant difference among meso positions that would be responsible for any kind of regioselectivity.

For a comparison, a degradation of TPP<sup>2-</sup> (**4**, path C) was also analyzed. For each path, five dianionic structures were optimized (**IA**–**VA**, **IB**–**VB**, and **IC**–**VC**, respectively) as well as starting dianions (**6** and **4**) and dioxygen molecule. The subsequent reaction steps included the following:

- 1) Dioxygen attack on the porphyrin dianion and its addition to a meso carbon, yielding a zwitterionic structure **I**. The attempted calculations assuming the addition to C<sub>α</sub> failed or eventually led to form **I**.
- 2) Ring closure by forming an O–C<sub>α</sub> (structure **II**) or O–C<sub>β</sub> bond (form **III**). Typically, a 4-membered (1,2-dioxetane) ring formation was considered a key step in the reaction of different olefins with singlet dioxygen.<sup>16</sup> However, a 5-membered (1,2-dioxolane) ring closure was also assumed in some oxygenation reactions,<sup>17</sup> and products containing this structural feature were isolated from reactions of unsaturated compounds with dioxygen.<sup>18</sup> Here, to explain the observed unusual degradation pathway, we postulate the structure of type **III**, which has not been previously discussed for the tetrapyrrolic substrates.
- 3) Breaking of O–O and C<sub>α</sub>–C<sub>meso</sub> bonds, leading to linear primary degradation ring-opened products **IV** (from **II**) and **V** (from **III**), which are converted to the observed final products, **5** or **7**, by addition of alcohol or water. These compounds were not included in DFT calculations. All structures of type **I**–**V** are isomeric, which makes possible the comparison of their energies.

Scheme 3



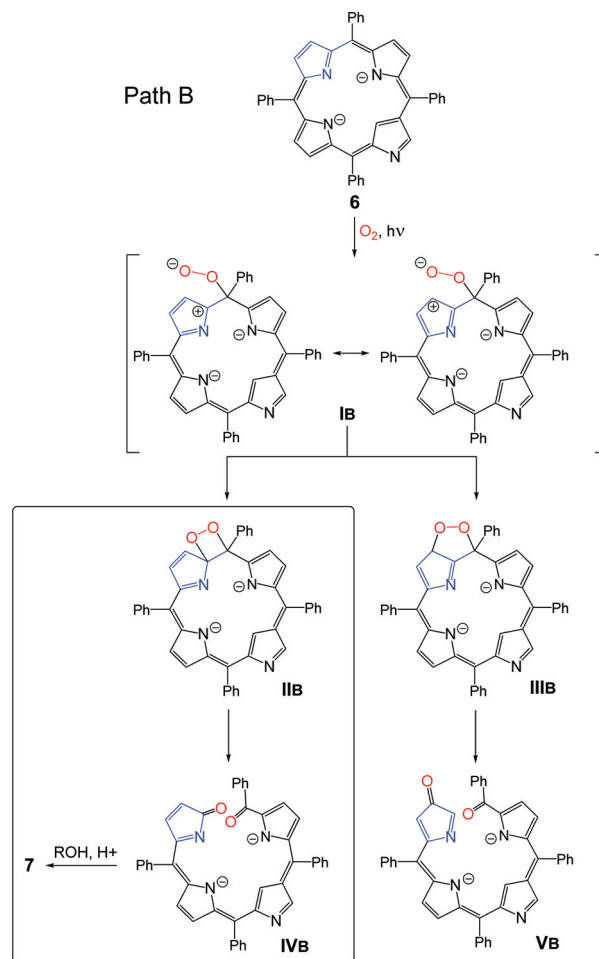
The three reaction paths are shown in Schemes 3–5. For structure I, two resonance structures differing by the bond and charge arrangement in the key pyrrole fragment are shown. Steps leading to products that are in fact observed (5 and 7) are indicated by frames.

The DFT optimized structures are shown in the Supporting Information, and the representative intermediates IIB and IIIA are presented in Figure 2. For structures of type I, the distances from terminal oxygen to C<sub>α</sub> and C<sub>β</sub> are comparable (in the range of 2.61–2.72 Å), and no preference for ring-closing direction is visible. The interruption of delocalization path in all structures results in a partial alternation of bond lengths. Oxygen–oxygen bond length in dianions I–III (1.49–1.55 Å) is comparable with the one observed in X-ray structures of peroxides, including cyclic ones.<sup>19,20</sup>

1,2-Dioxetane rings in structures II exhibit a typical, nonplanar (puckered) conformation.<sup>19</sup> For example, dihedral angles between two halves of 4-membered ring in IIB are in the range of 11–16.5°. For structures III, a half-chair conformation was found for 5-membered 1,2-dioxalane ring.<sup>20</sup> In IIIB, the angle between C(10)–C(11)–C(12) plane and the mean plane of C(10)–O–O–C(12) fragment equals 35°.

Compounds IVB and VB are characterized by different configurations of C<sub>meso</sub>–C<sub>α</sub> bonds as compared to the rest of open structures (Figures 2 and 5S–7S in the Supporting Information). In all cases, structures of type II or III with the broken O–O and C–C bonds were used as starting points for the calculations. In fact, the stereochemistry of these degradation products remains unknown because (if they are

Scheme 4



formed) they are readily converted to compounds 5 or 7, in which the 15-carbon atom has a sp<sup>3</sup> hybridization. The question of configuration becomes less important if we only compare the energy of structures belonging to one of the proposed degradation paths.

The relative energies calculated for the considered structures are given in Table 1. The energy diagrams for the three paths are shown in Figures 3–5.

When path A is taken into account, the formation of 5-membered 1,2-dioxolane ring should be preferred over 4-membered one (the energy of IIIA is 16.9 kcal/mol lower than IIA). The ring-opened product VA has also a considerably lower energy (by 12.9 kcal/mol) than IVA containing an N-confused pyrrole (its formation was not detected in our experiments).

In track B, IIIB is also more stable than IIB, but the energy difference is much smaller (3.7 kcal/mol). In the case of TPP<sup>2-</sup> degradation (path C), the energies of IIC and IIIC are practically identical. In both cases, form IV exhibits lower energy than V by ca. 6 kcal/mol. Again, only compounds 7 (formed from IVB) and 5 (resulting from the conversion of IVC) were isolated in our experiments. Certainly, it does not mean that other forms cannot be produced from the reaction with dioxygen, as some tetrapyrrolic products can be further converted to smaller ones (like tripyrrinone formed by the elimination of N-confused pyrrole).<sup>13,21</sup>

Scheme 5

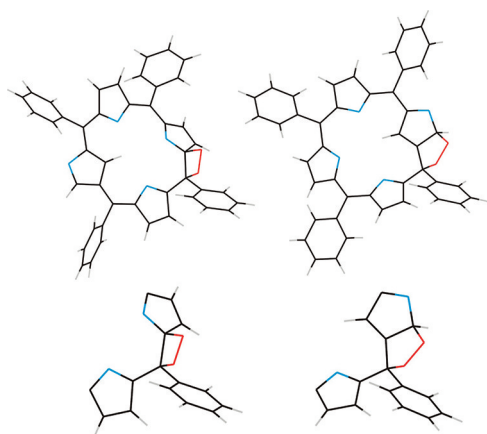
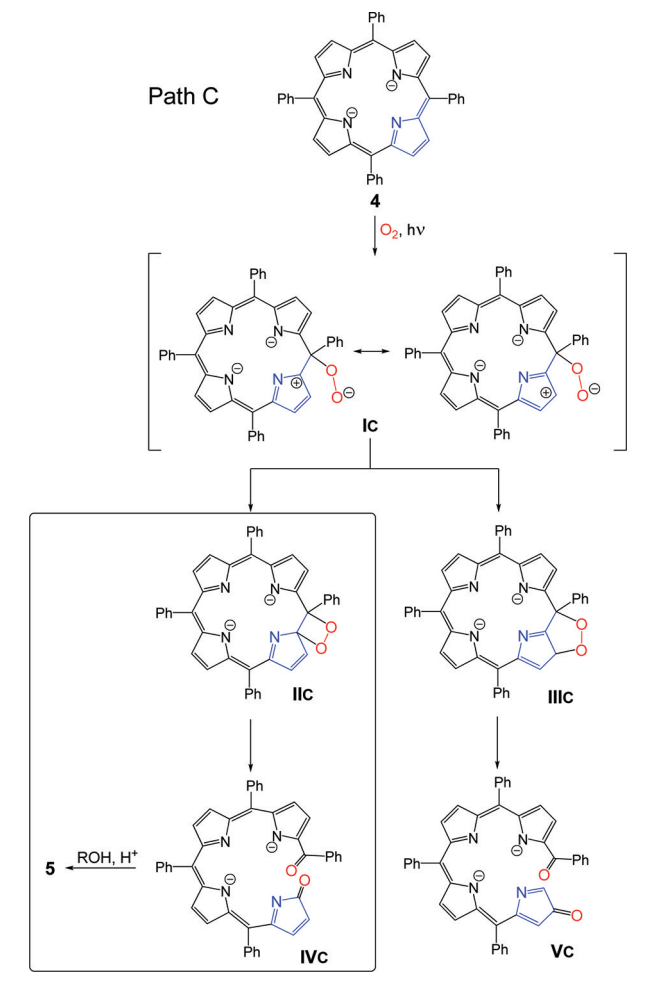


Figure 2. DFT calculated structures IIB (left) and IIIA (right), shown above the expansions of the key bipyrrolic fragments.

## CONCLUSION

The experimental study on the photooxidation of N-confused porphyrin dianion revealed two different mechanisms operating in one molecule. Apart from 1,2-dioxygen addition, which is common for tetrapyrrolic macrocycles, the rare 1,3-addition was also observed. DFT calculations used to analyze the degradation process show that the proposed reaction pathway, including the formation of 5-membered dioxolane ring, is reasonable and can

Table 1. DFT Calculated Energies (kcal/mol)<sup>a</sup>

	path A		path B		path C
6 + O <sub>2</sub>	0.0	6 + O <sub>2</sub>	0.0	4 + O <sub>2</sub>	0.0
IA	-21.2	IB	-21.0	IC	-20.7
IIA	-15.7	IIB	-20.7	IIC	-25.3
IIIA	-32.6	IIIB	-24.4	IIIC	-25.7
IVA	-122.1	IVB	-119.7	IVC	-141.8
VA	-135.0	VB	-113.5	VC	-136.3

<sup>a</sup>In each case, the energies were related to the substrates.

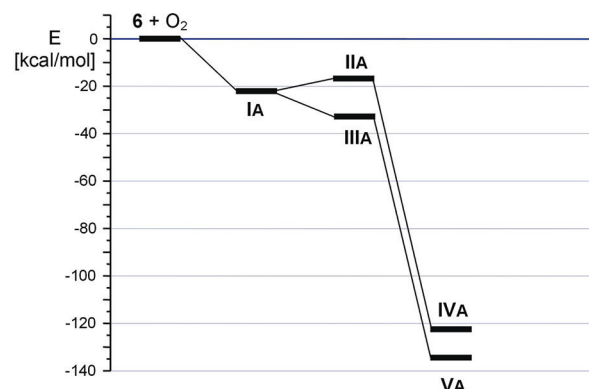


Figure 3. Energy diagram for path A.

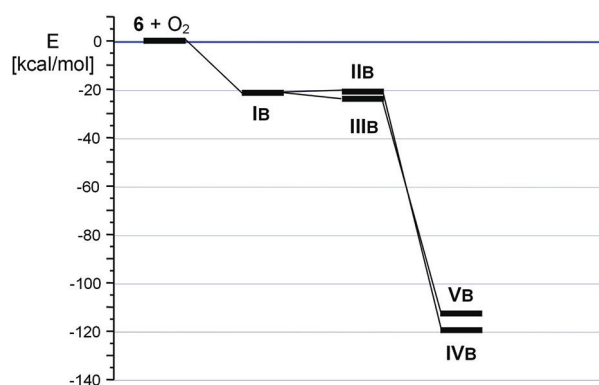


Figure 4. Energy diagram for path B.

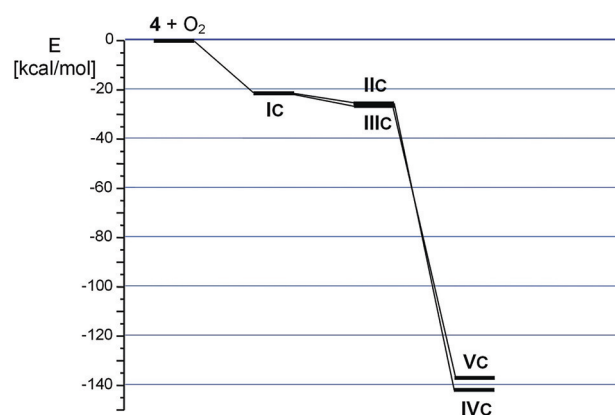


Figure 5. Energy diagram for path C.

be used to explain the formation of unexpected degradation product 5. This new example of a specific reactivity of the 3-position of NCTPP<sup>2-</sup> at the same time creates an interesting link between the chemistries of the two porphyrin isomers.



## EXPERIMENTAL SECTION

All  $^1\text{H}$  NMR (600 MHz) and  $^{13}\text{C}$  NMR (150 MHz) measurements were performed using a spectrometer equipped with a broadband inverse gradient probehead. The data were collected at 300 K, with the chemical shift referenced to a residual solvent signal ( $\text{CDCl}_3$ ,  $\delta$  ( $^1\text{H}$ ) = 7.26 ppm,  $\delta$  ( $^{13}\text{C}$ ) = 77.16 ppm). Mass spectra were measured using the electrospray technique.

DFT calculations were performed with the Gaussian 03 program.<sup>22</sup> Starting geometries were taken from molecular mechanics calculations. Geometry optimizations were carried out within unconstrained  $C_1$  symmetry. Becke's three-parameter exchange functional<sup>23</sup> with the gradient-corrected correlation formula of Lee, Yang, and Parr (B3LYP)<sup>24</sup> was used with the 6-31G\*\* basis set. The structures were found to have converged to a minimum on the potential energy surface; the resulting zero-point vibrational energies were included in the calculation of relative energies. The Cartesian coordinates for the calculated structures are given in the Supporting Information.

The preparation of N-confused tetraphenylporphyrin followed the described procedure.<sup>25</sup> The photooxidation of the respective dianion was performed as described previously.<sup>13</sup> To a solution of 2-aza-21-carba-5,10,15,20-tetraphenylporphyrin (100 mg, 0.16 mmol) in 200 mL of dry tetrahydrofuran, 0.23 g (4.3 mmol) of sodium methoxide in 2 mL of dry methanol was added. A stream of air was slowly bubbled through the resulting green solution, which was irradiated using 60 W tungsten lamp. No filters were applied, and the light source was located ca. 3 cm from the 500 mL round-bottom flask containing the reaction mixture. After 1 h, the resulting brown solution was diluted with dichloromethane (100 mL) and washed with water (3  $\times$  150 mL). The organic phase was dried with  $\text{MgSO}_4$  and evaporated to dryness, and the solid residue was chromatographed on a basic alumina column (activity III). The chromatographic separation of degradation products on basic alumina column (activity III) led to four major fractions, containing the unreacted substrate (38 mg), tripyrrinone dimethyl acetal (12 mg, 21%), tripyrrinone (16 mg, 30%), and a purple fraction that was identified as a mixture of **7a** (17 mg, 25%) and **5a** (4 mg, 6%). The dichloromethane solution of these tetrapyrroles was then shaken with 1 M aqueous HCl, washed three times with water, dried, and evaporated. The resulting mixture of compounds **7b** and **5b** was separated on a silica column. Dichloromethane containing 0.5% methanol eluted compound **5b**. Its spectral characteristics were in agreement with literature data.<sup>10d</sup> Increasing the methanol content to 2% yielded a fraction containing **7b**.

For **5b**:  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  75.0 ( $C_{15}$ ), 109.9 ( $C_{17}$ ), 111.8 ( $C_{13}$ ), 119.8 ( $C_{18}$ ), 121.3 ( $C_5$ ), 124.4 ( $C_2$ ), 125.2 ( $C_{12}$ ), 126.0 ( $C_7$ ), 127.0 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 127.8 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.18 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.24 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.3 ( $C_{\text{para}}$ ), 128.6 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.7 ( $C_{\text{para}}$ ), 128.9 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 129.1 ( $C_{\text{para}}$ ), 130.4 ( $C_{16}$  or  $C_{19}$ ), 131.0 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 131.4 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 131.7 ( $C_{\text{para}}$ ), 132.1 ( $C_{11}$  or  $C_{14}$ ), 134.7 ( $C_8$ ), 136.2 ( $C_{\text{ipso}}$ ), 137.2 ( $C_{\text{ipso}}$ ), 137.8 ( $C_3$ ), 138.5 ( $C_{\text{ipso}}$ ), 139.4 ( $C_4$ ), 142.4 ( $C_{10}$ ), 142.7 ( $C_{\text{ipso}}$ ), 143.5 ( $C_{16}$  or  $C_{19}$ ), 149.7 (2  $\times$   $C_{\text{ar}}$ ;  $C_6$  or  $C_9$ ,  $C_{11}$  or  $C_{14}$ ), 164.8 ( $C_6$  or  $C_9$ ), 173.3 ( $C_1$ ), 184.6 ppm ( $C_{\text{ortho}}$  at  $C_{20}$ ).

For **7b**: UV-vis  $\lambda_{\text{max}}$  (log  $\epsilon$ ) 321 (4.08), 535 (3.91) nm. The  $^1\text{H}$  NMR spectrum was found to be concentration-dependent, apparently due to partial dimerization:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) for  $c = 5$  mM,  $\delta$  4.22 (bs, 1H, 15-OH), 5.96 (dd, 1H,  $J_1 = 3.7$  Hz,  $J_2 = 2.7$  Hz,  $H_{17}$ ), 6.20 (d, 1H,  $J = 5.7$  Hz,  $H_2$ ), 6.26 (d, 1H,  $J = 4.6$  Hz,  $H_7$ ), 6.51 (d, 1H,  $J = 1.3$  Hz,  $H_{23}$ ), 6.71 (d, 1H,  $J = 4.6$  Hz,  $H_8$ ), 6.73 (dd, 1H,  $J_1 = 3.7$  Hz,  $J_2 = 2.6$  Hz,  $H_{18}$ ), 6.94 (d, 1H,  $J = 5.7$  Hz,  $H_3$ ), 7.05 (d, 1H,  $J = 1.3$  Hz,  $H_{13}$ ), 7.25–7.33 (m, 4H, Ph), 7.39–7.46 (m, 13H, Ph), 7.52 (t, 1H,  $J = 7.5$  Hz,  $p$ -H at  $C_{20}$ ), 7.77 (d, 2H,  $J = 7.1$  Hz,  $o$ -H at  $C_{20}$ ), 10.08 (bs, 1H, NH), 10.45 (s, 1H, NH,  $H_{24}$ ), 11.68 ppm (bs, 1H, NH); for  $c = 0.7$  mM,  $\delta$  3.36 (bs, 1H, 15-OH), 6.05 (dd, 1H,  $J_1 = 3.7$  Hz,  $J_2 = 2.6$  Hz,  $H_{17}$ ), 6.22 (d, 1H,  $J = 5.7$  Hz,  $H_2$ ), 6.27 (d, 1H,  $J = 4.6$  Hz,  $H_7$ ), 6.52 (d, 1H,  $J = 1.3$  Hz,  $H_{23}$ ), 6.72 (d, 1H,  $J = 4.5$  Hz,  $H_8$ ), 6.76 (dd, 1H,  $J_1 = 3.7$  Hz,  $J_2 = 2.6$  Hz,  $H_{18}$ ), 6.96 (d, 1H,  $J = 5.7$  Hz,  $H_3$ ), 7.11 (d, 1H,  $J = 1.3$  Hz,  $H_{13}$ ), 7.25–7.33 (m, 4H, Ph), 7.39–7.46 (m, 13H, Ph), 7.52 (tt, 1H,  $J_1 = 7.4$  Hz,  $J_2 = 1.3$  Hz,  $p$ -H at  $C_{20}$ ), 7.82 (d, 2H,  $J = 7.0$  Hz,  $o$ -H at  $C_{20}$ ), 9.87 (s, 1H, NH,  $H_{24}$ ), 10.09 (bs, 1H,

NH), 11.60 ppm (bs, 1H, NH);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  74.4 ( $C_{15}$ ), 110.6 ( $C_{17}$ ), 120.3 ( $C_5$ ), 120.4 ( $C_{18}$ ), 122.0 ( $C_{23}$ ), 125.0 ( $C_2$ ), 126.5 ( $C_7$ ), 126.6 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 127.8 ( $C_{\text{para}}$ ), 127.9 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.1 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.2 (2  $\times$   $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 128.3 ( $C_{13}$ ), 129.0 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 129.4 ( $C_{\text{para}}$ ), 129.5 ( $C_{\text{para}}$ ), 130.4 ( $C_{16}$  or  $C_{19}$ ), 131.2 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 131.3 ( $C_{\text{ortho}}$  or  $C_{\text{meta}}$ ), 131.7 ( $C_{\text{para}}$ ), 134.0 ( $C_{11}$  or  $C_{14}$ ), 134.1 ( $C_{\text{ipso}}$ ), 135.5 ( $C_8$ ), 136.3 ( $C_{\text{ipso}}$ ), 137.1 ( $C_{\text{ipso}}$ ), 137.5 ( $C_3$ ), 138.3 ( $C_{\text{ipso}}$ ), 139.9 ( $C_4$ ), 142.1 ( $C_{11}$  or  $C_{14}$ ), 144.7 ( $C_{16}$  or  $C_{19}$ ), 145.8 ( $C_{10}$ ), 150.5 ( $C_6$  or  $C_9$ ), 166.3 ( $C_6$  or  $C_9$ ), 172.3 ( $C_1$ ), 185.0 ppm ( $C_{\text{ortho}}$  at  $C_{20}$ ); HRMS (ESI)  $m/z$  647.24431 ( $[\text{M}-\text{OH}]^+$ ), calculated for  $\text{C}_{44}\text{H}_{31}\text{N}_4\text{O}_2$  ( $[\text{M}-\text{OH}]^+$ )  $m/z$  647.24463.

The selective deuteration of NCTPPH<sub>2</sub> (**2**) was performed according to the described procedure,<sup>1a</sup> yielding 80% isotope labeling at C-21. Photooxidation of the respective deuterated dianion, 21-D-**6**, performed as described above for **6**, and further conversion with HCl led to isolation of tetrapyrrolic products 3-D-**5b** and 23-D-**7b** with spectral characteristics identical to that found for **5b** and **7b**, respectively, with exceptions due to selective deuteration.

3-D-**5b**:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  6.15–6.18 (m, 3H,  $H_2$ ,  $H_{13}$ ,  $H_{17}$ ), 6.30 (d, 1H,  $J = 4.4$  Hz,  $H_7$ ), 6.33 (s, 1H, 15-OH), 6.46 (d, 1H,  $J = 4.1$  Hz,  $H_{12}$ ), 6.76 (d, 1H,  $J = 4.6$  Hz,  $H_8$ ), 6.82 (dd,  $J_1 = 3.5$  Hz,  $J_2 = 2.5$  Hz), 6.85 (d, 0.2 H, residual  $H_3$ ), 7.33–7.55 (m, 18H, Ph), 7.86 (d, 2H,  $J = 7.1$  Hz,  $o$ -H at  $C_{20}$ ), 9.87 (s, 1H, NH), 10.82 (bs, 1H, NH), 12.46 ppm (bs, 1H, NH); HRMS (ESI)  $m/z$  648.2496 ( $[\text{M}-\text{OH}]^+$ ), calculated for  $\text{C}_{44}\text{H}_{30}\text{DN}_4\text{O}_2^+$  ( $[\text{M}-\text{OH}]^+$ )  $m/z$  648.2509).

23-D-**7b**:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) for  $c = 0.7$  mM,  $\delta$  3.36 (bs, 1H, 15-OH), 6.05 (bs,  $H_{17}$ ), 6.22 (d, 1H,  $J = 5.5$  Hz,  $H_2$ ), 6.27 (d, 1H,  $J = 4.6$  Hz,  $H_7$ ), 6.52 (s, 0.2H, residual  $H_{23}$ ), 6.72 (d, 1H,  $J = 4.6$  Hz,  $H_8$ ), 6.76 (bs, 1H,  $H_{18}$ ), 6.96 (d, 1H,  $J = 6.0$  Hz,  $H_3$ ), 7.11 (s, 1H,  $H_{13}$ ), 7.25–7.33 (m, 4H, Ph), 7.39–7.46 (m, 13H, Ph), 7.52 (t, 1H,  $J = 7.3$  Hz,  $p$ -H at  $C_{20}$ ), 7.82 (d, 2H,  $J = 7.3$  Hz,  $o$ -H at  $C_{20}$ ), 9.86 (s, 1H, NH,  $H_{24}$ ), 10.09 (bs, 1H, NH), 11.58 ppm (bs, 1H, NH); HRMS (ESI)  $m/z$  648.2491 ( $[\text{M}-\text{OH}]^+$ ), calculated for  $\text{C}_{44}\text{H}_{30}\text{DN}_4\text{O}_2^+$  ( $[\text{M}-\text{OH}]^+$ )  $m/z$  648.2509).

## ASSOCIATED CONTENT

### Supporting Information

$^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra of compounds **5b** and **7b**, DFT optimized structures **IA–VA**, **IB–VB** and **IC–VC**, and Cartesian coordinates all structures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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## ACKNOWLEDGMENTS

Financial support from the Ministry of Science and Higher Education (Grant No. N N204 021939) is kindly acknowledged. DFT calculations were carried out at the Supercomputer Center of Poznań.

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- (15) The most intense peak in the ESI spectrum of 23-D-**7b** was found at  $m/z$  648.2491, which correlates with the value calculated for  $C_{44}H_{30}DN_4O_2^+$  ( $[M - OH]^+$ ,  $m/z$  648.2509).
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