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To be cited as: Angew. Chem. Int. Ed. 10.1002/anie.201710530 Angew. Chem. 10.1002/ange.201710530

Link to VoR: http://dx.doi.org/10.1002/anie.201710530 http://dx.doi.org/10.1002/ange.201710530

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# Oxime Ether Radical Cations Stabilized by *N*-Heterocyclic Carbene

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**Abstract:** *N*-heterocyclic carbene 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<sup>+</sup>][OTf<sup>-</sup>] upon the reaction with NHCNO. This study adds an important example of stable singlet carbenes stabilizing main group radicals due to their  $\pi$ -conjugating effect, the synthesis and structures of which have never been elucidated 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  $R_2C$ :, are another very reactive species of interest.<sup>[1]</sup> 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.<sup>[2]</sup> Very interestingly, singlet carbenes offer a versatile platform for stabilizing reactive species.<sup>[3]</sup> One of the most common singlet carbenes, *N*heterocyclic carbenes (NHCs), can stabilize reactive species by donating electrons, which 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.<sup>[4]</sup> With the aid of NHCs, boryl, silyl, and phosphoryl radical cations were successfully characterized including X-ray crystal structures (**Scheme 1**).<sup>[5]</sup> Herein, we report the synthesis and characterization of oxime ether radical cations **H** from the addition of different electrophiles to the parent radical. Previously, oxime

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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.<sup>[6]</sup>



**Scheme 1.** Examples of structurally characterized NHC-stabilized main group radical cations. (Dipp = 2,6-diisopropylphenyl; 'Bu = *tert*-butyl; 'Pr = isopropyl; TMS = trimethylsilyl; TIPS = triisopropylsilyl)

reported the synthesis Recently, our group and characterization of the stable N-heterocyclic carbene stabilized nitric oxide radicals (NHCNOs).<sup>[7]</sup> Interestingly, NHCNO 1 reacts with trimethylsilyl triflate (TMSOTf) or triisopropylsilyl triflate (TIPSOTf) to generate the corresponding radical cations 2a or 2b, respectively (Scheme 2). This reactivity resembles the addition of various reagents to N-heterocyclic carbene nitrous oxides (NHCN<sub>2</sub>O), which was intensively studied by the Severin group.<sup>[8]</sup> When 1 was treated with a stoichiometric amount of silvl triflate in THF solution under N<sub>2</sub> atmosphere, the color of the reaction mixture changed immediately to dark brown. The product was crystallized by addition of pentane, and subsequently washed with pentane to yield 2a or 2b as a brown solid. The structure of the radical cations 2a and 2b were unambiguously determined by X-ray crystallography (Figure 1a,b). The C1-N3 bond length of 2a (1.334(4) Å) and 2b (1.332(5) Å) is slightly shorter than that of 1 (1.350(6) Å), and N3-O1 bond length is slightly longer in 2a (1.358(3) Å) and **2b** (1.363(4) Å) than **1** (1.309(5) Å), while both bond lengths indicate a bond order of 1.5. The O1-Si1 bond length of **2b** (1.747(3) Å) is slightly longer than that of **2a** (1.734(2) Å) presumably due to the large size of the triisopropylsilyl group. The (imidazole ring)-N-O-Si groups of 2a and 2b are planar, which suggests delocalization of the radical through  $\pi$ conjugation. The molecular structures of 2a and 2b are also in good agreement with the structures from density functional theory (DFT) calculations at B3LYP/6-31G(d,p) level of theory. The calculated Wiberg bond orders for C1-N3 (1.51 for both 2a and 2b), N3-O1 (1.46 for 2a; 1.48 for 2b), and O1-Si1 (0.83 for 2a; 0.80 for 2b) are consistent with the bond length data from the single crystal X-ray structure analysis.

#### 10.1002/anie.201710530

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Scheme 2. Syntheses of the Radical Cations 2 and 3. a. Isolated yields.



**Figure 1.** Characterization of the radical cations **2a** and **2b**. (a) Molecular structure of **2a** and (b) **2b** from X-ray crystallography. The thermal ellipsoids are set at a 50% probability level. Triflate anions were omitted for clarity. (c) Experimental (bottom) and simulated (top) EPR spectra of **2a** (g = 2.0083; hyperfine coupling constants:  $a(^{14}N) = 27.1$ , 9.5, 7.7 MHz,  $a(^{1}H) = 10.5$ , 6.8 MHz) and (d) **2b** (g = 2.0092; hyperfine coupling constants:  $a(^{14}N) = 26.7$ , 9.6, 7.9 MHz,  $a(^{1}H) = 10.3$ , 6.4, 1.5, 1.5 MHz). See the Supplementary Information for the details.

The electronic structure of the radical cations 2a and 2b were also confirmed by electron paramagnetic resonance (EPR) spectroscopy (Figure 1c,d). The experimental EPR spectra were recorded using saturated benzene solution of the radical cations at room temperature. The EPR signals of 2a and 2b were very similar; 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  $a(^{14}N) = 27.1, 9.5$ , 7.7 MHz;  $a(^{1}H) = 10.5$ , 6.8 MHz. DFT calculations suggest that N3 has larger hyperfine coupling constant than other nitrogen atoms, 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, which 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 molecular plane (**Figure S8**). The radical cations **2a** and **2b** are moisture-sensitive, and should be stored under inert atmosphere of nitrogen. They slowly decompose in ambient atmosphere to generate a mixture of imidazolium salt (*I*PrH+OTf-; 1,3-bis(2,6-diisopropylphenyl)imidazolium triflate) and other unidentified products. In the presence of an excess amount of water, **2a** decomposes to give the imidazolium salt (*I*PrH+OTf-) in 91% isolated yield.

Up to date, there have been no report of 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 FeCl<sub>3</sub>, AlCl<sub>3</sub>, and B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> to form neutral radical adducts.<sup>[9]</sup> In contrast to aminoxyl radicals, both nitrogen and oxygen atom of iminoxyl radicals may act as a nucleophilic center. DFT calculations at B3LYP/6-31G(d,p) level of theory revealed that O-addition is thermodynamically more favorable than N-addition by 19.8 kcal/mol for TMS derivatives. This is presumably due to both steric hindrance and oxophilic nature of silicon.

After the isolation and characterization of the NHC-stabilized silvl oxime ether radicals 2a and 2b, we wanted to expand this reactivity between NHCNO 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 benzene solution was well matched with the simulated spectra of the expected products (Figure 2), 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 pentane into the reaction mixture. The C1–N3 bond length (1.345(2) Å) and N3–O1 bond length (1.353(2) Å) of 3b indicate a bond order of 1.5, while DFT calculation also revealed the bond order of 1.51 and 1.45 for C1-N3 and N3-O1, respectively. SOMOs of 3a and 3b from DFT calculation were delocalized through the molecular plane, similar to the silyl analogues (Figure S8). The experimental EPR spectrum of 3b shows 14 peaks, while 3a shows 16 peaks due to the additional hyperfine interaction with the nearby methyl hydrogens.

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**Figure 2.** Characterization of the radical cations **3a** and **3b**. (a) Molecular structure of **3b** from X-ray crystallography. The thermal ellipsoids are set at a 50% probability level. Triflate anions were omitted for clarity. (b) Experimental (bottom) and simulated (top) EPR spectra of **3a** (g = 2.0094; hyperfine coupling constants:  $a(^{14}N) = 26.1, 9.2, 7.2$  MHz,  $a(^{1}H) = 11.1, 7.1, 6.3, 6.3, 6.3$  MHz) and (c) **3b** (g = 2.0096; hyperfine coupling constants:  $a(^{14}N) = 25.7, 9.1, 7.3$  MHz,  $a(^{1}H) = 10.3, 9.3, 6.5, 1.5$  MHz). See the Supplementary Information for the details.

The cyclic voltammogram of **2a** and **3b** showed one reversible redox peak at  $E_{1/2} = 0.406$  V and 0.563 V, respectively, versus Ag/AgCl (saturated) electrode, which 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, neutral oxime ether **4** was isolated in 66% yield and successfully characterized.



Figure 3. Cyclic voltammogram of 2a and 3b. Recorded using dry and degassed THF solution (0.1 M  $NBu_4PF_6$  as electrolyte; potential versus saturated Ag/AgCl; scan rate = 0.5 V/s).



Scheme 3. One-electron Reduction of 2a. a. Isolated yield.

The isolation of both silvl 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 1 and a stoichiometric amount of LutHOTf resulted in a 1:1 mixture of two non-radical products: [/PrNO<sup>+</sup>][OTf<sup>-</sup>] (6) and [/PrNHOH<sup>+</sup>][OTf<sup>-</sup>] (7). It is notable that this reactivity resembles the disproportionation of aminoxyl radicals triggered by strong acids.<sup>[10]</sup> Both 6 and 7 were obtained in 37% yields as measured by <sup>1</sup>H NMR, and characterized by high resolution mass spectrometry. Although the isolation of 6 or 7 in reasonable yields was not successful, we were able to obtain their single crystals suitable for X-ray crystallography, and so confirmed the structures of both 6 and 7 (Figure 4).



Scheme 4. Attempted Synthesis of the Oxime Radical Cation 5. a. <sup>1</sup>H NMR yields obtained from a mixture of 6 and 7.

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Figure 4. (a) Molecular structure of 6 and (b) 7 from X-ray crystallography. The thermal ellipsoids are set at a 50% probability level. Triflate anions, solvent molecules (toluene), and minor disorders were omitted for clarity. Bond lengths and bond angles are described in the Supplementary Information.

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 **1** to **6** and **7**, two different mechanisms were proposed. One possible mechanism starts with the protonation of **1** 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 the intermediate **5** and remaining **1** to generate **6** with oxime **8**.<sup>[10c]</sup> It is notable that **1** undergoes reversible one-electron oxidation (E<sub>1/2</sub> = 0.327 V vs. saturated Ag/AgCl),<sup>[7]</sup> and **5** may act as a one-electron oxidant in the reaction to generate **6**. In comparison with **2a** (E<sub>1/2</sub> = 0.406 V) or **3b** (E<sub>1/2</sub> = 0.563 V), **5** is expected to be a stronger oxidant, due to 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 1 with silicon or carbon electrophiles, respectively. Single crystal X-ray and computational studies suggest that the spin density of compounds 2 and 3 are delocalized over the molecular plane. The well-defined 1e redox behavior suggests the potential application of the radical cations as a tunable organic oxidant. On the other hand, 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, which 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.

#### Acknowledgements

This work was supported by the Institute for Basic Science (IBS) [IBS-R007-D1]. X-ray diffraction experiment with synchrotron

radiation was performed at the Pohang Accelerator Laboratory (Beamline 2D and 6D). We thank Gregory B. Boursalian and Dmitry V. Yandulov for helpful discussions.

**Keywords:** carbenes • iminoxyl radicals • nucleophilic addition • radical cations • radicals

- a) D. Bourissou, O. Guerret, F. P. Gabbaï, G. Bertrand, *Chem. Rev.* 2000, 100, 39-92; b) M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* 2014, *510*, 485-496.
- [2] a) A. Igau, H. Grutzmacher, A. Baceiredo, G. Bertrand, J. Am. Chem. Soc. 1988, 110, 6463-6466; b) A. J. Arduengo, R. L. Harlow, M. Kline, J. Am. Chem. Soc. 1991, 113, 361-363; c) J. Huang, S. P. Nolan, J. Am. Chem. Soc. 1999, 121, 9889-9890; d) V. Lavallo, Y. Canac, C. Prasang, B. Donnadieu, G. Bertrand, Angew. Chem. Int. Ed. 2005, 44, 5705-5709; e) T. W. Hudnall, C. W. Bielawski, J. Am. Chem. Soc. 2009, 131, 16039-16041.
- a) D. Martin, M. Soleilhavoup, G. Bertrand, *Chem. Sci.* 2011, *2*, 389-399;
  b) C. D. Martin, M. Soleilhavoup, G. Bertrand, *Chem. Sci.* 2013, *4*, 3020-3030;
  c) H. Song, Y. Kim, J. Park, K. Kim, E. Lee, *Synlett* 2016, *27*, 477-485;
  d) O. Back, B. Donnadieu, M. von Hopffgarten, S. Klein, R. Tonner, G. Frenking, G. Bertrand, *Chem. Sci.* 2011, *2*, 858.

 [4] a) M. Schäfer, M. Drayß, A. Springer, P. Zacharias, K. Meerholz, *Eur. J.* Org. Chem. 2007, 2007, 5162-5174; b) M. Schmittel, A. Burghart, Angew. Chem. Int. Ed. 1997, 36, 2550-2589; c) T. D. Beeson, A. Mastracchio, J. B. Hong, K. Ashton, D. W. Macmillan, *Science* 2007, 316, 582-585.

- [5] a) O. Back, M. A. Celik, G. Frenking, M. Melaimi, B. Donnadieu, G. Bertrand, J. Am. Chem. Soc. 2010, 132, 10262-10263; b) O. Back, B. Donnadieu, P. Parameswaran, G. Frenking, G. Bertrand, Nat. Chem. 2010, 2, 369-373; c) R. Kinjo, B. Donnadieu, G. Bertrand, Angew. Chem. Int. Ed. 2010, 49, 5930-5933; d) R. Kinjo, B. Donnadieu, M. A. Celik, G. Frenking, G. Bertrand, Science 2011, 333, 610-613; e) H. Tanaka, M. Ichinohe, A. Sekiguchi, J. Am. Chem. Soc. 2012, 134, 5540-5543; f) D. Martin, C. E. Moore, A. L. Rheingold, G. Bertrand, Angew. Chem. Int. Ed. 2013, 52, 7014-7017; g) P. Bissinger, H. Braunschweig, A. Damme, C. Horl, I. Krummenacher, T. Kupfer, Angew. Chem. Int. Ed. 2015, 54, 359-362.
- a) J. L. Hofstra, B. R. Grassbaugh, Q. M. Tran, N. R. Armada, H. J. P. de Lijser, *J. Org. Chem.* 2015, *80*, 256-265; b) H. J. P. de Lijser, C. K. Tsai, *J. Org. Chem.* 2004, *69*, 3057-3067; c) H. J. P. de Lijser, F. H. Fardoun, J. R. Sawyer, M. Quant, *Org. Lett.* 2002, *4*, 2325-2328.
- J. Park, H. Song, Y. Kim, B. Eun, Y. Kim, D. Y. Bae, S. Park, Y. M. Rhee,
  W. J. Kim, K. Kim, E. Lee, J. Am. Chem. Soc. 2015, 137, 4642-4645.
- [8] a) A. G. Tskhovrebov, E. Solari, M. D. Wodrich, R. Scopelliti, K. Severin, Angew. Chem. Int. Ed. 2012, 51, 232-234; b) A. G. Tskhovrebov, B. Vuichoud, E. Solari, R. Scopelliti, K. Severin, J. Am. Chem. Soc. 2013, 135, 9486-9492; c) A. G. Tskhovrebov, L. C. Naested, E. Solari, R. Scopelliti, K. Severin, Angew. Chem. Int. Ed. 2015, 54, 1289-1292.
- a) J. J. Scepaniak, A. M. Wright, R. A. Lewis, G. Wu, T. W. Hayton, J. Am. Chem. Soc. 2012, 134, 19350-19353; b) X. Tao, G. Kehr, X. Wang, C. G. Daniliuc, S. Grimme, G. Erker, Chem. Eur. J. 2016, 22, 9504-9507; c) W.-w. Huang, H. Henry-Riyad, T. T. Tidwell, J. Am. Chem. Soc. 1999, 121, 3939-3943.
- a) V. A. Golubev, R. I. Zhdanov, V. M. Gida, E. G. Rozantsev, *Russ. Chem. Bull.* **1971**, *20*, 768-770; b) V. A. Golubev, V. D. Sen, I. V. Kulyk, A. L. Aleksandrov, *Russ. Chem. Bull.* **1975**, *24*, 2119-2126; c) V. D. Sen, V. A. Golubev, *J. Phys. Org. Chem.* **2009**, *22*, 138-143.

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Nucleophilic addition of NHC-stabilized nitric oxide radical (NHC-NO) to silyl and alkyl triflates generate silyl and alkyl oxime ether radical cations. In addition, disproportionation occurs when NHCNO reacts with lutidinium triflate, generating NHC-stabilized nitrosyl cation (NHC-NO<sup>+</sup>) and a hydroxylamine derivative (NHC-NHOH+).