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The First Metal Chelation by a Neutral Porphyrin Analogue

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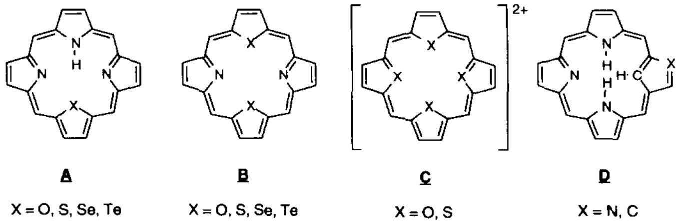
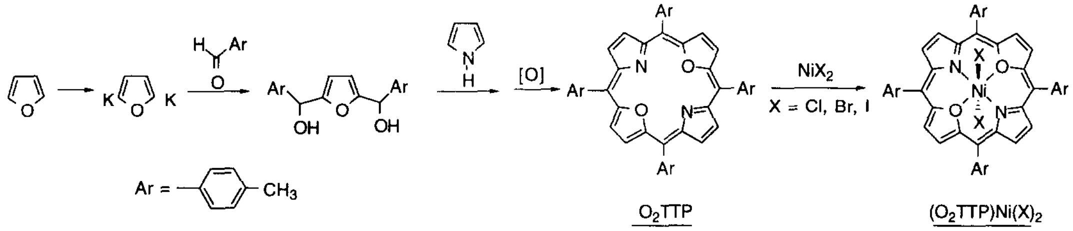
Abstract: The preparation and spectroscopic characterization of O_2TTP— a modified porphyrin in which the two NH groups are replaced by oxygen atoms— and its dihalonickel(II) complexes lead to the conclusion that 21,23-dioxaporphyrins are exceptionally well suited for metal complexation and for stabilization of divalent nickel in paramagnetic pseudo-octahedral geometries.

Porphyrins and the related chlorin and corrin rings are the major biological metal-binding macrocycles. The chelating core in these macrocycles— invariably consisted of four nitrogen atoms— is either diprotonic (porphyrins, chlorophylls) or monoprotonic (Vitamin B_{12}). A primary factor in governing the characteristics of metal ions is the identity of the atoms in their immediate coordination sphere. Accordingly, inner-core modified porphyrins, in which some of the macrocycle's nitrogens are replaced by other atoms, are receiving increased attention during the last years.[1] Thus, both the tetraoxa- and the most recently reported tetrathia-porphyrins (**C** in Scheme 1) display very interesting features.[2] These derivatives are however cationic and accordingly can not bind metal ions. The monoprotonic thiaporphyrins (**A**, X=S in Scheme 1)[3] and triprotonic carbaporphyrins (**D** in Scheme 1)[4] were shown to form metal complexes with some quite unique properties. For example, thiaporphyrins stabilize monovalent nickel,[5] and in the nickel(II) complex of carbaporphyrins the inner carbon atom is best described as a carbene.[6] For preparation of neutral porphyrine-like ligands, substitution of the two opposite NH's by group 16 (VI A) atoms (**B**, X = O, S, Se, Te in Scheme 1) seems most attractive. It was however shown that for X = S, Se, and Te, the inner core of these neutral macrocycles is too small to accommodate metal ions.[1a] Because of the similar size of nitrogen and oxygen, this should not be the case for X = O, i.e. 21,23-dioxaporphyrins. Surprisingly, there exists only one report of any 21,23-dioxaporphyrin, and attempts to insert metals into this very asymmetric derivative were not successful.[7]



Scheme 1

We report now the preparation of 21,23-dioxa-5,10,15,20-tetra-(4-tolyl)porphyrin (O_2TTP) and show that it readily binds metal ions. The methodology for preparation of the macrocycle followed the long established procedures for the synthesis of the related 21,23-dithia-5,10,15,20-tetraphenylporphyrin (S_2TPP),[8] as outlined in Scheme 2. Thus, double alkylation of the dianion of furan with *p*-tolualdehyde afforded the bis-alcohol **1**,[9] whose one-pot acid-catalyzed cyclocondensation with pyrrole[10] resulted in the desired product.[11] Characterization of O_2TTP was mainly based on the expected ^1H NMR features. Similar to S_2TPP and monooxatetraphenylporphyrin OTTPH,[12] both the furan and the pyrrole ring experienced a significant diamagnetic current due to the aromaticity of the macrocycle, somewhat larger for the furan than for the pyrrole ring (Table 1). The relative assignment of the furan and pyrrole CH protons was assured by synthesis of pyrrole-deuterated O_2TTP via the condensation of **1** with pyrrole-d_5.



Scheme 2

For metal insertion into O_2TTP we have decided to concentrate on nickel because of the following reasons: a) Nickel complexes have only one preferred oxidation state, Ni^{2+}. b) The complexes were anticipated to be paramagnetic, due to the pseudo-octahedral geometry enforced by occupation of all equatorial positions by the neutral macrocycle, leaving the axial positions for the anionic ligands. c) The ^1H NMR spectra of the related paramagnetic hexa-coordinated nickel(II) porphyrins are well resolved.[13] The consequence of these three factors is that structural characterization of the reaction products was expected to be relatively easy.

The reactions of O_2TTP with $Ni(Cl)_2$, $Ni(Br)_2$, and $Ni(I)_2$ in a mixture of 2-propanol and MeOH proceeded smoothly, and purification of the *trans*-dihalonickel(II) complexes— $(O_2TTP)Ni(Cl)_2$, $(O_2TTP)Ni(Br)_2$, and $(O_2TTP)Ni(I)_2$— required only one recrystallization.[14] All three products were stable both in the solid state and in non-coordinating solvents, but addition of alcohols or imidazole induced de-metallation. The structures of the complexes were easily elucidated from their magnetic moments and ^1H NMR spectra. Thus, the magnetic moments of 2.74, 2.71, and 2.69 B.M. for the chloro, bromo, and iodo complexes, respectively, correspond nicely to hexa-coordinated high-spin d^8 nickel(II). Both the paramagnetism and the high symmetry proposed for the $(O_2TTP)Ni(X)_2$ complexes were also apparent in the ^1H NMR spectra, as demonstrated in Figure 1 and Table 1. The protons of both the pyrrole— assigned by metallation of the above mentioned pyrrole-deuterated O_2TTP— and the furan rings were located at very low field due to paramagnetic interactions with the metal ion, while the observation of only one signal for each of the phenyl's *meta*-H and *ortho*-H were indicative of the high symmetry (D_{2h}).

NMR spectroscopy is known to be an excellent tool for determination of structural and electronic parameters of paramagnetic complexes.[13] In the present series, it can be safely concluded from the NMR spectra that the furan ring is coordinated to the metal in an η^1 fashion, without any serious out-of-plane tilting. This conclusion is based on the fact that the signals due to both the pyrrole and furan protons are paramagnetically shifted to low field. Contradistinctively, in paramagnetic nickel(II) complexes of carba-, thia-, and Nmethylporphyrins the modified-pyrrole's protons appear at high field. In these complexes, the corresponding rings are tilted out of the plane defined by the nitrogen atoms of the three regular pyrrole rings by as much as 50°.[15] Additional information about the nickel(II) complexes of O_2TTP is provided by the observation that the signals due to the pyrrole protons are noticeable broader and shifted to lower field than the furan protons (Figure 1). The isotropic shift— the difference in chemical shift of a particular proton between the para- and diamagnetic molecules— of pyrrole protons in high spin nickel(II) porphyrins is dominated by σ spin-transfer from the singly occupied $d_{x^2-y^2}$ orbital to the macrocycle. Relative linewidths in such complexes are inversely proportional to r^6, the metal-CH distance. Thus, the relative isotropic shifts clearly show that spin-transfer to pyrrole is more efficient than to furan, while the larger linewidth of the pyrrole CH's suggest that their distance from the metal is smaller than that of the furan. The effects of the halide anions on the NMR spectra of the complexes are also quite revealing. The comparison of $(O_2TTP)Ni(Cl)_2$, $(O_2TTP)Ni(Br)_2$, and $(O_2TTP)Ni(I)_2$ shows that the sum of the isotropic shifts experienced by the pyrrole and furan rings is reduced in the series— 70.2, 68.9, and 67.5 ppm, respectively— while the isotropic shift of the pyrrole CH's are progressively decreased (less shifted to low field) and that of the furan ring increased (Table 1). This reduces the differences in the isotropic shifts of the two rings from 13.8 ppm in $(O_2TTP)Ni(Cl)_2$ to 9.1 ppm in $(O_2TTP)Ni(I)_2$.

Table 1. ^1H NMR chemical shifts (δ, ppm) for O_2TTP and its nickel(II) complexes. Values in parentheses are isotropic shifts, the difference between identical protons in the nickel complexes and O_2TTP.

	pyrrole-H	*furan*-H	*ortho*-H	*meta*-H	*para*-CH_3
$(O_2TTP)Ni(Cl)_2$	50.39 (42.00)	37.31 (28.18)	8.75 (0.71)	7.67 (0.14)	2.85 (0.18)
$(O_2TTP)Ni(Br)_2$	48.85 (40.46)	37.52 (28.39)	8.59 (0.55)	7.80 (0.27)	2.80 (0.13)
$(O_2TTP)Ni(I)_2$	46.66 (38.27)	38.30 (29.17)	8.45 (0.41)	7.76 (0.23)	2.78 (0.11)
O_2TTP	8.39	9.13	8.04	7.53	2.67

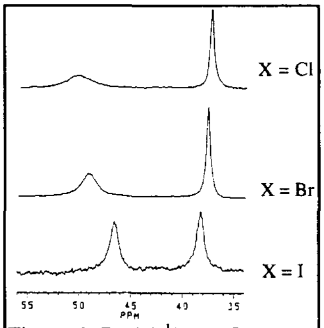


Figure 1. Partial ^1H NMR spectra of the $(O_2TTP)Ni(X)_2$ complexes, emphasizing the pyrrole (lower field) and furan protons.

All these phenomena are understandable by simple ligand field and molecular orbital considerations. The major interaction responsible for the isotropic shifts of the pyrrole and furan protons is between electrons in the high-energy $d_{x^2-y^2}$ metal orbital and the low-energy O and N sp orbitals of O_2TTP. The larger spin-transfer into the pyrrole ring is most probably due to the fact that sp(N) is higher in energy than sp(O), and accordingly in stronger interaction with $d_{x^2-y^2}$. An increase in the axial Ni-X bond length (I > Br > Cl) leads to larger splitting of the d_σ orbitals by lowering the energy of d_{z^2} and increasing that of $d_{x^2-y^2}$. A larger difference in energy between the singly occupied $d_{x^2-y^2}$ and the doubly occupied O and N sp orbitals will lead to less ligand character in the σ^* combination, thus explaining the reduced total isotropic shift in $(O_2TTP)Ni(I)_2$. The trend toward more equal spin transfer into the pyrrole and furan rings by moving from $(O_2TTP)Ni(Cl)_2$ to $(O_2TTP)Ni(I)_2$ has probably the same origin, as it seems reasonable that as the energy of the $d_{x^2-y^2}$ orbital increases (I > Br > Cl), the difference between the $d_{x^2-y^2} \pm sp(O)$ and $d_{x^2-y^2} \pm sp(N)$ combinations becomes smaller. Thus, in the absence of crystallographic data for the nickel complexes, NMR spectroscopy provides very useful information about their structural and electronic properties.

Concluding, this is the first report of metal complexes of any porphyrin derivative in which two of the inner nitrogens are replaced by heteroatoms.[16] In sharp contrast to all other paramagnetic metal complexes of inner-core modified porphyrins, the furan rings are not severely deviating from the main plain of the macrocycle. This feature and the neutrality of the macrocycle were shown to affect stabilization of the high-spin nickel(II) pseudo-octahedral coordination geometry, unfavored for the related nickel porphyrins. Ongoing attention in our laboratory is given to other metal complexes of O_2TTP, such as palladium(II), platinum(II), and the iron triad.

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11. 0.16 g (0.2 mmol, 16% yield) of O_2TTP were obtained from 1.54 g (5 mmol) **1** and 0.35 g (5.2 mmol) pyrrole applying the Lindsey procedure.[10] Elution with $CH_2Cl_2/EtOAc$ (9:1), followed by a second chromatographic treatment with $CH_2Cl_2/EtOAc/Et_3N$ (7.0/2.9/0.1) and recrystallization from $CHCl_3$/hexane afforded the desired product, O_2TTP, as purple solid.R_f = 0.56 (alumina, $CH_2Cl_2/EtOAc/Et_3N$ 7/2.9/0.1); UV-Vis (CH_2Cl_2): λ_{max} (log ε) = 420 (4.90), 496 (4.17), 524 (4.11) nm; The ^1H NMR (200 MHz, CD_2Cl_2) data is presented in Table 1.
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14. A hot solution of 21.8 mg (35 μmol) O_2TTP in 2 mL 2-propanol was added dropwise to a hot solution of the appropriate dry Ni(II) halide (9.5-12.5 mg, 40 μmol) in a mixture of 3 mL 2-propanol and 2 mL MeOH and heated under N_2 for additional 3-5 hours, followed by solvent evaporation and recrystallization from $CHCl_3$/heptane. The isolated yields were 51, 70, and 65%, for the chloro, bromo, and iodo complexes, respectively. The ^1H NMR (200 MHz, $CDCl_3$) data for all three complexes is presented in Table 1. The magnetic moments were determined in CH_2Cl_2 solutions by the Evans' method (Evans, D. F. *J. Chem. Soc.* **1959**, 2003). Other physical data: $(O_2TTP)Ni(Cl)_2$: MS^- (DCI, isobutane): *m/z* (%) (clusters with characteristic Ni and Cl isotopes): 764.9 (83%) [M^- -Cl], 729.9 (100) [M^- -2Cl], 674.0 (40) [M^- -2Cl, -Ni]; UV-Vis (CH_2Cl_2): λ_{max} (log ε) = 416 (5.18), 498 (4.41), 528 (3.97) nm. $(O_2TTP)Ni(Br)_2$: MS^- (DCI, isobutane): *m/z* (%) (clusters with characteristic Ni and Br isotopes): 810.9 (100) [M^- -Br], 730.0 (55) [M^- -2Br], 674.0 (10) [M^- -2Br, -Ni]; UV-Vis (CH_2Cl_2) λ_{max} (log ε) = 418 (5.26), 502 (4.6), 534 (4.23) nm. $(O_2TTP)Ni(I)_2$: MS^- (DCI, isobutane): *m/z* (%) (clusters with characteristic Ni isotopes): 856.7 (100) [M^- -I], 729.9 (38) [M^- -2I], 674.0 (5) [M^- -2I, -Ni]; UV-vis (CH_2Cl_2): λ_{max} (log ε) = 410 (5.03), 484 (4.25) nm.
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16. It was recently brought to our attention that work describing dichloronickel(II) complexes of dioxaporphyrins is *in press* in *Chem. Eur. J.*.

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