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Effects of *N*-Oxidation on Heteroaromatic Macrocycles: Synthesis, Electronic Structures, Spectral Properties, and Reactivities of Tetraazaporphyrin *meso-N*-Oxides

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Abstract: Heteroaromatic N-oxides such as pyridine and quinoline N-oxides are well studied in organic chemistry, and N-oxide formation has long been utilized for tuning the reactivities of heteroaromatics. However, the scope of aromatic N-oxidation is still restricted to relatively small azine or azole skeletons, and there has been little investigation of the photophysical/chemical effects of Noxidation on larger heteroaromatic systems. Here, we report synthesis and unique properties of novel macrocyclic heteroaromatic N-oxides, tetraazaporphyrin (TAP) meso-N-oxides. N-Oxidation of TAP reduced the 18π -aromaticity of the TAP ring compared with that of the parent TAP due to the cross-conjugated resonance structure. The optical properties of TAPs were significantly changed by Noxidation: the N-oxides did not exhibit azaporphyrin-like optical properties, but instead exhibited porphyrin-like optical properties, i.e., weak Q absorption bands, strong Soret absorption bands, and weak fluorescence. These features can be explained by the neardegenerate frontier molecular orbitals resulting from N-oxide formation. Singlet oxygen quantum yields were greatly increased to almost quantitative levels by N-oxidation. The N-oxides showed near-IR-responsive photoredox properties, and worked as both oxidants and sensitizers for oxidation reactions. Protonation of the N-oxides restored TAP-like intense Q bands and red fluorescence, offering a potential design strategy for fluorescence switches.

heterocyclic chemistry, and are utilized in pharmaceuticals,^[1] receptors and ligands,^[2] and oxidants.^[3] In general, N-oxidation of heteroaromatics increases dipole moment, decreases basicity and facilitates both electrophilicity and nucleophilicity at the highly polarized C=N bond, due to guaternary nitrogen cation formation and mesomeric release of N-oxide oxygen, respectively.^[4] Many methods are available for N-oxidation of heteroaromatics and for removal of oxygen from N-oxides.^[5] Thus, N-oxidation is well established as a strategy to modify the reactivities of nitrogen-containing heteroaromatics. On the other hand, utilization of *N*-oxidation for tuning photophysical/chemical properties is not common, though it is known that the introduced oxygen atom often results in red-shifted absorption bands due to intramolecular charge transfer.^[4] One reason for this situation is the fact that availability of N-oxides is generally limited to rather small heteroaromatics consisting of 6π-aromatic azine or azole skeletons, which usually absorb high-energy UV light. In contrast the chemistry of heteroaromatic macrocyclic N-oxides has not been investigated in detail, despite its potential for contributing to the development of functional visible/near-IR dyes.

Introduction

Heteroaromatic *N*-oxides such as pyridine *N*-oxides and quinoline *N*-oxides form an important domain of aromatic

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Pyridine N-Oxide

Tetraazaporphyrin (TAP) N-Oxide

We focused on porphyrins, especially azaporphyrins, as representative heteroaromatic macrocycles suitable for Noxidation. Azaporphyrins, composed of four pyrrole subunits interconnected at the meso positions via nitrogen bridges, are representative 18n-heteroaromatic macrocycles. They have attracted considerable attention due to their aromatic/highly conjugated properties, as well as their absorption/emission in the visible/near-IR region, and have been extensively employed as biomedical tools and optoelectronic materials.^[6] However, meso-N-oxides of azaporphyrins, which can be considered as extended 18π-heteroaromatic N-oxides, are almost unexplored.^[7] To our knowledge, the only example is diazaporphyrin meso-N-oxide, obtained as a side product during the synthesis of a diazaporphyrin.^[8] Therefore, the chemistry, generality, and properties of macrocyclic azaporphyrin N-oxides are still unclear.

Herein, we report the first *N*-oxidation of *meso*-nitrogens of azaporphyrins. Tetraazaporphyrin (TAP), the simplest

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azaporphyrin, which has four nitrogens at the *meso* positions,^[9] was selected as a model compound. The TAP *meso*-nitrogens were easily converted to the corresponding *N*-oxides with *m*CPBA. We found that the *N*-oxidation significantly alters the electronic structures and photophysical properties of 18π -aromatic TAPs. Intriguingly, TAP *N*-oxide exhibited near-IR photo-oxidative properties, releasing the oxygen atom and sensitizing molecular oxygen. Protonation of the *N*-oxides restored absorption and fluorescence emission in the red region. Our findings indicate that *N*-oxidation is a simple but robust method for controlling the photophysical/chemical properties of heteroaromatic macrocycles.



Scheme 1. Synthesis of TAP *meso-N*-oxides. Reagents and conditions: *m*CPBA (1.1 eq.), CH₂Cl₂ (for 1H₂, 1'H₂), THF (for 1Zn, 1'Zn), rt, 24 h.

Results and Discussion

Synthesis and Characterization

In the reaction between mCPBA and H₂TAP with no peripheral substituents, generation of the desired N-oxide was indicated by MALDI-MS and UV-vis measurements, but its poor solubility hampered further purification and analysis. In addition, gradual decomposition was observed during the reaction due to increased electrophilicity of the macrocycle at pyrrole rings, arising from installation of the N-oxide functionality. In order to improve the solubility and suppress oxidative/nucleophilic degradation, we focused on the introduction of *t*-butyl (^tBu) groups onto the TAP pyrrole rings. H₂TAP(^tBu)₄ was synthesized as a mixture of four regioisomers and separated into three fractions (D_{2h} , $C_s + C_{2v}$, and C_{4h} structures) by standard column chromatography on silica gel (see the Supporting Information (SI)). ZnTAP(^tBu)₄ was prepared by insertion of a Zn ion into H₂TAP(^{*i*}Bu)₄. Scheme 1 shows the synthesis of TAP *N*-oxides. All the reactions were performed using mCPBA at room temperature. Other typical oxidants used for synthesis of pyridine N-oxides,^[5] such as peracetic acid, trifluoroperacetic acid, H₂O₂, Oxone, and dimethyldioxirane, did not afford the

desired N-oxides at all. The D_{2h} isomers $1H_2$ and 1Zn reacted at the less hindered meso-nitrogens to give mono-N-oxides 2H₂ and 2Zn in moderate yields, respectively. 1Zn additionally afforded 3Zn, but 1H₂ did not yield the corresponding di-N-oxide. The $C_s + C_{2\nu}$ isomers 1'H₂ and 1'Zn only gave mono-N-oxides 2'H2 and 2'Zn, presumably because the other three mesonitrogens are sterically hindered by the bulky ^tBu groups. The C_{4h} isomer of H₂TAP(^tBu)₄ did not react with mCPBA at all. These oxidation reactions afforded TAP N-oxides and unreacted TAPs as isolable compounds, and no major byproducts were detected in the reaction mixtures (See the SI). It should be noted that N-oxidation of the TAPs did not occur at the pyrrolic nitrogen atoms, in contrast to the reported reaction between octaethylporphyrin and mCPBA.[7c] These meso-N-oxides are stable under ambient conditions, and were characterized by ESI-MS, ¹H and ¹³C NMR, and UV-vis spectroscopic methods. We confirmed that the positions of the ^tBu groups have little effect on the physical properties of these compounds.



Figure 1. a) X-ray structure of **2H**₂. The thermal ellipsoids are drawn at the 50% probability level. All the hydrogens and one of the two disordered oxygen atoms are omitted for clarity. b) Selected bond lengths (Å) of H₂TAP (top) and H₂TAP mono-*N*-oxide (bottom) calculated at the B3LYP/6-31G^{**} level. c) Two possible resonance structures of H₂TAP mono-*N*-oxide.

The introduction of an oxygen atom at the less-hindered *meso*-nitrogen was unambiguously confirmed by X-ray diffraction analysis of crystals obtained by slow diffusion of methanol into a toluene solution of $2H_2$ (Figure 1a). The *N*-oxide molecule has a crystallographic-inversion center, and the symmetry brings about a disordering of the entire molecule by superimposing a pair of mirror images. This prohibits our discussing the bond lengths of the skeleton in detail. In order to obtain geometrical information, we calculated the structures of H₂TAP and its *N*-oxide (Figure 1b). The calculated N–O distance of 1.28 Å in H₂TAP *N*-oxide is similar to the N–O distances

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observed in pyridine *N*-oxides.^[10] The C–N(O) bond lengths were estimated to be 1.38 and 1.39 Å, longer than the C–N(*meso*) bonds of H₂TAP (1.32 and 1.34 Å). This increased single-bond character of the C–N bonds can be attributed to a cross-conjugated resonance structure with an N=O double bond (Figure 1c), in which the 18 π -aromatic circuit of the TAP skeleton is disrupted by the oxygen atom. The IR spectrum of **2'H**₂ displays an intense absorption band at 1234 cm⁻¹, assigned to the N–O stretching vibration, as commonly seen in pyridine *N*-oxides (Figure S4-1).^[11]



Figure 2. ¹H NMR spectra of a) 1H₂ and b) 2H₂ in CDCI₃ at room temperature.

Figure 2 shows ¹H NMR spectra of **1H**₂ and **2H**₂ in CDCl₃ at room temperature. The internal N-H protons, ^tBu protons, and external pyrrole β protons of **1H**₂ were observed at -2.40, 2.23, and 8.95 ppm, respectively, clearly indicating the existence of a strong diatropic ring current typical of 18π-aromatic porphyrinoids. As for $2H_2$, the pyrrole β protons gave two split signals at 8.55 and 9.05 ppm, reflecting their different environments due to the oxygen atom. Judging from the chemical shifts of the internal N-H protons (-0.15 ppm) and the ^tBu protons (2.10 ppm), the ring current strength of **2H**₂ is slightly decreased compared to that of 1H2. The nucleus-independent chemical shift (NICS)^[12] values of H₂TAP and H₂TAP mono-Noxide at 1 Å above the center of the skeleton were estimated to be -13.49 and -10.52 ppm, respectively (Figure S6-1), which are consistent with the slightly diminished diatropic properties of 2H₂. Calculated ¹H chemical shifts also agreed with the observed weaker ring current effects upon N-oxidation (Figure S6-2). This reduced 18π-aromatic ring current of 2H₂ is likely associated with the contribution of the cross-conjugated resonance structure discussed above. A similar tendency was reported⁴ and computed for pyridine and its *N*-oxide (NICS(1): – 11.08 and -8.43 ppm, respectively) (Figure S6-1).





Figure 3. Electronic absorption (solid) and fluorescence (broken) spectra of (a) $1'H_2$ (gray) and $2'H_2$ (blue) in CHCl₃, (b) 1'Zn (gray) and 2'Zn (blue) in THF and (c) 3Zn (blue) in THF.

Photophysical Properties

To investigate the effects of the N-oxide functionality on the optical properties, we measured absorption and fluorescence spectra of TAPs and their N-oxides (Figure 3). TAPs displayed intense Q bands (1'H₂: 622, 553 nm; 1'Zn: 591 nm) and Soret bands (1'H₂: 336 nm; 1'Zn: 336 nm), which are characteristic of azaporphyrinoids.[13] Interestingly, TAP N-oxides showed significantly altered electronic properties. 2'H₂ and 2'Zn exhibited weaker and red-shifted Q bands in the 720-520 nm region, while the red-shifted Soret bands in the 500-400 nm region remained strong compared with those of the parent TAPs These drastic spectral changes are in marked contrast to the optical properties of meso-N-protonated TAPs, which usually retain their intense Q and Soret bands.^[14] The absorption spectrum of di-N-oxide 3Zn gave even more red-shifted and weaker bands in the near-IR region up to 829 nm. These behaviors of N-oxides are reminiscent of standard porphyrin systems with meso-carbons, which generally show weak Q bands and intense Soret bands. The magnetic circular dichroism (MCD) spectra of N-oxides 2'H2 and 2'Zn both show coupled Faraday B terms in the Q and Soret band regions, similarly to porphyrins (Figure S4-2).^[15] 2'H₂ and 2'Zn displayed fluorescence at 705 nm and 695 nm, respectively, but the

quantum yields (**2**'**H**₂: Φ_F = 0.007; **2**'**Zn**: Φ_F = 0.005) were much smaller than those of TAPs (**1**'**H**₂: Φ_F = 0.244; **1**'**Zn**: Φ_F = 0.224) (Table 1), probably due to the decreased extinction coefficients of the red-shifted Q bands. No fluorescence was detectable for **3Zn**.

Table 1. Fluorescence and singlet oxygen quantum yields.							
	1'H₂	1'Zn	2'H₂	2'Zn	3Zn		
$oldsymbol{\Phi}_{ extsf{F}}^{[a]}$	0.244 ^[b]	0.224 ^[b]	0.007 ^[c]	0.005 ^[c]	n.d. ^[c]		
$oldsymbol{\Phi}_{\!\!\Delta}{}^{[d]}$	0.21	0.59	0.93	0.96	0.85		

[a] Fluorescence quantum yields using oxazine 170 as a standard ($\Phi_F = 0.579$ in ethanol).^[16] [b] Measured in CHCl₃. [c] Measured in THF. [d] Singlet oxygen quantum yields determined from singlet oxygen luminescence measured in pyridine using ZnPc as a standard ($\Phi_{\Delta} = 0.61$ in pyridine).^[17]

The quite low fluorescence quantum yields of N-oxides imply the possibility of facilitated intersystem crossing from the S1 state to the T1 state upon N-oxidation, which might lead to enhanced phosphorescence and singlet oxygen generation. TAP 1'H₂ and 1'Zn exhibited no detectable phosphorescence and low to moderate singlet oxygen generation (**1'H**₂: ϕ_{Δ} = 0.21; **1'Zn**: ϕ_{Δ} = 0.59) at room temperature (Table 1), as observed for common azaporphyrins.^[18] The increased singlet oxygen quantum yield upon metalation is explained by heavy atom effects. In sharp contrast, all the N-oxides showed quite high singlet oxygen quantum yields (**2'H**₂: ϕ_{Δ} = 0.93; **2'Zn**: ϕ_{Δ} = 0.96; **3Zn**: ϕ_{Δ} = 0.85), although phosphorescence was not observed. The Φ_{Δ} value of **2'H**₂ is quite large for a porphyrinoid with no heavy atom, and is greater than that of free-base tetraphenylporphyrin, which is frequently used as a photosensitizer ($\Phi_{\Delta} = 0.63$).^[19] These improved singlet oxygen yields after N-oxidation can be partly rationalized by the change from azaporphyrin-like optical properties to porphyrin-like optical properties, since porphyrins generally sensitize oxygen more efficiently than azaporphyrins due to their forbidden Q band absorptions.[19]

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Figure 4. Frontier π -system molecular orbitals and energy levels of ZnTAP (left) and ZnTAP mono-*N*-oxide (right) calculated at the B3LYP/6-31G^{**} level. [a] σ -Orbitals.

Molecular Orbital Analysis

In order to gain insight into the altered electronic properties, we performed molecular orbital (MO) calculations of ZnTAP and ZnTAP mono-N-oxide (Figure 4). The optical properties of porphyrins and azaporphyrins are reasonably well explained by Gouterman's four-orbital model.^[20] The intense Q band of ZnTAP is derived from the doubly degenerate transition from the non-degenerate HOMO to the degenerate LUMOs (LUMO and LUMO+1). N-Oxidation of the meso-nitrogen significantly destabilizes the HOMO-1 owing to the out-of-phase interaction between the oxygen and the meso-nitrogen, while the HOMO, LUMO, and LUMO+1 are slightly stabilized. In other words, the inductive effect of the electronegative quaternary nitrogen cation leads to general stabilization of the MOs, while the electrondonating character of the oxygen anion of the N-oxide destabilizes the HOMO-1 selectively through the mesomeric effect. Such phenomena/interactions are well known for pyridine N-oxide (Figure S6-3). These changes in the energy levels coincidentally cause near-degeneracy of the HOMOs and LUMOs, which accounts for the forbidden Q band absorption and allowed Soret band absorption, as seen in regular porphyrin systems. H₂TAP mono-N-oxide has similar MOs to ZnTAP mono-N-oxide (Figure S6-4), and time-dependent density functional theory (TD-DFT) calculations of N-oxides agreed well with the observed absorption spectra (Figure S6-5). Cyclic voltammetry (CV) measurements of 2'H₂ showed a slight anodic shift of the first reduction potential compared with a reported TAP^[21] (Figure S4-3), which supports the calculation results on the stabilized LUMOs of TAP N-oxides.

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Scheme 2. Reduction of TAP N-oxide 2'H₂ to TAP 1'H₂.



Scheme 3. Catalytic near-IR oxidation with TAP N-oxide.

Reactivities and Photoreactivities

We expected that the TAP N-oxides would exhibit unique reactivities, especially under light irradiation, corresponding to their physicochemical properties. The metal-free N-oxide 2'H₂ was selected for investigation of the reactivities. A strong reductant, PCl₃, immediately reacted with 2'H₂ to give TAP 1'H₂ in 89% yield (Scheme 2). Interestingly, the reduction to 1'H₂ was also achieved in the presence of weaker reductants, Ph₃P and Et₃N, upon near-IR light irradiation under an Ar atmosphere, generating Ph₃PO and acetaldehyde, respectively.^[22] During the photo-reduction with Ph₃P, we noticed that 2'H₂ oxidized more than 1 equivalent of Ph₃P under an aerobic condition, suggesting participation of O2 in the reaction. In fact, Ph3P was completely converted to Ph₃PO with a catalytic amount of 2'H₂ under an O₂ atmosphere upon near-IR irradiation (Scheme 3). The mechanism could involve reaction of singlet oxygen with Ph₃P or single electron transfer from Ph₃P to excited N-oxide followed by quenching of Ph₃P⁺ with triplet oxygen, as proposed for catalytic oxidation of triarylphosphine under UV/visible light irradiation.[23] Singlet oxygen generation by near-IR light irradiation was further demonstrated for endoperoxide formation on 9,10-diphenylanthracene. The photoreactions did not proceed in the dark. These results indicate that TAP N-oxides can be utilized as near-IR responsive photo-oxidizing sensitizers.



Scheme 4. Methylation of TAP N-oxide 2'H2.

We then examined modification at the N-oxide moiety (Scheme 4). Meerwein's salt methylated the oxygen atom of $2'H_2$ to afford $2'H_2$ -Me⁺, though the product was difficult to completely purify and isolate due to its rapid decomposition in the presence of water. This instability contrasts with the stability of various isolable *N*-methoxypyridinium salts.^[24] The electronic absorption spectrum of 2'H₂-Me⁺ showed H₂TAP-like characteristics, i.e., two intense Q bands and a Soret band (Figure S4-4), since the attached methyl group suppresses electron donation from the oxygen atom to the macrocycle and reduces the contribution of the cross-conjugated structure with an N=O double bond, as confirmed by the calculated bond lengths (Figure S6-6). The internal N-H protons of 2'H2-Me⁺ were observed at -1.90 ppm in the ¹H NMR spectrum, also indicating recovery of strong 18π-aromaticity, comparable to that of TAP 1'H₂.



Figure 5. a) Electronic absorption (top) and fluorescence (bottom) spectra of $2^{\prime}H_2$ in CHCl₃ (blue) and in 0.2% TsOH-CHCl₃ (red). b) Electronic absorption (top) and fluorescence (bottom) spectra of $2^{\prime}Zn$ in THF (blue) and in 0.2% H₂SO₄-THF (red). c) Photographs of $2^{\prime}Zn$ in THF (left) and in 0.2% H₂SO₄-THF (right) under visible (top) and UV (bottom) light.

Switching Optical Properties Using the *N*–Oxide Functionality

The result of methylation prompted us to investigate protonation of TAP *N*-oxides. Figure 5 shows absorption and fluorescence spectra of $2'H_2$ and 2'Zn upon addition of acid. Both protonated compounds exhibited much more intense Q bands than the neutral forms, presumably due to structural changes caused by protonation of the oxygen atoms. The TAP-like intense Q bands of the protonated and methylated TAP *N*-oxides were further confirmed by TD-DFT calculations (Figure S6-7). Fluorescence quantum yields were also enhanced by protonation, and, surprisingly, the red fluorescence of 2'Zn became approximately

50 times more intense upon protonation (neutral: $\Phi_{\rm F}$ = 0.005; protonated: $\Phi_{\rm F}$ = 0.245). To our knowledge, these TAP *N*-oxides are the first porphyrinoids that enable switching between porphyrin-like optical properties and azaporphyrin-like optical properties.

Conclusions

We have prepared TAP meso-N-oxides using mPCBA as an oxidant to investigate the effects of N-oxidation on the properties of extended heteroaromatic macrocycles. This is the first report of substitution at the meso-nitrogen atoms of azaporphyrins. The 18π-aromaticity of these N-oxides is decreased compared with that of the parent TAPs due to the contribution of the crossconjugated resonance structure. The N-oxides exhibit porphyrinlike weak Q bands and intense Soret bands originating from nearly degenerate pairs of HOMOs and LUMOs. Much weaker fluorescence was observed while singlet oxygen quantum yields were greatly enhanced upon N-oxidation. The oxygen moiety can be easily removed by photoreduction under near-IR light irradiation, and the N-oxide itself works as a photosensitizer for oxidation reactions. In addition, the porphyrin-like optical properties are converted to azaporphyrin-like optical properties upon protonation, enabling fluorescence switching in the red region. These studies indicate that the classical chemistry of pyridine N-oxides can provide clues for improving the physicochemical properties of heteroaromatic macrocycles. Further studies on N-oxidation of other extended conjugated dyes and work to utilize TAP N-oxides as near-IR responsive photo-oxidizing agents are in progress.

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Keywords: conjugation • fluorescence • *N*-oxides • porphyrinoids • singlet oxygen

- a) Y. Pan, P. Li, S. Xie, Y. Tao, D. Chen, M. Dai, H. Hao, L. Huang, Y. Wang, L. Wang, Z. Liu, Z. Yuan, *Bioorg. Med. Chem. Lett.* 2016, *26*, 4146; b) A. M. Mfuh, O. V. Larionov, *Curr. Med. Chem.* 2015, *22*, 2819; c) S. Cretton, L. Breant, L. Pourrez, C. Ambuehl, L. Marcourt, S. N. Ebrahimi, M. Hamburger, R. Perozzo, S. Karimou, M. Kaiser, M. Cuendet, P. Christen, *J. Nat. Prod.* 2014, *77*, 2304.
- [2] a) X. Chi, H. Zhang, G. I. Vargas-Zúñiga, G. M. Peters, J. L. Sessler, J. Am. Chem. Soc. 2016, 138, 5829; b) J. J. Henkelis, S. A. Barnett, L. P. Harding, M. J. Hardie, Inorg. Chem. 2012, 51, 10657; c) A. V. Malkov,

P. Ramírez-López, L. Biedermannová, L. Rulíšek, L. Dufková, M. Kotora, F. Zhu, P. Kočovský, *J. Am. Chem. Soc.* 2008, *130*, 5341; d) H.
W. Roesky, M. Andruh, *Coord. Chem. Rev.* 2003, *236*, 91.

- a) Z. Xu, H. Chen, Z. Wang, A. Ying, L. Zhang, J. Am. Chem. Soc.
 2016, *138*, 5515; b) T. Kojima, K. Nakayama, M. Sakaguchi, T. Ogura, K. Ohkubo, S. Fukuzumi, J. Am. Chem. Soc. **2011**, *133*, 17901; c) R. Ito, N. Umezawa, T. Higuchi, J. Am. Chem. Soc. **2005**, *127*, 834.
- [4] A. Albini, S. Pietra, *Heterocyclic N-Oxides*, CRC Press, Florida, **1991**.
- [5] a) J. A. Bull, J. J. Mousseau, G. Pelletier, A. B. Charette, *Chem. Rev.* **2012**, *112*, 2642; b) S. Youssif, *Arkivoc* **2001**, *i*, 242; c) A. R. Katritzky, J. N. Lam, *Heterocycles* **1992**, 33, 1011.
- [6] a) J. Fernández-Ariza, R. M. Krick Calderón, M. S. Rodríguez-Morgade, D. M. Guldi, T. Torres, J. Am. Chem. Soc. 2016, 138, 12963; b) Y. Zhang, M. Jeon, L. J. Rich, H. Hong, J. Geng, Y. Zhang, S. Shi, T. E. Barnhart, P. Alexandridis, J. D. Huizinga, M. Seshadri, W. Cai, C. Kim, J. F. Lovell, Nat. Nanotechnol. 2014, 9, 631; c) A. Varotto, C.-Y. Nam, I. Radivojevic, J. P. C. Tomé, J. A. S. Cavaleiro, C. T. Black, C. M. Drain, J. Am. Chem. Soc. 2010, 132, 2552.
- [7] N-Oxide formation at the internal pyrrolic nitrogen of porphyrins has been known for many years. a) S. Banerjee, M. Zeller, C. Brückner, J. Org. Chem. 2009, 74, 4283; b) A. L. Balch, Y. W. Chan, M. Olmstead, M. W. Renner, J. Am. Chem. Soc. 1985, 107, 2393; c) L. E. Andrews, R Bonnett, R. J. Ridge, E. H. Appelman, J. Chem. Soc., Perkin Trans. 1 1983, 103; d) R. Bonnett, R. J. Ridge, E. H. Appelman, J. Chem. Soc. Chem. Commun. 1978, 310.
- [8] T. Okujima, G. Jin, S. Otsubo, S. Aramaki, N. Ono, H. Yamada, H. Uno, J. Porphyrins Phthalocyanines 2011, 15, 697.
- [9] R. P. Linstead, M. Whalley, J. Chem. Soc. 1952, 4839.
- [10] a) J. F. Chiang, J. J. Song, J. Mol. Struct. 1982, 96, 151; b) D. Ülkü, B.
 P. Huddle, J. C. Morrow, Acta Crystallogr. Sect. B: Struct. Sci. 1971, B27, 432.
- [11] C. L. Wild, M. Spahis, R. D. Blankenship, J. W. Rogers, R. J. Williams, Polyhedron 1983, 2, 379.
- [12] P. v. R. Schleyer, C. Maerker, A. Dransfeld, H. Jiao, N. J. R. v. E. Hommes, J. Am. Chem. Soc. 1996, 118, 6317.
- [13] J. Mack, M. J. Stillman, N. Kobayashi, Coord. Chem. Rev. 2007, 251, 429.
- [14] a) P. A. Stuzhin, Yu. B. Ivanova, I. S. Migalova, V. B. Sheinin, *Russ. J. Gen. Chem.* 2005, 75, 1300; b) P. A. Stuzhin, O. G. Khelevina, B. D. Berezin in *Phthalocyanine. Properties and Applications, Vol. 4* (Eds.: C. C. Leznoff, A. B. P. Lever), VCH Publications, New York, 1996, Chapter 2, pp. 19–78; c) P. A. Bernstein, A. B. P. Lever, *Inorg. Chim. Acta.* 1992 198-200, 543.
- [15] J. Mack, Y. Asano, N. Kobayashi, M. J. Stillman, J. Am. Chem. Soc. 2005, 127, 17697.
- [16] K. Rurack, M. Spieles, *Anal. Chem.* **2011**, *83*, 1232.
- [17] A. Ogunsipe, D. Maree, T. Nyokong, J. Mol. Struct. 2003, 650, 131.
- [18] K. Ishii, N. Kobayashi in *The Porphyrin Handbook, Vol. 16* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, New York, **2003**, Chapter 102, pp. 1–42.
- [19] M. C. DeRosa, R. J. Crutchley, Coord. Chem. Rev. 2002, 233–234, 351.
- [20] M. Gouterman, J. Mol. Spectrosc. **1961**, 6, 138.
- [21] H. Miwa, E. A. Makarova, K. Ishii, E. A. Luk'yanets, N. Kobayashi, *Chem. Eur. J.* **2002**, *8*, 1082.
- [22] Heteroaromatic *N*-oxides increase oxidizing ability under UV irradiation. a) M. Sako, S. Ohara, K. Shimada, K. Hirota, Y. Maki, *J. Chem. Soc., Perkin Trans 1* **1990**, 863; b) A. Albini, M. Alpegiani, *Chem. Rev.* **1984**, 84, 43.
- [23] a) S. M. Bonesi, S. Protti, A. Albini, J. Org. Chem. 2016, 81, 11678.; b)
 K. Ohkubo, T. Nanjo, S. Fukuzumi, S. Bull. Chem. Soc. Jpn. 2006, 79, 1489; c) S. Yasui, S. Tojo, T. Majima, J. Org. Chem. 2005, 70, 1276.
- [24] E. D. Lorance, W. H. Kramer, I. R. Gould, J. Am. Chem. Soc. 2002, 124, 15225.

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FULL PAPER



Macrocyclic heteroaromatic *N***-oxides:** Tetraazaporphyrin (TAP) *meso-N*-oxides were synthesized by direct oxidation of TAPs. The introduction of an oxygen atom significantly alters the physicochemical properties: the *N*-oxides exhibited weaker red/near-IR absorption and fluorescence while singlet oxygen quantum yields were greatly enhanced. The *N*-oxides showed near-IR-responsive photoredox properties, and protonation of the *N*-oxides restored TAP-like intense red absorption and fluorescence.

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Effects of *N*-Oxidation on Heteroaromatic Macrocycles: Synthesis, Electronic Structures, Spectral Properties, and Reactivities of Tetraazaporphyrin *meso-N*-Oxides