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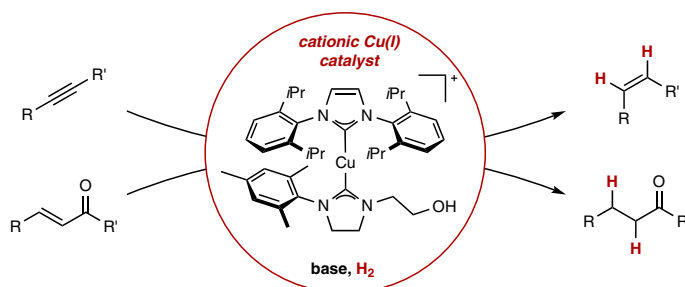
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# Catalytic Hydrogenations with Cationic Heteroleptic Copper(I)/N-Heterocyclic Carbene Complexes

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**Abstract** A new heteroleptic cationic copper(I) complex bearing two N-heterocyclic carbene (NHC) ligands has been prepared. In situ, a Cu–O bond can be generated which enables the complex to catalytically activate H<sub>2</sub>. The resulting complex shows activity in catalytic chemo- and stereoselective alkyne semihydrogenations as well as conjugate reductions of enones.

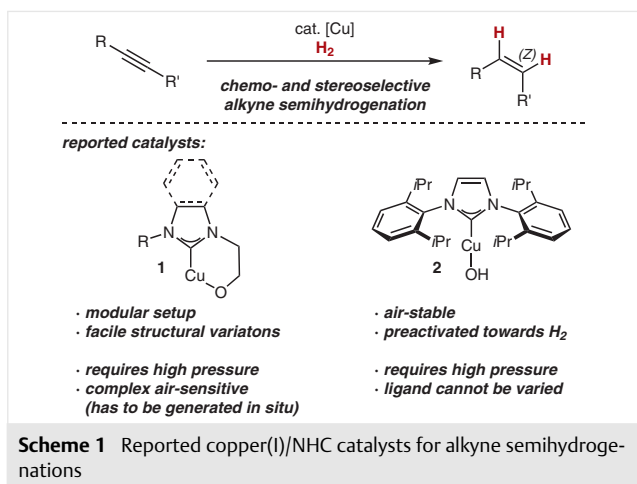
**Key words** copper, NHC ligands, hydrogenation, homogeneous catalysis, alkynes, enones

Well-defined copper(I) complexes bearing N-heterocyclic carbene (NHC) ligands have emerged as powerful catalysts for a variety of transformations.<sup>2</sup> While the vast majority of the complexes reported bear one NHC ligand (leading to Cu(NHC)X complexes, where X is an additional anionic ligand), also the corresponding cationic complexes of the general formula Cu(NHC)<sub>2</sub><sup>+</sup> have been investigated as catalysts, albeit to a much lesser extent.<sup>3,4</sup> Our group and others have identified copper(I)/NHC complexes bearing a Cu–O bond as useful catalysts for the activation of H<sub>2</sub> and subsequent hydrogenations or other reductive transformations.<sup>5–7</sup> For catalytic chemo- and stereoselective alkyne semihydrogenations, two general types of complexes have been disclosed: i) copper(I) complexes such as **1** based on bidentate (“tethered”) NHC ligands bearing additional heteroatom tethers<sup>6a,e,8</sup> that were generated in situ from the corresponding imidazol(in)ium salts and a suitable copper(I) precursor (Scheme 1, bottom left); ii) the simple and preactivated copper(I) hydroxide complex [IPrCuOH]<sup>9</sup> (**2**, Scheme 1, bottom right).<sup>6b,d</sup> Both catalysts lead to a variety of Z-alkenes from internal alkynes in a highly stereoselective manner and are characterized by their negligible tendency for overreduction to the corresponding alkanes. For a

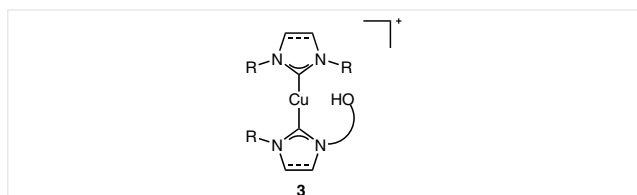


**Johannes Teichert** is currently Juniorprofessor at Technische Universität Berlin. He has studied at Philipps-Universität Marburg and at Université Paul Sabatier in Toulouse, France. In 2006, he joined the group of Prof. Ben L. Feringa at Rijksuniversiteit Groningen, the Netherlands for his PhD in the field of asymmetric catalysis. After a postdoctoral stay with Prof. Jeffrey Bode at ETH Zurich, he started his independent research group in Berlin. Johannes' research interests include method development in organic synthesis, transition metal catalysis and especially reductive transformations employing H<sub>2</sub>.

systematic optimization, however, both catalysts pose particular challenges: Complexes of the type **1** with a tethered ligand have so far not been isolated due to their tendency to oxidize to the corresponding (inactive) copper(II) counterparts.<sup>6a</sup> In addition, this catalyst requires high H<sub>2</sub> pressure (generally 50–100 bar), which impedes the practicability of the overall catalytic hydrogenation. However, this catalyst type is modular and can easily be varied both structurally as well as electronically through a variety of substituents.<sup>6c</sup> While the second type of catalyst (**2**) is air-stable and can therefore be operated without special precautions, it shares the limitation of being active only at elevated H<sub>2</sub> pressure.<sup>6b,d</sup> In addition, with the exception of one closely related complex,<sup>10</sup> copper(I) hydroxide/NHC complexes based on other NHC ligands are highly unstable, which hampers their use and systematic optimization.

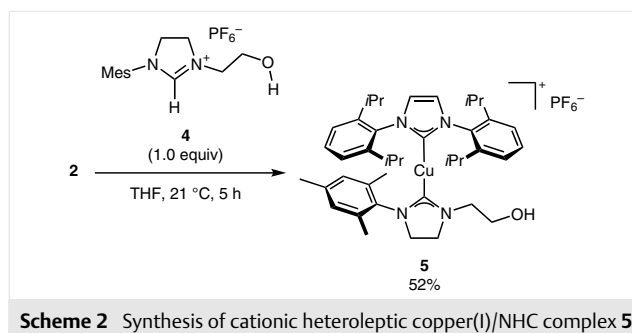


We therefore decided to investigate cationic copper(I)/NHC complexes **3** (Figure 1), with the aim to take advantage of a possible air stability while maintaining viable pathways for derivatizations. Such a setup, with two different NHC ligands coordinated to one copper(I) atom (heteroleptic complex), could serve as ideal platform for rapid and systematic optimization of catalysts for a catalytic transformation of choice. At the same time, at least one of the NHC moieties would have to be bidentate, with an additional alkoxide moiety available for the generation of a Cu–O bond required for H<sub>2</sub> activation.

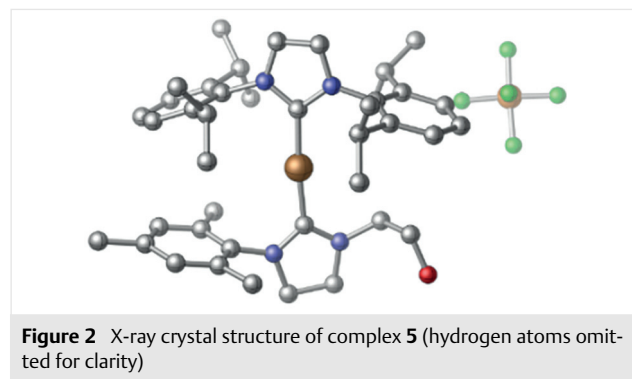


**Figure 1** Envisaged heteroleptic cationic copper(I)/(NHC)<sub>2</sub> complexes

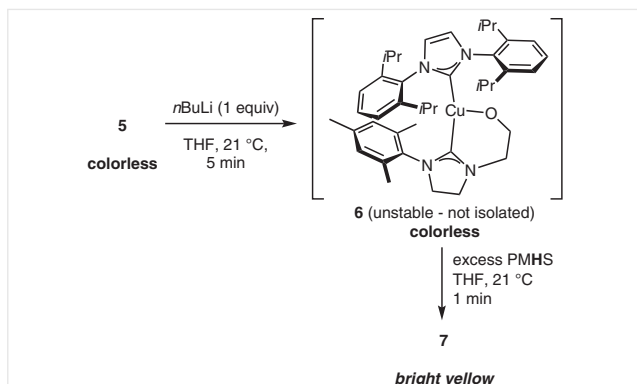
We decided to take advantage of the high basicity<sup>9a</sup> of the [IPrCuOH] complex (**2**) for the preparation of the envisaged cationic copper(I) complexes, and therefore anticipated that **2** could itself deprotonate an imidazolium salt such as **4**<sup>11</sup> to generate the desired complex **5** (Scheme 2). Indeed, when [IPrCuOH] (**2**) and imidazolium salt **4** were reacted in THF at room temperature, we were able to isolate the new heteroleptic cationic copper(I) complex **5** in 52% yield. We did not detect any copper(I) alkoxide complex which could form through direct deprotonation of the alcohol moiety of ligand precursor **4**.<sup>12</sup> Heteroleptic cationic copper(I) complex **5** was susceptible to X-ray crystal-structure analysis (Figure 2).<sup>13</sup> The C–Cu–C angle was found to be 175°, and no interaction between the copper and the oxygen atom was found. The new cationic copper(I) complex was found to be bench-stable under air for months.



For catalytic activity with H<sub>2</sub>, the formation of a Cu–O bond emanating from complex **5** was necessary. We therefore decided to deprotonate **5** with *n*-butyllithium as in our earlier protocol.<sup>6a,e</sup> While full conversion of **5** was detected after 5 minutes, the new complex **6** turned out to be too reactive to be isolated (Scheme 3). When polymethylhydrosiloxane (PMHS) was added to the reaction mixture at room temperature, a fast appearance of a yellow color, indicative for a possible (most probably dimeric)<sup>14</sup> copper(I) hydride complex **7**, could be observed.<sup>15</sup> Copper(I) hydrides are known to be formed from complexes bearing a Cu–O bond in the presence of hydrosilanes.<sup>16</sup> At present, the structure and bonding situation of the intermediately formed complex **6** are unknown. The unknown intermediate **6** could possess a Cu–O bond in a possible T-shape or trigonal coordination mode.<sup>17</sup>

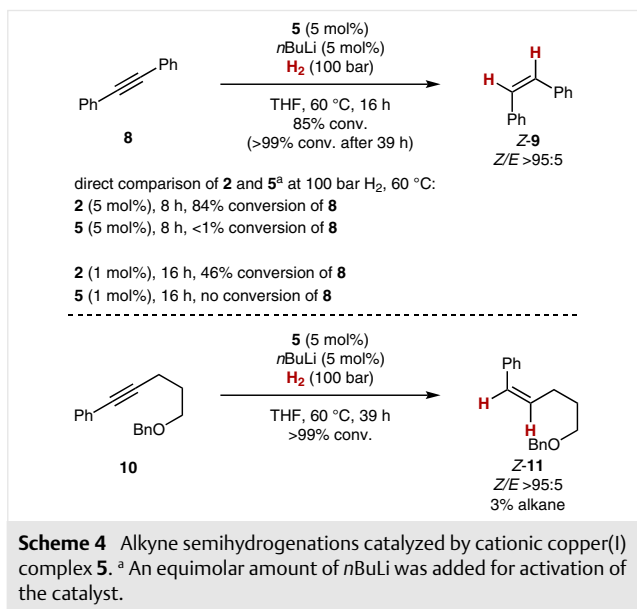


To assess the catalytic activity of the new cationic complex **5**, we decided to activate it in situ to generate the putative active complex **6** and then directly carry out an alkyne semihydrogenation with tolane (**8**) and pentynol derivative **10** as representative internal alkynes. With 100 bar H<sub>2</sub> pressure at 60 °C, we found that tolane (**8**) showed 85% conversion to *Z*-stilbene (**9**) with excellent stereoselectivity (*E/Z* >95:5, Scheme 4), and no overreduction to the corresponding alkane (not shown) detected. Without the addition of *n*-butyllithium, no catalytic alkyne semihydrogenation was observed. Full conversion of **8** was reached after 39 hours reaction time. Under these conditions, alkyne **10** was also fully converted with similar stereoselectivity, albeit in this



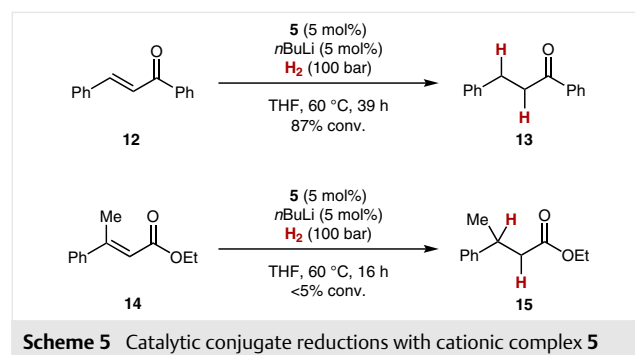
**Scheme 3** Attempted isolation of copper(I)/alkoxide complex **6** and evidence for copper(I) hydride formation (PMHS = polymethylhydrosiloxane)

case with 3% alkane detected in the reaction mixture. Cationic complex **5** therefore shows the known characteristics of a copper(I)/NHC complex in catalytic alkyne semihydrogenations (high chemo- and stereoselectivity). When comparing the present catalyst **5** with the parent complex **2** under similar conditions, two features of **5** become clear: i) complex **5** is comparatively less reactive than **2** (as evident from the significantly higher conversion of **8** under all conditions). ii) complex **5** becomes active after a substantial initiation period (of at least 8 hours). One reasonable explanation for these results could be that one of the NHC ligands on the cationic complex **5** acts as a 'sacrificial' ligand, which is lost prior to the actual catalysis, leading to an active catalyst. The observed induction period supports such an explanation.<sup>18</sup>



**Scheme 4** Alkyne semihydrogenations catalyzed by cationic copper(I) complex **5**.<sup>a</sup> An equimolar amount of *n*BuLi was added for activation of the catalyst.

One of the hallmark reactions of the so-called 'copper hydride catalysis' is the conjugate reduction of  $\alpha,\beta$ -unsaturated carbonyl or carboxyl derivatives.<sup>15</sup> We therefore decided to test the new cationic complex for these transformations as well. Chalcone (**12**) and cinnamic ester **14** were chosen as model substrates. Under similar reaction conditions as before (100 bar H<sub>2</sub>, 60 °C, THF), chalcone (**12**) could be reduced to ketone **13** with 87% conversion, while no 1,2-reduction of the ketone was observed (Scheme 5). The less reactive and sterically more demanding enoate **14** showed negligible conversion, displaying that the activity of the cationic complex **5** is limited at present in comparison to related neutral copper(I)/NHC complexes.<sup>6f</sup> Nevertheless, the observed reactivity of the new catalyst with enone **12** gives an important indication that copper(I) hydride complexes are indeed present after H<sub>2</sub> activation.



**Scheme 5** Catalytic conjugate reductions with cationic complex **5**

In summary, we have demonstrated that cationic, heteroleptic copper(I) complexes bearing two NHC ligands can be employed as catalysts for H<sub>2</sub> activation and alkyne semihydrogenations as well as conjugate reductions. The new complex presented herein serves as an ideal platform for further systematic development of well-defined copper(I)/NHC catalysts, as it offers several advantages: The catalyst precursor is air-stable and does not require special handling and additionally bears a multitude of sites for systematic variation of electronic and steric parameters of the resulting catalysts. This variation could stem from different NHC backbones, N-substituents, and/or the alkoxide tether.

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## Supporting Information

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## References and Notes

- (1) Present address: Stratingh Institute for Chemistry, Rijksuniversiteit Groningen, The Netherlands.
- (2) For reviews, see: (a) Egbert, J. D.; Cazin, C. S. J.; Nolan, S. P. *Catal. Sci. Technol.* **2013**, *3*, 912. (b) Lin, J. C. Y.; Huang, R. T. W.; Lee, C. S.; Bhattacharyya, A.; Hwang, W. S.; Lin, I. J. B. *Chem. Rev.* **2009**, *109*, 3561.
- (3) For a review, see: Lazreg, F.; Nahra, F.; Cazin, C. S. J. *Coord. Chem. Rev.* **2015**, *293*, 48.
- (4) For selected examples, see: (a) Díez-González, S.; Stevens, E. D.; Scott, N. M.; Petersen, J. L.; Nolan, S. P. *Chem. Eur. J.* **2008**, *14*, 158. (b) Grandbois, A.; Mayer, M.-E.; Bédard, M.; Collins, S. K.; Michel, T. *Chem. Eur. J.* **2009**, *15*, 9655. (c) Díaz Velázquez, H.; Ruiz García, Y.; Vandichel, M.; Madder, A.; Verpoort, F. *Org. Biomol. Chem.* **2014**, *12*, 9350.
- (5) For the formulation of the mechanistic hypothesis of H<sub>2</sub> activation along Cu–O bonds, see: (a) Halpern, J. J. *Phys. Chem.* **1959**, *63*, 398. (b) Chalk, A. J.; Halpern, J. J. *Am. Chem. Soc.* **1959**, *81*, 5852. (c) Goeden, G. V.; Caulton, K. G. *J. Am. Chem. Soc.* **1981**, *103*, 7354.
- (6) For catalytic hydrogenations with copper(I)/NHC complexes, see: (a) Pape, F.; Thiel, N. O.; Teichert, J. F. *Chem. Eur. J.* **2015**, *21*, 15934. (b) Thiel, N. O.; Teichert, J. F. *Org. Biomol. Chem.* **2016**, *14*, 10660. (c) Wakamatsu, T.; Nagao, K.; Ohmiya, H.; Sawamura, M. *Organometallics* **2016**, *35*, 1354. (d) Thiel, N. O.; Kemper, S.; Teichert, J. F. *Tetrahedron* **2017**, *73*, 5023. (e) Pape, F.; Teichert, J. F. *Synthesis* **2017**, *49*, 2470. (f) Zimmermann, B.; Teichert, J. F. *Chem. Commun.* **2019**, *55*, 2293. For a related copper(I)-catalyzed alkyne semihydrogenation employing phosphine ligands, see: (g) Semba, K.; Kameyama, R.; Nakao, Y. *Synlett* **2015**, *26*, 318.
- (7) For related reductive transformations with copper(I)/NHC complexes, see: (a) Nguyen, T. N. T.; Thiel, N. O.; Pape, F.; Teichert, J. F. *Org. Lett.* **2016**, *18*, 2455. (b) Korytiakova, E.; Thiel, N. O.; Pape, F.; Teichert, J. F. *Chem. Commun.* **2017**, *53*, 732. (c) Nguyen, T. N. T.; Thiel, N. O.; Teichert, J. F. *Chem. Commun.* **2017**, *53*, 11686.
- (d) Das, M.; Kaicharla, T.; Teichert, J. F. *Org. Lett.* **2018**, *20*, 4926.
- (e) Pape, F.; Brechmann, L. T.; Teichert, J. F. *Chem. Eur. J.* **2019**, *25*, 985.
- (8) For reviews on 'tethered' NHC ligands, see: (a) Pape, F.; Teichert, J. F. *Eur. J. Org. Chem.* **2017**, 4206. (b) Hameury, S.; Frémont, P.; de Braunstein, P. *Chem. Soc. Rev.* **2017**, *46*, 632. (c) Liddle, S. T.; Edworthy, I. S.; Arnold, P. L. *Chem. Soc. Rev.* **2007**, *36*, 1732.
- (9) (a) Fortman, G. C.; Slawin, A. M. Z.; Nolan, S. P. *Organometallics* **2010**, *29*, 3966. For a review on transition metal hydroxides, see: (b) Nelson, D. J.; Nolan, S. P. *Coord. Chem. Rev.* **2017**, *353*, 278.
- (10) Santoro, O.; Lazreg, F.; Minenkov, Y.; Cavallo, L.; Cazin, C. S. J. *Dalton Trans.* **2015**, *44*, 18138.
- (11) Clavier, H.; Coutable, L.; Toupet, L.; Guillemin, J.-C.; Mauduit, M. *J. Organomet. Chem.* **2005**, *690*, 5237.
- (12) For an investigation of the deprotonation behavior of 'tethered' NHC precursors, see: Arnold, P. L.; Casely, I. J.; Turner, Z. R.; Carmichael, C. D. *Chem. Eur. J.* **2008**, *14*, 10415.
- (13) CCDC 1890624 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/getstructures](http://www.ccdc.cam.ac.uk/getstructures).
- (14) Mankad, N. P.; Laitar, D. S.; Sadighi, J. P. *Organometallics* **2004**, *23*, 3369.
- (15) For reviews on copper(I) hydride chemistry, see: (a) Jordan, A. J.; Lalic, G.; Sadighi, J. P. *Chem. Rev.* **2016**, *116*, 8318. (b) Deutsch, C.; Krause, N. *Chem. Rev.* **2008**, *108*, 2916. (c) Rendler, S.; Oestreich, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 498.
- (16) (a) Rendler, S.; Plefka, O.; Karatas, B.; Auer, G.; Fröhlich, R.; Mück-Lichtenfeld, C.; Grimme, S.; Oestreich, M. *Chem. Eur. J.* **2008**, *14*, 11512. (b) Gathy, T.; Peeters, D.; Leyssens, T. *J. Organomet. Chem.* **2009**, *694*, 3943. (c) Vergote, T.; Nahra, F.; Merschaert, A.; Riant, O.; Peeters, D.; Leyssens, T. *Organometallics* **2014**, *33*, 1953.
- (17) For a related T-shaped copper(I) complex, see: (a) Lake, B. R. M.; Willans, C. E. *Chem. Eur. J.* **2013**, *19*, 16780. A trigonal planar coordination of the ligands in **6** would also be viable. For examples of trigonal copper(I)/NHC complexes, see: (b) Marion, R.; Sguerra, F.; Di Meo, F.; Sauvageot, J.-F.; Lohier, R.; Daniellou, R.; Renaud, J.-L.; Linares, M.; Hamel, M.; Gaillard, S. *Inorg. Chem.* **2014**, *53*, 9181.
- (18) For another example of catalyst activation by loss of one NHC ligand from a cationic copper(I) complex, see ref. 4b.