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Dissociation Energies and Charge Distribution of the Co−NO Bond for Nitrosyl-α,*β*,*γ*,*δ*-tetraphenylporphinatocobalt(II) and Nitrosyl-α,*β*,*γ*,*δ*-tetraphenylporphinatocobalt(III) in Benzonitrile Solution

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Abstract: The first two series of Co−NO bond dissociation enthalpies in benzonitrile solution were determined for 12 cobalt(II) nitrosyl porphyrins and for 12 cobalt(III) nitrosyl porphyrins by titration calorimetry with suitable thermodynamic cycles. The results display that the energy scales of the heterolytic $Co^{III}-NO$ bond dissociation, the homolytic $Co^{III}-NO$ bond dissociation, and the homolytic $Co^{II}-NO$ bond dissociation are 14.7−23.2, 15.1−17.5, and 20.8−24.6 kcal/mol in benzonitrile solution, respectively, which not only indicates that the thermodynamic stability of cobalt(II) nitrosyl porphyrins is larger than that of the corresponding cobalt(III) nitrosyl porphyrins for homolysis in benzonitrile solution but also suggests that both cobalt(III) nitrosyl porphyrins and cobalt(II) nitrosyl porphyrins are excellent NO donors, and in addition, cobalt(III) nitrosyl porphyrins are also excellent NO^+ contributors. Hammett-type linear free energy analyses suggest that the nitrosyl group carries negative charges of 0.49 ± 0.06 and 0.27 ± 0.04 in $T(G)PPCo^{II}NO$ and in $T(G)PPCo^{III}NO$, respectively, which indicates that nitric oxide is an electron-withdrawing group both in $T(G)PPCo^{II}NO$ and in $T(G)PPCo^{III}NO$, behaving in a manner similar to Lewis acids rather than to Lewis bases. The energetic and structural information disclosed in the present work is believed to furnish hints to the understanding of cobalt nitrosyl porphyrins' biological functions in vivo.

Introduction

The discoveries that nitric oxide serves important roles in mammalian bioregulation of functions such as vasodilation, bronchodilation, and neurotransmission[1] have stimulated intense interest in the chemistry and biochemistry of NO and derivatives such as metal nitrosyl complexes.[2] Especially of interest are nitrosylmetalloporphyrin complexes that can serve to deliver NO to biological targets on demand.[3] Studies into the binding of nitric oxide (NO) by metalloporphyrins would have aided our understanding of how NO interacts with heme-containing biomolecules, such as hemoglobin, myoglobin, and soluble guanylate cyclase.[4,5] Many iron nitrosyl porphyrins have been examined as model compounds during such studies,[6] but other metalloporphyrins such as cobalt porphyrins are also known to form nitrosyl derivatives.[7] The substitution of iron by cobalt in heme and synthetic porphyrins has also gained prominent attention in a biological setting; for example, cobalt nitrosyl

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porphyrin has been explored as an isoelectronic model for oxygenated protoheme.[8] In fact, the NO adducts of cobalt-substituted myoglobin and hemoglobin are also known.[9] Injection of cobalamin Cbl(III) in rodents can prevent and reverse pathological results caused by an overproduction of NO.[10] Cbl(III) can quench NO-mediated inhibition of leukemia cell proliferation[11] and prevent and reverse the relaxation of isolated smooth muscle by NO and NO-donating compounds.[12] Addition of an i.v. dose of Cbl(III) to intact conscious dogs significantly increased resistance to blood flow, which was suggested to result from interference with endogenous NO.[13] Such biological effects have been interpreted to result from the formation of Cbl(III)−NO from Cbl(III) and NO.[12,13] Importantly some cobalt nitrosyl porphyrins such as (protoporphyrin-IX)Co(NO) were found to activate soluble guanylate cyclase to a greater extent than do the Fe and Mn analogues.[14] Since cobalt tetraphenylporphyrins can act as model compounds for cobalamins and especially vitamin B_{12} and because cobalt nitrosyl porphyrins are present and because of their biological importance in vivo,[15] development of the Co−NO bond energy scale in solution for a series of cobalt nitrosyl porphyrins has been a strategy goal in our research program for a long time.

In our previous papers,[16] we have conducted a study on heterolytic and homolytic Y−NO bond (Y = N, O and S) dissociation energies for a series of *alpha* π-acceptor-bearing N-, O-, and S-nitroso compounds. In this paper, we wish to report the first direct determination for the Co−NO bond dissociation energies of nitrosyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatocobalt(II) [T(G)PPCo^{II}NO] and nitrosyl-$\alpha,\beta,\gamma,\delta$-tetraphenylporphinatocobalt(III) [T(G)PPCo^{III}NO] in benzonitrile solution in terms of calorimetric measurement of cation (NO^+) and T(G)-PPCo^{II} coordination incorporated with electrochemistry through a thermodynamic cycle and clarify the nature of the Co−NO bond in T(G)PPCo^{II}NO and T(G)PPCo^{III}NO using Hammett-type linear free energy analyses.

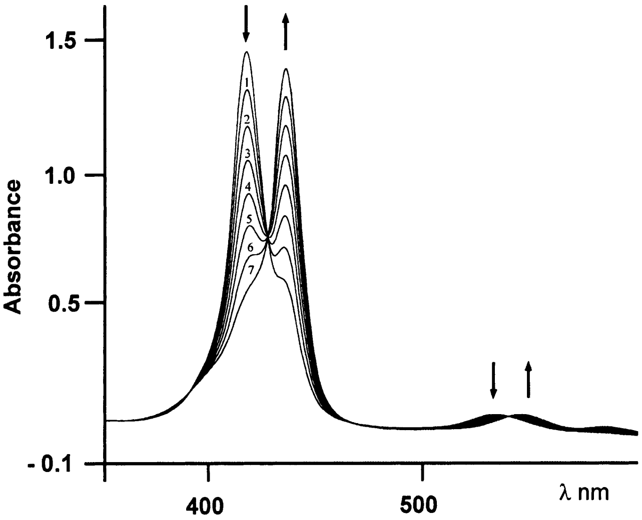

Figure 1. Absorption spectral changes observed for a benzonitrile solution of 2.25×10^{-6} M T(*p*-OCH_3)PPCo^{II} at various NO^+ concentrations (see the arrows in the figure). Initial: $[NO^+] = 0.25 \times 10^{-6}$ M; **1**: $[NO^+] = 0.50 \times 10^{-6}$ M; **2**: $[NO^+] = 0.75 \times 10^{-6}$ M; **3**: $[NO^+] = 1.0 \times 10^{-6}$ M; **4**: $[NO^+] = 1.25 \times 10^{-6}$ M; **5**: $[NO^+] = 1.5 \times 10^{-6}$ M; **6**: $[NO^+] = 1.75 \times 10^{-6}$ M; **7**: $[NO^+] = 2.0 \times 10^{-6}$ M.

Results and Discussion

T(*p*-OCH_3)PPCo^{II} reacts with NO^+ to yield T(*p*-OCH_3)PPCo^{III}-NO,[17] which is subjected to UV−vis analysis to exhibit peaks at 419 and 535 nm for T(*p*-OCH_3)PPCo^{II} and peaks at 438 and 545 nm for T(*p*-OCH_3)PPCo^{III}NO in benzonitrile solution. Figure 1 shows the absorption spectral changes observed for a benzonitrile solution of 2.25×10^{-6} M T(*p*-OCH_3)PPCo^{II} at various NO^+ concentrations. With the increase of $[NO^+]$, the electron spectra showed a decrease in absorbance at 419 and 535 nm with a concomitant increase at 438 and 545 nm and gave two good isosbestic points suggesting a 1:1 stoichiometry of the reaction of T(*p*-OCH_3)PPCo^{II} with NO^+ that can be simply expressed as eq 1. Obviously, according to reaction 1, the heterolytic Co^{III}−NO bond dissociation energy of T(*p*-OCH_3)PPCo^{III}NO is just equal to the reaction enthalpy change (ΔH_{rxn}) of T(*p*-OCH_3)PPCo^{II} with NO^+ simply by switching the sign of ΔH_{rxn} (eq 5),[18] and the latter can be directly determined by titration calorimetry. The homolytic Co^{III}−NO and Co^{II}−NO bond dissociation energies of T(G)PPCo^{III}NO and T(G)PPCo^{II}NO can be obtained according to eqs 6 and 7, which were derived from the suitable thermodynamic cycles as shown in Schemes 1, respectively. It should be pointed out herein that we used the term free energy change ΔG_{eT} to replace the enthalpy change ΔH_{eT} in eqs 6 and 7 for the electron transfer processes. The validation of using free energy change ΔG_{eT} instead of enthalpy change ΔH_{eT} for electron transfer processes is that entropies associated with electron transfer are negligible,

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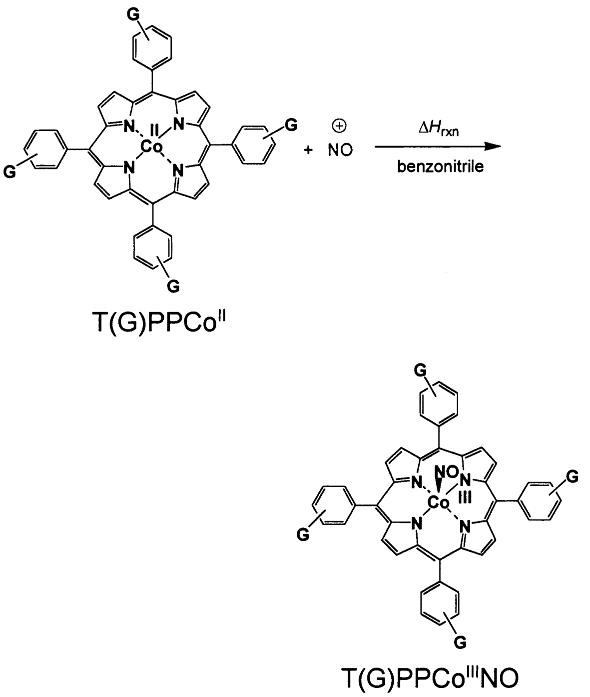
[18] In Figure 1, T(*p*-OCH_3)PPCo^{II} in benzonitrile solution gives peaks at 419 and 535 nm, which are close to the corresponding characteristic absorption peaks of free T(*p*-OCH_3)PPCo^{II} in toluene at 417 and 531 nm, respectively, suggesting that no coordination effects of benzonitrile as an axial ligand on T(*p*-OCH_3)PPCo^{II} occur in the benzonitrile solution of T(*p*-OCH_3)PPCo^{II}, which is also supported by Walker and Kadish's work.[27] Since benzonitrile does not coordinate to T(*p*-OCH_3)PPCo^{II}, the heterolytic Co^{III}−NO bond dissociation energy of T(*p*-OCH_3)PPCo^{III}NO in benzonitrile solution unambiguously is equal to the reaction enthalpy change (ΔH_{rxn}) of T(*p*-OCH_3)PPCo^{II} with NO^+ simply by switching the sign of ΔH_{rxn}.

and ΔG_{eT} can be combined directly with ΔH_{eT}, which has been verified by Arnett's work.[19]



(1)

The three types of Co−NO bond dissociation energy investigated in this study are the following:

$$T(G)PPCo^{III}NO \rightarrow T(G)PPCo^{II} + NO^{+} \qquad \Delta H_{het}(Co^{III}-NO) = ? \quad (2)$$

$$T(G)PPCo^{III}NO \rightarrow T(G)PPCo^{III} + NO \qquad \Delta H_{homo}(Co^{III}-NO) = ? \quad (3)$$

$$T(G)PPCo^{II}NO \rightarrow T(G)PPCo^{II} + NO \qquad \Delta H_{homo}(Co^{II}\text{-}NO) = ? \quad (4)$$

where G = p-OCH_3, p-CH_3, H, p-Cl, p-Br, p-NO_2, p-iPr, m-OCH_3, m-CH_3, m-Cl, m-Br, and m-NO_2, and the Roman numeral indicates the charge on the cobalt.

$$\Delta H_{het}(Co^{III}-NO) = -\Delta H_{rxn} \quad (5)$$

$$\Delta H_{homo}(Co^{III}-NO) = \Delta H_{het}(Co^{III}-NO) - 23.06[E_{1/2}(NO^{+}/NO) - E_{1/2}(TPPCo^{II})] \quad (6)$$

$$\Delta H_{homo}(Co^{II}-NO) = \Delta H_{het}(Co^{III}-NO) - 23.06[E_{1/2}(NO^{+}/NO) - E_{1/2}(TPPCo^{II}NO)] \quad (7)$$

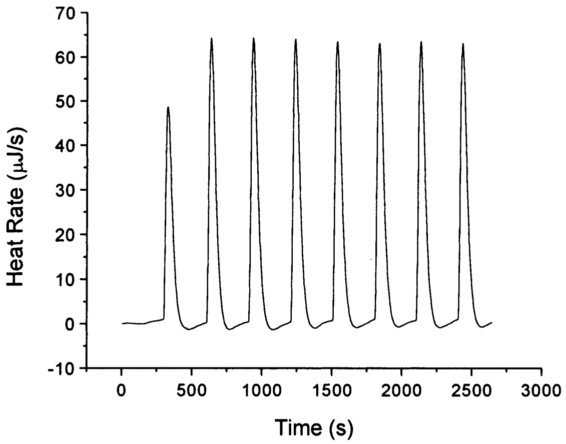


Figure 2. Isothermal titration calorimetry (ITC) for the reaction of $NO^{+}ClO_4^{-}$ with T(p-CH_3)$PPCo^{II}$ in benzonitrile solution at 25 °C. Titration was conducted by adding 10 μL of $NO^{+}ClO_4^{-}$ (2.24 mM) every 300 s into the benzonitrile solution containing T(p-CH_3)$PPCo^{II}$ (1.37 mM).

Table 1. Reaction Heat of $NO^{+}ClO_4^{-}$ with $T(G)PPCo^{II}$ (kcal/mol) along with Redox Potentials of $T(G)PPCo^{II}$ and $T(G)PPCo^{II}NO$ in Benzonitrile Solution

no.	substituent (G)	$-\Delta H_{rxn}$[a]	$E_{1/2}(T(G)PPCo^{II}NO)$[b]	$E_{1/2}(T(G)PPCo^{II})$[c]
1	p-OCH_3	23.2	0.887	0.581
2	p-CH_3	21.9	0.923	0.621
3	p-iPr	21.9	0.925	0.608
4	m-CH_3	20.8	0.945	0.646
5	p-H	20.3	0.962	0.676
6	m-OCH_3	20.1	0.967	0.684
7	p-Cl	18.5	1.014	0.731
8	p-Br	18.9	1.015	0.733
9	m-Cl	18.1	1.055	0.772
10	m-Br	17.5	1.058	0.775
11	m-NO_2	14.7	1.105	0.844
12	p-NO_2	14.1	1.131	0.872

[a] Measured in benzonitrile solution at 25 °C in kcal/mol by titration calorimetry. The data given are average values of at least two independent runs, each of which was again an average value of 7 consecutive titrations. The reproducibility was ≤0.4 kcal/mol. [b,c] Measured in benzonitrile solution at 25 °C in volts by CV vs ferrocenium/ferrocene redox couple. Reproducible to 5 mV or better.

The titration calorimetry was performed in benzonitrile solution at 25 °C on a CSC 4200 isothermal titration calorimeter. Prior to use, the instrument was calibrated against an internal heat pulse, and the functional response was verified by determination of the heat of dilution of a concentrated sucrose solution and comparison with the literature value.[20] The reaction heat was determined following eight automatic injections and obtained by area integration of each peak except the first one (calibration graph, see Figure 2). Twelve reaction heats ($-\Delta H_{rxn}$) of $T(G)PPCo^{II}$ with NO^{+} in benzonitrile solution and redox potentials of $T(G)PPCo^{II}$ and $T(G)PPCo^{II}NO$ in benzonitrile solution are listed in Table 1. Heterolytic and homolytic Co^{III}−NO bond dissociation energies for $T(G)PPCo^{III}NO$ and homolytic Co^{II}−NO bond dissociation energies for $T(G)PPCo^{II}NO$ as well as the free energy changes of one-electron transfer from $T(G)PPCo^{II}$ to NO^{+} to form $T(G)PPCo^{III}$ and NO are summarized in Table 2.

Table 2 shows that $\Delta H_{het}(Co^{III}-NO)$'s, $\Delta H_{homo}(Co^{III}-NO)$'s of 12 $T(G)PPCo^{III}$−NO, and $\Delta H_{homo}(Co^{II}-NO)$'s of 12 $T(G)PPCo^{II}$−NO in benzonitrile solution cover a range of 14.1−23.2 kcal/mol (henceforth abbreviated as kcal), a range of 15.1−17.5 kcal, and a range of 20.8−24.6 kcal, respectively. Comparing the $\Delta H_{het}(Co^{III}-NO)$'s, $\Delta H_{homo}(Co^{III}-NO)$'s, and $\Delta H_{homo}(Co^{II}-NO)$'s with those of the N−NO bonds in N-nitrosophenylureas [ΔH_{het}(N−NO) of 52.4−62.0 kcal, ΔH_{homo}(N−NO) of 23.1−33.1 kcal],[16b−d] those of the O−NO bonds in O-nitrosobenzoates [ΔH_{het}(O−NO) of 25.7−32.3 kcal,

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Table 2. Heterolytic and Homolytic $Co^{III}-NO$ and $Co^{II}-NO$ Bond Dissociation Energies (kcal/mol) of $T(G)PPCo^{III}NO$ and $T(G)PPCo^{III}NO$ along with Free Energy Change of One-Electron Transfer from $T(G)PPCo^{II}$ to NO^+ (kcal/mol) in Benzonitrile Solution[21]

no.	substituent	ΔH_{het} (Co^{III}–NO) [a]	ΔH_{homo} (Co^{III}–NO)[b]	ΔH_{homo} (Co^{II}–NO)[c]	ΔG_{eT}[d]
1	*p*-OCH_3	23.2	17.5	24.6	−5.7
2	*p*-CH_3	21.9	17.2	24.1	−4.7
3	*p*-*i*Pr	21.9	16.9	24.2	−5.0
4	*m*-CH_3	20.8	16.6	23.5	−4.2
5	*p*-H	20.3	16.8	23.4	−3.5
6	*m*-OCH_3	20.1	16.8	23.3	−3.3
7	*p*-Cl	18.5	16.3	22.8	−2.2
8	*p*-Br	18.9	16.7	23.3	−2.2
9	*m*-Cl	18.1	16.8	23.4	−1.3
10	*m*-Br	17.5	16.3	22.8	−1.2
11	*m*-NO_2	14.7	15.1	20.8	0.4
12	*p*-NO_2	14.1	15.2	21.1	1.1

[a] Taken as $-\Delta H_{rxn}$ (from eq 5). The data given are average values of at least two independent runs, each of which was again an average value of 7 consecutive titrations. The reproducibility is $\leq$0.4 kcal/mol. [b,c] Derived from eqs 6 and 7 from Scheme 1, taking $E_{1/2}(NO^+/NO) = 0.8265$ V vs $Fc^{+/0}$ in benzonitrile solution. Uncertainty is estimated to be $\leq$0.5 kcal/mol. [d] Free energy change of one-electron transfer from $T(G)PPCo^{II}$ to NO^+ in benzonitrile solution, which was approximately equal to the difference between ΔH_{homo} and ΔH_{het} for the $Co^{III}-NO$ bond.

$\Delta H_{homo}(O-NO)$ of 32.5−38.6 kcal],[16e] and those of the S−NO bonds in *S*-nitrosophenylthiols [$\Delta H_{het}(S-NO)$ of 38.7−55.0 kcal, $\Delta H_{homo}(S-NO)$ of 18.0−25.9 kcal][16a] demonstrates that the Co−NO bonds in both $T(G)PPCo^{III}NO$ and $T(G)PPCo^{II}NO$ are much weaker than the N−NO and O−NO bonds in terms of heterolysis or homolysis, but the strength of the $Co^{II}-NO$ bond is close to that of the S−NO bond for homolysis.[22] These results indicate that both cobalt(III) nitrosyl porphyrins and cobalt(II) nitrosyl porphyrins are a better NO donor than the series of *alpha* π-acceptor-bearing N-, O-, and S-nitroso compounds,[16] and additionally, the former is also a better NO^+ contributor than the N-, O-, and S-nitroso compounds, which not only supports the previously experimental observation that cobalt nitrosyl porphyrins can activate nitric oxide in its transfer process in vivo[14] but also provides guidance on the direction of NO transfer among different NO carries (such as N, O, S, and Co) in vivo.

Examining ΔH_{het}'s of $Co^{III}-NO$ and the corresponding ΔH_{homo}'s of $Co^{III}-NO$ in columns 3 and 4 in Table 2, we found that the ΔH_{het}'s of $Co^{III}-NO$ are generally larger than the corresponding ΔH_{homo}'s of $Co^{III}-NO$, but the difference is not large, which is remarkably different from the cases of N−NO, O−NO, and S−NO bond dissociations mentioned above. Inspecting of the relationship of ΔH_{het}'s and ΔH_{homo}'s of $Co^{III}-NO$ with the remote substituent G in detail, it is interesting to find that when the substituent G is an electron-donating group (EDG) or a weak electron-withdrawing group (EWG), the ΔH_{het} of $Co^{III}-NO$ is larger than the corresponding ΔH_{homo} of $Co^{III}-NO$, but when the substituent G is a strong EWG (such as NO_2), the ΔH_{het}'s of $Co^{III}-NO$ become smaller than the corresponding ΔH_{homo}'s. This result suggests that when the substituent G is a EDG or weak a EWG, $T(G)PPCo^{III}NO$ has good $NO^\bullet$-releasing property, but when the substituent G is a strong EWG, the $T(G)PPCo^{III}NO$ becomes a good donator of the cation NO^+. The reason is that when the substituent G is a EDG or a weak EWG, the oxidation potential of $T(G)PPCo^{II}$ is smaller than the reduction potential of NO^+ ($E_{1/2}(NO^+/NO) = 0.8265$ V vs $Fc^{+/0}$), which, of course, results in one-electron transfer from $T(G)PPCo^{II}$ to NO^+ to yield the products that were formed directly by homolytic $CO^{III}-NO$ bond dissociation. However, when the substituent G is a strong EWG, the oxidation potential of $T(G)PPCo^{II}$ becomes larger than the reduction potential of NO^+, and $T(G)PPCo^{II}$, of course, is stable together with NO^+ in benzonitrile solution. Obviously, whether NO^+ or NO is released from $T(G)PPCo^{III}NO$ can be regulated by changing the remote substituent G.

As is well known, there exist two type important species of cobalt nitrosyl porphyrins in vivo, i.e., cobalt(III) nitrosyl porphyrins and cobalt(II) nitrosyl porphyrins. To compare the thermodynamic stability of cobalt(III) nitrosyl porphyrins with cobalt(II) nitrosyl porphyrins in vivo, examination of $\Delta H_{homo}(Co^{II}-NO)$'s and $\Delta H_{homo}(Co^{III}\text{-}NO)$'s was conducted. The results show that $\Delta H_{homo}(Co^{II}-NO)$'s are generally quite larger than the corresponding $\Delta H_{homo}(Co^{III}-NO)$'s, indicating that the stability of $T(G)PPCo^{II}NO$ is larger than that of the corresponding $T(G)PPCo^{III}NO$. This result not only validates the previous prediction that the thermodynamic stability of cobalt(II) nitrosyl porphyrins is larger than that of the corresponding cobalt(III) nitrosyl porphyrins in vivo but also suggests that cobalt porphyrin takes part in transport of NO in vivo potentially by the following channel: cobalt(II) porphyrin captures an NO molecule from a free NO molecule, S-nitroso compound, or other activated NO-donor such as activated iron(III) nitrosyl porphyrins to form a cobalt(II) nitrosyl porphyrin, which then directly delivers NO or contributes NO and NO^+ after oxidation by one-electron transfer to biological targets.[23] According to the magnitudes of $\Delta H_{homo}(Co^{III}-NO)$ and $\Delta H_{het}(Co^{III}-NO)$, it is conceived that NO would be released more easily than NO^+ from cobalt(III) nitrosyl porphyrins, since $\Delta H_{het}(Co^{III}-NO)$ is generally larger than the corresponding $\Delta H_{homo}(Co^{III}-NO)$ for $T(G)PPCo^{III}NO$, except the complex where the remote substituent (G) is a strong electron-withdrawing group (such as group NO_2).

To clarify the nature of the Co−NO bond in cobalt nitrosyl porphyrins, the effects of the remote substituents (G) on the Co−NO bond dissociation energies were examined. A Hammett-type free energy analysis for the $\Delta H_{het}(Co^{III}-NO)$, $\Delta H_{homo}(Co^{III}-NO)$, and $\Delta H_{homo}(Co^{II}-NO)$ provides three excellent lines with slope values of -2.056 ± 0.07, -0.481 ± 0.07, and -0.792 ± 0.09, respectively (Figure 3), which shows that the Hammett linear free energy relationship holds in the three Co−NO bond dissociation reactions (eqs 2, 3, 4). The negative slopes

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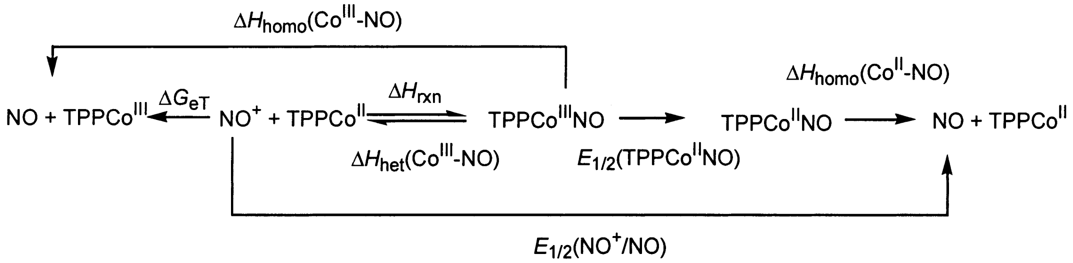
(21) The values of Co−NO bond energies offered in Table 2 are the values in solution rather than in the gas phase, and the solvation effects are included rather than cleaned up. As is well known, the concept of *bond energy in solution* is different from the classical concept of *bond energy in the gas phase*; the former contains solvation effects, but the latter does not contain solvation effects. In fact, the concept of *bond energy in solution* has been extensively used in the literature, and the energy scales of many different types of bond dissociation energies in solution [such as Y−H, Y−O, and Y−C (Y = N, O, S, C, etc.) in H_2O, DMSO, CH_3CN, etc.] have been established by many research groups in the world. The reason is that the values of *bond energy in solution*, sometimes, are much more important than the values of *bond energy in the gas phase* in many chemical or biochemical reactions in which chemists are interested, because they occur in solution.

(22) The values of N−NO and S−NO bond dissociation energies offered herein were determined in acetonitrile.[16] Since the polar solvation constants of acetonitrile ($\epsilon = 37.5$) are much larger than that of benzonitrile ($\epsilon = 25.2$) (see: Isaacs, N. S. *Physical Organic Chemistry*, 1st ed.; John Wiley & Sons: New York, 1987; Chapter 5, p 180), the values of N−NO and S−NO bond energies in benzonitrile solution, in fact, should be larger than the values in acetonitrile.

(23) Mu, X. H.; Kadish, K. M. *Inorg. Chem.* **1990**, *29*, 1031−1036.

Scheme 1



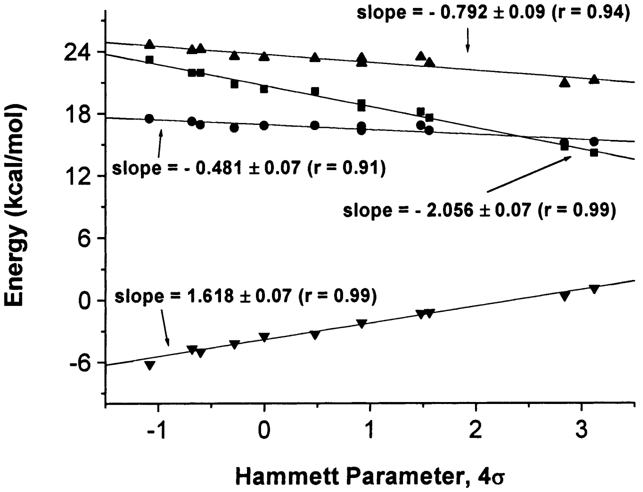
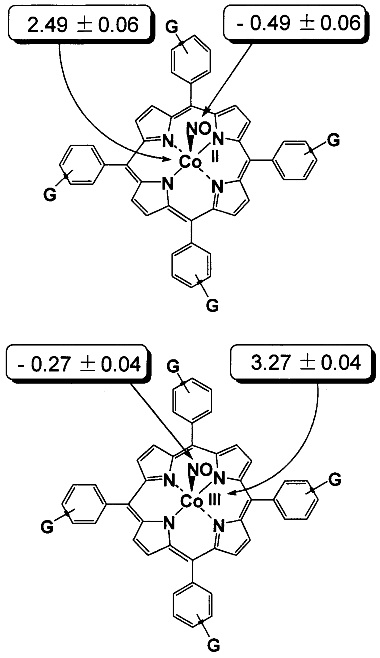


Figure 3. Hammett plots of $\Delta H_{het}(Co^{III}-NO)$ (■), $\Delta H_{homo}(Co^{III}-NO)$ (●), $\Delta H_{homo}(Co^{II}-NO)$ (▲), and ΔG_{eT} (▼) vs 4σ. The compound numbers and half-wave potentials are listed in Table 2.

for $\Delta H_{het}(Co^{III}-NO)$, $\Delta H_{homo}(Co^{III}-NO)$, and $\Delta H_{homo}(Co^{II}-NO)$ reflect the effective positive charge decrease at the cobalt in the three Co−NO bond dissociation processes, and the magnitude of the slope values is a measure of the effective charge change at the cobalt atom, because the only difference is the oxidation number of the cobalt atom and the nitric oxide for the three dissociation reactions.[24] Comparing the magnitudes of the three slope values, it is found that the absolute value of the three line slopes is $|\mathrm{slope}(\Delta H_{het}(Co^{III}-NO)| > |\mathrm{slope}(\Delta H_{homo}(Co^{II}-NO)| > |\mathrm{slope}\ (\Delta H_{homo}(Co^{III}-NO)|$, indicating that the charge change at the cobalt would decrease in the following order: $TPPCo^{III}NO$ (heterolysis) > $TPPCo^{II}NO$ (homolysis) > $TPPCo^{III}NO$ (homolysis) in the Co−NO bond dissociation processes. To quantitatively describe the effective charge change at the cobalt in the three dissociation reactions, a Hammett-type free energy analysis was done on the one-electron-transfer reaction of $T(G)PPCo^{II}$ with NO^+ (see Figure 3). The line slope of ΔG_{eT} vs 4σ is 1.618 ± 0.07, which indicates that the slope value of 1.618 is equivalent to the oxidation number increase of one unit at the cobalt atom on going from $T(G)PPCo^{II}$ to $T(G)PPCo^{III}$, and from which it is easily available that the slope of −2.056 ± 0.07 for $T(G)PPCo^{III}$-NO heterolysis is equivalent to the oxidation number decrease of 1.27 ± 0.04 units at the cobalt atom from $T(G)PPCo^{III}NO$ to $Co^{II}(G)TPP$. Similarly, the slope of −0.792 ± 0.09 for Co^{II}-NO(G)TPP homolysis is equivalent to oxidation number decreases of 0.49 ± 0.06 units at the cobalt atom from T(G)-$PPCo^{II}NO$ to $T(G)PPCo^{II}$. These results directly mean that the oxidation number of the cobalt atom in $T(G)PPCo^{II}NO$ and in $T(G)PPCo^{III}NO$ is 2.49 ± 0.06 and 3.27 ± 0.04 rather than 2 and 3, respectively, and as viewed from the other side, the nitrosyl group carries a negative charge of 0.49 ± 0.06 units in $T(G)PPCo^{II}NO$ and a negative charge of 0.27 ± 0.04 units in $T(G)PPCo^{III}NO$ (Scheme 2).[25] This result suggests that NO in both $T(G)PPCo^{II}NO$ and $T(G)PPCo^{III}NO$ is an electron-withdrawing group behaving in a manner similar to Lewis acids rather than to Lewis bases, which well clarified an important and debatable question: Is the nature of NO in metal nitrosyl porphyrins more similar to Lewis bases or Lewis acids?[26]

Scheme 2. Charge Distritbution of the Co−NO Bond in Nitrosyl-α,β,γ,δ-tetraphenylporphinatocobalt(II) and Nitrosyl-α,β,γ,δ-tetraphenyl Porphinatocobalt(III) in Benzonitrile Solution



To support the above proposal that NO is an electron-withdrawing group in $T(G)PPCo^{II}NO$ and $T(G)PPCo^{III}NO$, we examined the oxidation potentials and the reaction center sites of the following two reactions:

$$\mathrm{T(G)PPCo^{II}NO} \rightarrow \mathrm{T(G)PPCo^{III}NO} + e^- \qquad E_{1/2}[\mathrm{T(G)PPCo^{III}NO/T(G)PPCo^{II}NO}]$$

$$\mathrm{T(G)PPCo^{II}} \rightarrow \mathrm{T(G)PPCo^{III}} + e^- \qquad E_{1/2}[\mathrm{T(G)PPCo^{III}/T(G)PPCo^{II}}]$$

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(24) Page, M.; Williams, A. *Organic and Bio-organic Mechanism*; Addison-Wesley Longman Limited: 1997; Chapter 3, pp 52−79.

(25) The main reason is that d-electrons of the cobalt atom partially feed into the empty orbits of NO in T(G)PPCoNO [see references: (a) Wayland, B. B.; Minkiewicz, J. V.; Abd-Elmageed, M. E. *J. Am. Chem. Soc.* **1974**, *96*, 2795. (b) Mingos, D. M. P. *Inorg. Chem.* **1973**, *12*, 1209. (c) Pierpont, G. C.; Eisenberg, R. *J. Am. Chem. Soc.* **1971**, *93*, 4905.

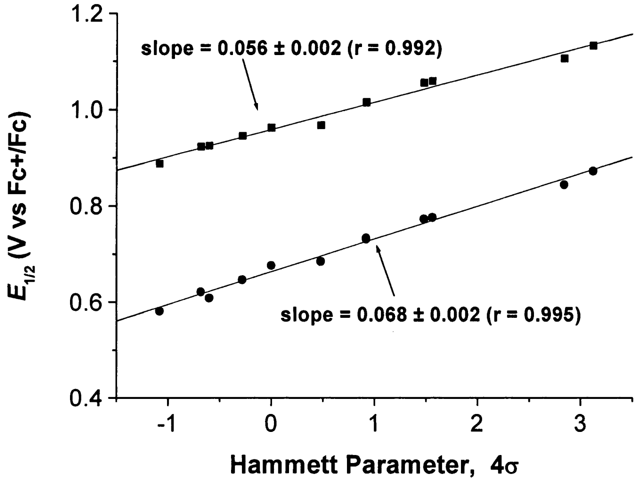

Figure 4. Hammett plots of $E_{1/2}$[T(G)PPCo^{III}NO/T(G)PPCo^{II}NO] (■) and $E_{1/2}$[T(G)PPCo^{III}/T(G)PPCo^{II}] (●) vs 4σ in benzonitrile solution, 0.1 M $Bu_4N^+ClO_4^-$. The compound numbers and half-wave potentials are listed in Table 1.

From columns 4 and 5 in Table 1, it is clear that the oxidation potential of T(G)PPCo^{II}NO is significantly larger than that of the corresponding T(G)PPCo^{II}, which indicates that T(G)PPCo^{II}NO is much more difficult to lose an electron than the corresponding T(G)PPCo^{II}; in other words, the electrochemical reaction center atom in the former reaction is a poorer electron donor than that in the latter reaction. To determine the reaction center site of electron transfer in the two oxidation reactions, Hammett-type redox potential analysis for the two reactions was made (Figure 4). The result provides two excellent straight lines with slopes of 0.056 ± 0.002 (r = 0.992) and 0.068 ± 0.002 (r = 0.995), respectively. Since the reaction center site of TPP(G)Co^{II} oxidation is at the metal cobalt atom,[27] it is conceived that the reaction center site of T(G)PPCo^{II}NO oxidation would also be at the cobalt atom rather than at the nitrosyl axial ligand in T(G)PPCo^{II}NO. The main reason is that a good Hammett linear free energy relationship holds in this reaction. If the reaction center were at the nitrosyl axial ligand rather than at the cobalt atom, no good Hammett linear free energy relationship could be unambiguously observed for this reaction, since the angle of Co−N−O in T(p-OCH$_3$)PPCo^{II}NO is about 119.6(4)°,[17] which indicates that the π-orbital of the nitrosyl axial ligand is not able to overlap significantly with porphyrin π-orbitals. According to the experimental results that the oxidation potential of T(G)PPCo^{II}NO is larger than that of the corresponding T(G)PPCo^{II} and the reaction center sites in the two reactions are all at the cobalt atom, a reasonable proposal can be made that the positive charge at the cobalt in T(G)PPCo^{II}NO assuredly is larger than that at the cobalt in the corresponding T(G)PPCo^{II}, which also suggests that NO would be an electron-withdrawing group behaving in a manner similar to a Lewis acid in T(G)PPCo^{II}NO. In fact, if we carefully inspect the line slope values for the two reactions, we would find that the line slope for T(G)PPCo^{II}NO oxidation (slope = 0.056 ± 0.002) is slightly smaller than that for T(G)PPCo^{II} oxidation (slope = 0.068 ± 0.002), which indicates that the electron density of the cobalt atom in T(G)PPCo^{II}NO would be smaller than that of the cobalt in T(G)PPCo^{II} on the basis of the reactivity−selectivity principle (RSP).[28]

Conclusions

The first two series of Co−NO bond dissociation enthalpies were determined in benzonitrile solution for 12 cobalt(II) nitrosyl porphyrins and for 12 cobalt(III) nitrosyl porphyrins by direct titration calorimetry with appropriate thermodynamic cycles. The results show that the energy scales of the heterolytic Co^{III}−NO bond dissociation, the homolytic Co^{III}−NO bond dissociation, and the homolytic Co^{II}−NO bond dissociation are 14.7−23.2, 15.1−17.5, and 20.8−24.6 kcal/mol in benzonitrile solution, respectively, which not only indicates that the stability of cobalt(II) nitrosyl porphyrins is larger than that of the corresponding cobalt(III) nitrosyl porphyrins for homolysis in benzonitrile solution but also suggests that both cobalt(III) nitrosyl porphyrins and cobalt(II) nitrosyl porphyrins are excellent NO donors, and in addition, cobalt(III) nitrosyl porphyrins are also excellent NO$^+$ contributors. Hammett-type linear free energy analyses on the nature of the Co−NO bond in T(G)PPCoNO suggest that the nitrosyl group carries negative charges of 0.49 ± 0.06 and 0.27 ± 0.04 in T(G)PPCo^{II}NO and in T(G)PPCo^{III}NO, respectively, which indicates that nitric oxide is an electron-withdrawing group in both T(G)PPCo^{II}NO and T(G)PPCo^{III}NO, behaving in a manner similar to Lewis acid, which, to our knowledge, appears to be the first work to quantitatively describe the charge distribution of cobalt nitrosyl porphyrins using experimental methods. The energetic and structural information disclosed in the present work is believed to furnish hints to the understanding of TPPCoNO biological functions in vivo.

Experimental Section

Materials. The para- and meta-substituted tetraphenylporphyrin free bases T(G)PPH$_2$, where G = p-OCH$_3$, p-CH$_3$, H, p-Cl, p-Br, p-NO$_2$, p-iPr, m-OCH$_3$, m-CH$_3$, m-Cl, m-Br, and m-NO$_2$, were synthesized by condensation of the precursor benzaldehydes and pyrrole using the method of Adler et al.[29] and chromatographed on silica gel with dichloromethane at least once before use. The corresponding cobalt derivative, T(G)PPCo^{II}, was obtained by refluxing the free-base porphyrins with $Co(CH_3CO_2)_2{\cdot}4H_2O$ in dimethylformamide by the method of Adler et al.[30] The products were chromagraphed at least three times as described above for T(G)PPH$_2$, the final time using benzene as the solvent. Each time only the center cut was retained. Visible spectra (λ_{max}, ϵ) of the T(G)PPCo^{II} complexes were very similar to those reported previously for T(p-OCH$_3$)PPCo^{II}.[31] T(G)PPCo^{II}NO was synthesized as described in the literature.[17] The nitrosating reagent $NO^+ClO_4^-$ was prepared by a literature method.[32] All solvents were treated according to standard procedures.

Spectrophotometric Titrations. Spectrophotometric titrations were performed on a U-3000 spectrophotometer, with digitized absorbance data being recorded on a Pentium-586 computer.

Isothermal Titration Calorimetry (ITC). Reaction of NO$^+$ ($NO^+ClO_4^-$) with α,β,γ,δ-tetraphenylporphinatocobalt(II) and its de-

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rivatives in benzonitrile solution was rapid and clean, giving the corresponding complex product nitrosyl-α,*β*,*γ*,*δ*-tetraphenylporphinatocobalt(III) in nearly quantitative yield.[33] ITC titration experiments were performed in benzonitrile solution at 25 °C on a CSC 4200 isothermal titration calorimeter. Prior to use, the instrument was calibrated against an internal heat pulse. Data points were collected every 2 s. The reaction heat was determined following eight automatic injections from a 200 μL injection syringe (containing 2.24 mM $NO^+ClO_4^-$) into the reaction cell (1.00 mL) containing 1.37 mM T(G)PPCo^{II}. Injection volumes (10 μL) were delivered at 0.5 s time intervals with 300 s between every two injections. The reaction heat was obtained by area integration of each peak except for the first one.

Electrochemical Experiments. All electrochemical experiments were carried out by CV (sweep rate, 100 mV/s) using a BAS-100B electrochemical apparatus in benzonitrile solution under an argon atmosphere. $Bu_4N^+ClO_4^-$ (0.1 M) was employed as the supporting electrolyte. A standard three-electrode assembly consisted of a glassy carbon disk as the working electrode, a platinum wire as counter electrode, and 0.1 M $AgNO_3$/Ag (in benzonitrile) as reference. All sample solutions were 1.0 mM. The ferrocenium/ferrocene redox couple ($Fc^{+/0}$) was taken as an internal standard. Reproducibility is generally smaller than 5 mV.

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[33] The formation of T(*p*-OCH_3)PPCo^{III}NO from the reaction of NO^+ with T(*p*-OCH_3)PPCo^{II} may be further confirmed according to the following experimental results: (i) The reaction product of NO^+ ($NO^+ClO_4^-$) with T(*p*-OCH_3)PPCo^{II} was reduced by the single-electron reducing agent ferrocene to give T(*p*-OCH_3)PPCo^{II}NO and ferrocenium in nearly quantitative yield. (ii) The reaction enthalpy change of T(*p*-OCH_3)PPCo^{II} with NO^+ was determined to be −23.2 kcal/mol much more negative than that of the one-electron transfer from T(*p*-OCH_3)PPCo^{II} to NO^+ ($\Delta G_{eT} = -5.7$ kcal/mol), which indicates that the final reaction product of T(*p*-OCH_3)PPCo^{II} with NO^+ unambiguously is the complex T(*p*-OCH_3)PPCo^{III}NO rather than the free T(*p*-OCH_3)PPCo^{III} and the free NO in benzonitrile.[17] Concerning the mechanism of T(*p*-OCH_3)PPCo^{III}NO formation, a reasonable proposal can be made according to the negative or little positive free energy change required for one-electron transfer from T(*p*-OCH_3)PPCo^{II} to NO^+ that the reaction of T(*p*-OCH_3)PPCo^{II} with NO^+ may be initiated by one-electron transfer to form T(*p*-OCH_3)PPCo^{III} and NO, which then rapidly combine into the final reaction product T(*p*-OCH_3)PPCo^{III}NO:

$$\mathrm{T(G)PPCo^{II}} + \mathrm{NO^+} \xrightleftharpoons{\mathrm{ET}} \mathrm{T(G)PPCo^{III}} + \mathrm{NO} \xrightleftharpoons{\mathrm{combining}} \mathrm{T(G)PPCo^{III}NO}$$