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## Metal free oxidation of vinamidine derivatives: a simple synthesis of $\alpha$ -keto- $\beta$ -diimine ligands†

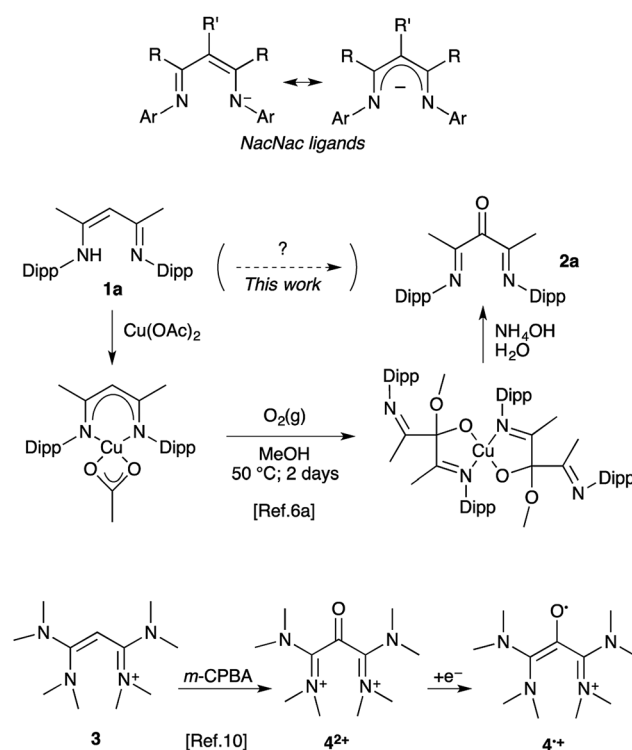
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Oxidation of vinamidinium salts with *meta*-chloroperbenzoic acid is the key synthetic step towards new persistent 1,3-di(amino)oxyallyl radical cations. When applied to parent vinamidines, this protocol allows for a simple straightforward synthesis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

$\beta$ -Diketiminates, so-called NacNac ligands (Scheme 1), have been a focus in coordination chemistry for decades.<sup>1</sup> Structural modifications include a large variety of N-substituents, as well as bulky,<sup>2</sup> electron-withdrawing,<sup>3</sup> or electron donating<sup>4</sup> 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.<sup>5</sup> The  $\alpha$ -keto- $\beta$ -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- $\alpha$ -olefins.<sup>6</sup> Interestingly, low-disperse semi-crystalline polymers could be obtained under living conditions and remarkable enantiomorphic site control could be achieved.<sup>7</sup>

The low availability of  $\alpha$ -keto- $\beta$ -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 ( $R' = H$ ).<sup>8</sup> 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**.<sup>6a,d,9</sup> 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.<sup>6a</sup> Recently, we released a patented, though in principle far simpler, oxidation of tetrakis(dimethylamino) vinamidinium **3** into di(amidinium)ketone **4**<sup>2+</sup> with *meta*-chloroperbenzoic acid (*m*-CPBA) as oxidant. Our initial focus was on the corresponding radical **4**<sup>•+</sup>, which was found remarkably air-persistent, despite minimal steric hindrance.<sup>10</sup> Herein we report how further assessment of such 1,3-(diamino)oxyallyl radical cations ultimately led to a straightforward protocol for the synthesis of  $\alpha$ -keto- $\beta$ -diimines from NacNac precursors.



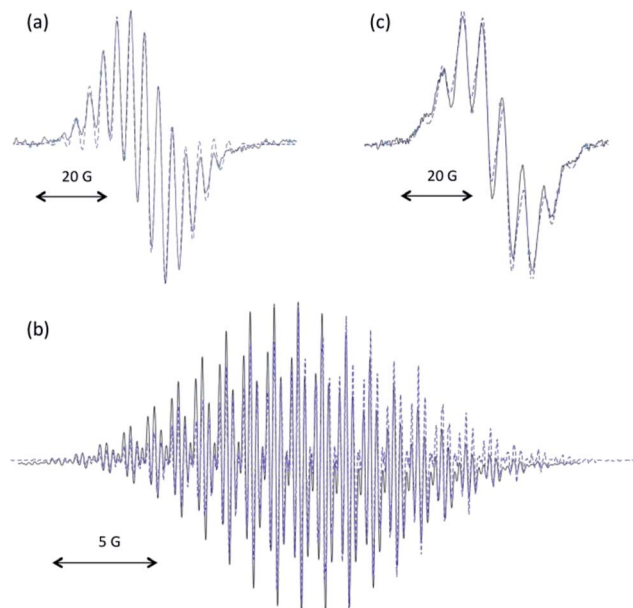
Scheme 1 Previously reported synthesis of  $\alpha$ -keto- $\beta$ -diimines and synthesis of air-persistent radical **4**<sup>•+</sup> from vinamidinium **3**.

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† Electronic supplementary information (ESI) available: <sup>1</sup>H and <sup>13</sup>C spectra of all new compounds, computational and crystallographic (CCDC 1866491–1866494) details. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c8ra08220k



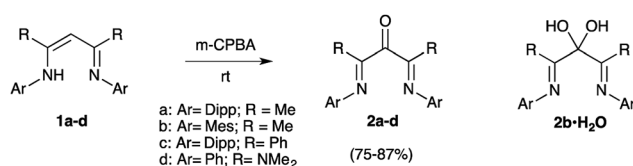




**Fig. 2** Experimental isotropic X-band EPR spectra in dichloromethane at room temperature (plain black line) of  $7^{+\bullet}$  (a),  $10^{+\bullet}$  (b) and a crude reaction mixture of *m*-CPBA and **1a** (c). Simulated spectra (dashed blue line) were obtained with (a) a Lorentzian line-broadening 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**<sup>22</sup> 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**· $\text{H}^+$ , 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  $\alpha$ -keto- $\beta$ -diimines **2a–d** from vinamidines **1a–d**.

The only few reported  $\beta$ -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.<sup>6d</sup> We applied our protocol to vinamidines **1b**<sup>21</sup> 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 <sup>13</sup>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<sub>2</sub>O<sub>5</sub> decreased the amount of impurity, allowing us to assign this latter to the corresponding hydrated *gem*-diol **2b**·H<sub>2</sub>O.<sup>23,24</sup>

Finally, we considered vinamidines **1c**<sup>25</sup> and **1d**,<sup>4b,d</sup> 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<sub>ATR</sub>:  $\nu = 1700$  cm<sup>-1</sup>; <sup>13</sup>C NMR  $\delta_{\text{CO}} = 194$ –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  $\alpha$ -keto- $\beta$ -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.

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