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Carboxylation of terminal alkynes promoted by silver carbamate at ambient pressure†

Giulio Bresciani,[ab] Fabio Marchetti[ab] and Guido Pampaloni*[ab]

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Transition metal carbamates constitute a class of compounds with unique properties, however their catalytic potential has been sparingly explored so far. The easily available silver *N*,*N*-dimethylcarbamate, $Ag(O_2CNMe_2)$, worked as a catalyst in the carboxylation reaction of terminal alkynes with CO_2 at atmospheric pressure. Different reaction parameters (solvent, base, temperature, time and the amount of catalyst) were investigated in order to establish the optimal conditions.

Introduction

The use of carbon dioxide as a nontoxic and inexpensive C1 synthon to obtain valuable chemicals represents a foremost topic of contemporary chemistry research, in view of developing new convenient and sustainable synthetic processes.[1] Among the large variety of studied organic reactions exploiting CO_2, the carboxylation of terminal alkynes to afford propiolic acids is one of the most intriguing ones in terms of added-value products. Indeed, propiolic acids are useful intermediates to produce polymers and molecules of pharmaceutical interest, such as flavones, coumarins, spirobenzofuranones and vinyl sulfide.[2] The classical synthetic strategy to access propiolic acids involves the oxidation of propargylic alcohols[3] or aldehyde derivatives,[4] and the carboxylation of terminal alkynes represents an alternative and more sustainable route. The latter involves alkyne deprotonation by a suitable base, with the resulting carbanion adding CO_2 to finally afford propiolic acids (Scheme 1).[2]

Saegusa and co-workers reported the first example of a metal-mediated carboxylation of terminal alkynes using a stoichiometric amount of copper(I) or silver(I) *tert*-butoxides.[5] The first catalytic reaction was published 20 years later exploiting silver(I) and copper(I) salts in the presence of an excess of K_2CO_3, at ambient CO_2 pressure at 100 °C.[6] Since this pioneering work, attention paid to carboxylation reactions of alkynes has exponentially increased, and several catalytic systems have been developed to reach satisfying conversions under mild conditions.[7] It is believed that copper and silver species may work as optimal catalysts due to the tendency of such metal centers to activate carbon–carbon triple bonds,[8] thus various Cu(I)[9] and Ag(I) complexes,[10] copper conjugated polymers[11] and silver nanoparticles[12] have been proposed in this regard. Nevertheless, also dinuclear Mo–alkoxides,[13] lanthanide amidates[14] and metal free systems[15] have been evaluated. Several of the efficient molecular metal compounds require CO_2 pressure >1 atm and temperatures above 100 °C in order to gain acceptable conversion values.[16]

Metal *N*,*N*-dialkylcarbamates are easily accessible and cost effective materials of general formula $M(O_2CNR_2)_n$, being usually obtained by treatment of a range of metal chloride precursors with dialkylamines in the presence of CO_2 at atmospheric pressure (eqn (1)).[17]

$$MCl_n + nCO_2 + 2nNHR_2 \rightarrow M(O_2CNR_2)_n + n(NH_2R_2)Cl \quad (1)$$

A limited number of transition metal carbamates have found application as catalytic precursors in various reactions, such as the hydrogenation of alkenes[18] and the polymerization of alkenes[19] and cyclic esters.[20]

Despite the fact that such a class of versatile metal complexes display interesting chemical–physical properties[17,21] and constitute in turn an intrinsic form of CO_2 activation, their employment in metal promoted carboxylation reactions is still in its infancy. However, we recently reported that $Fe(O_2CNEt_2)_3$ is effective in the synthesis of cyclic carbonates by CO_2 addition to epoxides at ambient temperature and pressure, in the presence of NBu_4Br as a co-catalyst.[22] Remarkably, the proposed catalytic system takes advantage of a dynamic pre-activation of carbon dioxide, incorporated within the metal structure as a carbamato ligand, as it has been outlined by DFT calculations and NMR spectroscopy. Analogously, carbamates of tin, aluminum and copper are active in the epoxide–CO_2 coupling process under mild conditions.[23]

[a] *Università di Pisa, Dipartimento di Chimica e Chimica Industriale, Via Moruzzi 13, I-56124 Pisa, Italy. E-mail: guido.pampaloni@unipi.it*
[b] *CIRCC, via Celso Ulpiani 27, I-70126 Bari, Italy*

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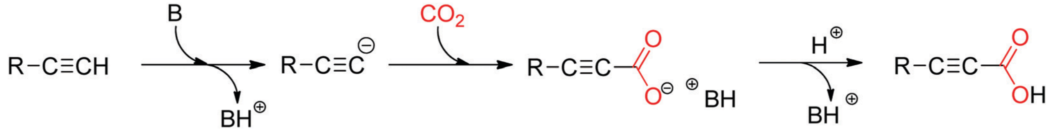


Scheme 1 Base(B)-assisted synthesis of propiolic acids by carboxylation of terminal alkynes.

Herein, we explore for the first time the catalytic potential of copper and silver carbamates, showing their performance in the carboxylation reactions of terminal alkynes.

Results and discussion

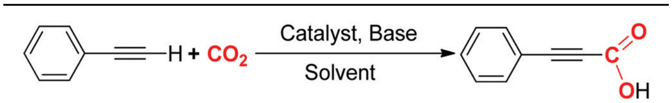
We selected silver and copper carbamates $Ag^{I}(O_2CNR_2)$, R = Me, Et, $Cu^{I}(O_2CN^{i}Pr_2)$ and $Cu^{II}(O_2CNEt_2)_2$ in order to assess their catalytic activity in the formation of phenylpropiolic acid from phenylacetylene and CO_2, selected as a model process. The reactions were carried out in a solvent (THF, DMSO or DMF) for 24 h at 50 °C and 1 atm, in the presence of a base (KOH or Cs_2CO_3), see Table 1.

The silver carbamate $Ag(O_2CNMe_2)$ is the best catalyst, leading to the isolation of phenylpropiolic acid in 60% yield, after work-up. DMF and Cs_2CO_3 were revealed to be the optimal solvent/base combination. A blank experiment (Table 1, entry 11) showed that a significant lower yield is achieved under the same conditions but in the absence of the catalyst. Since the silver carbamate exhibited a higher catalytic activity with respect to copper complexes, we used the former for additional studies. First, we investigated the effect of temperature (Table 2).

The results reported in Table 2 indicate that temperatures above 50 °C are detrimental in terms of yield; this trend might be associated with a very rapid decrease of CO_2 solubility in DMF over 50 °C.[24]

The influence of the amount of catalyst on the product yield was evaluated from a minimum of 0.5 mol% to a maximum of 5 mol% (Table 3).

Table 1 Carboxylation of phenylacetylene catalyzed by Ag(I), Cu(I) and Cu(II) carbamates[a]



Entry	Catalyst	Base	Solvent	Yield[b] [%]
1	$Cu(O_2CNEt_2)_2$	KOH	THF	—
2	$Ag(O_2CNMe_2)$	KOH	THF	—
3	$Cu(O_2CNEt_2)_2$	KOH	DMSO	2
4	$Ag(O_2CNMe_2)$	KOH	DMSO	1
5	$Ag(O_2CNMe_2)$	KOH	DMF	—
6	$Ag(O_2CNMe_2)$	Cs_2CO_3	DMSO	45
7	$Cu(O_2CN^{i}Pr_2)$	Cs_2CO_3	DMF	37
8	$Cu(O_2CNEt_2)_2$	Cs_2CO_3	DMF	20
9	$Ag(O_2CNMe_2)$	Cs_2CO_3	DMF	60
10	$Ag(S_2CNEt_2)$	Cs_2CO_3	DMF	54
11	—	Cs_2CO_3	DMF	15

[a] Reaction conditions: phenylacetylene (0.22 mL, 2.0 mmol), catalyst 1 mol%, base 3.0 mmol, solvent 10 mL, T = 50 °C, $p(CO_2)$ = 1 bar, t = 24 h. [b] Referred to isolated products after work-up (see Experimental for details).

Table 2 Yield of phenylpropiolic acid at different temperatures using $Ag(O_2CNMe_2)$ as the catalyst[a]

Entry	Temperature [°C]	Yield[b] [%]
1	25	10
2	50	60
3	80	20
4	120	19

[a] Reaction conditions: phenylacetylene (0.22 mL, 2.0 mmol), $Ag(O_2CNMe_2)$ 1 mol%, Cs_2CO_3 3.0 mmol, DMF 10 mL, $p(CO_2)$ = 1 bar, t = 24 h. [b] Referred to isolated products after work-up (see Experimental for details).

Table 3 Yield of phenylpropiolic acid using different amounts of catalyst[a]

Entry	Amount of $Ag(O_2CNMe_2)$ [mol%]	Yield[b] [%]
1	0.5	39
2	1	60
3	2	77
4	5	53

[a] Reaction conditions: phenylacetylene (0.22 mL, 2.0 mmol), Cs_2CO_3 3.0 mmol, DMF 10 mL, $p(CO_2)$ = 1 bar, t = 24 h. [b] Referred to isolated products after work-up (see Experimental for details).

The data indicate a favourable effect of the increase of catalyst amount up to 2 mol% (Table 3, entry 3). However, a further increase to 5 mol% determines a negative effect.

The reactions carried out in DMSO or THF under the optimized conditions afforded slightly lower yields compared to the reaction performed in DMF (Table 4). On the other hand, replacing the methyl groups with ethyl ones within the carbamato ligand resulted in moderate lowering of the product yield (Table 4, entry 4).

Having established that $Ag(O_2CNMe_2)$, in combination with Cs_2CO_3, is an effective system for the carboxylation of phenylacetylene, we decided to expand the scope of the present study to other terminal alkynes (Table 5).

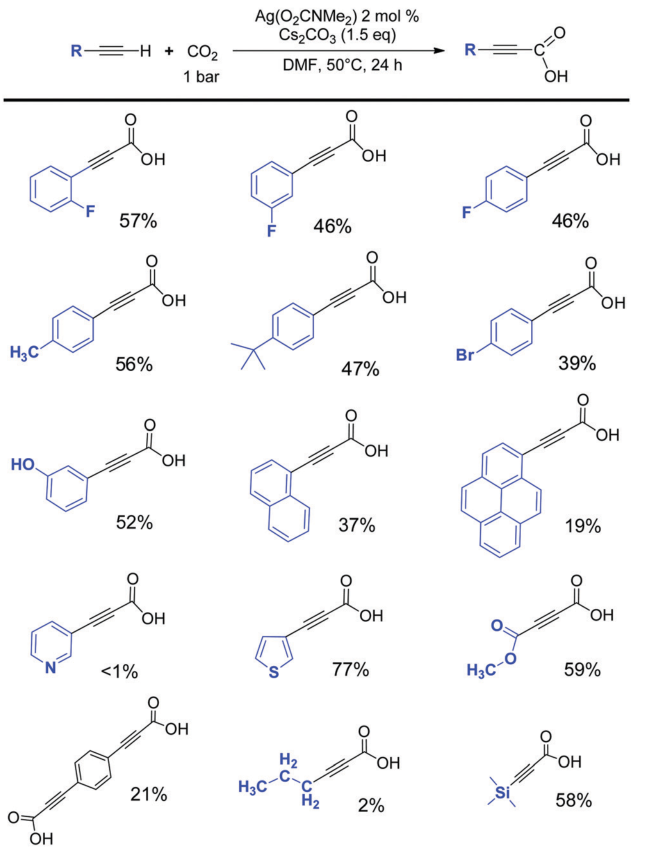
The results show that, in general, phenylacetylenes are prone to carboxylation, leading to the isolation of the corresponding

Table 4 Yield of phenylpropiolic acid under various conditions[a]

Entry		Solvent	Temperature [°C]	Yield[b] [%]
1[c]	$Ag(O_2CNMe_2)$	DMF	50	35
2	$Ag(O_2CNMe_2)$	DMSO	50	66
3	$Ag(O_2CNMe_2)$	THF	50	72
4	$Ag(O_2CNEt_2)$	DMF	50	65
5	$Ag(O_2CNMe_2)$	DMF	80	20
6	$Ag(O_2CNMe_2)$	DMF	50	77

[a] Reaction conditions: phenylacetylene (0.22 mL, 2.0 mmol), catalyst 2 mol%, Cs_2CO_3 3.0 mmol, solvent 10 mL, T = 50 °C, $p(CO_2)$ = 1 bar, t = 24 h. [b] Referred to isolated products after work-up (see Experimental for details). [c] Cs_2CO_3 4.0 mmol.

Table 5 Yield of propiolic acids obtained by carboxylation of terminal alkynes using $Ag(O_2CNMe_2)$ as the catalyst



propiolic acids in satisfying yields, irrespective of the position and nature of the substituents. Likewise, the reaction worked well with alkynes containing electron-withdrawing groups, *i.e.* trimethylsilylacetylene and methyl propiolate. Lower yields were achieved with alkynes substituted with fused aromatic rings, alkyl chains and a pyridine moiety.

Interestingly, the reaction with 1,4-diethynylbenzene supplied almost quantitative selectivity for the diacid derivative, since only traces of the other possible monoacidic product were detected by ^1H NMR.

It is presumable that the $Ag(O_2CNMe_2)$-mediated formation of propiolic acid proceeds through the generally accepted catalytic cycle reported in Scheme 2.[1a] However, a CO_2 dynamic exchange (see the Introduction)[22] might be working too.

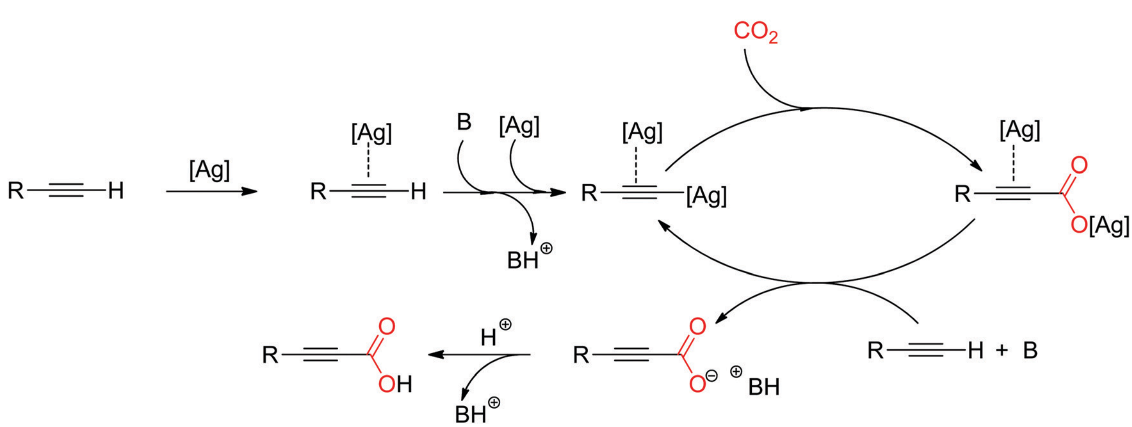
Conclusions

The use of carbon dioxide as a convenient C1 synthon in organic synthesis is a topic of great interest due to environmental and economic issues, and in this context the carboxylation of terminal alkynes represents an attractive strategy to afford propiolic acids. On the other hand, transition metal carbamates are easily accessible materials representing an intrinsic form of CO_2 activation and possessing unique properties. However, the catalytic potential of transition metal carbamates remains largely investigated. Herein, we have assessed silver and copper complexes containing carbamato ligands as catalysts for the carboxylation of a series of terminal alkynes at ambient CO_2 pressure. $Ag(O_2CNMe_2)$, in combination with Cs_2CO_3 in DMF solution, was found to be the most efficient system, and the produced propiolic acids were isolated in moderate to good yields after work-up.

Experimental section

General experimental details

All the operations were carried out under an atmosphere of pre-purified nitrogen. The reaction vessels were oven dried at 140 °C prior to use, evacuated (10^{-2} mmHg) and then filled with nitrogen. CO_2 (99.99%) was purchased from Rivoira (Chivasso, Italy). Deuterated solvents and organic and inorganic reactants were commercial products (Sigma Aldrich, TCI Europe or Strem) of the highest purity available and stored under a nitrogen atmosphere as received. Solvents (Sigma Aldrich) were distilled before use over appropriate drying agents. $Cu(O_2CNEt_2)_2$,[25] $Cu(O_2CN^iPr_2)$[26] and $Ag(O_2CNMe_2)$[26] were prepared according to literature procedures. Infrared spectra (solid state) were recorded at room temperature on



Scheme 2 Possible mechanism of Ag-promoted carboxylation of terminal alkynes.

a FTIR-PerkinElmer Spectrometer, equipped with an UATR sampling accessory. NMR spectra were recorded at 298 K on a Bruker Avance II DRX400 instrument equipped with a BBFO broadband probe. Chemical shifts (expressed in ppm) are referenced to the residual solvent peaks.[27]

Synthesis and characterization of $Ag(O_2CNEt_2)$

$Ag(O_2CNEt_2)$ was prepared by a slight modification of the procedure reported in the literature.[26] A solution of diethylamine (8.0 mL, 78 mmol) in heptane (120 mL) was cooled to 0 °C and saturated with CO_2. When the gas absorption was terminated, the reaction flask was carefully covered with aluminum foil and Ag_2O (3.0 g, 13 mmol) was added to the solution. The mixture was allowed to slowly return to room temperature during the stirring (20 h). The resulting solution was evaporated under vacuum, and the residue was suspended in 50 mL of pentane, filtered and dried *in vacuo* at room temperature. A light brown solid was collected and stored in the dark under an N_2 atmosphere. Anal. calcd for $C_5H_{10}AgNO_2$: C, 26.81; H, 4.50; N, 6.25. Found: C, 26.73; H, 4.45; N, 6.33.

Reaction between terminal alkynes and carbon dioxide

The appropriate amounts of catalyst and base were introduced into a Schlenk tube with the solvent (10 mL). The tube was evacuated and filled with CO_2. The vacuum/CO_2 sequence was repeated twice. Alkyne (2 mmol) was added under a stream of carbon dioxide, and the resulting mixture was stirred at 50 °C and ambient pressure. After 24 h, the mixture was treated with a potassium carbonate solution (2 M, 10 mL). The resulting mixture was stirred for 1 hour and washed with dichloromethane (3 × 20 mL). The aqueous layer was acidified with concentrated HCl to pH = 1 and extracted with diethyl ether (3 × 10 mL). The organic phases were collected, dried over Na_2SO_4 and filtered. The volatiles were evaporated under vacuum affording the desired carboxylic acid. The purity of the products was checked by NMR spectroscopy (see the ESI,† Table S1).

Conflicts of interest

There are no conflicts to declare.

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