

A dinitrosyl iron complex as a platform for metal-bound imidazole to N-heterocyclic carbene conversion†

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An N-alkyl imidazole bearing a neutral {Fe(NO)₂}¹⁰ dinitrosyliron complex (DNIC) when treated with sodium *t*-butoxide undergoes base-promoted conversion to the N-heterocyclic carbene (NHC)–DNIC, while maintaining the Fe(NO)₂ unit intact. Subsequent alkylation led to the isolation of the NHC–DNIC product; further nitrosylation led to trinitrosyl (NHC)Fe(NO)₃⁺. Both were isolated and structurally characterized.

While the most famous application of N-heterocyclic carbenes (NHCs) as ligands is arguably towards the 2nd generation Grubbs catalyst, they have been described as “some of the most versatile ligands in the toolkit of the synthetic chemist”.^{1,2} With respect to iron, developments continue to expand in homogeneous catalysis and bio-mimetic chemistry.¹ Within the first coordination sphere the planar NHCs mimic ligands such as imidazole, which itself is a surrogate for histidine, and in composition and steric character a C₃N₂ heterocycle similar to NHC.³ Of particular interest in this regard is the study by Li *et al.*, which explored the synthesis and characterization of a series of dinitrosyl iron complexes, DNICs, bearing imidazole derivatives (*e.g.*, 4-methyl imidazole, imidazole, and benzimidazole).⁴ In this series, only Fe(NO)₂(1-MeIm)₂ (1-MeIm = 1-methyl imidazole), with the DNIC moiety in the reduced, {Fe(NO)₂}¹⁰ (Enemark–Feltham notation),⁵ form could be isolated and characterized by single crystal X-ray diffraction. All derivatives displayed the now classic EPR signature of {Fe(NO)₂}⁹ complexes, an isotropic signal of *g* = 2.03, indicative of the ease of oxidation of neutral {Fe(NO)₂}¹⁰.⁶ To address this difficulty of isolating pure imidazole bound DNICs, Hess *et al.* found that NHCs supported DNICs at both redox levels, *i.e.*, {Fe(NO)₂}¹⁰ and {Fe(NO)₂}⁹.⁷ This ability is uncommon, the [(2,6-diisopropylphenyl)–NC(Me)]₂CH (Ar-nacnac) ligand reported by Lippard *et al.* being another such example.⁸ Furthermore, we have noted that NHCs were superior ligands to DNICs, readily replacing imidazoles in competition studies involving the oxidized and reduced DNICs.⁷

Gas phase calculations of the energetics of the free imidazole molecule have shown that it is *ca.* 30 kcal mol^{−1} lower in energy than its NHC tautomer,⁹ which suggests that tautomerization to NHC is thermodynamically unfavoured. In contrast, from studies by Crabtree *et al.* addressing the existence of C-bound imidazoles in metalloproteins, it was concluded that this thermodynamic preference may be reversed when each is bound to a metal center.¹⁰ Nevertheless this preference is metal dependent; for large chloride coordination environments, first row transition metals were found to favor binding *via* N, while second and third row metals preferred binding *via* C.¹⁰ Experimental studies by Ruiz *et al.* and Lopez *et al.* have led to the development of a protocol wherein conversion of an imidazole ligand bound to manganese- or rhenium-carbonyls has been effected.^{11,12} Similar inter-conversions were reported by Brill *et al.* and Hällér *et al.*^{13,14} Given the aforementioned order of reactivity observed for imidazole and NHC-bearing synthetic DNICs, as well as the biological significance of DNICs, we have pursued the possibility of conversion of an imidazole to an NHC on the dinitrosyl iron platform, when provided with necessary conditions.

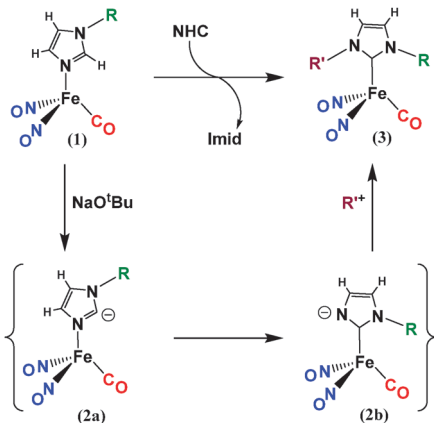
The experimental protocol for conversion of metal-bound imidazoles to NHCs established by Ruiz *et al.* was followed (Scheme 1).^{11,15} The imidazole containing DNIC **1** (R = *−mesityl*) was obtained by reacting 1-mesitylimidazole (synthesized *via* a literature procedure)¹⁶ with Fe(CO)₂(NO)₂ in a 1:1 ratio,⁷ in THF solution, to yield a dark brown product, complex **1**. Its formation could be monitored by IR spectroscopy, $\nu(\text{CO})$: 1994 cm^{−1}; $\nu(\text{NO})$: 1747, 1701 cm^{−1} (Fig. 1). The product was further characterized by ¹H-NMR spectroscopy.

Deprotonation of **1** using NaO^{*t*}Bu results in a color change of the solution from brown to teal green (Fig. 1. IR $\nu(\text{CO})$: 1854 cm^{−1}; $\nu(\text{NO})$: 1687, 1675 cm^{−1}). We assign the change in the positions and pattern of the IR bands accompanying this colour change to the formation of anionic intermediates **2a/2b** (Scheme 1) analogous to those proposed by Ruiz *et al.*^{11,15} However, owing to its extreme air sensitivity and instability, we were unable to further characterize the intermediate species.

The reaction process is consistent with the calculations by Ruiz *et al.*,¹⁷ as well as our own preliminary DFT calculations,

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Scheme 1 Conversion of metal-bound imidazoles to NHCs on a DNIC.

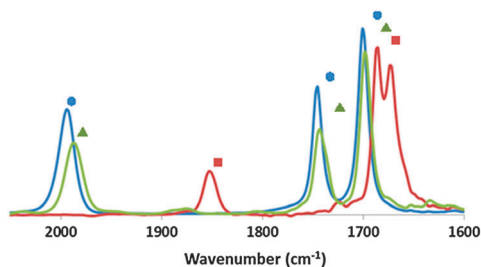
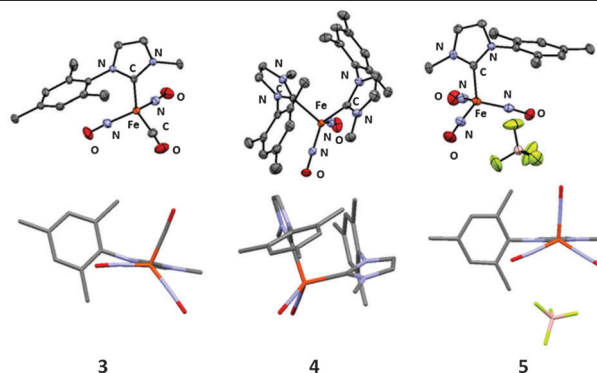


Fig. 1 Overlaid IR spectra of 1, 2a/2b and 3 in THF. [●, blue: 1: $\nu(\text{CO})$: 1994 (s), $\nu(\text{NO})$: 1747 (s), 1701 (vs) cm^{-1}], [■, red: 2a/2b: $\nu(\text{CO})$: 1854 (w), $\nu(\text{NO})$: 1687 (vs), 1675 (s) cm^{-1}], [▲, olive: 3: $\nu(\text{CO})$: 1988 (s), $\nu(\text{NO})$: 1743 (s), 1690 (vs) cm^{-1}].

wherein it is found that the removal of a proton from the C2 on the imidazole ring produces a ‘free carbene’ that is unstable and isomerizes to the metal-bound carbene. In the case of the Ruiz study, a *cis* carbonyl at 90° is said to facilitate this process.¹⁷ However, such bond formation is less likely in the tetrahedral geometries of our compounds.

The color of the green solution changed to dark brown upon addition of one equivalent of trimethyloxonium tetrafluoroborate as a methylating agent with a corresponding shift in the IR features to $\nu(\text{CO})$: 1988 cm^{-1} ; $\nu(\text{NO})$: 1743, 1690 cm^{-1} (Fig. 1). This can be attributed to the formation of complex 3 (Scheme 1), which is an NHC-containing species. As expected, the NHC-bound species was seen to possess comparatively lower IR frequencies than the corresponding imidazole, consistent with its higher σ donor ability and earlier studies.⁷ X-ray quality crystals were grown by cooling a saturated solution of hexanes at $-35\text{ }^\circ\text{C}$ for three days. The molecular structure of 3 (Table 1) shows an asymmetric NHC bound iron dinitrosyl compound, which provides conclusive evidence for the ability of the dinitrosyl iron platform to support the conversion of the imidazole to an NHC upon deprotonation. The diamagnetic character of 3 was confirmed by sharp signals in the $^1\text{H-NMR}$ spectrum (see ESI[†]). Its CO lability, as established for symmetric NHCs,⁷ accounted for decomposition during attempted crystallization by slow evaporation of a concentrated diethyl ether–hexanes solution (1:1) at $-35\text{ }^\circ\text{C}$ over a period of 3 weeks. Using this procedure X-ray quality crystals were obtained for the neutral, di-substituted, bis-NHC–DNIC, [(MeMes–NHC)₂Fe(NO)₂] (complex 4), the molecular structure of which is shown in Table 1. This complex

Table 1 Selected bond distances, angles and molecular structures of 3, 4 (packing solvent omitted for clarity) and 5: (top) ORTEP with thermal ellipsoids drawn at 50% probability (H atoms omitted); (bottom) capped stick renditions



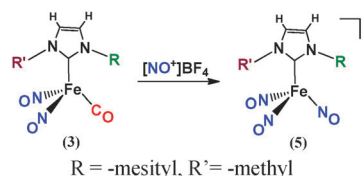
Bond distances (Å)			
Fe–C _{NHC}	1.991(1)	1.990(1) ^a	2.006(2)
Fe–NO ^a	1.660(1)	1.651(2)	1.695(2)
Fe–CO	1.834(2)	—	—
N–O ^a	1.179(2)	1.203(2)	1.148(2)
Bond angles (deg)			
N–Fe–N	120.3(1)	118.5(1)	113.0(1) ^a
Fe–N–O ^a	174.8(2)	172.2(2)	173.1(2)
C _{carb} –Fe–NO ^a	107.5(1)	110.3(1)	105.6(1)

^a Average distances or angles (the maximum deviations from the average distances and angles are shown in the table. Full lists of metric parameters are given in the ESI).

may be directly prepared by reaction of 2 equiv. of the NHC with Fe(CO)₂(NO)₂ (see ESI[†]).⁷

In complex 3, isoelectronic replacement of CO by NO⁺, upon the addition of one equivalent of [NO⁺]BF₄, led to the formation of the trinitrosyl iron complex (TNIC) 5 (Scheme 2). This can be characterized by $^1\text{H}/^{13}\text{C-NMR}$ and IR spectroscopies. The latter shows 1914 and 1814 cm^{-1} in the $\nu(\text{NO})$ region with the typical two band (A + E) pattern, indicating the *C*_{3v} symmetry typical for TNICs (see ESI[†]). X-ray quality crystals of 5 were obtained in THF–pentane at $-35\text{ }^\circ\text{C}$. The metrics of TNIC 5 (Table 1) are comparable to those of the known IMes (IMes = 1,3-dimesitylimidazol-2-ylidene) and I¹Pr (I¹Pr = 1,3-diisopropylimidazol-2-ylidene) analogues.^{7,18}

The molecular structures of 3, 4 and 5 are displayed and metric parameters are given in Table 1. All are tetrahedral complexes where the CN₂C₂ plane of the NHC bisects the N–Fe–N angle of the trigonal base of 5. This plane is approximately aligned with one Fe–NO vector of 3. The planes of the ‘wing-tip’ mesitylene in both 3 and 5 are roughly perpendicular to the CN₂C₂ plane and appear to umbrella the Fe(NO)₂L motif on one side. In the bis-NHC complex 4, the two



Scheme 2 Conversion of DNIC to TNIC.

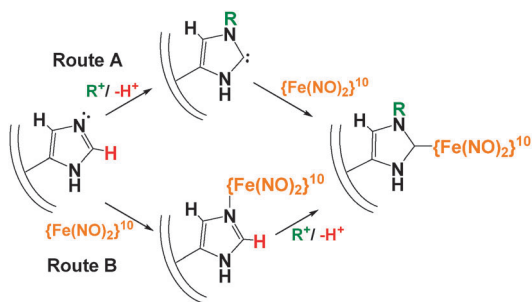


Chart 1

CN₂C₂ planes are perpendicular to each other, each having a mesitylene perpendicular to the respective CN₂C₂ plane. Each CN₂C₂ plane in **4** is aligned with one Fe–NO vector and the phenyl rings of the two mesitylenes are also oriented perpendicular and ‘trans’ to each other. The average Fe–N–O angles of **3**, **4** and **5** are similar (174.8°, 172.2° and 173.1° respectively). Upon comparing the metric data of two isoelectronic species **3** and **5**, we note that the Fe–NO_{avg} distance of complex **3** is shorter by 0.035 Å and the N–O_{avg} distance is longer by 0.031 Å than those of complex **5**. Furthermore, the ¹³C NMR spectra of complexes **3** and **5** show the carbene carbon chemical shifts at 190.7 and 142.3 ppm, respectively. Baker and Huynh found that the ¹³C NMR chemical shifts of the carbene carbon in Au and Pd complexes decrease with the increase in Lewis acidity of its metal center.^{19,20} Although the assignment of the oxidation state of Fe in these two isoelectronic species **3** and **5** cannot be based solely on the chemical shifts of the carbene carbon and the structurally linear NO ligands (*i.e.* linear NO is usually assigned as NO⁺),^{21,22} we can conclude that the electron density of the Fe center of neutral complex **3** is greater than that of cationic complex **5**. The changes of Fe–NO and N–O distances are as expected on the basis of back-bonding arguments.

In our previous work, the trinitrosyl [{Fe(NO)₃}¹⁰⁺] complex was found to have greater NO lability upon the addition of nucleophiles when compared to the reduced dinitrosyl [{Fe(NO)₂}¹⁰⁰], the latter needing one electron oxidation to trigger NO release in the presence of an NO trapping agent, *e.g.* metalloporphyrin.¹⁸ It is noteworthy that TNICs are inherently thermally unstable species as seen in the complexes of the XFe(NO)₃ type reported by Beck *et al.*²³ and other TNICs reported by Hayton, Legzdins *et al.*²⁴ and Berke *et al.*²⁵ Also, the trinitrosyl analogue cannot be obtained from direct reaction of [(imidazole)Fe(NO)₂(CO)] with [NO⁺]BF₄.⁷ Therefore, the ability of the NHC to stabilize otherwise unstable TNICs further validates the premise that NHCs have advantages over their imidazole counterparts on di/trinitrosyl iron platforms.

In conclusion, the type of reactivity seen in this study may have implications for processes taking place in biological DNICs with histidine donors when exposed to alkaline media. We have provided evidence for the occurrence of a base-promoted conversion of an imidazole to an NHC on a dinitrosyl iron platform. The integrity of

the dinitrosyl iron unit, a metallo-unit for which evidence of its biological significance accrues, is maintained throughout, thereby proving it to be stable under base treatment. Chart 1 presents this possibility as well as the typical method for NHC synthesis *via* deprotonation of imidazolium salts. We maintain that either route A or B is a potential pathway for the biosynthesis of {Fe(NO)₂}-NHC derivatives. Whether or not these are likely to be natural processes, the potential for labeling biomolecules at histidine to NHC converted sites is of significance.

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