

Copper(0) Nanoparticles Supported on Al₂O₃ as Catalyst for Carboxylation of Terminal Alkynes

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Abstract The copper particles, supported on Al_2O_3 were for the first time used as heterogeneous, highly active, easily available, and recyclable copper catalyst of direct carboxylation of various terminal alkynes with CO_2 (2 bar) in the presence of cesium carbonate, allowing for the synthesis of alkyl 2-alkynoates. The catalyst contains largescale CuNPs covered by oxide layer and less prone to erosion, resulting in its high selectivity and efficiency unusual for the particles of this size.

Graphical Abstract



Keywords Carboxylation · Terminal alkyne · CuNPs · Supported nanoparticles · Heterogeneous catalysis

1 Introduction

Recently, reactions involving CO_2 as the most available and cheap source of C1 attract attention of many research groups [1, 2]. Many routes of CO_2 application in fine organic synthesis such as reactions with alkenes [3–5], alkynes [6–8], dienes and allenes [9–11], aromatic [12, 13] and heteroaromatic compounds [14, 15] have already been found. However, taking into account kinetic and thermodynamic stability of the molecule, it is evident that either

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¹ Department of Chemistry, Lomonosov Moscow State University, 1 Leninskie Gory, GSP-2, Moscow, Russia 119992 active substrates, primarily organometallic compounds [16], or active catalysts [17] should necessarily be used in the reactions. In the last case, availability and recyclability are important in addition to the catalyst efficiency.

Naturally, organic molecules functionalization involving CO_2 cannot affect such processes as global warming and can hardly solve the problem of binding greenhouse vapors, but the use of nontoxic carbon dioxide in organic synthesis as an alternative for phosgene or isocyanate seems to be an important area of its application.

Since the reactions involving CO_2 molecule are greatly variable, it is evident that different catalytic systems would be needed for each specific reaction [18]. For example, the carboxylation of epoxides needs another catalytic system than the activation of C–H bonds. The copper and silver salts turned out to be optimum catalysts for the widely studied carboxylation of terminal alkynes [19]. Silver complexes with carbene ligands efficiently catalyse the carboxylation processes and exhibit high yields in mild conditions [20–22].

Saegusa and coauthors in 1974 pioneered this field [23] in describing stoichiometric alkyne carboxylation in the presence of the copper salts and showed [24] reversibility of the reaction even at 35 °C, which can partially be avoided by "capturing" the formed carboxylate by alkyl halide. Only 20 years later, in 1994, Inoue and coworkers used catalytic amounts (4 mol%) of the copper(I) and silver(I) salts in the carboxylation of terminal acetylenes [25]. The intensive search for mild reaction conditions (room temperature, CO₂ pressure of 1 bar) and, if possible, for avoiding reversibility has started only in the XXI century. Different copper salts [26, 27] and their complexes with various ligands [28-30] were tested in the reaction and the systems with carbenes CuCl-polyNHC were most efficient [30]. Exclusive importance of base and of DMA and DMF as solvent was also reported [25]. There are examples of the reactions in ionic liquids [31] and supercritical CO₂ [27].

It should be mentioned that the system CuCl-polyNHC [30] was heterogeneous and manifested considerable advantages since it catalyzed the reactions even with electronwithdrawing alkynes (for example, nitrophenylacetylene) in the presence of small catalyst amounts (0.5 mol%); however, the authors [30] did not perform recycling. Another heterogeneous system consisting of CuBr on active carbon was recycled five times without a significant loss in activity [32].

The chemistry of metallic nanoparticles has recently become very important in synthesis, catalysis, and medicine [33]. The catalytic properties of the nanoparticles were especially pronounced in the palladium catalysis where the variation of the support and reaction conditions made it possible to carry out reactions of poorly substrates such as aryl chlorides [34, 35] in the absence of any ligands, while for more active substrates fantastic values of TON and TOF can be obtained under mild conditions [36, 37].

Thus, the advantages of the heterogeneous catalysts (easy separation of the catalyst from the reaction product and recyclability) are accompanied by the high catalytic activity quite comparable with that of the homogeneous catalysts, whereas such a high activity is not observed for the last in the absence of toxic and/or expensive ligands.

Copper(II) nanooxide was successfully used as a catalyst in the C–S cross-coupling [38, 39], arylation of active methylene compounds [40] and syntheses of thiol esters in ionic liquid [41] and flavanones [42]. In addition, nano-CuO can be applied as sensor [43]. In the most cases, the use of complicated ligands is not required for successful reactions in the presence of these systems.

CuNPs can catalyze "click" process but the authors note that the reactions involved a film containing copper oxide(s) on the CuNPs surface [44, 45], which is thermodynamically more stable than the non-oxidized metallic copper surface [46]. The observed activity of these catalysts significantly exceeds the catalytic activity of CuO and Cu₂O.

Similar particles, as well as nanoparticles CuNPs/Cu₂O, exhibit synergic properties [47] and, hence, can be used as efficient catalysts. For example, the Cu/Cu₂O nanoparticles can manifest high activity in the photocatalytic reactions due to the properties of the corresponding redox pair [48, 49]. The calculated data for carbon dioxide adsorption on the copper(I) oxide show that the geometry of the adsorbate molecule is influenced by its coordination at the surface copper and oxygen atoms [50]. The electron transfer due to the coordinatively unsaturated copper atoms occurs when the carbon dioxide molecule gains bent form [51].

In continuation of our work with transition metal nanoparticles [52, 53] we decided to try copper NPs in alkyne carboxylation. We focused on a catalyst based on CuNPs covered by a thin layer of copper oxide assuming that alkyne would interact with the copper surface not covered by oxides (for example, in crystal defects), while carbon dioxide, on the contrary, would be adsorbed on copper oxide. And this symbiotic microreactor would provide a good selectivity of direct carboxylation.

2 Results and Discussion

CuNPs obtained by the method earlier proposed by us for AuNPs [54] (impregnation of the support with an aqueous solution of CuSO₄ followed by evaporation and heating at 300 °C in a hydrogen flow) gave rather large (up to 50 nm) copper crystallites which turned out to be active in the carboxylation of *para*-methoxyphenylacetylene **1a** in DMF at 60 °C, 2 atm. CO₂ and Cs₂CO₃ as a base



Scheme 1 CuNPs catalyzed carboxylation of 4-methoxy-1-ethynylbenzene



Fig. 1 Screening of the catalyst activity in the carboxylation of 4-methoxy-1-ethynylbenzene

(Scheme 1, Fig. 1). CuNPs/Al₂O₃ catalyzed the reaction to give the corresponding ester **2a** in an almost quantitative yield. The catalysts on the carbon supports also showed high activity: the yields of the product for CuNPs/C and CuNPs/GrOx (GrOx-graphite oxide) were 76 and 86%, respectively. These yields significantly exceeded both the yields obtained using other supports (Cu/CaCO₃, Cu/TiO₂, and Cu/SiO₂) and those for unsupported CuO and Cu₂O, as well as the yields for nano-Cu₂O/SiO₂ (note that the last three exhibited similar catalytic activity) (Fig. 1).

Our attempts to use CuNPs supported on the surface of TiO_2 , Al_2O_3 and zeolite prepared according to a known method [44] that gives small particles (~1.5 nm) active in click reactions [45] were unsuccessful, and we failed to perform the carboxylation of alkyne **1a** in the presence of

these catalysts under standard conditions (Scheme 1). On the other hand, the Sonogashira reaction and azide–alkyne addition ("click" reaction, CuAAC) [45] which can be performed with the small nanoparticles did not occur in the presence of CuNPs/Al₂O₃ (50 nm) obtained by our method mentioned above.

The SEM, XPS, and XRD studies were carried out for the most efficient catalysts. The copper particles in the CuNPs/Al₂O₃ catalyst sample observed in the SEM image (Fig. 2a) are fairly large (about 50–100 nm) (Fig. 2b), whereas the crystallites in the CuNPs/C and CuNPs/GrOx samples are larger and beyond the nano dimensionality range (~250–500 nm) (Fig. 2b, c), and the smaller effective surface area of these particles results in decrease of their catalytic activity. These catalysts are also difficult to recycle and we excluded them from further investigations.

The powder XRD pattern of the CuNPs/Al₂O₃ sample (Fig. 3) exhibits characteristic peaks (marked by blue) of the metallic phase of CuNPs corresponding to 2θ values of 43.4°, 50.5°, and 74.2° and signals of the aluminoxide support (2θ values of 14.5°, 28.2°, 38.3°, 45.8°, 48.8°, 49.2°, 51.7°, 55.2°, 60.5°, 64.2°, 64.9°, 66.9°, 67.7°, 72.0°, 72.2°, and 79.2° marked by red) corresponding to the typical spectrum of the amorphous sandwich-like form of alumina, boehmite, formed under high-temperature conditions of catalyst calcination under hydrogene atmosphere. The oxygen ions located in the octahedral layers are bound to the aluminum ions only, whereas the external oxygen ions are also linked to the hydrogen ions [55]. The layered structure of boemite and presence



Fig. 2 SEM micrograph of the CuNPs in CuNPs/Al₂O₃ (a), CuNPs/C (b) and CuNPs/GrOx (c)

(Coupled TwoTheta/Theta)



Fig. 3 X-ray diffraction patterns of the powder sample of CuNPs/Al₂O₃

O-H-O-H-O bonds on its surfaces promote better adsorption of metal ions, which makes it the best support for our catalyst.

The presence of an oxide layer with different Cu(I)/ Cu(II) ratios on the catalyst surface was shown by XPS (Fig. 4): 41/59% for CuNPs/C and 51/49% for CuNPs/ Al₂O₃ (signal of Cu⁺ from 930 to 935 eV and that of Cu²⁺ from 931 to 947 eV). Note that the reaction was successfully performed by using the special nanoparticles and supports as well as certain base and solvent. We showed that K_2CO_3 , Bu_4NOAc and DABCO widely used in copper catalysis were quite inactive as bases in our case. The results indicated were obtained using two equivalents of Cs_2CO_3 (Fig. 1) (using only 1 equiv. of base sharply decreased the yield of the product). As it was shown [56] the reaction can be



Fig. 4 XPS spectra of the surface of the CuNPs/C (a) and CuNPs/Al₂O₃ (b) catalysts

performed in non-catalytic conditions in the presence of cesium carbonate only but requires high temperature (120 °C), whereas our reaction conditions are much milder. We also confirmed the importance of CuNPs catalysis by carrying out the reaction in the presence of Cs₂CO₃ and support (Al_2O_3) only and obtaining a negligible yield (<5%) within 6 h). Except for DMF and DMA, all other tested solvents turned out to be inactive. In the case of CuNPs/C, the DMF and DMA solvents showed similar results (86 and 89%, respectively, within 6 h). The reaction catalyzed by CuNPs/Al₂O₃ turned out to be more sensitive to the solvent nature, and the yield close to quantitative (97%) was obtained in DMF only. Therefore, all other catalysts were also tested in the Cs₂CO₃ (2 equiv.)-DMF system (Scheme 1).

Kinetic studies of three selected catalysts (Fig. 5) showed that the kinetic curves resembled each other, as a whole, but the carbon supports exhibited a specific feature already noted in previous publications [32], namely, the yield relatively rapidly reached a maximum after which began to decrease with time. This effect is explained by the equilibrium between the carboxylation and backward decarboxylation [24]. The study of the latter process, which has also been performed previously [57], showed that, in

square)

our case in the absence of CO₂ under standard conditions, product 2a decarboxylated almost completely within 6 h.

Our attempt to reduse CO₂ pressure to 1.5 atm. resulted in decrease of alkynoate yield to 75% what probably caused by reversibility of the process.

The study of the temperature dependence was also carried out for the most promising catalyst CuNPs/Al₂O₃ (Fig. 6). At 80 °C the maximum conversion was achieved within 1.5 h, at 70°C it took 2 h, and at 60°C-16 h (Fig. 5). At temperatures below 40°C, the reaction was very slow and the yield of the product did not exceed 20% even in 16 h. It should be mentioned that at 80 and 70 °C after reaching the maximum the yield began to decrease (Fig. 6), which was also observed for the carbon supports [32] and can be explained by an increase in the decarboxylation rate with temperature.

We proposed the mechanism for the direct catalytic carboxylation of terminal alkynes on the surface of nanocrystalline copper covered by copper oxides (Fig. 7). Terminal alkyne appears to be coordinated on the copper surface and carbon dioxide is adsorbed on Cu₂O surface [49, 50]. To check the possibility of leaching from the catalyst surface, a hot centrifugation test was carried out. It showed that the reaction did not occur in the





Fig. 7 Mechanism proposed for direct alkyne carboxylation on the surface of nanocrystalline copper covered by the thin oxide layer

centrifugate of the reaction mixture sampled after 2 h from reaction start with a new portion of the base and heating for 4 h (Fig. 6). The absence of copper traces in the centrifugate was also confirmed by inductively coupled plasma mass spectroscopy analysis (ICP/MS).

According to the SEM data, the isolated catalyst samples contain a significant amount of adsorbed salts on its surface even after washing with an aqueous-alcohol solution (Fig. 8). Washing of the catalyst by other solvents except DMF influenced dramatically its recyclization, probably because traces of alcohols and oxygen were destroying the catalyst surface. Therefore, the CuNPs/ Al_2O_3 catalyst was recycled with washing it by DMF only.

The yield of the product upon recycling was determined within kinetic-controlled region at the time of half completion $\tau_{1/2}$ (2 h, 60 °C). The results of these experiments presented in Fig. 9 show that the catalyst activity changes insignificantly after five cycles.

The carboxylation of a series of terminal alkynes was carried out under the found optimum conditions (2 equiv. Cs_2CO_3 , 5 mol% CuNPs/Al₂O₃, 1.2 equiv. BuBr, 2 atm. CO_2 , 60 °C, DMF) (Fig. 10). Whereas for alkynes **1a–d** reaction was completed after 6 h, for alkynes **1e–m** needed at least 16 h.



Fig. 8 SEM micrograph of the $CuNPs/Al_2O_3$ sampled from the reaction

Thus in the case of phenylacetylene **1b** and aromatic alkynes with electron-donating substituents **1a**, **c**–**d**, the corresponding esters **2a**–**d** were obtained in high yields of 78–92%. However, in the case of 4-*tert*-butyl-substituted phenylacetylene **1e**, the reaction time had to be increased to 16 h to obtain an almost quantitative yield of 97%,



Fig. 9 Recovery of NPs Cu/Al₂O₃ in 4-methoxy-1-ethynylbenzene 1a carboxylation at 60 °C for 2 h with a negligible loss in catalytic efficiency

which can be explained by a larger volume of the *tert*-butyl group having weak electron-donor properties and impeding adsorption on the catalyst surface. Less reactive alkynes with the electron-withdrawing substituents, aliphatic alkyne and heteroaromatic (thienyl, pyrazolyl, quinolil-substituted) alkynes reacted somewhat more slowly: the corresponding products 2f-m were formed within 16 h in 61–96% yields. Both the elongation of the reaction time and an increase in the temperature and CO₂ pressure to 80 °C and 4 atm., respectively, were needed for heteroaromatic alkyne 11 and aliphatic alkyne 1m. However in all cases, the reactions proceeded without by-product formation.



Fig. 10 Direct carboxylation of terminal alkynes with CO₂ catalyzed by CuNPs/Al₂O₃

3 Experimental

3.1 Materials and Methods

All starting materials were purchased from Sigma Aldrich except graphite oxide, 97% purchased from NPO Unichemtech (http://www.unichimtek.ru) and 4-ethynyl-1-methyl-1H-pyrazole obtained by Bestmann-Ohira method [58]. Solvents were dried and deoxygenated using standard procedures. Carbon dioxide gas 99,99% purity was used. Carboxylation reactions were performed in 15 mL capacity glass low pressure reactor RLP25ML (http://www.openscience.ru) equipped with gas feeding system, magnetic stirrer and manometer. For all products NMR spectra were recorded on a Bruker Avance 400 and Agilent 400MR spectrometers (¹H NMR 400 MHz and ¹³C NMR 100.6 MHz) at ambient temperature in CDCl₃ and DMSO-d₆. Chemical shifts are reported in ppm relative to SiMe₄ in the ¹H NMR spectra and to chemical shifts of the solvent peaks as a secondary standard in the ¹³C NMR spectra. ESI-TOF spectra were recorded with a Thermo Scientific Orbitrap Elite instrument. Column chromatography was carried out on Merck silica gel 60 (40–63 µm) with mixture of petroleum ether (60-90°C) and ethylacetate 20:1 as eluent. For the catalytic carboxylation reactions, the reaction mixtures were analyzed by gas chromatography, using a Chromatec Crystal 5000 GC instrument. The melting point was measured using capillary sealed at one end in an Electrothermal 9100 melting point indicator. Target-oriented approach was utilized for the optimization of the analytic measurements [59]. Before measurements the samples were mounted on a 25 mm aluminum specimen stub and fixed by carbon conductive paste. Samples morphology was studied under native conditions to exclude metal coating surface effects [60]. The observations were carried out using Hitachi SU8000 field-emission scanning electron microscope (FE-SEM). Images were acquired in secondary electron mode at 1, 2, 3, 5 and 15 kV accelerating voltage and at working distance 2-9 mm. X-ray photoelectron spectra (XPS) were recorded on a Kratos Axis Ultra DLD. The X-ray diffraction data were collected on an X-ray diffractometer DRON-3 (Co-Kα radiation, θ/2θ scanning technique). Detection of copper in reaction mixture was performed on inductively coupled plasma mass spectrometer (ICP-MS)-element-2 (Thermo Fisher Scientific).

3.2 Preparation of Cu/Support Catalysts

To 0.125 g CuSO₄ dissolved in water 0.95 g of support was added. The mixture was stirred for 1 h, the solvent was then removed in vacuo. The dried catalyst was heated at 300 °C for 2–3 h in a stream of hydrogen (15–20 mL min⁻¹) using a tubular furnace.

3.2.1 Preparation of CuO/SiO₂ Catalyst

To 0.125 g CuSO₄ dissolved in water 0.95 g of SiO₂ was added. The mixture was stirred for 1 h, 1 M KOH solution was then added to alkaline the reaction. The precipitate was centrifuged and calcined in air to dark-brown colour.

3.3 Carboxylation Reactions

3.3.1 General Procedure of Alkyne Carboxylation

To a low pressure reactor equipped with magnetic stirrer alkyne (0.15 mmol), Cs_2CO_3 (0.30 mmol), copper catalyst (0.0075 mmol), *n*-BuBr (0.18 mmol) and DMF (2 mL) were added. CO_2 (2 atm.) was introduced into the reaction mixture by triply purging the reactor with CO_2 . The reaction mixture was stirred at 60 °C for 6 h or 16 h. After the reaction, the mixture was cooled to room temperature and diluted with DMF. After centrifugation, the organic phase was concentrated under reduced pressure and purified by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1). Isolated product was dried under vacuum.

3.3.2 Spectral Characteristics of Carboxylation Products

3.3.2.1 Butyl 3-(4-methoxyphenyl)propionate 2a White solid, ¹H NMR (400 MHz, CDCl₃, δ): 7.54 (d, J=8.8 Hz, 2H), 6.88 (d, J=8.8 Hz, 2H), 4.22 (t, J=6.8 Hz, 2H), 3.83 (s, 3H), 1.72–1.65 (m, 2H), 1.47–1.38 (m, 2H), 0.95 (t, J=7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 161.4, 154.5, 134.9, 114.2, 111.4, 86.9, 80.1, 65.8, 55.4, 30.5, 19.1, 13.7. The spectroscopic data matched those reported in the literature [CAS: 1359848-70-6].

3.3.2.2 Butyl 3-phenylpropionate **2b** Colorless oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.59–7.56 (m, 2H), 7.46–7.41 (m, 1H), 7.38–7.34 (m, 2H), 4.23 (t, *J*=6.8 Hz, 2H), 1.73–1.65 (m, 2H), 1.47–1.38 (m, 2H), 0.95 (t, *J*=7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.2, 132.9, 130.5, 128.5, 119.6, 86.0, 80.7, 65.9, 30.5, 19.0, 13.6. The spectroscopic data matched those reported in the literature [CAS: 80220-93-5].

3.3.2.3 Butyl 3-(*p*-tolyl)propionate 2*c* Light yellow solid, ¹H NMR (400 MHz, CDCl₃, δ): 7.48 (d, *J*=8.2 Hz, 2H), 7.17 (d, *J*=8.0 Hz, 2H), 4.22 (t, *J*=6.7 Hz, 2H), 2.36 (s, 3H) 1.72–1.65 (m, 2H), 1.47–1.38 (m, 2H), 0.95 (t, *J*=7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.3, 141.2, 132.9, 129.3, 116.5, 86.6, 80.3, 65.8, 30.5, 21.7, 19.0, 13.6. The spectroscopic data matched those reported in the literature [CAS: 1359848-69-3].

3.3.2.4 Butyl 3-mesitylpropionate **2d** Colorless oil, ¹H NMR (400 MHz, CDCl₃, δ): 6.87 (s, 2H), 4.23 (t, J=6.8 Hz, 2H), 2.43 (s, 6H), 2.28 (s, 3H), 1.73–1.66 (m, 2H), 1.48–1.38 (m, 2H), 0.96 (t, J=7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.6, 142.4, 140.4, 127.9, 116.5, 88.2, 84.5, 65.7, 30.5, 21.5, 20.8, 19.1, 13.7. HRMS: Calcd. for C₁₆H₂₀O₂: 244.1505, found: 244.1498.

3.3.2.5 Butyl 3-(4-(tert-butyl)phenyl)propionate 2e Colorless oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.53 (d, J=8.2 Hz, 2H), 7.39 (d, J=8.2 Hz, 2H), 4.22 (t, J=6.7 Hz, 2H), 1.73–1.65 (m, 2H), 1.47–1.38 (m, 2H), 1.3 (s, 9H), 0.95 (t, J=7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.4, 154.2, 132.9, 125.6, 116.5, 86.6, 80.3, 65.9, 35.0, 31.0, 30.5, 19.1, 13.7. HRMS: Calcd. for C₁₇H₂₂O₂: 258.1643, found: 258.1648.

3.3.2.6 Butyl 3-(4-(trifluoromethyl)phenyl)propionate **2f** Colorless oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.70 (d, J=8.1 Hz, 2H), 7.64 (d, J=8.3 Hz, 2H), 4.25 (t, J=6.7 Hz, 2H), 1.73–1.66 (m, 2H), 1.48–1.39 (m, 2H), 0.95 (t, J=7.5 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 153.7, 133.1, 125.6-125.5, 83.8, 82.3, 66.2, 30.4, 19.0, 13.6. HRMS: Calcd. for C₁₄H₁₃F₃O₂: 270.0965, found: 270.0959.

3.3.2.7 *Methyl* 4-(3-butoxy-3-oxoprop-1-yn-1-yl)benzoate **2g** Colorless oil, ¹H NMR (400 MHz, CDCl₃, δ): 8.04 (d, J=8.3 Hz, 2H), 7,65 (d, J=8.3 Hz, 2H), 4.24 (t, J=6.7 Hz, 2H), 3.92 (s, 3H), 1.73–1.65 (m, 2H), 1.48–1.38 (m, 2H), 0.95 (t, J=7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 166.1, 153.8, 132.8, 131.6, 129.6, 124.2, 84.5, 82.7, 66.1, 52.4, 30.4, 19.0, 13.6. HRMS: Calcd. for C₁₅H₁₆O₄: 260.1038, found: 260.1042.

3.3.2.8 Butyl 3-(4-cyanophenyl)propionate **2h** Colorless oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.66 (s, 4H), 4.24 (t, J=6.7 Hz, 2H), 1.72–1.65 (m, 2H), 1.47–1.37 (m, 2H), 0.95 (t, J=7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 153.5, 133.2, 133.2, 124.5, 117.8, 113.9, 83.7, 83.1, 66.3, 30.4, 19.0, 13.6. The spectroscopic data matched those reported in the literature [CAS: 1359848-71-7].

3.3.2.9 Butyl 3-(4-fluorophenyl)propionate 2i Yellow oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.59–7.56 (m, 2H), 7.08–7.04 (m, 2H), 4.22 (t, J=6.7 Hz, 2H), 1.72–1.65 (m, 2H), 1.47–1.38 (m, 2H), 0.95 (t, J=7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 165.1, 162.6, 154.1, 135.3, 116.2, 85.0, 80.6, 66.0, 30.4, 19.0, 13.6. The spectroscopic data matched those reported in the literature [CAS: 1449127-55-2].

3.3.2.10 Butyl 3-(3-thienyl)propionate 2j Yellow oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.73–7.72 (m, 1H), 7.31– 7.29 (m, 1H), 7.22–7.20 (m, 1H), 4.21 (t, *J*=6.7 Hz, 2H), 1.71–1.64 (m, 2H), 1.46–1.36 (m, 2H), 0.94 (t, *J*=7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.2, 133.6, 130.1, 126.0, 118.8, 81.5, 80.7, 65.9, 30.4, 19.0, 13.6. The spectroscopic data matched those reported in the literature [CAS: 1359848-76-2].

3.3.2.11 Butyl 3-(1-methyl-1H-pyrazol-4-yl)propionate **2k** Yellow oil, ¹H NMR (400 MHz, CDCl₃, δ): 7.68 (s, 1H), 7.64 (s, 1H), 4.19 (t, J=6.7 Hz, 2H), 3.89 (s, 3H), 1.69–1.62 (m, 2H), 1.45–1.35 (m, 2H), 0.93 (t, J=7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.3, 143.5, 135.0, 99.9, 82.7, 79.2, 65.7, 39.3, 30.4, 19.0, 13.6. HRMS: Calcd. for C₁₁H₁₄N₂O₂: 206.1133, found: 206.1140.

3.3.2.12 Butyl 3-(quinolin-3-yl)propionate 2l Brown solid, m.p. 92–93 °C, ¹H NMR (400 MHz, DMSO-*d*6, δ): 8.79 (s, 1H), 8.03 (t, *J*=9.1 Hz, 2H), 7.92 (s, 1H), 7.86 (t, *J*=7.3 Hz, 1H), 7.68 (t, *J*=7.5 Hz, 1H), 4.20 (t, *J*=6.8 Hz, 2H), 1.64–1.49 (m, 2H), 1.38–1.29 (m, 2H), 0.87 (t, *J*=7.4 Hz, 3H). ¹³C NMR (100 MHz, DMSO-*d*6, δ): 153.5, 151.7, 147.3, 141.8, 132.1, 129.0, 128.6, 128.1, 126.5, 112.8, 83.3, 83.1, 66.1, 29.9, 18.7, 13.6. HRMS: Calcd. for C₁₆H₁₅NO₂: 253.1161, found: 206.1155.

3.3.2.13 Butyl oct-2-ynoate **2m** Colorless oil ¹H NMR (400 MHz, CDCl₃, δ): 4.13 (t, J=6.7 Hz, 2H), 2.30 (t, J=7.2 Hz, 2H), 1.66–1.53 (m, 4H), 1.42–1.26 (m, 6H), 0.93–0.86 (m, 6H). ¹³C NMR (100 MHz, CDCl₃, δ): 154.0, 89.5, 73.1, 65.6, 31.0, 30.4, 27.2, 22.1, 19.0, 18.6, 13.8, 13.6. The spectroscopic data matched those reported in the literature [CAS: 127794-10-9].

3.4 Recyclization Studies and Leaching Experiments

For the studies of the catalysts recyclization, the following procedure was used. After 2 h from the start of the carboxylation reaction, the reactor was allowed to rest, organic phase was decanted to separate it from the solid catalyst. The solid residue was twice washed with DMF. Combined organic layers were concentrated and analyzed by GLC. A fresh charge of reagents was introduced into reactor and the reaction was carried as described previously. This was repeated for every recycle reaction.

The possibility of leaching from the catalyst surface was studied by centrifugation of the hot reaction mixture at 333 K by abruptly stopping the reaction at ~50% conversion. The collected centrifugate of the reaction mixture was heated for 4 h with CO_2 (2 atm.) and a new portion of the base filtered and no reaction was observed. The filtrate of the mixture was analyzed by ICP-MS (inductively coupled

plasma for atomic emission spectroscopy) investigation and no copper signal was detected in it.

4 Conclusions

The first CuNPs catalyzed direct carboxylation reaction of terminal alkynes was carried out. A comparison of the activity of a number of oxide- and carbon-based supports was performed. The best of the tested catalytic supports, i.e., highly active, selective, easily available, and recyclable was the Cu/Al₂O₃ containing medium and large CuNPs particles (up to 50–100 nm) covered by the thin oxide layer. The catalyst was successfully applied in the carboxylation of various terminal alkynes with CO₂ affording the corresponding alkyl 2-alkynoates in good yields. A possible mechanism was proposed for the reaction that, according to leaching tests, occurred on the catalyst surface.

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