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Mannich Reaction of Secondary Amines, Aldehydes and Alkynes in Water Using Cu/C Nanoparticles as a Heterogeneous Catalyst

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The use of 2 mol% of Cu/C nanoparticles, as an easily accessible and inexpensive heterogeneous catalyst, promoted a one-pot three-component condensation of an amine, aldehyde, and an alkyne in water to produce the corresponding propargylamine in good to high yields. This method was proved to be applicable to a wide range of substrates and is especially practical for the synthesis of new azacrown ether derivatives. The catalyst was quantitatively recovered from the reaction by a simple filtration and reused for at least ten times with almost consistent activity.

Keywords: Mannich reaction, Cu/C nanoparticles, Heterogeneous catalyst, Water, Azacrown ether and anthraquinone derivatives

INTRODUCTION

One-pot multicomponent coupling reactions (MCRs) have received much attention in recent years [1]. Especially, multicomponent reactions that can be run under solvent-free conditions or in water for achieving atom economy and the identification of catalytic procedures are ideal protocols for the development of environmentally friendly and economical advantageous chemical processes [2].

One of the best examples of such a process is three-component coupling of aldehydes, alkynes, and amines (A^3-coupling) *via* C-H bond activation [3]. The resultant propargylamines acquired from A^3-coupling reactions are frequent skeletons [4] and act as synthetically adaptable key intermediates [5] for the production of many nitrogen-containing biologically active compounds such as conformationally restricted peptides, oxotremorine analogues, β-lactams, isosteres, therapeutic drug molecules and natural products [4b,6].

Several examples of propargylamines synthesis *via* A^3-coupling and transition metal catalysis, iridinum [7a], copper [7b,7c,7d], silver [7e], gold [7f,7g] and zinc [7h], have also been reported very recently [7].

To improve the recovery for reusing, catalyst species have been immobilized onto various supports such as hydroxyapatite [8], layered double hydroxide [9], 12-tungstophosphoric acid [10], alumina [11], silica [2g,12] and zeolites [13].

These heterogeneous catalysts three-component Mannich reactions require functional groups immobilized on a supports. Thus, there is a growing need to find an inexpensive and novel catalyst for the Mannich, one-pot, three-component coupling reactions of formaldehyde, secondary amines and terminal alkynes, in which the reaction should be fast, occur in a single step under mild and convenient conditions.

In the course of our studies on the development of

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heterogeneous [14] catalyzed organic syntheses and as a continued interest to develop Mannich reaction [15], herein we report a highly efficient three-component coupling of aldehydes, alkynes, and amines (A^3-coupling), catalyzed by heterogeneous Cu/C nanoparticles in water for the preparation of propargylamines *via* activation of alkynes under an atmosphere of air.

EXPERIMENTAL

Instrumentation, Analyses and Starting Materials

NMR spectra were recorded on a Bruker Avance DPX-250 (^{1}H NMR 250 MHz and ^{13}C NMR 62.9 MHz) spectrometer in pure deuterated solvents with tetramethylsilane as an internal standard. IR spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instruments at 70 or 20 eV. Melting points determined in open capillary tubes in a Büchi-535 circulating oil melting point apparatus. X-Ray diffraction (XRD, D8, Advance, Bruker, axs) was obtained for characterization of the heterogeneous nanocatalyst. The ICP analysis data were obtained using a Varian Vista-pro analyzer. TEM images were obtained using a transmission electron microscopy (TEM, CN-10, Philips, 100 KV).

The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica gel PolyGram SILG/UV 254 plates. Column Chromatography was carried out on short columns of silica gel 60 (70-230 mesh) in glass columns (2-3 cm diameter) using 15-30 g of silica gel per one gram crude mixture.

The chemicals used were purchased from Fluka, Aldrich and Merck Companies. The activated carbon was also purchased from Merck (Atr. No. 9631, 0.3-.05 mm).

Determination of the Copper Content in Cu/C Catalyst

The Cu/C (100 mg) was extracted with concentrated HCl (5 × 2 ml) in a screw-capped vessel, followed by treatment with concentrated nitric acid (2 ml) to digest the metal complex. The mixture was then transferred into a volumetric flask (100 ml), diluted 1:50 for the second time and was determined by the ICP analysis. The copper concentration was determined an atomic emission wavelength of 324.754 nm with references to a linear (R = 0.99) calibration curve over 1-4 ppm. CuI was also prepared in a manner identical to the sample preparation.

General Procedure

Alkyne (1 mmol), amine (1 mmol), aqueous formaldehyde (37%, 0.4 ml) and catalyst (0.044 g) (2 mol%) were dissolved in 1 ml of water or a mixture of water:EtOH (1:1) and stirred for the indicated time at room temperature or 75 °C. After the reaction completed the whole reaction mixture directly passed through a celite and rinsed with acetone (3 × 15 ml). The recovered nanocatalyst was then dried and stored for another consecutive reaction runs. The acetone was removed by rotation evaporator under vacuum and the residue was purified by chromatography.

4-(3-Phenyl-2-propynyl)morpholine (1). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (20/1), gave compound **1** in 91% yield. IR (neat): 694(s), 760(s), 860(s), 910(w), 1007(m), 1072(m), 1115(s), 1238(m), 1450(s), 1716(s), 2858(s), 2932(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.63 (t, 4H, J = 4.6 Hz), 3.48 (s, 2H), 3.74 (t, 4H, J = 4.5 Hz), 7.25-7.42 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.7, 52.1, 66.5, 83.7, 85.7, 122.8, 128.2, 131.6. Anal. Calcd. for $C_{13}H_{15}NO$ (201.264): C, 77.58; H, 7.51. Found: C, 77.67; H, 7.39.

1-(3-Phenyl-2-propynyl)piperidine (2). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (20/1), gave compound **2** in 90% yield. IR (neat): 690(s), 756(s), 860(m), 995(m), 1034(m), 1111(s), 1304(m), 1443(s), 1678(w), 2797(s), 2854(s), 2935(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.33-1.37 (m, 2H), 1.49-1.57 (m, 4H), 2.46 (t, 4H, J = 4.7 Hz), 3.36 (s, 2H), 7.4-7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 23.8, 25.8, 48.4, 53.3, 84.8, 84.9, 123.2, 127.9, 128.1, 131.6. Anal. Calcd. for $C_{14}H_{17}N$ (199.292): C, 84.37; H, 8.60. Found: C, 84.49; H, 8.47.

N,N-Dibutyl-3-phenyl-2-propyn-1-amine (3). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (20/1), gave compound **3** in 88% yield. IR (neat): 690(s), 756(s), 910(m), 1092(m), 1323(w), 1377(w), 1466(m), 1678(w), 2226(w), 2816(m), 2866(s), 2932(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.93 (t, 6H, J = 7.2 Hz), 1.22-1.55 (m, 8H), 2.54 (t, 4H, J = 7.2 Hz), 3.62 (s, 2H), 7.24-7.68 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 14.0, 20.7, 29.7, 42.6, 53.5,

84.6, 84.9, 123.4, 127.8, 128.1, 131.4. Anal. Calcd. for $C_{17}H_{25}N$ (243.387): C, 83.89; H, 10.35. Found: C, 83.98; H, 10.17.

N,N-Diethyl-3-phenyl-2-propyn-1-amine (4). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (20/1), gave compound **4** in 89% yield. IR (neat): 690(s), 756(s), 1068(m), 1319(m), 1381(w), 1489(m), 1597(w), 2338(w), 2820(m), 2935(s) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 0.98 (t, 6H, J = 7.1 Hz), 2.44 (q, 4H, J = 7.1 Hz), 3.49 (s, 2H), 7.11-7.31 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 12.6, 41.8, 47.2, 84.3, 84.9, 127.4, 127.9, 131.6. Anal. Calcd. for $C_{13}H_{17}N$ (187.281): C, 83.37; H, 9.15. Found: C, 83.52; H, 8.98.

2,2'-(3-Phenyl-2-propynylazanediyl)diethanol (5). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **5** in 88% yield. IR (neat): 760(w), 1072(s), 1048(m), 1570(m), 1655(m), 2878(m), 2943(m), 3356(br) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.78 (t, 4H, J = 5.3 Hz), 3.56-3.71 (m, 6H), 4.37 (s, 2H), 7.26-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 50.6, 55.3, 58.7, 59.6, 83.9, 85.3, 122.8, 128.1, 128.2, 131.6. Anal. Calcd. for $C_{13}H_{17}NO_2$ (219.280): C, 71.21; H, 7.81. Found: C, 71.36; H, 7.68.

1,4-Bis(3-phenyl-2-propynyl)piperazine (6). Purification by flash column chromatography, eluted with n-hexane/ethyl acetate (1/1), gave compound **6** as white powder in 85% yield. M.p.: 103 °C. IR (KBr): 690(s), 752(s), 795(m), 1007(s), 1134(s), 1284(m), 1315(s), 1439(m), 1485(m), 1593(w), 2820(m), 2881(m), 2905(m), 3047(w) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.76 (s, 8H), 3.55 (s, 4H), 7.26-7.45 (m, 10H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.7, 51.9, 84.4, 85.4, 123.1, 128.1, 128.2, 131.3, 131.7. Mass m/z (%): 315 (M^++1, 0.3), 314 (M^+, 3.6), 313(7.4), 312(4.2), 285(2.7), 244(2.8), 209(7.1), 199(23.1), 170(3.9), 149(7.2), 115(100), 94(14.1), 69(17.0). Anal. Calcd. for $C_{22}H_{22}N_2$ (314.424): C, 84.04; H, 7.05. Found: C, 83.89; H, 6.91.

N-Benzyl-N-ethyl-3-phenyl-2-propyn-1-amine (7). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **7** in 82% yield. IR (neat): 694(s), 756(s), 787(s), 1053(w), 1099(w), 1130(w), 1323(m), 1454(m), 1489(m), 1597(w), 2361(w), 2820(m), 2932(m), 2970(m), 3028(w) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.04 (t, 3H, J = 7.2 Hz), 2.56 (q, 2H, J = 7.2 Hz), 3.42 (s, 2H), 3.58 (s, 2H), 7.04-7.37 (m, 10H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 13.1, 41.9, 58.4, 84.7, 85.8, 123.7, 127.3, 127.6, 128.5, 129.4, 131.9, 139.1. Anal. Calcd. for $C_{18}H_{19}N$ (249.350): C, 86.70; H, 7.68. Found: C, 86.87; H, 7.81.

N-Benzyl-3-phenyl-N-(2-phenylethyl)-2-propyn-1-amine (8). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **8** in 79% yield. IR (neat): 694(s), 756(s), 1030(w), 1072(w), 1119(m), 1323(m), 1454(s), 1493(s), 1601(m), 2361(w), 2824(m), 2932(m), 3028(m), 3059(m) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.8(s, 4H), 3.52 (s, 2H), 3.68 (s, 2H), 7.08-7.38 (m, 15H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 34.5, 42.6, 55.6, 58.4, 84.8, 86.0, 123.7, 126.3, 127.7, 128.3, 128.8, 129.4, 129.9, 132.0, 139.0, 140.6. Anal. Calcd. for $C_{24}H_{23}N$ (325.446): C, 88.57; H, 7.12. Found: C, 88.71; H, 6.97.

N-Benzyl-N-ethyl-2-heptyn-1-amine (9). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **9** in 78% yield. IR (neat): 698(s), 737(s), 1030(w), 1323(m), 1601(w), 2361(w), 2820(m), 2932(s), 2962(s), 3028(w) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ= 0.85 (t, 3H, J = 7.2 Hz), 1.01 (t, 3H, J = 7.2 Hz), 1.14-1.43 (m, 4H), 2.15 (t, 2H, J = 2.1 Hz), 2.49 (q, 2H, J = 7.2 Hz), 3.21 (t, 2H, J = 2.2 Hz), 3.53 (s, 2H), 7.11-7.29 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 12.9, 13.9, 18.4, 22.3, 31.2, 41.3, 47.3, 57.7, 74.4, 85.4, 126.7, 127.9, 129.2, 131.8, 138.9. Anal. Calcd. for $C_{16}H_{23}N$ (229.361): C, 83.79; H, 10.11. Found: C, 83.92; H, 9.97.

4-[Benzyl(ethyl)amino]-2-butyn-1-ol (10). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **10** in 80% yield. IR (neat): 698(s), 737(s), 1026(s), 1103(s), 1327(w), 1454(s), 1659(w), 2368(w), 2831(m), 2932(m), 3383(br) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.01(t, 3H, J = 7.2 Hz), 2.50 (q, 2H, J = 7.2 Hz), 3.25 (t, 2H, J = 1.8 Hz), 3.53 (s, 2H), 3.79 (s, 1H), 4.19 (t, 2H, J = 1.8 Hz), 7.11-7.55 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 12.4, 41.1, 47.3, 50.4, 57.6, 79.3, 84.5, 127.3, 128.5, 129.4, 137.4. Anal. Calcd. for $C_{13}H_{17}NO$ (203.280): C, 76.81; H, 8.43. Found: C, 76.67; H, 8.58.

5-[Benzyl(ethyl)amino]-2-methyl-3-pentyn-2-ol (11). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **11** in 79% yield. IR (neat): 698(s), 737(s), 949(s), 1169(s), 1230(m), 1327(w), 1362(m), 1454(s), 2380(w), 2824(m), 2932(s) 3028(w), 3383

(br) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 1.29 (t, 3H, J = 7.2 Hz), 1.76 (s, 6H), 2.80 (q, 2H, J = 7.2 Hz), 3.40 (s, 1H), 3.53 (s, 2H), 3.79 (s, 2H), 7.42-7.59 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 12.6, 31.9, 40.9, 47.3, 57.6, 64.7, 76.1, 90.9, 127.9, 128.2, 129.6, 138.4. Anal. Calcd. for $C_{15}H_{21}NO$ (231.333): C, 77.88; H, 9.15. Found: C, 78.02; H, 9.29.

4-[4-(4-Chlorophenoxy)-2-butynyl]morpholine (12). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **12** in 79% yield. IR (neat): 825(s), 864(m), 1007(s), 1115(s), 1223(s), 1288(m), 1454(w), 1493(s), 1593(w), 2361(w), 2854(m), 2924(m) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.43 (t, 4H, J = 4.7 Hz), 3.23 (t, 2H, J = 1.9 Hz), 3.64 (t, 4H, J = 4.8 Hz), 4.62 (t, 2H, J = 1.9 Hz), 6.82 (dd, 2H, J_1 = 6.8, J_2 = 2.3 Hz), 7.17 (dd, 2H, J_1 = 6.8, J_2 = 2.3 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.4, 52.2, 56.3, 66.4, 79.8, 82.7, 114.5, 116.3, 126.3, 129.3, 156.1. Anal. Calcd. for $C_{14}H_{16}ClNO_2$ (265.735): C, 63.28; H, 6.07. Found: C, 63.09; H, 6.22.

4-[4-(4-Nitrophenoxy)-2-butynyl]morpholine (13). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **13** in 75% yield. IR (neat): 690(m), 752(s), 860(s), 1003(m), 1111(s), 1230(s), 1454(m), 1512(s), 1593(s), 2341(w), 2816(m), 2854(m), 2920(m), 3082(w) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.44 (t, 4H, J = 4.6 Hz), 3.27 (t, 2H, J = 1.9 Hz), 3.64 (t, 4H, J = 4.8 Hz), 4.76 (t, 2H, J = 1.9 Hz), 6.98 (dd, 2H, J_1 = 9.3, J_2 = 2.3 Hz), 8.13 (dd, 2H, J_1 = 7.1, J_2 = 2.2 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.1, 52.0, 56.5, 66.5, 78.8, 83.5, 114.3, 125.6, 141.7, 162.4. Mass m/z (%): 278 (M^++2, 0.5), 277 (M^++1, 5.5), 276 (M^+, 10.6), 259(11.3), 167(2.2), 149(10.1), 138(59.6), 108(85.6), 86(53.5), 69(44.4), 53(100). Anal. Calcd. for $C_{14}H_{16}N_2O_4$ (276.288): C, 60.86; H, 5.84. Found: C, 60.71; H, 5.68.

4-[4-(4-Methylphenoxy)-2-butynyl]morpholine (14). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **14** in 77% yield. IR (neat): 814(s), 864(s), 1007(s), 1115(s), 1176(w), 1219(m), 1292(w), 1454(m), 1512(s), 1612(w), 1713(w), 2361(w), 2812(m), 2854(m), 2924(m) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.28 (s, 3H), 2.51 (t, 4H, J = 4.7 Hz), 3.30 (t, 2H, J = 1.8 Hz), 3.71 (t, 4H, J = 4.7 Hz), 3.46 (t, 2H, J = 1.8 Hz), 6.86 (d, 2H, J = 8.6 Hz), 7.08 (d, 2H, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 20.5, 47.4, 52.3, 56.2, 66.8, 80.5, 82.1, 114.8, 128.2, 129.8, 130.6, 131.7, 155.5. Anal. Calcd. for $C_{15}H_{19}NO_2$ (245.317): C, 73.44; H, 7.81. Found: C, 73.26; H, 7.63.

1-Chloro-4-{[4-(4-morpholinyl)-2-butynyl]oxy}-9H-thioxanthen-9-one (15). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **15** in 80% yield. M.p.: 120-122 °C. IR (KBr): 740(m), 818(m), 856(m), 945(m), 1007(m), 1041(m), 1115(s), 1253(s), 1292(s), 1431(s), 1577(s), 1647(vs), 2827(m), 2924(m) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.49 (t, 4H, J = 4.7 Hz), 3.31 (t, 2H, J = 1.9 Hz), 3.67 (t, 4H, J = 4.7 Hz), 4.93 (t, 2H, J = 1.9 Hz), 7.13 (dd, 1H, J_1 = 8.7, J_2 = 2.2 Hz), 7.40-7.58 (m, 4H), 8.42 (dd, 1H, J_1 = 8.0, J_2 = 0.8 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.3, 52.2, 57.6, 66.6, 78.9, 83.8, 114.1,125.8, 126.5, 128.2, 129.0, 129.4, 130.7, 131.9, 135.3, 150.8, 179.9. Mass m/z (%): 401 (M^++2, 1.0), 400 (M^++1, 3.6), 399 (M^+, 11.7), 364(1.6), 314(7.1), 262(41.3), 234(12.1), 205(20.1), 170(19.1), 138(100), 100(90.5), 55(93.5). Anal. Calcd. for $C_{21}H_{18}ClNO_3S$ (399.891): C, 63.07; H, 4.54. Found: C, 63.21; H, 4.45.

4-Methyl-1-{[4-(4-morpholinyl)-2-butynyl]oxy}-9H-thioxanthen-9-one (16). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **16** in 84% yield. IR (neat): 864(m), 1007(m), 1072(w), 1115(s), 1273(m), 1439(m), 1678(vs), 2361(w), 2854(m), 2951(m) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.17 (s, 3H), 2.24 (t, 4H, J = 4.6 Hz), 3.05 (t, 2H, J = 1.8 Hz), 3.44 (t, 4H, J = 4.7 Hz), 4.68 (t, 2H, J = 1.9 Hz), 6.79 (d, 1H, J = 8.3 Hz), 7.09-7.32 (m, 4H), 8.18 (d, 1H, J = 7.9 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 19.2, 47.4, 52.2, 57.7, 66.7, 80.2, 82.9, 112.0, 120.6, 125.3, 125.8, 126.3, 126.7, 129.3, 131.5, 133.4, 134.9, 138.4, 158.0, 180.9. Mass m/z (%): 381(M^++2, 0.6), 380 (M^++1, 1.1), 379 (M^+, 1.0), 264(2.7), 184(15.1), 137(100), 107(25.9), 79(12.2), 53(26.6). Anal. Calcd. for $C_{22}H_{21}NO_3S$ (379.473): C, 69.63; H, 5.58. Found: C, 69.76; H, 5.74.

2-{[4-(4-Morpholinyl)-2-butynyl]oxy}-9H-thioxanthen-9-one (17). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **17** in 78% yield. M.p.: 94-95 °C. IR (KBr): 741(m), 860(w), 1003(m), 1115(s), 1207(w), 1292(w), 1331(s), 1473(s), 1597(m), 1643(s), 2854(w), 2912(w) cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz): δ = 2.51 (t, 4H, J = 4.7 Hz), 3.31 (t, 2H, J = 1.8 Hz), 3.68 (t,

4H, J = 4.7 Hz), 4.85 (t, 2H, J = 1.9 Hz), 7.29 (dd, 1H, J_1 = 10.5, J_2 = 2.9 Hz), 7.46-7.60 (m, 4H), 8.16 (d, 1H, J = 2.8), 8.38 (dd, 1H, J_1 = 8.2, J_2 = 0.8 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.4, 51.9, 56.4, 66.7, 79.6, 83.0, 111.9, 122.9, 125.9, 126.1, 127.3, 128.5, 129.5, 130.0, 132.0, 137.3, 156.2, 179.3. Mass m/z (%): 366 (M^++1, 0.9), 365 (M^+, 3.6), 279(23.7), 228(30.2), 200(25.8), 171(40.9), 138(100), 100(26.5), 56(32.9). Anal. Calcd. for $C_{21}H_{19}NO_3S$ (365.447): C, 69.02; H, 5.24. Found: C, 69.18; H, 5.39.

1,8-Bis{[4-(4-morpholinyl)-2-butynyl]oxy}anthra-9,10-quinone (18). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **18** in 79% yield. IR (neat): 744(m), 860(m), 964(m), 1007(m), 1038(m), 1115(s), 1238(s), 1273(s), 1311(s), 1454(m), 1585(s), 1670(vs), 2357(w), 2854(m), 2920(m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.41(t, 8H, J = 4.7 Hz), 3.23 (t, 4H, J = 1.7 Hz), 3.61 (t, 8H, J = 4.7 Hz), 4.9 (t, 4H, J = 1.5 Hz), 7.41 (dd, 2H, J_1 = 8.4, J_2 = 1.0 Hz), 7.58 (t, 2H, J = 7.8 Hz), 7.82 (dd, 2H, J_1 = 7.7, J_2 = 1.0 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 47.1, 51.9, 57.2, 66.4. 79.6, 83.3, 119.7, 120.7, 124.6, 133.5, 134.5, 156.9, 162.1, 181.9, 183.2. Anal. Calcd. for $C_{30}H_{30}N_2O_6$ (514.569): C, 70.02; H, 5.88. Found: C, 69.89; H, 6.03.

7-{4-[(8-{[4-(3,11-Dioxo-3,4,5,6,9,10,11,12-octahydro-2H-1,13,4,7,10-benzodioxatriazacyclopentadecin-7(8H)-yl)-2-butynyl]oxy}-9,10-dioxo-9,10-dihydro-1-anthracenyl) oxy]-2-butynyl}-5,6,7,8,9,10-hexahydro-2H-1,13,4,7,10-benzodioxatriazacyclopentadecine-3,11(4H,12H)-dione (19). M.p.: 261 °C. IR (KBr): 579(w), 667(w), 744(m), 968(w), 1045(m), 1126(m), 1261(s), 1315(w), 1443(w), 1504(m), 1585(w), 1674(vs), 2338(w), 2851(w), 2924(w), 3404(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.9 (t, 8H, J = 5.3 Hz), 3.44 (t, 8H, J = 5.3 Hz), 3.51 (s, 4H), 4.40 (s, 8H), 4.98 (s, 4H), 6.76-6.98 (m, 8H), 7.38 (s, 4H), 7.43 (d, 2H, J = 8.4 Hz), 7.66 (t, 2H, J = 8.1 Hz), 7.89 (d, 2H, J = 7.6 Hz). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 35.1, 37.4, 51.8, 57.5, 66.6, 80.7, 81.5, 112.3, 120.3, 122.0, 124.6, 130.5, 133.6, 134.7, 145.8, 157.2, 167.2, 182.0, 182.5. Anal. Calcd. for $C_{50}H_{50}N_6O_{12}$ (944.965): C, 64.79; H, 5.44. Found: C, 64.93; H, 4.36.

7-(3-Phenyl-2-propynyl)-5,6,7,8,9,10-hexahydro-2H-1,13,4,7,10-benzodioxatriazacyclopentadecine-3,11(4H, 12H)-dione (20). M.p.: 185-186 °C. IR (KBr): 571(w), 689(w), 756(s), 818(m), 1045(m), 1126(m), 1215(m), 1261(s), 1323(w), 1435(m), 1508(s), 1686(vs), 2338(w), 2847(w), 2905 (w), 3410(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.59-2.63 (m, 4H), 3.54-3.61 (m, 4H), 3.68 (s, 2H), 4.49 (s, 4H), 6.85-7.02 (m, 4H), 7.28-7.45 (m, 5H), 7.51 (s, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 35.1, 37.5, 47.4, 51.6, 52.3, 66.7, 77.6, 80.9, 112.3, 122.0, 146.0, 167.2. Mass m/z (%): 409 (M^++2, 0.8), 408 (M^++1, 3.3), 407 (M^+, 4.4), 337(0.8), 307(0.9), 294(0.2), 293(0.4), 292(0.9), 251(1.0), 183(12.1), 156(25.3), 115(100), 85(71.4), 56(58.5). Anal. Calcd. for $C_{23}H_{25}N_3O_4$ (407.462): C, 67.80; H, 6.18. Found: C, 67.63; H, 6.34.

7-[4-(4-Morpholinyl)-2-butynyl]-5,6,7,8,9,10-hexa-hydro-2H-1,13,4,7,10-benzodioxatriazacyclopenta-decine-3,11(4H,12H)-dione (21). Purification by plate chromatography, eluted with n-hexane/ethyl acetate (10/1), gave compound **21** in 74% yield. M.p.: 177-178 °C. IR (KBr): 571(w), 671(w), 748(m), 818(w), 1003(w), 1049(m), 1115(s), 1215(m), 1257(s), 1319(w), 1524(s), 1686(vs), 2338(w), 2851(m), 2908(m), 3414(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 2.47 (t, 4H, J = 4.7 Hz), 2.77-2.80 (m, 4H), 3.26 (t, 2H, J = 1.8 Hz), 3.38-3.43 (m, 6H), 3.66 (t, 4H, J = 4.7 Hz), 4.41 (s, 4H), 6.75-6.96 (m, 4H), 7.46 (s, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 35.1, 37.5, 47.4, 51.6, 52.3, 66.7, 77.6, 80.9, 112.3, 122.0, 146.0, 167.2. Mass m/z (%): 432 (M^++2, 3.8), 431 (M^++1, 4.8), 430(M^+, 0.6), 345(4.5), 306(8.8), 299(2.7), 293(0.3), 292(0.8), 277(4.9), 251(5.7), 225(3.2), 206(8.2), 163(5.2), 137(100), 100(30.7), 56(61.7). Anal. Calcd. for $C_{22}H_{30}N_4O_5$ (430.498): C, 61.38; H, 7.02. Found: C, 61.51; H, 6.89.

4-(1-Hexyl-3-phenyl-2-propynyl)morpholine (22). Purification by plate chromatography, eluted with n-hexane/ ethyl acetate (10/1), gave compound **22** in 76% yield. IR (neat): 690(s), 756(s), 1003(w), 1119(s), 1254(w), 1454(m), 1724(w), 2854(s), 2928(s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.82 (t, 3H, J = 7.0 Hz), 1.18-1.67 (m, 10H), 2.49-2.73 (m, 4), 3.44 (t, 1H, J = 7.4 Hz), 3.67-3.73 (m, 4H), 7.22-7.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 14.1, 22.6, 26.5, 29.0, 31.7, 32.8, 49.6, 67.0, 86.3, 86.9, 123.1, 127.9, 128.2, 131.7. Anal. Calcd. for $C_{19}H_{27}NO$ (285.424): C, 79.95; H, 9.53. Found: C, 80.11; H, 9.39.

RESULT AND DISCUSSION

We have recently reported the synthesis of a new heterogeneous Cu/C nanosatalyst [16]. Impregnation of

activated carbon (Merck, 0.3-0.5 mm) with CuI in absolute EtOH using an oil bath under reflux and N_2 condition leads, after distillation of EtOH and drying, to nanoparticle-sized Cu/C. Both CuI and Cu have been proposed as the species present within the activated carbon matrix.

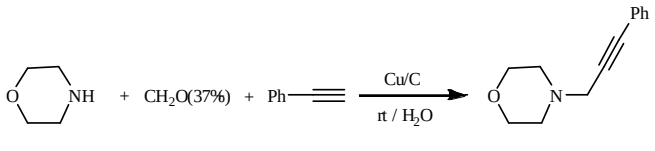
In order to optimize the reaction conditions, the condensation of morpholine (1 mmol), formalin (37%) and phenylacetylene (1 mmol) was studied as a model reaction to provide compound **1** (Scheme 1).
The results are shown in Table 1.

During our optimization studies, various solvents were examined and it was found that the solvent plays a significant role in terms isolated yield. Water clearly stands out as a solvent of choice with its high yield, cheapness, green character and environmental acceptability. Increasing the catalyst amount did not enhance the yield significantly.

Thus, careful analysis of the optimized reactions revealed that the optimum conditions for this one-pot procedure are the addition of phenylacetylene (1 mmol) to a solution of morpholine (1 mmol) and formalin (37%) (0.4 ml) in the presence of 2 mol% of Cu/C nanoparticles at room temperature in water. The reaction was stirred for 3 h. By using this reaction conditions, we were able to prepare the corresponding propargylamine in 91% yield.

In addition, no other additives were needed for this system, and the experimental process was quite simple and easy.

A variety of amines and alkynes bearing different functional groups was employed as the reaction substrates to explore the scope and generality for the catalyst application. All the results are summarized in Table 2.



1

Scheme 1. Mannich reaction of a model compound in the presence of Cu/C nanoparticles

In a similar manner, morpholine and piperidine were reacted with phenylacetylene under the influence of the Cu/C nanocatalyst to produce the corresponding product **2** in 90% yields (Table 2, entry 2).

As expected, various dialkylamines were found to react with formalin and phenylacetylene in the presence of a catalytic amount of Cu/C to give the corresponding propargylamines in good to excellent yields. For example, the reaction of dibutylamine with formalin and phenylacetylene catalyzed by Cu/C in water at room temperature for 3 h, produced **3** in 88% yield (Table 2, entry 3).

The use of piperazine as an amine afforded bridged propargylamine **6** in 85% yield (Table 2, entry 6). As clearly seen from Table 2, in the case of liquid compounds, the hydrophilicity of water is so high that results in some positive interactions among organic species as lipophilic compounds to promote the efficiency organic reactions. Whereas, for solid reagents with low solubility in water, a mixture of water:

Table 1. Mannich Reaction of Morpholine (1 mmol), Formalin (37%) (0.4 ml) and Phenylacetylene (1 mmol) at Room Temperature for 3 h

Entry	Catalyst	Condition	Yield (%)
1	Cu/C (2 mol%)	Dioxane	75
2	Cu/C (2 mol%)	THF	83
3	Cu/C (2 mol%)	*t*-BuOH	74
4	Cu/C (2 mol%)	EtOH (96%)	80
5	Cu/C (2 mol%)	CH_3CN	85
6	Cu/C (2 mol%)	DMSO	86
7	Cu/C (2 mol%)	H_2O	91
8	Cu/C (5 mol%)	H_2O	92

Table 2. Mannich Reaction of Amines (1 mmol), Formalin (37%) (0.4 ml) and Alkynes (1 mmol) in the Presence of 2 mol% of Cu/C

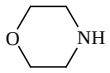
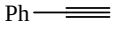
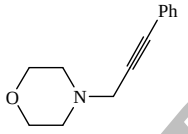
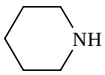
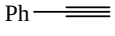
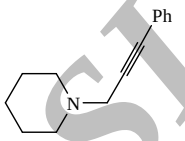
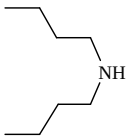
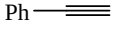
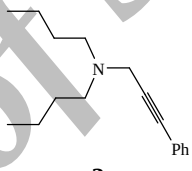
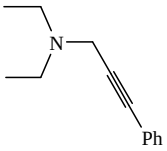
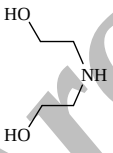
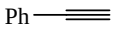
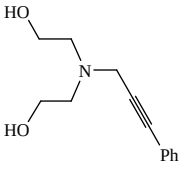
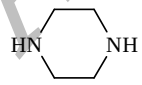
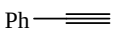
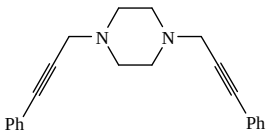
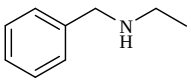
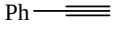
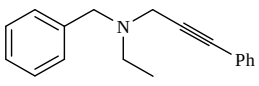
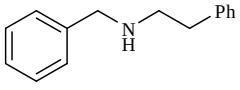
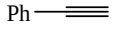
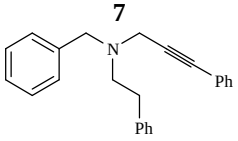
Entry	Amine	Alkyne	Product	Time (h)	Yield (%)[a]
1			 **1**	3	91
2			 **2**	3	90
3			 **3**	3	88
4			 **4**	3	89
5			 **5**	3	88
6[b]			 **6**	2	85
7			 **7**	4	82
8			 **8**	6	79

Table 2. Continued

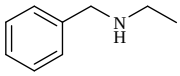
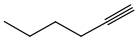
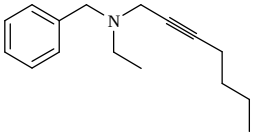
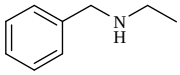
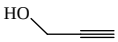
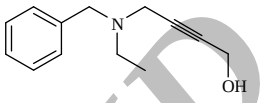
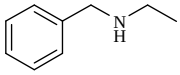
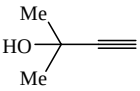
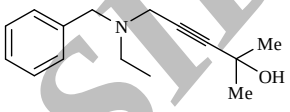
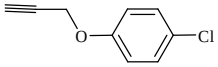
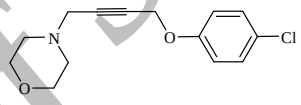
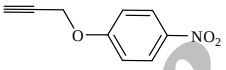
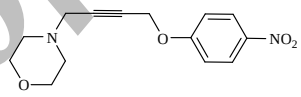
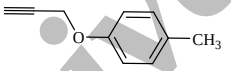
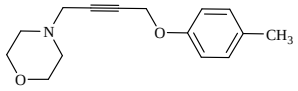
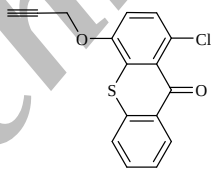
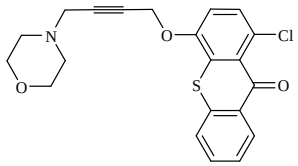
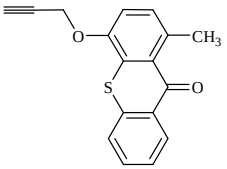
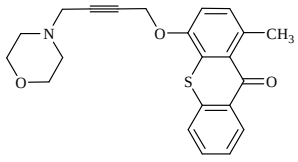
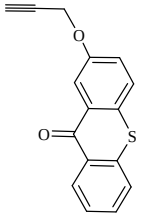
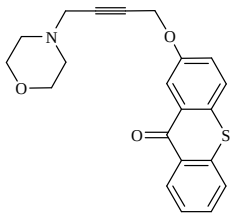
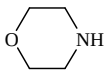
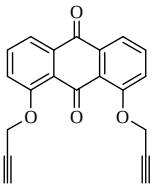
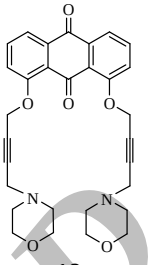
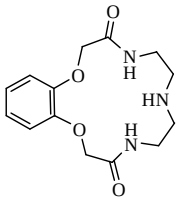
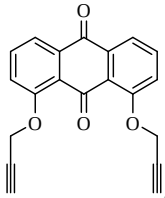
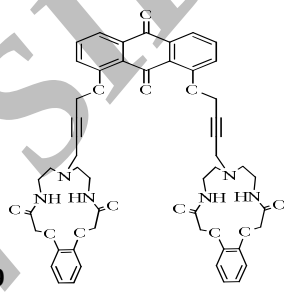
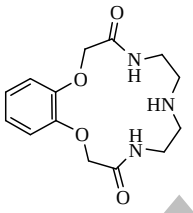
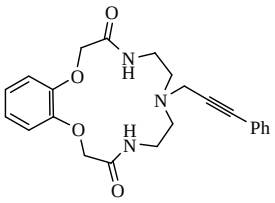
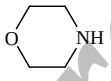
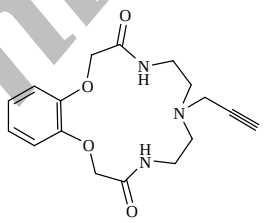
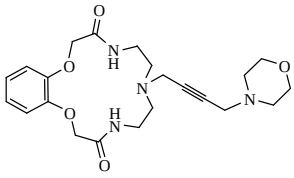
9[c]			 **9**	5	78
10[c]			 **10**	5	80
11[c]			 **11**	5	79
12[c]			 **12**	6	79
13[c]			 **13**	8	75
14[c]			 **14**	5	77
15[b,c]			 **15**	3	80
16[b,c]			 **16**	3	84
17[b,c]			 **17**	3	78

Table 2. Continued

18[b,c]			 **18**	3	79
19[b,c]			 **19**	5	75
20[b]			 **20**	3	78
21[b,c]			 **21**	3	74

[a]Isolated yields. [b]The reaction was carried out at mixture of water:EtOH (1:1). [c]The reaction was carried out at 75 ºC.

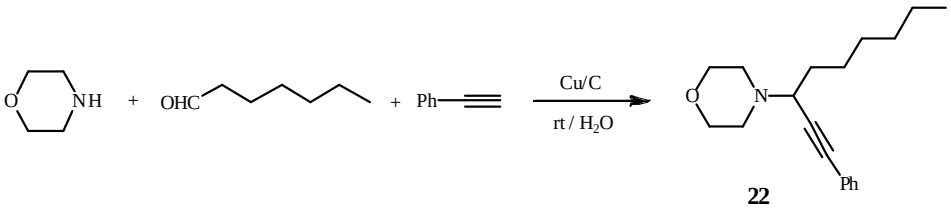
EtOH (1:1) was selected as appropriate green solvent.

This methodology can also be extended to the use of other amines, which provides a facile one-pot route to convert *N*,*N*-benzylethyl amine into corresponding propargylamine in high yield (Table 2, entry 7).

Subsequently, a variety of aliphatic alkynes was also examined for the coupling using formalin solution and morpholine as model substrates. In these cases, the reactions proceeded smoothly to give the corresponding propargylamines in good to high yields.

Although the aliphatic alkynes afforded propargylamines with good to high yields; the reactions proceeded at low rates in comparison with aromatic alkynes at room temperature. Thus, we carried out the reaction with aliphatic alkynes at a higher temperature (75 °C).

We subsequently tried to investigate novel substrates for Mannich reaction in water using a similar method. Therefore, thioxanthone [17] and propargylether derivatives were selected for examination. It is interesting to note that, this method exhibited high yields (Table 2, entries 15-17).



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Scheme 2. Mannich reaction of an aliphatic aldehyde in the presence of Cu/C nanoparticles

The coupling of anthraquinone [18] dipropargylether, formalin solution and morpholine proceeded smoothly to afford the corresponding bispropargylamines in good yields under standard conditions (Table 2, entry 18).

To expand the scope of amine substrates, we used the sterically hindered amines such as azacrown ethers [15]. It is worth mentioning that, through our methodology, it was possible to prepare new bis azacrown ether that attached to anthraquinone (Table 2, entry 19).

The above methodology may provide a new class of azacrown ethers incorporated triple bond derivatives with high yields, which may find potential utilities in the pharmacological areas. We then applied the Cu/C nanocatalyzed protocol to the coupling of azacrown ethers and azacrown ether propargylamines with phenylacetylene and morpholine, respectively (Table 2, entries 20 and 21).

Reactions using an aliphatic aldehyde such as heptanal gave the desired products in high yields using only 2 mol% of the copper nanocatalyst (Scheme 2). In this experiment, a large degree of the deposited Cu(I) is considered as active catalytic species in the Mannich reaction of morpholine. Also, the metallic Cu nanoparticles, synthesized by the disproportionation reaction of Cu(I), act as active species for increasing the active surface area of the solid catalyst to setup the organic reaction. Therefore, the more use of the catalyst in the synthesis of organic compounds, the superior is the active surface area of the catalyst. This consequently results to get higher catalytic activity for the catalyst. However, some phenomena such as formation Cu(II) species act as by-product species, due to the disproportionation reaction, as well as oxidation of Cu(I) by water dissolved oxygen during the synthesis of organic compounds in water media.

The recyclability of the Cu/C nanoparticles was also tested in the Mannich reaction of phenylacetylene, morpholine and formalin (37%). The activated carbon supported copper species was simply recovered by filtration after each experiment, and after washing with acetone and drying in air, was reused directly without further purification for the propargylamine syntheses in more than 10 successive reactions. After 10 consecutive reactions, the recovered Cu/C was found to contain 9.84% (w/w) of Cu species based on the ICP analysis, which was comparable to the initial value of 9.97% (w/w) [16], indicative of less than 1.30% leaching, based on the disproportionation reaction, during the reaction cycles. This is also due to the oxidation of Cu(I) to Cu(II) by water dissolved oxygen during its use in the synthesis of organic compounds in water media.

The recyclability of the copper nanoparticles is related to the structure of copper species supported on activated carbon. The size of the deposited copper species is usually dependent on the roughness of the support. The original morphology (roughness) of the activated carbon support plays a significant role in evaluation of the friction coefficient of the substrate for controlling the size and the morphology of the copper nanoparticles deposited on the carbon support. The more the surface roughness, the superior is the friction coefficient. Usually, flat surfaces, developing large continuous junctions, originating large amounts of deposited nanoparticles, while original rough surfaces, form many small junctions, producing many small nanoparticles [19]. In this study, the observed process for the deposition of copper nanoparticles cannot be explained (i) without including the processes such as the roughness of activated carbon support [19-22], and also (ii) without investigation of the Cu-O bond formed due to the formation of carboxylic acid functional groups during the activation process of carbon by nitric acid, as evidenced from

the results of different technical spectroscopies.

The FT-IR spectrum (Fig. 1), Raman spectrum (Fig. 2) and the patterned X-ray diffraction (XRD) (Fig. 3) of the copper nanocatalyst supported on activated carbon, analyzed after its use as catalyst in organic reactions for at least 10 times, were similar to the corresponding spectra for the copper species initially supported on activated carbon.

In the FT-IR spectrum (Fig. 1), the strong peak at around 3444 cm^{-1} is related to the hydroxyl group. The peak at around 1616 cm^{-1}, is also related to the carboxylic functional group. The results exhibited that, a wide and strong peak positioned at around 1110-700 cm^{-1} is mainly related to the formation of CuI (around 1037 cm^{-1}) and, more or less, to the electronic interactions occurred between the different copper species on activated carbon, as investigated in our previous study [16].

Also, strong chemical interactions are expected due to the deposition of copper onto activated carbon [23]. The results also reveal that the weak peak at 667 cm^{-1} is related to the Cu-O bond [16]. This can be considered as another proof for the reusability of the nanocatalyst used in several organic reactions. For more confidence about the chemical bond between copper nanoparticles and activated carbon, the Raman spectrum of the copper supported on activated carbon is shown in Fig. 2.

According to the Raman spectrum shown in Fig. 2, the broadening of the ~380 cm^{-1} band is related to the Cu-O formation due to the deposition of copper on activated carbon [24,25]. Also the broad peak at 1300 cm^{-1} (D-band) is related to the disposition of copper species on the activated carbon. The Raman spectrum exhibits the tangential (1450-1650 cm^{-1}, G band) and disorder (1250-1350 cm^{-1}) modes, the ratio of which indicates the extent of defects of the activated carbon. The relative intensity of tangential mode/disorder mode, called G/D ratio, is a good indicator for the quality and also the morphology of carbon support during its activation process [26,27], in terms of preservation of sp^2 hybridization. The G/D ratio was calculated as 0.82, for the initial carbon, and 1.27, for carbon powder activated with nitric acid. This indicated that the activation process promotes the active sites of the carbon support, which makes it suitable for the deposition of copper species.

As investigated in detail in our previous study [16], different morphologies were detected according to the XRD

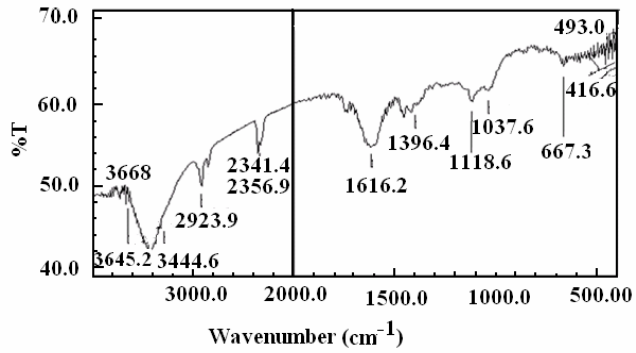


Fig. 1. The FT-IR spectrum of copper nanoparticle supported on activated carbon after its use as catalyst for at least 10 times.

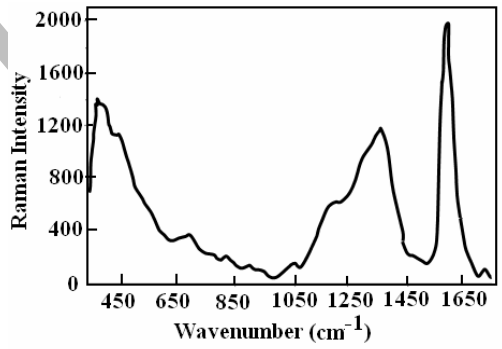


Fig. 2. The Raman spectrum of copper nanoparticles supported on activated carbon after 10 times reused.

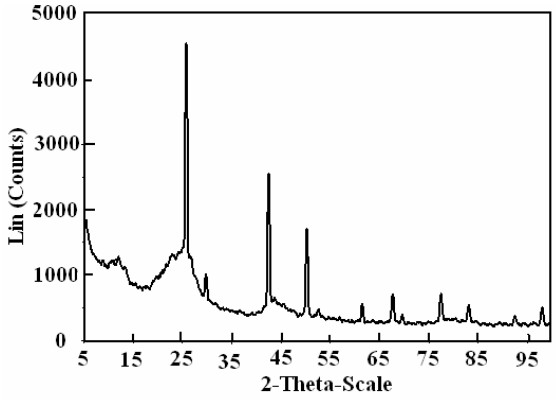


Fig. 3. The XRD pattern of copper nanoparticles supported on activated carbon after 10 times reused.

Table 3. Analysis of XRD Patterns Related to CuI/Cu on Activated Carbon after 10 Times Reuse

2-Theta-Scale (2θ)	Matrix and morphology			Ref.
	C	Cu	CuI/CuI_3	
25.5	(002)	-	(111)	[28a,28b]
29.5	(422)	-	(200)	[28a]
40	-	(111)	(220)	[28a]
50.2	(008)	(200)	(311)	[28,29]
52.1	-	-	(222)	[29]
61.2	-	-	(400)	[28a]
67.2	-	-	(331)	[29]
69.2	-	-	(420)	[29]
77	-	(220)	-	[28c,29]

pattern of copper species supported on activated carbon. The results corresponding to carbon, copper and CuI/CuI_3 are reported in Table 3. The same result was also observed for the XRD analysis of the catalyst after at least 10 times reused. This result is considered as another evident for the recyclability of the copper nanoparticles in Mannich reaction.

Figure 4A shows the TEM image of the Cu nanoparticles initially deposited on activated carbon. As clearly seen, there is good correlation between the diameter of Cu nanoparticles observed in the TEM images, with the results obtained based on the SEM and AFM images reported in our previous study [16].

Also Fig. 4B illustrated the TEM image of Cu nanoparticles after at least 10 times use as catalyst in the Mannich reaction. Comparing the two TEM images shown in Fig. 4 reveals this fact that the multiple uses of the catalyst in the syntheses of organic compounds do not affect the size of copper nanoparticles, and also increases the number of copper nanoparticles during the use of copper as catalyst. This enhancing effect in the number of copper nanoparticles is considered as another evident for the formation of copper nanoparticles based on the disproportionation reaction of Cu(I) in polar solvents.

To access the feasibility of applying this method in a preparative scale, we carried out the reaction of morpholine, phenyl acetylene and formalin (37%) in 100 mmol scale in the presence of the heterogeneous Cu/C catalyst. As expected, the reaction proceeded similar to the case in a smaller scale, and

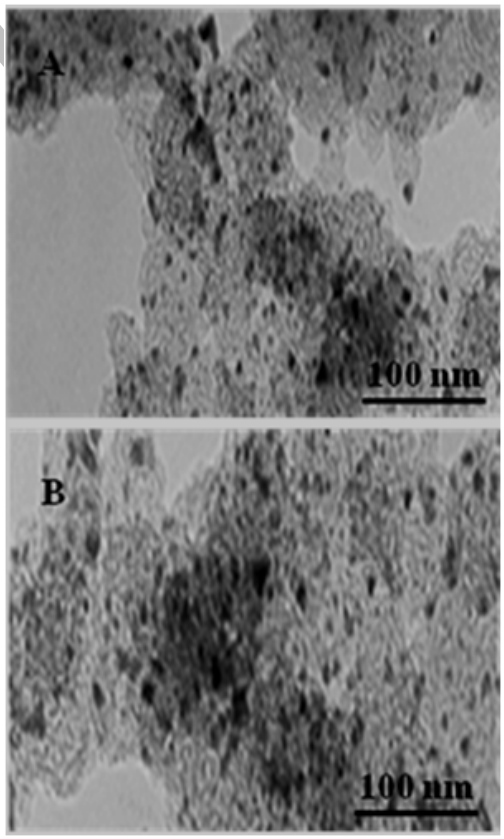
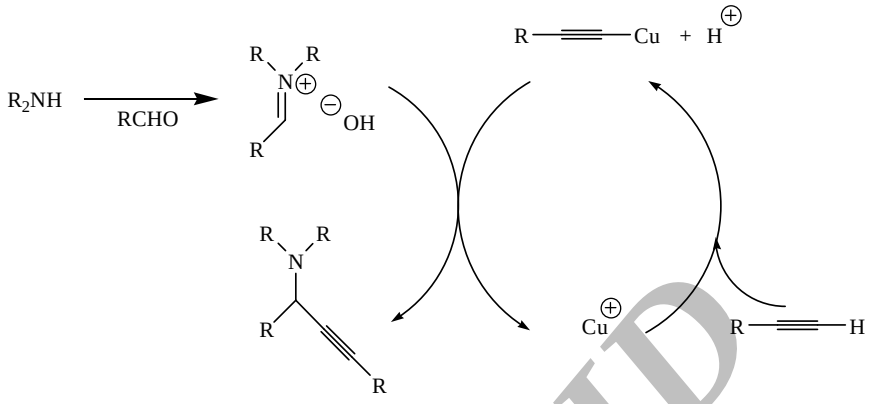


Fig. 4. TEM images of Cu/C nanoparticles A: after deposited on activated carbon, B: after at least 10 time use as catalyst in the synthesis of organic compounds.



Scheme 3. A tentative mechanism for synthesis of propargylamines in the presence of Cu/C nanoparticles

the desired propargylamine was obtained in 89% isolated yield in 3.5 h.

According to the TEM images shown in Fig. 4 and also based on the SEM images reported in our previous work [16], the active area of activated carbon is so high that large degree of copper is deposited. On the other hand, the nanoscale copper species formed according the proposed reaction, promotes the capability of copper catalyst to act as appropriate catalyst in the synthesis of organic compounds. The results revealed that the observed 1.3% conversion, due to the disproportionation reaction of Cu(I) as well as the effect of water dissolved oxygen, does not have any effect on the efficiency of the organic reactions catalyzed by Cu/C based on the proposed mechanism. Also the metallic copper nanoparticles synthesized by the disproportionation reaction during the catalytic activity of the copper species, supported on activated carbon, provides larger active surface area that results in only 1.3% conversion for Cu(I).

A tentative mechanism was proposed involving the exchange of H of the C-H bond of alkyne by a Cu(I) species [7a,7d]. The copper acetylide intermediate thus generated reacted with the iminium ion generated *in situ* from aldehydes and secondary amines to give the corresponding propargylamine and regenerate the Cu(I) nanocatalyst for further reactions (Scheme 3).

CONCLUSIONS

Highly efficient Cu/C nanoparticles were found to catalyze the three-component coupling of aldehydes, alkynes, and amines in water *via* the C-H activation. The process was simple and generated a diverse range of propargylamines in excellent yields. Water is the only byproduct in this novel three-component reaction. Furthermore, Cu/C nanoparticles can be recovered and recycled by simple filtration of the reaction solution and reused in at least ten consecutive trials without significant decrease in the activity.

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REFERENCES

[1] a) G.H. Posner, Chem. Rev. 86 (1986) 831; b) R.W. Armstrong, A.P. Combs, P.A. Tempest, S.D. Brown, T.A. Keating, Acc. Chem. Res. 29 (1996) 123; c) H. Bienayme, C. Hulme, G. Oddon, P. Schmitt, Chem. Eur. J. 6 (2000) 3321; d) J. Zhu, H. Bienayme (Eds.), Multicomponent Reactions, Wiley-VCH: Weinheim, 2005.

[2] a) C.J. Li, Chem. Rev. 93 (1993) 2023; b) J. Metzger, Angew. Chem., Int. Ed. 37 (1998) 2975; c) K. Tanaka, F. Toda, Chem. Rev. 100 (2000) 1025; d) C.J. Li, Chem. Rev. 105 (2005) 3095; e) H.R. Hobbs, N.R.

Thomas, Chem. Rev. 107 (2007) 2786; f) B. Yan, Y. Liu, Org. Lett. 9 (2007) 4323.

[3] C. Wei, L. Zhang, C.J. Li, Synlett (2004) 1472.

[4] a) M.A. Huffman, N. Yasuda, A.E. DeCamp, E.J.J. Grabowski, J. Org. Chem. 60 (1995) 1590; b) M. Konishi, H. Ohkuma, T. Tsuno, T. Oki, G.D. VanDuyne, J. Clardy, J. Am. Chem. Soc. 112 (1990) 3715.

[5] a) M. Miura, M. Enna, K. Okuro, M. Nomura, J. Org. Chem. 60 (1995) 4999; b) A. Jenmalm, W. Berts, Y.L. Li, K. Luthman, I. Csoregh, U. Hacksell, J. Org. Chem. 59 (1994) 1139.

[6] a) G. Dyker, Angew. Chem. Int. Ed. 38 (1999) 1698; b) T. Naota, H. Takaya, S.I. Murahashi, Chem. Rev. 98 (1998) 2599; c) M. Wang, P. Li, L. Wang, Eur. J. Org. Chem. (2008) 2255.

[7] a) S. Sakaguchi, T. Mizuta, M. Furuwan, T. Kubo, Y. Ishii, Chem. Commun. (2004) 1638; b) L. Shi, Y.-Q. Tu, M. Wang, F.-M. Zhang, C.-A. Fan, Org. Lett. 6 (2004) 1001; c) L.W. Bieber, M.F. da Silva, Tetrahedron Lett. 45 (2004) 8281; d) S.B. Park, H. Alper, Chem. Commun. (2005) 1315; e) X. Yao, C.-J. Li, Org. Lett. 7 (2005) 4395; f) V.K.-Y. Lo, Y. Liu, M.-K. Wong, C.-M. Che, Org. Lett. 8 (2006) 1529; g) E. Ramu, R. Varala, N. Sreelathaa, S.R. Adapa, Tetrahedron Lett. 48 (2007) 7184.

[8] B.M. Choudary, C. Sridhar, M.L. Kantam, B. Sreedhar, Tetrahedron Lett. 45 (2004) 7319.

[9] M.L. Kantam, B.V. Prakash, C.R.V. Reddy, B. Sreedhar, Synlett (2005) 2329.

[10] K.M. Reddy, N.S. Babu, I. Suryanarayana, P.S. Sai Prasad, N. Lingaiah, Tetrahedron Lett. 47 (2006) 7563.

[11] a) G.W. Kabalka, L. Wang, R.M. Pagni, Synlett (2001) 676; b) G.W. Kabalka, L.-L. Zhou, L. Wang, R.M. Pagni, Tetrahedron 62 (2006) 857; c) Y. Zhou, T. He, Z. Wang, Arkivoc xiii (2008) 80.

[12] P. Li, L. Wang, Tetrahedron 63 (2007) 5455.

[13] K.M. Patil, M. Keller, B.M. Reddy, P. Pale, Sommer, J. Eur. J. Org. Chem. (2008) 4440.

[14] a) H. Sharghi, M.H. Beyzavi, M.M. Doroodmand, Eur. J. Org. Chem. (2008) 4126; b) H. Sharghi, M. Aberi, M.M. Doroodmand, Adv. Synth. Catal. 350 (2008) 2380; c) H. Sharghi, M. Hosseini-Sarvari, F. Moeini, Can. J. Chem. 86 (2008) 1044; d) H. Sharghi, M.H. Beyzavi, A. Safavi, M.M. Doroodmand, R. Khalifeh, Adv. Synth. Catal. 351 (2009) 2391.

[15] a) H. Sharghi, R. Khalifeh, Heterocycles, 71 (2007) 1601; b) H. Sharghi, A.R. Salimi Beni, R. Khalifeh, Helv. Chim. Acta 90 (2007) 1373; c) H. Sharghi, R. Khalifeh, Can. J. Chem. 86 (2008) 426; d) H. Sharghi, S. Ebrahimpourmoghaddam, Helv. Chim. Acta 91 (2008) 1363; e) H. Sharghi, R. Khalifeh, A.R. Salimi Beni, J. Iran. Chem. Soc. 7 (2010) 275. Available from www.ics-ir.org/jics...

[16] H. Sharghi, R. Khalifeh, M.M. Doroodmand, Adv. Synth. Catal. 351 (2009) 207.

[17] a) H. Sharghi, A.R. Salimi Beni, Synthesis (2004) 2900; b) H. Sharghi, A.R. Salimi Beni, J. Iran. Chem. Soc. 5 (2008) S33, Available form www.ics-ir.org/jics.

[18] a) H.R. Pouretedal, A. Forghaniha, H. Shargi, M. Shamsipur, Analytical Lett. 31 (1998) 2591; b) M. Shamsipur, F. Raoufi, H. Sharghi, Talanta 52 (2000) 637; c) M. Shamsipur, A. Siroueinejad, B. Hemmateenejad, A. Abbaspour, H. Sharghi, K. Alizadeh, S. Arshadi, J. Electroanal. Chem. 600 (2007) 345.

[19] M. Akbulut, A.R.G. Alig, J. Israelachvili, J. Chem. Phys. 124 (2006) 174703.

[20] S. Olliges, P.A. Gruber, S. Orso, V. Auzelyte, Y. Ekinci, H.H. Solak, R. Spolenak, Scripta Materialia. 58 (2008) 175.

[21] R. Kohli, Part. Sci. Technol. 25 (2007) 21.

[22] R. Spolenak, C.A. Volkert, S. Ziegler, C. Panofen, W.L. Brown, Mat. Res. Soc. Symp. Proc. 673 (2001) 1.4.1.

[23] J. Sarkany, Phys. Chem. Chem. Phys. 1 (1999) 5251.

[24] M.A. Karakassides, A. Saranti, I. Koutselas, J. Non-Cryst. Solids 347 (2004) 69.

[25] I. Ardelean, C. Andronache, C. Cimpean, P. Pascuta, Mod. Phys. Lett. B18 (2004) 45.

[26] J.E. Herrera, L. Balzano, F. Pompeo, D.E. Resasco, J. Nanosci. Nanotech. 3 (2003) 133.

[27] Y. Kobayashi, D. Takagi, Y. Ueno, Y. Homma, Phys. E 24 (2004) 26.

[28] a) M. Gu, D.X. Wang, Y.T. Huang, R. Zhang, Cryst.

Res. Technol. 39 (2004) 1104; b) S. Hussain, A.K. Pal, Bull. Mater. Sci. 29 (2006) 553; c) M. Samim, N.K. Kaushik, A. Maitra, Bull. Mater. Sci. 30 (2007) 535.

[29] P.S. Kumar, Y.L. Saraswathi, C.S. Sunandana, Mater. Phys. Mech. 4 (2001) 71.