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Cu-NHC Azide Complex: Synthesis and Reactivity

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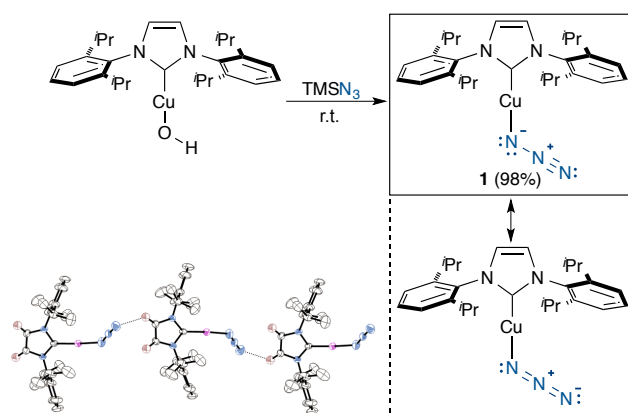
Herein we report the first example of a NHC-based copper azide complex. The synthetic protocol leading to [Cu(N₃)(IPr)] and the reactivity of this complex with various compounds is described.

Copper azide species were first structurally characterised in 1964 when the molecular structure of [Cu(N₃)(NH₃)₂]_n was elucidated.¹ A few years later, Agrell described the structure of [Cu(N₃)₂]_n.² In both cases, the compounds were found to be polymeric and shock sensitive (explosive). The first well-defined copper azide species was reported in 1971, stabilised by triphenylphosphine. The complex obtained has the following formula: [Cu(μ-N₃)(PPh₃)₂]₂,³ where the azide fragments are bridging the Cu-centers through their terminal nitrogen atoms. This work was followed by a number of reports on the use of *P*- and *N*-based ligands to stabilise the CuN₃ core,^{4,5} and also focused on exploring its fascinating reactivity. Studies have been mostly limited to these heteroatom-based donor ligands.

N-heterocyclic carbene (NHC) ligands have an outstanding ability to stabilise highly reactive transition metal complexes, including copper complexes⁶ used as catalysts in numerous organic transformations.⁷ However, to the best of our knowledge, no copper(I)-NHC azide complex has been reported to date. In 2009, Gray and co-workers reported the synthesis of silver and gold azide complexes bearing NHC ligands⁸ while recently, the reactivity of a gold-NHC azide complex in a [3+2] cycloaddition reaction using terminal alkynes was reported, affording gold-NHC triazole complexes.⁹ Considering the ability of NHC-Cu hydroxide complex to act as a fairly general synthon,¹⁰ we explored its potential to generate a NHC-Cu azide species. Herein, we report on the isolation and characterisation of such a compound, and its

reactivity with organic and organometallic fragments.

The synthesis of [Cu(N₃)(IPr)] (**1**) (IPr = *N,N'*-bis[(2,6-(di-*iso*-propyl)phenyl)]imidazol-2-ylidene) was achieved by reacting [Cu(OH)(IPr)]¹⁰ with trimethylsilylazide (TMSN₃) in toluene for 16 h (Scheme 1). The reaction was done under inert conditions; however, the final complex (**1**) is air-stable in the solid-state. The product was characterised by NMR, and the structure was determined by X-ray diffraction of single crystals obtained by slow diffusion of hexane into a saturated THF solution of the complex. The complex thus obtained is monomeric, with only one *N*-atom per N₃-fragment involved in metal bonding. This structure is similar those obtained with group 11 congeners (Ag and Au) bearing a NHC.⁸ The complex obtained here, [Cu(N₃)(IPr)] **1**, attests again to the unique ability of *N*-heterocyclic carbenes to stabilise low valent species. This is in marked contrast with the tetrahedral geometry observed for Cu-azide complexes supported by *P*- and/or *N*-donor ligands.^{5b} Indeed, in **1**, the copper atom adopts an almost linear coordination with the two ligands (C1-Cu1-N30 = 175.85(7)°), which are nearly equidistant from the copper center (C1-Cu1 = 1.8688(15) Å, Cu1-N30 = 1.8488(15) Å). The azide ligand adopts an asymmetrical canonical form N=N=N⁻,¹¹ with NN bond distances of 1.192(2) and 1.154(2) Å.¹²



Scheme 1. Synthetic access to **1** and its molecular structure. Selected bond lengths (Å) and angles (°): C1-Cu1, 1.8688(15); Cu1-N30, 1.8488(15); N30-N31, 1.192(2); N31-N32, 1.154(2); C1-Cu1-N30, 175.85(7); N30-N31-N32, 175.86(18); Cu1-N30-N31, 125.1(1).¹²

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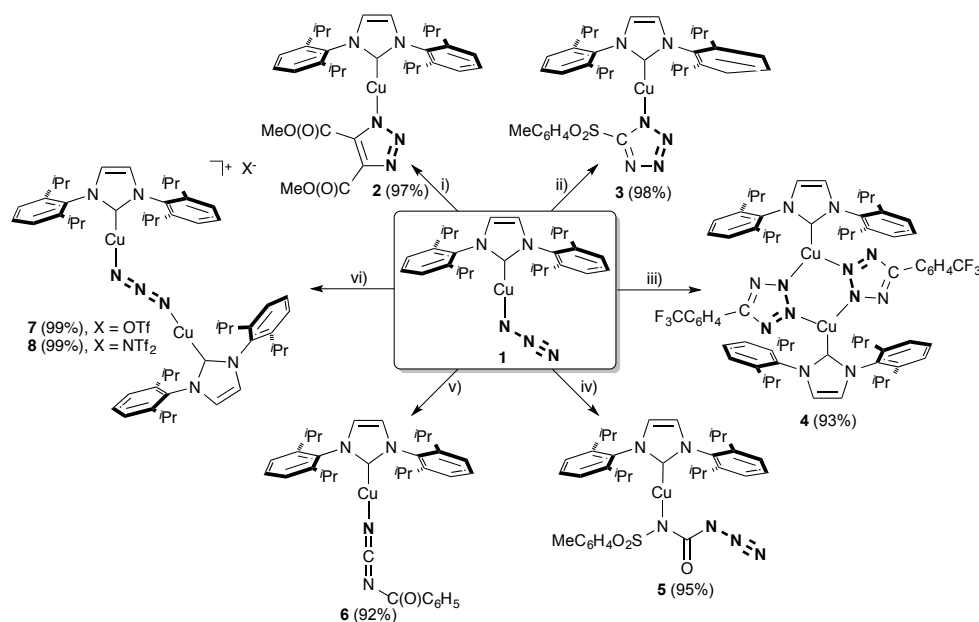
Electronic Supplementary Information (ESI) available: Synthesis and characterisation of complexes, crystal data and NMR spectra. See DOI: 10.1039/x0xx00000x

As expected, the longest NN bond distance is found between the nitrogen atom coordinated to the metal centre and its neighbour.¹¹ The Cu-N-N angle is 125.1(1)°, which is within the expected range for trigonally hybridised nitrogen. The solid-state packing of **1** presents an intermolecular hydrogen bonding interaction between a hydrogen atom of the IPr ligand backbone (H³) and the terminal azide nitrogen of a neighbouring molecule (Scheme 1).¹² A similar interaction was observed in the analogous [Au(N₃)(IPr)],⁸ with the noticeable difference that, in the Au case, all azide moieties have the same orientation. Concerning both distances and angles, they are found similar to all group 11 congeners, with the exception of the M-N bond length, which is considerably shorter in **1** compared that found in Ag and Au analogues.

Considering the ability of NHCs to stabilise reactive species, the use of [Cu(N₃)(IPr)] **1** as synthon to access intermediate complexes involved in catalysis was examined. Our attention first turned to the Cu-catalysed [3+2] cycloaddition of azides and alkynes (CuAAC).¹³ In this transformation, it is proposed that the metal activates the alkyne forming a copper-acetylide intermediate, which adds to the azide.¹⁴ Here an orthogonal approach was envisioned, with the copper-azide **1** reacting with the alkyne. It should be noted that no selective reaction was obtained using terminal alkynes. For example, 1-ethynyl-4-fluorobenzene did not react with **1** at rt, and when the reaction mixture was heated to 50 °C two unknown species were detected by ¹⁹F-¹H} NMR; however, full conversion of **1** was not reached even after three days. Regarding internal alkynes, the cycloaddition reaction is more difficult using copper and thus ruthenium is usually the metal of choice (RuAAC);¹⁵ therefore, not surprisingly, diphenylacetylene failed to react with **1** at 50 °C. However, **1** reacted immediately at room temperature with dimethyl acetylenedicarboxylate, an activated alkyne, to form the triazolite copper complex **2**

(Scheme 2), the structure of which was confirmed by XRD on single crystal.¹² While the Cu-C_{carbene} bond distances are comparable (1.8688(15) and 1.877(2) Å), the Cu-N bond length in **2** is slightly longer than the one observed in **1** (1.887(2) vs 1.8488(15) Å), and a dihedral angle of 126.7(3)° is observed between the two heterocycles. This result might suggest that the reaction proceeds through the nucleophilic addition of the Cu(I)-activated azide onto the electrophilic alkyne rather than a typical 1,3-dipolar cycloaddition.

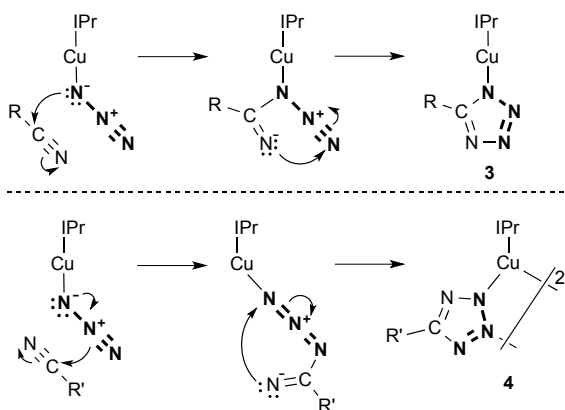
We next turned our attention to nitrile derivatives in order to access tetrazolate complexes, compounds that have been proposed as key intermediates in the Cu-catalysed cycloaddition of nitriles and azides.¹⁶ Reaction of [Cu(N₃)(IPr)] **1** with the activated *p*-toluenesulfonyl cyanide led quantitatively to **3** upon mixing, while the less activated 4-(trifluoromethyl)benzonitrile required heating and longer reaction times (50 °C, 16 h) to form **4** in high yield (Scheme 2). In contrast, when *p*-tolunitrile was used, no reaction occurred, denoting the same reactivity trend previously observed with internal alkynes. The nature of the nitrile does not only govern reactivity, but also selectivity, as shown with the different structures obtained with *p*-toluenesulfonyl cyanide and 4-(trifluoromethyl)benzonitrile. Indeed, while the latter leads to a dimeric species with a N²-N³ bridging tetrazole (**4**), the former leads to a N¹-bound tetrazole complex which is monomeric due to the steric hindrance brought about by the C⁵-substituent (**3**).¹⁷ The difference of regioselectivity is rationalised by the attack of the nitrile carbon atom which can be done by either the proximal azide nitrogen or the distal one, depending on the steric nature of R group (Scheme 3). Since there is no evidence of **4** being dimeric in solution, another possibility would be that both reactions follow a similar mechanism, followed by a rearrangement in the case of the reaction leading to complex **4**.



Scheme 2. Reactivity of [Cu(N₃)(IPr)], **1**.

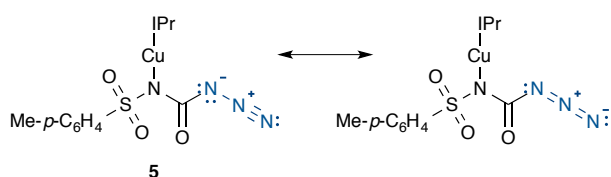
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The crystal structure of **3** shows similarity with the structural features found in **1** and **2**. Complex **4**, on the other hand, displays a significantly longer Cu-C_{carbene} (2.000(3) Å) and orthogonality of the bridging ligand with the carbene core (90.8(3)^o).¹²



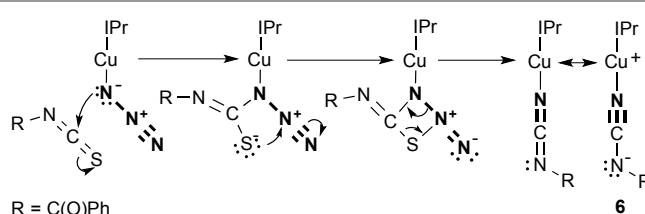
Scheme 3. Selectivity of the cycloaddition of nitriles and azide.

Our attention next focused on the use of iso(thio)cyanate substrates for the [3+2] cycloaddition.¹⁸ *p*-Toluenesulfonyl isocyanate was reacted with **1**, leading instantaneously to full conversion. Crystals suitable for X-Ray analysis were obtained by slow diffusion of pentane into a saturated CH₂Cl₂ solution, confirming the formation of **5** (Scheme 4). As for complex **1**, **5** displays an asymmetrical canonical (NN bond distances of 1.247(6) and 1.104(7) Å) with the longest NN bond length found in the Cu vicinal bond.



Scheme 4. Canonical forms of N₃ in complex **5**.

Benzoyl isothiocyanate also reacts instantaneously with **1** at room temperature, leading to the formation of the cyanamido derivative **6** with concomitant release of S=N=N (Scheme 5). Such reactivity has been reported when isothiocyanates react with sodium bis(trimethylsilyl)amide, releasing Me₃Si-SiMe₃ and affording the correspondent cyanamide.¹⁹ Metal cyanamide intermediates have been postulated in the palladium-catalysed synthesis of cyanamides from isocyanates and TMSN₃, but no characterisation data has been reported to date on such species.²⁰



Scheme 5. Proposed mechanism for the formation of **6**.

We next turned our attention to the ability of **1** to lead to dimeric species. Such complexes are of particular interest as they are reactive intermediates in a number of Cu-catalysed reactions.^{21–24} However, while a number of Cu dimeric species have been reported,^{17c} to the best of our knowledge, no azide-bridged NHC-Cu dimer has been reported to date. In this respect, **1** proved to be an excellent synthon, and reaction with [Cu(X)(NHC)] (X = OTf, NTf₂) led to dimers [(Cu(NHC))₂(μ-N₃)]OTf **7** and [(Cu(NHC))₂(μ-N₃)]NTf₂ **8** in quantitative yield of microanalytically pure form (Scheme 2). In the case of **7** and **8**, the N₃ unit is expected to be symmetrical, of the form N=N=N. To ascertain this, single crystals suitable for XRD studies were grown. While the data sets obtained do not allow to comment on the N₃ bond lengths, in **8**, the central nitrogen sits on a centre of symmetry thus providing symmetric bond distances. However, considering the data show neither thermal motion of the azide nitrogens along the axis of the N₃, nor electron density peaks which would suggest disorder of a symmetric azide, it is thus likely that **7** and **8** adopt a symmetrical canonical N=N=N form.

In summary, the copper(I)-NHC azide complex [Cu(N₃)(IPr)] was successfully synthesised and fully characterised, completing the last entry in the coinage metal-NHC azide series. It exhibits similar features as its gold and silver congeners. Moreover, the reactivity of [Cu(N₃)(IPr)] was investigated (Scheme 2). It reacts with various organic substrates, following a cycloaddition pathway leading to a triazole-based complex when an activated alkyne is used and tetrazole-based complexes when reacted with nitriles. In the case of isocyanates, a nucleophilic attack of the azide moiety onto the carbon of the isocyanate occurs, while when the reaction partner is an isothiocyanate, a rearrangement takes place to afford a cyanamide bound to the copper centre. Finally, dinuclear copper complexes, with the azide moiety bridging the two copper atoms, were readily synthesised by reacting [Cu(N₃)(IPr)] with a cationic copper fragment. In all cases, crystal structures¹² and full characterisation were obtained, thus shedding much-needed light on this area of research, highlighting the interesting reactivity displayed by this family of complexes and finally showcasing the unique

stabilising effect brought about in Cu-NHC coordination that permits the synthesis and isolation of complexes bearing usual organic fragments.

Conflicts of interest

There are no conflicts to declare.

Notes and references

- C. Brosset, I. Agrell, *Nature*, 1964, **202**, 1210.
- I. Agrell, *Acta Chem. Scand.*, 1967, **21**, 2647.
- R. F. Ziolo, A. P. Gaughan, Z. Dori, C. G. Pierpont, R. Eisenberg, *Inorg. Chem.*, 1971, **10**, 1289.
- (a) A. P. Gaughan, R. F. Ziolo, Z. Dori, *Inorg. Chem.*, 1971, **10**, 2776; (b) R. F. Ziolo, J. A. Thich, Z. Dori, *Inorg. Chem.*, 1972, **11**, 626; (c) J. Green, E. Sinn, S. Woodward *Inorg. Chim. Acta*, 1995, **230**, 231.
- (a) G. La Monica, G. Ardizzioia, S. Cenini, F. Porta, *J. Organomet. Chem.*, 1984, **273**, 263; (b) C. Pettinari, *Polyhedron*, 2001, **20**, 2755.
- For selected examples of NHC-copper(I) complexes see: (a) T. Vergote, F. Nahra, A. Welle, M. Luhmer, J. Wouters, N. Mager, O. Riant, T. Leyssens, *Chem. Eur. J.*, 2012, **18**, 793; (b) N. P. Mankad, T. G. Gray, D. S. Laitar, J. P. Sadighi, *Organometallics*, 2004, **23**, 1191; (c) G. Venkatachalam, M. Heckenroth, A. Neels and M. Albrecht, *Helv. Chim. Acta* 2009, **92**, 1034; (d) O. Santoro, A. Collado, A. M. Z. Slawin, S. P. Nolan, C. S. J. Cazin, *Chem. Commun.* 2013, **49**, 10483; (e) G. C. Fortman, A. M. Z. Slawin, S. P. Nolan, *Organometallics*, 2010, **29**, 3966; (f) D. S. Laitar, P. Müller, J. P. Sadighi, *J. Am. Chem. Soc.*, 2005, **127**, 17196; (g) G. G. Dubinina, H. Furutachi, D. A. Vicić, *J. Am. Chem. Soc.*, 2008, **130**, 8600; (h) C. Gibard, H. Ibrahim, A. Gautier, F. Cisnetti, *Organometallics*, 2013, **32**, 4279; (i) A. C. Badaj, S. Dastgir, A. J. Lough, G. G. Lavoie, *Dalton Trans.*, 2010, **39**, 3361; (j) S. Díez-González, E. C. Escudero-Adán, J. Benet-Buchholz, E. D. Stevens, A. M. Z. Slawin, S. P. Nolan, *Dalton Trans.*, 2010, **39**, 7595.
- For selected review regarding NHC-copper(I) in catalysis see: (a) L. Zhang, Z. Hou, *Chem. Sci.*, 2013, **4**, 3395; (b) J. Egbert C. S. J. Cazin, S. P. Nolan, S. P. *Catal. Sci. Tech.*, 2013, **3**, 912; (c) F. K. Zinn, M. S. Viciu, S. P. Nolan, *Annu. Rep. Prog. Chem., Sect. B*, 2004, **100**, 231; (d) H. Clavier, S. P. Nolan, *Annu. Rep. Prog. Chem., Sect. B*, 2007, **103**, 193; (e) L. Zhang, Z. Hou, *Pure Appl. Chem.*, 2012, **84**, 1705; (f) H. Jacobsen, A. Correa, A. Poater, C. Costabile, L. Cavallo, *Coord. Chem. Rev.*, 2009, **253**, 687; (g) X. Bantreil, J. Broggi, S. P. Nolan, *Annu. Rep. Prog. Chem., Sect. B*, 2009, **105**, 232.
- D. V. Partyka, T. J. Robilotto, J. B. Updegraff III, M. Zeller, A. D. Hunter, T. G. Gray, *Organometallics*, 2009, **28**, 795.
- T. J. Robilotto, N. Deligonul, J. B. Updegraff III, T. G. Gray, *Inorg. Chem.*, 2013, **52**, 9659.
- G. C. Fortman, A. M. Z. Slawin, S. P. Nolan, *Organometallics*, 2010, **29**, 3966.
- Z. Dori, R. F. Ziolo, *Chem Rev.*, 1973, **73**, 247.
- CCDC-1541281 (1), CCDC-1541282 (2), CCDC-1541283 (3), CCDC-1541284 (4), CCDC-1541285 (5), CCDC-1541286 (6), CCDC-1541287 (7), CCDC-15412818 (8) contain the supplementary crystallographic data for this contribution.
- For selected examples of CuAAC see: (a) E. Haldón, M. C. Nicasio, P. J. Pérez, *Org. Biomol. Chem.*, 2015, **13**, 9528; (b) J. E. Hein, V. V. Fokin, *Chem. Soc. Rev.*, 2010, **39**, 1302; (c) M. – L. Teyssot, A. Chevy, M. Traïkia, M. El-Ghozzi, D. Avignant, A. Gautier, *Chem. Eur. J.*, 2009, **15**, 6322; (d) F. Lazreg, A. M. Z. Slawin, C. S. J. Cazin, *Organometallics*, 2012, **31**, 7969; (e) Y. D. Bidal, M. Lesieur, M. Melaimi, F. Nahra, D. B. Cordes, K. S. A. Arachchige, A. M. Z. Slawin, G. Bertrand, C. S. J. Cazin, *Adv. Synth. Catal.*, 2015, **357**, 3155.
- a) R. Berg, B. F. Straub, *Beilstein J. Org. Chem.*, 2013, **9**, 2715; b) L. Zhu, C. J. Brassard, X. Zhang, P. M. Guha, R. J. Clark, *Chem. Rec.*, 2016, **16**, 1501.
- B. C. Boren, S. Narayan, L. K. Rasmussen, L. Zhang, H. Zhao, Z. Lin, G. Jia, V. V. Fokin, *J. Am. Chem. Soc.*, 2008, **130**, 8923.
- T. Jin, F. Kitahara, S. Kamijo, Y. Yamamoto, *Chem. Asian J.*, 2008, **3**, 1575.
- (a) M. Trose, F. Lazreg, T. Chang, F. Nahra, D. B. Cordes, A. M. Z. Slawin, C. S. J. Cazin, *ACS Catal.*, 2017, **7**, 238; (b) M. Trose, F. Nahra, A. Poater, D. B. Cordes, A. M. Z. Slawin, L. Cavallo, C. S. J. Cazin, *ACS Catal.*, 2017, **7**, 8176; (c) M. Trose, F. Nahra, C. S. J. Cazin, *Coord. Chem. Rev.*, 2018, **355**, 380.
- a) P. Kreutzer, C. Weis, H. Boehme, T. Kemmerich, W. Beck, C. Spencer, R. Mason, *Z. Naturforsch.*, 1972, **27b**, 745; b) P. H. Kreutzer, J. C. Weis, H. Bock, J. Erbe, W. Beck, *Chem. Ber.*, 1983, **116**, 2691; c) Kim, Y.-J.; Lee, S.-H.; Lee, S.-H.; Jeon, S. I.; Lim, M. S.; Lee, S. W. *Inorg. Chim. Acta*. 2005, **358**, 650.
- C.-Y. Chen, F.-F. Wong, J.-J. Huang, S.-K. Lin, M.-Y. Yeh, *Tetrahedron Lett.*, 2008, **49**, 6505.
- S. Kamijo, T. Jin, Y. Yamamoto, *Angew. Chem. Int. Ed.*, 2002, **41**, 1780.
- For selected examples of dinuclear cationic copper(I)-NHC complexes see: (a) C. M. Wyss, B. K. Tate, J. Bacsa, T. G. Gray, J. P. Sadighi, *Angew. Chem. Int. Ed.*, 2013, **52**, 12920; (b) C. M. Wyss, B. K. Tate, J. Bacsa, M. Wieliczko, J. P. Sadighi, *Polyhedron*, 2014, **84**, 87; (c) A. M. Suess, M. R. Uehling, W. Kaminsky, G. Lalic, *J. Am. Chem. Soc.*, 2015, **137**, 7747.
- M. Lee, M. Nguyen, C. Brandt, W. Kaminsky, G. Lalic, *Angew. Chem. Int. Ed.*, 2017, **56**, 15703.
- A. M. Suess, M. R. Uehling, W. Kaminsky, G. Lalic, *J. Am. Chem. Soc.*, 2015, **137**, 7747.
- L. Jin, D. R. Tolentino, M. Melaimi, G. Bertrand, *Sci. Adv.*, 2015, **1**, 1.