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Solvent-free synthesis of propargylamines via A^3 coupling reaction and organic pollutant degradation in aqueous condition using Cu/C catalyst

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The present report focuses on the efficient and operationally simple synthesis of biomass-derived carbon as support to immobilize copper particles as a catalyst for the one-pot synthesis of propargylamines from furfural via the A^3 coupling reaction. This new catalyst showed remarkable catalytic performance leading to a 97% yield within 5 h at 80 °C using 5 mg (0.0022 mmol Cu) of Cu/C catalyst under solvent-free condition. Moreover, nitro-substituted compounds such as 4-nitrophenol (4-NP) are highly toxic and not easily degradable. Hence, a quick and effective method is required to neutralize these toxic compounds. The synthesized active support Cu/C catalyst having various electron-donating groups containing small amounts of Cu plays an essential role in the catalytic reduction of 4-NP (0.1 g). Using only 3 mg (0.0013 mmol Cu) of Cu/C catalyst and $NaBH_4$ (10 mmol), a 99% yield (100% selectivity) in the aqueous condition at 25 °C was achieved. The catalytic reduction follows the pseudo-first-order kinetics with reaction rate constant of $0.028\ s^{-1}$. Moreover, results demonstrate that the Cu/C catalyst has superior catalytic activity due to the presence of electron-donating molecules such as O, S, and N atoms, which enable synergistic effect in enhancing the overall catalytic performance. Notably, the recoverability and recyclability of the synthesized catalyst were evaluated for up to four cycles, which confirmed its stability in these cycles.

KEYWORDS
4-Nitrophenol, Cu/C catalyst, D-glucose, propargylamines, xylose

1 | INTRODUCTION

The development of sustainable, green, biomass-derived compounds into chemicals, biofuels, drugs, and various materials is a significant research objective in modern organic chemistry.[1] For example, one-pot synthesis of propargylamines derived from aldehyde derivatives or xylose is an important study area because propargylamines are used in the synthesis of chemicals such as a peptides, isosteres, β-lactams, and natural products.[2–4] Moreover, numerous propargylamines have been utilized to deal with neuropsychiatric disorders such as anxiety, Parkinson's disease, and depression. Moreover, they have been successfully applied in drugs such as rasagiline, a potent cardiovascular drug.[5] Because of their vital role in many applications, numerous synthetic methods for the preparation of propargylamines have been established.[6–9] However, improvements to these synthetic methods continue to be explored. One approach to the synthesis of propargylamines is the aldehyde–alkyne–amine (A^3) coupling reaction which utilizes various kinds of metal-based catalysts such as Ag(I) salts,

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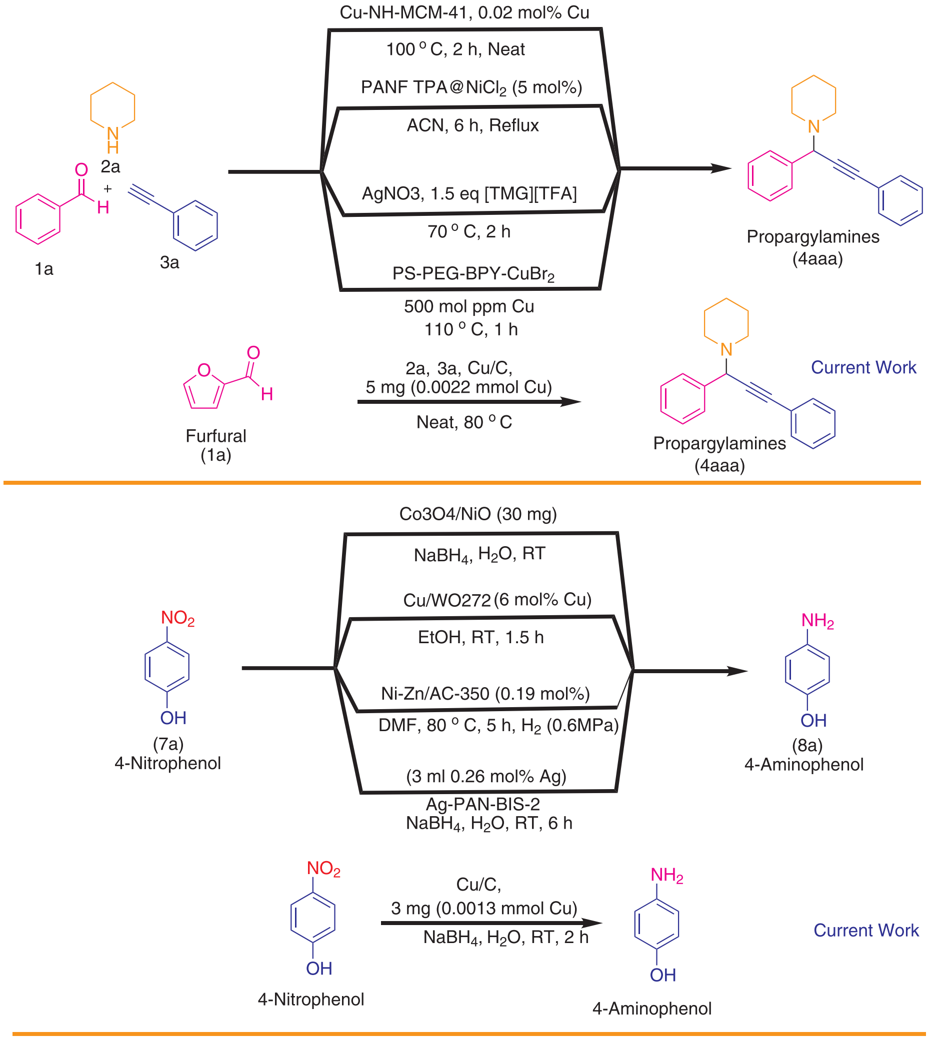
Cu(I) salts, and Fe(III) salts.[10–12] For example, Li et al.[13] reported the A^3 coupling reaction to produce propargylamines catalyzed by AgI at 100 °C in the presence of H_2O for 14 h. Furthermore, Wang et al.[14] established an $InCl_3$-catalyzed direct A^3 coupling reaction in toluene at 120 °C for 14 h. However, all these reported catalysts were used in homogeneous form. For this reason, the catalysts (i) were difficult to recover, regenerate and reutilize; (ii) require large amounts of reagents; (iii) need highly moisture-sensitive reagents; and (iv) require exact reaction conditions that unfortunately restrict their commercial application. To overcome these issues, efforts have been devoted to construct various heterogeneous metal catalysts for the A^3 coupling reaction such as Cu–HAP,[15] nanocrystalline CuO,[16] silica-immobilized NHC CuI complex,[17] Ni–Y zeolite,[18] AgY zeolite, and supported Au/MIL-53.[19] However, these heterogenous catalysts required toxic solvents, high metal loading, various additives, and tedious catalyst separation, all of which limit their utilization and applicability. Therefore, robust and highly efficient heterogenous catalysts are still being actively sought[20] (Scheme 1).

Meanwhile, rapid industrialization and innovative advancements that have led to many improvements in humanity's living conditions have also come at the cost of several environmental impacts such as H_2O scarcity, water pollution, air pollution, and climate change. These environmental impacts often stem from the release of large amounts of industrial chemicals to the environment that are difficult to degrade. Many of these industrial chemicals are nitro-substituted compounds which are among the most toxic and hazardous of chemicals. Nitro-substituted compounds cause severe health hazards to humans, animals, and aquatic life. For these reasons, effective and efficient methods for the treatment of such toxic compounds need to be developed. One treatment strategy is via catalyzed reduction reactions.

The development of the catalytic reduction reactions for converting nitro-substituted compounds to benign and sometimes industrially important chemicals is usually



SCHEME 1 Previous protocols compared with the present work. ACN: Acetonitrile; AgNO3: Silver nitrate; Ag-PAN-BIS-2: polymer supported silver complex; Co3O4/NiO: 3D hierarchical Co3O4/NiO microspheres; Cu/NH2/MCM-41: Amine-Functionalized Mesoporous Silica as a Support Copper(I); Cu/WO272: bimetallic NP catalyst; DMF: Dimethylformamide; EtOH: Ethanol; NaBH4: Sodium borohydride; Neat: Solvent-free; NI-Zn/AC-350: Activated carbon supported bimetallic catalysts; PANF TPA@NiCl2: fiber-supported Ni(II) complex catalyst; PS-PEG-BPY-CuBr2: copper(II) –bipyridine complex immobilized on amphiphilic polystyrene –poly(ethylene glycol) (PS–PEG) resin; RT: Room temperature; [TMG][TFA]: Ionic Liquid (IL)

performed using the test molecule 4-nitrophenol (4-NP). In these catalyzed reduction reactions, 4-NP is converted to 4-aminophenol (4-AP), which has a lower toxicity level and may be utilized as a pharmaceutical intermediate.[21] Catalysts that have been used for these reactions include Au nanoparticles,[22] SiO_2@CuxO@TiO_2 heterostructures,[23] Ag nanoparticles, and Ni nanoparticles.[24] All these reported systems require high-temperature and high-pressure reactors, strong acid media, toxic solvents, and high catalyst loadings, but generally produce low yields.[25] In addition, these reported technologies dealt only with the catalytic reduction of 4-NP, and without separation and purification of resulting products. As such, the development of more effective heterogenous catalysts for the reduction of nitro-substituted compounds remains an important area of concern.

The choice of suitable supports is a significant parameter in the design of high-performance heterogeneous catalysts. Recently, many types of materials that include new inorganic supports, novel polymers, and hybrid materials have been actively explored for the immobilization of catalytic species. However, tedious preparation methods and high production costs eventually prevent their widespread application. Because of this, one of the hottest topics nowadays in the area of heterogenous catalyst development is the utilization of novel support materials with excellent stability and high immobilization capacity for more facile heterogeneous catalysis. Carbon materials and carbonaceous catalysts have recently gained enormous attention due to their ease of synthesis. Some carbon-based catalysts may in fact be prepared via one-pot synthesis. Meanwhile, the development of highly effective non-noble metal catalysts which can significantly reduce the catalyst loading is highly required.

In this study, we prepared carbonized D-glucose with para-toluenesulfonic acid (*p*-TSA) via a one-pot process wherein structures embedded with the highly active –OH, –COOH, and –SO_3H sites were formed.[26] These functional groups provide not only anchor sites but also electronic effects that aid in catalytic activity.[27] The catalyst surface was then modified with 3-aminopropyltriethoxysilane (APTES) to produce the catalyst anchor sites for the immobilization of a small amount of copper ($CuCl_2{\cdot}2H_2O$ in EtOH). This heterogenous catalyst was evaluated for two potential applications, namely, (i) A^3 coupling reactions, and (ii) reduction of nitro-substituted compounds. By contrast, performing organic conversion without the use of harmful solvents is also a primary concern in green organic synthesis. Despite widespread investigations into solvent-free catalytic reactions, the reduction of catalyst loadings in solvent-free A^3 coupling reactions with non-noble metal catalysts has not been sufficiently examined. The synthesis of an extremely efficient Cu/C catalyst that promotes A^3 coupling reactions with low Cu loading in solvent-free catalytic transformations is undoubtedly desired to achieve ideal and practical catalytic synthesis of propargylamines.[28,29] We believe that it would be very promising in terms of green technology, environmental impact, process economics, and reaction efficiency to examine a one-pot synthesis of important industrial chemicals from biomass-derived intermediates such as furfural via the A^3 coupling reaction. Therefore, one objective of this research work was to develop a Cu-immobilized catalyst with low metal loading (2.86 wt. %Cu) for the one-pot synthesis of propargylamines from furfural at low temperature and under solvent-free conditions. To the best of our knowledge, the utilization of non-noble metals alone without suitable support is not effective for the reduction of 4-NP to 4-AP. So far, we have not encountered the utilization of active support with low metal loading in the catalytic reduction of substituted nitro-compounds. Active supports having various functional groups that enhance catalytic activity are expected to exhibit superior catalytic reduction of 4-NP with $NaBH_4$ in aqueous condition under mild reaction conditions.

Finally, we determined whether the synergistic effect between immobilized Cu and the active carbon support in our Cu/C catalyst is preserved over four reuse cycles and observed no loss in catalytic activity in both the A^3 coupling and nitro-reduction reactions. This means that our heterogenous catalyst offers a new path for catalytic synthesis of propargylamines and the degradation of organic pollutants.

2 | EXPERIMENTAL SECTION

2.1 | Materials

All reagents or chemicals were of laboratory grade and were utilized without further purification. $CuCl_2{\cdot}2H_2O$, glucose, xylose, furfural, para-toluenesulfonic acid (*p*-TSA), (3-aminopropyl)triethoxysilane (APTES), 4-nitrophenol (4-NP), dimethyl sulfoxide (DMSO), $NaBH_4$, toluene, and ethanol were obtained from Sigma-Aldrich (Korea).

2.2 | General procedure for the synthesis of propargylamines (4aaa)

Furfural (1.04 mmol), piperidine (1.07 mmol), and phenylacetylene (1.02 mmol) were allowed to react solvent free at 80 °C with 5 mg (0.0022 mmol Cu) of Cu/C catalyst. The propargylamine (**4aaa**) product was isolated by flash chromatography (ethyl acetate–hexane).

2.3 | Catalytic reduction of 4-NP (7a)

4-NP (0.1 g), Cu/C catalyst (3 mg; 0.0013 mmol Cu), and $NaBH_4$ (10 mmol) were allowed to react in H_2O at 25 °C. Thin-layer chromatography was used to monitor the progress of the reaction. The 4-AP (**8a**) product was extracted using ethyl acetate and the solvent was removed by evaporation under vacuum.

3 | RESULTS AND DISCUSSION

Synthesis of biomass-derived copper catalyst (Cu/C) from glucose is promising in terms of sustainability, availability, cost, and ease of preparation. Furthermore, the Cu/C catalyst consists of a carbon skeleton that is easily separable, stable, and insoluble in most acidic/basic aqueous environments as well as organic solvents. The synthesized Cu/C catalyst was characterized by various analytical techniques such as Fourier transform infrared (FT-IR), X-ray diffraction (XRD), scanning electron microscopy (SEM), SEM–energy-dispersive X-ray (EDX), thermogravimetric analysis (TGA), X-ray photoelectron spectroscopy (XPS), and inductively coupled plasma-mass spectrometry (ICP-MS). Cu/C catalyst showed extraordinary performance in the one-pot, multistep synthesis of propargylamines **(4aaa)** from furfural within 5 h at 80 °C under solvent-free condition using only 5 mg (0.0022 mmol Cu) of catalyst and in the selective catalytic reduction of 4-NP using only 3 mg (0.0013 mmol Cu) of catalyst and $NaBH_4$ (10 mmol) in the presence of water at 25 °C (Scheme 2).

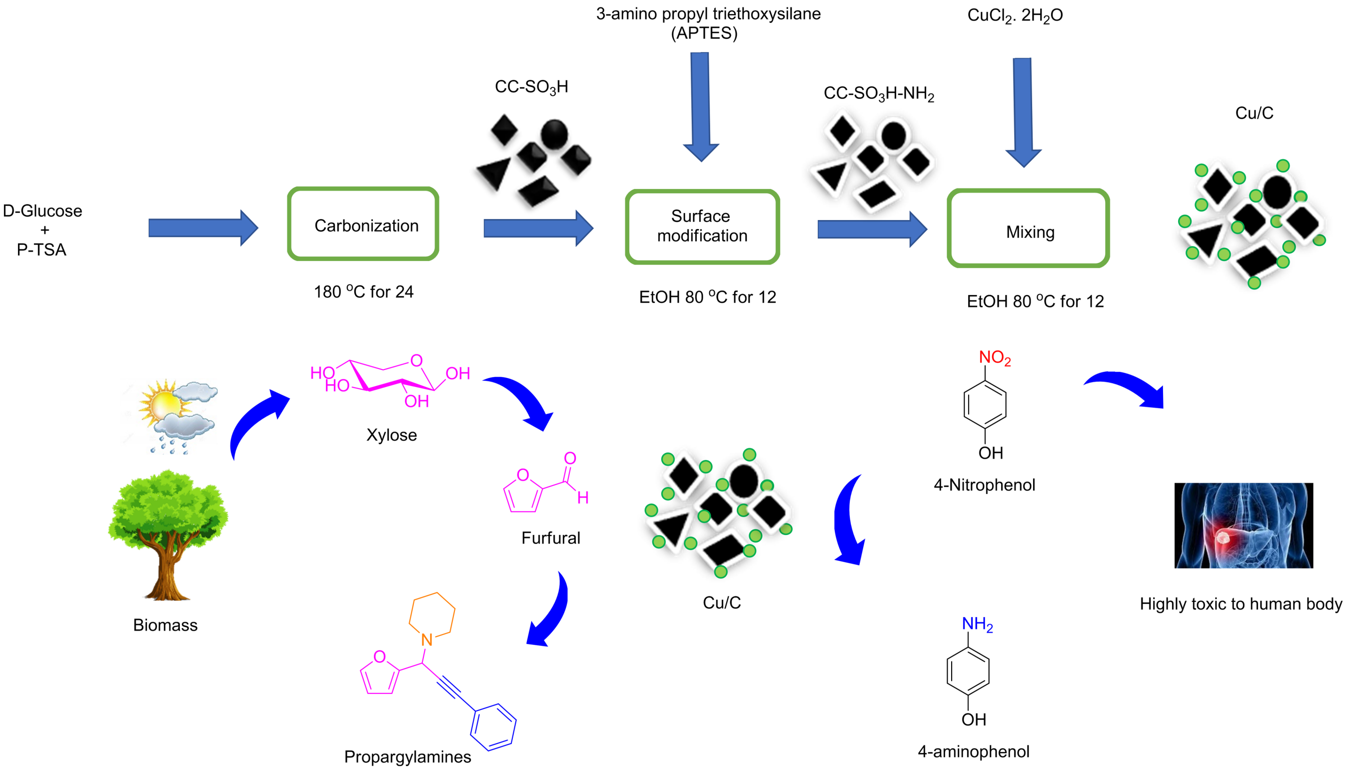
The FT-IR spectra of the synthesized Cu/C catalyst is shown in Figure 1a. The peaks at 1009 and 1100 cm^{-1} correspond to O=S=O stretching vibration of $–SO_3H$ and $–SO_2$, respectively, indicating the presence of sulfonic acid on the catalyst surface. The peak at 1636 and 1480 cm^{-1} are attributed to C=C stretching vibrations in aromatic carbon and C–H bending vibration of alkyl groups of terminal silanes, respectively. The peak at 1018 cm^{-1} corresponds to the Si–O stretching vibration, whereas the peaks at 681 and 610 cm^{-1} are attributed to the Si–O–C stretching and bending vibrations, respectively, after silanization of the catalyst surface. A strong peak observed at 3425 cm^{-1}, which is attributed to O–H stretching, affirms the existence of –OH functionalities on the catalyst surface. The XRD pattern analysis of the as-prepared Cu/C catalyst is shown in Figure 1b. The crystal structure and purity of the samples could be easily obtained by XRD measurement. The Cu/C catalyst showed the characteristic reflection for $CuCl_2$ at $2\theta = 17°, 22°, 29°, 32°$, and 39°, corresponding to the planes (220), (101), (210), (210) (111), and (200) of cubic $CuCl_2$ structures.[30–33] The XRD peaks at 50° and 53.3° represent CuO which comes from surface oxidation of the catalyst due to exposure to moisture/air. The results confirm that the Cu/C catalyst was successfully synthesized.

The surface morphology and the chemical composition of the Cu/C catalyst were characterized by SEM–EDX analysis. Figure 2(a–c) shows the SEM image of morphology of the Cu/C catalyst such that Cu particles assemble as irregular spheres on the surface of the substrate. EDX analysis (Figure 2d) confirms the presence of carbon (56.2%), oxygen (25.2%), nitrogen (5.07%), sulfur (0.95%), silicon (3.12%), copper (5.53%), and chloride (3.87%). The thermal stability of the synthesized Cu/C catalyst was examined by TGA and details are presented in the supporting information (Figure S1). The initial weight loss up to 100 °C was ascribed to the evaporation of H_2O. Subsequent weight loss in the 150–250 °C range may be ascribed to the carbonization of glucose, and further weight loss was due to the carbonization and evaporation of carbon.[34] The next degradation step was allocated to the decomposition of the hydroxyl and sulfuric groups and the molecular chains of APTES.

XPS was utilized to determine the surface components of the Cu/C sample and the results are shown in Figure 3. The Cu/C sample was prepared in KBr pellets prior to XPS analysis. The survey spectra of Cu/C catalyst revealed the presence of Cu2p, O1s, N1s, C1s, S2p, and Si2p photoelectrons with binding energies 930.6, 932.6, 529.8, 399.8, 282, 166.5, and 100.0 eV, respectively, as shown in Figure 3a. XPS peaks at 285, 529.8, and 166.5 eV correspond to C, O, and S atoms of the Cu/C catalyst.[35] The peak at 399.8 eV shown by the presence of N1s confirms the immobilization of APTES on the surface of the Cu/C catalyst.[36] The peaks at 100.0 eV correspond to the binding energy of Si. Copper exists in Cu^{2+} oxidation state, which was confirmed by the presence of Cu $2p^{1/2}$ and Cu $2p^{3/2}$ peaks with binding corresponding energies of 952.6 eV and 932.6 along with their satellite peaks at 940.8 and 960.6 eV, respectively, as shown in the high-resolution spectra of the Cu2p region.[37–39] The XPS spectra also showed binding energy of 930.6 eV, which corresponds to copper present in the metallic state on the catalyst surface as shown in Figure 3b–f.[40] The loading of Cu in the synthesized Cu/C catalyst was found to be 2.86 wt.%, as determined by ICP-MS.

3.1 | Synthesis of propargylamines (4aaa) from carbonyl compounds

Using the Cu/C catalyst, we investigated the multicomponent reaction of various aldehydes, amines, and



SCHEME 2 Preparation of biomass-derived copper (Cu/C) catalyst

alkynes. Initially, the catalytic activity of Cu/C catalyst was studied for the A^3 coupling reaction of furfural (1.04 mmol), piperidine (1.05 mmol), and phenylacetylene (1.02 mmol) as model substrates for optimizing reaction conditions such as solvent, temperature, catalyst loading, and time (Table 1). The required product was not obtained for the reaction without the Cu/C catalyst (Table 1, entry 1). By contrast, the reaction yield reached 49% simply by using 10 mg (0.0045 mmol Cu) of Cu/C catalyst in the presence of toluene at 80 °C (Table 1, entry 2). The reaction product was initially examined using gas chromatography (GC)–MS (Figure S3). Under similar reaction conditions utilizing Cu/C catalyst in various other solvents (EtOH, tetrahydrofuran [THF], DMSO, and H_2O) product yields was lower (Table 1, entries 3–6). Meanwhile, the reaction carried out under solvent-free condition at 80 °C for only 3 h gave a high yield of **4aaa** (Table 1, entry 7). Moreover, when the amount of Cu/C catalyst added was reduced to 5 mg (0.0022 mmol Cu) under the same reaction conditions, a similar product yield (91%) of **4aaa** was obtained (Table 1, entry 8). The catalytic reaction continued to occur quantitatively when the temperature was at 90 and 100 °C with yields of 92% and 91%, respectively (Table 1, entries 9 and 10). Consequently, we identified the optimal A^3 coupling reaction conditions using our

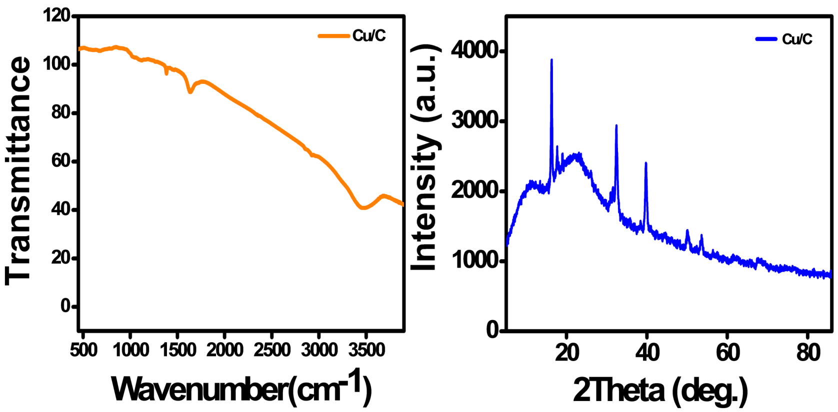
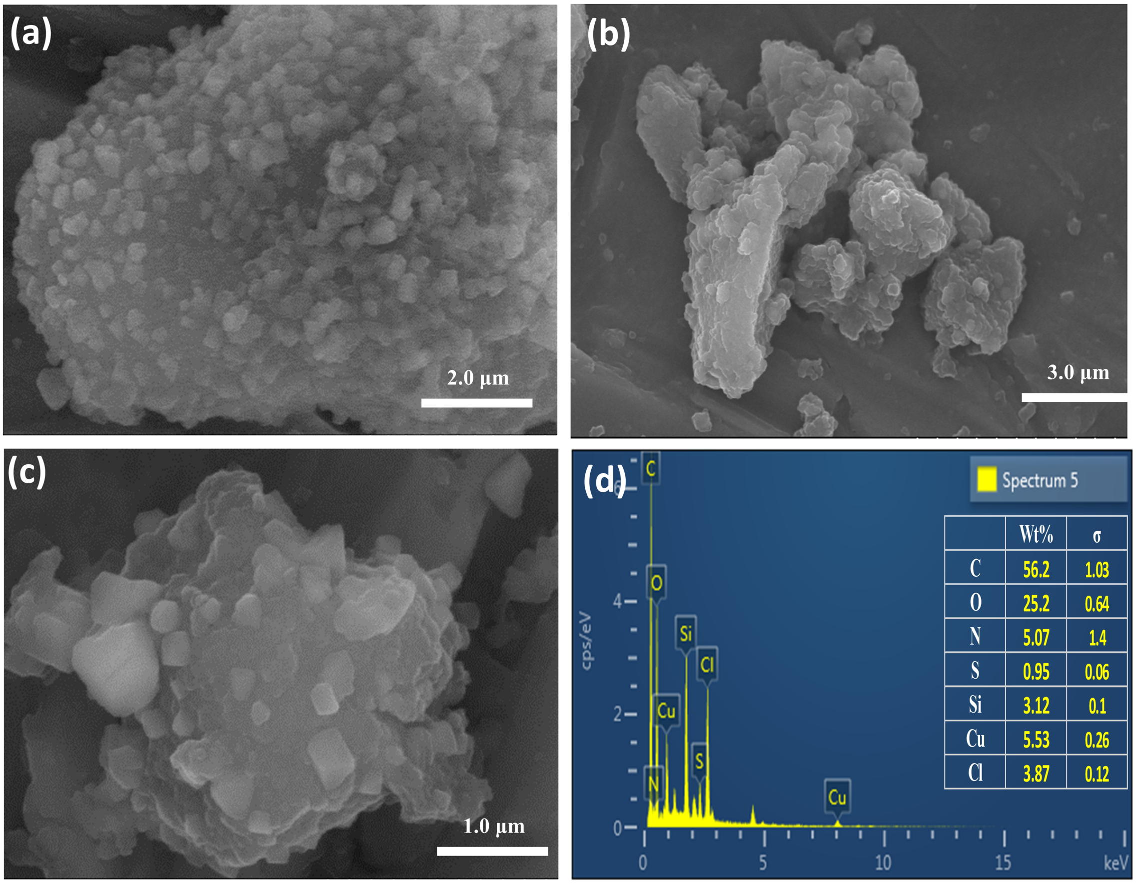


FIGURE 1 (a) Fourier transform infrared spectrum of the Cu/C catalyst, and (b) X-ray powder diffraction spectrum of the Cu/C catalyst



	Wt%	σ
C	56.2	1.03
O	25.2	0.64
N	5.07	1.4
S	0.95	0.06
Si	3.12	0.1
Cu	5.53	0.26
Cl	3.87	0.12

FIGURE 2 Scanning electron microscopy (a–c) image of Cu/C catalyst, and (d) energy-dispersive X-ray image of the Cu/C catalyst

heterogenous catalyst to be 5 mg (0.0022 mmol Cu) of Cu/C catalyst under solvent-free conditions at 80 °C. These results suggest that the synthesized Cu/C catalyst provides a promising approach to the solvent-free A^3 coupling reaction at low metal loadings.

To expand the scope of the synthesis of propargylamines (**4aaa**) in solvent-free condition via the A^3 coupling reaction, we studied various aldehydes which were reacted with phenylacetylene and different amines under the optimized catalytic conditions: 5 mg (0.0022 mmol Cu) of Cu/C catalyst loading, solvent-free condition, and at 80 °C (Table 2). The initial investigation of the biomass-derived furfural, with piperidine and phenylacetylene, has been utilized as model substrate for the study of A^3 coupling reaction. Utilizing various amines such as the cyclic (piperidine, *n*-methyl aniline, diphenylamine) and acyclic (diethylamine and diisobutylamine) secondary amines provided good yield (isolated) of products (**4aaa–4aea**) under the reaction solvent-free conditions. A^3 coupling of benzaldehyde (**1b**) and (piperidine) **2a**, (n-methyl aniline) **2b**, (aniline) **2f**, and (benzylamine) **2g** with (phenylacetylene) **3a** provided the corresponding coupling products (**4baa**, **4bba**, **4bfa**, and **4bga**) in excellent yields. We have additionally studied the primary amines such as aniline and benzylamine in the solvent-free A^3 coupling reaction. It is determined in the literature that it is difficult to produce coupling products using primary amines because primary amine typically produces imine rather than iminium species, which are very less environment friendly as compared with iminium species, to initiate the further reaction with the terminal alkyne. The results indicate that aromatic aldehyde with functional groups such as $-NO_2$, –Cl, and –OH demonstrate good to excellent yield (**4caa, 4daa, and 4eaa**). The isolated reaction products were analyzed by ^1H and ^{13}C nuclear magnetic resonance (Supporting information).

3.2 | One-pot synthesis of furyl-containing propargylamines (6aaa) from xylose (5a)

Achieving one-pot synthesis of furyl-containing propargylamines (**6aaa**) from xylose (**5a**) remains a challenge, as one has to overcome the issues related to the separation and purification of intermediates (i.e. furfural), while saving cost, time, energy, and solvent. For the one-pot synthesis of **6aaa** from **5a**, which is an important

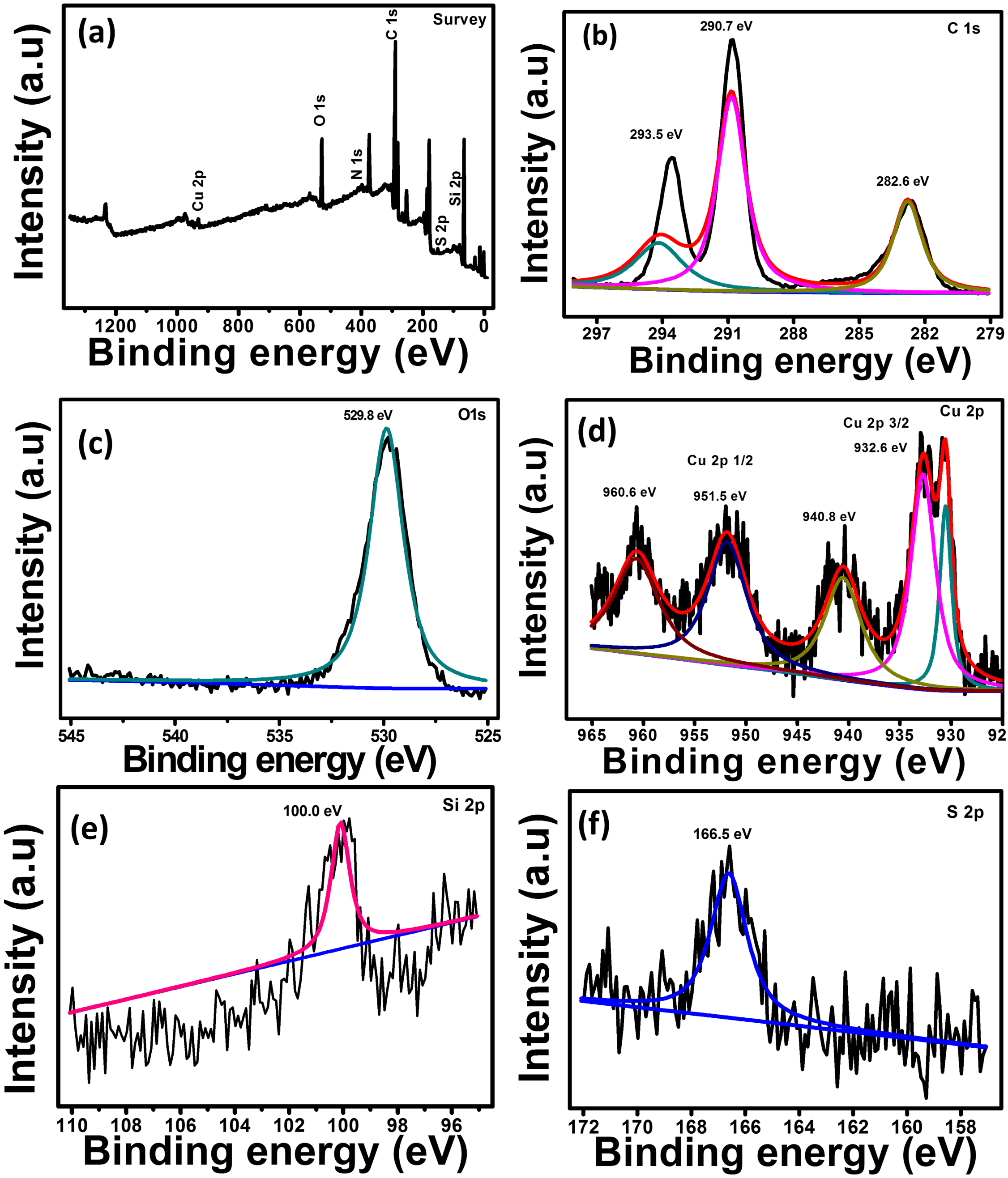
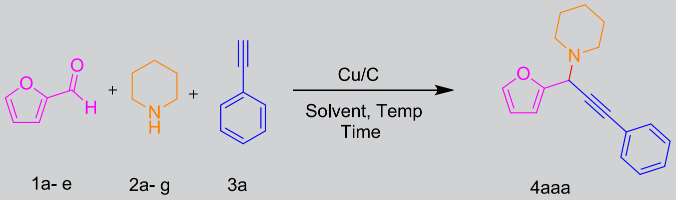


FIGURE 3 High-resolution X-ray photoelectron spectroscopy (XPS) spectra: (a) survey XPS spectra of Cu/C catalyst, and (b–f) high-resolution XPS of C1s, O1s, Cu2p, Si2p, and S2p, respectively

component of biomass and is also inexpensive and easily available, we initially selected xylose, piperidine, and phenylacetylene as substrates to screen reaction conditions. The results are presented in Table S1. Initially, we have studied the effect of different solvents in the reaction using 10 mg (0.0045 mmol Cu) of Cu/C catalyst at 100 °C. EtOH, THF, toluene, DMSO, and H_2O were screened, among which DMSO provided the good yield (Table S1, entries 1–5). Further, we have optimized the reaction temperature for **6aaa** formation and yields of 46% (110 °C), 82% (120 °C), and 81%(130 °C) were achieved in the presence of 10 mg (0.0045 mmol Cu) of catalyst (Table S1, entries 6–8). With increased Cu/C catalyst loading, the product yield did not significantly improve (Table S1, entry 9). However, if it was reduced from 10 to 5 mg, the product yield decreased to 42% (Table S1, entry 10). Subsequently, we have optimized 10 mg (0.0045 mmol Cu) of Cu/C catalyst in the presence of DMSO as solvent at 120 °C, which was an ideal condition for the one-pot synthesis of **6aaa** from **5a**. The synthesis of **6aaa** using **5a** via the A^3 coupling reaction is one of the most appealing reactions as it consistently involves multistep. The dehydration

TABLE 1 Optimization of the A^3 coupling reaction condition [a]



S. no	Solvent (5 mL)	Cu/C (mg)	Temp (°C)	Time (h)	Yield[b] (%)
1	Toluene	—	80	24	—
2	Toluene	10	80	24	49
3	Ethanol	10	80	24	37
4	Tetrahydrofuran	10	80	24	12
5	Dimethyl sulfoxide	10	80	24	43
6	Water	10	80	24	Trace
7	Neat	10	80	3	92
8	Neat	5	80	5	91
9	Neat	5	90	5	92
10	Neat	5	100	4	91

[a] Reaction conditions: furfural (1.04 mmol), piperidine (1.05 mmol), phenylacetylene (1.02 mmol), Cu/C (5 mg, 0.0022 mmol Cu), N_2 atmosphere.

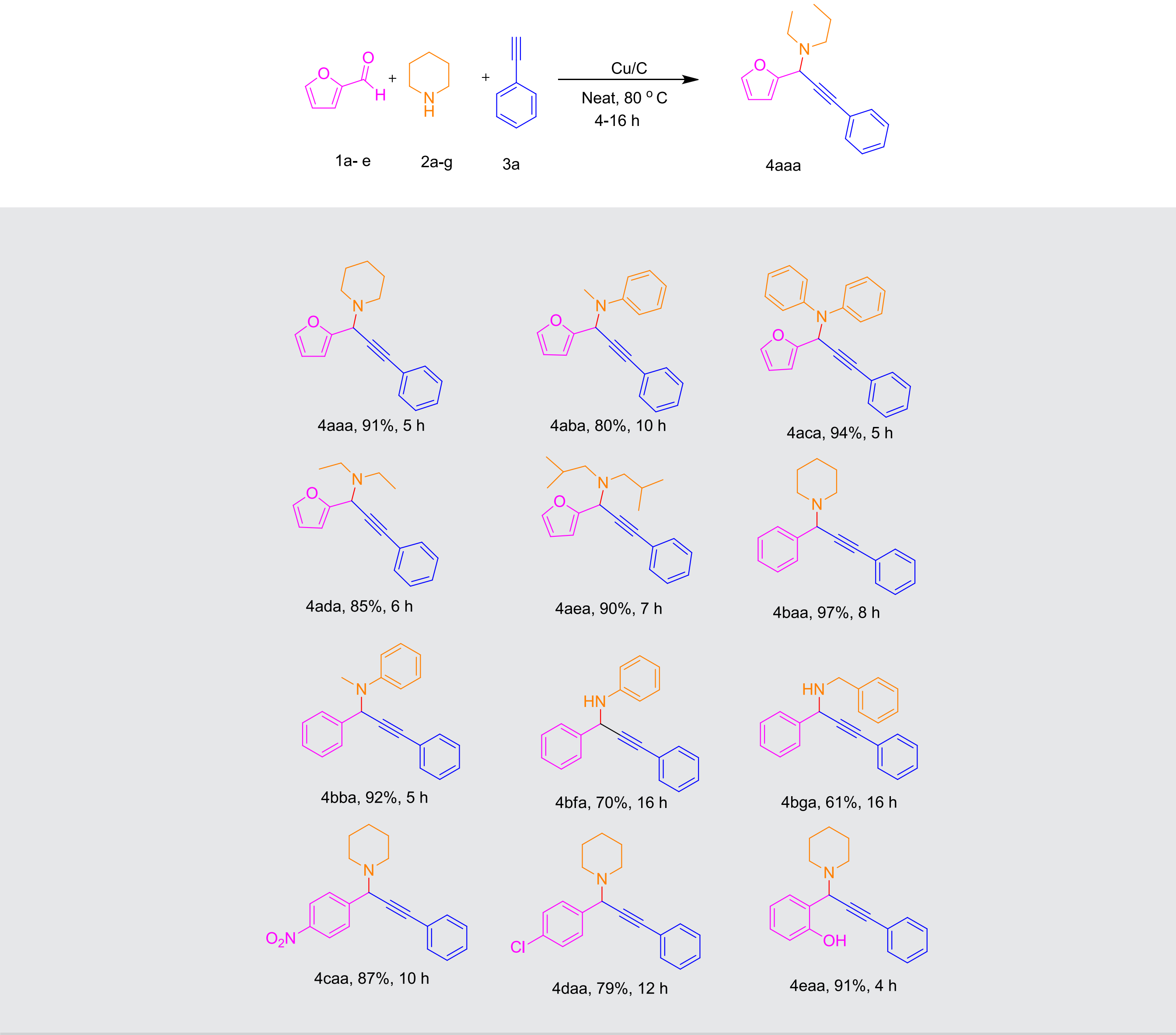
[b] Isolated yields.

of **5a** to furfural is the initial step (the furfural was examined using GC–MS and high-performance liquid chromatography; Figures S4 and S5), and subsequent steps involve the reaction of furfural with a secondary amine to produce iminium intermediate. By contrast, the Cu/C catalyst can activate the terminal C–H bond of phenylacetylene through the formation of Cu–acetylide as an intermediate. The desired **6aaa** products can be achieved via the coupling reaction of Cu–acetylide and iminium.[41] However, several transformations could be performed in a sequence as it avoids isolation of intermediate.

We have expanded the scope of the synthesis of **6aaa** from **5a** via the A^3 coupling reaction as shown in Table 3. Dehydration of **5a** to furfural involved coupling reaction with amines and phenylacetylene to give the corresponding furyl-containing propargylamines (**6aaa, 6aca, 6ada,** and **6aca**) in isolated yield as shown in Table 3. A^3 coupling of (xylose) **5a** and piperidine (**2a**), diphenylamine (**2c**) with phenylacetylene (**3a**) provided the corresponding coupling products **6aaa** and **6aca** in excellent yields. In addition, we have studied aliphatic amine **2d** and **2h** (diethylamine and diisopropylamine, respectively) substituents that underwent the A^3 coupling reaction and produced products **6ada** and **6aha** in good isolated yield. These clearly show that the A^3 coupling reaction using only 10 mg (0.0045 mmol Cu) of Cu/C catalyst loading is successful.

The plausible reaction mechanism is illustrated in Scheme 3. We thus believe it should be very promising in terms of sustainable chemistry to examine the one-pot, multistep reaction involving **5a** for the formation of **6aaa**. The one-pot synthesis of the biologically critical intermediate from **5a** is also very essential aspect. The synthesis of **6aaa** using **5a** via the A^3 coupling reaction is one of the most appealing methods; besides, it consistently involves multistep processes. The dehydration of **5a** to furfural is the initial step. The subsequent step involves the reaction of furfural with a secondary amine to produce iminium intermediate; meanwhile, the Cu/C catalyst can activate the terminal C–H bond of phenylacetylene through the formation of Cu–acetylide as an intermediate. The desired **6aaa** products can be achieved via the coupling reaction of Cu–acetylide and iminium.[42] Cu particles in the synthesized biomass-derived Cu/C catalyst coordinate with electronegative atom, such as the nitrogen in the amine functionality on the surface of the catalyst. The electron-donating character improves the catalytic activity of copper especially in the

TABLE 2 Study of substituted scope for the A^3 coupling reaction product[a]



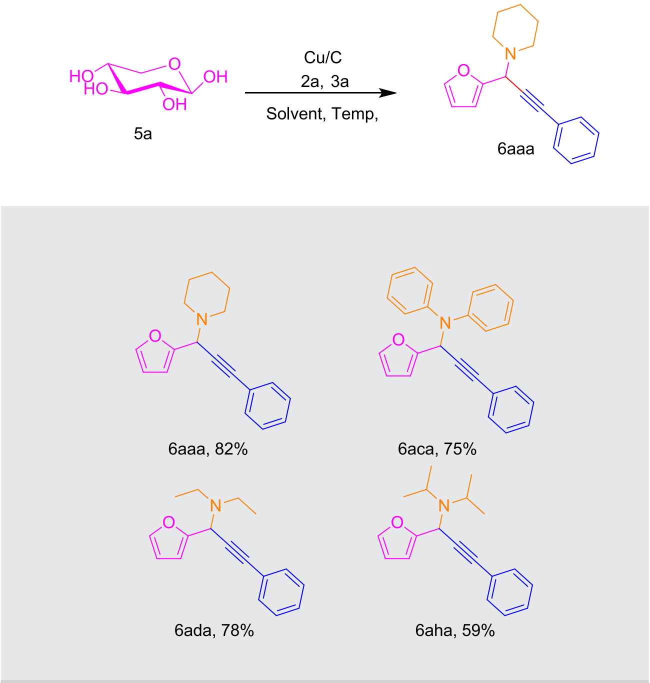
[a] Reaction conditions: furfural (1.04 mmol), piperidine (1.07 mmol), phenylacetylene (1.02 mmol), Cu/C (5 mg, 0.0022 mmol Cu), 80 °C, neat, N_2 atmosphere, isolated yields are reported.

A3-coupling reaction.[43] Economical point of view, one-pot synthesis of furyl-containing propargylamines is highly significant.

3.3 | Catalytic reduction of 4-NP

Substituted nitro compounds are utilized in the manufacture of pesticides, pharmaceutical solvents, and drugs. Among the nitroarenes, 2-NP and 4-NP are considered significant class of environmental pollutants by the US Environmental Protection Agency. In the catalytic degradation process, 4-NP can be transformed to 4-AP, which is less toxic and can be utilized as a valuable pharmaceutical intermediate (e.g. paracetamol).[25,44] To date, noble metals or transition metals have received much attention for the catalytic reduction of 4-NP. However, developing simple, low metal loading, low-cost, green process with less hazardous catalysts having superior performance for the catalytic reduction of 4-NP is still highly demanded. In our study, we achieved the selective catalytic reduction of 4-NP in the presence of only 3 mg (0.0013 mmol Cu) of Cu/C catalyst and sodium borohydride (10 mmol) under mild reaction conditions.

TABLE 3 One-pot synthesis of furyl-containing propargylamines from xylose[a]



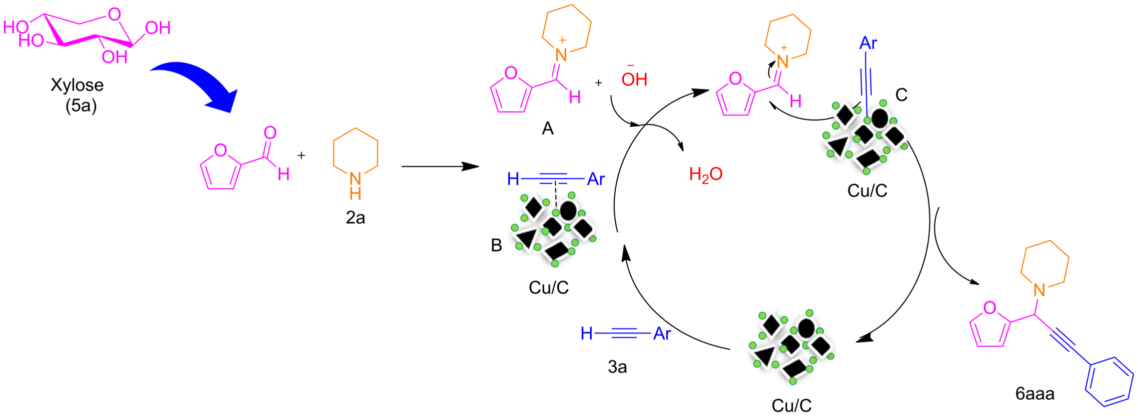
[a]Reaction conditions: xylose (0.1 mmol), piperidine (1.07 mmol), phenylacetylene (1.02 mmol), Cu/C 10 mg (0.0045 mmol Cu), dimethyl sulfoxide (5 mL), 20 h, 120 °C, N_2 atmosphere, isolated yields are reported.

3.4 | Catalytic performances and reduction reaction mechanism

We next examined the activity of Cu/C catalyst in the reduction of the 4-NP in the presence of $NaBH_4$ as model substrate by UV–Vis spectroscopy analysis. The 4-NP solution showed a light-yellow color and exhibited the absorbance at 316 nm. When the reducing agent ($NaBH_4$) was added into 4-NP, the absorbance peak shifted to 400 nm, and the reaction mixture became bright yellow. This color change is attributed to the production of 4-nitrophenolate ions at increased alkalinity of the mixture (Figure 4a, c). Moreover, the peak intensity of 4-nitrophenolate ions (400 nm) without utilizing a Cu/C catalyst did not show any change for a long period. This suggests that without the Cu/C catalyst, the catalytic reduction of 4-NP did not proceed (as presented in Figure 4b). However, when a small amount of Cu/C catalyst was added into the reaction mixture, the absorbance peak intensity at 400 nm drastically decreased and a new absorbance peak at 305 nm gradually increased, which can be attributed to 4-AP (Figure 4d). The catalytic reduction of 4-NP was accomplished within 100 s using the Cu/C catalyst. After the reduction reaction, the reaction solution becomes colorless. The reduction of 4-NP using the Cu/C catalyst under mild optimal conditions (Figure 4e, f) exhibited a linear relationship between $\ln(C_t/C_0)$ and reaction time t. The reaction rate constant calculated from the equation $\ln(C_t/C_0) = k_t$ was $0.028\ s^{-1}$. The catalytic reduction reaction follows the pseudo-first-order kinetics. The rate constant (k) is calculated using the following equation

$$dC_t/d_t = k\,C_t \text{ or } \ln(C_t/C_0) = \ln(A_t/A_0) = \text{-}kt$$

The rate constants of the samples were calculated from the from the slope of $\ln(C_t/C_0)$ versus time, where C_t refers to the absorbance at time $t_{(sec)}$, and C_0 refers to the initial absorbance. Thus, the low-metal-loaded catalyst presented superior catalytic activity for the reduction of 4-NP to 4-AP with $NaBH_4$ in the presence of H_2O. The catalytic reduction of 4-NP utilizing the Cu/C catalyst is an electron-transfer process. The reduction process involved several steps (Scheme 4). In the initial process, 4-NP and BH_4^- diffuse from an aqueous solution to the surface of a Cu/C catalyst via π–π stacking interactions.



SCHEME 3 The plausible reaction mechanism for the synthesis of furyl-containing propargylamines

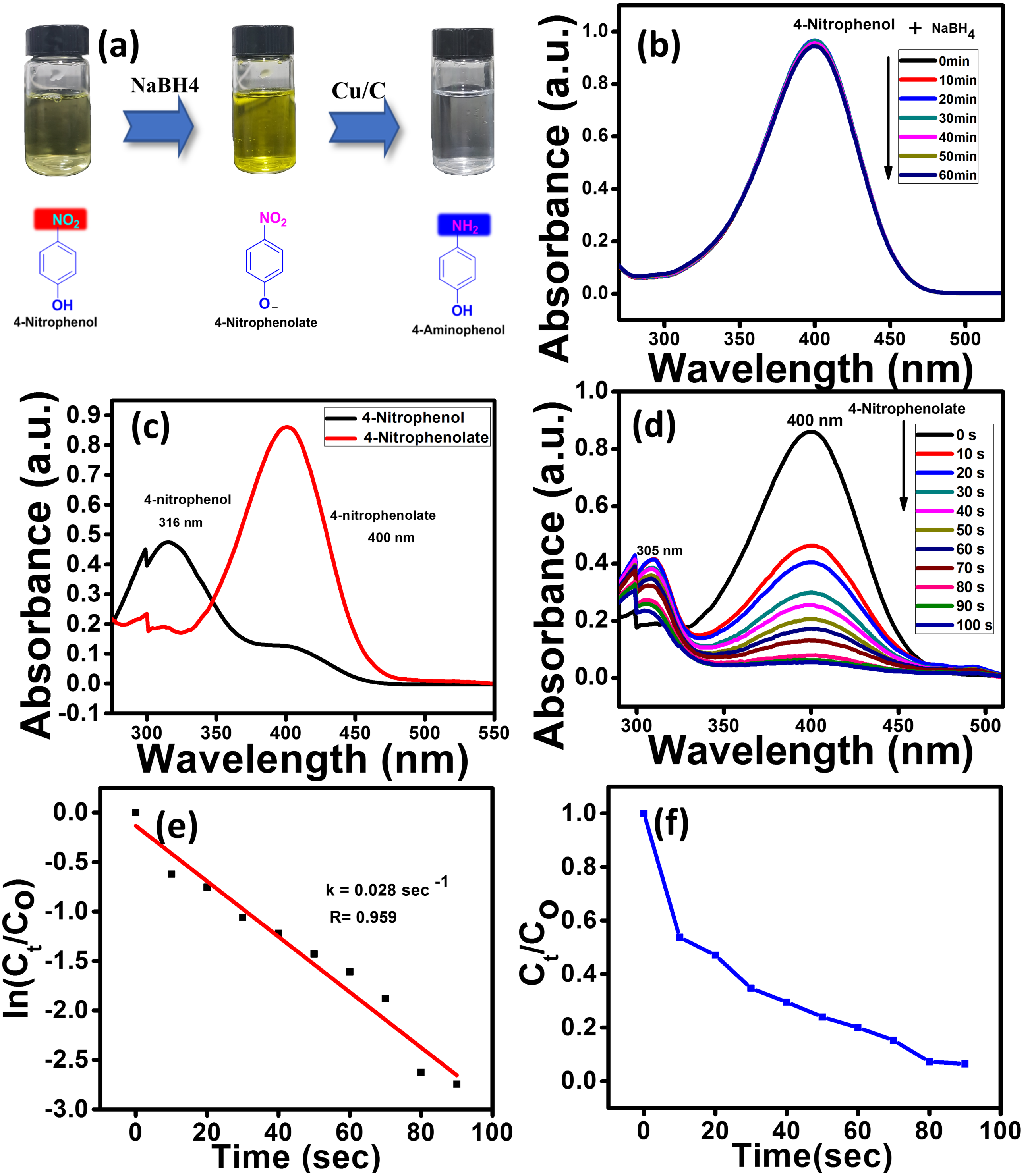
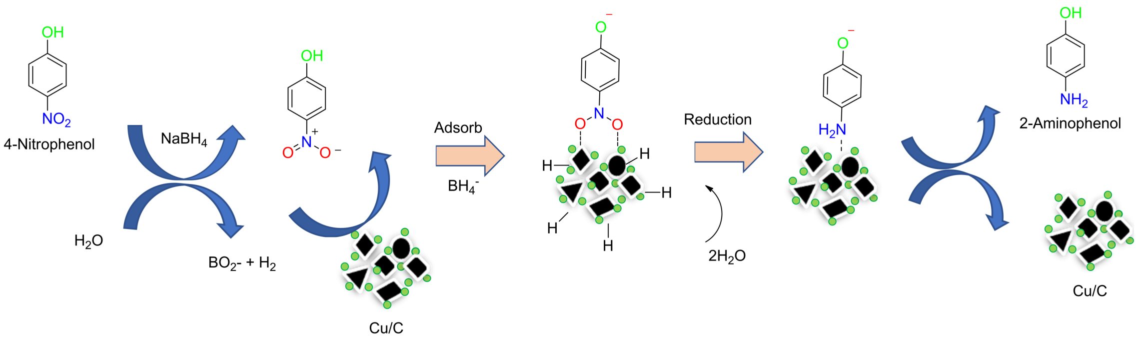


FIGURE 4 UV–Visible (UV–Vis) spectra of (a) 4-nitrophenol (4-NP) before and after addition of $NaBH_4$ solution, (b) 4-NP with $NaBH_4$ without the addition of any catalysts (4-nitrophenolate), (c) 4-NP before and after addition of $NaBH_4$ solution, and (d) time-dependent UV–Vis absorption spectra for the catalytic reduction, (e, f) linear relationship between $\ln(C_t/C_0)$ and reaction time t

In the subsequent step, after electron transfer from BH_4^- and 4-NP near the Cu/C catalyst as the electron mediator, the hydrogen atoms, which are from BH_4^-, attack 4-NP and reduce it. Finally, the corresponding 4-AP was desorbed from the surface of the catalyst.[45]

3.5 | Catalytic reduction of substituted nitro compounds

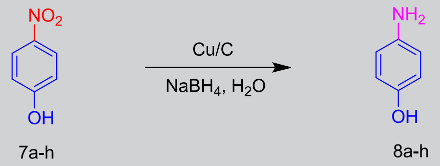
The general applicability of the Cu/C catalyst for catalytic reduction of 4-NP with $NaBH_4$ was evaluated and the



SCHEME 4 A plausible mechanism for the catalytic reduction of 4-nitrophenol

best reaction condition has been screened, with results summarized in Table 4. Initially, we examined the reaction solvent (Table 4). The utilization of solvent (EtOH) as reaction medium in the presence of 10 mg of Cu/C catalyst (0.0045 mmol Cu) achieved only 43% of 4-NP to 4-AP conversion in 1 h at 25 °C. This is due to the complete insolubility of $NaBH_4$ in EtOH (Table 4, entry 1). When we used the biphasic solvent system with the ratio of H_2O:EtOH (1:1), the conversion of 4-NP increased to 65% in 1 h (Table 4, entry 2). Moreover, using THF and MeOH solvent as the reaction medium, the catalytic reduction of 4-NP was 3.5% and 29%, respectively, in 1 h. It can be seen that when utilizing only H_2O as the solvent, the conversion was 79% in 1 h. By increasing the reaction time to 1.5 h, the catalytic reduction of 4-NP was 99% (Table 4, entries 3–6). After identifying the ideal reaction solvent, we optimized the catalyst concentration (Table 4, entries 7 and 8). The best reaction conditions for the catalytic reduction of 4-NP (0.1 g) are as follows: H_2O (reaction solvent), 10 mmol of $NaBH_4$, and only 3 mg (0.0013 mmol Cu) of catalyst at 25 °C. Table 4, entries 9 and 10 show that without utilizing a Cu/C catalyst and in the absence of $NaBH_4$, the catalytic reduction reaction did not show any conversion. The excellent performance of the synthesized Cu/C catalyst can be attributed to the following reasons: first, the electron-rich amino groups act as an electron donor to enrich the electron of the Cu species on the catalyst, and second, the

TABLE 4 Optimization of the 4-nitrophenol reduction reaction[a]



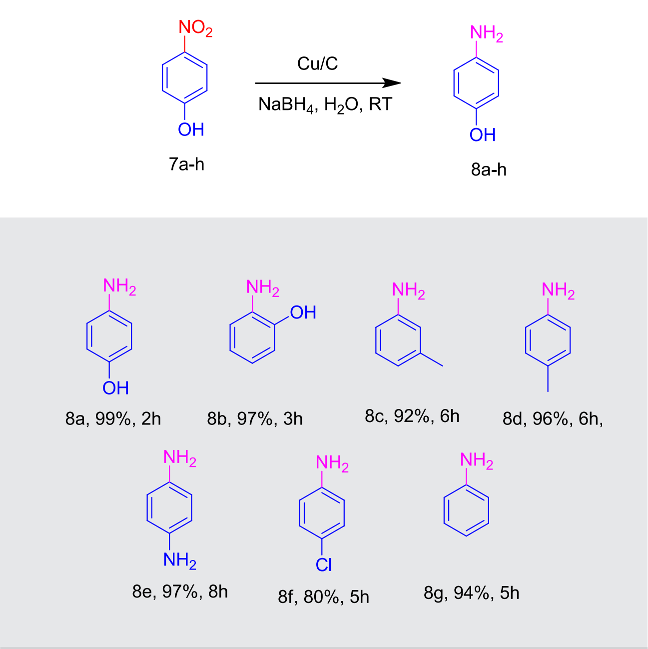
S. no	Cu/C (mg)	Solvents (5 mL)	Time (h)	Yield[b] (%)	Selectivity[b] (%)
1	10	Ethanol	1	43	100
2	10	Ethanol/Water	1	65	100
3	10	Water	1	79	100
4	10	Tetrahydrofuran	1	3.5	100
5	10	Methanol	1	29	100
6	10	Water	1.5	99	100
7	5	Water	2	99	100
8	3	Water	2	99	100
9	—	Water	1	—	—
10[c]	3	Water	1	—	—

[a] Reaction conditions: 4-nitrophenol (0.1 g), Cu/C (3 mg, 0.0013 mmol Cu), $NaBH_4$ (10 mmol), H_2O (10 mL), room temperature.
[b] Isolated yields.
[c] Without $NaBH_4$.

4-NP is likely to adsorb on the Cu/C catalyst with rich electron density as a result of its strong electron-withdrawing properties. Consequently, outstanding selectivity could be attained.[46]

To expand the scope of Cu/C catalyst application for substituted nitro compounds reduction (Table 5), the reduction of 2-NP utilizing the catalyst was also evaluated. A lower yield compared with the catalytic reduction of 4-NP at room temperature (**8a**, **8b**) was achieved. Furthermore, for the catalytic reduction of 3-nitrotoluene and 4-nitrotoluene, no demethylation was observed, with achieved yields of 92% and 96%, respectively, at room temperature and without affecting the C–CH_3 bond (**8c** and **8d**). Moreover, for 4-nitroaniline, the catalytic reduction reaction was complete in 6 h (**8e**). The Cu/C catalyst was extremely active for the reduction of substituted nitro compounds while functional groups such as –CH_3, –OH, and –NH_2 were not affected. Furthermore, it is worth noting that selective reduction of a nitro compound having halogen functionalities (Cl) with good yield was successfully achieved under optimal reaction conditions (**8f**). The nitrobenzene reduction in the presence of catalyst gave a yield of 94% at 25 °C in 5 h (**8g**). All these nitro-substituted compounds were reduced in the presence of Cu/C catalyst (3 mg, 0.0013 mmol Cu) with excellent yields and afforded highly selective products. Synthesized biomass-derived Cu/C catalysts having electron-donating functional groups have strong coordination of copper species that have a positive effect on the surface of the catalyst.[47] Furthermore, when dispersed in water, catalyst surface becomes highly negatively charged as a result of ionization of phenolic hydroxyl groups, sulfuric acid, carboxylic acid, and amine on the Cu/C catalyst sheets. Because of the electron-donating character, the catalytic activity of copper is improved, especially in the catalytic reduction of 4-NP.[48] The significance of electron-donating support groups offer a promising approach for attractive catalytic performance in other reactions.[27] A comparative study of the reported synthesis of propargylamines and reduction of 4-NP is summarized in Table S2. These results clearly suggest that the Cu/C catalyst is extremely active for the synthesis of propargylamines and catalytic reduction of 4-NP. Recycling experiments for the synthesis of propargylamines (**4aaa**) from furfural and reduction of 4-NP using Cu/C catalyst were conducted under the aforesaid optimal condition. After the completion of reactions, Cu/C catalyst can be recovered using filtration, followed by washing with EtOH and drying in vacuum at 60 °C. Then, the catalyst was directly used in the next run as presented in Figure 5. We also performed XRD characterization of the Cu/C catalyst after the fourth cycle. As seen from Figure S2, whereas the intensity of

TABLE 5 Substrate scope for the reduction of nitroarenes[a]



[a]Reaction conditions: 4-nitrophenol (0.1 g), Cu/C (3 mg, 0.0013 mmol Cu), H_2O (10 mL), $NaBH_4$ (10 mmol), room temperature, isolated yields reported with 100% selectivity.
Abbreviation: RT, room temperature.

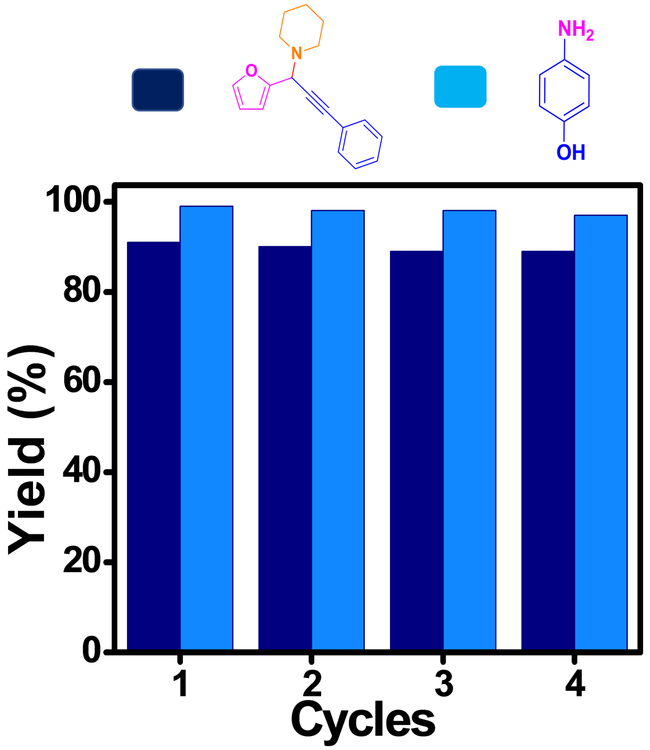


FIGURE 5 Catalytic reusability study of the Cu/C catalyst for the A^3 coupling reaction and catalytic reduction of 4-nitrophenol (4-NP) under optimal conditions

some peaks was reduced, the crystal structure of the catalyst remained intact, which confirms its stability even after four cycles.

4 | CONCLUSION

We have demonstrated a sustainable process for the synthesis of Cu/C catalyst from renewable D-glucose as a precursor. The chemical and structural properties of the prepared Cu/C catalyst were characterized by various analytical techniques such as FT-IR, XRD, SEM, SEM–EDX, TGA, XPS, and ICP-MS. The catalyst showed excellent performance in the synthesis of (**4aaa**) products from furfural via the A^3 coupling reaction, which utilized only 5 mg (0.0022 mmol Cu) of Cu/C catalyst at 80 °C under the solvent-free condition. In addition, the superior catalytic reduction of 4-NP using only 3 mg (0.0013 mmol Cu) of Cu/C catalyst and $NaBH_4$ achieved a 99% yield (100% selectivity) in the aqueous condition at 25 °C and follows the pseudo-first order kinetics. The significant properties of the presented approach are as follows: (i) results support that the synthesized catalyst is cost-effective and environmentally friendly, which is an excellent alternative to classical noble or Cu-based catalysts; (ii) good to excellent yield of the products; (iii) performing organic conversions without the use of harmful solvents (solvent free and with water) under low temperature conditions is also a significant process for green organic synthesis; and (iv) the catalyst is easily recoverable and reusable.

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AUTHOR CONTRIBUTIONS

Pramod Rathod: Conceptualization; investigation; methodology. **John Marc Puguan:** Conceptualization; visualization. **Hern Kim:** Funding acquisition; resources; supervision.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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