Green Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

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An efficient and recyclable thiourea supported copper(I) chloride catalyst for the azide–alkyne cycloaddition reactions†

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A reaction between two equivalents of bulky thiourea *i.e.,* 1-3-bis(2,6-dimethylphenyl)thiourea(L) [L = {$(ArNH)_2C=S$); (Ar = 2,6-$Me_2C_6H_3$)}] and $CuCl_2$ or CuCl in THF solvent afforded a bulky thiourea stabilized copper(I) halide complex, LCu(Cl)L(**1**). Compound **1** was characterized by NMR spectroscopy, mass spectrometry and X-ray structural analysis. Further, we tested the catalytic activity of this well defined compound **1** for azide-alkyne cycloaddition (AAC) reactions in solvent free conditions. Compound **1** shows a high catalytic activity for the synthesis of 1,4-di and 1, 4, 5-trisubstituted-1, 2, 3-triazoles in good to excellent yields from azides (aliphatic or aromatic) and alkynes (both terminal and di-substituted). Furthermore, three component CuAAC reactions were successfully carried out to obtain both 1, 4-di and 1, 4, 5- trisubstituted 1, 2, 3-triazoles in good to excellent yields from an organic halide, sodium azide and alkyne (both terminal and di-substituted) in greener solvent water. More importantly, the catalyst can be reused efficiently up to ten consecutive cycles with negligible loss of catalytic activity.

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†Electronic supplementary information (ESI) available: Analysis data and NMR spectra (^1H and $^{13}C\{^1H\}$) for compounds **4a – 4y, 6a-6c, 8a-8e.** CCDC 1425735; X-ray crystal data, TGA and Powder XRD for compound **1**

Introduction

In 2001, Sharpless[1] was introduced the term "Click chemistry" and signifies a set of reactions widely utilized, able to join moieties together in a very efficient and reliable manner. These examples of reactions include cycloadditions,[2] nucleophilic ring opening,[3] chemistry of non-aldol type[1] and carbon–carbon additions.[4] A set of reactions mentioned above, particularly, a well known copper catalyzed azide alkyne cyaloaddition (CuAAC) reaction is often considered as "Click chemistry". In 1963, Huisgen[5] reported the uncatalysed reaction of 1, 3-dipolar cycloaddition of organic azides with alkynes. This reaction is a slow, high temperature and not regioselective. However, CuAAC reaction is faster, facile and regioselective. In this context, in 2002, two research groups Sharpless[2a] and Meldal[6] have shown that the copper catalyzed 1, 3-dipolar cycloaddition of azides with terminal alkynes, independently. Since then, CuAAC reaction has been gaining huge attention among synthetic chemists.[7] Very recently, Nicasio and Perez et al.[8] thoroughly updated the CuAAC reactions and described that the nature of the catalyst has been classified into copper (I) and copper salts or complexes, metallic or nano particulate copper and other solid supported copper systems. Most of the cases in all copper based systems mentioned above, an active catalyst species is copper(I) metal ion in CuAAC reactions. In more recent times in particular, there is a huge attention towards design of well defined Cu(I) catalysts in CuAAC reactions, advantages that include not only avoid excess use of ligand and/or additives, but also better control of the nature of species present in the reaction medium. In this context, in 2011, Diez-Gonzalez reviewed on well defined copper(I) complexes for click azide-alkyne cyclcoaddition reactions.[9] Preformed copper (I) complexes bearing nitrogen, phosphrous, carbon and oxygen based ligands have been employed in CuAAC reactions.

The most employed molecularly defined Cu(I) complexes as catalysts in CuAAC reactions are those bearing carbon based neutral N-heterocyclic carbene(NHC) ligands. In, 2006,

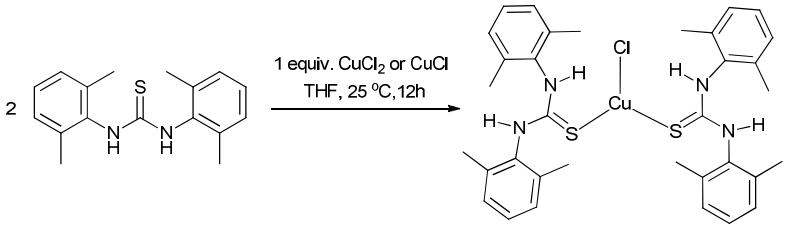
Nolan[10] reported [(SIMes)CuBr] (SIMes = N,N"-bis(2,4,6-tri-metylphenyl)-4,5-dihydro-imidazol-2-ylidene) as catalyst in CuAAC reactions. Later, [IAd)CuI] (IAd = N,N'-bis (adamant-1-yl)imidazol-2ylidene) was reported to have better catalytic activity than that of the SIMes analogue under the same reaction conditions.[11]

To improve the catalytic activity of [(SIPr)CuCl] in water, Li and co-workers[12] synthesized a series of ammonium salt tagged [(SIPr)CuCl] complexes. Straub and co-workers synthesized and structurally characterized bis-NHC –dicopper complexes and utilized as catalysts.[13] And also, copper(I) complexes bearing abnormal N-heterocyclic carbene as ligands were also reported to use as catalysts in CuAAC reactions.[14] However, a very few sulphur based ligands employed in CuAAC reactions.[15] Therefore, herein we report a well defined bulky thioureas supported copper(I) chloride(**1**) complex as a catalyst for azide-alkyne cycloaddition reactions to produce 1,4-di and 1,4,5-tri substituted 1,2,3-triazoles at room temperature in good to excellent yields either in water or under neat conditions. More importantly, catalyst was reused up to ten consecutive cycles and it retains its catalytic activity without any decomposition. Furthermore, we have also shown one pot synthesis that uses halides and sodium azide for direct cycloaddition with alkynes in water as a solvent. To the best our knowledge there have been no reports on bulky thioureas supported copper(I) chloride catalyzed azide-alkyne cycloaddition reactions.

Results and discussion

Synthesis and X-ray crystal structure of complex 1

Ligand (L) [L = {$(ArNH)_2C=S$); (Ar = 2,6-$Me_2C_6H_3$)}] was prepared using a similar procedure that described in the literature for its Mes and Dipp analogues MesN(H)C(S)N(H)Mes (Mes = 2,4,6 trimethyl aniline) or DippN(H)C(S)N(H)Dipp (Dipp = 2,6-$^{i}Pr_2C_6H_3$) by the reaction of drop wise addition of carbon disulphide to a solution of aromatic amine and triethylamine in water/acetonitrile.[16]



Scheme 1 Synthesis of bulky thiourea supported copper(I)chloride complex (**1**)

Two equivalents of 1,3-bis(2,6-dimethylphenyl)thiourea *i.e.,* [L = $(ArNH)_2C=S$); (Ar = 2,6-$Me_2C_6H_3$)] in THF was added dropwise to a solution of $CuCl_2$ in THF at room temperature. The reaction mixture was stirred at room temperature for 12 h and a clear solution was noticed. After filtration through Celite, the filtrate was concentrated and stored at room temperature to afford crystalline compound LCu(Cl)L(**1**) (see Scheme 1), which is confirmed by X-ray crystal structure (*vide infra*). Not surprisingly, in this reaction Cu metal ion is reduced to Cu(I) ion. It is clearly established that the preparation of complexes of Cu^{I} with thiourea derivatives can be easily achieved by the reaction between ligand and Cu^{II} salt, where Cu^{II} is reduced to Cu^{I} ion.[17] Further, synthesis of LCu(I)ClL in good yield was achieved by reacting two equivalents of L with CuCl in THF.

Compound **1** is thermally stable and melts at the range of 210 - 214 ^{o}C. It is not soluble in water and sparingly soluble in methanol, ethanol and dichloromethane. However, complex **1** is soluble in THF, DMSO and acetonitrile solvents. Compound **1** was characterized by ^{1}H and ^{13}C{^{1}H} NMR spectroscopy analyses. The ^{1}H NMR spectrum of **1** exhibits resonances at δ = 8.78 & 9.95 ppm for N-*H* protons, 2.14 & 2.32 ppm for Ar-CH_3 and remaining expected peaks for Ar-*H* (7.03-7.08 ppm) and THF (1.76 & 3.60 ppm). ^{13}C{^{1}H} NMR spectrum of **1** shows a characteristic peak at 177 ppm for *C*=S moiety. The other chemical shifts are typical for both bulky thiourea ligands. Compound **1** was further characterized by X-ray structural and mass spectrometry analyses. Single crystals were obtained from saturated THF solution at room temperature. Compound **1** crystallizes in triclinic space group $P\bar{1}$ with one THF molecule in the unit cell. The molecular structure of **1** is illustrated in Fig. 1. Selected bond lengths and bond angles are listed in Fig. 1 caption.

Compound **1** is a mononuclear three coordinated copper(I) chloride complex, in which copper atom is coordinated by two sulphur atoms of each bulky thiourea ligand and one chlorine atom (Fig. 1), thus it is exhibiting a trigonal planar molecular configuration with a butterfly structure. The driving force for this structure might be due to the intamolecular hydrogen bonds between Cl1 and N1/N4 atoms to form pseudo-six membered rings (NHClCuSC). Hydrogen bonds D···A distances (Å) and D–H···A angles (^{o}):N4–H4···Cl1 [3.1811 (21), 158] N1–H1···Cl1 [3.2184(22), 152]. Cu–Cl bond distance 2.3058(10) Å is slightly shorter than that of Cu–Cl bond distance of recently published Roesky's[18] *N*-(2,6-disisopropylphenyl)-*N*'-benzoylthiourea (2.2236 Å). And also, S1–C2 1.706(3) Å and S2–C1 1.709(2) Å bond distances are in good agreement with those in related compounds.[19]

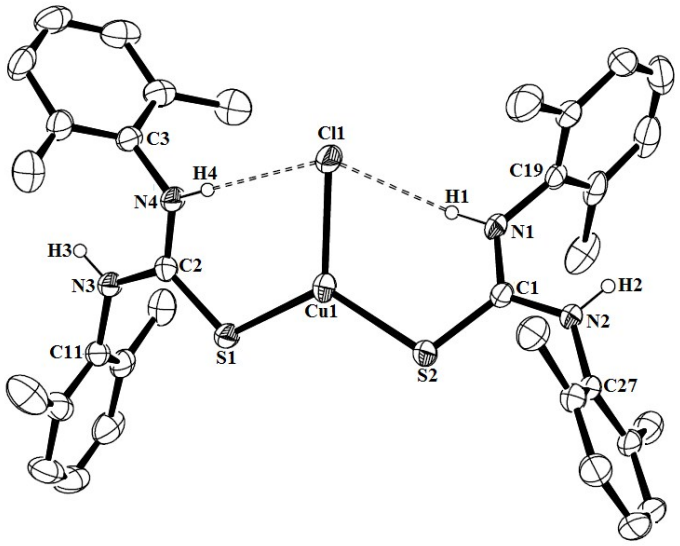


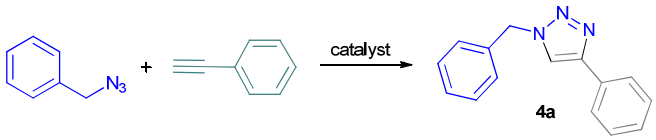
Fig. 1 Molecular structure of **1** with thermal ellipsoids drawn at 30% probability. Hydrogen atoms have been omitted for clarity (except N–H). Selected bond lengths (Å) and bond angles(°): Cu1–Cl1 2.3059(10), Cu1–S1 2.2250(9), Cu1–S2 2.2401(8), S1–C2 1.706(3), S2–C1 1.709(2), N2 –C1 1.334(3), N2–C27 1.436(3), N1–C1 1.331(3), N3 –C2 1.340(3), N4 –C2 1.332(3), N4–C3 1.435(3); S1–Cu1–S(2) 125.30(3), S1–Cu1–Cl1 118.20(4), S2–Cu1–Cl1 116.45(4), C1–S2–Cu1 107.91(8), N1–C1–N2 117.4(2), N1–C1–S2 121.05(17), N3 –C2 –N4 117.8(2), C2 –N4–C3 125.98(19), C2–N3–C11 124.8(2). Hydrogen bonds D···A distances (Å) and D–H···A angles (°):N4–H4···Cl1 [3.1811 (21), 158] N1–H1···Cl1 [3.2184(22), 152]

Thermo gravimetric analysis (TGA) and Powder XRD

To probe thermal stability of the compound **1** thermo gravimetric analysis (TGA) was performed (see ESI†; Fig. S1) at 30 – 800 ^{o}C. Compound **1** exhibits two steps decomposition in the range of 166 – 320 ^{o}C where the first step is the decomposition of the chlorine atom at temperature range 166 – 184 ^{o}C which accounts for 6.16 % weight loss (calc. 5.3 %) and in the second step decomposition of the thiourea moiety at temperature range 221 – 305 ^{o}C which accounts for the 76.26 % weight loss (calc. 75.57 %). The powder X–ray diffraction pattern for compound **1** is in good agreement with simulated pattern (see ESI; Fig. S2), this is generated from the single crystal X-ray data.

Copper complexes have been utilized as catalysts in various organic transformations due to their low cost, facile reactivity, and broad tolerance of functional groups on substrates.[7f, 20] In this perspective, our interest is to employ compound **1** as a catalyst for azide-alkyne cycloaddition reaction. We initially carried out LCu(Cl)L (**1**) catalysed cycloaddition of benzyl azide with phenyl acetylene as a model reaction either in water or under neat conditions (Table 1). In both cases the reaction is going very smoothly with quantitative yield of product formation (**4a**). From the Table 1, it is very clear that in solvent free condition shorter reaction time is required when compared to the water media for the product (**4a**) formation.

Table 1 Complex **1** catalyzed cycloaddition of benzyl azide with phenyl acetylene: Optimization studies[a]



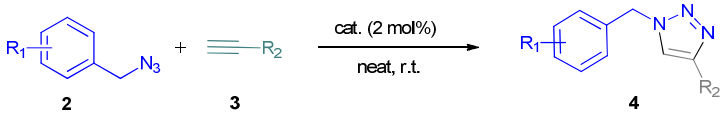
Entry	Catalyst	Cat. (mol%)	Solvent	Time (h)	Yield[b] (%)
1	**1**	1	neat	4	94
2	**1**	2	neat	1.5	99
3	**1**	5	neat	0.5	99
4	**1**	2	water	3	96
5	**1**	5	water	1.5	97
6	CuCl	2	neat	2	36
7	**1**	2	ethanol	10	65
8	**1**	2	methanol	10	67
9	**1**	2	DCM	8	87
10	**1**	2	CH_3CN	8	95

[a]Reaction conditions: benzyl azide (0.5 mmol), phenyl acetylene (0.6 mmol), solvent (1 mL). [b]Isolated yield

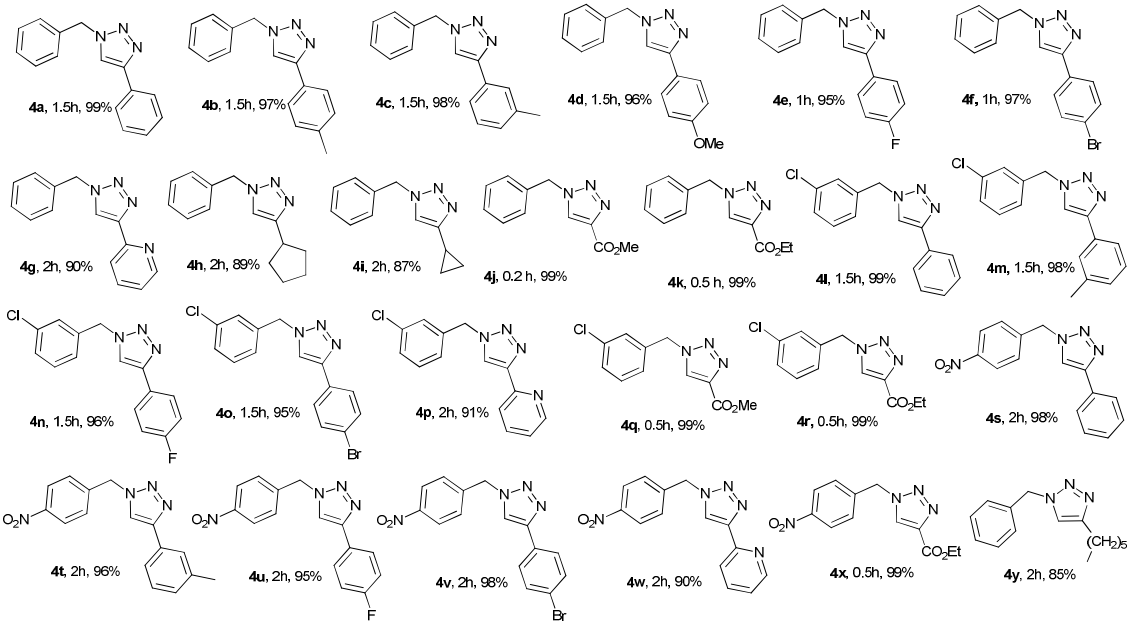
We observed that a less amount of triazole product (**4a)** formation under these conditions using ligand free CuCl (Table 1, Entry 6) as a catalyst for the reaction of benzylazide with phenyl acetylene as substrates, such observations also reported in earlier studies.[14c, 21] Further, we explored the same reaction in various organic solvents such as ethanol, methanol, dichloromethane and acetonitrile. We noticed that less product (**4a**) formation and longer reaction time is required for the compound **1** catalyzed cylcloaddition of benzylazide with phenyl acetylene in solvent media such as ethanol (Table 1, Entry 7), methanol (Table 1, Entry 8) and dichloromethane(DCM) (Table 1, Entry 9). However, 95% yield conversion of **4a** at similar reaction conditions was observed when the reaction performed in acetonitrile (Table 1, Entry 10).

Further, we explored the scope of the reaction by carrying out reactions of benzyl azide, 4-nitrobenzylazide and 3-chlorobenzylazide with a variety of terminal alkynes using 2 mol% of **1** as catalyst under solvent free conditions. The results of the catalytic reactions are summarized in Table 2. We noticed that during the reaction of formation of triazole the initial substrates were liquid and subsequently the liquid reaction mixture solidified after consumption of the starting material. Solid reaction mixture dissolved in ethyl acetate and passed through silica gel column. After removal of solvent in vacuum and washing the residue with *n*-hexane afforded pure desired products (**4a-4y**).

Table 2 Complex **1** catalyzed [3 + 2] cycloaddition of aliphatic azide with alkyne[a]



2 3 4

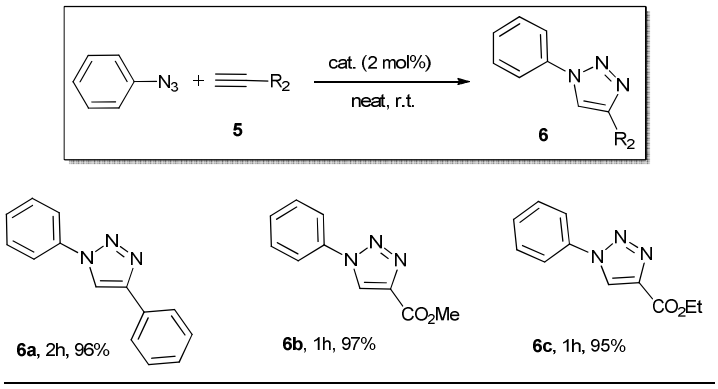


[a] Reaction conditions: azide (1 mmol), alkyne (1.15 mmol), LCu(Cl)L (2 mol%), neat, isolated yield.

Further, we investigated the catalytic efficacy of compound **1** for the reaction of alkynes with aromatic azides and results are illustrated in Table 3.

Compound **1** catalyzed (2 mol %) reaction of phenyl azide with phenyl acetylene in solvent free condition at room temperature led to the formation of triazole product **6a** in 96% yield in two hours**.** Similarly, compound **1** catalyzed reactions of phenyl azide with methyl carboxylate azide and ethylcarboxylate azide afforded the triazole products **6b** (97%) and **6c** (95%), respectively in 1 hour

Table 3 Complex **1** catalyzed [3 + 2] cycloaddition of aromatic azide with alkyne

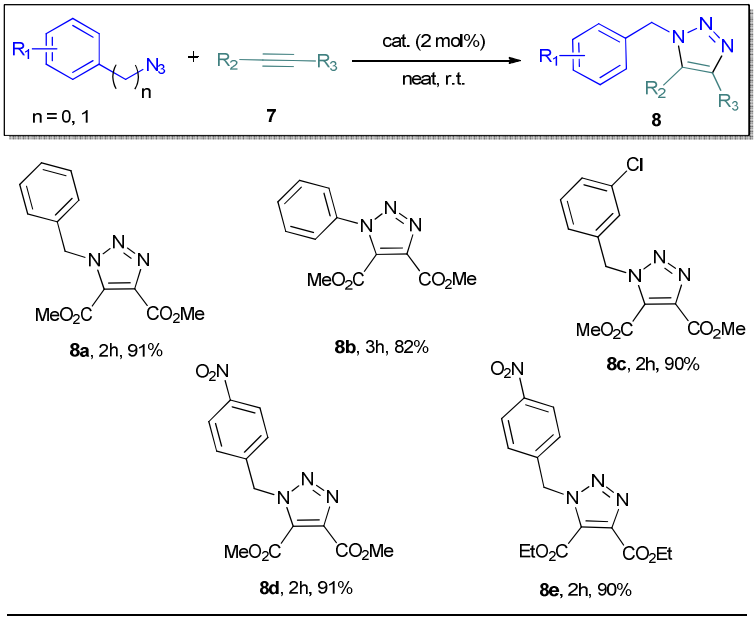


[a] Reaction conditions: Phenyl azide (1 mmol), alkyne (1.15 mmol), LCuCl (2 mol%), neat, isolated yield.

In the literature it is reported that a wide range of copper based catalysts have been utilized for cycloaddition of azides with terminal alkynes.[22] However, a very limited number of copper based catalysts have been developed for cycloaddition of azides with internal alkynes.[23] In view of this our attention turned towards compound **1** catalysed cycloaddition reactions of azides with internal alkynes. Our initial attempt was 2 mol% of **1** catalysed

reaction of benzyl azide with dimethyl acetylenedicarboxylate in solvent free conditions. This reaction leads to the formation 1, 4, 5-trisubstituted 1, 2, 3-triazole (**8a**) in excellent yield (91%) in two hours. And also, 2 mol% of **1** catalysed reaction of phenyl azide with dimethyl acetylenedicarboxylate afforded the desired triazole product (**8b)** in good yield. Furthermore, 2 mol% of **1** catalysed reactions of chloro and nitro substituted benzyl azides with either dimethyl acetylenedicarboxylate or diethyl acetylenedicarboxylate have been investigated. These reactions are also carried out in neat conditions and produced desired products (**8c-8e**) in very good yields. However, 2 mol% of **1** catalysed reaction of phenyl azide with diphenyl acetylene affords the desired product in very low yield (15%) at 70 ^{o}C.

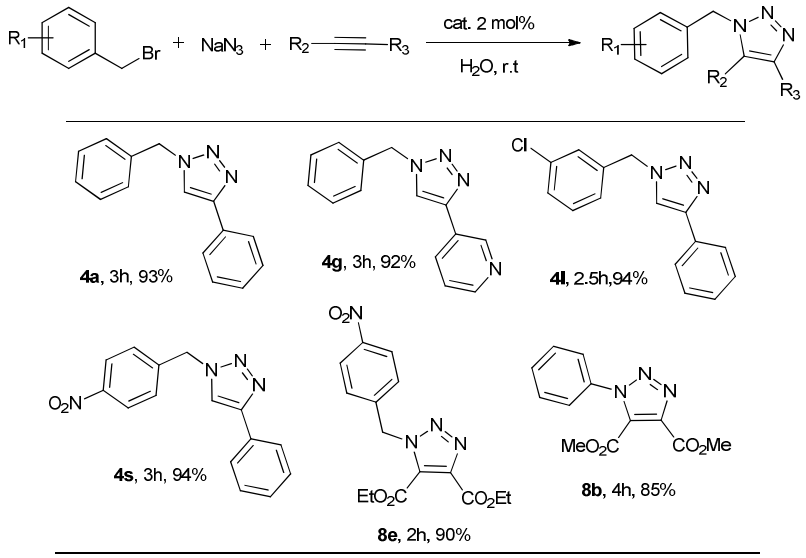
Table 4 Results of the CuAAC reaction of azides with disubstituted alkynes using **1** as a catalyst



[a]Reaction conditions: azide (1.0 mmol), di-substituted alkyne (1.15 mmol), isolated yield.

Organic azides are generally safe and stable towards water and oxygen,[24] but low molecular weight organic azides are explosive and difficult to handle.[25] Therefore, the synthetic protocol that avoids azides isolation is very much desirable. In this context, chemists developed copper catalysed synthesis of triazoles *via* a three-component reaction (organic bromide, sodium azide and an alkyne).[12, 26] In view of this, we tested the catalytic activity of complex **1** in three component reaction and results are summarized in Table 5. All reactions were performed at room temperature in water by using organic bromide, sodium azide and alkyne with 2 mol% of catalyst and triazoles products were isolated in good to excellent yields.

Table 5 Three-component CuAAC from organic halides as azido precursors with complex **1** catalyst



[a]Reaction conditions: azide (1 mmol), alkyne (1.15 mmol), H_2O(2mL). [b]Isolated yield.

Overall, there was no considerable difference of reactivity was noticed for the studied reactants with different electronic properties, electron-rich and electron-poor azides and alkynes, and the results prove that the thiourea stabilized copper complex (**1**) is a highly

efficient catalytic system for the cycloaddition of aliphatic and as well as aromatic azides with various alkynes.

More importantly, we checked the catalytic longevity by performing the *in situ* recycling experiments in the same reaction vial. The catalyst was reused up to ten consecutive cycles without any appreciable loss of reactivity, using 2 mol% catalyst for benzyl azide and methylacetylenecarboxylate. For this experiment we noticed 15 minutes was taking to achieve quantitative yield up to 6 catalytic cycles. After six catalytic cycles to complete the reaction it took 20 minutes.

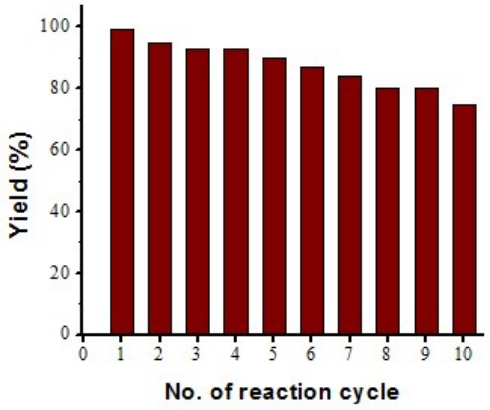


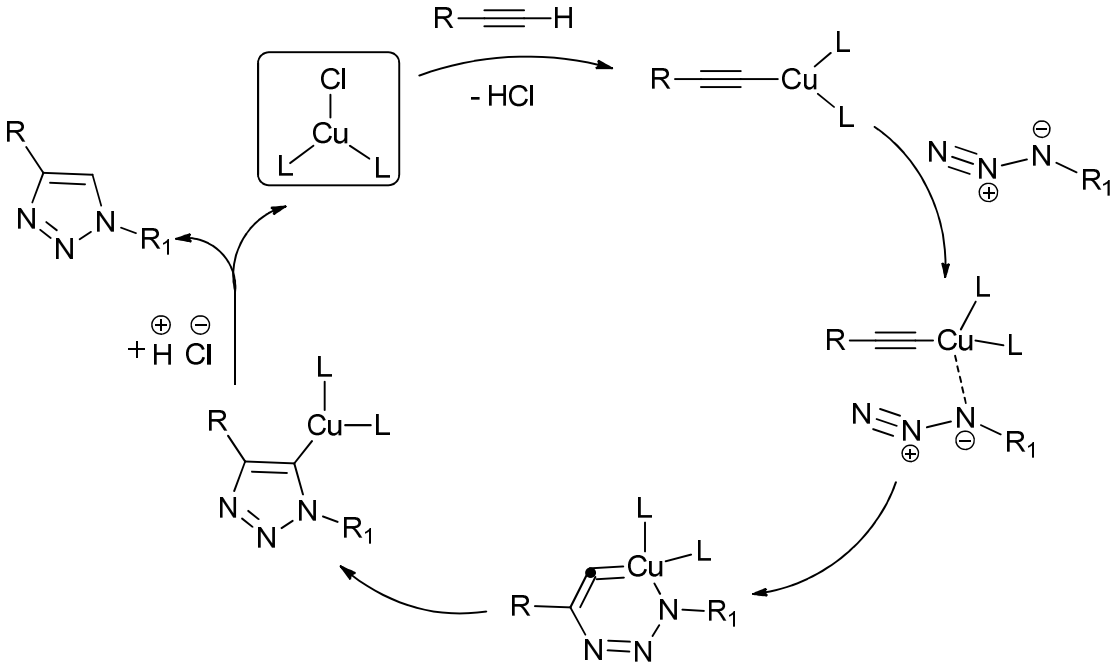
Fig. 2 The recyclability test of complex **1**
Reaction Conditions: benzyl azide (1 mmol) and methylacetylenecarboxylate (1.15 mmol), catalyst 0.02 mmol

Procedure for catalyst longevity experiment between benzyl azide and methyl propiolate

Catalyst **1** (0.02 mmol), benzylazide (1.0 mmol) and methyl propiolate (1.15 mmol) were taken in screw cap vial and stirred at room temperature. The reaction mixture was monitored by ^{1}H NMR spectroscopy by taking aliquots of the reaction mixture after 15 min intervals

and the reaction was stopped when the consumption of substrates was complete. During this period, a solid product was formed. Second time a fresh batch of substrates benzylazide (1.0 mmol) and methyl propiolate (1.15 mmol) was added for the next cycle without adding any further catalyst into the reaction vial. This procedure was repeated for a total ten consecutive catalytic runs.

Many investigations toward elucidation of the mechanism of the CuAAC with terminal alkynes have been documented. The mechanistic pathway for the complex **1** catalyzed azide-alkyne cycloadition is depicted in Fig 3.



L = {$(ArNH)_2C=S$); (Ar = 2,6-$Me_2C_6H_3$)}

Fig 3. Proposed mechanism for the complex **1** catalyzed azide-alkyne cycloaddition reaction

In the first step, LCu(Cl)L complex (**1**) upon reaction with alkyne would lead to the formation of acetylide-copper complex. In the second step, acetylide-copper complex interact

with the azide, in which it favours the nucleophilic attack of alkyne carbon atom to the end nitrogen atom of the azide. Subsequent ring contraction of the generated metallacycle would allow to a copper-triazolide complex. Finally, copper-triazolide abstracts a proton from HCl that lead to the formation of the desired triazole product and subsequently regeneration of LCu(Cl)L complex completes the catalytic cycle. It is worth mentioning that despite the highly reactive intermediates within catalytic cycle of CuAAC, some research groups isolated and characterized the copper-actylide and –triazolide intermediates.[27] Further, proposed mechanism for the compound **1** catalysed cyloaddition of azides with internal alkynes is depicted in Fig S3. (see ESI†).[28]

Conclusion

In conclusion, we have synthesized and structurally characterized a neutral, air & moisture stable and monomeric copper (I) chloride complex (**1**) bearing two bulky thiourea ligands. And also, we have shown that complex **1** exhibits a highly efficient catalyst for the synthesis of a wide range of both 1,4 –di and 1,4,5-tri substituted 1,2,3-triazoles from azides (aliphatic or aromatic) and alkynes (terminal or internal) in solvent free at room temperature conditions. Further, three component CuAAC reactions were successfully performed to obtain triazoles from organic bromide, sodium azide and alkynes in greener solvent water. Furthermore, the catalyst longevity has been checked up to ten consecutive cycles for the reaction of benzylazide and methylpropiolate substrates and noticed that a marginal loss of catalytic activity.

Experimental

General

All manipulations were carried out under air and using technical grade solvents without any particular precautions to prohibit oxygen or moisture. Chemicals were purchased from Sigma-Aldrich, Alfa-Aesar and used as received unless otherwise stated. Column chromatography and TLC were performed on silica gel (100-200) and using UV light. ^{1}H, $^{13}C\{^{1}H\}$ NMR spectra were recorded on Bruker AV-400 (^{1}H: 400 MHz, $^{13}C\{^{1}H\}$: 100.6 MHz) and were referenced to the resonances of the solvent used. IR Spectra were recorded in Perkin-Elmer FT-IR Spectrometer. Mass spectra were recorded on Bruker micrOTOF-Q II Spectrometer. 1-3-bis(2,6-dimethylphenyl)thiourea(L) [**L** = {$(ArNH)_2C=S$); (Ar = 2,6-$Me_2C_6H_3$)}] was synthesized according to the literature procedure[16]. Benzyl azide[22c], 3-chlorobenzyl azide[29] and 4-nitrobenzylazide[30] were prepared according to the literature procedures. All alkynes were used directly as received.

X-ray crystallographic details

The crystal data for the compound **1** has been collected on a Bruker SMART CCD diffractometer (MoKα radiation, λ = 0.71073 Å). The structure was solved by direct methods using the program SHELXS-97 and refined by full-matrix least-squares methods against F^2 with SHELXL-97.[31] Hydrogen atoms were fixed at calculated positions and their positions were refined by a riding model. All non-hydrogen atoms were refined with anisotropic displacement parameters. The crystal data and the cell parameters for compound **1** is summarized in Table S1 (See ESI†).

TGA and Powder XRD details

Thermogravimetric analysis (TGA) was carried out under nitrogen atmosphere, a ramp rate of 10 °C/min using a Discovery TGA by TA Instruments-Waters Lab. Powder X-ray diffraction data for compound **1** has been collected on a Bruker D8 Advance with DIVINCI design fitted with HTK 16 temperature chamber X-ray powder diffractometer using CuKα radiation (λ = 1.5418 Å).

Synthesis of complex 1

Method A: Two equivalents of thiourea 1-3-bis(2,6-dimethylphenyl)thiourea [L = $(ArNH)_2C{=}S$); (Ar = 2,6-$Me_2C_6H_3$)] (1 g, 3.52 mmol) in THF(25 mL) was added drop by drop to a solution of $CuCl_2$ (0.236 g, 1.76 mmol) in THF (10 mL) at room temperature. The reaction mixture was stirred at room temperature for 12 hours and a clear solution was noticed. After filtration through Celite, the filtrate was concentrated and stored at room temperature. Pale yellow colour crystals of compound **1** were isolated after one day. Further product was obtained by crystallization from mother liquor at 0 ^oC. The total yield is 0.99 g (85 %).

Method B: Complex **1** was synthesised by following similar procedure that employed in method A and using precursors CuCl (0.088g, 0.88mmol) and L (0.5g , 1.76mmol) yield (1.05 g, 90 %).

m.p = 210 **-** 214 ^oC. ^1H NMR (400 MHz, DMSO-D_6, 25 ^oC) δ 9.95 (s, 2H, N*H*), 8.78 (s, 2H, N*H*), 7.25–7.18 (m, 6H, Ar–*H*), 7.08–7.03 (m, 6H, Ar–*H*), 3.60 (t, *J* = 6.6 Hz, 4H, OC*H*$_2$CH$_2$), 2.32 (s, 12H, Ar–C*H*$_3$), 2.14 (s, 12H, Ar–C*H*$_3$), 1.76 (t, *J* = 6.6 Hz, 4H, OCH$_2$C*H*$_2$). ^{13}C NMR (101 MHz, DMSO-D_6, 25 ^oC) δ 177.1 (*C*=S), 136.5 (Ar–*C*), 136.4

(Ar–*C*), 135.9 (Ar–*C*), 133.7 (Ar–*C*H_3), 128.6 (Ar–*C*), 128.5 (Ar–*C*), 127.8 (Ar–*C*), 127.3 (Ar–*C*H_3), 67.0 (O*C*H_2CH_2), 25.1(OCH_2*C*H_2), 18.1 (Ar–*C*H_3), 17.8 (Ar–*C*H_3); IR (KBr) ν (cm^{-1}): 626(m), 697(m), 711 (s), 761(m), 813(m), 902(s), 924(m), 990(m), 1032(m), 1066(m), 1100(m), 1167(m), 1209(m), 1243(w), 1298(m), 1379(m), 1442(w), 1472(w), 1560(w), 1636(w), 1849(s), 1926(s), 2309(w), 2730(m), 2855(m), 2925(w), 3261(w), 3581(w). HRMS (ESI-TOF-Q) *m*/*z*: [M –Cl] calcd for $C_{34}H_{40}CuN_4S_2Cl$ 631.1931; found: 631.1985.

General procedure for the 3 + 2 cycloaddition of azides(aliphatic or aromatic) and terminal alkynes

Catalyst **1** (0.02 mmol), azide (1 mmol) and an alkyne (1.15 mmol) were placed in a screw cap vial. The reaction mixture was stirred at room temperature and the progress of the reaction was monitored by TLC. Solid mass was dissolved in ethyl acetate and passed through silica gel column. After removal of the solvent *in vacuo* and washing the residue with *n*-hexane afforded pure desired products. All the products were characterized by ^{1}H and ^{13}C NMR and ESI-MS spectra.

General procedure for the 3 + 2 cycloaddition of azides (aliphatic or aromatic) and internal alkynes

Catalyst **1** (0.02 mmol), azide (1 mmol) and an alkyne (1.15 mmol) were placed in a screw cap vial. The reaction mixture was stirred at room temperature and the progress of the reaction was monitored by TLC. Solid mass was dissolved in ethyl acetate and passed through silica gel column. After removal of the solvent *in vacuo* and washing the residue with *n*-hexane afforded pure desired products. All the products were characterized by ^{1}H and ^{13}C NMR and ESI-MS spectra.

General procedure for the three component click reaction catalyzed by complex 1

Catalyst **1** (0.02 mmol), organic bromide (1.0 mmol), NaN_3 (1.2 mmol) and an alkyne (1.2 mmol) and water (2 mL) were placed in a screw cap vial. The reaction was carried out at room temperature and monitored by TLC. After completion of the reaction, 10 mL of water was added to the reaction mixture and further stirred for 30 min to precipitate the product completely, which was collected by suction filtration and washed with 10 mL of water several times affording the desired trizole. All the products were characterized by ^1H and ^{13}C NMR and ESI-MS spectra.

The analysis data for compounds **4a-4l, 4r-4s, 4u, 4x-4y, 6a-6c, 8a-8d** were in agreement with those described in the literature[14a, 22a, 22c, 22e, 23, 26c, 32] (see supporting information)

Compound 4m; 1-(3-chlorobenzyl)-4-(m-tolyl)-1H-1,2,3-triazole

^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 9.0 Hz, 2H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.22 (dd, *J* = 12.4, 5.4 Hz, 3H), 7.14 – 7.04 (m, 2H), 5.47 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 138.6, 136.7, 135.1, 130.5, 130.3, 129.2, 129.1, 128.8, 128.1, 126.5, 126.1, 122.9, 119.6, 53.6, 21.5. HRMS (ESI-TOF-Q) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{14}ClN_3$ 284.0935; found 284.0949.

Compound 4n; 1-(3-chlorobenzyl)-4-(4-fluorophenyl)-1H-1,2,3-triazole

^1H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.66 (s, 1H), 7.36 – 7.27 (m, 3H), 7.19-7.16 (m, 1H), 7.13 – 7.05 (m, 2H), 5.53 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8(d, *J* = 246Hz), 147.6, 136.6, 135.1, 130.6, 129.1, 128.2, 127.6(d, *J* = 8Hz), 126.7(d, *J* = 3Hz), 126.2, 119.4, 115.9(d, *J* = 22Hz), 53.6 ppm. HRMS (ESI-TOF-Q) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{11}ClFN_3$ 288.0699; found 288.0698.

Compound 4o; 4-(4-bromophenyl)-1-(3-chlorobenzyl)-1H-1,2,3-triazole

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.64 (m, 3H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.36 – 7.28 (m, 3H), 7.18 (d, *J* = 6.8 Hz, 1H), 5.54 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.5, 135.2, 132.1, 130.6, 129.35 (d, *J* = 18.6 Hz), 128.2, 127.3, 126.2, 122.3, 119.7, 53.7; HRMS (ESI-TOF-Q) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{11}ClN_4$ 347.9842; found 347.9898.

Compound 4p; 2-(1-(3-chlorobenzyl)-1H-1,2,3-triazol-4-yl)pyridine

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.56 (d, *J* = 3.9 Hz, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 7.80 (s, 1H), 7.39 – 7.28 (m, 4H), 7.19 (d, *J* = 6.6 Hz, 1H), 5.57 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.2, 146.9, 145.4, 136.4, 135.2, 133.3, 130.6, 129.3, 128.2, 126.7, 126.2, 124.0, 120.0, 53.8; HRMS (ESI-TOF-Q) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{11}ClN_4$ 271.0756; found 271.0745.

Compound 4q; methyl 1-(3-chlorobenzyl)-1H-1,2,3-triazole-4-carboxylate

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.37 – 7.29 (m, 2H), 7.26 (d, *J* = 3.4 Hz, 1H), 7.16 (d, *J* = 7.1 Hz, 1H), 5.55 (s, 2H), 3.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 135.7, 135.3, 130.7, 129.5, 128.4, 127.6, 126.3, 53.8, 52.3.HRMS (ESI-TOF-Q) *m*/*z*: $[M + H]^+$ calcd for $C_{11}H_{10}ClN_3O_2$ 252.0539; found 252.0534.

Compound 4t; 1-(4-nitrobenzyl)-4-(m-tolyl)-1H-1,2,3-triazole

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.2 Hz, 2H), 7.76 (s, 1H), 7.66 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 5.69 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 141.8, 138.8, 129.9, 129.4, 128.9, 128.7, 126.6, 124.4, 123.0, 53.3, 21.5. HRMS (ESI-TOF-Q) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{14}N_4O_2$ 295.1178; found 295.1190.

Compound 4v; 4-(4-bromophenyl)-1-(4-nitrobenzyl)-1H-1,2,3-triazole

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.7 Hz, 2H), 7.77 (s, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 5.69 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 141.6, 132.2, 129.2, 128.7, 127.3, 124.5, 122.5, 53.4. HRMS (ESI-TOF-Q) *m*/*z*: $[M + H]^+$ calcd for $C_{15}H_{11}BrN_4O_2$ 359.0091; found 359.0138

Compound 4w; 2-(1-(4-nitrobenzyl)-1H-1,2,3-triazol-4-yl)pyridine ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.58 (s, 1H), 8.24 (d, *J* = 8.6 Hz, 2H), 8.20 (d, *J* = 7.9 Hz, 1H), 7.86 (s, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.37 (dd, *J* = 7.4, 4.9 Hz, 1H), 5.72 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 148.3, 147.1, 145.8, 141.5, 133.3, 128.8, 124.6, 124.0, 120.2, 53.5. HRMS (ESI-TOF-Q) *m*/*z*: $[M + H]^+$ calcd for $C_{14}H_{11}N_5O_2$ 282.0988; found 282.0986.

Compound 8e; diethyl 1-(4-nitrobenzyl)-1H-1,2,3-triazole-4,5-dicarboxylate ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 5.92 (s, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 158.3, 148.2, 141.2, 141.0, 129.3, 129.0, 124.2, 63.2, 62.2, 53.0, 14.2, 13.9. HRMS (ESI-TOF-Q) *m*/*z*: calcd for $[M + H]^+$ $C_{15}H_{16}N_4O_6$ 349.1186; found 349.1143.

Acknowledgments

The authors thank the National Institute of Science Education and Research (NISER), Bhubaneswar for supporting this work. We also thank the anonymous reviewers for their helpful suggestions.

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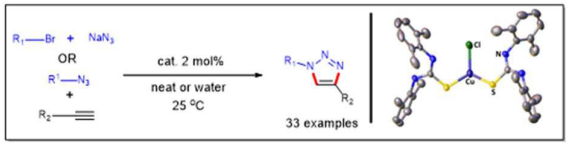

We have shown that air stable bulky thioureas supported copper (I) chloride complex as an efficient catalyst for the synthesis of five membered heterocycles from alkynes and azides.