Effect of Ring Configuration on Axial Ligand Binding to Nickel(II) Octaethylisobacteriochlorins

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Introduction

Tetrapyrrolic macrocycles serve as the functional groups in a wide variety of biological systems. These macrocycles are involved in activities that include oxygen binding and transport, electron transfer, catalysis, and light harvesting.[1,2] Recently, there has been considerable interest in how the conformations of nonplanar tetrapyrrolic rings influence their functional characteristics.[3-5] For example, Barkigia et al. have shown that the optical and redox properties of zinc(II) porphyrins are strongly perturbed by distortions from planarity.[3c,d] Highly nonplanar macrocycles exhibit Q bands that are $\sim$1500 cm^{-1} to the red of less distorted rings. The former species are also $\sim$200 mV easier to oxidize than the latter. Shiemke et al. have found that the axial ligand binding affinity of cofactor F_{430} of methylreductase is larger by a factor of $\sim$40 than that of a closely related configurational isomer (the 12,13-diepimer).[4b] Conformation-dependent changes of this magnitude in the absorption characteristics, redox potentials, or ligand binding affinities could profoundly influence the functional behavior of biologically active tetrapyrrolic ring systems.

The nickel complexes of *trans*-octaethylisobacteriochlorin, Ni(OEiBC) (and related macrocycles), have frequently been used as a model systems for cofactor F_{430}.[3a,c,4] The tetrahydroporphyrin ring system supports the formation of a Ni(I) species[6] which is thought to be an intermediate in the turnover of methyl reductase.[8] Spectroscopic and reactivity studies on Ni(OEiBC) and other metallo(OEiBC) complexes have typically been conducted on mixtures containing nearly equal amounts of the two different configurational isomers of *trans*-OEiBC.[6,9-12] These two isomers differ in the configuration of the trans-ethyl substituents on one saturated pyrrole ring versus the other (trans–trans–trans vs trans–cis–trans).[13] X-ray crystallographic studies of Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) indicate that both isomers are highly nonplanar; however, the degree of distortion is similar for the two macrocycles (the average deviation of the 24-atom skeleton is 0.455 Å for Ni(*ttt*-OEiBC) and 0.428 Å for Ni(*tct*-OEiBC[13b]). Given these structural similarities,[14] the utilization of mixtures of Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) seems inherently reasonable because it might be suspected that the physicochemical properties of the two forms should also be similar. In this connection, we have been examining the electronic and vibrational properties of Ni(OEiBC) and other metallo(OEiBC) complexes.[11] In the course of these studies, we have found that the axial ligand binding capabilities of Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) are in fact quite different. In this note, we report the results of these latter studies.

Experimental Section

Free base *trans*-OEiBC was synthesized and purified as described in ref 9a. Insertion of Ni(II) was accomplished as described in ref 6c. Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) were separated on a MgO column by using a 1:1 mixture of benzene–hexanes as the eluent. The latter isomer is the faster moving component as described in ref 16. Resonance Raman (RR) spectra were acquired as described in ref 11b,c. Ligand binding curves were obtained by sealing a degassed sample of Ni(OEiBC) in toluene in an optical cell and adding 100 μL aliquots of degassed pyridine (piperidine) from a calibrated syringe. A large number of spectra were taken over a wide range of ligand concentrations; for pictorial clarity, only five representative curves are shown for each isomer in Figure 3. The equilibrium constants for ligand binding (K_{eq}) were obtained by simulating the absorption spectra and fitting the data to the relation $K_{eq} = [Ni(OEiBC)L_2]/[NiOEiBC][L]^2$.

Results and Discussion

The absorption spectra of four-coordinate Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) are shown in Figure 1. The spectra are essentially identical except for a slight red-shift ($\sim$2 nm) of the Q_y-band maximum of the former complex versus the latter. The RR spectra of four-coordinate Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) are shown in Figure 2. As can be seen, the frequencies of the structure-sensitive skeletal modes are essentially identical for the two isomers. The absorption (and RR) spectra of six-coordinate Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) are also essentially indistinguishable (not shown). These spectra are, however, distinctively different from those of the four-coordinate species because the binding of axial ligands changes the spin state of the Ni(II) ion.[11c] The absorption changes that occur upon titrating Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) with pyridine are shown in Figure 3. As the pyridine concentration increases, the Soret absorption maximum

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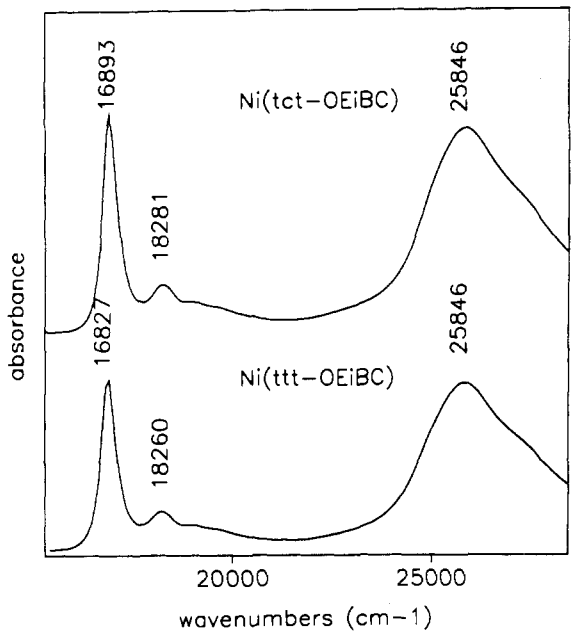

Figure 1. Absorption spectra of Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) in toluene at room temperature.

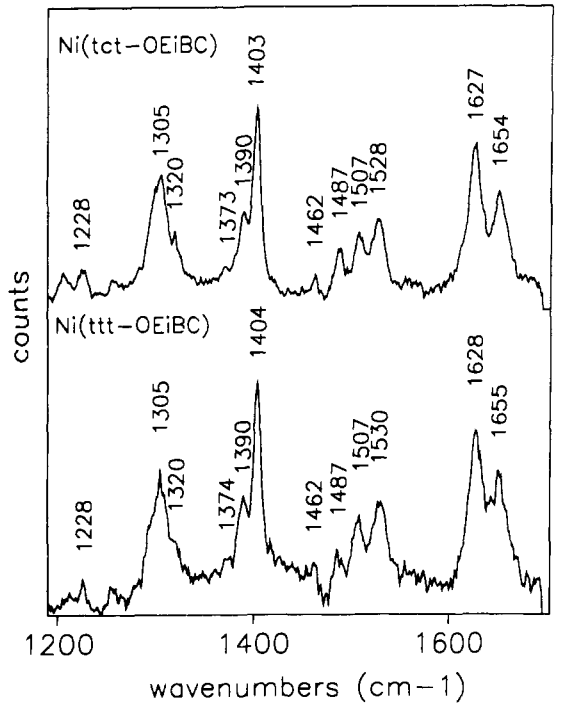

Figure 2. Visible-excitation (λ_{ex} = 552 nm) resonance Raman spectra of Ni(*ttt*-OEiBC) and Ni(*tct*-OEiBC) in toluene at room temperature.

shifts from ~25 900 cm^{-1} to ~25 000 cm^{-1}. The titration curves for both isomers exhibit several isosbestic points and vary quadratically (as expected[5a]) with the concentration of axial base. However, with the same concentration of base, it is clear that the spectrum of the six-coordinate species is far more developed for Ni(*ttt*-OEiBC) than for Ni(*tct*-OEiBC). Titrations with pyridine and piperidine indicate that the equilibrium constants for both bases are relatively small; however, the binding constants for Ni(*ttt*-OEiBC) [K_{eq}(pyridine) = 0.18 ± 0.02 M^{-2}; K_{eq}(piperidine) = 17.5 ± 1.8 M^{-2}] are 4–6 times larger than those for Ni(*tct*-OEiBC) [K_{eq}(pyridine) = 0.048 ± 0.006 M^{-2}; K_{eq}(piperidine) = 2.8 ± 0.2 M^{-2}]. The resulting free energy differences for ligand binding to Ni(*tct*-OEiBC) versus Ni(*ttt*-OEiBC) are in the range $\Delta\Delta G$ ~ 0.8–1.1 kcal/mol. These $\Delta\Delta G$'s are quite large considering the similarities in the vibrational and electronic properties of the two configurational isomers.

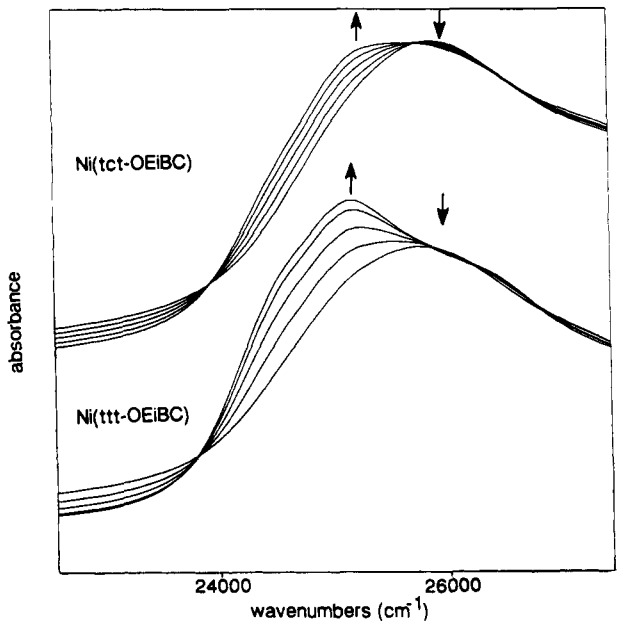

Figure 3. Soret absorption spectra of Ni(*ttt*-OEiBC) (3.3×10^{-6}) and Ni(*tct*-OEiBC) (5.8×10^{-6} M) in toluene:pyridine mixtures. The pyridine concentrations are 0.62, 1.2, 1.7, 2.1, and 2.5 M.

The origin of the enhanced ligand-binding capabilities of Ni(*ttt*-OEiBC) versus Ni(*tct*-OEiBC) is not immediately apparent. It is possible that steric constraints imposed by the orientation of the ethyl groups on the saturated pyrrole rings are different for the two forms. In this regard, both faces of Ni(*ttt*-OEiBC) are nominally equivalent whereas the two faces of Ni(*tct*-OEiBC) are inequivalent. For the latter isomer, the ethyl group orientation makes one face more accessible than the other. [The more accessible face of Ni(*tct*-OEiBC) is presumably also more accessible than either face of Ni(*ttt*-OEiBC).] The relative inaccessibility of one face of Ni(*tct*-OEiBC) could impede the binding of the second axial ligand. However, this explanation is not particularly satisfactory because the ethyl groups are not large enough to significantly screen the ligand binding site(s).

Another possible origin for the different ligand binding capabilities of the two configurational isomers is that their conformations and/or degrees out-of-plane distortion are different in solution. However, the fact that the electronic and vibrational spectra of the two isomers in the four-coordinate state are quite similar as are those of the two isomers in the six-coordinate state suggests that the conformations of the two four (six)-coordinate species are similar in solution. It must be emphasized, however, that the spectral properties of the four- versus six-coordinate species are quite different.[11c] This is expected because the macrocycle must become more planar upon binding two axial ligands. Collectively, these observations suggest that the difference in ligand binding affinities of the two configurational isomers lies in the detailed characteristics of the conformational potential energy surfaces. In particular, different ligand binding affinities would result if one configurational isomer energetically favors a non-planar conformation (four-coordinate species) over a planar conformation (six-coordinate species) more than does the other isomer. Regardless, of the exact origin of the altered ligand binding capabilities, the results herein exemplify the fact that relatively subtle changes in the structure of tetrapyrrolic macrocycles can significantly alter their reactivity. This in turn has important implications for the functional characteristics of both synthetic and natural nickel-containing macrocycles.

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