Oxime Ether Radical Cations Stabilized by N-Heterocyclic Carbenes

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Abstract: N-heterocyclic carbene (NHC) nitric oxide (NHCNO) radicals, which can be regarded as iminoxyl radicals stabilized by NHCs, were found to react with a series of silyl and alkyl triflates to generate the corresponding oxime ether radical cations. The structures of the resulting oxime ether radical cations were determined by X-ray crystallography, along with EPR and computational analysis. In contrast, lutidinium triflate produced a 1:1 mixture of [NHCNO]+-[OTf−] and [NHCNHOH]+[OTf−] upon the reaction with NHCNO. This study adds an important example of stable singlet carbenes for stabilizing main-group radicals because of their π-conjugating effect, the synthesis and structures of which have not been reported previously.

Exploring the nature of highly reactive species is always a common interest of chemists. In particular, radicals are one of the most important reactive species in the field of chemistry and biology. In general, the vast majority of radicals are thermodynamically and kinetically unstable. Therefore, the isolation and structural characterization of novel radicals has remained a challenge.

Carbenes, having the general formula R2C=, are another very reactive species of interest.[1] Although carbenes were traditionally considered as highly unstable species because of their coordinative unsaturation and incomplete octet, numerous stable carbenes are now being synthesized and applied in various fields, thanks to the pioneering discoveries of Bertrand’s and Arduengo’s singlet carbenes.[2] Very interestingly, singlet carbenes offer a versatile platform for stabilizing reactive species.[3] One of the most common singlet carbenes, N-heterocyclic carbenes (NHCs), can stabilize reactive species by donating electrons, and has led to the successful isolation and characterization of several reactive radicals.

Radical cations are of particular interest because they occur as transient species, mainly in electron-transfer reactions, or in several ionization techniques for mass spectrometry.[4] With the aid of NHCs, boryl, silyl, and phosphoryl radical cations were successfully characterized, including X-ray crystal structures (Scheme 1).[5] Herein, we report the synthesis and characterization of the oxime ether radical cations E from the addition of different electrophiles to the parent radical. Previously, oxime radical cations and oxime ether radical cations had never been isolated or characterized, and were only proposed as intermediates of various photochemical reactions of oximes and oxime ethers.[5]

Recently, our group reported the synthesis and characterization of the stable N-heterocyclic carbene stabilized nitric oxide radicals (NHCNOs).[6] Interestingly, NHCNO (1) reacts with trimethylsilyl triflate (TMSOTf) and triisopropylsilyl triflate (TIPSOTf) to generate the radical cations 2a or 2b, respectively (Scheme 2). This reactivity resembles the addition of various reagents to N-heterocyclic carbene nitrous oxides (NHCN=O), reactivity which was intensively studied by the group of Severin.[8] When 1 was treated with a stoichiometric amount of silyl triflate in THF solution under a N2 atmosphere, the color of the reaction mixture changed immediately to dark brown. The product was crystallized by addition of n-pentane, and subsequently washed with n-pentane to yield either 2a or 2b as a brown solid. The structures of the radical cations 2a and 2b were unambiguously determined by X-ray crystallography (Figura...
The electronic structures of 2a and 2b were also confirmed by electron paramagnetic resonance (EPR) spectroscopy (Figures 1c,d). The experimental EPR spectra were recorded using a saturated benzene solution of the radical cations at room temperature. The EPR signals of 2a and 2b were very similar as they both split to 13 peaks, mainly due to the coupling with three nitrogen atoms and several hydrogen atoms. The hyperfine coupling constants for 2a were calculated to be $a(1^4N) = 27.1, 9.5, 7.7$ MHz, $a(1^4H) = 10.5, 6.8$ MHz. DFT calculations suggest that N3 has a larger hyperfine coupling constant than other nitrogen atoms, and is in consistent with the largest spin density on N3 (50%). It is notable that the vinyl protons of the imidazole ring show significant contribution on the hyperfine coupling, and confirms the stabilization power of NHC by spin delocalization. Calculation also shows that the singly occupied molecular orbitals (SOMOs) of 2a and 2b are both delocalized through the molecular plane (see Figure S8 in the Supporting Information). The radical cations 2a and 2b are moisture-sensitive, and should be stored under an inert atmosphere of nitrogen. They slowly decompose under an ambient atmosphere to generate a mixture of imidazolium salts (Pr-H•OTf •1,3-bis(2,6-disopropylphenyl)imidazolium triflate) and other unidentified products. In the presence of an excess amount of water, 2a decomposes to give the imidazolium salt (PrH•OTf •1) in 91% yield.

To date, there have been no reports on the nucleophilic reactivity of iminoxyl radicals, while the nucleophilic addition of aminoxyl radicals to Lewis acids are well studied. For example, TEMPO ([2,2,6,6-tetramethylpiperidin-1-yl]oxyl radical] reacts with neutral electrophiles such as FeCl3, AlCl3, and B(C6F5)3 to form neutral radical adducts[9]. In contrast to aminoxyl radicals, both the nitrogen and oxygen atom of iminoxyl radicals may act as a nucleophilic center. DFT calculations at the B3LYP/6-31G(d,p) level of theory revealed that O addition is thermodynamically more favorable than N addition by 19.8 kcal mol−1 for TMS derivatives. This preference is presumably a result of both the steric hindrance and oxophilic nature of silicon.

After the isolation and characterization of 2a and 2b, we wanted to expand this reactivity between 1 and silicon electrophiles toward lighter, carbon analogues. In a manner similar to the synthesis of 2, methyl (3a) and isopropyl (3b) analogues were successfully isolated (Scheme 2). The experimental EPR spectra of 3a and 3b in a benzene solution was well matched with the simulated spectra of the expected products (Figure 2), thus suggesting that the reactivity between NHCNOs and silicon electrophiles can indeed be expanded to analogous carbon electrophiles. Unfortunately, attempts to grow single crystals of 3a for X-ray crystallography were unsuccessful, but single crystals of 3b were successfully obtained after slowly layering n-pentane into the reaction mixture. The C1-N3 (1.345(2) Å) and N3-O1 bond lengths (1.353(2) Å) of 3b indicate a bond order of 1.5, whereas DFT calculations also revealed the bond order of 1.51 and 1.45 for C1-N3 and N3-O1, respectively. The SOMOs, derived from DFT calculations, of 3a and 3b were delocalized through the molecular plane, similar to the silyl analogues (see Figure S8). The experimental EPR spectrum of 3b shows 14 peaks, while 3a shows 16 peaks resulting the additional hyperfine interactions with the nearby methyl hydrogens.

The cyclic voltammograms of 2a and 3b show one reversible redox peak at $E_{1/2} = 0.406$ V and 0.563 V, respectively, versus the Ag/AgCl (saturated) electrode, and indicates that one-electron reduction reactions of the radical cations are possible (Figure 3). Compared to 2a, 3b has a higher oxidizing power, as expected for the isopropyl group being a weaker electron-donor than the trimethylsilyl group. These results suggest the potential application of the oxime
ether radical cations as a tunable organic oxidant since the redox potential of the radicals can be easily adjusted by changing either the electrophile or the NHC. It is notable that their reduction potential is comparable or higher than conventional one-electron oxidants such as ferrocenium (0.44 V) and tetracyanoethylene (0.17 V).

To verify the redox behavior of the radical cations, a THF solution of 2a was treated with 1.1 equivalents of ferrocene as a one-electron donor (Scheme 3). The color of the reaction mixture changed from dark brown to dark green, and after work up, the neutral oxime ether 4 was isolated in 66% yield and successfully characterized.

The isolation of both silyl oxime ether radical cations, 2a,b, and alkyl oxime ether radical cations, 3a,b, encouraged us to attempt the synthesis of the unprotected oxime radical cation 5 (Scheme 4). However, reaction of 1 with neither triflic acid (HOTf) nor lutidinium triflate (LutHOTf) afforded 5, as the products from both reactions exhibited no EPR signal. Instead of the radical cation 5, the reaction between I and a stoichiometric amount of LutHOTf resulted in a 1:1 mixture of two non-radical products: [PrNO]±[OTf −] (6) and [PrNHOH+][OTf −] (7). It is notable that this reactivity resembles the disproportionation of aminoxyl radicals triggered by strong acids.[10] Both 6 and 7 were obtained in 37% yields as measured by 1H NMR spectroscopy. Although the isolation of 6 and 7 in reasonable yields was not successful, we were able to obtain single crystals suitable for X-ray crystallography, and so confirmed the structures of both 6 and 7 (Figure 4). It is interesting that the structural parameters of 6 and 7 are distinctly different. The C1-N3 bond length of 6 (1.412(3) Å) is longer than that of 7 (1.348(4) Å), while the N3-O1 bond length of 6 (1.228(3) Å) is much shorter than that of 7 (1.405(4) Å). The most significant structural difference is that the (imidazole ring)-N-O fragment is almost planar in 6 (N2-C1-N3-O1 torsion angle: 1.8(3)), but is twisted in 7 (N2-C1-N3-O1 torsion angle: 35.8(4)). These structural parameters were well reproduced in the DFT calculations at B3LYP/6-31G(d,p) level of theory.

For the disproportionation of I to 6 and 7, two different mechanisms were proposed. One possible mechanism starts with the protonation of I to generate the radical cation 5 as a transient intermediate, followed by disproportionation (i.e., hydrogen-atom transfer) to generate 6 and 7. Another plausible mechanism is the single-electron transfer between 5 and remaining I to generate 6 with the oxime (PrNHOH; 1,3-bis(2,6-diisopropylphenyl)imidazol-2-one oxime) which forms 7 after protonation.[11] It is notable that I undergoes reversible one-electron oxidation ($E_{1/2} = 0.327$ V vs. saturated Ag/AgCl).[7] and 5 may act as a one-electron oxidant in the

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**Figure 2.** Characterization of 3a and 3b. a) Molecular structure of 3b from X-ray crystallography.[11] The thermal ellipsoids are shown at a 50% probability level. Triflate anions were omitted for clarity. Experimental (bottom) and simulated (top) EPR spectra of 3a (b; g = 2.0094; hyperfine coupling constants: $a(^{1}H) = 26.1, 9.2, 7.2$ MHz, $a(^{1}P) = 11.1, 7.1, 6.3, 6.3$ MHz) and 3b (c; $g = 2.0096$; hyperfine coupling constants: $a(^{1}H) = 25.7, 9.1, 7.3$ MHz, $a(^{1}P) = 10.3, 9.3, 6.5, 1.5$ MHz). See the Supporting Information for the details.

**Figure 3.** Cyclic voltammogram of 2a and 3b. Recorded using dry and degassed THF solution (0.1 M NBu2PF6 as electrolyte; potential versus saturated Ag/AgCl; scan rate = 0.5 V s$^{-1}$).

**Scheme 3.** One-electron Reduction of 2a. a) Yield of isolated product.

**Scheme 4.** Attempted Synthesis of the oxime radical cation 5. a) Yields of a mixture of 6 and 7 as determined by $^{1}$H NMR spectroscopy.
reaction to generate 6. In comparison with either 2a ($E_{1/2} = 0.406$ V) or 3b ($E_{1/2} = 0.563$ V), 5 is expected to be a stronger oxidant because of the absence of the electron-donating silyl or alkyl groups.

In summary, we have presented the synthesis of silyl and alkyl oxime ether radical cations (2 and 3), from the reaction of the NHC-stabilized nitric oxide radical I with either silicon or carbon electrophiles. Single-crystal X-ray and computational studies suggest that the spin densities of 2 and 3 are delocalized over the molecular plane. The well-defined one-electron redox behavior suggests the potential application of the radical cations as a tunable organic oxidant. In contrast, the reaction of 1 toward a simple proton yielded a 1:1 mixture of NHC-bound nitrosyl (6) and hydroxylamine (7) derivatives. This work is the first demonstration of the nucleophilicity of iminoxyl radicals, and thus extends our understanding of the reactive radical species, and was enabled by the aid of the novel properties of N-heterocyclic carbenes. The reactivity of the iminoxyl radicals toward other interesting electrophiles is now under active investigation.

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Conflict of interest

The authors declare no conflict of interest.

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[11] CCDC 1554040 (2a), 1554041 (2b), 1554042 (3a), 1554043 (6), and 1554044 (7) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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