ORGANIC
LETTERS

2004
Vol. 6, No. 9
1393−1396

Demetalation of the Regioselective Oxygenation Product of an N-Confused Porphyrin Complex

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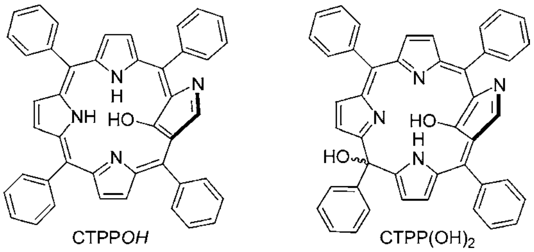
Received February 11, 2004

ABSTRACT



The demetalation of M^{III}(*H*CTPP*O*)Br (M = Mn or Fe) afforded two hydroxylated N-confused porphyrinoids. CTPP*OH* retains the tautomer form of the N-confused porphyrin with a hydroxyl group substituted in the inner-core carbon. The further attack of OH^- to the *meso* carbon afforded a dihydroxylated N-confused macrocycle, $CTPP(OH)_2$.

Investigations into the chemistry of N-confused porphyrins (NCPs) have progressed rapidly in recent years.[1,2] Important results from the studies of NCPs include the nontraditional coordination modes of the NCP complexes,[3,4] the stabilization of abnormal metal oxidation states,[5] the formation of organometallic metal carbon bonds,[6] and the formation of dinuclear or polynuclear N-confused porphyrin complexes through nitrogen coordination on an inverted pyrrole ring.[7] One particularly intriguing result from the study of NCP complexes is the unusual reactivity of the internal carbon on an inverted pyrrole ring. Reactions including halogenation,[8] cyanization,[9] oxygenation,[10] and internal fusion[11] have been reported. Recently, Furuta and co-workers reported the oxidative liberation of tripyrrinone metal complexes from NCP.[12] More recently, novel ring reduction on the manganese NCP complex to form a phlorine-type porphyrin core has been reported by Ziegler et al.[13] All of these reactions provide routes to obtain novel porphyrin macrocycles, which are difficult to access from other approaches. However, there are only a few reports available for the demetalation reaction of N-confused porphyrin complexes to obtain the free base form of novel macrocycles. Recently, we have found that the iron(II) and manganese(II) complexes of NCP react with dioxygen in a sequential two-step process. The metal center of five coordinated M^{II}(*H*CTPP*H*)Br (M = Fe or Mn) is oxidized

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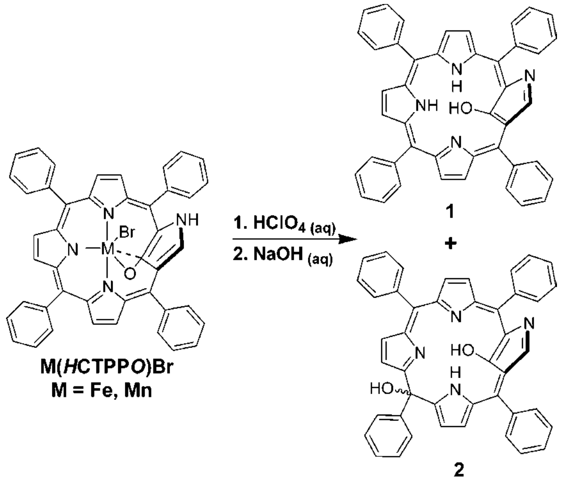
(1) Chmielewski, P. J.; Latos-Grażyński, L.; Rachlewicz, K.; Głowiak, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 779.
(2) Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994**, *116*, 767.
(3) Furuta, H.; Maeda, H.; Osuka, A. *Chem. Commun.* **2002**, 1795.
(4) Chen, W.-C.; Hung, C.-H. *Inorg. Chem.* **2001**, *40*, 5070.
(5) Furuta, H.; Ogawa, T.; Uwatoko, Y.; Araki, K. *Inorg. Chem.* **1999**, *38*, 2676.
(6) Chmielewski, P. J.; Latos-Grażyński, L.; Głowiak, T. *J. Am. Chem. Soc.* **1996**, *118*, 5690.
(7) Furuta, H.; Ishizuka, T.; Osuka, A. *J. Am. Chem. Soc.* **2002**, *124*, 5622.
(8) Furuta, H.; Ishizuka, T.; Osuka, A.; Ogawa, T. *J. Am. Chem. Soc.* **1999**, *121*, 2945.
(9) Xiao, Z.; Patrick, B. O.; Dolphin, D. *Chem. Commun.* **2003**, 1062.
(10) Hung, C.-H.; Chen, W.-C.; Lee, G.-H.; Peng, S.-M. *Chem. Commun.* **2002**, 1516.
(11) Furuta, H.; Ishizuka, T.; Osuka, A.; Ogawa, T. *J. Am. Chem. Soc.* **2000**, *122*, 5748.
(12) Furuta, H.; Maeda, H.; Osuka, A. *Org. Lett.* **2002**, *4*, 181.
(13) Harvey, J. D.; Ziegler, C. J. *Chem. Commun.* **2003**, 2890.

10.1021/ol049757b CCC: $27.50

followed by inner C−H deprotonation to form M^{III}(*H*CTPP)-Br.[14] Further dioxygen activation inserts an oxygen atom into the iron−carbon bond to form Fe^{III}(*H*CTPP*O*)Br.[15] As an attempt to isolate the free base of the oxygenation product for future coordination chemistry study, here we report the isolation and characterization of the oxygenation product, CTPP*OH*. A novel CTPP(OH)$_2$ compound with an insertion of the second hydroxylation group into a *meso* carbon of the tripyrrin unit is also reported.

Scheme 1



The method of treating M(*H*CTPP*O*)Br with HClO$_4$ in a solvent mixture of CH_2Cl_2/THF (3:1) was used for the demetalation reactions. The color of the solution changed immediately from dark green to yellow-green when HClO$_4$ was added. The reaction mixture was neutralized with NaOH$_{(aq)}$ and then washed with H_2O. After column chromatography the products **1** and **2** (ratio 3:2) can be obtained. Demetalations of both manganese(III) and iron(III) complexes were carried out with a similar procedure. The results showed higher yields (**1**, 54%; **2**, 38%) for iron(III) complexes in comparison with manganese(III) complexes (**1**, 30%; **2**, 18%). Preliminary study reveals that the isolated products are relatively stable. The exposure of toluene solutions of **1** and **2** to air gave no significant change in UV−vis spectra during the course of 12 h. The mass spectra clearly indicated the presence of hydroxyl substituents on the isolated products. The UV−vis spectra shown in Figure 1 are distinctively different from the starting M(*H*CTPP*O*)-Br.[15] Both compound **1** and **2** showed split Soret bands with absorption coefficients lower than that of CTPP*H*. The Soret bands for both compounds are blue-shifted and broadened, suggesting the diminishing of aromatic π system. The further blue-shifted Soret peak of **2** agrees with a shorter and discrete conjugate system.

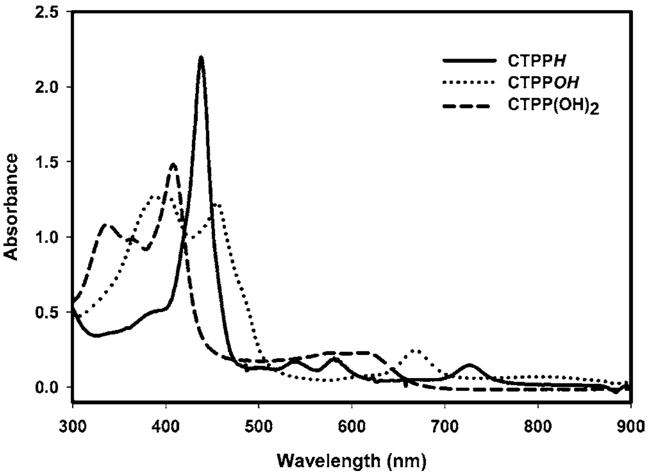


Figure 1. Absorption spectra of CTPP*H* free base, CTPP*OH* (**1**) and CTPP(OH)$_2$ (**2**).

To have an insight of the structures, compound **1** and **2** were characterized by NMR spectroscopy. The chemical shifts of compound **1** spanned the region of δ 0−12 with unusually broad peaks. The lowering of temperature down to −50 °C did not significantly sharpen the peaks. A rapid flipping of the pyrroles or phenyl rings might be attributed to the peak broading. Also, rapid interconversion between keto- and enol-tautomer forms cannot be ruled out. Outside the aromatic region, three peaks at δ 11.29, 11.88, and 2.05 are visible. These chemical shifts originate from the two pyrrolic NH and a hydroxyl proton, which are confirmed by isotope exchange experiments.

In contrast to **1**, the half-widths of ^{1}H NMR signals for **2** are in the normal range. Noticeably, the β-pyrrolic protons are significantly upfield shifted to 6−7 ppm, an indication of diminished aromatic π system. As shown in Figure 2, the β-pyrrolic protons on the dipyrrin fragment are located as

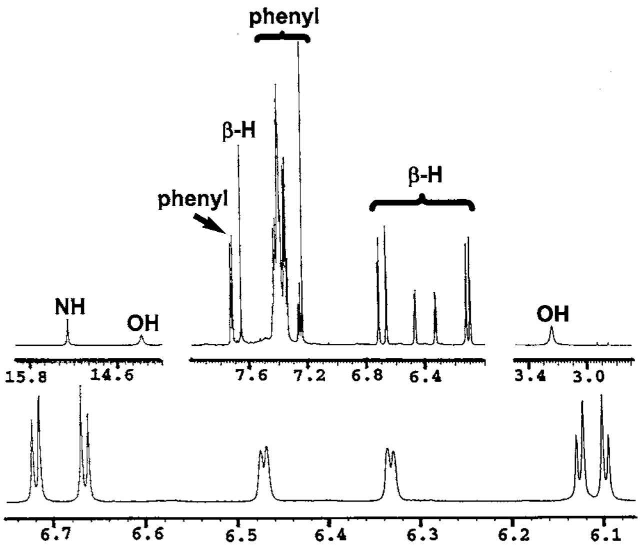


Figure 2. NMR spectrum of CTPP(OH)$_2$ (**2**) in selected region.

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[14] Bohle, D. S.; Chen, W.-H.; Hung, C.-H. *Inorg. Chem.* **2002**, *41*, 3334.

[15] Rachlewicz, K.; Wang, S.-L.; Ko, J.-L.; Hung, C.-H.; Latos-Grażyński, L. *J. Am. Chem. Soc.* **2004**, *126*, 4420.

two pairs of *AB* pattern at δ (6.667, 6.719) and (6.099, 6.125). The much broader pair of doublet at δ 6.472 and 6.332 is assigned to the β-pyrrole protons between the two hydroxyl groups. The COSY spectrum showed that these two protons further coupled to a peak at δ 15.284. The peak at 15.284 ppm was therefore assigned to the pyrrolic N−H on the same pyrrole ring. A singlet integrated into one proton at δ 7.661 was assigned to the pyrrolic proton on the inverted pyrrole ring and therefore suggested the presence of an imino nitrogen on the inverted pyrrole ring. Two broadened peaks at 14.278 and 3.245 ppm were assigned to the hydroxyl protons on the inner carbon and *meso* carbon, respectively.

The explicit evidence of the structure was obtained from the X-ray single-crystal analysis. CTPP*OH*, **1**, crystallized in triclinic $P\bar{1}$ with one molecule in the unit cell.[16] The molecule sits on a center of symmetry and only a half molecule was located from the electron density map. The hydroxyl group on the inner carbon of inverted pyrrole ring was refined to an occupancy factor of 0.5 in agreement with a crystallographic disorder involving the inverted pyrrole ring and the pyrrole ring *trans* to it. As depicted in Figure 3, the distance of 1.497(4) Å for C23−O1 suggested a hydroxyl group with diminutive keto form contribution. The planarity of O1−C23−C19−C22 as well as the distance of 1.397(3) Å for both C23−C19 and C23−C22 agree with a sp^2 carbon on C23. CTPP*OH* exhibits a distorted porphyrin ring. Whereas the pyrrole rings of N1 and N1A are nearly coplanar to the porphyrin mean plane, the inverted pyrrole ring and the N3A pyrrole are tilted, in the opposite direction, away from the mean plane. The angle between the inverted pyrrole ring and the plane of other core atoms is 12°. The oxygen is deviated 0.96 Å from the mean porphyrin plane.

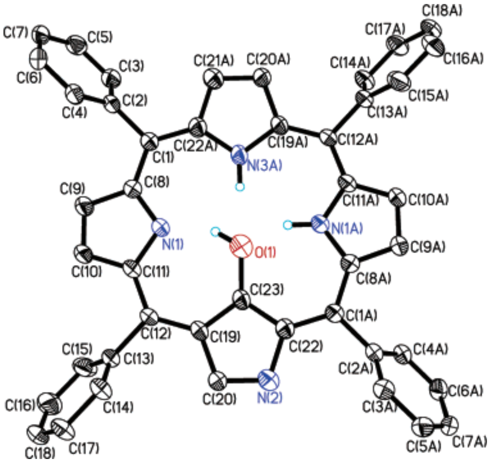

Figure 3. Structure of CTPP*OH* (**1**) in 35% thermal ellipsoids.

Six enol tautomers (Figure 4) were examined using ab initio quantum chemistry at the MP2/6-31G(d) level.[17] To our surprise, a keto structure was obtained during our study. The relative energies of species (in kcal/mol, with respect to **3H-3**) are shown in Figure 4. Our result shows that the **3H** form tautomers are significantly more stable than those with the **2H** form. The inner core hydrogen bonding interactions may play an essential role to the stabilization energies as in the case of *H*CTPP*H*.[18] **3H-2**, **3H-3**, and the keto form are the most stable tautomers at the MP2/6-31G(d) level. When we include the solvation free energy with isodensity surface polarized continuum model (IPCM) at the dielectric constant of THF,[19] **3H-3** is 4.3 and 2.8 kcal/mol lower in energy than **3H-2** and the keto, respectively. The computational result of **3H-3** as lowest energy form is in good agreement with the crystal structure parameters. The observation of peaks at 3426 and 1080 cm^{-1} in the IR spectrum of **1** provides further evidence of an enol form structure.

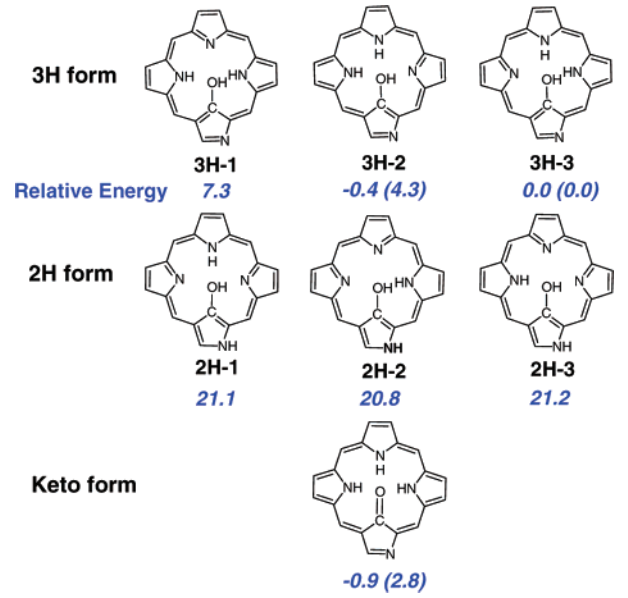

Figure 4. Relative energies (in kcal/mol, with respect to **3H-3**) of the tautomers of CTPP*OH* (**1**) at the MP2/6-31G(d) level. In parentheses are energies including solvation free energy of THF.

The dihydroxyl compound **2** crystallized in monoclinic space group $P2_1/n$ with four molecules in a unit cell.[20] A toluene that disordered into two positions was located in the crystal lattice. As depicted in Figure 5, the most intriguing part of the structure is the reaction on *meso* C13 atom to form a sp^3 carbon with a hydroxyl group substituted on the equatorial position and the phenyl ring tilted to nearly perpendicular to the mean porphyrin plane. The geometry of C13 is a distorted tetrahedron with an angle of 118.2(4)°

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[16] Crystal data for **1**: $C_{44}H_{30}N_4O$, $M_w = 630.72$, triclinic $P\bar{1}$, $a = 6.1556$ (6), $b = 10.6385(11)$, $c = 12.5323$ (13) Å, $V = 791.60(14)$ Å^3, $D_c = 1.323$ Mg/m^3, $Z = 1$, $R = 0.0676$, w$R = 0.1869$, GOF = 1.018 ($I > 2\sigma(I)$).

[17] All computations were performed using the Gaussian98 suite of programs.

[18] Ghosh, A.; Wondimagegn, T.; Nilsen, H. J. *J. Phys. Chem. B* **1998**, *102*, 10459.

[19] Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. J. *J. Phys. Chem.* **1996**, *100*, 16098.

[20] Crystal data for **2**: $C_{44}H_{30}N_4O_2{\cdot}0.5$ toluene, $M_w = 692.79$, monoclinic $P2_1/n$, $a = 6.6176$ (17), $b = 24.138(6)$, $c = 22.081$ (6) Å, $V = 3499.9$-(15) Å^3, $D_c = 1.315$ Mg/m^3, $Z = 4$, $R = 0.0582$, w$R = 0.0695$, GOF = 0.517 ($I > 2\sigma(I)$).

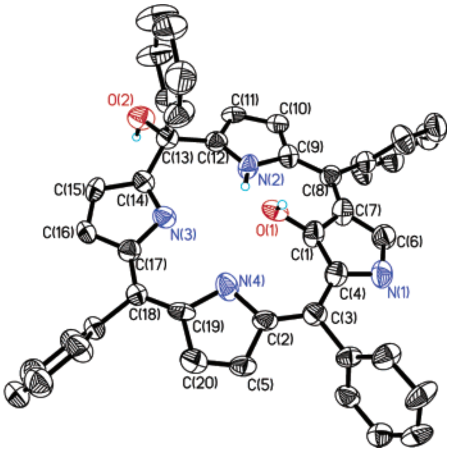

Figure 5. Structure of one of the enantiomers of CTPP(OH)$_2$ (**2**) in 50% ellipsoids.

for C14−C13−C12. The distance of 1.440(5) Å for C13−O2 is close to the C−O bond distance on methoxy-substituted isoporphyrin.[21] The inner core hydroxyl group is disordered into two positions with 50% occupancy on each site. The second site of the inner hydroxyl oxygen was located on the N4 pyrrole ring and suggested a cocrystallization of the enantiomers. The distance of 1.418(6) Å from O1 to C1 is significantly shorter than the corresponding distance in **1**. The shorter distance of the inner C−O bond suggests a higher degree of contribution of keto tautomer form. The porphyrin core of the macrocycle displays a roof-like geometry with atoms of C13 and C3 at the top deviated 0.550 and 0.183 Å, respectively, from the mean plane defined by the 24 atoms porphyrin plane. Interestingly, as shown in Figure 6, the porphyrins exhibit ladder-type polymeric chains in the crystal lattice linked by hydrogen bonding between two hydroxyl groups. Although the orientation of hydrogen atoms on hydroxyl groups cannot be precisely determined because of the disorder, the distance (2.812 Å between O1 and O2) and direction of hydroxyl groups strongly suggest hydrogen bonding interactions. In the ladder, the porphyrin rings partially overlap neighboring molecules with an averaged separation of 3.749 Å while the perpendicular phenyl rings sit nearly coplanar with each other.

In conclusion, two novel N-confused porphyrinoids, CTPP*OH* and CTPP(OH)$_2$, are isolated from the demetalation of M^{III}(*H*CTPP*O*)Br (M = Fe or Mn). Both porphyrinoids showed diminished aromaticity and split Soret bands. Theoretical calculation suggested that the keto form would have the lowest energy in the gas phase. However, the spectroscopic data as well as the solid-state crystal structure suggest that a 3H enol form is the isolated product. The further hydroxylation via nucleophilic addition of the OH$^-$ in the presence of base afforded the dihydroxylated CTPP(OH)$_2$. Presumably, the regioselectivity of **2** originates from the electron-donating ability of the inner hydroxyl group of **1**, which makes further nucleophilic attack on the *meso* carbons neighboring to the hydroxylated inverted pyrrole ring unlikely. The porphyrinoid **2** has a sp^3 *meso* carbon with the phenyl substituent tilted nearly perpendicular to the porphyrin plane. The solid state of the dihydroxylated product exhibits an unusual ladder polymeric chain linked by hydrogen bonding between the hydroxyl groups.

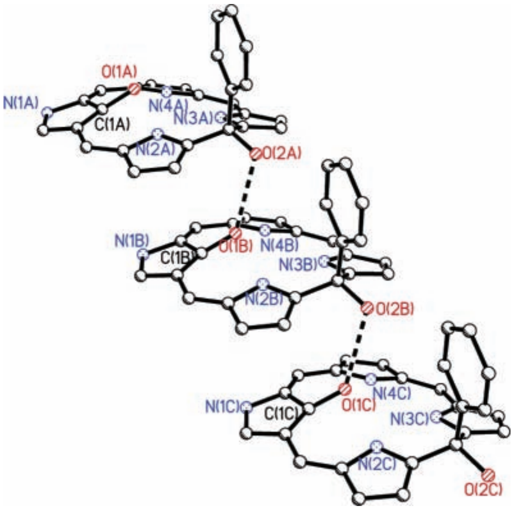

Figure 6. Polymeric chain of **2** linked by hydrogen bonding interactions between two hydroxyl groups. (Unrelated phenyl groups are omitted for clarity).

Acknowledgment. Support of this work by the National Science Council of Taiwan under Grant NSC 92-2113-M-018-003 (C.-H.H.) is gratefully acknowledged. NMR measurements were performed by Mrs. Mei-Yueh Chien at the Instrument Center, National Chung-Hsing University.

Supporting Information Available: Synthetic procedures and spectral data of CTPP(OH) (**1**) and CTPP(OH)$_2$ (**2**) and CIF files for the X-ray structural data of **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[21] Ema, T.; Senge, N. Y.; Ogoshi, H.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1879.