科技部補助專題研究計畫成果報告
期末報告

雙亞硝基鐵化合物與氧氣、超氧化物、過氧化物之反應與生化反應相關性探討

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中 文 摘 要 ： 由於近來發現一氧化氮在人體的許多生理及病理方面扮演著重要的角色，因此引起許多研究者再度對一氧化氮化學的濃厚興趣，其中包含了一氧化氮跟金屬作用產生的金屬硝基化合物。到目前為止一氧化氮確定在人體內扮演的角色包含了對血管舒張收縮的調節、中樞及周遭神經系統的傳導，以及對病原體的免疫。一氧化氮在人體內由一氧化氮合成酶所產生，而雙亞硝基鐵化合物（DNICs）及硫醇亞硝基(RSNO)通常被視為扮演生物體內的一氧化氮載體或貯存槽的角色。生物體內的酪胺酸蛋白硝基化
(protein tyrosine nitration (PTN))對於許多病理現象(包含發炎現象、神經退化、心血管疾病)來說也是一個相當重要的轉譯後蛋白質修飾(post-translational modification)。日前化學家根據所做的化學反應實驗結果大膽推測雙亞硝基鐵化合物（DNICs）也可能在生物體內扮演促進酪胺酸蛋白硝基化(protein tyrosine nitration (PTN))的反應。此外，生物化學家亦發現雙亞硝基鐵化合物可促進生物體內的半胱氨酸氧化(cysteine oxidation) 。我們已經成功合成一系列結構相同、不同電子組態或電子環境略微差異的單核雙亞硝基鐵化合物(DNICs 1-5),並且以單晶X-ray繞射確定其立體結構。接下去將利用各種物理方法去分析這些化合物上各原子的電子密度分布，期待分析的結果可以用以解釋不同DNICs與O2、O2-、O22-反應的反應機構及進行酚類亞硝基化反應、半胱氨酸氧化的差異性。

中 文 關 鍵 詞 ： 雙亞硝基鐵化合物,氧氣,過氧化合物,超氧化合物

英 文 摘 要 ： The discoveries that NO plays a key role for a surprising range of physiological and pathological processes in humans have led many researchers to revisit the chemistry of NO and its derivatives such as dinitrosyl iron complexes (DNICs) in recent years. Till now, NO has been found to play an important role in vascular system regulation, signaling between nerves in both the peripheral and central nerve system, and in immune response to pathogen. Dinitrosyl iron complexes (DNICs) and S-nitrosothiols (RSNO) have been suggested as one of the possible forms for storage and transport of NO in biological system. Recently, Prof. Kim has demonstrated that the {Fe(NO)2}10 DNICs served as a nitrating agent to convert 2,4-di-tert-butylphenol to 2,4-di-tert-butyl-6-nitro-phenol in the presence of O2, and claimed that cellular DNICs could provide the possible route to generate protein tyrosine nitration (PTN) which is an important post-translational modification associated with various pathological conditions. In addition, Prof. Kim also showed the possible biological function
of cysteine oxidation. In this work, we have synthesized a series of mononuclear dinitrosyl iron complexes (DNICs 1-5) with analogous coordination geometry but different electronic configuration. The further work will focus on the study of the O2, O2- and O22- reactivity and the

ability serving as the nitrating agent in the phenol nitrating reaction and as the oxidant in the thiolate oxidizing reaction. The formal charge of Fe atom, NO group and thiolate on these iron nitrosyl complexes will also be scrutinized on the basis of EPR, SQUID, DFT computation and Fe/N K-edge X-ray absorption spectroscopy (XAS). Also, the physical characterization will be correlated to the relationship between the ability of phenol nitration, thiolate oxidation mediated by DNICs and the electronic structure of
DNICs.

英文關鍵詞：Dinitrosyl iron complex, dioxygen, peroxide, superoxide

Biochemical insight into the reactivity of dinitrosyl iron complexes with dioxygen, superoxide and peroxide

Introduction

The physiological and biological functions of nitric oxide in living organisms are an area of intense investigation, because of the discovery of more and more function of nitric oxide including principal neurotransmitter mediating erectile function,[1] a critical endogenous regulator of blood flow and thrombosis,[2, 3] a major path physiological mediator of inflammation and host defense.[4] The naturally cellular NO is almost produced by NO synthases via a five electron oxidation of L-arginine.[5] However, the increasing evidence suggests that NO can also behave as a cytotoxic effector and/or a pathogenic mediator under NO overproduction. [6, 7] The cytotoxicity of NO is supposed to relate to the formation of some reactivity nitrogen species (RNS) such as peroxynitrite or nitric dioxide. It is believed that the presence of reactive oxygen species (ROS) such as superoxide radical($O_2^{\bullet-}$) and hydrogen peroxide (H_2O_2), and transition metal centers are required for the produce of the reactive nitrogen species (RNS) from NO. [6, 7] In addition, reactive nitrogen species (RNS) and reactive oxygen species (ROS) are involved in the *in vivo* oxidative reaction in biological system and play an important role in aging and the development of diseases.[8] At high concentrations, ROS/RNS can induce oxidative damage to DNA, lipids, and proteins, a phenomenon named as oxidative /nitrative stress, while at low/moderate concentrations, ROS/RNS are important messengers for signal transduction.[6, 9]

Recently, RNS mediated nitration of biological phenols, such as seen in protein tyrosine nitration (PTN), has been observed in a variety of human diseases associated with oxidative stress, such as inflammatory, neurodegenerative, and

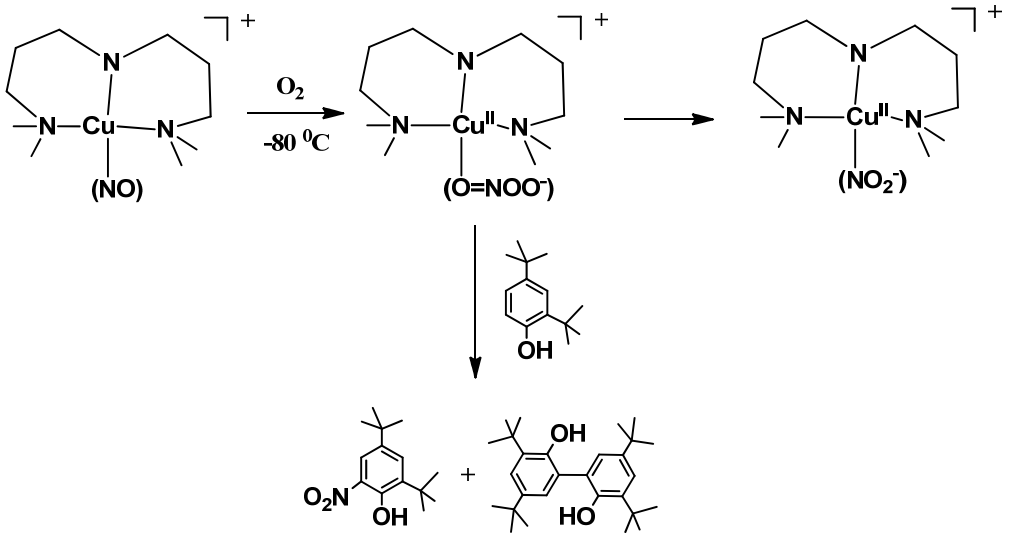
cardiovascular conditions.[6, 10-16] In addition, PTN is also usefully diagnostic biomarker for Alzheimer's, and Parkinson's diseases.[17-19] Recent reports indicate that distinct cellular nitrating agents could be responsible for it specificity at various sites.[13, 20] Although the underlying mechanism of protein tyrosine nitration *in vivo* is still unclear, two reactive nitrogen compounds, the peroxynitrite anion ($ONOO^-$) and nitrogen dioxide (•NO2), are thought to be involved.[21] $\bullet NO_2$ may be generated via several mechanism, including oxidation of •NO with oxygen,[22] the decomposition of peroxynitrite ($ONOO^-$),[21, 23, 24] and the oxidation of nitrite (NO_2^-) by hydrogen peroxide (H_2O_2) catalyzed with peroxidases.[25] However, peroxynitrite doesn't react directly with tyrosine. The mechanism of tyrosine nitration was first found to mediate via peroxynitrite on a free radical based mechanism but it turned out that heme-containing proteins facilitated this reaction by the formation of ferryl intermediates. Prostacyclin synthase was proven sensitive to nitration by peroxynitrite which could be efficiently prevented by an inhibitory substrate analogue. This result indicated that tyrosine nitration was a metal-mediated process in close proximity to the active heme-iron site.[26-28]

Peroxynitrite ($ONOO^-$) is generally generated *in vivo* from the diffusion-controlled reaction between superoxide (O_2^-) and nitric oxide (•NO).[21, 29, 30] Peroxynitrite is both an oxidant and nucleophile and these chemical properties dictate to the formation of secondary free radical intermediates such as nitrogen dioxide and carbonate radicals.[31] Peroxynitrite has been shown to oxidize various biomolecules including lipids, thiols, amino acid residues, DNA bases, as well as low- molecular weight antioxidants. The most prominent protein modifications mediated by peroxynitrite are the nitration and dimerization of tyrosine residues, the oxidation of cysteine thiol group, as well as the oxidation of methionine sulfur groups.[26]

In chemistry, the reactivity of dioxygen toward metal nitrosyl complexes has been thoroughly investigated, in particular because of the possible use of these complexes to activate dioxygen.[32] In addition, heme proteins and their models have been studied extensively to evaluate the role of transition metal ions in generation, stabilization, and activation for substrate oxidation and thermal isomerization of peroxynitrite ($ONOO^-$).[33] In 2000, Prof. Koppenol reported the rare discrete structurally characterized metal−peroxynitrite complex, cobalt−peroxynitrite (tris(tetraethylammonium) pentacyanoperoxynitritocobaltate(III)).[34]

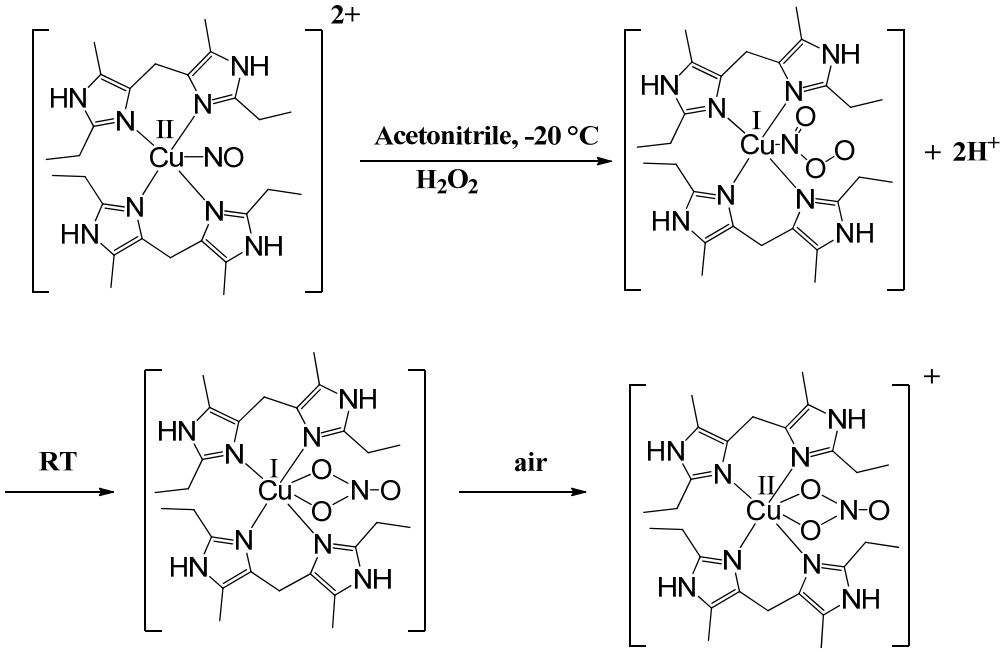
In addition to the stable cobalt−peroxynitrite complex, iron (e.g., heme), manganese, and copper complexes have been studied with respect to bio(chemical) O$=NOO^-$ mediated chemistry. For examples, $[Cu^{I}(AN)(NO)]^+$ (AN = 3,3'-iminobis(N,N'-dimethylpropylamine)) has been synthesized by Prof. Karlin in 2009 and then be used to react with dioxygen at -80°C affording $[Cu^{II}(AN)(O=NOO^-)]^+$. After the thermal transformation of $[Cu^{II}(AN)(O=NOO^-)]^+$, $[Cu(AN)(NO_2)]^+$ was afforded.[35] In the meantime, addition of 2, 4-di-tert-butylphenol in to $[Cu^{II}(AN)(O=NOO^-)]^+$ led to 2,4-di-tert-butyl-6-nitro-phenol (Scheme1) via phenol nitration.

Scheme 1.

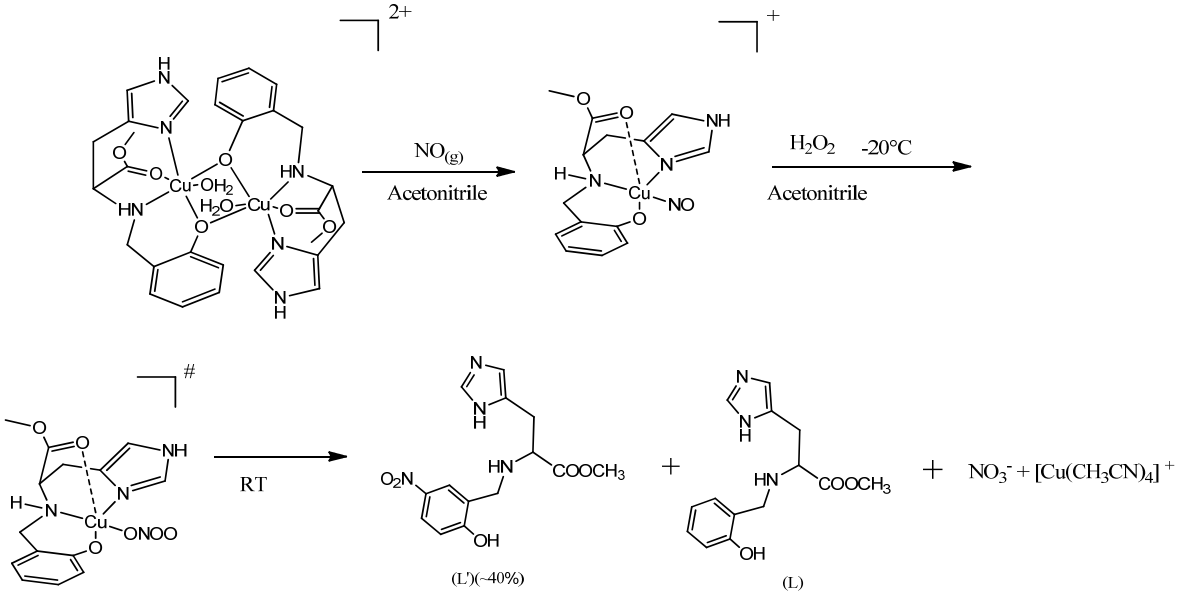


Also, the putative formation of a copper(I)–peroxynitrite intermediate via reaction of the mononuclear copper(II)−nitrosyl complexes with H_2O_2 at -20℃ was reported by Prof. Mondal in 2012 and 2013, respectively(Scheme 2 and 3).[36, 37] Formation of the peroxynitrite intermediate has been confirmed by its characteristic phenol ring nitration reaction as well as isolation of corresponding Cu(I)–nitrate and nitrate ion, respectively. Recently, Prof. Kim also reported the formation of the putative iron-peroxynitrite intermediate via reaction of the dinitrosyl iron complexes in 2011.[38]

Scheme 2.



Scheme 3.



DNICs are NO derivatives of biological relevance, found in various tissues and cells during NO overproduction by the inducible nitric oxide synthase. [39-45] *In vivo*, the naturally occurring DNICs are classified into protein-bound DNICs and low-molecular-weight DNICs (LMW-DNICs).[46-49] Protein-bound DNICs derived from NO-mediated degradation of Fe-S cluster containing proteins are considered as the storage of NO or $\{Fe(NO)_2\}$ moiety, and LMW-DNICs yielded via the displacement of protein-bound DNICs with free thiols/thiolates are served probably as the donor of NO or $\{Fe(NO)_2\}$ moiety.

Up to now, only one example of the crystallographically characterized protein-bound DNIC, derived from introducing an exogeneously formed $(glutathione)_2Fe(NO)_2$ into human glutathione S-transferase (GST P1-1), has been reported.[50] Although the protein-bound DNIC with [S,O] ligation mode was well characterized by X-ray diffraction, it is still difficult for isolation and structural determination of the DNICs derived from NO-mediated biological processes. The difficulty has inspired the efforts in the syntheses of adequate DNICs to serve the

spectroscopic references for the intermediates in the NO-mediated biological processes and the study of potential NO delivery systems.

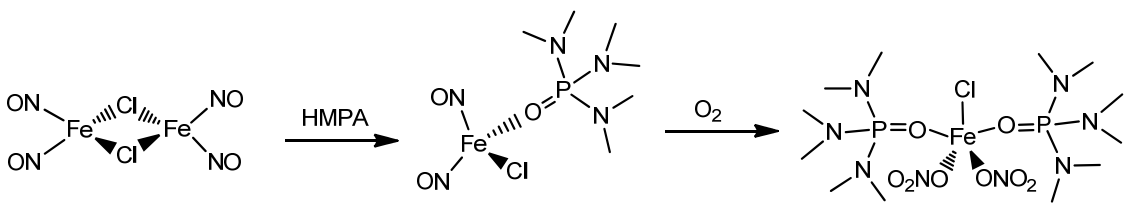
Recently, dinitrosyl iron complexes (DNICs) with different kinds of coordinated ligands (S-/O-/N-containing ligands) have been synthesized and are classified into the paramagnetic, oxidized form DNICs ($\{Fe(NO)_2\}^9$ DNICs) and the diamagnetic, reduced from DNICs ($\{Fe(NO)_2\}^{10}$ DNICs), based on the Enemark-Fetham notation. In the meanwhile, the interconversion between dinuclear DNICs (RREs, anionic RREs, dianionic RREs) and mononclear DNICs (oxidized and reduced form DNICs) has been also demonstrated.[51-59]

Also, these synthetic DNICs were employed to study the possible reactivity and formation pathways of nature occurring DNIC in biological systems. In 2006, Prof. Liaw and Lippard showed the conversion of biomimetic oxidized- and reduced-form rubredoxin $[Fe(SR)_4]^{2-/1-}$ into DNICs in the presence of $NO_{(g)}$ or RSNO, meanwhile, the intermediate mononitrosyl tris(thiolate) complexes $[Fe(SR)_3(NO)]^-$ of nitrosylation were isolated and the reactivity was elucidated.[60, 61] Prof. Liaw and Lippard also demonstrated the formation of DNICs from [2Fe-2S] clusters by reaction of biomimetic [2Fe-2S] ferredoxins $[S_5Fe(\mu\text{-}S)_2FeS_5]^{2-}$/ $[(PhS)_2Fe(\mu\text{-}S)_2Fe(SPh)_2]^{2-}$ with $NO_{(g)}$ or RSNO.[62, 63] At the same time, Prof. Lippard found that [2Fe-2S] clusters reacted with $NO_{(g)}$ yielding Roussin's black salt (RBS) instead of DNIC under dilute NO concentrations (< 100 μM). Prof. Lippard also investigated the nitorsylation of [4Fe-4S] clusters and found that reaction of the [4Fe-4S] clusters, $[Fe_4S_4(SR)_4]^{2-}$, with $NO_{(g)}$ afforded Roussin's black salt (RBS), while reaction of the [4Fe-4S] clusters, $[Fe_4S_4(SR)_4]^{2-}$, with $NO_{(g)}$ in the presence of 4 equiv of $[SR]^-$ yielded DNIC. [72] In contrast, the transformation of DNICs into [4Fe-4S] clusters, $[Fe_4S_4(SPh)_4]^{2-}$ in the presence of $[Fe(SR)_4]^{2-/1-}$ and S-donor species S_8 via the reassembling process $([(NO)_2Fe(SPh)_2]^- \rightarrow [Fe_4S_3(NO)_7]^-$/ $[Fe_4S_3(NO)_7]^{2-} \rightarrow [Fe_4S_4(NO)_4]^{2-}$

$\rightarrow$[$Fe_4S_4(SPh)_4$]$^{2-}$) was demonstrated by Prof. Liaw and co-workers.[64] The study of DNIC-to-RSNO transformation which utilized Brønsted acid and Lewis base $(Me_2NCS_2)_2$ to trigger one-thiolate containing DNIC to convert into S-nitrosothiol may reasonably rationalize that the 70% protein-SNO are surrounded within 6 Å by negatively and positively charged amino acids which are proposed to regulate the DNIC-to-RSNO transformation.[65] In addition, study on repair of DNICs yielding biomimetic [2Fe-2S] $[Fe_2(\mu\text{-}S)_2(SR)_4]^{2-}$ reveals that the anionic mixed thiolate-sulfide-bridged RREs acts as a key intermediate in the transformation of DNICs into [2Fe-2S] clusters.[66] Studies of the nitrite-containing DNICs, MNICs and interconversion of the nitrite-containing $\{Fe(NO)_2\}^9$ and $\{Fe(NO)_2\}^{10}$ DNICs indicated that the nitrite-to-nitroxyl-to-nitric oxide conversion pathway is activated by the $\{Fe(NO)_2\}^9$ DNIC and accompanied by transformation off $\{Fe(NO)_2\}^9$ to $\{Fe(NO)_2\}^{10}$; the nitrite-to-nitrosonium-to-nitric oxide conversion pathway is activated by the $\{Fe(NO)_2\}^{10}$ DNIC and accompanied by transformation off $\{Fe(NO)_2\}^{10}$ to $\{Fe(NO)_2\}^9$.[67, 68]

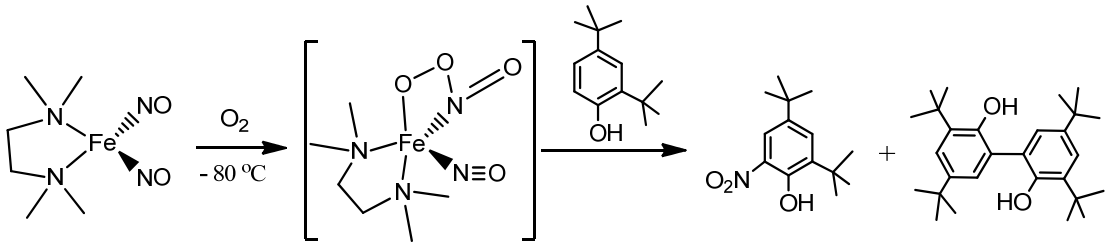
Although the synthesized DNICs have been widely studied to offer important chemical and biological insights, the study on the O_2 reactivity of DNICs is limited to few examples. In 1989, Prof. Postel reported the first example of DNICs toward O_2. As shown in Scheme 4, oxidation by oxygen of the unstable DNIC $[Fe(NO)_2Cl(HMPA)]$, afforded from reaction of $[Fe_2Cl_2(NO)_4]$ with HMPA, resulted in the formation of the nitrato-complex $[Fe(NO_3)Cl_2(HMPA)]$.[69]

Scheme 4.



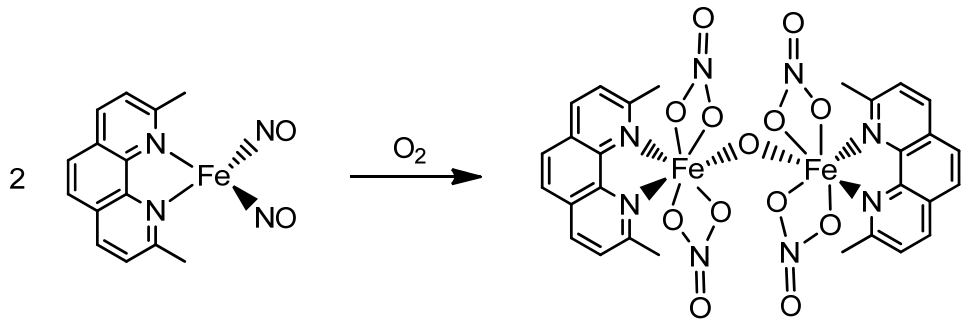
In 2011, Prof. Kim studied the dioxygen reactivity of an N-bound $\{Fe(NO)_2\}^{10}$ DNIC, $[Fe(TMEDA)(NO)_2]$ (TMEDA = N,N,N',N'-tetramethylethylenediamine).[38] As presented in Scheme 5, the report demonstrated the formation of a stable five-coordinate iron-peroxynitrite [Fe(TMEDA)(NO)(ONOO)], characterized by FTIR and Fe K-edge X-ray absorption spectroscopy when $[Fe(TMEDA)(NO)_2]$ reacted with dioxygen at -80 °C. In addition, when dioxygen is added to a mixture of $[Fe(TMEDA)(NO)_2]$ and DBP (2,4-di-tert-butylphenol) at -80 °C and then is subsequently warmed to room temperature, NO_2-DBP (2,4-di-tert-butyl-6-nitro-phenol) is observed along with 3,3',5,5'-tetra-tert-butyl-1,1'-biphenyl. This result reasonably suggested that DNICs act as mobile nitrating reagent in cells, in addition to the role of NO storage and transfer.

Scheme 5.



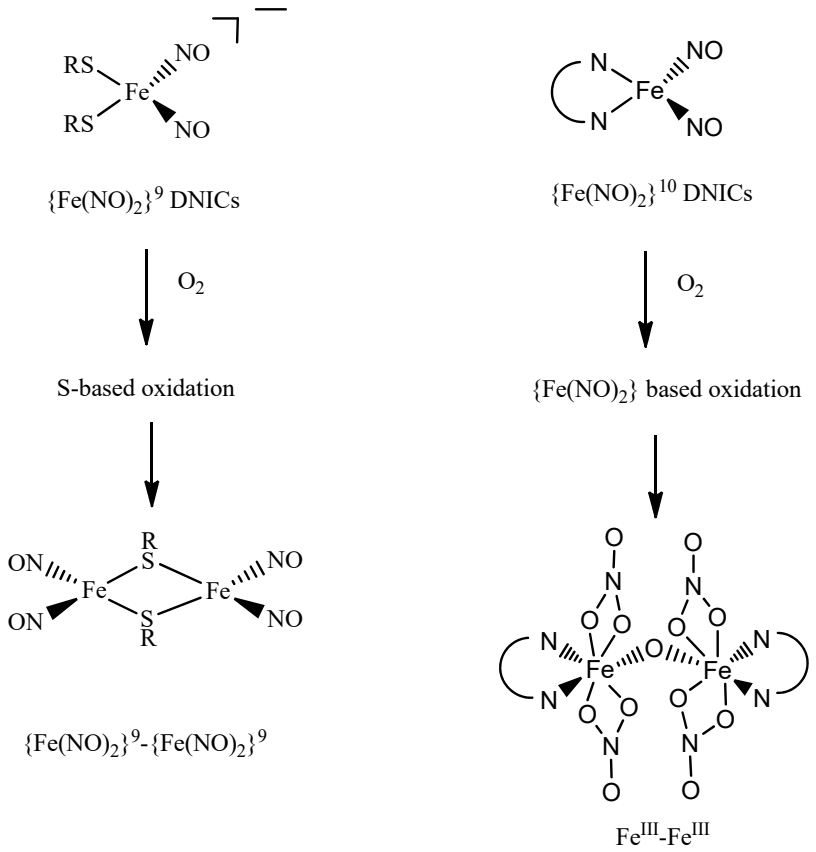
In 2012, Prof. Kim demonstrated the reaction of another $\{Fe(NO)_2\}^{10}$ DNIC $[Fe(dmp)(NO)_2]$ with dioxygen. As shown in Scheme 6, the reaction resulted in the formation of the room-temperature-stable nitrato-containing complex $[Fe_2O(NO_3)_4(dmp)_2]$. It is noted that $[Fe_2O(NO_3)_4(dmp)_2]$ is incapable of nitrating DBP to NO_2-DBP, but $[Fe(dmp)(NO)_2]$ in the presence of dioxygen does effectively nitrate DBP to NO_2-DBP. This result reveals that the iron-peroxynitrite species plays a critical role in phenol nitration and it forms prior to the formation of $[Fe_2O(NO_3)_4(dmp)_2]$.[70]

Scheme 6.



In 2013, Prof. Kim proceeded the dioxygen reactivity of thiolate-contaning $\{Fe(NO)_2\}^9$ DNICs. As shown in scheme 7, reaction of dioxygen with $[Fe(NO)_2(SR)_2]^-$ (R = t-Bu, Et, Ph) afforded $[Fe(NO)_2(SR)]_2$. Based on the study of dioxygen reactivity of N-bound $\{Fe(NO)_2\}^{10}$ and S-bound $\{Fe(NO)_2\}^9$ DNICs, the research group concluded that N-bound DNICs oxidation by dioxygen occurs at the NO group of $\{Fe(NO)_2\}$ unit and S-bound DNICs oxidation by dioxygen occurs at the S-bound ligands.[71]

Scheme 7.



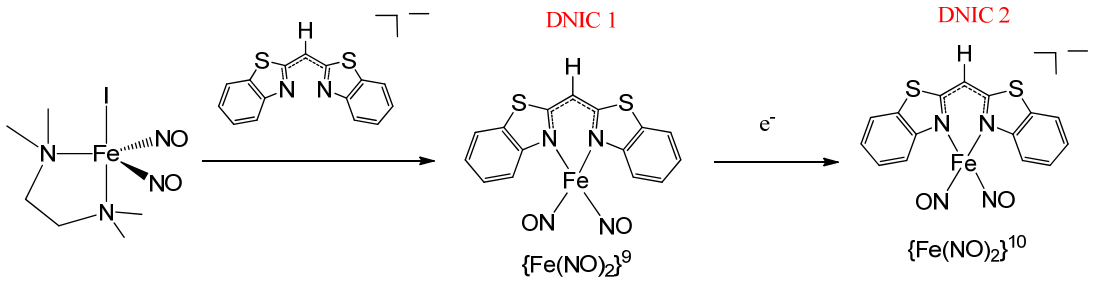
The study on the reactivity of DNICs with molecular oxygen by Prof. Kim inspires us to consider the following questions. (1) It has found that [N,N]-bound $\{Fe(NO)_2\}^{10}$ DNICs could react with molecular oxygen to form iron-peroxynitrite and proceeded the phenol nitration. Could the [N,N]-bound $\{Fe(NO)_2\}^{9}$ DNICs demonstrate the same chemical properties? And are $\{Fe(NO)_2\}^{9}$ DNICs more effective in phenol nitration then $\{Fe(NO)_2\}^{10}$ DNICs? (2) Will the subtle variations of the formal oxidation state of Fe and the charge of NO in [N,N]-bound $\{Fe(NO)_2\}^{9}$ and $\{Fe(NO)_2\}^{10}$ DNICs give influences on the reactivity of DNICs with molecular oxygen and the mechanism of phenol nitration? (3) Though the reactivity of DNICs with dioxygen has been investigated, the reactivity of DNICs with superoxide and peroxide has not been present. In addition, the study on the reactivity of DNICs with superoxide may give valuable biological relevance because peroxynitrite ($ONOO^-$) is generated generally *in vivo* from the diffusion-controlled reaction between superoxide (O_2^-) and nitric oxide (•NO),[21, 29, 30] We designed the following experiments to answer these questions and to the purse the specific objectives mentioned above.

The experimental method included the syntheses and physical characterization of a series of mononuclear [N,N]-bound DNICs containing $\{Fe(NO)_2\}^{9}$/$\{Fe(NO)_2\}^{10}$ electronic configurations. The physical characterization of the synthetic DNICs will allow us to distinguish the variations of formal oxidation state of Fe and the charge of NO in $\{Fe(NO)_2\}$ motifs of the synthetic DNICs with different electronic configurations and relate to the possibly different reactivity of dioxygen, superoxide, and peroxide with DNICs and efficiency of phenol nitration induced by the variations of formal oxidation state of Fe and the charge of NO in $\{Fe(NO)_2\}$ motifs of DNICs.

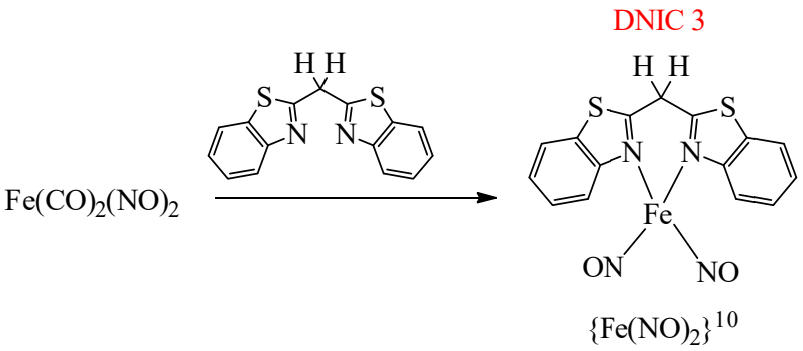
Results and discussion

Though the redox reactivity of DNICs has been studied, the study on redox reactivity of DNICs is limited to the reaction of DNIC with reductant and oxidant.[57, 59] The reactivity of DNICs with dioxygen, superoxide and peroxide is rare. In order to study the different reactivity toward dioxygen, superoxide and peroxide induced by the distinct electronic configuration of DNICs ($\{Fe(NO)_2\}^9$/$\{Fe(NO)_2\}^{10}$ DNICs), it is necessary to prepare the $\{Fe(NO)_2\}^9$/$\{Fe(NO)_2\}^{10}$ DNICs with the same coordinating environment(homologous DNIC redox-partners). The following homologous DNIC redox-partner DNICs **1** and **2** were prepared according to scheme 8. Reaction of FeI(NO)(TMEDA) with the deprotonated 2,2'-Methylenebisbenzothiazole afforded the $\{Fe(NO)_2\}^9$ DNIC **1**. The further reduction of DNIC **1** with BH_4^- afforded $\{Fe(NO)_2\}^{10}$ DNIC **2**. In addition, the DNIC with a modified similar ligand will also be prepared to evaluate the influence on the formal oxidation state of Fe and the charge of NO induced by the modified ligand. DNIC **3** with $\{Fe(NO)_2\}^{10}$ fragment was prepared by reaction of $Fe(CO)_2(NO)_2$ with 2,2'-Methylenebisbenzothiazole as shown in scheme 9. The formation of DNIC 1, DNIC 2, and DNIC 3 have been structurally characterized by single-crystal X-ray diffraction and the structures are depicted in Figures 1 - 3.

Scheme 8.



Scheme 9.



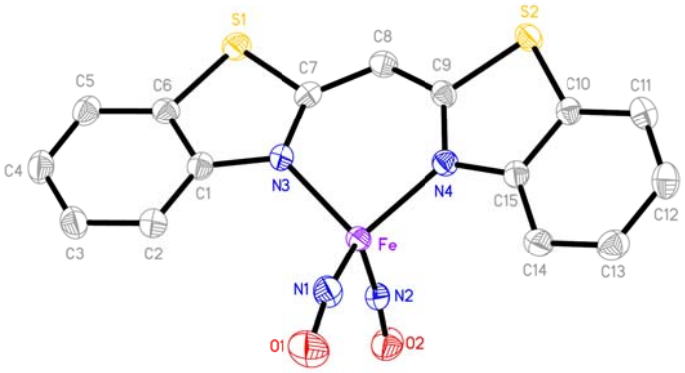
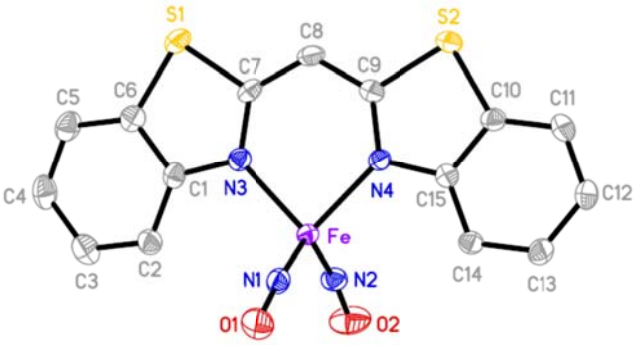


Figure 1. ORTEP drawing and labeling scheme of DNIC **1** with thermal ellipsoids drawn at 50 % probability level.



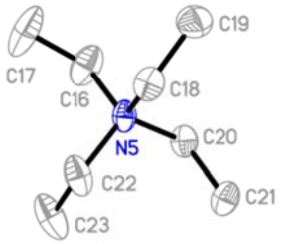


Figure 2. ORTEP drawing and labeling scheme of DNIC **2** with thermal ellipsoids drawn at 50 % probability level.

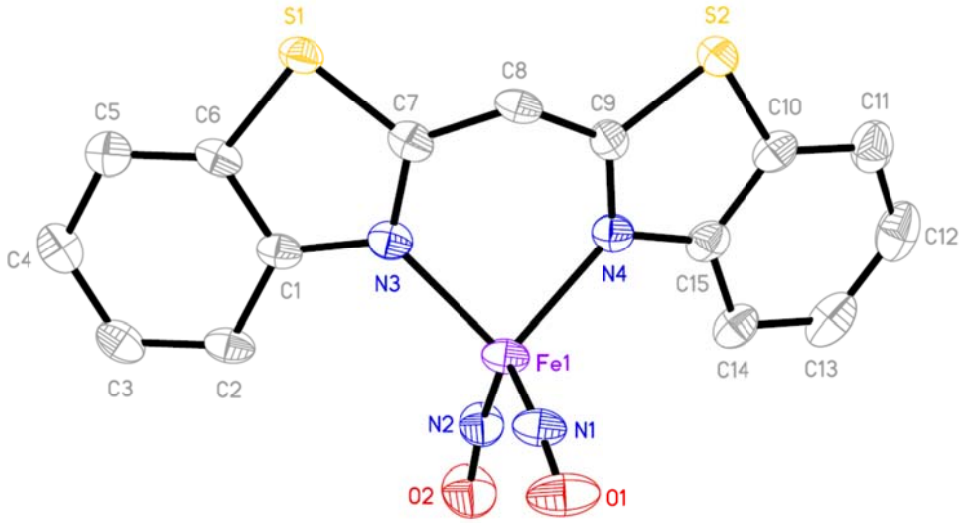
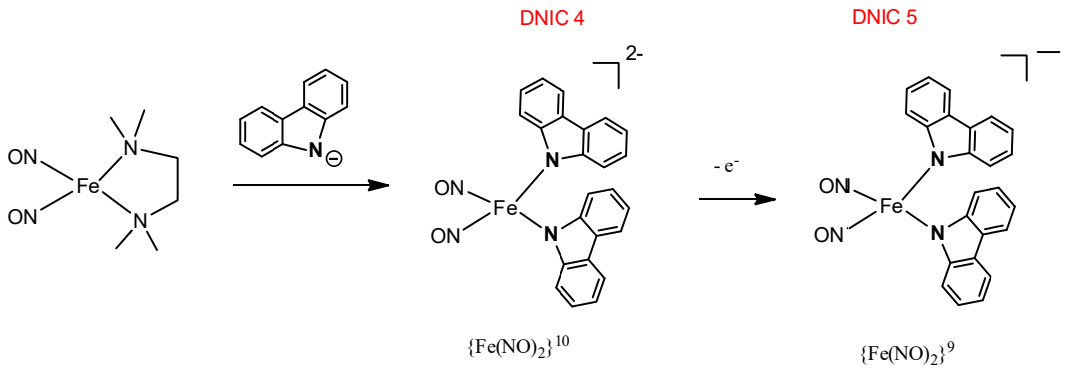


Figure 3. ORTEP drawing and labeling scheme of DNIC **3** with thermal ellipsoids drawn at 50 % probability level.

In addition, the other homologous monomeric [N,N]-bound DNICs redox partners could be prepared as shown in scheme 10.[59] Reaction of $Fe(TMEDA)(NO)_2$ and carbazolate afforded $\{Fe(NO)_2\}^{10}$ DNIC **4**. The further oxidation of $\{Fe(NO)_2\}^{10}$ DNIC **4** with Cp_2FeBF_4 resulted in $\{Fe(NO)_2\}^{9}$ DNIC **5**. The structures of DNIC **4** and DNIC **5** were characterized by single-crystal X-ray diffraction and the ORTEP drawing and labeling schemes were shown in Figures **4** and **5**. In a similar fashion, these DNICs will react with dioxygen, superoxide and peroxide. We expect the reaction results could be consistent with the physical characterization of these DNICs.

Scheme 10



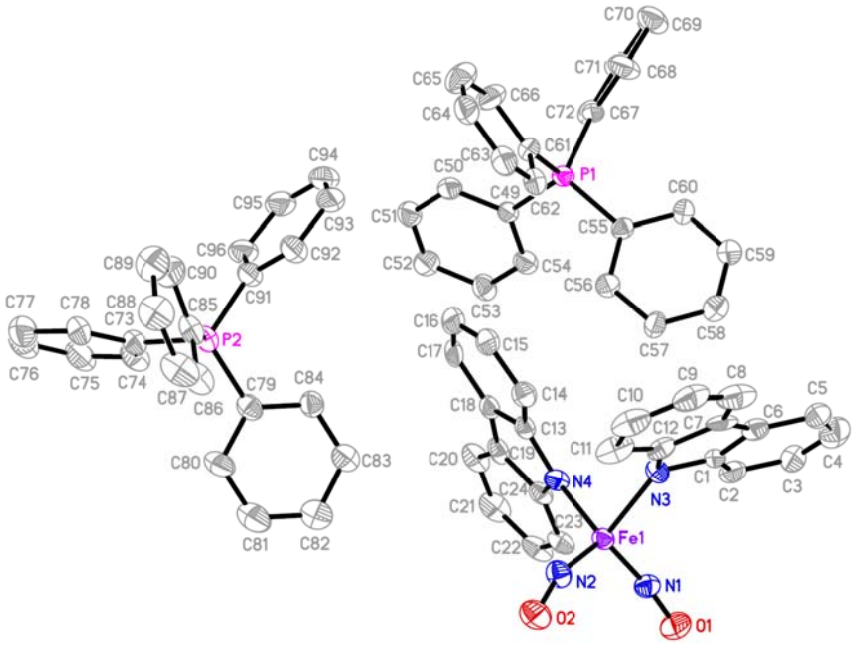


Figure 4. ORTEP drawing and labeling scheme of DNIC **4** with thermal ellipsoids drawn at 50 % probability level.

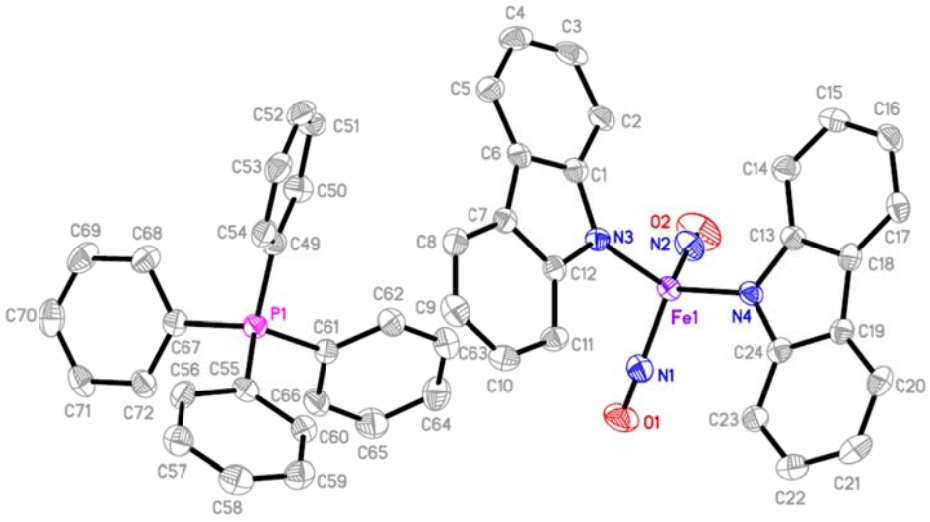


Figure 5. ORTEP drawing and labeling scheme of DNIC **5** with thermal ellipsoids drawn at 50 % probability level.

Conclusions

A series of mononuclear four coordinate mononuclear $\{Fe(NO)_2\}^9/\{Fe(NO)_2\}^{10}$ DNICs (DNICs **1-5**) have been synthesized successfully and characterized by IR, UV/vis, ^{1}H NMR, EPR. The SQUID measurements of DNICs **1-5** and studies on the

electronic structure (NO/Fe oxidation states) of the series of $\{Fe(NO)_2\}^9/\{Fe(NO)_2\}^{10}$ DNICs by X-ray absorption spectroscopy and DFT calculations are ongoing. Also, the reactivity of dioxygen, superoxide and peroxide toward $\{Fe(NO)_2\}^9/\{Fe(NO)_2\}^{10}$ motifs are currently being investigated in our laboratory. Similarly, phenol nitration and thiolate oxidation induced by the possible iron-peroxonitrite intermediate resulting from the reaction of dioxygen, superoxide and peroxide with DNICs 1-5 will be studied to correlate the relationship between the yields of nitro-phenol/cysteine sulfinic acid and the formal charge of Fe atom and NO group in DNICs 1-5.

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104年度專題研究計畫成果彙整表

計畫主持人：陳建宏	**計畫編號：**104-2113-M-040-003-
計畫名稱：雙亞硝基鐵化合物與氧氣、超氧化物、過氧化物之反應與生化反應相關性探討	

成果項目					量化	單位	質化 （說明：各成果項目請附佐證資料或細項說明，如期刊名稱、年份、卷期、起訖頁數、證號...等）
國內	學術性論文	期刊論文			0	篇	
		研討會論文			0		
		專書			0	本	
		專書論文			0	章	
		技術報告			0	篇	
		其他			0	篇	
	智慧財產權及成果	專利權	發明專利	申請中	0	件	
				已獲得	0		
			新型/設計專利		0		
		商標權			0		
		營業秘密			0		
		積體電路電路布局權			0		
		著作權			0		
		品種權			0		
		其他			0		
	技術移轉	件數			0	件	
		收入			0	千元	
國外	學術性論文	期刊論文			0	篇	
		研討會論文			0		
		專書			0	本	
		專書論文			0	章	
		技術報告			0	篇	
		其他			0	篇	
	智慧財產權及成果	專利權	發明專利	申請中	0	件	
				已獲得	0		
			新型/設計專利		0		
		商標權			0		
		營業秘密			0		
		積體電路電路布局權			0		
		著作權			0		
		品種權			0		
		其他			0		

	技術移轉	件數	0	件	
		收入	0	千元	
參與計畫人力	本國籍	大專生	2	人次	訓練學生實驗室基本技巧及其搜索資料整理資料能力
		碩士生	2		訓練學生實驗室基本技巧及其搜索資料整理資料能力
		博士生	0		
		博士後研究員	0		
		專任助理	0		
	非本國籍	大專生	0		
		碩士生	0		
		博士生	0		
		博士後研究員	0		
		專任助理	0		
其他成果 （無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。）					

科技部補助專題研究計畫成果自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現（簡要敘述成果是否具有政策應用參考價值及具影響公共利益之重大發現）或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估
   ■達成目標
   □未達成目標（請說明，以100字為限）
   　□實驗失敗
   　□因故實驗中斷
   　□其他原因
   說明：

2. 研究成果在學術期刊發表或申請專利等情形（請於其他欄註明專利及技轉之證號、合約、申請及洽談等詳細資訊）
   論文：□已發表　□未發表之文稿　■撰寫中　□無
   專利：□已獲得　□申請中　■無
   技轉：□已技轉　□洽談中　■無
   其他：（以200字為限）

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性，以500字為限）
   所合成的一系列雙亞硝基鐵化合物仍屬於較少數的特殊例子,可供對於電子環境的些微差異導致的反應性變化作探討.

4. 主要發現
   本研究具有政策應用參考價值：■否　□是，建議提供機關
   （勾選「是」者，請列舉建議可提供施政參考之業務主管機關）
   本研究具影響公共利益之重大發現：□否　□是
   說明：（以150字為限）