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Structural and electronic control of 1-(2-pyridyl)benzotriazole bidentate ligand in copper chemistry with application to catalysis in the A³ coupling reaction

Stavroula I. Sampani,^[a] Victor Zdorichenko,^[b] Jack Devonport,^[a] Gioia Rossini,^[a] Matthew C. Leech,^[c] Kevin Lam,^[c] Brian Cox,^[a,b] Alaa Abdul-Sada,^[a] Alfredo Vargas*^[a] and George E. Kostakis*^[a]

In memory of Prof. Jim Hanson

- [a] S. I. Sampani, J. Devonport, G. Rossini, Prof. B. Cox, Dr. A. Abdul-Sada, Dr. A. Vargas, Dr. G. E. Kostakis, Department of Chemistry, School of Life Sciences, University of Sussex, Brighton BN1 9QJ, UK. E-mail: Alfredo.Vargas@sussex.ac.uk & G.Kostakis@sussex.ac.uk
- [b] Dr. V. Zdorichenko, Prof. B. Cox
Photodiversity Ltd c/o Department of Chemistry, School of Life Sciences, University of Sussex, Brighton BN1 9QJ, UK.
- [c] Dr. M. C. Leech, Dr. K. Lam,
School of Science, Department of Pharmaceutical Chemical and Environmental Sciences, University of Greenwich, Central Avenue, Chatham Maritime, ME4 4TB, UK.

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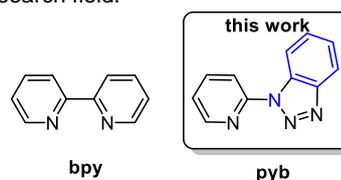
Abstract: We introduce the hybrid bidentate 1-(2-pyridyl)benzotriazole (pyb) ligand in well-characterized 3d-transition metal catalysis. Specifically, [Cu(II)(OTf)₂(pyb)₂](CH₃CN) (**1**) enables the synthesis of a wide range of propargylamines, via the A³ coupling reaction, at room temperature, in the absence of additives. Experimental and high-level theoretical calculations suggest that the bridging N atom of the ligand imposes exclusive *trans*-coordination at Cu and allows ligand rotation, while the N atom of the pyridine group modulates charge distribution and flux, thus orchestrating structural and electronic pre-catalyst control permitting alkyne binding with simultaneous activation of the C–H bond via a transient Cu(I) species.

Introduction

Copper is a labile transition metal, plural in oxidation states that promotes a variety of organic transformations either as a metal salt, *in situ* formed or well-characterized complexes.^[1,2] In its dominant oxidation state(II), the d⁹ electronic configuration confers elongated or shorten axial axes, known as Jahn and Teller effect,^[3] and depending on the coordinating ligands various geometries and stereoisomers, i.e. *cis* – *trans* for CuX₂(N-N)₂ where N-N is a bidentate ligand, can be obtained. 2,2'-bipyridine (2,2'-bpy) has been extensively used in coordination chemistry as a bidentate ligand^[4] and in catalysis.^[5] The catalytic protocols that involve *in situ* blending of bpy, copper salts and substrates achieve high yields and new products;^[6] however, the role of each component in the catalytic cycle is questioned. Well-characterized Cu(II) and bpy based complexes have been used as models for the aerobic oxidation of alcohols^[7] and other organic transformations.^[8] In some occasions, well-characterized Cu(II)-bpy complexes surpass the catalytic performance of isostructural compounds built with similar N,N'-bidentate ligands. This differentiation in catalytic efficacy may be a result of electronic and/or steric effects; however, the formation of different stereoisomers cannot be ignored.^[9]

The importance of developing the coordination chemistry of new bidentate ligands and identifying better catalysts is fundamental. Our groups initiated a combined experimental and theoretical project to provide an in-depth description and

understanding of the properties that govern the chemistry of the 1-(2-pyridyl)benzotriazole (pyb) ligand (Scheme 1) and the resulting coordination complexes. When compared with bpy, pyb has the following differences: a) additional N atoms that can participate in H-bonding interactions, b) additional phenyl group that enforces an electron-rich character of the framework but also permits participation in stacking interactions, and c) the two, pyridine and benzotriazole, units are linked via an N atom which imposes flexibility via the C–N bond, yielding different coordination behavior when compared with the rigid C–C based bpy ligand. Steel, in his pioneer work, identified pyb-based compounds to be more electron-deficient when compared with that of 2,2'-bpy;^[10] however, the use of well-characterized pyb-based complexes as catalysts or *in situ* made catalysts containing pyb is almost an unexplored research field.^[11–14]



Scheme 1. The traditional bidentate ligand 2,2'-bipyridine (bpy) and the bidentate ligand (right) used in this work.

The A³ coupling is a very well known, atom efficient, reaction that yields propargylamines^[15–17] with one molecule of water as a side product. Methodologies that involve Cu(II) sources for the C–H activation have been reported,^[18–22] however, the emphasis, in these studies, is given in the final product and achieving excellent yields, irrespectively of the extreme reaction conditions, i.e. elevated temperatures, prolonged time, high catalyst loadings. Knochel's pioneer work determines the activation of the acetylide on the coordination sphere of the Cu(I) centre and subsequently the coupling with the corresponding imine.^[23] Besides, copper reduction may occur in the presence of alkynes, and this process depends on temperature and concentration.^[24]

In this work, we introduce the pyb ligand in well-characterized 3d-transition metal catalysis and report the synthesis and characterization of [Cu(II)(OTf)₂(pyb)₂](CH₃CN) (**1**) which enables the synthesis of a wide range of

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propargylamines, via the A^3 coupling reaction, at room temperature, in the absence of additives.

Results and Discussion

The ligand pyb (Fig S1) can be synthesized in one step,^[10] and its reaction with $\text{Cu}(\text{OTf})_2$ in a molar ratio 2 : 1, in CH_3CN under aerobic conditions yields $[\text{Cu}(\text{II})(\text{OTf})_2(\text{pyb})_2]2(\text{CH}_3\text{CN})$ (**1**) (85%). We characterized compound **1** by single-crystal x-ray diffraction (Fig 1), ESI-MS (Fig S2-4), UV-Vis (Fig S5), IR (Fig S6), thermogravimetric (Fig S7) and elemental analysis and cyclic voltammetry (Fig 2). Copper adopts a *trans* geometry and sits in the centre of an octahedron; the equatorial positions are occupied by two pyb ligands, while two OTf^- anions hold the axial positions. There is a significant relative difference between the Cu–N and the Cu–O bonds, which is characteristic of the Jahn-Teller distortion. Solution studies identify that **1** retains its structure in solution. The UV-Vis spectrum in a solution of dichloromethane shows a very broad (550-850 nm) peak with the maximum at 685nm, characteristic of a Cu(II) with Jahn Teller distortion (Fig S5), while bond valence calculations are in line for a Cu(II) oxidation state. Besides, the cyclic voltammogram of **1** shows a reversible one-electron curve (Fig 2).

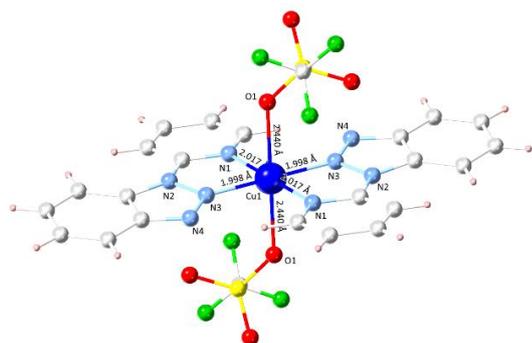


Figure 1. The X-ray structure of compound **1**. The CH_3CN lattice molecules are omitted for clarity.

Taking into account that copper salts are less efficient in the A^3 coupling reaction with primary amines, we chose cyclohexanecarboxaldehyde, aniline and phenylacetylene as model substrates to evaluate the title reaction in a molar ratio 1 : 1.1 : 1.2.

Table 1. Solvent screening.

Entry	Solvent	Yield
1	MeOH	16
2	EtOH	22
3	i-PrOH	29
4	CH_3CN	traces
5	DCM	93
6	Ethyl acetate	47

^aRelative yield calculated by $^1\text{H-NMR}$ based on the remaining **2a** and the intermediate Schiff base derived from **2a** and **3a**; ^bReaction conditions: **1** (1.5 mol%), 1.0 mmol aldehyde, 1.1 mmol amine, 1.2 mmol alkyne, 2 mL solvent, 25°C, 24 hours, concentration 0.5 M based on aldehyde, in the presence of molecular sieves 4A.

To make the protocol more user-friendly, reactions were carried out in open air and room temperature. Reactions in various solvents (Table 1) afforded the anticipated product in good to moderate yields, and therefore DCM, a non-coordinating solvent, was chosen from this screening process. Variation of catalyst loading determines the optimum condition when a 1.5% loading is applied (Table 2, Entries 1-5), while reactions in less time cause a significant drop in the yield of **5aaa**. (Table 2, Entries 4,6,7) The reaction with copper salts provided similar yields; however, this was only achieved with higher catalyst loadings (10%), almost one order of magnitude more loading, which is in line with previous results (Table 2, Entry 8).^[25] Given that the activation of alkynes is highly dependent on concentration,^[26] the next step was to identify the limits of this catalytic system. Thus, we performed a reaction in higher concentration (1M) which yielded **5aaa** in moderate yields and identifying that the chosen 0.5M concentration is the optimum (Table 2, Entry 9). This methodology applies to a variety of primary and secondary amines, and its scope is extended affording twenty substrates, out of which three are synthesized and characterized for the first time (Table 3 and ESI for more details Fig S13-S45).

Table 2. Optimization of Reaction Conditions

Entry	Loading (mol %)	Time (h)	Yield (%) ^{a,b}
1	5	24	53 ^c
2	3	24	74 ^c
3	2	24	95 ^c
4	1.5	24	93 ^c
5	1	24	53 ^c
6	1.5	12	52 ^c
7	1.5	6	30 ^c
8	10	24	99 ^d
9	1.5	24	81 ^e

^aRelative yield calculated by $^1\text{H-NMR}$ based on the remaining **2a** and the intermediate Schiff base derived from **2a** and **3a**; ^bReaction conditions: **1** (x mol%), 1.0 mmol aldehyde, 1.1 mmol amine, 1.2 mmol alkyne, molecular sieves 4A, DCM and concentration 0.5 M based on aldehyde; ^c25°C and concentration 0.5 M; ^dReaction with 10 mol% $\text{Cu}(\text{OTf})_2$; ^e25°C and concentration 1 M.

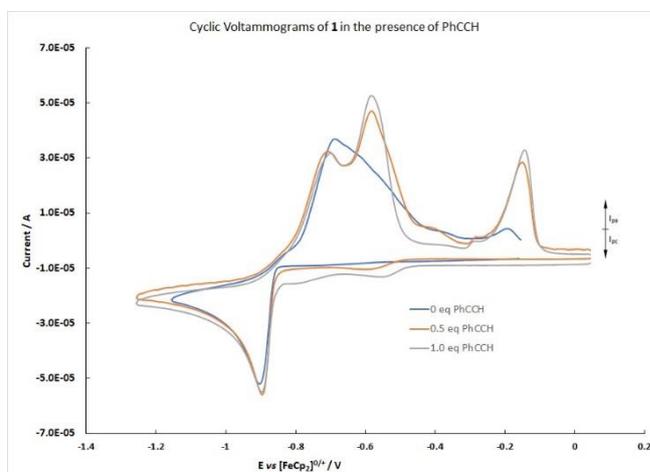


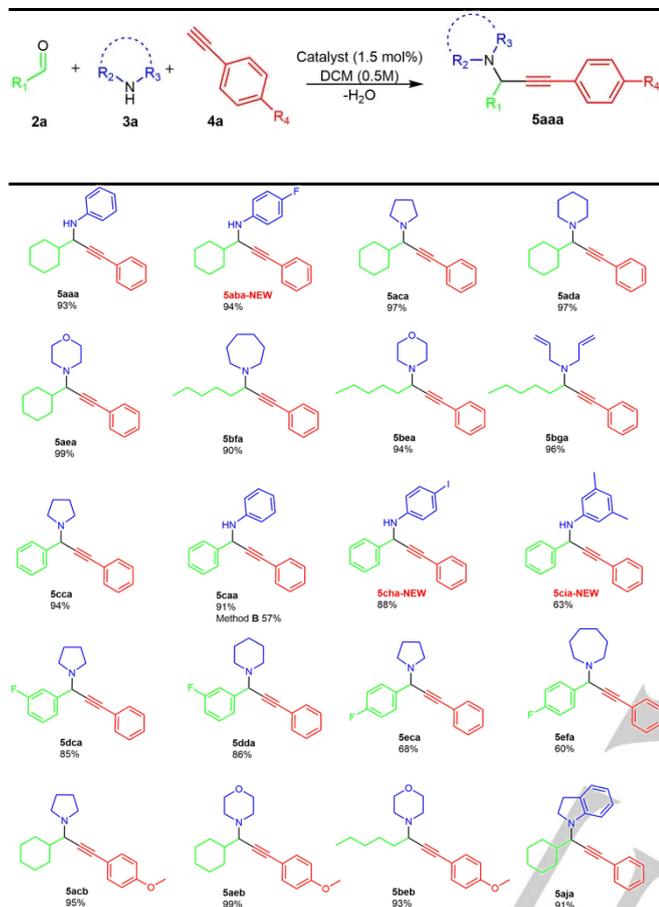
Figure 2 The cyclic voltammogram of **1** in the presence of phenylacetylene.

Then we performed reactions at elevated temperatures or microwave conditions as this has been noted in previous Cu(II)

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systems.^[18–22] Indeed, under heating (Table 4, entry 1) and microwave (Table 4, entry 2) conditions, the prototype reaction that affords **5aaa** is completed within one hour in excellent yields.

Table 3. Scope of the reaction with aldehydes, amines and alkynes.



Isolated yields. Reaction conditions: 1.0 mmol aldehyde, 1.1 mmol amine, 1.2 mmol alkyne, molecular sieves (4Å), solvent DCM, concentration 0.5M based on aldehyde, catalyst loading 1 (1.5 mol%). stirring in open-air at 25°C for 24 hours.

Based on evidence from our recent studies,^[27] we performed a series of reactions to gain mechanistic insights. A reaction for the synthesis of **5cca**, in the presence of a radical trap (TEMPO, 10mol% based on aldehyde, Table 4, Entry 3), afforded the desired product (Figure S42), thus excluding the formation of a radical species. The reactions at elevated temperature, under N₂ or Ar atmosphere, yielded product **5aaa** in a similar yield (Table 4, Entry 4), excluding the activation of the catalyst via bonding to dioxygen.^[28] Finally, we performed a reaction under N₂ at room temperature for only two hours, and **5aaa** was obtained in a moderate yield (Table 4, Entry 5). The same reaction was repeated under Ar atmosphere (Table 4, Entry 6), providing the anticipated product in a similar yield. This unprecedented result provides a time-efficient synthetic protocol for the synthesis of propargylamines, and we will explore its full potential in future studies. However, to shed light into this very exciting result, we performed among others cyclic voltammetry titrations, under N₂ atmosphere, of **1** in the presence of phenylacetylene (Figure 3). This study confirms a structural change into the catalytic system when one equivalent of phenylacetylene is added and could be explained based on ligand dissociation upon reduction of the

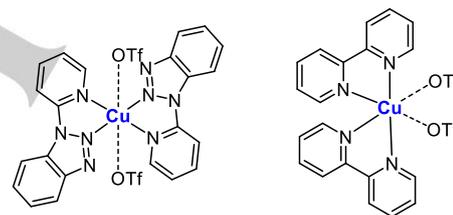
copper centre and the formation of a {Cu(II/II)(py)_x(Ph-C≡C-H)_y} species.

Table 4. Various experiments to obtain mechanistic evidence.

Entry	Time (h)	Atmosphere	Catalyst	Yield (%) ^{a,b}
1	1	Open air	1	95 ^c
2	1	Open air	1	96 ^d
3	1	Open air	1	96 ^e
4	2	N ₂ /Ar	1	98 ^c
5	2	N ₂	1	65 ^f
6	2	Ar	1	68 ^f
7	2	Ar	6	Traces ^g
8	2	Ar	Cu(OTf) ₂	Traces ^h

^aRelative yield calculated by ¹H-NMR based on the remaining **2a** and the intermediate Schiff base of **2a** and **3a**, ^bReaction conditions: **1** (1.5 mol%), 1.0 mmol cyclohexanecarboxaldehyde, 1.1 mmol aniline, 1.2 mmol phenylacetylene, molecular sieves 4Å, solvent DCM 2 mL, concentration 0.5 M, ^c80°C, ^dMicrowave conditions 80°C, ^e(TEMPO, 10mol%), ^froom temperature, ^gLoading 2 mol%, room temperature ^hLoading 1 mol%, room temperature

An attempt to rationalize how the A³ coupling reaction is promoted by **1**, we decided to examine the catalytic efficacy of compound [Cu(OTf)₂(bpy)₂] (**6**).^[9,29] (Scheme 2).



Scheme 2. A chemical diagram of **1** and **6**, showcasing the *trans* and *cis* geometries.

Compound **6** has a *cis*-octahedral geometry. The catalytic reactions at room temperature under Ar atmosphere with **6** (2% loading, Table 4, entry 7) failed to provide the expected product, and no precipitate or bpy moiety was found in the solution (crude ¹H-NMR). Besides, despite compound **6** showing a reversible CV signal,^[9] a titration CV study with phenylacetylene identified a non-reversible signal (Figure 3). This can be attributed to the fact that complex **6** is stable and forms a very stable {Cu(II)(bpy)_x(HC≡CPh)_y}⁺ species which prevents alkyne activation. Given the short reaction time (2h), these results indicate that the stereochemistry of the pre-catalyst is a parameter that should be taken into account, during the catalytic process, which is in line with literature evidence.^[30,31] Given that even 1 mol% of the catalyst **1** still performs well while the other Cu(II) salts have been reported to perform poorly at this level (Table 4, entry 8),^[25] this discards a possible full ligand dissociation in **1** but favours the formation of a stable Cu(I)-complex which possibly is the active catalytic species. This suggestion can be further evidenced by the presence of pure ligand peaks in the crude NMR and LCMS data (Figures S44 and S45). Efforts to trap, monitor, isolate and characterize this Cu(I)-complex were unsuccessful. Besides, the absence of bulky groups in the pyridine or benzotriazole moieties, that would contribute steric effects and

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possibly prevent two different ligands from coordinating to the Cu(I) centre, prevented us from isolating and characterizing this species in reactions with Cu(I) salts; this possibility will be explored in future studies.

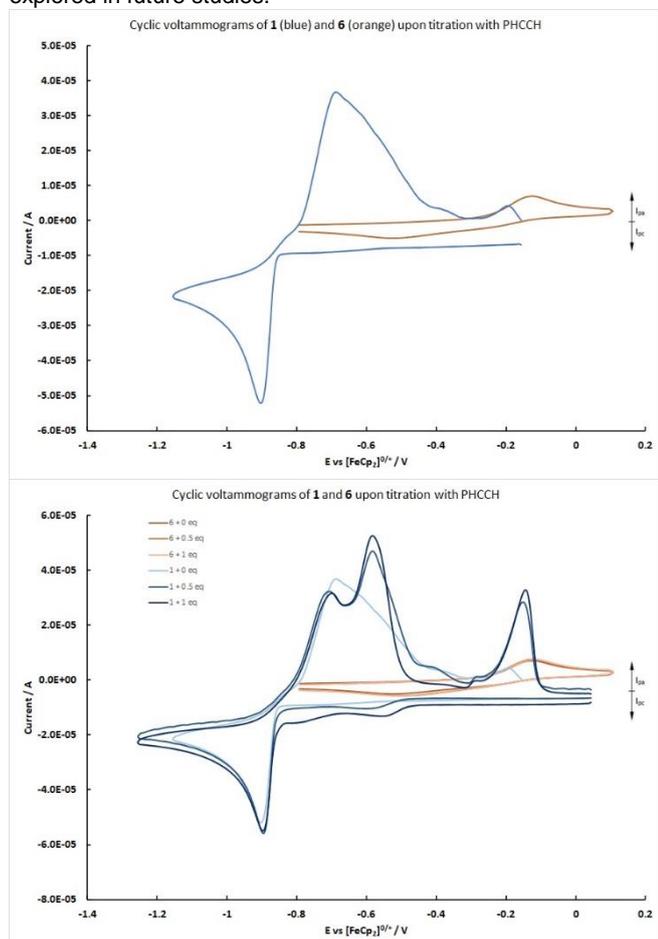
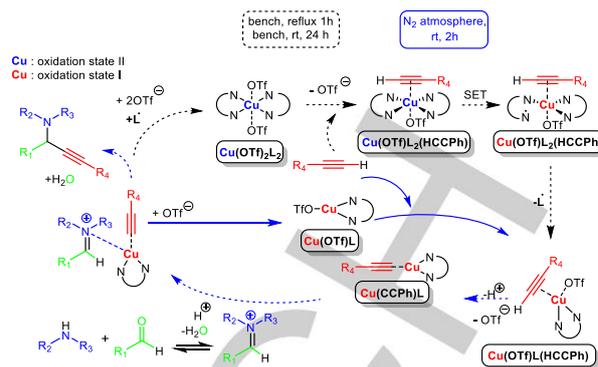


Figure 3 (upper) The cyclic voltammogram of **1** and **6**. (lower) The cyclic voltammogram of **1** and **6** in the presence of 6 equivalents of phenylacetylene

Based on all these observations and bearing in mind that a) Cu should simultaneously bind both nucleophile (phenylacetylide) and electrophile (imine),^[23] b) the benzotriazole entity can act as an acid or a weak base^[32,33] and possibly form radicals,^[32] c) the reaction proceeds in the absence of additives, and d) previous mechanisms based on Cu(I) or Cu(II) sources^[15–22] we propose the catalytic mechanism shown in Scheme 3. This mechanism has two but interlinked pathways. The external path (highlighted in dashed lines) involves the following steps: one OTf⁻ dissociation, alkyne binding, a copper reduction via a Single Electron Transfer (SET) process,^[34,35] ligand dissociation, OTf⁻ dissociation and acetylide activation, reaction with the imine and catalyst regeneration. The internal pathway (highlighted in blue) initiates when the {Cu(I)(OTf)(pyb)} species is formed in the first path and discards the reduction-oxidation process of the Cu centre but incorporates the triflate ion for the regeneration of the catalyst and alkyne activation purposes. Taking into account that the reduction of Cu(II) to Cu(I) by alkynes is a prolonged procedure,^[26] we consider the formation of the Cu(I)-intermediate as the rate-determining step under ambient conditions (24h for completion), while under inert atmosphere the catalytic cycle can be achieved in almost 2 hours.



Scheme 3. A proposed mechanism, highlighting the two interlinked paths, dashed and blue lines. The blue/dashed arrows present the shared part of these two paths.

Additionally, we wanted to investigate, by carrying out theoretical calculations, some aspects of the chemistry of the compounds and look at the possible catalytic driving forces that support the proposed experiment-based mechanism. At the OLYP/ZORA/TZP level of theory in the gas-phase, the structure of **1** presents a non-planar geometry concerning the pyb ligands (Fig. S9), showcasing conformational lability through rotation around the central C–N bond; a feature not offered by bpy in **6**. Such flexibility should thus allow dispersion interactions with neighbouring atoms; furthermore, this should allow conformational changes to accommodate excess charge and/or spin density during the activation process. Indeed, upon OTf⁻ abstraction, the two ligands show a slightly non-equivalent deviation from planarity which points to one critical asset; these neutral ligands can act as efficient charge sinks given the extended π system and the ability to modulate conjugation through the C–N rotation, thus affording to accommodate charge density upon change of oxidation state or of any reductive process. This can be depicted for instance by considering the molecular electrostatic potential on the calculated [Cu(I)(OTf)(pyb)₂]⁺ and [Cu(II)(OTf)(pyb)₂] (Fig 4); the metal centre is relatively unchanged whereas the ligands can get highly charged with high accumulation on the unbound nitrogen.

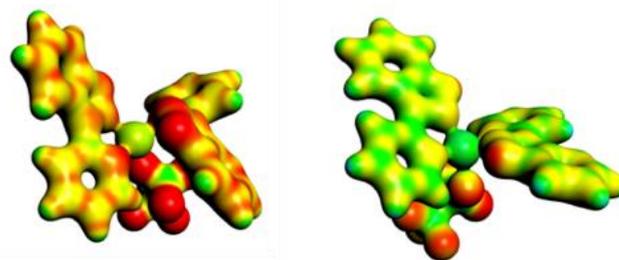


Figure 4. The molecular electrostatic potential (MEP) of [Cu(I)(OTf)(pyb)₂]⁺ (left) and [Cu(II)(OTf)(pyb)₂] (right)

In terms of electronic structure, an inspection of molecular orbitals of (**MO**) **1** (Fig. 5) shows the presence of doubly degenerate levels which per se points to spontaneous symmetry lowering with concomitant lowering in energy, hence providing a potential towards reactivity. Moreover, the diagram indicates a low-lying unoccupied beta (spin down) MO. Upon removal of one OTf⁻ (**1a**) for instance, the degenerate levels split (see Fig. S10), but even in the lowered symmetry, the characteristics of this unoccupied level is conserved. That is, given the unhindered

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quasi-planar geometry and the alignment of in-phase p(N)-d(Cu)-p(N) as the main components spanning this unoccupied MO, binding to electron-rich molecules should thus be facilitated (see Fig. S10). Indeed, comparing the levels of **1** with those of the reduced $[\text{Cu(II)(OTf)(pyb)}_2(\text{HC}\equiv\text{CPh})]^+$ shows the expected electronic structure, i.e. the highest unoccupied spin-down level gets occupied, the degeneracies are lifted, and the intercalation of levels centred on the ligands is conserved (see Fig. S11). This latter observation further supports the idea of the active role played by the ligands upon change of oxidation state. The stability gained upon reduction is enormous, the $[\text{Cu(II)(OTf)(pyb)}_2(\text{HC}\equiv\text{CPh})]^+$ to $[\text{Cu(I)(OTf)(pyb)}_2(\text{HC}\equiv\text{CPh})]$ transformation is associated to a free Gibbs energy amounting to 135 kcal/mol in favour of the Cu(I) species. Such a large energy barrier is mainly due to the structural rearrangement of the ligands. Incidentally, upon removal of the alkyne, the energy difference in terms of full electronic energy is increased by 6 kcal/mol, hinting to a SET mechanism. Detailed calculations regarding the SET mechanism are beyond the scope of the current manuscript and will be communicated in the future. Finally, it can be noticed that in the $[\text{Cu(II)(OTf)(pyb)}_2(\text{HC}\equiv\text{CPh})]^+$ the OTf^- is not displaced and the metal centre adopts a see-saw geometry; on the other hand, in the $[\text{Cu(I)(OTf)(pyb)}_2(\text{HC}\equiv\text{CPh})]$ intermediate, the OTf^- is displaced, leaving a tetrahedral $[\text{Cu(I)(pyb)}_2]^+$, the loss of the OTf^- is associated with an increase in charge is aided by an additional stabilization induced by the two flanking ligands through dispersive interaction as suggested by the geometry. These observations highly suggest that the reaction proceeds through alkyne capture and hydrogen abstraction proceed uniquely with Cu(I) and is not feasible with Cu(II). We assessed the gas-phase viability of some of the species in the mechanism (see Fig. S12), and given the strong influence of the environment, a full mechanism study without explicit solvent molecules would be merely conjectural.

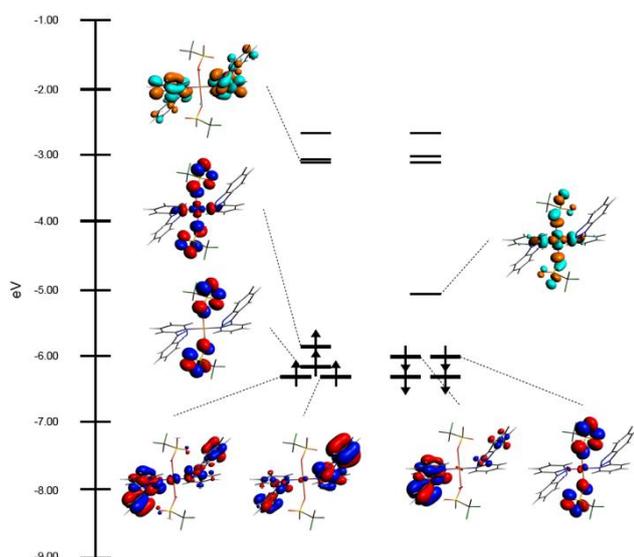


Figure 5. Molecular orbital levels of **1**.

Conclusion

We report the first example of a Cu(II) complex built from pyb that efficiently promotes the synthesis of propargylamines at room temperature through the A^3 coupling reaction. The N_{bridging} atom of this hybrid ligand imposes exclusive *trans*-coordination at Cu and allows ligand rotation, while the overall construct of the ligand, in particular, the presence of the N_{pyridine} atom modulates charge distribution and flux, thus orchestrating structural and electronic pre-catalyst control permitting alkyne binding with simultaneous activation of the C–H bond through an *in situ* catalytic active $[\text{Cu(I)(OTf)(pyb)}]$ species. This notion is not feasible in the *cis*- $[\text{Cu(II)(OTf)}_2(\text{bpy})_2]$ indicating that the stereochemistry of the pre-catalyst and the nature of the *N,N*-bidentate ligand are parameters to be taken into account when designing such catalysts. The results presented herein shall pave the way for future discoveries and explorations in Coordination Chemistry, for bidentate ligands, and Catalysis, for reactions requiring substrate activation.

Experimental Section

Synthesis and characterization of 1-(2-Pyridyl)benzotriazole

The ligand 1-(2-Pyridyl)benzotriazole (pyb) was synthesized by two different methods (i) and (ii), appropriate for synthesis in large and small scale respectively: Method (i): Reflux under N_2 using a round-bottomed flask equipped with a magnetic stirbar. The round bottom flask was charged with 3.15 g (20.0 mmol) of 2-bromopyridine, 12 g (86.2 mmol) K_2CO_3 , 0.5 g (3 mmol) KI and 4.76g (40.0 mmol) benzotriazole in 20 mL of acetone. The flask was heated at reflux for 8 hours. The reaction mixture was dissolved in ethyl acetate (250mL), washed with cold 10% KOH (2 x 150 mL), dried MgSO_4 and evaporated to afford the pure product as a white solid which was recrystallized from $\text{H}_2\text{O}/\text{EtOH}$. Yield = 4.65 g (79%) based on 2-bromopyridine.

Method (ii): A 5 ml sealed vessel equipped with magnetic stir bar was charged with 0.32 g (2.0 mmol) 2-bromopyridine and 0.48 g (4.0 mmol) benzotriazole and was exposed to microwave irradiation at 160°C for 3 hours, under solvent-free, non-inert conditions, according to previously reported protocol.^[36] After reaction completion, the cooled to ambient temperature mixture was, diluted in 1 mL DCM and purified by flash column chromatography. The product is isolated through silica gel using a diethyl ether/petroleum ether (fraction 40-60) mixture as the gradient eluent (01:99-30:70 v/v). The pyridyl-benzotriazole was obtained as a white solid. Isolated yield = 5.06g (86%) based on 2-bromopyridine. $^1\text{H NMR}$ (600 MHz, Chloroform-*d*) δ 8.66 (dt, J = 8.4, 1.0 Hz, 1H), 8.64 – 8.60 (m, 1H), 8.31 (dt, J = 8.4, 0.9 Hz, 1H), 8.12 (dt, J = 8.4, 0.9 Hz, 1H), 7.94 (ddd, J = 8.4, 7.4, 1.8 Hz, 1H), 7.61 (ddd, J = 8.1, 6.9, 1.0 Hz, 1H), 7.46 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H), 7.33 (ddd, J = 7.4, 4.8, 0.9 Hz, 1H), 1.54 (d, J = 0.6 Hz, 2H). MS (LCMS) m/z : $([\text{M} + \text{H}]^+)$ calcd for $\text{C}_{11}\text{H}_9\text{N}_4$, 197.2; found, 197.1, R_t = 2.64 min.

Synthesis and characterization of **1**.

$[\text{Cu(II)L}_2(\text{OTf})_2]\cdot 2(\text{CH}_3\text{CN})$ (**1**) was synthesized by the following procedure: L (0.2 mmol, 39 mg) and Cu(OTf)_2 (0.1 mmol, 36 mg) were added in acetonitrile (10ml), using a round-bottomed flask equipped with a magnetic stirbar. The resulting mixture was stirred for 1 hour. The solution mixture was filtered, and the green filtrate was then collected and underwent slow evaporation, forming green block-shaped crystals after four days. Yield = 75mg, 85% based on Cu^{II}. Elemental analysis for

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Cu₂₈H₂₈F₆N₁₀O₆S₂: C 39.93, H 3.35, N 16.63; found C 40.01, H 3.31, N 16.66. ESI-FTMS of (1) in methanol m/z: ([M]⁺) calcd for [Cu₂₃H₁₆N₈F₃O₃S]⁺, 604.0314; found, 604.0338.

X-Ray crystallography

The precipitate of **1** was recrystallized by slow evaporation in CH₃CN solution. Data for **1** were obtained at the University of Sussex by use of an Agilent Xcalibur Eos Gemini Ultra diffractometer with CCD plate detector under a flow of nitrogen gas at 173(2) K using Cu K α radiation ($\lambda = 1.54184\text{\AA}$). CRYSLIS CCD and RED software was used respectively for data collection and processing. Reflection intensities were corrected for absorption by the multi-scan method. The crystal structure was then refined on Fo² by full-matrix least-squares refinements using SHELXL.^[37] Geometric/crystallographic calculations were performed using Olex2,^[38] graphics were prepared with Crystal Maker.^[39] Structure **1** has been given CCDC deposition number 2018589.

General Catalytic protocol

A mixture of aldehyde (1 mmol), amine (1.1 mmol), alkyne (1.2 mmol), **1** (1.5 mol%, based on aldehyde), and CH₂Cl₂ (dry, 2 mL) was placed in a sealed tube equipped with 4 Å molecular sieves (50 mg) and magnetic stir bar and was stirred at 25°C (method A) for 24 hours or (method B) for 2 hours under Ar atmosphere. In each case the reaction was monitored by thin-layer chromatography (TLC). After completion, the slurry was filtered through filter paper (to withhold the molecular sieves) and subsequently upon a short pad of silica (to withhold the catalyst). The resultant solution is concentrated under reduced pressure, and the residue is then loaded into a flash column chromatography. The product is isolated through silica gel using a diethyl ether/petroleum ether (fraction 40-60) mixture as the gradient eluent (01:99-30:70 v/v). Propargylamines were obtained as red or yellow oils, which solidified on standing. ¹H NMR, ¹³C NMR, HRMS (ESI-FTMS) and LCMS spectra are reported for the propargylamines, synthesized for the first time. ¹H NMR spectra are presented for the already reported propargylamines.^[27]

Acknowledgements

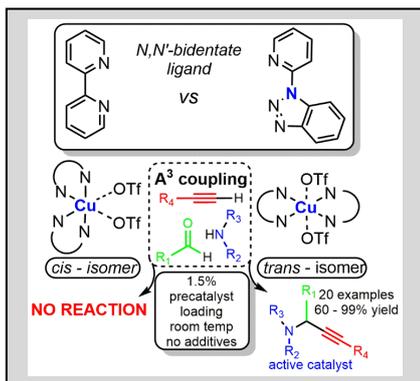
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Keywords: copper • N,N'-bidentate ligands • A³ coupling • DFT • OLYP/TZP

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Entry for the Table of Contents



[Cu(II)(OTf)₂(pyb)₂]₂(CH₃CN) (**1**), pyb is 1-(2-pyridyl)benzotriazole, enables the synthesis of a wide range of propargylamines, via the A³ coupling reaction, at room temperature and absence of additives. This hybrid *N,N'*-bidentate ligand imposes exclusive *trans*-coordination at Cu, can rotate and can modulate charge distribution and flux, thus orchestrating structural and electronic pre-catalyst control permitting activation of the C–H bond.