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1-D Copper(I) coordination polymer based on bidentate 1,3-dithioether ligand: Novel catalyst for azide-alkyne-cycloaddition (AAC) reaction

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ABSTRACT

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Introduction

The 1,2,3-triazoles are known to be an important heterocyclic scaffolds from biological and pharmaceutical viewpoints; such as anti-allergic,¹ anti-bacterial,² and anti-HIV activity,³ and selective β3-adrenergic receptor agonism.⁴ The atom-efficient 1,3-dipolar Huisgen cycloaddition reaction between alkynes and organyl azides (commonly known as AAC) is one of the most straightforward methods for the synthesis of 1,2,3-triazoles.⁵ While AAC reaction gives a mixture of 1,4- and 1,5-disubstituted 1,2,3-triazoles, the use of Cu(I) catalysts under mild conditions selectively forms the 1,4-disubstituted 1,2,3-triazoles in excellent yields and this is commonly known as 'click reaction'. The simplest example of Cu(I) catalyzed click triazole synthesis was effectively achieved by excess of CuSO₄ and sodium ascorbate, where sodium ascorbate reduces the Cu(II) to Cu(I) and inhibits the aerobic oxidation of Cu(II) species.⁶ For well-defined Cu(I) catalytic systems, various ligands like PPh3, NHC, S- and Nbased molecules have been used so far, though P-based ligands afford unwanted Staudinger reaction.⁶⁻⁹ The coordination chemistry of sulfur ligands has been studied extensively and their copper complexes are attractive due to the reducing power of sulfur group as well as prevent further oxidation of Cu(I) to Cu(II) in the absence of any base.¹⁰ This promoted the synthesis and application of Copper(I)-thioamide catalytic complex in AAC reaction.¹¹ Mononuclear complexes like $[CuX_2(SNS)]$ (X = Cl, Br), [Cu(OTf)₂(H₂O)(SNS)] and 1-D Cu(I)-coordination polymer, $[Cu_2I_2(SNS)]_n$ have been used as effective catalyst for the AAC reaction.¹² Hybrid nitrogen-sulfur (NS) ligands supported Cu(I)/ Cu(II) complexes have also been used for AAC reaction.¹³ But in some cases, the hybrid SNS-based Cu(I)

A novel 1,3-bis(4-fluorophenylthio)-propane ligand based CuI 1–D polymeric coordination complex having formula ([(CuI)₂{ArS(CH₂)₃SAr}₂]_n, Ar = 4-F-C₆H₄) has been synthesized and characterized by ¹H-NMR, ¹³C-NMR and single crystal XRD techniques. This complex has been employed for the first time as suitable catalyst for base-free one–pot three-component regioselective azide-alkyne cycloaddition (AAC) reaction. A novel 1,2,3–triazole compound with sulfur functionalized pendant arms has also been prepared using our catalytic system in a multicomponent manner via one–pot two–step reaction.

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catalyst met with the problems of undesired alkyne-alkyne homocoupling reaction. $^{\rm 14}$

Hor et al reported the synthesis of novel pyridyl and thioether hybridised 1,2,3-triazole ligands based Cu(I) coordination polymers and its application in azide-alkyne cycloaddition reactions.¹⁵ It opened a new dimension for the polymeric coordination complex catalyzed AAC reactions. Due to strong coordination power of sulfur atoms, sulfur containing ligands are generally used for the preparation of Cu(I)-coordination polymer.¹⁶ Knorr et al illustrated the coordination mode of aromatic dithioether ligands of the type PhS(CH₂)_nSPh.¹⁶ Apart from the structural and photophysical properties, the catalytic activity of these types of dithioether based copper complexes in the AAC reaction has not been reported yet. Herein we report the synthesis, characterization of a new type of 1,3-dithioether based CuI coordination polymer and find its application to one pot azide-alkyne cycloaddition reaction in a multicomponent fashion. Our 1,3-bis(4-fluorophenylthio)-propane ligand based CuI coordination polymeric complex having molecular formula, $([(CuI)_{2}{ArS(CH_{2})_{3}SAr}_{2}]_{n}, Ar = 4-F-C_{6}H_{4})$ was first synthesized and characterized by NMR and single crystal X-ray diffraction pattern. The catalyst works efficiently in AAC reaction under base-free condition in water/acetonitrile solvent mixture at 50 °C to afford selectively 1,4-disubstituted 1,2,3triazole products. In scheme 1, the AAC reaction performed by various Cu(I) complexes with S, NS and SNS ligand is presented. NN- and SNS-based polymeric Cu(I) complexes have been found as catalyzing the AAC reaction but interestingly, polymeric Cu(I) complex with SS-based bidentate ligands, used as AAC reaction is not found in literature.



Scheme 1: Various ligand based copper complex catalyzed AAC reaction.

Results and discussion

Synthesis of the copper complex

The 1,3-bis(4-fluorophenylthio)-propane ligand (L) was synthesized according to our previously reported procedure.¹⁷ This compound was characterized by ¹H- and ¹³C-NMR spectroscopy. This ligand has been reacted with CuI in 1:2 metal to ligand ratio in acetonitrile solvent to obtain the desired 1-D polymeric CuI-1,3-dithioether complex. The as-synthesized Cu-complex was characterized by ¹H-NMR, ¹³C-NMR and single crystal XRD techniques. The NMR spectra of bare ligand and copper(I) complex are given in Supporting Information.

This complex crystallizes in the monoclinic space group P $2_{1/c}$, and shows a polymeric propagation in the form of

[(CuI)₂{ArS(CH₂)₃SAr}₂]_n metallopolymer (Fig 1). The 1Dnetwork is built up upon dimeric Cu₂I₂ units which are interconnected via dithioether ligands. The framework consists of Cu₂(μ -I)₂ prismatic part connected with the dithioether ligands. Within the cluster core, the Cu—I bond lengths range between 2.5867 (5) and 2.6443 (12) Å. The Cu....Cu distance between the two Cu (I) centers, 2.7812 (10) Å falls significantly below the sum of the vander Waals radius (2.8 Å). The mean Cu—S bond length of range between 2.3339 (11) to 2.3551 (12) Å similar to [{Cu(μ -I)₂Cu}₂{ μ -PhS(CH₂)₃SPh}₂]_n (2.3465 Å).^{16a} The angle between Cu...I...Cu is 64.23° and I...Cu...I 115.77° in the metallocluster. The crystal data, data collection and structure refinement for the polymeric complex is given in the Supporting Information.



Figure 1. View of (a) monomeric picture of the complex and (b) infinite 1-D chain of the complex incorporating dinuclear $Cu(\mu_2-I)_2Cu$ motifs along 'b' axis.

The catalytic activity of the copper complex

The catalytic activity of the complex towards one-pot multicomponent AAC reaction under base-free conditions was optimized by the model reaction of benzyl bromide, NaN_3 and phenylacetylene with varying catalyst loading under different temperature and solvent conditions (Table 1). The reaction was first studied at neat condition and higher temperature (60 °C)

with 5 mg of the complex. After 5 hours, 84% of the product was isolated under this condition (entry 1). When methanol was used as solvent relatively less conversion was achieved compared to the neat condition (70%, entry 2). Similarly the reactions in acetonitrile and water gave 87% and 80% yield of the product respectively (entry 3 & 4). A binary solvent mixture of acetonitrile and water (1:1) resulted excellent yield of the desired triazole product with lesser time (entry 5). The same experiment

on microwave reactor yielded lesser amount of yield than conventional thermal heating (entry 6). Decreasing the temperature to 50 $^{\circ}$ C also gave excellent yield (97%) in 3 hours (entry 7). The product conversion was dropped when the reaction was carried out at room temperature (entry 8). The catalyst loading was also performed from entry 8 to entry 10 and the catalytic activity has been found to be very effective with only 0.5 mg of the complex catalyst for this reaction (entry 11). While using CuI as the catalyst, the product was obtained in relatively lower yield (entry 12). Performing the reaction by doubling the reactants and keeping the catalyst quantity same (0.5 mg) also afforded the desired product in poor yield (entry 13).

Table 1

Optimization of reaction conditions for the Cu(I)-complex catalyzed one-pot three-component AAC reaction.

| | ∼ + NaN ₃ + ===⟨ Br | $(CuI)_{2} {ArS(CH)}$ $Ar = 4-F-4$ $x mg$ Solvent, Temp | $[I_2)_3 SAr \}_2]_n$ $C_6 H_4$ perature | N N N N | |
|-----------------|-----------------------------------|---|--|------------------|------------------------|
| Entry | Solvent | Complex/CuI in (mg) | Temp. (°C) | Time (h) | Yield ^a (%) |
| 1 | Neat | 5 | 60 | 5 | 84 |
| 2 | Methanol | 5 | 60 | 5 | 70 |
| 3 | Acetonitrile | 5 | 60 | 5 | 87 |
| 4 | Water | 5 | 60 | 8 | 80 |
| 5 | Acetonitrile: water | 5 | 60 | 3 | 97 |
| 6 | Acetonitrile: water | 5 | 60 | 0.5 | 92 ^b |
| 7 | Acetonitrile: water | 5 | 50 | 3 | 97 |
| 8 | Acetonitrile: water | 5 | RT | 5 | 85 |
| 9 | Acetonitrile: water | 3 | 50 | 3 | 97 |
| 10 | Acetonitrile: water | 1 | 50 | 3 | 96 |
| 11 | Acetonitrile: water | 0.5 | 50 | 3 | 96 |
| 12 ^c | Acetonitrile: water | 0.5 | 50 | 3 | 79 |
| 13 ^d | Acetonitrile: water | 0.5 | 50 | 4 | 65 |

Reaction conditions: Phenyl acetylene (1 mmol), NaN₃ (1.2 mmol) and benzyl bromide (1.1 mmol),

Cu-complex [5.0 mg (1.0 mol%) to 0.5 mg (0.1 mol%)], Acetonitrile:H₂O (1:1, 2 mL).

^aIsolated yield after purification through column chromatography by silica gel.

^bReaction tried on focused microwave reactor.

^cCuI was used as catalyst.

^dPhenyl acetylene (2 mmol), NaN₃ (2.4 mmol) and benzyl bromide (2.2 mmol).

The complex is air stable and can tolerate a range of benzyl, allyl, cinnamyl and alkyl halides under mild reaction conditions (Table 2). The terminal alkynes have participated in this reaction very smoothly (Table 2). Phenyl acetylene, 4-ethynyl toluene and 2-bromo phenyl acetylene gave excellent yield (entry 1 to 3). 4-nitro-phenyl acetylene also gave excellent yield but slightly lesser than the previous entries (entry 4). Apart from aromatic alkynes, alphatic alkynes responded also to this reaction smoothly (entries 5, 13 and 14). Allyl bromide was found to be very reactive as a coupling partner in this AAC reaction (entry 6 **Table 2**

and 7). Benzyl chlorides have been found to be reactive as benzyl bromides (entry 8 and 9). But the same reaction when carried out with diphenyl acetylene (internal alkyne) no reaction occurred even after 12 hours (entry 10). This methodology has been also applied for cinnamyl chlorides (entry 11 and 12). *n*-Octyl iodide, an aliphatic halide also responded well to this cycloaddition reaction (entry 15). All the reactions proceeded without any difficulty and the products were isolated in good to excellent yields in high purity through column chromatography.

Catalytic activities of the Cu(I)-complex catalyzed one-pot three-component AAC reaction.

$$R^{1} \land X + NaN_{3} + R^{2} = H \xrightarrow{[(Cul)_{2} \{ArS(CH_{2})_{3}SAr\}_{2}]_{n}}_{Action trile: water (1:1)} R^{1} \land N \land R^{2}$$

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|---------------------|----------------------------------|---|----------|---|------------------------|--|--|--|--|
| Entry | R ¹ CH ₂ X | R ² ———————————————————————————————————— | Time (h) | Product | Yield ^a (%) | | | | |
| 1 | PhCH ₂ Br | Ph-=== | 3 | Ph N Ph | 97 | | | | |
| 2 | PhCH ₂ Br | p-Tol— | 3 | Ph $N \rightarrow p$ -Tol N = N | 96 | | | | |
| 3 | PhCH ₂ Br | o-Br-Ph-=== | 4 | $Ph N \rightarrow o-Br-Ph N = N [2c]$ | 96 | | | | |
| 4 | PhCH ₂ Br | <i>p</i> -O ₂ N-Ph | 4 | $Ph \longrightarrow N \longrightarrow p-NO_2-P$ N = N [2d] | h 91 | | | | |
| 5 | PhCH ₂ Br | Ph | 4 | Ph $N \rightarrow Ph$ $N=N OH$ | 90 | | | | |
| 6 | Br | Ph-=== | 4 | $N \rightarrow Ph$ N = N | 81 | | | | |
| 7 | Br | p-Tol— | 4 | $[2t]$ $N \longrightarrow p-Tol$ $N = N$ $[2g]$ | 83 | | | | |
| 8 | PhCH ₂ Cl | Ph-== | 3.5 | $Ph \underbrace{N}_{N=N}^{[2g]} Ph \underbrace{N}_{[2a]}^{[2g]}$ | 95 | | | | |
| 9 | PhCH ₂ Cl | p-Tol-=== | 3.5 | Ph N p -Tol N=N [2b] | 94 | | | | |
| 10 | PhCH ₂ Br | Ph-=Ph | 12 | NR | _ | | | | |
| 11 | PhotoCl | Ph-=== | 4 | Ph $N \rightarrow Ph$ N = N [2h] | 84 | | | | |
| 12 | Ph | p-Tol— | 4 | Ph $N \rightarrow p-T$ | °ol 85 | | | | |
| 13 | PhCH ₂ Br | | 4 | $\begin{array}{c} \begin{array}{c} [21] \\ Ph & N \\ N \\ N \\ N \\ [2j] \end{array} \\ \end{array} \\ O \\ \end{array} $ | 72 | | | | |
| 14 | PhCH ₂ Br | CI A | 4 | Ph $N \rightarrow N^{*}N^{*}N^{*}N^{*}N^{*}N^{*}N^{*}N^{*}$ | 81 Cl | | | | |
| 15 | \sim | ∕I Ph—≡ | 4 | H_6 $N \rightarrow Ph$ N=N | 76 | | | | |

4

Reaction conditions: Teminal alkynes (1 mmol), NaN₃ (1.2 mmol) and benzyl/allyl/cinnamyl/alkyl halide (1.1 mmol), Cu–complex (0.5 mg, 0.1 mol%), Acetonitrile:H₂O (1:1, 2 mL).

^aIsolated yield after purification through column chromatography by silica gel.

Mechanism

A probable mechanism for this multicomponent azide-alkynecycloaddition reaction was proposed in Scheme 2. It was presumed that the reaction was initiated by the metalation of phenylacetylene in the presence of the 1D-CuI dithioether polymeric complex giving copper acetylide. In the next step, benzyl/allyl/cinnamyl/alkyl azide was formed *in-situ* by the substitution reaction between benzyl/allyl/cinnamyl/alkyl halide and sodium azide. The polymeric copper acetylide moiety reacted with benzyl/allyl/cinnamyl/alkyl azide *via* cycloaddition fashion followed by elimination of the complex catalyst give rise to 1,4–disubstituted 1,2,3–triazoles as the main product.



Scheme 2. A plausible mechanistic path for the Cu(I)-complex catalyzed one-pot three-component AAC reaction.

Synthesis of sulfur functionalized 1,2,3-triazole

1,2,3-triazoles containing diverse functional groups have strong potential as steel corrosion inhibitors or suitable ligands for transition-metal chemistry.¹⁸ We have prepared sulfur functionalized pendant arms of 1,2,3-triazole compounds in a multicomponent approach via one-pot two-step reaction using our catalyst. Benzenethiol (1.1 mmol) was first reacted with propargyl bromide (1 mmol) in presence of triethyl amine (2 mmol) in water at room temperature. After 2 hours, benzyl bromide (1.1 mmol) and sodium azide (1.2 mmol) and Cu(I)-complex (0.5 mg, 0.1 mol%) were added to the reaction mixture. The progress of the reaction was monitored by TLC and finally the desired product was isolated in column chromatography (82% yield). The preparation methodology is presented in Scheme 3.



Scheme 3. One-pot two-step synthesis of sulfur functionalized 1,2,3-triazole derivative.

Conclusion

In conclusion, we have synthesized a suitably designed Cu(I) coordination polymer based on dithioether ligands (SS, bidentate), which can be used as efficient catalyst for AAC reaction. The polymeric complex has been well characterized and applied in variety of substrates and the desired 1,4–disubstituted 1,2,3–triazole products are obtained in excellent yields. Low temperature and low catalyst loading for the reaction are noteworthy besides demonstrating the catalytic activity of S,S-based Cu(I) coordination polymer. Further application of the polymeric complex is under active pursuits.

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Highlights

1-D Copper(I) coordination polymer based on bidentate 1,3-dithioether ligand: Novel catalyst for azide-alkyne-cycloaddition (AAC) reaction Sankar saha, Kinkar Biswas,* Baudeb Basu* Department of Chemistry, North Bengal University, Darjeeling 734013, India

- ▶ New Cu complex from CuI and 1,3-Dithioether, characterized by single crystal X-ray
- Acts as a catalyst in AAC at low concentration and ambient temperature
- First example of SS-based Cu complex used as catalyst in AAC
- Extended to the synthesis of Sfunctionalized pendent arms of 1,2,3triazole

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