



Tandem CuI – Zinc dust as a sustainable catalyst for the preparation of propargylamine derivatives via an A³ coupling reaction, under neat conditions

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ABSTRACT

The cooperative activity of two proximal metal ions is well-known to exhibit highly efficient and synergistic catalytic activities in living organisms. Owing to this knowledge, tandem Cu–Zn systems have been widely used to catalyze a diversity of chemical transformations. This report describes the use of CuI and zinc dust as a sustainable tandem catalyst for the preparation of propargylamines via a three-component coupling reaction under neat conditions. This reaction proceeds at low temperature, and produces good yields with a number of aliphatic and aromatic aldehydes. The reactivity of a number of amines and alkynes has also been explored under these reaction conditions, resulting in 33 fully characterized compounds prepared in the process. Among the ketones tested during this study, only cyclohexanone was able to produce the expected product in a decent yield. The catalytic system reported here represents one of the sustainable approaches to the preparation of propargylamines, as it involves the use of naturally abundant metals as a tandem catalyst, at a low temperature and under neat conditions.

1. Introduction

Copper-zinc superoxide dismutase (SOD1 protein) is one of the three human superoxide dismutase identified and characterized since 1969 [1–3]. This abundant copper- and zinc-containing protein is primarily found in the cytosol, nucleus, peroxisomes, and mitochondrial intermembrane space of human cells [4,5]. Its primary function is to act as an antioxidant enzyme, lowering the steady-state concentration of superoxide [6–9]. It has been established that Cu is responsible for the primary function of SOD1, with the cell membrane acting as a scaffold in the process of Cu transfer to apo-SOD1 [6,8,10,11]. A mutation leading to the loss of Zn from the protein is often followed by misfolding and aggregation, a process associated with amyotrophic lateral sclerosis [12–16]. However, studies have shown that the removal of Zn from SOD1 does not lead to an immediate unfolding, but rather to an immediate deactivation of the enzyme through a combination of subtle structural and electronic effects [12–16], suggesting that SOD1 exerts its catalytic properties through a synergistic cooperation between the two metals. In fact, the cooperative activity of two proximal metal ions has been shown to display highly efficient synergistic catalytic properties in living organisms [10,17,18], and as such, Cu–Zn systems have been

explored as a catalyst for a diversity of chemical transformations [19–26].

Propargylamines such as pargyline, rasagiline, and selegiline are well known to increase the survival of dopaminergic cells by protecting damaged neurons from apoptosis, increasing protein and mRNA levels for the new synthesis of neuroprotective proteins, and as such, they are used as treatment options to manage neurodegenerative disorders such as Parkinson's and Alzheimer's diseases [27–31]. These molecules have been shown to exert their neuroprotective effects by irreversibly inhibiting monoamine oxidase and cholinesterase [27,32–35]. In addition to the wide range of biological and pharmaceutical properties associated with these compounds, propargylamines are prominent precursors in the synthesis of a range of nitrogen-containing compounds, and also serve as key intermediates in the preparation of various natural products. As such, a number of approaches have been used in the preparation of propargylamines, with the structurally simple ones synthesized via the amination of propargylic halides, propargylic phosphates, or propargylic triflates, while the much complex compounds are prepared using more elaborated methods [36,37]. Nevertheless, the catalytic coupling of the aldehyde–alkyne–amine system, also known as A³ coupling reaction, has progressively established itself as a simple and efficient

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method for the preparation of a diversity of propargylamines, as it is known to tolerate a wide range of functional groups, and proceed under highly tunable reaction conditions [38–44]. While various catalytic systems have been utilized, copper-based catalysts have played a critical role in this area [45–50], with the enantioselective preparation of tertiary propargylamines via a three-component coupling reaction, using CuBr as the catalyst and quinap as a ligand developed by Gommermann et al. [49,51,52], being among the most prominent examples. However, many of these methods not only require the addition of a ligand and a solvent, but their scopes are primarily limited to secondary amines, leading to tertiary propargylamines, with often long reaction times (up to six days) [49,51,52]. In order to facilitate access to secondary propargylamines, a number of catalytic systems involving imine intermediates have been developed [53–55]. In fact, Lui et al. [53] reported the enantioselective synthesis of secondary propargylamines from imine intermediates, using Cu(II)-pyridine containing *N*-tosylated aminoimine ligand complex as the catalyst, Benaglia et al. [54] used Cu(OTf)₂ with Bidusenko et al. [55] managing to develop a metal-free method for the preparation propargylamines from imine intermediates, under strongly basic conditions.

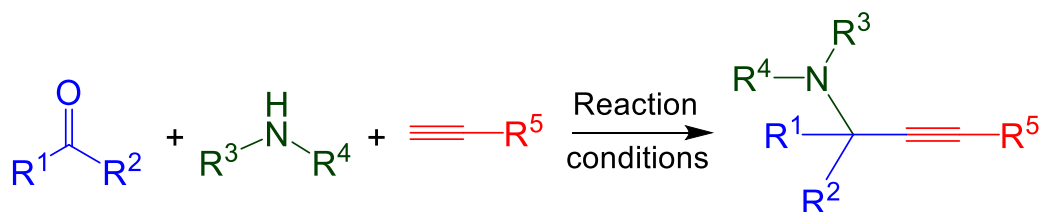
However, CuI supported on a range of materials or in the presence of a diversity of additives has received the most attention, as illustrated in Fig. 1. This includes the use of imine-functionalized silica (SiO₂-Py-CuI) as reported by Likhar et al. [56], Amberlyst A-21 as studied by Bosica and Abdilla [57], sulfur-functionalized halloysite nanoclay with 3-mercaptopropyl trimethoxysilane, explored by Bahri-Laleh and Sadjadi [58], protonated trititanate nanotubes investigated by Reddy et al. [59], and polyimidoamine dendrimer and trypsin enzyme supported on magnetic nanosilica (Fe₃O₄@SiO₂@DNHCS-Tr@CuI) studied by Peiman et al., [60]. These catalysts have demonstrated a diverse level of efficiency toward the synthesis of propargylamines via A³ (aldehyde, amine, and acetylene) coupling reactions. Furthermore, the synthesis of propargylamines via A³ coupling has also been successfully achieved using CuI in the presence of additives such as succinic acid as reported by Ren et al. [48], or [MEA][H₂PO₄] ionic liquid as shown by Zhu et al.

[61]. However, the scope of many of these reactions appeared also to be limited to the exploration of aldehydes in the presence of secondary amines, resulting in the synthesis of tertiary propargylamines, often with no mention of the behavior of primary amines under these reaction conditions. In fact, among the recently reported CuI-catalyzed methods for the preparation of propargylamines via A³ coupling, only Bosica and Abdilla [57] mentioned the exploration of a single primary amine, namely (4-methoxyphenyl)methanamine, in their report using Amberlyst A-21.

Meanwhile, Kantam et al. [62] managed to synthesize propargylamines using only zinc dust as a catalyst in acetonitrile as the solvent, without the need for any support, co-catalyst or ligand involvement. However, the scope of this latter reaction was also restricted to the investigation of secondary amines, with no indication of any attempt to explore primary amines, ketones or any alkyne other than phenylacetylene under these conditions.

Our research group has been very interested in the use of reactive substrates as starting materials in a reductive functionalization of CO₂ [63,64], and one of these reactive intermediates appears to be propargylamines, used in the preparation of oxazolidinones. Due to the limited availability of these starting materials from major chemical suppliers, we set about to prepare these reaction intermediates in our lab.

Since only secondary propargylamines are needed in our study, an attempt to expand the scope of the reaction by Kantam et al. [62] to include these needed intermediates failed systematically. As our research group is extremely green-and-sustainable oriented, it was important for us to utilize a method that complies with a number of green and sustainable chemistry principles, including the use of naturally abundant metals, at a low temperature and under neat conditions. In the search for such a catalytic system, we came across a report by Cheng et al. [65] using copper nanoparticles supported on MOF-5, a three-dimensional cubic porous framework with Zn₄O-clusters linked together through 1,4-benzenedicarboxylate-ligands metal-organic framework derived nanoporous carbon, as catalyst for the synthesis of



Previous work

Ref. [56] SiO ₂ -Py-CuI/MeCN, 90 °C (Likhar et al., 2007)	Ref. [57] CuI/A-21 (10 mol%)/ neat, 98 °C (Bosica & Abdilla, 2017)	Ref. [58] CuI@HNTs-S/EtOH, r.t (ultrasonic irradiation) (Bahri-Laleh & Sadjadi, 2018)
Ref. [59] CuI/ HTNT-5/ neat, 70 °C (Reddy et al., 2017)	Ref. [60] Fe ₃ O ₄ @SiO ₂ @DNHCS-Tr@CuI/ neat, 80 °C (Peiman et al., 2022)	Ref. [48] CuI/succinic acid/ Toluene, 100 °C (Ren et al., 2009)
Ref. [61] CuI/ [MEA][H ₂ PO ₄], 50 °C (Zhu et al., 2023)	Ref. [62] Zn dust/ CH ₃ CN, reflux (Kantam et al., 2008)	This work CuI/ Zn dust /neat, 60 °C ○ Bimetallic catalytic system ○ Simplistic and Broader scope

Fig. 1. Various reaction conditions involving the use of CuI in the synthesis of propargylamine via A³ coupling reactions.

propargylamines, via an A³ (aldehyde, amine and acetylene) coupling reaction. The XRD and XPS analysis of the surface of such a material indicated that Zn, ZnO, Cu and CuO coexisted in the Cu@MOF-5-C sample, and that the synergistic cooperation between different species of these two metals might be responsible for the observed catalytic effect [65]. The current report describes a unique and simplistic bimetallic catalytic system, which leverages the synergistic activity between two proximal metal centers, to facilitate the preparation of propargylamines via a three-component coupling reaction, at a lower temperature under neat conditions.

2. Results & discussion

The starting point for this study was an attempt in our lab to use the conditions from Kantam et al.'s [62] paper, a one pot synthesis of propargylamines using zinc dust as the sole catalyst. As such, refluxing *p*-tolualdehyde, piperidine (1.1 eqv), phenylacetylene (1.2 eqv) and Zn dust (15 mol%) in acetonitrile resulted in the corresponding propargylamine in a decent yield, as illustrated in Scheme 1. However, the reaction produced only traces of the expected product at best, when piperidine was substituted by a primary amine, with the corresponding imine intermediate observed as the major product.

Since CuI complexes [50,66] or supported on different types of materials [58,59,65,67] have recently been reported as efficient catalysts for the one pot synthesis of propargylamines via A³-coupling, it seems auspicious that the replacement of Zn dust by CuI as the catalyst could improve the yield of the reaction. Consequently, refluxing *p*-tolualdehyde, allylamine (1.1 eqv), phenylacetylene (1.2 eqv) and CuI (20 mol%) in acetonitrile as illustrated in Scheme 2, produced the corresponding propargylamine, with about 63% yield after 12 h (Table 1, entry 1).

Reactions were performed under a nitrogen atmosphere, using 100 mg of *p*-tolualdehyde (1.0 eqv). ^aIn relationship to the number of moles of *p*-tolualdehyde. ^bPercent conversions determined by GC-MS, using tridecane as an internal standard. ^cNo *p*-tolualdehyde was present upon reaction completion as indicated by GC-MS. ^dN.R. = No Reaction.

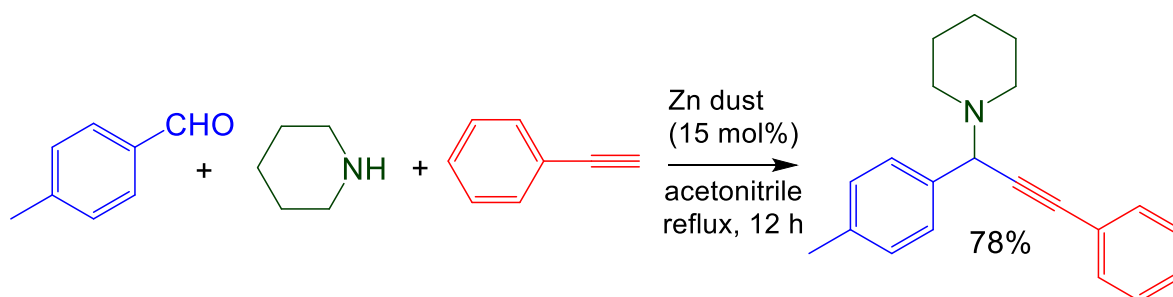
The yield of the reaction did not significantly improve with the variation of the solvent, including toluene, THF, dioxane, DMF or methanol, even after 18 h (Table 1, entries 2, 3, 4, 5 and 6). That is when, supported by the above-mentioned literatures, an intuitive decision to add zinc dust as a co-catalyst, in a single pot reaction, was made. As such, the mixture was refluxed either in toluene (entry 7) or under neat conditions (entry 8) resulting in a significant increase in the percent yield of the reaction. Using exactly 1.0 equivalent of either allylamine (entry 9) or phenylacetylene (entry 10) in relationship to the number of moles of *p*-tolualdehyde, resulted in lower yields. In fact, the reaction was able to reach completion only when 1.2 equivalent of allylamine and 2.0 equivalent of phenylacetylene (entry 12) were used, as indicated by the GC-MS spectrum of the crude product in each attempt. The reaction also produced a noticeable amount of diphenylacetylene side product, explaining the use of two equivalents of phenylacetylene under the optimal conditions. The reduction of the amount of CuI to 10 mol% (entry 13) or zinc dust to 5 mol% (entry 14) has a negative impact on the

reaction, with the effect being more dramatic in a complete absence of zinc dust (entry 17). The reaction systematically failed when no CuI was present (entry 18). The reduction of the reaction time from 18 to 12 h also resulted in a reduced yield (entry 16), and the reaction failed at room temperature as well (entry 15). As a result, the conditions in entry 12 were selected for the exploration of the scope of the reaction. It should be mentioned that the conditions in entry 12 produced lower yields with either CuBr (72%), CuCl (52%) or Cu(OAc)₂ (32%), suggesting that the nature of the copper ion and the solubility of the copper salt might be important for the reaction to proceed.

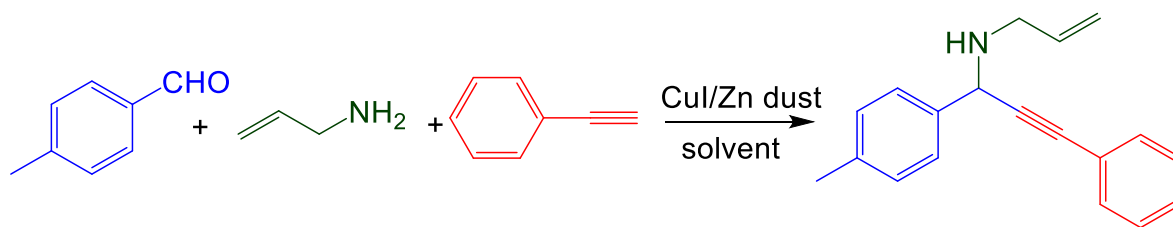
With the optimal reaction conditions in hand, the exploration of the scope of the reaction was initiated, using a wide range of starting materials. The electronic effects of diverse groups on the reaction were investigated using benzaldehyde derivatives, substituted at different positions by either an electron donating or electron withdrawing group, while keeping phenylacetylene and allylamine as the other coupling partners, using the optimal reaction conditions in entry 12. It appears that the reaction produces a better yield with benzaldehyde bearing electron-donating groups, as illustrated in Fig. 2.

In fact, compounds **1**, **2**, **8** and **11** obtained while using activated benzaldehyde derivatives, namely *p*-tolualdehyde, *p*-anisaldehyde, *m*-anisaldehyde and *o*-anisaldehyde, respectively, consistently produced a better yield than their counterparts **3**, **4**, **5**, **6**, **12**, **13** and **14** obtained from deactivated benzaldehyde derivatives. Among the activated benzaldehyde derivatives, an electron-donating group at the *para*-position **2** (90%), produced a better yield than when the same group was at a *meta*- **8** (79%) or *ortho*- **11** (77%) position, respectively. The reaction also tolerates a free hydroxyl group as shown with compound **9** (53%). Furthermore, as the group on the benzaldehyde ring become more electron-withdrawing [**3**: *p*-Cl (63%), **4**: *p*-Br (60%), **5**: *p*-F (59%), **6**: *p*-CF₃ (35%), or **14**: 2,4-di-Cl (47%)], the yield of the reaction gradually decreases, with the reaction failing to produce the expected product with *p*-nitrobenzaldehyde (**7**). The position of the electron-withdrawing group on the ring does not appear to have a significant impact on the reaction, as illustrated with compounds **10** (*m*-Cl, 55%), **12** (*o*-Br, 65%) or **13** (*o*-F, 60%) as compared to compounds **3** (*p*-Cl, 63%), **4** (*p*-Br, 60%) and **5** (*p*-F, 59%), respectively. In addition, 2-bromo-4-nitrobenzaldehyde, pyridine-4-carbaldehyde and 3-chloroisonicotinaldehyde, which are extremely deactivated systems, also failed to produce the expected products, as illustrated with **15**, **16** and **17**, respectively. On the other hand, all the aliphatic aldehydes, namely cyclohex-1-ene-1-carbaldehyde, cyclohexanecarbaldehyde, isobutyraldehyde and octanal, produced good yields, as shown with compound **18** (78%), **19** (73%), **20** (85%) and **21** (69%). This is not surprising as alkyl groups are primarily electron-donating by nature.

When exploring the reactivity of different amines towards the synthesis of propargylamines under the optimal reaction conditions, it appears that the reaction produced decent to good yields with almost all the secondary amines tested, except with *N*-methylaniline which failed to produce the expected product, and the starting materials were collected at the end of the reaction. In fact, the reaction produced a very good yield with piperidine, morpholine, thiomorpholine, and



Scheme 1. Initial reaction conditions from Kantam et al.'s [62].



Scheme 2. Reaction conditions involving the use of copper iodide and zinc dust as co-catalysts for the preparation of propargylamines.

Table 1
Optimization of the reaction conditions as depicted by Scheme 2.

Entry	Allylamine (eqv) ^a	Phenylacetylene (eqv) ^a	CuI (mol%) ^a	Zn (mol%) ^a	Solvents (1.0 M) ^a	Temp. (°C)	Time (h)	Yield (%) ^b
1	1.1	1.2	20	none	acetonitrile	reflux	18	63
2	1.1	1.2	20	none	toluene	reflux	18	56
3	1.1	1.2	20	none	THF	reflux	18	59
4	1.1	1.2	20	none	dioxane	reflux	18	47
5	1.1	1.2	20	none	DMF	reflux	18	65
6	1.1	1.2	20	none	methanol	reflux	18	NR ^d
7	1.1	1.2	20	10	toluene	reflux	18	90
8	1.1	1.2	20	10	Neat	60	18	87
9	1.0	1.2	20	10	neat	60	18	83
10	1.1	1.0	20	10	neat	60	18	74
11	1.2	1.0	20	10	neat	60	18	77
12	1.2	2.0	20	10	neat	60	18	98 ^c
13	1.2	2.0	10	10	neat	60	18	65
14	1.2	2.0	20	5	neat	60	18	78
15	1.2	2.0	20	10	neat	rt	18	trace
16	1.2	2.0	20	10	neat	60	12	73
17	1.2	2.0	20	none	neat	60	18	60
18	1.2	2.0	none	10	neat	60	18	NR ^d

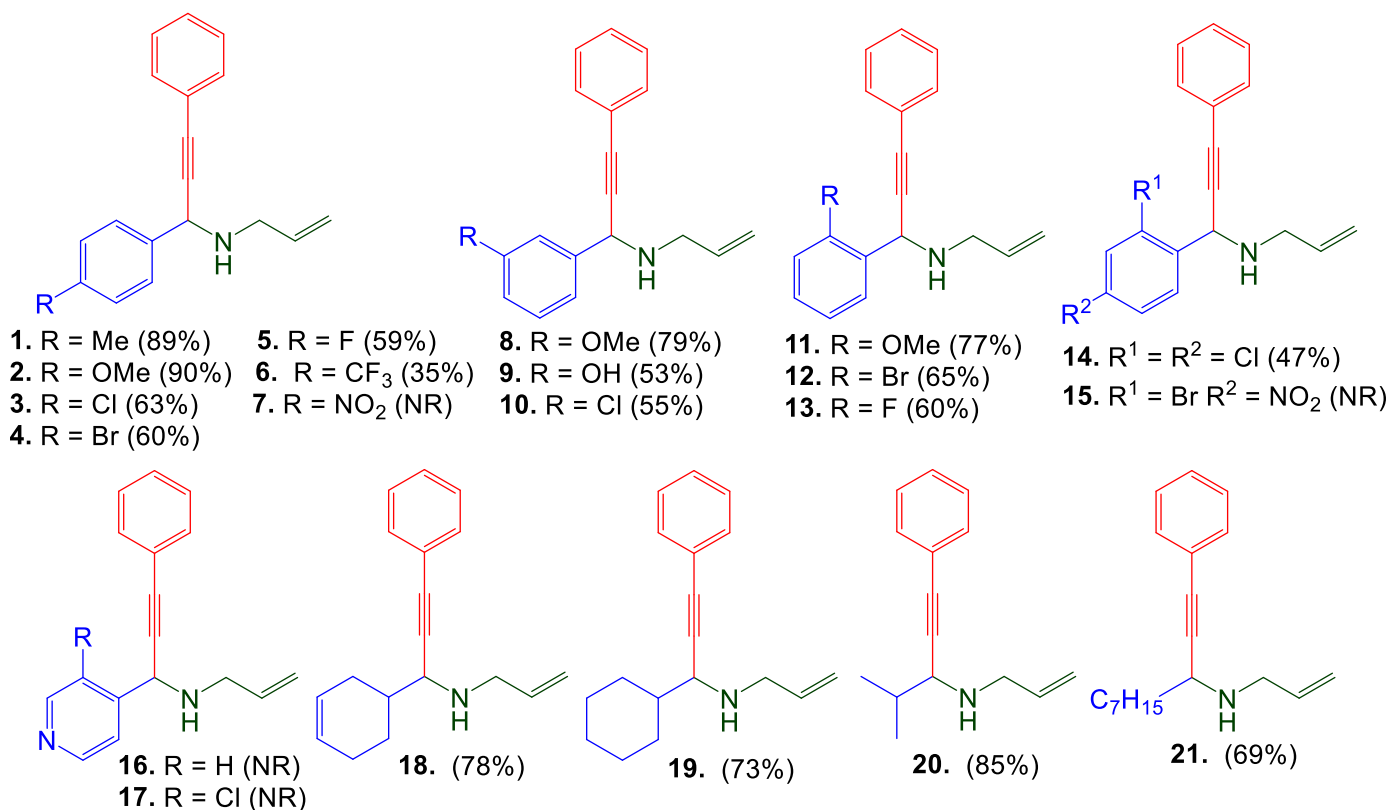


Fig. 2. Exploration of the electronic effects of different groups on the CuI/Zn-catalyzed one-pot synthesis of propargylamines. (All reactions are conducted at 60 °C, and the listed yields are isolated. N.R. indicates that the expected product was not observed. However, the imine intermediate was obtained almost in each of these cases, unless otherwise stated).

diallylamine in the presence of *p*-tolualdehyde, as shown by compounds **32** (88%), **35** (88%), **36** (72%) and **37** (88%), respectively (Fig. 3). These reaction conditions also tolerate a free hydroxyl group on the amine coupling partner, as indicated by compounds **33** (53%) and **39** (48%), but the yield was much lower.

The reaction also produced a lower yield with *N*-methylbenzylamine (**37**: 58%), but failed completely with *N*-methylaniline (**38**), with the combined observations from these two latter reactions suggesting a probable adverse effect from steric hindrance resulting from the proximity of the benzene ring of *N*-methylbenzylamine to the reaction center. It is obvious that the reaction does not work well with primary amines as it does with secondary amines. While allylamine produced a

good yield with a range of aldehydes, only octylamine (**22**: 57%) was able to produce the expected product under the standard optimal conditions. It is possible that a peripheral π -stacking type of interaction with the C=C in allylamine might be involved in the stabilization of the transition state of the reaction, thus explaining the observed reactivity. In the case of octylamine, a weak peripheral σ -type interaction might be just enough to explain the success of the reaction, with the other amines lacking the ability to provide either a π -type or a weak σ -type of stabilizing interaction. While the failure of reactions involving aniline and pyridin-2-amine derivatives might be explained by the already mentioned potential sterics as a result of the proximity of the aromatic ring to the reaction center, there is no logical explanation as to why 2-

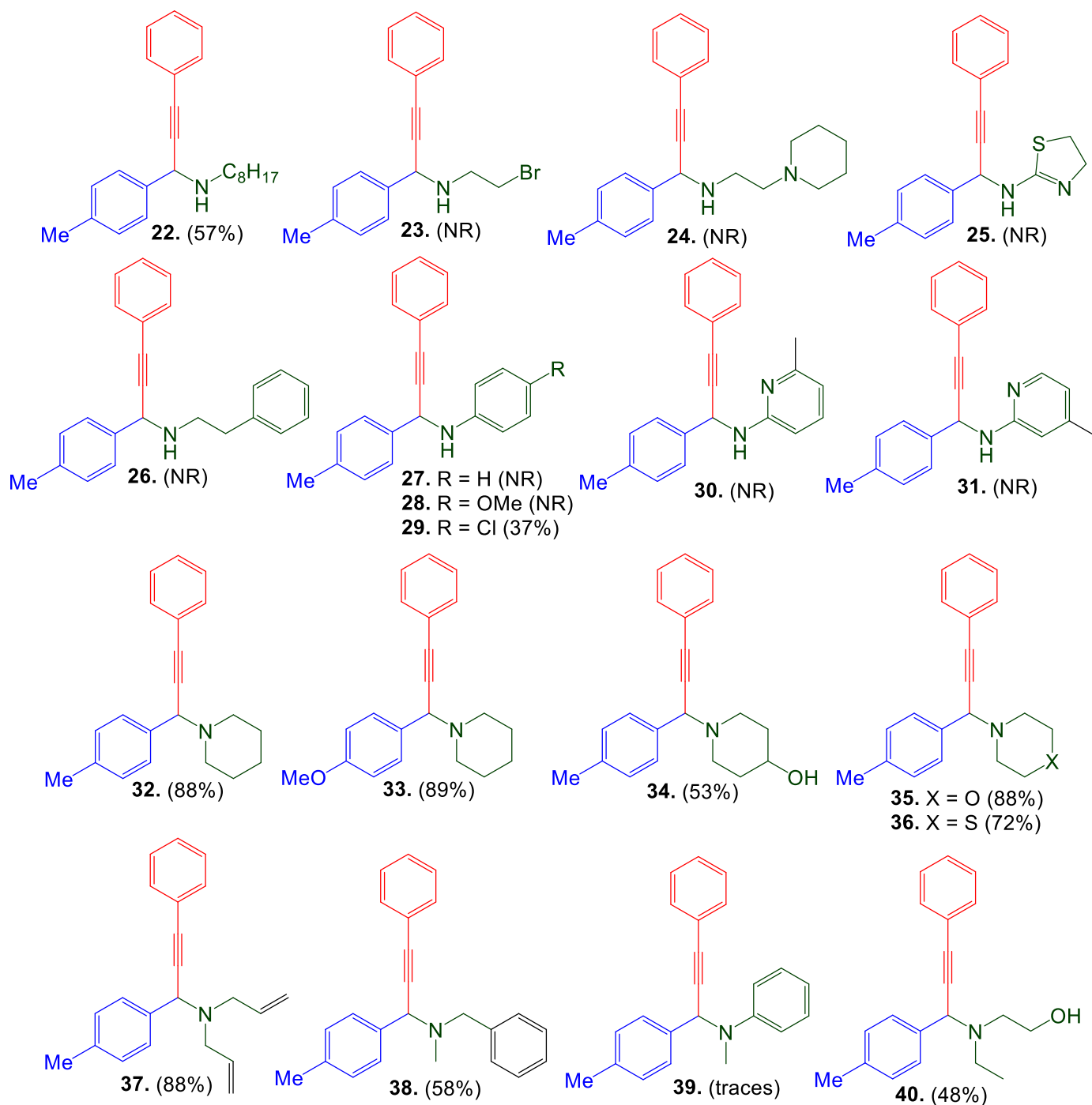


Fig. 3. Exploration of the reactivity of different amines towards the synthesis of propargylamines under CuI/Zn-catalyzed one-pot reaction conditions. (All reactions are conducted at 60 °C, and the listed yields are isolated. N.R. indicates that the expected product was not observed).

bromoethylamine (23), 2-(piperidin-1-yl)ethan-1-amine (24) and 2-phenylethylamine (26) failed to produce the corresponding propargylamine, with the imine intermediate collected at the end of the reaction in each of these cases. We speculated that these later amines were unable to generate a strong-enough σ -type peripheral interaction to stabilize the transition state, suggesting that the stability of the imine intermediate plays a key role in the progression of the second step of the reaction. Since secondary amines produce a not-very-stable iminium intermediate, this might explain why secondary amines readily produce the expected propargylamine, while primary amines systematically fail, except for allylamine and octylamine. It is worth mentioning that reactions involving aniline and 4-methoxyaniline failed to produce the expected product even after 72 h, with the starting material and only trace of the imine intermediate observed at the end of the reaction. Under similar conditions however, 4-chloroaniline produced the expected product (29: 37%), with a very low yield.

To investigate the effect of alkyne coupling partners on the reaction, the reactivity of a number of monosubstituted acetylene derivatives was explored. It appears that 1-ethynyl-4-methoxybenzene produced the expected product with a better yield than phenylacetylene (41: 92%), while the derivative bearing a fluoro group at the *para*-position on the benzene ring failed to produce the expected product. This might suggest a potential positive electronic effect on the reaction by the electron

donating group. It also appeared that the proximity of a benzene ring on the alkyne is beneficial to the reaction, as prop-2-yn-1-ylbenzene (43) and but-3-yn-1-ylbenzene (not shown) failed to produce the expected products in the presence of allylamine, and the imine intermediate was collected at the end of the reaction in each case. The replacement of phenylacetylene with 3-bromoprop-1-yne (44), hex-1-yne (45), 3,3-dimethylbut-1-yne (46), ethynyltrimethylsilane (47) or 2-methylbut-3-yn-2-amine (48), in the presence of allylamine, all failed to produce the expected product, with the corresponding imine intermediate collected at the end of each reaction. It should however be noticed that, when allylamine (primary amine) was substituted by piperidine (secondary amine), many of these alkynes produced the expected propargylamine in good yield, as illustrated by 49 (79%), 50 (83%) and 51 (75%), respectively (Fig. 4).

It is noteworthy that the reaction failed to produce the expected product whenever the aldehyde coupling partner was replaced by a ketone, including octan-2-one, acetophenone or 4-methoxyacetophenone. Only cyclohexanone was able to produce the expected product in the presence of either allylamine (52) or piperidine (53), with phenylacetylene used as the alkyne coupling partner. However, the reaction failed or produced only traces of the product when phenylacetylene was replaced by either 3,3-dimethylbut-1-yne (54), and ethynyltrimethylsilane (55) in the presence of allylamine.

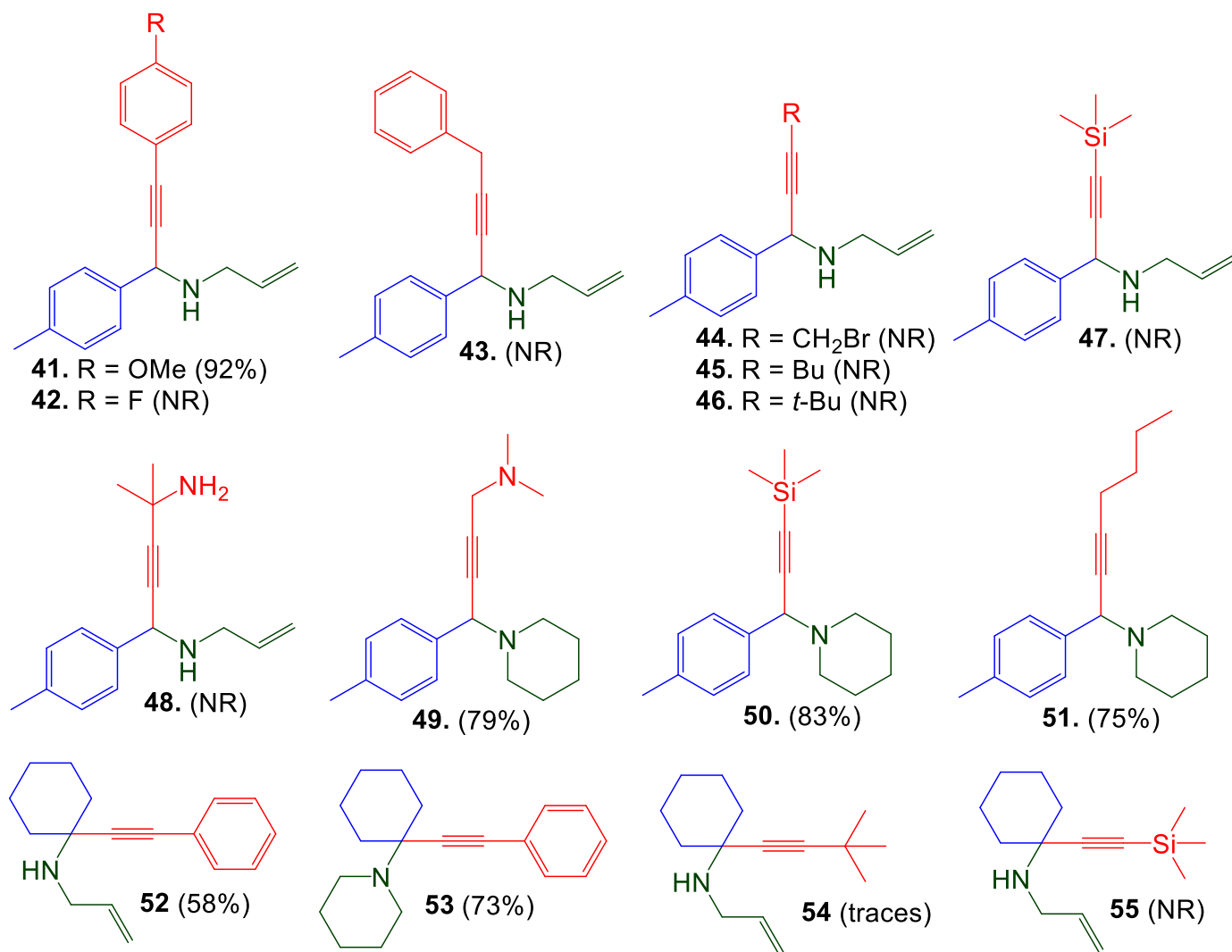


Fig. 4. Exploration of the reactivity of different alkynes towards the synthesis of propargylamines under CuI/Zn-catalyzed one-pot reaction conditions. (All reactions are conducted at 60 °C, and the listed yields are isolated. N.R. indicates that the expected product was not observed. However, the imine intermediate was obtained almost in each of these cases, unless otherwise stated).

Attempts at recycling the catalyst failed, as a colloidal sticky material was collected at the end of each reaction after centrifugation and several washes, making it almost impossible to perform the next reaction. As for the mechanism of the reaction, although the CuZn catalytic process is been known for more than a century, and despite intensive efforts devoted to the topic [68–70], the catalytic nature, the mechanism, and active sites of such a system are not yet fully understood [23,70–72]. It has however, been demonstrated that the addition of Zn in a copper catalytic system goes beyond the merely role of particle disperser, and acts as a chemically active promoter of the reaction through a CuZn synergistic effect [73,74]. The formation of CuZn alloy within the reaction mixture through the reduction of the Cu ion at the defective Zn sites was proposed [70,74,75], although there are still arguments about the chemical state of Zn in such a catalytic process [23,72,76]. It is unclear whether Zn remains in its metallic state as a surface alloy or a bulk alloy, even though Zn diffusion and Zn spillover on the Cu surface have been observed under various conditions, suggesting that the system can have a strong dynamic character [26,71–73]. Based on these observations, and inspired by previously reported mechanisms for copper catalyzed synthesis of propargylamines [38,44,49,51,77,78], a potential mechanism for the catalytic system described in this study is proposed in Scheme 3.

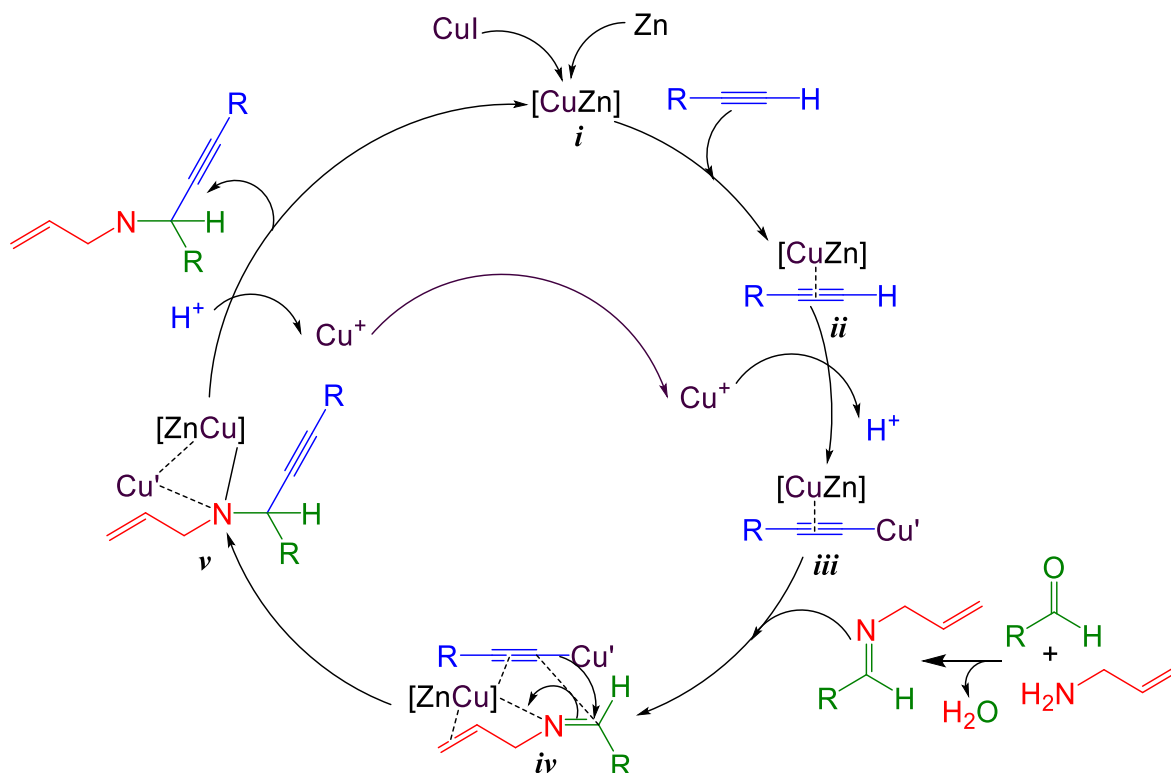
It is well documented in click chemistry involving azides as coupling partner that copper(I) readily complexes with terminal alkynes to generate highly aggregated species, engaging a range of σ - and π -interactions [79–81]. A required second copper atom in the transition state complex provides additional stabilization [79–81]. In fact, DFT studies of such catalytic systems indicated that the second Cu center facilitates the formation of the cupracycle in the rate-determining step and stabilizes the metallacycle intermediate itself [79–81]. Inspired by these observations, we conjectured that, in the catalytic system here reported, copper(I) is creating active species with a strong dynamic character with Zn dust (species **i**) via a single electron exchange, forming either a surface alloy or a bulk alloy. The presence of the alkyne coupling partner stabilizes this metal-to-metal intermediate through a π -type

interaction, leading to species (**ii**). Since the reaction conditions are optimal only when there are 2 equivalents of CuI for each equivalence of Zn dust, we concluded that there must be two copper centers present in the transition state of this reaction [79–81], with the remaining copper (I) attaching itself at the non-substituted end of the alkyne via an acid-base reaction, resulting species (**iii**), which eventually reacts with the imine intermediate resulting in species (**iv**). This intermediate rearranges into species (**v**), which, through an acid-base reaction, regenerate the copper(I) active species, followed by a reductive elimination to produce the expected propargylamine while recreating the CuZn active species, and thus closing the catalytic cycle (Scheme 3).

It should be clarified that this is only a proposed mechanism, and it is still possible that copper is solely responsible for catalysis, with zinc involved in the heterogeneous surface, providing the observed stabilization and elevated reactivity to the copper centers. We are currently exploring a collaborative effort, which involves the use of the equilibrium density functional theory (DFT), coupled with the dynamic density functional theory (DDFT) to investigate the viability of the different species proposed in this initial mechanism. The obtained results will be reported in due course.

3. Conclusion

A tandem Cu(I)/Zn dust catalytic system for the synthesis of propargylamines via a three-component coupling reaction has been developed. The reaction works well with a diversity of aldehyde, at low temperature and under neat conditions. Aliphatic and aromatic aldehydes bearing electron donating groups provided a better yield than deactivated benzaldehyde derivatives, with the reaction failing when the aromatic ring bearing the aldehyde functional group is extremely deactivated. The reaction also failed to produce the expected products with a number of primary amines. In fact, the reaction works preferably well with allylamine, suggesting a potential peripheral stabilization of the transition state via a π -type of interaction. Furthermore, only phenylacetylene derivatives were able to work as the alkyne coupling



Scheme 3. Proposed mechanism for the copper (I)-zinc-dust catalytic system used for the synthesis of propargylamines.

partner in the presence of a primary amine, with any other alkyne tried in this study failing to produce the expected product. However, these alkynes readily produce the expected propargylamine in the presence of a secondary amine. Furthermore, among the ketones tried as substrates in this study, only cyclohexanone produced the expected product in the presence of phenylacetylene, but failed when the alkyne coupling partner was changed to either 3,3-dimethylbut-1-yne or ethynyltrimethylsilane. A potential mechanism for the catalytic system involved in the transformation here reported is proposed, although it still needs to be fully investigated. Nevertheless, this reaction represents an environmentally friendlier approach toward the synthesis of propargylamines, as in involves the use of naturally abundant metals as a tandem catalyst, at a low temperature and under neat conditions.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.tgchem.2023.100027>.

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