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

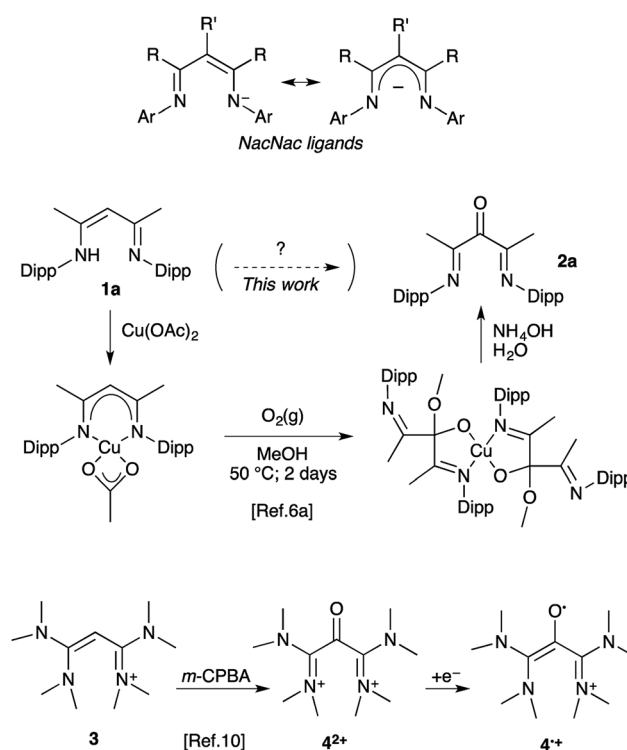
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Oxidation of vinamidinium salts with *meta*-chloroperbenzoic acid is the key synthetic step towards new persistent 1,3-di(amino)oxyallyl radical cations. When applied to parent vinamidines, this protocol allows for a simple straightforward synthesis 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.



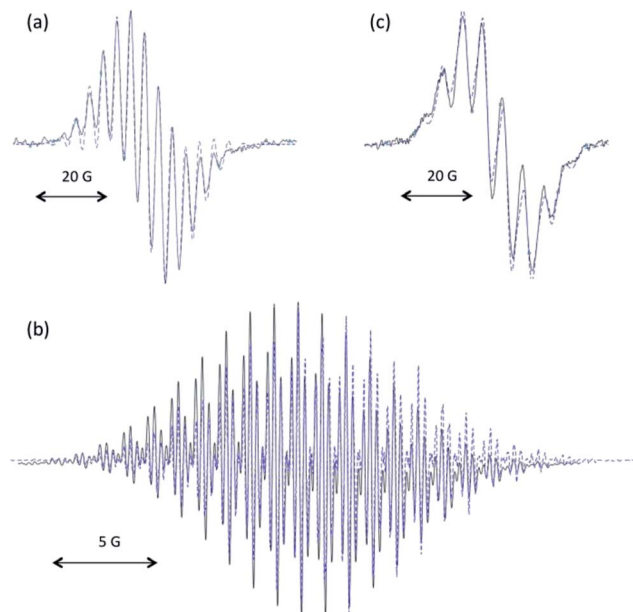
Scheme 1 Previously reported synthesis of  $\alpha$ -keto- $\beta$ -diimines and synthesis of air-persistent radical **4**<sup>•+</sup> from vinamidinium **3**.

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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



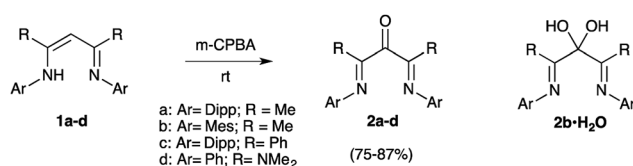




**Fig. 2** Experimental isotropic X-band EPR spectra in dichloromethane at room temperature (plain black line) of  $7^{+\bullet}$  (a),  $10^{+\bullet}$  (b) and a crude reaction mixture of *m*-CPBA and **1a** (c). Simulated spectra (dashed blue line) were obtained with (a) a Lorentzian line-broadening 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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## Notes and references

- (a) L. Bourget-Merle, M. F. Lappert and J. R. Severn, *Chem. Rev.*, 2002, **102**, 3031; (b) D. J. Emslie and W. E. Piers, *Coord. Chem. Rev.*, 2002, **233–234**, 131; (c) H. W. Roesky, S. Singh, V. Jancik and V. Chandrasekhar, *Acc. Chem. Res.*,



- 2004, **37**, 969; (d) D. J. Mindiola, *Acc. Chem. Res.*, 2006, **39**, 813; (e) C. J. Cramer and W. B. Tolman, *Acc. Chem. Res.*, 2007, **40**, 601; (f) P. L. Holland, *Acc. Chem. Res.*, 2008, **41**, 905; (g) Y. C. Tsai, *Coord. Chem. Rev.*, 2012, **256**, 722.
- 2 For examples with R = *tert*-butyl, see: (a) J. Vela, J. M. Smith, Y. Yu, N. A. Ketterer, C. J. Flaschenriem, R. J. Lachicotte and P. L. Holland, *J. Am. Chem. Soc.*, 2005, **127**, 7857; (b) Y. M. Badiei, A. Dinescu, X. Dai, R. M. Palomino, F. W. Heinemann, T. R. Cundari and T. H. Warren, *Angew. Chem., Int. Ed.*, 2008, **47**, 9961; (c) G. Zhao, F. Basuli, U. J. Kilgore, H. Fan, H. Aneetha, J. C. Huffman, G. Wu and D. J. Mindiola, *J. Am. Chem. Soc.*, 2006, **128**, 13575.
- 3 For some representative examples, see: (a) D. S. Laitar, C. J. N. Mathison, W. M. Davis and J. P. Sadighi, *Inorg. Chem.*, 2003, **42**, 7354; (b) S. Hong, L. M. R. Hill, A. K. Gupta, B. D. Naab, J. B. Gilroy, R. G. Hicks, C. J. Cramer and W. B. Tolman, *Inorg. Chem.*, 2009, **48**, 4514; (c) D. T. Carey, E. K. Cope-Eatough, E. Vilaplana-Mafé, F. S. Mair, R. G. Pritchard, J. E. Warren and R. J. Woods, *Dalton Trans.*, 2003, 1083; (d) H. A. Chiong and O. Daugulis, *Organometallics*, 2006, **25**, 4054; (e) A. G. M. Barrett, M. R. Crimmin, M. S. Hill, P. B. Hitchcock and P. A. Procopiou, *Angew. Chem., Int. Ed.*, 2007, **46**, 6339; (f) S. Kernbichl, M. Reiter, F. Adams, S. Vagin and B. Rieger, *J. Am. Chem. Soc.*, 2017, **139**, 6787; (g) S. Kundu, W. Y. Kim, J. A. Bertke and T. H. Warren, *J. Am. Chem. Soc.*, 2017, **139**, 1045; (h) K. S. Choung, M. D. Islam, R. W. Gou and T. S. Teets, *Inorg. Chem.*, 2017, **56**, 14326.
- 4 (a) V. Regnier, Y. Planet, C. E. Moore, J. Pecaut, C. Philouze and D. Martin, *Angew. Chem., Int. Ed.*, 2017, **56**, 1031; (b) D. C. H. Do, A. Keyser, A. V. Protchenko, B. Maitland, I. Pernik, H. Niu, E. L. Kolychev, A. Rit, D. Vidovic, A. Stasch, C. Jones and S. Aldridge, *Chem.–Eur. J.*, 2017, **23**, 5830; (c) I. Pernik, B. Maitland, A. Stasch and C. Jones, *Can. J. Chem.*, 2018, **96**, 513; (d) M. Tripathi, V. Regnier, C. Lincheneau and D. Martin, *New J. Chem.*, 2017, **41**, 15016.
- 5 (a) C. M. Byrne, S. D. Allen, E. B. Lobkovsky and G. W. Coates, *J. Am. Chem. Soc.*, 2004, **126**, 11404; (b) R. Jiao, X. Shen, M. Xue, Y. Zhang, Y. Yao and Q. Shen, *Chem. Commun.*, 2010, **46**, 4118; (c) M. M. Rodriguez, E. Bill, W. W. Brennessel and P. L. Holland, *Science*, 2011, **334**, 780; (d) L. A. Harris, E. C. Y. Tam, M. P. Coles and J. R. Fulton, *Dalton Trans.*, 2014, **43**, 13803; (e) K. Grubel, W. W. Brennessel, B. Q. Mercado and P. L. Holland, *J. Am. Chem. Soc.*, 2014, **136**, 16807; (f) A. Kalita, V. Kumar and B. Mondal, *RSC Adv.*, 2015, **5**, 643.
- 6 (a) J. D. Azoulay, R. S. Rojas, A. V. Serrano, H. Ohtaki, G. B. Galland, G. Wu and G. C. Bazan, *Angew. Chem., Int. Ed.*, 2009, **48**, 1089; (b) J. D. Azoulay, Y. Schneider and G. C. Bazan, US20090299020A1, 2009; (c) J. D. Azoulay, G. C. Bazan and G. B. Galland, *Macromolecules*, 2010, **43**, 2794; (d) A. Sokolohorskyj, O. Zeleznik, I. Cisarova, J. Lenz, A. Lederer and J. Merna, *J. Polym. Sci., Part A: Polym. Chem.*, 2017, **55**, 2440.
- 7 (a) J. D. Azoulay, Y. Schneider, G. B. Galland and G. C. Bazan, *Chem. Commun.*, 2009, 6177; (b) J. D. Azoulay, H. Y. Gao, Z. A. Koretz, G. Kehr, G. Erker, F. Shimizu, G. B. Galland and G. C. Bazan, *Macromolecules*, 2012, **45**, 4487.
- 8 For the reaction of dioxygen with NacNac–cobalt complexes, see: (a) M. C. Weiss and V. L. Goedken, *J. Am. Chem. Soc.*, 1976, **98**, 3389; (b) B. Durham, T. J. Anderson, J. A. Switzer, J. F. Endicott and M. D. Glick, *Inorg. Chem.*, 1977, **16**, 271; (c) J. A. Switzer and F. J. Endicott, *J. Am. Chem. Soc.*, 1980, **102**, 1181 NacNac–iron complexes: (d) D. P. Riley and D. H. Busch, *Inorg. Chem.*, 1983, **22**, 4141; (e) D. B. MacQueen, C. Lange, M. Calvin, J. W. Otvos, L. O. Spreer, C. B. Allan, A. Ganse and R. B. Frankel, *Inorg. Chim. Acta*, 1997, **263**, 125 For lanthanides: (f) J. Zhang, Z. Zhang, Z. Chen and X. Zhou, *Dalton Trans.*, 2012, **41**, 357 For alkaline earths: (g) B. Liu, V. Dorcet, L. Maron, J. F. Carpentier and Y. Sarazin, *Eur. J. Inorg. Chem.*, 2012, 3023.
- 9 S. Yokota, Y. Tachi and S. Itoh, *Inorg. Chem.*, 2002, **41**, 1342.
- 10 V. Regnier, F. Molton, C. Philouze and D. Martin, *Chem. Commun.*, 2016, **52**, 11422.
- 11 (a) D. Martin, C. E. Moore, A. L. Rheingold and G. Bertrand, *Angew. Chem., Int. Ed.*, 2013, **52**, 7014; (b) J. K. Mahoney, D. Martin, F. Thomas, C. Moore, A. L. Rheingold and G. Bertrand, *J. Am. Chem. Soc.*, 2015, **137**, 7519.
- 12 For the reaction of stable carbenes with CO, see also: (a) V. Lavallo, Y. Canac, B. Donnadieu, W. W. Schoeller and G. Bertrand, *Angew. Chem., Int. Ed.*, 2006, **45**, 3488; (b) T. W. Hudnall and C. W. Bielawski, *J. Am. Chem. Soc.*, 2009, **131**, 16039; (c) U. Siemeling, C. Färber, C. Bruhn, M. Leibold, D. Selent, W. Baumann, M. von Hopffgarten, C. Goedecke and G. Frenking, *Chem. Sci.*, 2010, **1**, 697; (d) T. Schulz, C. Färber, M. Leibold, C. Bruhn, W. Baumann, D. Selent, T. Porsch, M. C. Holthausen and U. Siemeling, *Chem. Commun.*, 2013, **49**, 6834; (e) T. Schulz, C. Färber, M. Leibold, C. Bruhn, P. Prochnow, J. E. Bandow, T. Schneider, T. Porsch, M. C. Holthausen and U. Siemeling, *Chem. Commun.*, 2014, **50**, 2341.
- 13 For the quest on stable 1,3-(diamino)oxyallyl derivatives, see: (a) V. Regnier and D. Martin, *Org. Chem. Front.*, 2015, **2**, 1536; (b) M. Devillard, V. Regnier, M. Tripathi and D. Martin, *J. Mol. Struct.*, 2018, **1172**, 3.
- 14 (a) H. Ahlbrecht, W. Raab and C. Vonderheid, *Synthesis*, 1979, 127; (b) R. Pajkert, T. Böttcher, M. Ponomarenko, M. Bremer and G.-V. Rösenthaller, *Tetrahedron*, 2013, **69**, 8943.
- 15 For the reaction of *m*-CPBA with halides see: (a) N. J. Bunce and D. D. Tanner, *J. Am. Chem. Soc.*, 1969, **91**, 6096; (b) M. Srebnik, *Synth. Commun.*, 1989, **19**, 197.
- 16 Experimental EPR spectra were fitted with the EasySpin simulation package: S. Stoll and A. Schweiger, *J. Magn. Reson.*, 2006, **178**, 42.
- 17 DFT calculations were performed using the program package Gaussian09: *Gaussian 09*, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, *et al.*, Gaussian Inc., Wallingford CT, 2009. See ESI† for complete citation and further details.



- 18 The trione is usually isolated as a mixture with its hydrate: Z. L. Wang, X. L. An, L. S. Ge, J.-H. Jin, X. Luo and W.-P. Deng, *Tetrahedron*, 2014, **70**, 3788.
- 19 (a) C. A. Dyker, V. Lavallo, B. Donnadiou and G. Bertrand, *Angew. Chem., Int. Ed.*, 2008, **47**, 3206; (b) W.-C. Chen, Y.-C. Hsu, C.-Y. Lee, G. P. A. Yap and T.-G. Ong, *Organometallics*, 2013, **32**, 2435.
- 20 A. K. Diba, C. Noll, M. Richter, M. T. Gieseler and M. Kalesse, *Angew. Chem., Int. Ed.*, 2010, **49**, 8367.
- 21 We propose that further reaction of  $13^{2+}$  with m-CPBA yields Bayer-Villiger type products, either (imidazolyl)-carbonates or carboxylate derivatives. These electrophiles being highly activated, they would readily undergo hydrolysis, affording 1,3-dimethylbenzimidazolium salts.
- 22 For a convenient protocole for the condensation of anilines with acetylacetone, see: L.-M. Tang, Y.-Q. Duan, X.-F. Li and Y.-S. Li, *J. Organomet. Chem.*, 2006, **691**, 2023.
- 23 Such compounds have been mentioned in patents: Y. Tang, Z. Chen, G. Ji, X. Sun, C. Xu and J. Li, WO 2015024517, 2015.
- 24 In parented Pt-complexes the  $^{13}\text{C}$  chemical shift of the central carbon is in the 80–110 ppm range: M. L. Scheuermann, U. Fekl, W. Kaminsky and K. I. Goldberg, *Organometallics*, 2010, **29**, 4749.
- 25 M. Arrowsmith, M. R. Crimmin, M. S. Hill and G. Kociok-Köhn, *Dalton Trans.*, 2013, **42**, 9720.

