

Cu^{II}-exchanged montmorillonite K10 clay-catalyzed direct carboxylation of terminal alkynes with carbon dioxide

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Received 8 June 2012; revised and accepted 29 June 2012

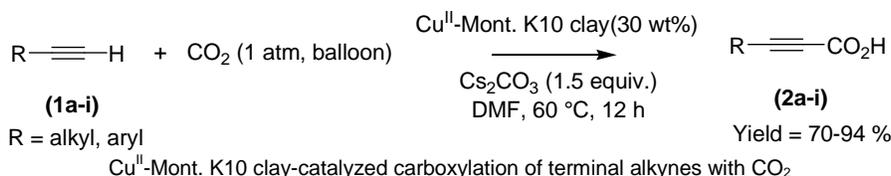
A new, simple and straight-forward protocol for direct carboxylation of terminal alkynes has been developed using Cu^{II}-montmorillonite K10 clay as a heterogeneous catalyst and CO₂ as the C1 carbon feedstock. Also coupling of terminal alkynes with CO₂ (1 atm) in the presence of alkyl halides has been achieved under the same reaction conditions, thereby providing access to a variety of functionalized alkyl-2-alkynoates in high yields.

Keywords: Catalysts, Montmorillonite clays, Carboxylation, Carbon dioxide activation, Alkyne C-H activation, Alkyl esters

Carbon dioxide is an attractive C1 building block in organic synthesis because it is an abundant, inexpensive and renewable feedstock.¹ It is highly inert due to its filled π orbitals, which are relatively low in energy and hence, its activation for forming new C-C bonds remains a challenging goal for synthetic chemists.² Alkynyl carboxylic acids (**2**) and their derivatives (**3**) are an important class of compounds in medicinal chemistry as well as in polymer synthesis.³ Traditionally, such compounds are synthesized in two-step processes: (i) addition of alkynes to formaldehyde followed by oxidation of the resulting propargylic alcohol,⁴ and, (ii) the oxidative carbonylation of alkynes.⁵ Other synthetic approaches include: (i) the carbonylation of unstable alkynyl halides,⁶ (ii) the lithiation of 1-alkynes followed by quenching with chloroformate,⁷ (iii) direct carboxylation of alkynyl Mg or Li reagents,⁸ and, (iv) Ni- or Pd-catalyzed alkylative carboxylation of alkynes using organozinc reagents under a CO₂ atmosphere.⁹ Quite recently, catalytic systems comprising Ag(I), Cu(I)/NHC and Cu(I)/TMEDA have been reported for the direct carboxylation of alkynes.¹⁰ However, these methods have many

disadvantages that include the use of expensive and sensitive organometallic reagents,¹¹ toxicity, and difficulty in handling of CO, etc. Therefore, the development of a reusable heterogeneous catalytic system for the direct carboxylation of alkynes with CO₂ under mild condition is highly desirable.

Montmorillonite clays have gained importance as catalysts for various useful organic transformations.¹² They often exhibit high surface acidity. Many clay minerals carry an excess negative electric charge owing to internal substitution by lower-valent cations and thereby lead to an, increase in internal reactivity for chemical combination and ion exchange. In particular, metal exchanged clays are useful catalysts, which can be recovered and reused several times without losing their activity.¹³ Under homogeneous conditions, Cu and Ag salts are proven to be effective catalysts for the carboxylation of terminal alkynes.¹⁰ In this context, we wish to report a Cu^{II}-exchanged montmorillonite K10 clay-catalyzed carboxylation of terminal alkynes (**1**) with CO₂ to produce the corresponding alkynyl carboxylic acids (**2**) and their derivatives (**3**) under heterogeneous conditions (Scheme 1).



Scheme 1

Materials and Methods

Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60–80 °C was used. All other chemicals were used as received. Melting points are uncorrected and recorded on a Buchi B-542 instrument. Infrared spectra were recorded on a Shimadzu FTIR-8400 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV-200 NMR spectrometer. Elemental analysis was carried out on a Carlo Erba CHNS-O analyzer. The electronic spectra of the catalyst were on a Shimadzu UV-vis recorded scanning spectrophotometer (model 2101 PC). Powder X-ray diffraction patterns of the catalysts were recorded using a Rigaku (model D/MAXIII VC, Japan), setup with Cu-K α radiation at a scan rate of 5° min $^{-1}$ and scanning in the 2θ range from 5 to 50°. Silicon was used to calibrate the instrument. The copper content in the clay samples was measured by an atomic absorption spectrometer (AAS-Hitachi, model Z-8000).

Preparation and characterisation of catalyst

All the metal-exchanged montmorillonite K10 clay catalysts were prepared and characterized following the reported procedures.¹⁴ For example, Cu^{II}-Mont. K10 clay was prepared by slurring acidic clay Mont. K10 (10 g) (purchased from Aldrich, USA) dried at 100 °C overnight with 0.5 M aqueous solution of Cu(OCOCH₃)₂ (50 mL) at 90 °C for 8 h. The slurry was then cooled to room temperature and filtered. This process was repeated twice to ensure maximum copper metal ion exchange. The solid obtained was filtered and washed several times with water and dried at 100 °C for 12 h and then calcined (300 °C for 4 h). The copper content of the Cu^{II}-Mont. K10 clay catalyst was measured by AAS and found to be 0.9 mmol/g.

The XRD profile of Mont. K10 showed a layered structure with a basal spacing (d_{001}) of 3.34 Å. After treatment with Cu(OCOCH₃)₂, the XRD studies of Cu-Mont. K10 showed that the layered structure is retained and the basal spacing of (d_{001}) was estimated to be 3.35 Å, which is comparable to that of the parent K10. The XRD of Cu-Mont. K10 catalysts after the reaction also retained the layered structure with a basal spacing (d_{001}) of 3.33 Å. The diffuse reflectance UV-vis spectra of Mont. K10 and Cu-Mont. K10 indicate the presence of copper in the catalyst sample. While Mont. K10 does not have any absorption band above 400 nm, Cu-K10 exhibits a strong band with a

maximum at 546 nm, which is attributed to the $d-d$ transitions of Cu(II).

General procedure for the preparation of alkynyl carboxylic acids, (2a-j)

To a stirred mixture of alkyne (3 mmol) and Cs₂CO₃ (4.5 mmol) in dry *N,N*-dimethylformamide (DMF; 3 mL), Cu^{II}-Mont. K10 clay (30 wt%) was added. The entire reaction mixture was stirred under CO₂ (1 atm) at 60 °C for 14 h. It was then cooled to room temperature and potassium carbonate solution (2*N*, 5 mL) was added slowly under stirring for 30 min. The reaction mixture was filtered to separate out the catalyst and the filtrate was then extracted with dichloromethane (3 × 25 mL) and the aqueous layer was acidified with 1 M HCl and again extracted with diethyl ether (3 × 25 mL). The combined organic layers were dried over anhydrous Na₂SO₄, and concentrated in vacuum to give the crude product, which was then purified by column chromatography over silica gel (100-200 mesh) using petroleum ether/EtOAc (1:1) to give alkynyl carboxylic acids (2a-j), which were fully characterized by ^1H and ^{13}C NMR, IR and elemental analyses.

3-Phenylpropionic acid (2a): Yield: 80 %; colourless solid; m.pt.: 137 °C (lit¹⁵: 136-138 °C); IR: (CHCl₃, cm $^{-1}$): ν_{max} 753, 919, 1209, 1305, 1417, 1673, 2201, 2235, 3069; ^1H NMR (200 MHz, DMSO-*d*₆): δ 7.44-7.65 (m, 5H), 13.82 (bs, 1H); ^{13}C NMR (50 MHz, CDCl₃): δ 80.2, 88.9, 119.2, 128.6, 131.0, 133.3, 158.6; Anal. (%): Calcd for C₉H₆O₂ requires C, 73.97; H, 4.14; found C, 74.08; H, 4.04.

General procedure for the preparation of alkynyl carboxylic esters, (3a-f)

To a stirred mixture of alkyne (3 mmol) and Cs₂CO₃ (4.5 mmol) in dry DMF (3 mL), Cu^{II}-Mont. K10 clay (30 wt%) was added. The reaction mixture was stirred under CO₂ (1 atm, balloon) at 60 °C for 14 h. After completion of the reaction, it was cooled to room temperature and alkyl iodide (3.0 mmol) was added. The resulting mixture was stirred for 2 h at room temperature under N₂ atmosphere. After completion of the reaction as monitored by TLC, the reaction mixture was filtered to separate out the catalyst and the filtrate was extracted with EtOAc (3 × 25 mL), washed with water and brine, dried over anhydrous Na₂SO₄ and concentrated to give the crude product. The crude product was then purified by column chromatography over silica gel

(100-200 mesh) using petroleum ether/EtOAc (9:1) to give alkynyl carboxylic esters, (**3a-f**), which were characterized by ¹H and ¹³C NMR, IR and elemental analyses.

Methyl 3-phenylpropiolate (**3aa**): Yield: 68 %; colourless liquid; IR: (CHCl₃, cm⁻¹): ν_{max} 689, 757, 1171, 1202, 1444, 1715, 2226; ¹H NMR (200 MHz, CDCl₃): δ 3.84 (s, 3H), 7.37-7.43 (m, 3H), 7.56-7.61 (m, 2H); ¹³C NMR (50 MHz, CDCl₃): δ 52.6, 80.5, 86.3, 119.7, 128.5, 130.6, 133.0, 154.2; Anal. (%): Calcd for C₁₀H₈O₂ requires C, 74.99; H, 5.03; found C, 74.89; H, 4.95.

Results and Discussion

Initially, the carboxylation reaction was carried out using phenyl acetylene (**1a**) as a test substrate, for determining the optimal conditions (Table 1). Thus, when phenyl acetylene (**1a**) was treated with Cu^{II}-Mont. K10 clay (10 wt%), CO₂ (1 atm, balloon) and Cs₂CO₃ (1.5 equiv.) in DMF at 60 °C, the corresponding acetylenic carboxylic acid (**2a**) was obtained in 30 % yield. However, the yield of (**2a**) could be significantly improved to 74 % when the catalyst quantity was increased to 20 wt% under the same reaction conditions. Interestingly, further increasing the catalyst concentration to 30 wt% resulted in a dramatic improvement in the yield of (**2a**) (94 %). In general, better yields were obtained with Cu^{II}-Mont. K10 clay (30 wt%) in all the cases studied. After several experimentations, it was found that a combination of alkyne (1 equiv.), Cu^{II}-Mont. K10 clay (30 wt%), CO₂ (1 atm, balloon) and Cs₂CO₃ (1.5 equiv.) in DMF at 60 °C and 12 h were the best reaction conditions in achieving a good conversion of alkynes with excellent product yield. In the absence of catalyst, negligible amount (<5%) of product (**2a**) was formed. A brief comparison of solvents and bases indicated that DMF and Cs₂CO₃ were the most suitable solvent and base, respectively for the carboxylation, as other solvents like *N,N*-dimethylacetamide (DMAc), dimethyl sulfoxide (DMSO), CH₃CN or bases like Et₃N and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were found to be less effective. Other metal-exchanged clay catalysts like Ag^I-Mont. K10 (30 wt%), Ru^{III}-Mont. K10 (30 wt%) and Cu^{II}-Pd^{II}-Mont. K10 clays (30 wt%), when carried out under similar reaction conditions, showed only moderate activity for the carboxylation of terminal alkynes with CO₂.

Substrate scope in the carboxylation of terminal alkynes was next examined using the conditions

Table 1 – Effect of reaction parameters on carboxylation of phenyl acetylene with CO₂. [React. cond.: Phenyl acetylene: 3 mmol; catalyst: 10-30 wt%; base: 4.5 mmol; CO₂: 1 atm, balloon; DMF: 10 mL; 60 °C; 14 h]

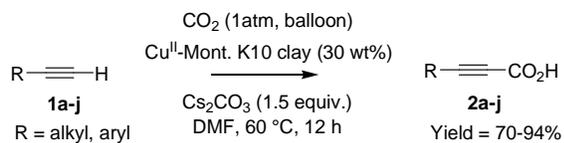
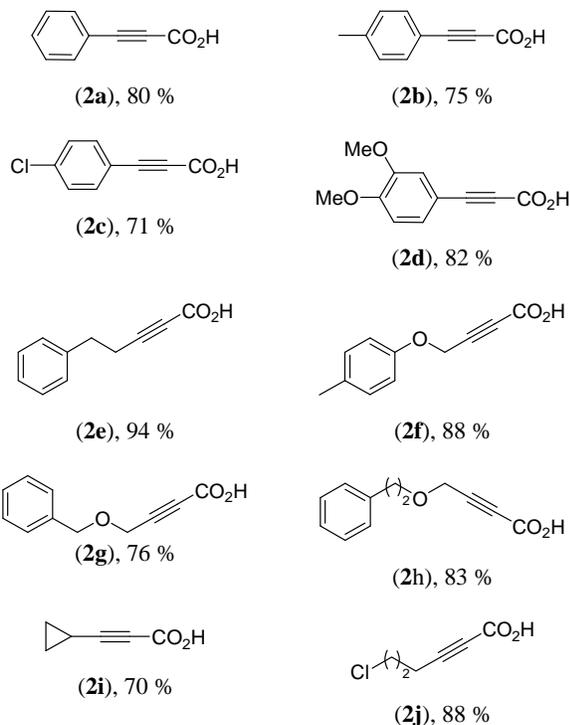
No.	Catalyst	Solvent	Base	Yield of (2a) (%) ^a
1	Nil	DMSO	Cs ₂ CO ₃	5
2	Cu ^{II} -Mont. K10 clay (10 wt%)	DMSO	Cs ₂ CO ₃	30
		DMF	Cs ₂ CO ₃	54
		CH ₃ CN	Et ₃ N	10
		DMAc	Cs ₂ CO ₃	20
		DMF	Cs ₂ CO ₃	74 ^b
3	Cu ^{II} -Mont. K10 clay (20 wt%)	DMF	Et ₃ N	40
		DMF	Cs ₂ CO ₃	74
		DMF	Cs ₂ CO ₃	94
4	Cu ^{II} -Mont. K10 clay (30 wt%)	DMAc	Cs ₂ CO ₃	68
		DMF	Cs ₂ CO ₃	15
5	Ag ^I -Mont. K10 clay (30 wt%)	DMF	DBU	15
		DMF	Cs ₂ CO ₃	15
6	Ru ^{III} -Mont. K10 clay (30 wt%)	DMF	DBU	15
		DMF	Cs ₂ CO ₃	10
7	Cu ^{II} -Pd ^{II} -Mont. K10 clay (30 wt%)	DMF	Cs ₂ CO ₃	10
		DMF	DBU	10

^aIsolated yields after chromatographic purification over silica gel (100-200 mesh) using petroleum ether/EtOAc (1:1).

^bReaction was carried out for 36 h.

optimized for phenyl acetylene. As can be seen from Table 2, a wide array of aromatic, cyclic, and acyclic terminal alkynes were readily carboxylated affording the corresponding carboxylic acids (**2a-j**) in good isolated yields. Higher yields, however, were obtained with electron-rich substrates (80-94 %) and acyclic terminal alkynes (88 %). Chloro substituted aliphatic alkyne (**2j**) also reacted well (88 %) under the reaction conditions. However, electron-deficient alkynes such as 4-chloro phenyl acetylene (**1c**) exhibited moderate activity (71 %).

Recently Kondo *et al.*^{10d} have reported a one-pot synthesis of propiolic esters (**3**) by coupling of terminal alkynes with CO₂ and primary halides using Cu-phosphine-based catalytic system. Encouraged by this result, we tested the applicability of our clay catalytic system for such processes. Thus, methyl iodide was added at the end of carboxylation reaction to quench the carbonate that was formed *in situ*. As expected, the corresponding methyl carboxylate (**3aa**) was obtained in 75 % yield. Other long chain primary

Table 2 – Cu^{II}-Mont. K10 clay-catalyzed carboxylation of terminal alkynes with CO₂Products (**2a-j**)^a

^aProducts were isolated after chromatographic purification over silica gel (100-200 mesh) using petroleum ether/EtOAc (1:1).

alkyl and allylic halides were then examined, which produced good yields of the respective alkynic carboxylic esters (**3a-f**) (50-77 %). Thus, several alkynic carboxylic esters (**3a-f**) were readily prepared and the results are summarized in Table 3. In addition to alkyl iodide, alkyl bromide was also found to be a suitable alkylating agent for the carboxylation process. However, alkyl chloride was found to be unreactive under the reaction conditions.^{10d}

The proposed catalytic cycle for the Cu^{II}-Mont. K10 clay-catalyzed carboxylation of terminal alkynes with CO₂ is shown in Fig. 1. The coordination of Cu(II) with alkynes enhances the acidity of its C-H bond, which readily assists in the formation of copper acetylide intermediate (**A**). This is followed by the insertion of CO₂ into alkyne-Cu bond to form copper propiolate intermediate (**B**), which subsequently

Table 3 – Cu^{II}-Mont. K10 clay-catalyzed carboxylative coupling of alkynes with alkyl halides and CO₂^a

No.	R (1a-f)	R'-X	Yield of (3a-f) (%) ^a
1	Ph	MeI EtI ⁿ BuBr ⁿ BuI ⁿ HeptylI AllylBr	75 (3aa) 68 (3ab) 50 (3ac) 77 (3ac) 72 (3ad) 62 (3ae)
2	4-MePh	EtI	89
3	4-ClPh	EtI	75
4	3,4-(OMe) ₂ Ph	EtI	79
5	4-MePh-O-CH ₂	EtI	85
6	PhCH ₂ -O-CH ₂	EtI	84

^a Isolated yield after chromatographic purification over silica gel (100-200 mesh) using petroleum ether/EtOAc (9:1).

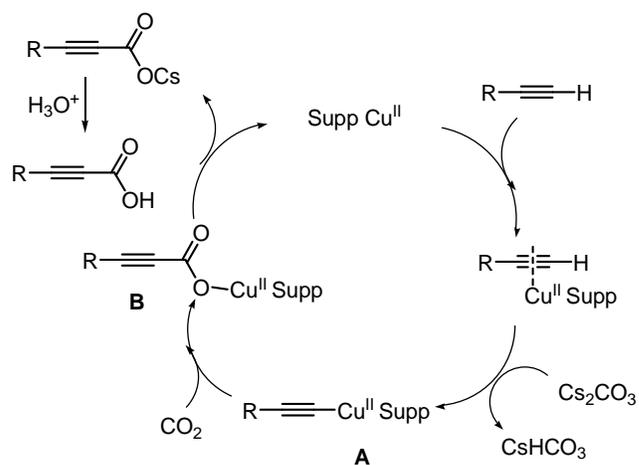


Fig. 1—Probable mechanism for the carboxylation of the terminal alkynes.

releases Cu-clay catalyst with the liberation of cesium propiolate, acidification of which finally affords propiolic acids.

Reusability of the catalyst

The reusability of the catalyst was also examined by filtering off the catalyst from the reaction mixture, washing with water and drying it in air. It was successfully reused three times without decreasing the catalytic activity. XRD characterization of the recovered catalyst after the third recycle indicated that

the catalyst did not show any substantial structural change after reuse. The copper content of the reused Cu^{II}-Mont. K10 clay catalyst was measured by AAS and found to be 0.88 mmol/g.^{14b}

Conclusions

In conclusion, Cu^{II}-Mont. K10 clay-catalyzed carboxylation of terminal alkynes with CO₂ (1 atm), R-X (for esters), and Cs₂CO₃ in DMF gives the corresponding alkynyl carboxylic acids (**2**) and their derivatives (**3**) in high yields. The protocol employs stable and readily accessible Cu^{II}-Mont. K10 clay as a truly heterogeneous catalyst for the carboxylation process via activation of C-H bond in terminal alkynes. The advantages of the current procedure include not only its cost effectiveness, but also green, efficient reusable catalyst for potential fixation of carbon dioxide.

Supplementary Data

Supplementary data associated with this article, viz., experimental data of the compounds **2(b-j)** and **3(b-f)** (¹H NMR, ¹³C NMR, IR and C, H, N analyses) are available in the electronic form at [http://www.niscair.res.in/jinfo/ijca/IJCA_51A_\(09-10\)_1325-1329_Suppl_Data.pdf](http://www.niscair.res.in/jinfo/ijca/IJCA_51A_(09-10)_1325-1329_Suppl_Data.pdf).

Acknowledgement

We sincerely thank CSIR, New Delhi, India, (NWP-0021B) and DST, New Delhi, India (No. SR/S1/OC-67/2010) for financial support. RDA, MHG and RSR thank CSIR, New Delhi, India, for research fellowships.

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