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[{Cu(IPr)}$_2$(μ-OH)][BF$_4$]: synthesis and halide-free CuAAC catalysis†

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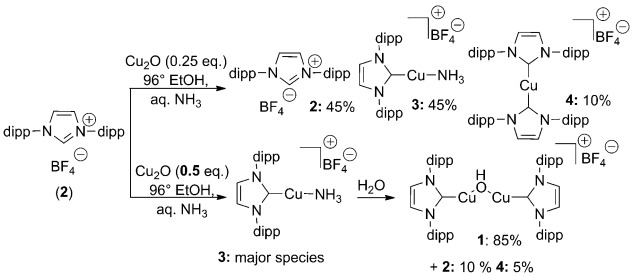
The preparation under protic conditions of the first μ-hydroxo dicopper(I)–NHC complex is reported. Its application as a CuAAC catalyst was investigated, evidencing a remarkable enhancement of catalytic efficiency in the presence of 4,7-dichloro-1,10-phenanthroline and highlighting the beneficial effect of the absence of coordinating halides.

Classically, the direct metalation of azolium salts involves the use of appropriate metal salts and strong bases under anhydrous anoxic conditions.[1a] This is particularly true for copper(I), which is prone to oxidation.[1b] Alternatively, Cu^I–NHC complexes may be obtained by transmetalation of silver precursors but this generates large amounts of inorganic waste.[1c] Recently, there has been a drive for the discovery of novel, alternative and simplified syntheses of Group 11 metal–NHC complexes,[2] as these offer unique catalytic opportunities. Mild bases and aqueous conditions have been highlighted as suitable media for the synthesis of Cu^I–NHC complexes. We have reported the preparation of hetero- and homoleptic Cu^I–NHCs in aqueous or ethanolic ammonia as basic and coordinating medium.[2d]

Previous reports have highlighted the potential of [M((S)IPr)(OH)] (M = Cu, Au) and [{Au(IPr)}$_2$(μ-OH)]$^+$ complexes in catalysis and as useful synthons.[3] To the best of our knowledge, no [{Cu(NHC)}$_2$(μ-OH)]$^+$ compound was reported. Such a complex would be of catalytic interest because of (i) the absence of halide ions – cationic halide-free complexes displayed improved activity in CuAAC and hydrosilylation reactions, which was rationalized by a more efficient pathway for the activation of the precatalyst[4] – and (ii) its possible equivalence with a combination of [Cu(NHC)]$^+$ and [Cu(NHC)(OH)], leading to [Cu(NHC)H$_2$O]$^+$ in water. We report in this communication the facile preparation of [{Cu(IPr)}$_2$(μ-OH)][BF$_4$] (**1**) by a two-step one-pot procedure (Scheme 1) and its catalytic potential for the copper-catalysed azide–alkyne cycloaddition (CuAAC) alone or in the presence of 4,7-dichloro-1,10-phenanthroline (phen*) as an additive. Indeed, it has been shown that the addition of Phenanthroline Enhances the Copper (''PECu'') performances toward CuAAC reactions.[5]



Scheme 1 Outcome of the metalation of **2**.

The synthesis of (**1**) was discovered serendipitously while studying an ammonia-based metalation in ethanol.[2d] Indeed, in contrast to (S)IMes·HBF$_4$, for which reaction with Cu$_2$O (0.25 eq.)/NH$_3$ in ethanol yielded the homoleptic complexes as filterable solids, IPr·HBF$_4$ (**2**) afforded a colorless solution. ^{1}H NMR of a sample of the reaction mixture revealed that it contained an equimolar amount of **2** and an unknown species (**3**) as well as a small amount (5–10%) of [Cu(IPr)$_2$]BF$_4$, **4**. Increasing the amount of Cu$_2$O to 0.5 eq. afforded **3** as the major component. The ^{1}H NMR signature of **3** was different from that of **4** and [Cu(IPr)OH] (**5**).† It displayed a broad signal (2.26 ppm) roughly integrating 3 protons. Therefore, **3** was tentatively identified to be [Cu(IPr)(NH$_3$)]$^+$. While treating the reaction mixture with water, a white solid separated. The ^{1}H-NMR spectrum revealed the presence of [Cu(IPr)$_2$]BF$_4$ (**4**) and **2** (5% and 10%, respectively) as well as a major new complex, **1**. Infrared analysis showed that **1** is a cationic complex with a BF$_4^-$ counter-ion (1051 cm^{-1}).

Preparative recrystallization affords prisms (**1**, majority) and needles (**4**, minority), both being stable for months on the benchtop.

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† Electronic supplementary information (ESI) available: Preparation and crystallographic data for **1**; the mechanism of formation of **1**, NMR spectra of **3** and the phenanthroline adduct of **1**. CCDC 989122. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4cc03346a

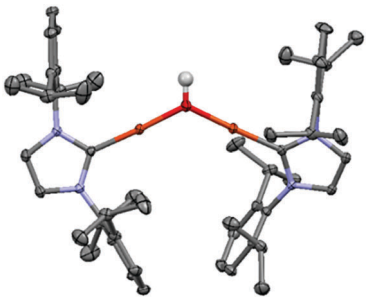
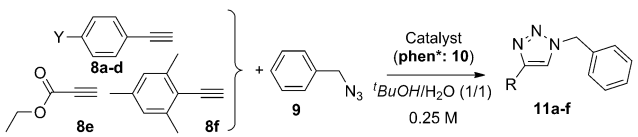


Fig. 1 Ellipsoid plot of [{Cu(IPr)}$_2$(μ-OH)](BF$_4$) (**1**) (50% probability level, BF$_4^-$ and most hydrogens omitted). Cu–C: 1.87 Å, Cu–O: 1.84 Å, C–Cu–O: 117° (average values), Cu–O–Cu: 127.87(8).

Identity and purity of **1** were established by X-ray crystallography (Fig. 1) and elemental analysis.† The structure is quite similar to [{Au(IPr)}$_2$(μ-OH)]$^+$.[3b] Optimization of the reaction conditions allowed this species to be obtained 95% pure in the crude solid. The formation of **1** could be explained by the replacement of the ammonia ligand of **3** by water furnishing [Cu(IPr)(OH$_2$)] (**6**) which is the conjugate acid of [Cu(IPr)OH], (**5**). The metal-bound water of **6** is expected to be displaced by **5** in an olation step furnishing the μ-OH complex **1** which precipitates from the reaction medium in the presence of a BF$_4^-$ counterion, thus providing a driving force for the reaction (Scheme S1, ESI†).

A first evaluation of the CuAAC potential of **1** under benchmark conditions such that the products are isolated by simple filtration was performed. It revealed that the catalyst allowed the CuAAC reaction to be performed under *true* click reaction conditions: open flask and pure products by filtration (Scheme 2, Table 1, entry 1).[6] For the sake of comparison, we tested [Cu(IPr)Cl][7] (**7a**) and [Cu(IPr)(O^{t}Bu)][8] (**7b**) under the same conditions (especially, the same metal loading). Entry 2 shows a low efficiency of **7a** whereas entry 3 displays a higher but still limited yield for the chloride free catalyst **7b** (19 *vs.* 53%). Catalyst **1** (entries 4 and 5) was more active furnishing good isolated yields of **11a** at loadings of 1 and 0.5 mol%. A shorter reaction time (entry 6) resulted in a lower isolated yield. The PECu effect was evaluated in entries 7–11. Addition of phen* to **7a** showed a better but still limited performance (entries 2 *vs.* 7), exhibiting a strong positive action on **7b** (entries 9, 10) and an even more marked effect on **1** (entries 11 and 12). Moderate yields were obtained only after 3 h using two equivalents of phen* per **1** (entry 13) while a lower yield was observed with 1 equivalent (entry 14). The lower limit of catalyst concentration was reached using 0.25 mol% (entry 15). Interestingly, chloride free catalysts **1** and **7b** perform better than [Cu(IPr)Cl] activated by phen* (90 and 53% *vs.* 39%; entries 1, 3 *vs.* 7). In the presence of chloride, the catalysis was totally inhibited (entries 4 *vs.* 16) highlighting the detrimental role



Scheme 2 Catalytic CuAAC experiments.

Table 1 CuAAC performed using Cu(IPr)-containing species

Entry	Catalyst	*x* (mol%) Cu	Alkyne	Time (h)	Yield[a] (%)
1	**1**	2	**8a** (–H)	19	90
2	**7a**	4	**8a** (–H)	19	19
3	**7b**	4	**8a** (–H)	19	53
4	**1**	1	**8a** (–H)	19	83
5	**1**	0.5	**8a** (–H)	19	46
6	**1**	1	**8a** (–H)	3	10
7	**7a** + **10** (4 mol%)	4	**8a** (–H)	19	39
8	**7a** + **10** (2 mol%)	2	**8a** (–H)	19	20
9	**7b** + **10** (4 mol%)	4	**8a** (–H)	19	80
10	**7b** + **10** (2 mol%)	2	**8a** (–H)	19	68
11	**1** + **10** (2 mol%)	1	**8a** (–H)	19	89
12	**1** + **10** (1 mol%)	0.5	**8a** (–H)	19	76
13	**1** + **10** (2 mol%)	1	**8a** (–H)	3	55
14	**1** + **10** (1 mol%)	1	**8a** (–H)	3	17
15	**1** + **10** (0.5 mol%)	0.25	**8a** (–H)	19	18
16	**1** + Cl$^-$[b]	1	**8a** (–H)	19	0
17	**1**	1	**8b** (–OMe)	19	76
18	**1**	1	**8c** (–NH$_2$)	19	70
19	**1**	1	**8d** (–F)	72	83
20	**1**	1	**8e**	72	70
21	**1**	1	**8f**	72	47

[a] Pure compound isolated by filtration. [b] NaCl or NH$_4$Cl (3.0 eq.).

of halides.[4b,9] As blank experiment we added **1** to NaCl solution and recovered [Cu(IPr)Cl] nearly instantaneously – the same observations applied for Br$^-$ or I$^-$ anions. The catalyst was also efficient with electron-rich (entries 17 and 18) as well as electron-poor alkynes, albeit at a lower rate (entries 19 and 20). The reaction hardly functions with bulky substituents (entry 21) compared to the triazolium-derived halide free homoleptic abnormal Cu^I–NHCs reported by Sarkar.[9a]

Having established **1** as a CuAAC catalyst, we decided to investigate the kinetic profile of the CuAAC reaction (Fig. 2) under homogenous conditions and at higher concentration.

Using **1**, the reaction starts after an induction period of ~20 minutes and reaches completion in approximately 120 min probably because **1** behaves as a precatalyst. Phen* exhibits a remarkable acceleration effect. At the same catalyst concentration, the inductive period is shortened to 4 min and completion reached in less than 7 min. A decrease of the catalyst loading lengthens

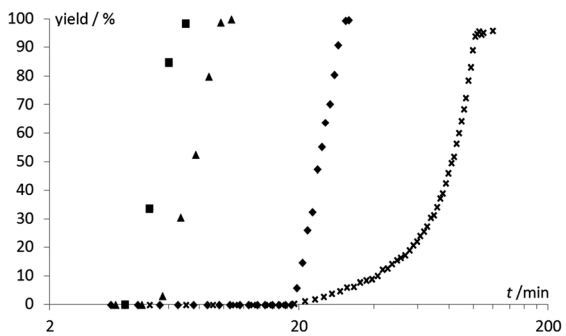
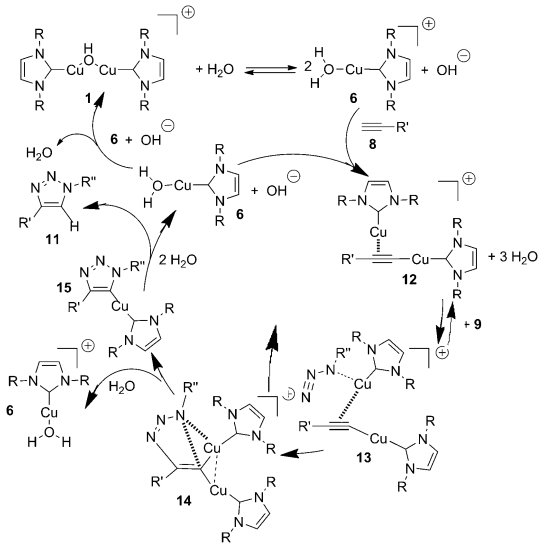


Fig. 2 ^{1}H NMR kinetic survey at 298 K (log scale) of the CuAAC reaction of phenylacetylene (**8a**) and benzyl azide (**9**) catalysed by **1**. [**8a**] = 0.5 M; [**9**] = 0.5 M, 1,4-dimethoxybenzene as internal standard, ^{t}BuOH/H$_2$O v/v 3 : 1.; ■: **1** (2 mol%) + phen* (4 mol%); ▲: **1** (1 mol%) + phen* (2 mol%); ◆: **1** (0.5 mol%) + phen* (1 mol%); ×: **1** (2 mol%).



Scheme 3 Proposed mechanistic path.

the inductive period and completion time by 10 min and 30 min (1 and 0.5 mol%), respectively.

A probable mechanism of catalysis by **1** is displayed in Scheme 3.[10] The reaction is expected to proceed through the formation of a σ, π dicuprated complex **12**. Reversible coordination of azide **9** followed by annulation through intermediate **14** and protonation of the resulting triazolide copper–NHC (**15**)[11] delivers the target 1,2,3-triazole **11** as well as the copper–NHC species **6** which could enter into the catalytic cycle through the coordination of a new alkyne delivering **12** or reforming **1**.

Addition of 2 eq. of phen* disrupts **1** into $[Cu(IPr)(phen^*)]^+$ (**16**)[12] – liberating simultaneously one equivalent of base which could facilitate alkyne deprotonation to access **12**. Phen* could also block the reformation of inactive **1** at the end of the catalytic cycle. Moreover, phen* may tune the electronic properties at several intermediates and transition states – especially, by analogy to previous reports, for the dicuprated complex **12** and the transition state between **13** and **14**[4a,b,9b]

In summary, we have reported the synthesis of $[\{Cu(IPr)\}_2(\mu\text{-}OH)](BF_4)$, (**1**), the first μ-hydroxo dicopper(I)–NHC. This species is easily synthesized in hydro alcoholic media using ammonia. Thanks to the absence of coordinating halides, the catalytic activity of (**1**) in CuAAC is greatly increased compared to [Cu(IPr)Cl], (**7**). Moreover, the addition of phen* to (**1**) leads to a marked enhancement of the catalytic efficiency. Compared to previously reported systems containing halides, such a PECu effect is optimally efficient. The synthesis of other $[\{Cu(NHC)\}_2(\mu\text{-}OH)]^+$ complexes is currently under investigation as well as their use as catalysts for other reactions under halide-free conditions. Applications pertaining to water-soluble functionalized Cu^I–NHCs may be of special interest.[13]

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