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Metal free oxidation of vinamidine derivatives: a simple synthesis of α -keto- β -diimine ligands†

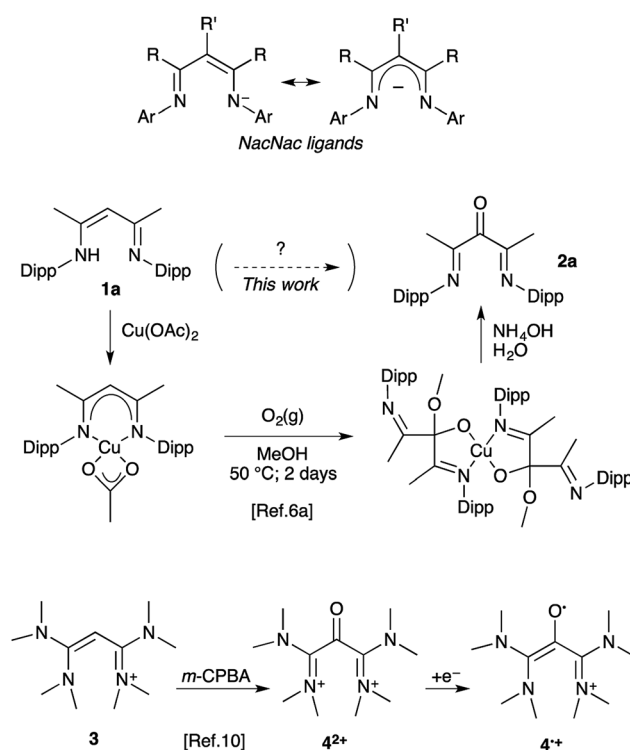
 Monika Tripathi, Vianney Regnier, Zakaria Ziani, Marc Devillard, Christian Philouze and David Martin *

Oxidation of vinamidinium salts with *meta*-chloroperbenzoic acid is the key synthetic step towards new persistent 1,3-di(amino)oxyallyl radical cations. When applied to parent vinamidines, this protocol allows for a simple straightforward synthesis of α -keto- β -diimine ligands, for which no convenient synthesis was previously available.

β -Diketiminates, so-called NacNac ligands (Scheme 1), have been a focus in coordination chemistry for decades.¹ Structural modifications include a large variety of N-substituents, as well as bulky,² electron-withdrawing,³ or electron donating⁴ R groups. Substitution at the central carbon atom ($R' \neq H$) has also been explored as a strategy to tame this reactive position and enhance the chemical stability of the complex.⁵ The α -keto- β -diimines are among rare representatives with a more significant modification at the central carbon. These electron-deficient ligands have found applications in the design of highly active nickel(II) initiators for the synthesis of high molecular weight polyethylenes and poly- α -olefins.⁶ Interestingly, low-disperse semi-crystalline polymers could be obtained under living conditions and remarkable enantiomorphic site control could be achieved.⁷

The low availability of α -keto- β -diimines has clearly hampered further development. Their metal complexes have been known for long, but only as occasional by-products from the air-decomposition of unprotected NacNac complexes ($R' = H$).⁸ To date only a rare selective oxygen-degradation of copper(II) complexes allows for the synthesis of a handful of 2,4-di(arylimino)pentan-3-ones **2** from the corresponding vinamidines **1**.^{6a,d,9} The procedure requires (i) the synthesis of the NacNac-Cu(II) complex, (ii) oxidation at the ligand with dioxygen in a methanol/dichloromethane mixture, (iii) the decomplexation and hydrolysis of the resulting hemiacetal ligand (Scheme 1). In turn, we had to synthesize 2,4-bis((2,6-diisopropylphenyl)imino)pentan-3-one **2a** and experienced firsthand the length and limitations of this methodology. Among the three steps, the oxidation of the NacNac-copper complex is especially inconvenient and wasteful, as it consists of a continuous bubbling of pure dioxygen

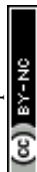
in a warm solution for two days.^{6a} Recently, we released a parent, though in principle far simpler, oxidation of tetrakis(dimethylamino) vinamidinium **3** into di(amidinium)ketone **4**²⁺ with *meta*-chloroperbenzoic acid (*m*-CPBA) as oxidant. Our initial focus was on the corresponding radical **4**^{•+}, which was found remarkably air-persistent, despite minimal steric hindrance.¹⁰ Herein we report how further assessment of such 1,3-(diamino)oxyallyl radical cations ultimately led to a straightforward protocol for the synthesis of α -keto- β -diimines from NacNac precursors.



Scheme 1 Previously reported synthesis of α -keto- β -diimines and synthesis of air-persistent radical **4**^{•+} from vinamidinium **3**.

Univ. Grenoble Alpes, CNRS, DCM, 38000 Grenoble, France. E-mail: david.martin@univ-grenoble-alpes.fr

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Prior to **4**⁺, only two oxallyl radical cations had been synthesized from the reaction of rare stable electrophilic carbenes with carbon monoxide.^{11–13} In principle, the oxidation of vinamidinium salts should provide for a more simple and general route, with no need of sophisticated N-substituents. To probe this assumption, we first considered the oxidative functionalization of the chloride salt of vinamidinium **5**⁺, which was synthesized from *N,N*-dimethyl-benzamide and 1-dimethylamino-1-phenylethene.¹⁴ Addition of *m*-CPBA at room temperature yielded 2-chlorovinamidium **6** in 71% yield (Scheme 2). This result indicated the competitive formation of *meta*-chlorobenzoyl hypochlorite Cl(C₆H₄)CO₂Cl, from the reaction of chloride anions with *m*-CPBA.¹⁵ Therefore we proceeded to an anion metathesis. The resulting tetrafluoroborate salt reacted with *m*-CPBA, but this time to afford **7**·H⁺, which was fully characterized and isolated in 74% yield. Of note, the NMR spectra of vinamidiniums **6** and **7**·H⁺ mostly differ in the ¹³C chemical shift of their central carbon: 94 and 127 ppm, respectively. They were unambiguously characterized by mass spectrometry analyses and X-ray diffraction studies (Fig. 1).

Solutions of $7\cdot\text{H}^+$ featured an EPR signal upon exposure to air. This slow reaction could be brought to fast completion in presence of potassium hydrogenocarbonate. The remarkable

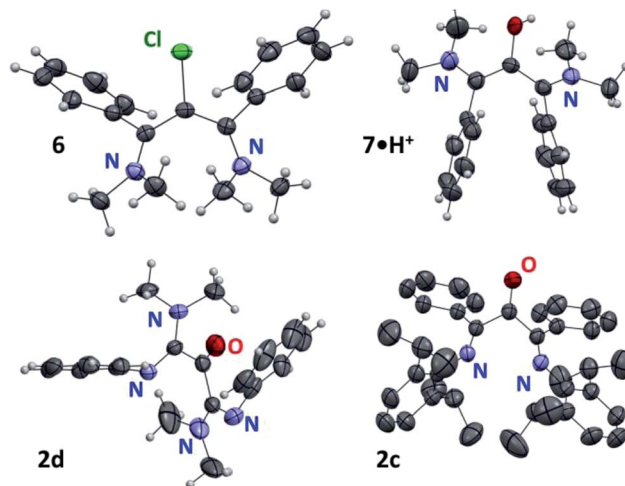
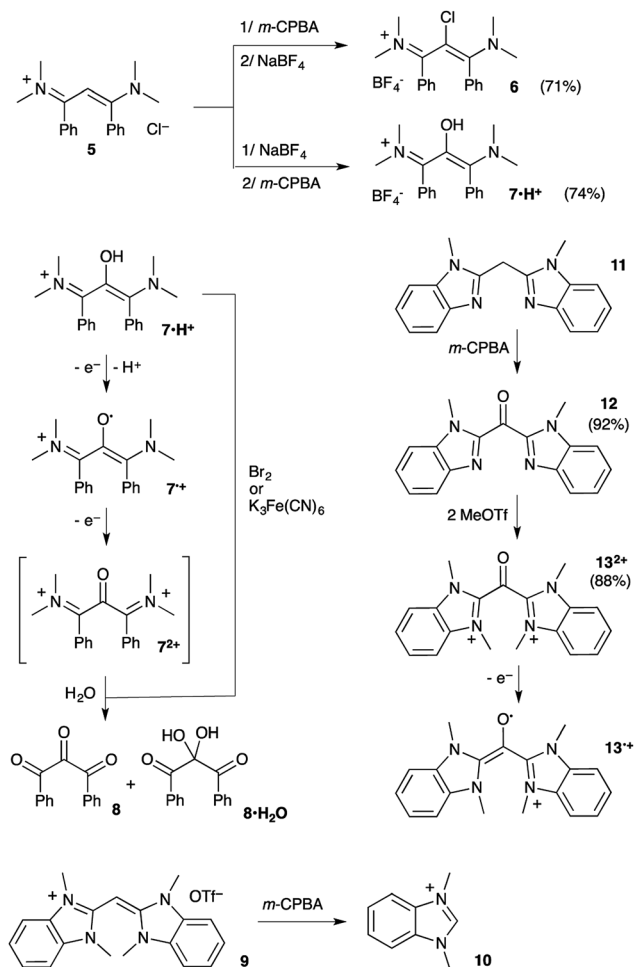


Fig. 1 X-ray structures of **6**, **7**·H⁺ and **2c,d** with thermal ellipsoids drawn at 50% probability level. Most hydrogen atoms, solvent molecules and counter-anions were omitted for clarity.

persistence under aerobic conditions of the resulting radical (in aerated solutions for several hours) was reminiscent of our previously reported stable oxyallyl radicals, some being similarly synthesized by auto-oxidation of parented enol-cations.^{11a} Therefore, we hypothesized the formation of radical $7^{+\bullet}$. Although the radical ultimately decayed and couldn't be isolated, the excellent fit between the experimental EPR hyperfine coupling constants¹⁶ and the calculated values¹⁷ for $7^{+\bullet}$ strongly supported this reasonable assumption (Fig. 2a). The reaction of $7 \cdot \text{H}^+$ with excess *meta*-chloroperbenzoic acid or stronger oxidants, such as dibromine or potassium ferricyanate, led to over oxidation and directly afforded EPR-silent mixtures of trione **8** and the corresponding hydrated *gem*-diol $8 \cdot \text{H}_2\text{O}$,¹⁸ likely through the formation and subsequent hydrolysis of electron-poor di(iminium)ketone 7^{2+} .

We turned to mono(methine)cyanine **9** featuring electron-rich benzimidazole patterns.¹⁹ However, the reaction of **9** with *m*-CPBA afforded known²⁰ 1,3-dimethyl- benzimidazolium **10**, and not the expected di(benzimidazolium)ketone **13**²⁺ (Scheme 2). Note that uncompleted, but clean, formation of **10** was still observed when adding sub-stoichiometric (one equivalent) *m*-CPBA over one hour at $-78\text{ }^{\circ}\text{C}$. Importantly, dication **13**²⁺ could be finally synthesized by the oxidation of di(imine) methane **11**¹⁹ by *m*-CPBA, followed by di(alkylation) of the resulting di(imine)ketone **12**. Given that **13**²⁺ was found almost unreactive towards water, the formation of **10** from **9** results from further oxidative cleavages of **13**²⁺, and not its hydrolysis.²¹ According to cyclic voltammetry experiments, **13**²⁺ undergoes successive reductions at $E_{1/2} = -0.12\text{ V vs. Fc/Fc}^{+}$ (reversible) and $E_{\text{pc}} = -0.9\text{ V}$ (with further chemical evolution), which we attributed to the formation of radical cation **13**^{•+} and zwitterionic oxyallyl **13**, respectively (see ESI[†]). We performed the electrochemical reduction of a solution of **13**²⁺ in acetonitrile at $E = -0.5\text{ V}$. The stoichiometry (one coulomb per mole of substrate), the observation of a strong EPR signal, as well as an excellent fit between experimental and theoretical hyperfine coupling constants, confirmed the formation of persistent **13**^{•+}



Scheme 2 Redox transformations of di(imidazole)methane and 1,3-di(phenyl) vinamidinium derivatives.

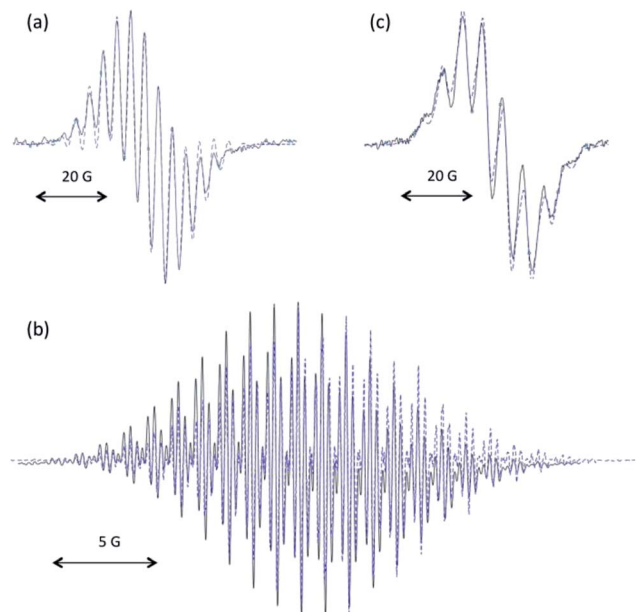
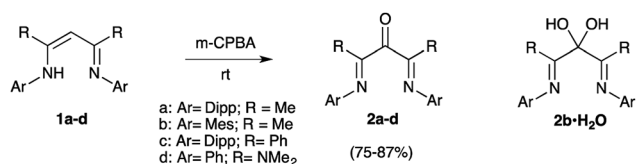


Fig. 2 Experimental isotropic X-band EPR spectra in dichloromethane at room temperature (plain black line) of $7^{\bullet+}$ (a), $10^{\bullet+}$ (b) and a crude reaction mixture of *m*-CPBA and **1a** (c). Simulated spectra (dashed blue line) were obtained with (a) a Lorentzian line-broadening parameter of 0.22 and the following set of hyperfine constants: $a(^{14}\text{N}) = 8.6$ MHz (2 nuclei) and $a(^1\text{H}) = 12.0$ MHz (12 nuclei); (b) with a Lorentzian line-broadening parameter of 0.013 and the following set of hyperfine constants: $a(^{14}\text{N}) = 3.1$ MHz (4 nuclei), $a(^1\text{H}) = 6.5$ MHz (12 nuclei) and $a(^1\text{H}) = 0.86$ MHz (4 nuclei); (c) with a Lorentzian line-broadening parameter of 0.37 and the following set of hyperfine constants: $a(^{14}\text{N}) = 7.8$ MHz (2 nuclei), $a(^1\text{H}) = 16.5$ MHz (1 nucleus) and $a(^1\text{H}) = 15.6$ MHz (6 nuclei).

(Fig. 2b), which ultimately decayed at room temperature after several hours.

The formation of di(imine)ketone **12** from **11** was so clean that it prompted us to explore further the direct oxidation of NacNac precursors. To our delight, treatment of **1a**²² afforded **2a** in 98% yield. In contrast with the former long and tedious syntheses from literature, the one-step reaction was completed after one hour at room temperature on multigram scales. EPR monitoring of the reaction showed the formation of a paramagnetic intermediate. Simulation of the hyperfine structure of the spectra required significant coupling with a single proton, in addition to two equivalent nitrogen atoms and six protons (Fig. 2c). This suggested the transient formation of N-protonated radical $1a\cdot\text{H}^{\bullet+}$, parented to $4^{\bullet+}$, $7^{\bullet+}$ and $13^{\bullet+}$, thus implying closely related pathways for the *m*-CPBA oxidation of vinamidiniums and vinamidines **1a**.



Scheme 3 One-step synthesis of α -keto- β -diimines **2a–d** from vinamidines **1a–d**.

The only few reported β -di(imine)ketones were derivatives of acetylacetone and ortho-substituted anilines. Apart from **1a**, which can be stored for several days, they were described as unstable ligands, to be used as soon as synthesized.^{6d} We applied our protocol to vinamidines **1b**²¹ with 2,4,6-trimethylaryl N-substituents and, indeed, the resulting ketone **2b** decayed into a complex mixture within hours. Fast work-up allowed for its isolation in 75% yield (Scheme 3). However, even freshly crystallized **2b** contained an impurity with similar NMR chemical shifts, except for a ^{13}C NMR signal (quarternary carbon) at 94 ppm in place of the CO band of **2b** at 194 ppm. Although the instability of **2b** limited further investigations, drying crystals *in vacuo* in presence of P_2O_5 decreased the amount of impurity, allowing us to assign this latter to the corresponding hydrated *gem*-diol **2b**· H_2O .^{23,24}

Finally, we considered vinamidines **1c**²⁵ and **1d**,^{4b,d} with phenyl and di(methyl)amino R groups, respectively. The corresponding di(imine)ketones **2c,d**, which are out of reach of previous methods, were isolated in 86–87% yield. They features similar key structural data (IR_{ATR} : $\nu = 1700\text{ cm}^{-1}$; ^{13}C NMR $\delta_{\text{CO}} = 194\text{--}191$ ppm). Their structures were asserted by a structural X-ray diffraction study (Fig. 1). Importantly, in ketones **2c,d** were found remarkably bench stable and have been stored for month with no noticeable degradation.

In conclusion, the synthesis and characterization of radicals $7^{\bullet+}$ and $13^{\bullet+}$ are further evidences that introducing 1,3-di(amino)oxyallyl patterns is a robust principle for the design of persistent radical cations. However, the outcome of the reaction of vinamidiniums with *m*-CPBA is too dependent of the substitution pattern to constitute a general route and over-oxidation is only manageable with extra electron-donating amino groups. In contrast, when applied to vinamidines, this protocol allows for a straightforward synthesis of α -keto- β -diimines. In addition to its simplicity, stable derivatives were isolated, with unprecedented bulky or electron-donating R groups. We are now evaluating these new ligands for nickel-initiated polymerization of ethylene.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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