A Journal of the Gesellschaft Deutscher Chemiker
Angewandte Chemie
GDCh
International Edition
www.angewandte.org

## Accepted Article

**Title:** Designed to react: Terminal Copper Nitrenes and their Application in Catalytic C-H Aminations

**Authors:** Sonja Herres-Pawlis, Julian Moegling, Alexander Hoffmann, Fabian Thomas, Nicole Orth, Patricia Liebhäuser, Ulrich Herber, Robert Rampmaier, Ivana Ivanovic-Burmazovic, Gerhard Fink, and Julia Stanek

**To be cited as:** *Angew. Chem. Int. Ed.* 10.1002/anie.201713171
*Angew. Chem.* 10.1002/ange.201713171

**Link to VoR:** http://dx.doi.org/10.1002/anie.201713171
http://dx.doi.org/10.1002/ange.201713171

WILEY-VCH

# Designed to react: Terminal Copper Nitrenes and their Application in Catalytic C–H Aminations

Julian Moegling,[a] Alexander Hoffmann,[a] Fabian Thomas,[a] Nicole Orth,[b] Patricia Liebhäuser,[a] Ulrich Herber,[a] Robert Rampmaier,[c] Julia Stanek,[a] Gerhard Fink,[a] Ivana Ivanović-Burmazović,[b] Sonja Herres-Pawlis*[a]

Dedicated to Prof. Dietmar Stalke on the occasion of his 60th birthday

**Abstract:** Heteroscorpionate ligands of the bis(pyrazolyl)methane family have been applied in the stabilisation of terminal copper tosyl nitrenes. These species are highly active intermediates in the copper catalysed direct C–H amination and nitrene transfer. Novel perfluoroalkyl-pyrazolyl and pyridinyl containing ligands have been synthesised, designed for the coordination to a reactive copper nitrene centre. Four distinct copper tosyl nitrenes have been prepared at low temperatures by the reaction with $SO_2t$BuPhINTs and copper(I) acetonitrile complexes. Their stoichiometric reactivity has been elucidated regarding imination and aziridination of phosphines and styrenes. The formation and thermal decay of the copper nitrenes were investigated by UV/Vis spectroscopy of the highly coloured species. Additionally, the compounds have been studied by cryo-UHR-ESI mass spectrometry and DFT. A mild catalytic procedure has been developed, where the copper nitrene precursors enable the C–H amination of cyclohexane and the aziridination of styrenes.

Functionalisation of unreactive C–H bonds plays a key role in the atom economical synthesis of organic compounds.[1]

A principal approach is the insertion of metal-bound nitrenes into C–H bonds[2], leading directly to the introduction of the *N*-group motif into organic substrates, which is of major importance for the fabrication of synthetically,[3] pharmaceutically[4] and biologically[5] relevant molecules. Due to its low toxicity, cost and environmental impact, copper compounds have been extensively studied and a rich chemistry for catalytic direct C–H amination[6] and *N*-group transfer[6g,7] has evolved. To date, tackling the full scope of organic substrates for the manipulation of unfunctionalised C–H compounds remains an important objective of chemical synthesis. Copper nitrenes are proposed to be key intermediates in Cu-catalysed C–H aminations and nitrene group transfers. This has been concluded by theoretical investigations[6c,6g,7a,8] and experiments.[9] Latest examples of their widespread reactivity comprise the formation of sulfonamides and isothiazoles from the long-known nitrene precursor PhINTs[10], the *α*-amination of acylpyrazoles[11] and the formation of oxazoles.[8b]

Particularly, the presence of *terminal copper nitrene* species has been evaluated as critical factor for reactivity.[6c,6g,7a,8-9] Taken together, the majority of reports on this topic are considering these discrete intermediates to mediate reactivity. So far, only few stable copper nitrenes have been reported (Figure 1), whereby none of them can be truly described as terminal copper nitrene. Pioneering work has been accomplished by the Warren group,[9b,12] who presented molecular structures of *μ*-nitrene bridged dicopper complexes by employing NacNac ligands. They inferred the catalytic reactivity in C–H aminations from the dissociation of the dimetallic species into a terminal copper nitrene. Although observed by Caulton et al.[6c] via ESI mass spectrometry, a comprehensive investigation of a cationic copper tosyl nitrene was achieved by the Ray group,[13] which was closely followed by the report of a copper mesityl nitrene,[14] both featuring a tridentate neutral amine ligand. Both systems were stabilised by the aid of Lewis acids and the former was later reassessed in terms of a tautomeric copper-imidyl form.[15] Bertrand et al. reported copper nitrenes originating from a metal-free phosphonitrene.[16] In solution, an equilibrium between a *μ*-nitrene bridged dicopper nitrene, a terminal nitrene and a twofold nitrene-coordinated copper(I) centre occurs. Attempts of isolating the terminal copper nitrene leads to its dismutation into the other isomers.[17] Most recently, Company, Ray and Ribas reported a room temperature stable phenyl copper nitrene incorporated into an aza-macrocycle.[18]

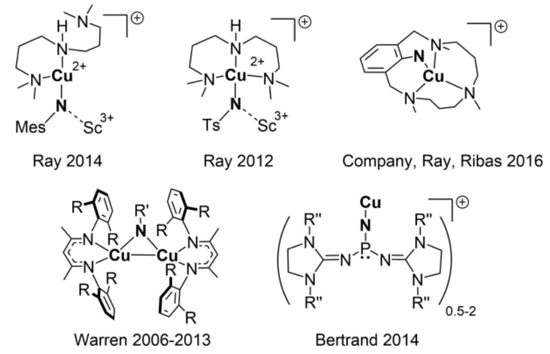


**Figure 1.** Synthetically and spectroscopically verified copper nitrenes.

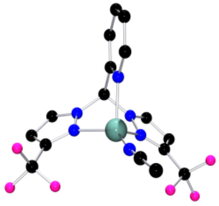
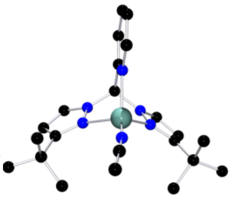
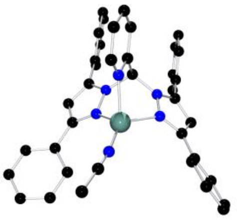
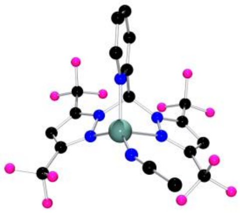
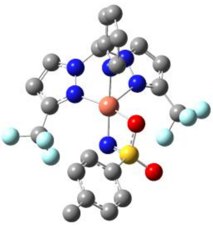
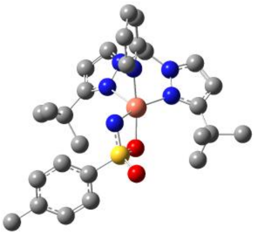
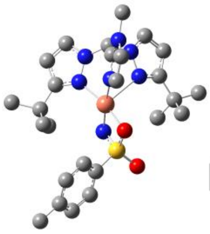
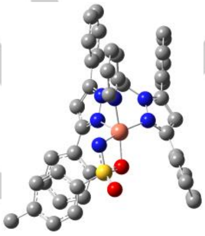
The occurrence and intermediacy of discrete Cu nitrenes is a fascinating object of research, but of the aforementioned stabilised Cu nitrenes, solely Warren's copper nitrenes allowed the development of an effective catalytic procedure.

---

[a] J. Moegling, Dr. A. Hoffmann, F. Thomas, P. Liebhäuser, Dr. U. Herber, J. Stanek, Dr. G. Fink, Prof. Dr. S. Herres-Pawlis
Institut für Anorganische Chemie
RWTH Aachen University
Landoltweg 1, 52074 Aachen (Germany)
E-mail:sonja.herres-pawlis@ac.rwth-aachen.de
[b] N. Orth, Prof. Dr. I. Ivanović-Burmazović
Department Chemie und Pharmazie
Friedrich-Alexander-Universität Erlangen-Nürnberg
Egerlandstraße 1, 91058 Erlangen (Germany)
[c] R. Rampmaier
Department für Chemie und Pharmazie
Ludwig-Maximilians-Universität München
Butenandtstraße 5-13, 81377 München (Germany)

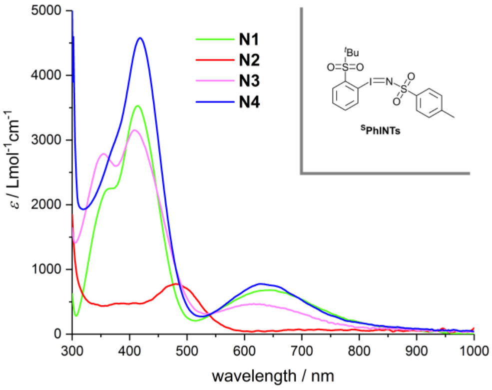
Supporting information for this article is given via a link at the end of the document.

**Table 1.** Top row: molecular structures of the cationic copper(I) bis(pyrazolyl)methane complexes [Cu{HC(3-CF$_3$Pz)$_2$(Py)}MeCN]$^+$ (**C1**), [Cu{HC(3-*t*BuPz)$_2$(Py)}MeCN]$^+$ (**C2**), [Cu{HC(3,5-PhPz)$_2$(Py)}MeCN]$^+$ (**C4**) and [Cu{HC(3,5-CF$_3$Pz)$_2$(Py)}MeCN]$^+$ (**C5**), which are used for the reaction with $^S$PhINTs. Bottom row: structures of the copper nitrenes in the singlet state and $\kappa^2$-*N*,*O* binding mode.

| ligand | HC(3-CF$_3$Pz)$_2$(Py) | HC(3-*t*BuPz)$_2$(Py) | HC(3-*t*BuPz)$_2$(1-MeIm) | HC(3,5-PhPz)$_2$(Py) | HC(3,5-CF$_3$Pz)$_2$(Py) |
|---|---|---|---|---|---|
| molecular structure (X-ray) |  |  | *no suitable crystals, but same structural motif (see Supp. Information for NMR, EA and MS)* |  |  |
| **complex** | **C1** | **C2** | **C3** | **C4** | **C5** |
| DFT structure |  |  |  |  | *does not form copper nitrene* |
| **nitrene** | **N1** | **N2** | **N3** | **N4** | |

This work contributes to the field of Cu nitrenes by introducing a new family of well-defined stable nitrenes featuring versatile bis(pyrazolyl)methane ligands. We present directly observed terminal copper nitrenes and provide with a mild catalytic protocol for the conversion of cyclohexane and toluene.

Bis(pyrazolyl)methanes were already demonstrated to support copper-peroxo cores,[19] representing the fastest Tyrosinase models for the catalytic phenol hydroxylation. Five ligands have been selected for the synthesis of tetrahedrally distorted copper(I) complexes with PF$_6^-$ or ClO$_4^-$ as non-coordinating anions (Table 1). Ligands HC(3-*t*BuPz)$_2$(Py)[20] and HC(3-*t*BuPz)$_2$(1-MeIm)[19c] have been reported previously and HC(3,5-PhPz)$_2$(Py) synthesised analogous to that procedure.[20-21] The ligands HC(3,5-CF$_3$Pz)$_2$(Py) and HC(3-CF$_3$Pz)$_2$(Py) have been synthesised for the purpose of providing inert, but sterically demanding groups pointing towards the metal centre.



$$[Cu\{L\}MeCN]PF_6 + SO_2{}^tBuPhI\mathbf{NTs} \xrightarrow[\text{-92 to -42 °C} \atop \text{10 to 60 min}]{\text{DCM}} [Cu\{L\}\mathbf{NTs}]PF_6 + SO_2{}^tBuPhI$$

**Figure 2.** Top: UV/Vis spectra of copper tosyl nitrenes (3 mmol L$^{-1}$ in [Cu(I){L}MeCN]PF$_6$, DCM). The molar absorption coefficient $\varepsilon$ is corrected to the estimated copper nitrene concentration derived from the ferrocene experiments (Figures S3-S6). Inset: Structural formula of $^S$PhINTs. Bottom scheme: formation of copper nitrenes from bis(pyrazolyl)methane copper(I) complexes.

A literature survey has shown methyl groups[6g,12b] and even *tert*-butyl groups[22] in the vicinity of a metal nitrene centre to be vulnerable towards intramolecular hydrogen atom abstraction.

The dichloromethane-soluble iminoiodinane 2-(*tert*-butylsulfonyl)(*p*-toluenesulfonyliminoiodo)benzene ($^S$PhINTs, see the inset of Figure 2 for the structure) was utilised as nitrene generating agent and exposed to the colourless Cu(I) complex solutions at low temperatures. An immediate reaction occurred and resulted in a colour change to green (**N1**, **N3** and **N4**) and red (**N2**). The distinct bands of the copper nitrenes were monitored by low-temperature UV/Vis spectroscopy and allowed further characterisation of the Cu nitrene reaction dynamics. The UV/Vis spectra (Figure 2) show strong absorption bands for **N1**, **N3** and **N4** centred around 400 nm (ε ~ 3000-4500 L mol$^{-1}$cm$^{-1}$) and weaker features ranging from 480 to 650 nm (ε ~ 750 L mol$^{-1}$cm$^{-1}$) for the four formed copper nitrenes.

Similar absorption features have been observed by Ray et al. for Sc$^{3+}$ trapped copper tosylnitrenes.[13] Curiously, the complex **C5** was not prone to undergo a reaction with $^S$PhINTs, which we relate to the inertness of this electron deficient Cu(I) complex towards oxidation. Cyclic voltammetry of **C1**-**C5** was performed and the potential of the oxidative waves of the irreversible electron transfer dissected (*E* versus Fc/Fc$^+$, Table S2). The highest oxidative peak potential was found for the electron deficient Cu(I) complexes **C1** (880 mV) and **C5** (1000 mV) and the lowest for **C4** (730 mV), thereby supporting the described trend in the copper nitrene formation. To further elucidate the Cu/nitrene stoichoimetry, we performed a titration, where $^S$PhINTs was used as titrant against the copper(I) complex (Figure S7 and S8). A slightly sigmoidal curve was obtained with the absorption maximum at the exact addition of 1.0 equivalents of titrant, which serves as further indicator for the formulation of a terminal nitrene with a 1:1 Cu/nitrene ratio. These nitrenes are almost indefinitely stable at -90 °C in dichloromethane solutions, but upon warming up above this temperature, thermal decay occurs (Figures S9-S12). The half-life of the Cu nitrenes has been determined at -42 °C to 10 min for **N3** and 38 min for **N2**. The decay of **N4** and

**N1** did not follow an exponential behaviour, with a rather too steep initial decay, giving 50 % of the initial absorption after 14 and 5 min, resp. For all nitrenes we observed decay to species with weaker absorption features, resulting in an almost complete loss of colour of the solutions. The quantification of nitrenes **N1**-**N4** and their respective products of the thermal decay was conducted by reduction, using an excess of ferrocene, and the detection of ferrocenium by UV/Vis (Table S3). This allows for the determination of the copper nitrene yield, assuming a single one-electron transfer by ferrocene. Ray et al. found a two-electron reduction process of a copper tosyl nitrene by ferrocene, whereby a reduction of the decayed product by ferrocene was only observed in the presence of a Lewis acid.[13] In our case the ferrocenium yields for the nitrenes range from 71-95 % and 63-75 % for the decayed products (except for the decayed product of **N4**), assuming a one-electron reduction. Considering the stoichiometry of the reaction, a two-electron transfer is discarded based on the high yields of ferrocenium of the decayed products, which would give yields of 150-180 % in this experiment when starting from nitrenes **N1**-**N3**. While being aware, that the product of one-electron reduction of **N1**-**N4** differs to the decayed products in terms of a proton (Scheme S4), the high amount of formation of the copper nitrenes **N1**-**N4** is also supported by the high yields of the stoichiometric $PPh_3$ imination by **N1** and **N3** and styrene aziridination by **N1** (described below).

To further evidence the formation of copper nitrenes, cryo-UHR-ESI mass spectrometry was used. The recorded spectra are given in the Supporting Information and herein exemplary discussed for **N2** (Figure S14, 1st spectrum). They do not exactly resemble the simulated one for the expected copper nitrene ion [**N2**]$^+$ (2nd spectrum). This can be explained by an overlay of [**N2**-H]$^+$ (3rd spectrum) and [**N2**+H]$^+$ (4th spectrum) which accompany the expected copper nitrene as minor contributors. These side-products are the result of nitrene decay by intra- or intermolecular hydrogen atom abstraction (for mechanism see Scheme S6) and protonation by traces of moisture in the ESI setup. Stavropoulos et al.[6g] also investigated copper nitrenes with cryo-spray ESI mass spectrometry and found a similar hydrogen atom abstraction pathway. In this case, an elusive putative copper nitrene was not stabilised, but found to completely decay to the product of the intramolecular C–H amination. The product of the decay was isolated on a preparative scale. In our case, such products were also detected by mass spectrometry of mixtures of the decayed nitrene **N2**. But, species of the type [**N2**-H] were neither found in worked-up samples nor by $^1$H NMR of mixtures of the decayed nitrene **N2**. **N1** could not be detected in the experiments, but upon dilution with THF, the protonated species [**N1**+H]$^+$ was detected (Figure S18). The same species could be produced by thermal decay. Every experiment was well reproduced with the isotopically labelled $^S$PhI$^{15}$NTs and gave the expected mass shift of 1 a.u. (Figures S14-S19). For **N1** the thermally decayed species is tentatively assigned to a copper amido complex [Cu{HC(3-$CF_3$Pz)$_2$(Py)}HNTs]$^+$. This is further supported by EPR spectroscopy, featuring an axial Cu(II) EPR spectrum (Figure S2).

Recently, Warren et al. reported the formation of masked copper nitrenes from Cu(I)-MeCN complexes by intramolecular insertion from the Cu nitrene moiety into the coordinated MeCN.[23] However in our case, such species could not be found in cryo-UHR-ESI or ESI mass spectra of decayed samples and $^1$H NMR spectra of worked-up mixtures.

The copper nitrenes **N1**-**N4** have been theoretically investigated by density functional theory (see SI Sections 9-10) using the TPSSh functional with a def2-TZVP GD3BJ basis set (PCM solvent-model for dichloromethane; empirical dispersion correction with Becke-Johnson damping), which has successfully described complicated copper systems with nearly identical ligands.[24] For all copper nitrenes, singlet, triplet and broken-symmetry states have been calculated and triplet ground states in $\kappa^1$-*N*,*O* binding mode are mostly stabilised. However, the different conformers and states are close in energy such that we assume conformational equilibria for the nitrenes such that the DFT results should not be overinterpreted. The spin state of the copper nitrenes **N1**-**N4** was probed by NMR and thereby assigned to a singlet by using the Evans' method[25] (Table S1). A distinct $\mu_{\text{eff}}$ was measured expectedly for the products of thermal decay of **N1**-**N4**, which are Cu(II)-amido complexes in the doublet state. The UV/Vis features of **N1**-**N4** were simulated with TD-DFT and found to give the correct number of absorptions and matching wavelength of the transitions for the singlet $\kappa^2$-*N*,*O* conformers of **N1**, **N3** and **N4** (Figures S21-S24).

The *N*-tosyl imination of $PPh_3$ serves as proxy for the oxidative ability of nitrido/nitrene complexes and has been monitored by UV/Vis spectroscopy, showing pseudo first-order reaction kinetics (Figure S13). The rate constants $k_{\text{obs}}$ were plotted against $[PPh_3]$ (Figure 3, right), which allows for the extraction of the second-order rate constants $k_2$, revealing the nitrenes **N3** and **N1** to be the fastest ($k_2 = 4.3 \pm 0.8$ L mol$^{-1}$s$^{-1}$ and $3.4 \pm 0.5$ L mol$^{-1}$s$^{-1}$) compared to **N2** ($k_2 = 0.6 \pm 0.1$ L mol$^{-1}$s$^{-1}$). The kinetics of **N4** could not be investigated, due to the competitive thermal decay. Taken together, **N2** displays the highest thermal stability and the slowest reaction rate with the reductant $PPh_3$ (in comparison to **N1** and **N3**). Next, we investigated the $TsNPPh_3$ formation, which did not exceed 34 and 50 % for the sluggish oxidants **N4** and **N2**, but gave high yields for **N3** and **N1** (84 and 79 %), as determined from $^{31}$P-NMR spectroscopy. ESI mass spectrometry shows peaks for $[TsNPPh_3]^+$ and the complex-product adduct [**C3**–$TsNPPh_3$]$^+$, which was further reproduced with the isotope labelled $^S$PhI$^{15}$NTs. To disprove the formation of $TsNPPh_3$ from the thermally decayed nitrenes, an experiment with the decayed nitrene of **N1**, the *N*-tosyl amido complex [Cu{HC(3-$CF_3$Pz)$_2$(Py)}HNTs]$^+$, was carried out at room temperature, showing only traces of the product. We propose the conformational flexibility to be key to reactivity, as found already earlier for $Cu_2O_2$ systems.[24]

A more synthetically applicable reaction is the aziridination of alkenes. The propensity of the investigated nitrenes to undergo aziridination reactions is rather low, but nevertheless styrenes containing electron withdrawing groups (EWG) in the *para*-position were employed and shown by UV/Vis spectroscopy to react with **N1** three times faster than the thermal decay. With **N1** being the fastest reactant in the stoichiometric aziridination, fair yields could be achieved for *p*-EWG-styrenes and a poor conversion for a styrene with *p*-electron donating group (*p*-OMe-styrene), owing to the competing thermal decay (Figure 3, left). A control experiment with the decayed nitrene **N1**, the *N*-tosyl amido complex [Cu{HC(3-$CF_3$Pz)$_2$(Py)}HNTs]$^+$ and *p*-$CF_3$-styrene gave only trace amounts of the corresponding aziridine. A further evaluation of the reactivity in stoichiometric reactions towards substrates for C–H amination reactions was impeded by the competing thermal decay.

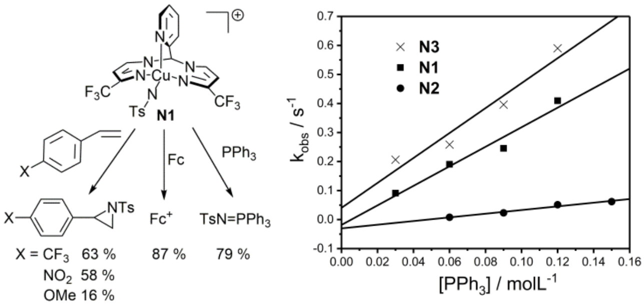
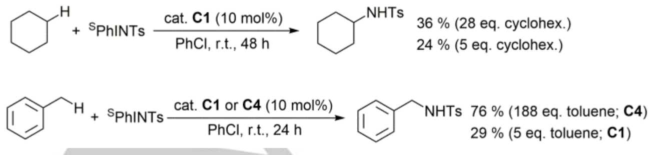


**Figure 3.** Left: yields of the stoichiometric reactions of **N1** with ferrocene, styrenes and $PPh_3$ (the latter are corrected to the estimated copper nitrene yield). Right: plot of pseudo first-order kinetic constants $k_{obs}$ versus the $PPh_3$ concentration with respect to **N1**-**N3**.

But in the next step, we found that the presented systems are primed for catalytic C–H aminations: with the aid of the Cu(I) precursor and $^S$PhINTs, we developed a catalytic procedure allowing the conversion of toluene and cyclohexane (Scheme 1). These substrates bear inert C–H bonds and a copper-catalysed C–H amination at room temperature has been rarely observed.[6g,6h] While some protocols require high temperatures,[6b,12b] elevated temperatures were not beneficial in our case. **C1** and **C4** excel in comparison to **C2**, **C3** and **C5** (Tables S5 and S6). The optimised protocol consists of PhCl as solvent and uses $^S$PhINTs. The overall modest yields of the challenging substrate cyclohexane are the consequence of the competing Cu(I)-catalysed cleavage of $^S$PhINTs into $^S$PhI and $H_2$NTs, where the latter was found quantitatively beside the product after stirring for 48 h. This Cu(I)-catalysed cleavage of an iminoiodiane has already been observed before and is a common side-reaction.[26] Additionally, the solubility of the starting materials is reduced by cyclohexane, denying the use of a vast excess of substrate. Besides the catalytic C–H amination, the catalytic aziridination of styrenes is easily accomplished by using PhINTs in dichloromethane (Table S4, entries 1-6). In the case of *p*-OMe-styrene the catalyst **C4** shows high product yields. Although **C5** does not act as suitable precursor for the stabilisation of a copper nitrene at low temperatures, a catalytic activity in C–H amination reactions and aziridination reactions at room temperature was observed (Tables S4-S6).



**Scheme 1.** Catalytic direct amination of cyclohexane and toluene. Reaction conditions: catalyst **C1** or **C4** (0.01 mmol); $^S$PhINTs (0.1 mmol); PhCl (0.15-1 mL); molecular sieves (3 Å). The yield was determined by $^1$H NMR spectroscopy, using an internal standard. See supporting information for details.

A remarkably interesting property is the instability of the nitrene **N1** with respect to ligand exchange. HC(3-$CF_3$Pz)$_2$(Py) is a much weaker ligand than HC(3-*t*BuPz)$_2$(Py) and can be replaced by the latter. We exploited this attribute for an unusual experiment inspired by the $Cu_2O_2$ core-capture experiment by Stack et al.[27] Such a transformation is also observed at the addition of ligand HC(3-*t*BuPz)$_2$(Py) to copper nitrene **N1** (Figure 4). The spectral features of **N1** completely disappear and **N2** evolves, accompanied by some decayed nitrene owing to the necessary temperature increase to enable the exchange reaction. Thereby, we present a novel Cu–NTs core-capture experiment, which is also supported by the application of isodesmic equations from DFT (Figure 4, inset, for the singlet $\kappa^2$-*N*,*O* conformers). The forward reaction was shown to be ca. 10 kcal mol$^{-1}$ more favoured compared to the back-reaction. A reversed reaction starting from **N2** is not observed experimentally. Hereby, **N1** might serve as nitrene precursor for metal complexes who are not capable to form metal nitrenes from iminoiodinanes.

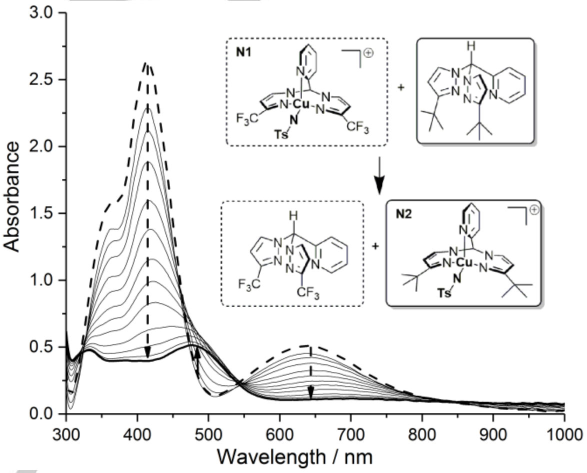


**Figure 4.** Cu–NTs core-capture starting from **N1**. The temperature is raised from -78 °C to -42 °C to initiate the reaction and form **N2**. See supporting information for details.

In summary, four distinct copper nitrenes, featuring tailored bis(pyrazolyl)methane ligands, were characterised regarding their stability, spectroscopy and reactivity. The herein reported unprecedented copper *N*-tosyl nitrenes exhibit a high thermal stability for terminal copper tosyl nitrenes, which exceeds that of the $Sc^{3+}$ stabilised system of Ray et al.[13] and preserve the monometallic structure. The compounds have been investigated by means of UV/Vis, cryo-UHR-ESI mass spectrometry and DFT and thereby assigned as terminal copper nitrenes. A mild catalytic procedure for the C–H amination of cyclohexane and toluene has been developed, underpinning the C–H activating capability of the investigated copper nitrenes. The latest discoveries on the copper tosyl nitrene mediated formation of sulfonamides and isothiazoles further corroborate the importance of this copper nitrene subclass. All in all, we were able to fill the gap for the long-standing search of terminal copper nitrenes and place bis(pyrazolyl)methane-supported copper nitrenes at the forefront of direct C–H aminations.

## Acknowledgements

Financial support by the Deutsche Forschungsgemeinschaft in the framework of the SFB 985 (Project A1), the SFB749 (Project B10), the RWTH Aachen in form of a Seed fund and the "Solar Technologies Go Hybrid" intiative by the State of Bavaria is gratefully acknowledged.

**Keywords:** terminal copper nitrenes• catalysis • C–H insertion • kinetics • N donor ligands • amination

[1] a) R. G. Bergman, *Nature* **2007**, *446*, 391-393; b) H. M. L. Davies, D. Morton, *J. Org. Chem.* **2016**, *81*, 343-350; c) N. V. Tzouras, I. K. Stamatopoulos, A. T. Papastavrou, A. A. Liori, G. C. Vougioukalakis, *Coord. Chem. Rev.* **2017**, *343*, 25-138.

[2] a) J. L. Roizen, M. E. Harvey, J. Du Bois, *Acc. Chem. Res.* **2012**, *45*, 911-922; b) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417-424.

[3] F. Collet, R. H. Dodd, P. Dauban, *Chem. Commun.* **2009**, 5061-5074.

[4] S. D. Roughley, A. M. Jordan, *J. Med. Chem.* **2011**, *54*, 3451-3479.

[5] R. Hili, A. K. Yudin, *Nat. Chem. Biol.* **2006**, *2*, 284-287.

[6] a) M. R. Fructos, S. Trofimenko, M. M. Díaz-Requejo, P. J. Pérez, *J. Am. Chem. Soc.* **2006**, *128*, 11784-11791; b) R. Bhuyan, K. M. Nicholas, *Org. Lett.* **2007**, *9*, 3957-3959; c) A. N. Vedernikov, K. G. Caulton, *Chem. Commun.* **2004**, 162-163; d) D. N. Barman, K. M. Nicholas, *Tetrahedron Lett.* **2010**, *51*, 1815-1818; e) R. T. Gephart, III, T. H. Warren, *Organometallics* **2012**, *31*, 7728-7752; f) I. Cano, M. C. Nicasio, P. J. Pérez, *Dalton Trans.* **2009**, 730-734; g) V. Bagchi, P. Paraskevopoulou, P. Das, L. Chi, Q. Wang, A. Choudhury, J. S. Mathieson, L. Cronin, D. B. Pardue, T. R. Cundari, G. Mitrikas, Y. Sanaki, P. Stavropoulos, *J. Am. Chem. Soc.* **2014**, *136*, 11362-11381; h) M. M. Díaz-Requejo, T. R. Belderraín, M. C. Nicasio, S. Trofimenko, P. J. Pérez, *J. Am. Chem. Soc.* **2003**, *125*, 12078-12079.

[7] a) P. Comba, C. Lang, C. Lopez de Laorden, A. Muruganantham, G. Rajaraman, H. Wadepohl, M. Zajaczkowski, *Chem. Eur. J.* **2008**, *14*, 5313-5328; b) H. Wu, L.-W. Xu, C.-G. Xia, J. Ge, W. Zhou, L. Yang, *Catal. Commun.* **2005**, *6*, 221-223; c) K. M. Gillespie, E. J. Crust, R. J. Deeth, P. Scott, *Chem. Commun.* **2001**, 785-786; d) N. Nebra, C. Lescot, P. Dauban, S. Mallet-Ladeira, B. Martin-Vaca, D. Bourissou, *Eur. J. Org. Chem.* **2013**, 984-990; e) E. Haldón, M. Delgado-Rebollo, A. Prieto, E. Álvarez, C. Maya, M. C. Nicasio, P. J. Pérez, *Inorg, Chem.* **2014**, *53*, 4192-4201; f) I. Arenas, M. Fuentes, E. Álvarez, Y. Díaz, A. Caballero, S. Castillón, P. J. Pérez, *Inorg, Chem.* **2014**, *53*, 3991-3999; g) B. M. Chanda, R. Vyas, A. V. Bedekar, *J. Org. Chem.* **2001**, *66*, 30-34; h) D. A. Evans, M. M. Faul, M. T. Bilodeau, *J. Am. Chem. Soc.* **1994**, *116*, 2742-2753; i) T. Ando, S. Minakata, I. Ryu, M. Komatsu, *Tetrahedron Lett.* **1998**, *39*, 309-312; j) L. D. Amisial, X. Dai, R. A. Kinney, A. Krishnaswamy, T. H. Warren, *Inorg, Chem.* **2004**, *43*, 6537-6539; k) A. N. Verdernikov, K. G. Caulton, *Org. Lett.* **2003**, *5*, 2591-2594; l) P. Comba, M. Merz, H. Pritzkow, *Eur. J. Inorg. Chem.* **2003**, 1711-1718; m) P. Comba, C. Haaf, A. Lienke, A. Muruganantham, H. Wadepohl, *Chem. Eur. J.* **2009**, *15*, 10880-10887.

[8] a) L. Maestre, W. M. C. Sameera, M. M. Díaz-Requejo, F. Maseras, P. J. Pérez, *J. Am. Chem. Soc.* **2013**, *135*, 1338-1348; b) I. Cano, E. Álvarez, M. C. Nicasio, P. J. Pérez, *J. Am. Chem. Soc.* **2011**, *133*, 191-193; c) P. Brandt, M. J. Södergren, P. G. Andersson, P.-O. Norrby, *J. Am. Chem. Soc.* **2000**, *122*, 8013-8020; d) D. N. Barman, P. Liu, K. N. Houk, K. M. Nicholas, *Organometallics* **2010**, *29*, 3404-3412; e) S. M. Tekarli, T. G. Williams, T. R. Cundari, *J. Chem. Theory Comput.* **2009**, *5*, 2959-2966.

[9] a) Z. Li, R. W. Quan, E. N. Jacobsen, *J. Am. Chem. Soc.* **1995**, *117*, 5889-5890; b) M. J. B. Aguila, Y. M. Badiei, T. H. Warren, *J. Am. Chem. Soc.* **2013**, *135*, 9399-9406.

[10] M. R. Rodríguez, Á. Beltrán, Á. L. Mudarra, E. Álvarez, F. Maseras, M. M. Díaz-Requejo, P. J. Pérez, *Angew. Chem. Int. Ed.* **2017**, *56*, 12842-12847; *Angew. Chem.* **2017**, *129*, 13022-13027.

[11] T. Tokumasu, R. Yazaki, T. Oshima, *J. Am. Chem. Soc.* **2016**, *138*, 2264-2669.

[12] a) Y. M. Badiei, A. Krishnaswamy, M. M. Melzer, T. H. Warren, *J. Am. Chem. Soc.* **2006**, *128*, 15056-15057; b) Y. M. Badiei, A. Dinescu, X. Dai, R. M. Palomino, F. W. Heinemann, T. R. Cundari, T. H. Warren, *Angew. Chem. Int. Ed.* **2008**, *47*, 9961-9964.

[13] S. Kundu, E. Miceli, E. Farquhar, F. F. Pfaff, U. Kuhlmann, P. Hildebrandt, B. Braun, C. Greco, K. Ray, *J. Am. Chem. Soc.* **2012**, *134*, 14710-14713.

[14] S.-L. Abram, I. Monte-Pérez, F. F. Pfaff, E. R. Farquhar, K. Ray, *Chem. Commun.* **2014**, *50*, 9852-9854.

[15] I. Monte-Pérez, S. Kundu, K. Ray, *Z. Anorg. Allg. Chem.* **2015**, *641*, 75-82.

[16] F. Dielmann, O. Back, M. Henry-Ellinger, P. Jerabek, G. Frenking, G. Bertrand, *Science* **2012**, *337*, 1526-1528.

[17] F. Dielmann, D. M. Andrada, G. Frenking, G. Bertrand, *J. Am. Chem. Soc.* **2014**, *136*, 3800-3802.

[18] T. Corona, L. Ribas, M. Rovira, E. R. Farquhar, X. Ribas, K. Ray, A. Company, *Angew. Chem. Int. Ed.* **2016**, *55*, 14005-14008; *Angew. Chem.* **2016**, *128*, 14211-14214.

[19] a) A. Hoffmann, C. Citek, S. Binder, A. Goos, M. Rübhausen, O. Troeppner, I. Ivanović-Burmazović, E. C. Wasinger, T. D. Stack, S. Herres-Pawlis, *Angew. Chem. Int. Ed.* **2013**, *52*, 5398-5401; *Angew. Chem.* **2013**, *125*, 5508-5512; b) C. Wilfer, P. Liebhäuser, H. Erdmann, A. Hoffmann, S. Herres-Pawlis, *Eur. J. Inorg. Chem.* **2015**, 494-502; c) C. Wilfer, P. Liebhäuser, A. Hoffmann, H. Erdmann, O. Grossmann, L. Runtsch, E. Pfaffenholz, R. Schepper, R. Dick, M. Bauer, M. Dürr, I. Ivanović-Burmazović, S. Herres-Pawlis, *Chem. Eur. J.* **2015**, *21*, 17639-17649; d) P. Liebhäuser, K. Keisers, A. Hoffmann, T. Schnappinger, I. Sommer, A. Thoma, C. Wilfer, R. Schoch, K. Stührenberg, M. Bauer, M. Dürr, I. Ivanović-Burmazović, S. Herres-Pawlis, *Chem. Eur. J.* **2017**, *23*, 12171-12183.

[20] A. Hoffmann, U. Flörke, M. Schürmann, S. Herres-Pawlis, *Eur. J. Org. Chem.* **2010**, 4136-4144.

[21] U. Herber, A. Hoffmann, S. Herres-Pawlis, *submitted* **2017**.

[22] D. T. Shay, G. P. A. Yap, L. N. Zhakarov, A. L. Rheingold, K. H. Theopold, *Angew. Chem. Int. Ed.* **2005**, *44*, 1508-1510.

[23] A. G. Bakhoda, Q. Jiang, J. A. Bertke, T. R. Cundari, T. H. Warren, *Angew. Chem. Int. Ed.* **2017**, *56*, 6426-6430; *Angew. Chem.* **2017**, *129*, 6526-6530.

[24] A. Hoffmann, S. Herres-Pawlis, *Phys. Chem. Chem. Phys.* **2016**, *18*, 6430-6440.

[25] a) D. F. Evans, *J. Chem. Soc.* **1959**, 2003-2005; b) J. Lölinger, R. Scheffold, *J. Chem. Edu.* **1972**, *49*, 646-647; c) D. F. Evans, D. A. Jakubovic, *J. Chem. Soc., Dalton Trans.* **1988**, 2927-2933.

[26] D. A. Evans, M. M. Faul, M. T. Bilodeau, *J. Org. Chem.* **1991**, *56*, 6744-6746.

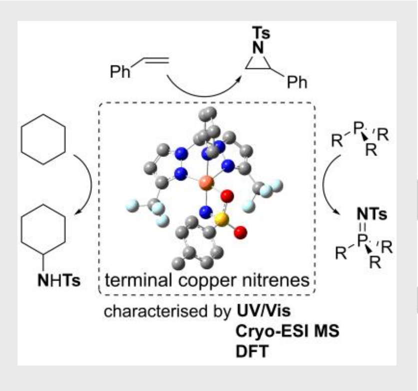
[27] a) L. Chiang, W. Keown, C. Citek, E. C. Wasinger, T. D. P. Stack, *Angew. Chem. Int. Ed.* **2016**, *55*, 10453-10457; *Angew. Chem.* **2016**, *128*, 10609-10613; b) C. Citek, B.-L. Lin, T. E. Phelps, E. C. Wasinger, T. D. P. Stack, *J. Am. Chem. Soc.* **2014**, *136*, 14405-14408; c) C. Citek, J. B. Gary, E. C. Wasinger, T. D. P. Stack, *J. Am. Chem. Soc.* **2015**, *137*, 6991-6994.

**Entry for the Table of Contents** (Please choose one layout)

Layout 1:

FULL PAPER

**Abstract:** Four distinct terminal copper tosyl nitrenes have been stabilised at low temperatures from heteroscorpionate ligands of the bis(pyrazolyl)methane family. They were investigated by UV/Vis spectroscopy, cryo-UHR-ESI mass spectrometry and DFT. A mild catalytic procedure has been developed, enabling the C–H amination of cyclohexane and toluene as well as the aziridination of styrenes.



*Julian Moegling, Alexander Hoffmann, Fabian Thomas, Nicole Orth, Patricia Liebhäuser, Ulrich Herber, Robert Rampmaier, Julia Stanek, Gerhard Fink, Ivana Ivanović-Burmazović, Sonja Herres-Pawlis*

***Page No. – Page No.***

**Designed to react: Terminal Copper Nitrenes and their Application in Catalytic C–H Aminations**