Mechanism of NO Transfer from NO-Donors (SNAP and G-MNBS) to Ferrous Tetraphenylporphyrin in CH$_3$OH

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ABSTRACT

The mechanism of NO transfer from NO-donors (SNAP and G-MNBS) to ferrous tetraphenylporphyrin (TPPFe$^{II}$) in CH$_3$OH is discovered for the first time by using a laser flash technique. The results show that the NO transfer is completed by NO$^+$ transfer followed by electron transfer rather than direct NO transfer in one step.

Nitric oxide (NO), which is among the simplest of molecules, has been found to have many important functions including blood pressure control, neurotransmission, and immune response in mammalian biology.$^{1}$ It is now believed that NO can activate the hemeproteins such as soluble-guanylyl cyclase (sGC) by binding its heme moiety.$^2$ Therefore, it is very important to understand the interaction mechanism of iron center proteins with NO. Much attention has been given to this aspect in the past two decades, and the iron complex, especially the iron porphyrin as a good model, has been widely used in the mechanistic studies.$^{1-10}$ In fact, the concentration of free NO in mammalian tissue is very low ($\sim$4 nM). The species most related to NO found in mammalian tissue are nitrate, nitrite, and NO-donors.$^5,11,12$ Since the NO-donor compounds, such as S-nitrosothioles, N-nitrosamines, etc., have shown many of the same biological properties as does NO alone and have been regarded as the best candidates for the endogenous storages and transports of NO,$^{12-14}$ it is certain that the interactions of hemeproteins


or iron porphyrin with widely existing NO-donors should be more common and important than that with free NO in vivo.\textsuperscript{(15a)} However, the investigation of this aspect is relatively rare.\textsuperscript{(15b)} One of the main reasons is that the ferrous porphyrin is extremely sensitive to oxygen and the pure compound is very difficult to obtain, which strictly limits experimental progress. But, in recent papers Hoshino et al.\textsuperscript{16,17} reported that the ferrous porphyrin can be quantitatively generated from TPPFe\textsuperscript{III}Cl in the degassed methanol solution by laser irradiation, which encouraged us to examine the reaction of NO-donors (G-MNBS and SNAP) with ferrous porphyrin in the degassed methanol solution by using a laser flash technique. Herein, we wish to report the detailed experimental results for the first time.

TPPFe\textsuperscript{III}Cl in the degassed methanol solution was treated by using a laser beam to quantitatively yield TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} ($\lambda_{\text{max}} = 425$ nm), which was confirmed by the previous work.\textsuperscript{16,17} The generated TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} is relatively stable without any decay over milliseconds after the laser pulse. However, when the NO-donor MNTS (N-methyl-N-nitroso-p-toluenesulfonamide) was added to the degassed methanol solution before the laser pulse, the formed absorption peak at 425 nm due to TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} decayed instantly, and at the same time, a new absorption peak at 414 nm appeared with an isoabsorptive point at 417 nm (Figure 1). The decay rate of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} was increased with increasing concentration of the added NO-donor, and finally approached the upper limit (Figure 2).

From Figure 1, it is clear that the formed TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} from TPPFe\textsuperscript{III}Cl is unstable in the presence of MNTS in Ar-saturated methanol and only remains several hundred microseconds after the laser pulse. Since the decay rate of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} is obviously dependent on the concentration of the NO-donor, it is conceivable that TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} decay is due to the reaction of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} with the NO-donor.\textsuperscript{18}

According to the previous study,\textsuperscript{19} the new absorption peak at 414 nm resulting directly from the decay of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} is due to $[\text{TPPFe}^{\text{II}}(\text{NO})(\text{CH}_3\text{OH})]^{+}$ ($\lambda_{\text{max}} = 414$ nm),\textsuperscript{19} which suggests that the decay of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} in the presence of MNTS in Ar-saturated methanol could be directly caused by NO$^+$ transfer from MNTS to TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2}. To further support this suggestion, the substituted N-methyl-N-nitrosobenzensulfonamides (G-MNBS) were used to replace MNTS to examine the Hammett substituent effect on the decay rate of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2}. The results are shown in Figure 3. From Figure 3, it is clear that the decay rate of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} is obviously increased as the substituent of G-MNBS goes from an electron-donating group (EDG) to an electron-withdrawing group (EWG) and the Hammett reaction constant $\rho$ (the line slope) is positive, which indicates...
that the negative charge on the G-MNBS was increased during the reaction of G-MNBS with TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2}, meaning that the break of the N—NO bond in G-MNBS during the reaction took place by heterolytic dissociation (NO\textsuperscript{+} transfer) rather than homolytic dissociation (neutral NO transfer). Evidently, this result strongly supports the suggestion above that the formation of [TPPFe\textsuperscript{II}(NO)(CH\textsubscript{3}OH)]\textsuperscript{+} was derived from NO\textsuperscript{+} transfer from G-MNTS releasing NO\textsuperscript{+} thermodynamically favorable (large. The practical pathway of NO\textsuperscript{+} transfer from MNTS to TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} has not been performed by the initial N—NO bond heterolytic fission of MNTS to release NO\textsuperscript{+} and the following combination of the released NO\textsuperscript{+} with TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} to form [TPPFe\textsuperscript{II}(NO)—(CH\textsubscript{3}OH)]\textsuperscript{+}. The reason is that the N—NO bond heterolytic dissociation energies of G-MNBs (range from 49.5 kcal/mol for p-OCH\textsubscript{3} to 44.3 kcal/mol for m-NO\textsubscript{2}) are quite large. The practical pathway of NO\textsuperscript{+} transfer from (G-MNBs) to TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} could be the concerted process of the heterolytic fission of the N—NO bond and the formation of the Fe—NO\textsuperscript{+} bond.

When we prolonged the observation on the formed absorption peak at 414 nm, it is clear that after about 400 \(\mu\)s from the beginning of the laser irradiation, the absorbance of [TPPFe\textsuperscript{II}(NO)(CH\textsubscript{3}OH)]\textsuperscript{+} at 414 nm began to decrease (Figure S2, Supporting Information). At the same time, the absorbance at 401 nm, owing to TPPFe\textsuperscript{II}NO,\textsuperscript{21} was increased (Figure S4, Supporting Information), meaning that the formed [TPPFe\textsuperscript{II}(NO)(CH\textsubscript{3}OH)]\textsuperscript{+} finally became the more stable product TPPFe\textsuperscript{II}NO\textsuperscript{22} by deriving an electron from the nitration G-MBSN\textsuperscript{−} formed in the former reaction. In fact, according to the reduction potential of TPPFe\textsuperscript{II}NO (\(E_{\text{red}} = 0.43\) V vs Fe\textsuperscript{3+/2+}\textsuperscript{22}) and the oxidation potential of the nitriations G-MBSN\textsuperscript{−} (\(E_{\text{ox}} = 0.201\) V vs Fe\textsuperscript{3+/2+} for p-H),\textsuperscript{20} the electron transfer from G-MBSN\textsuperscript{−} to [TPPFe\textsuperscript{II}(NO)(CH\textsubscript{3}OH)]\textsuperscript{+} give TPPFe\textsuperscript{II}NO and the neutral radical G-MBSN\textsuperscript{•} is thermodynamically favorable (\(\Delta G = -5.3\) kcal/mol). The formed radical G-MBSN\textsuperscript{•} was easy to dimerize to release energy, which can further promote the former reaction. According to the statements above, the mechanism of the NO transfer from MNBS to iron porphyrin TPPFeCl\textsubscript{2} initiated by laser irradiation may be proposed as shown in Scheme 1. Since similar phenomena were observed when SNAP, another very important NO-donor,\textsuperscript{12} was used to replace G-MNBs to react with TPPFe\textsuperscript{II}NO (Figure 2, as well as Figures S1, S3, and S5 in the Supporting Information), the two reaction systems should have a similar mechanism.

Scheme 1 shows that an equilibrium exists between TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} and TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} in methanol solution.\textsuperscript{24} The decay rate \((k_{\text{obs}})\) of TPPFe\textsuperscript{II}(CH\textsubscript{3}OH)\textsubscript{2} can be expressed by eq 1 according to the steady-state approximation.

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k_{\text{obs}} = \frac{k_{3}[\text{NO-donor}]}{k_{2} + k_{4}[\text{NO-donor}]}
\]

(1)

This reaction is the rate-determining step of the NO transfer from NO-donor to iron porphyrin TPPFe\textsuperscript{II}NO. The practical pathway for the NO transfer contains two separate steps: initial NO\textsuperscript{+} transfer followed by electron transfer. The thermodynamic analysis shows that both reaction steps are thermodynamically favorable. Considering that the hemoproteins and NO-donors widely exist in vivo,\textsuperscript{5—15} the NO transfer from NO-donors via the hemoprotein to the target molecules should be both very common and important. The present study could give important insight into a greater understanding of the interaction of NO-donors with hemoprotein and the possible mechanism of NO transfer in vivo.

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Note Added after ASAP Publication. The reference citation at the end of the first page was incorrectly shown as “22—14” in the version published ASAP June 7, 2006; the corrected version was published ASAP June 12, 2006.

Supporting Information Available: Experimental details including transient absorption spectra of the TPPFe\textsuperscript{II} decay in the presence of SNAP as well as the kinetic trace. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) The photochemical behavior of the NO-donors (SNAP or G-MNBs) alone in the reaction system was examined, and the results showed that no obvious decomposition of the NO-donors was found within hundreds of microseconds after the laser pulse.
(22) TPPFe\textsuperscript{II}NO can be easily obtained from the reaction of TPPFeCl\textsubscript{2} with NO in methanol and is quite stable in methanol solution. See: Wayland, B. B.; Olson, L. W. J. Chem. Soc., Chem. Commun. 1973, 897.