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Silver(I)-Catalyzed Synthesis of β-Oxopropylcarbamates from Propargylic Alcohols and CO_2 Surrogate: A Gas-Free Process

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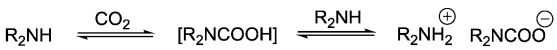
The utilization of carbon dioxide poses major challenges owing to its high thermodynamic stability and kinetic inertness. To circumvent these problems, a simple reaction system is reported comprising ammonium carbamates as carbon dioxide surrogates, propargylic alcohols, and a silver(I) catalyst, for the effective conversion of a wide range of alcohols and secondary amines into the corresponding β-oxopropylcarbamates. A key feature of this strategy includes quantitative use of a carbon resource with high product yields under gas-free and mild reaction conditions. Notably, this catalytic protocol also works well for the carboxylative cyclization of propargylic amines and carbon dioxide surrogates to afford 2-oxazolidinones.

Carbon dioxide is as an easily available, abundant, safe, and renewable carbon resource. These factors make it a highly attractive C_1 building block for exploitation in chemical transformations.[1] However, the utilization of CO_2 poses major challenges owing to its high thermodynamic stability and kinetic inertness. There are well-established protocols with vigorous catalysts including (transition) metals such as palladium, silver, copper, ruthenium, rhodium, iridium; active molecules with high free energy such as *N*-heterocyclic carbenes (NHCs); organic bases; and drastic reaction conditions such as high pressures for the incorporation of CO_2 into organic compounds.[2] Although great achievements have been made, most procedures require an excess of CO_2; that is, high CO_2 pressures. Therefore, discovering effective methodologies that use feedstocks that are low in CO_2 content, especially stoichiometric CO_2 resources, and low energy inputs is a significant, promising, and challenging area in both catalysis and sustainable chemistry.

The exploration of green, effective strategies for the reaction of quantitative CO_2 is a very attractive topic. Recently, Yoshida's group reported a methodology for the synthesis of oxazolidinone by the silver/1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)-promoted reaction of propargylic amines and CO_2 in air.[2f,3] A large amount of DBU was initially employed to trap CO_2 to form a DBU–CO_2 complex, which acted as CO_2 source for the reaction.[4] Subsequently, CO_2 captured directly from exhaust gas by aqueous ethanolamine solution was used for the carboxylation of alkynes as efficiently as pure CO_2 gas from a commercial source.[5] Newly, NH_2COONH_4 and $(NH_4)_2CO_3$ were reported as carbon source and hydrogenated to produce ammonium formate with molecular hydrogen through carbon-supported palladium nanocatalysts in aqueous alcohol solutions.[6] Our group has also developed catalytic strategies for high-efficiency chemical conversion of captured CO_2, that is, a CO_2 capture and utilization (CCU) strategy, into value-added chemicals such as ureas, oxazolidinones, formate, and others.[7] In these protocols, the fixed CO_2, a potential activated form, could be stoichiometrically incorporated into value-added chemicals/fuels under mild reaction conditions, getting rid of the desorption step. These findings pave the way for the development of green processes and technological innovations towards low-energy, highly effective catalytic methods for CO_2 conversion. Although CCU strategies offer much potential as effective catalytic protocols for the utilization of low concentrations of CO_2, the examples are limited and more studies are required.

Alkyl-substituted ammonium carbamates are the product of reactions between gaseous CO_2 and secondary aliphatic amines, which react rapidly (and exothermically) via unstable alkylcarbamic acids (Scheme 1).[8] These alkyl-substituted ammonium carbamates have found widespread application. For example, dimethylammonium dimethylcarbamate (DIMCARB), a commercially available dialkylammonium carbamate, is well-known to be a useful dimethylamine source for preparative amidation of carboxylic acids or ester derivatives, and a reagent in the Willgerodt–Kindler synthesis of *N*,*N*-dimethylthiocarboxamides.[9] In addition, DIMCARB has attracted attention as a self-associated, distillable ionic medium in natural product extractions.[8b,10] Furthermore, this ammonium salt can promote aldol condensations, Mannich-type condensations. and Knoevenagel condensations for metal-free syntheses of valuable



Scheme 1. Formation of carbamic acid and salts.

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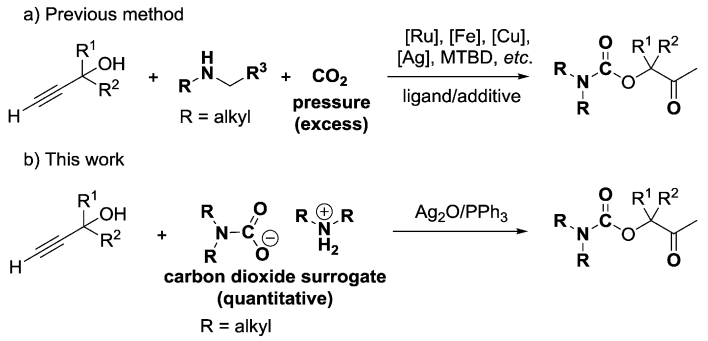
compounds, for example, [*n*]-shogaols.[11] Although dialkylammonium carbamates are potentially valuable as reagents, reaction media, promoters, or catalysts, their use in organic synthesis is limited. To the best of our knowledge, the use of alkyl-substituted ammonium carbamates as both carbonyl and nitrogen source in organic synthesis under gas-free conditions has not yet been reported. More importantly, the ammonium carbamate could be more active in lieu of free CO_2, leading to reactions that run smoothly under extremely mild conditions.[7b]

On the other hand, the chemical conversion of CO_2 has great significance, particularly in catalytic C–N bond formation with the production of value-added products such as oxazolidinones, quinazolines, carbamates, isocyanates, and polyurethanes.[12] One of the most promising examples is the three-component reaction of propargylic alcohols, secondary amines, and CO_2 to access β-oxopropylcarbamates with perfect atom economy (Scheme 2a), These compounds represent an important class of carbamate compounds in agriculture and pharmacology, are useful intermediates in organic synthesis, and serve as protective groups of an amine function in peptide chemistry.[13] In this context, several systems have already been developed, including catalytic metal complexes of ruthenium,[14] iron,[15] copper,[16] silver,[17] lanthanum,[18] catalytic nonmetal systems such as bicyclic guanidines,[19] and noncatalytic systems.[20] In general, these protocols have severe limitations: the inevitable use of high pressure (≥2 MPa) with large amount of additional energy to get the satisfied yields. Therefore, effective methodologies using CO_2 as a feedstock under atmospheric pressure (preferable with quantitative CO_2) with low energy input are highly desired.



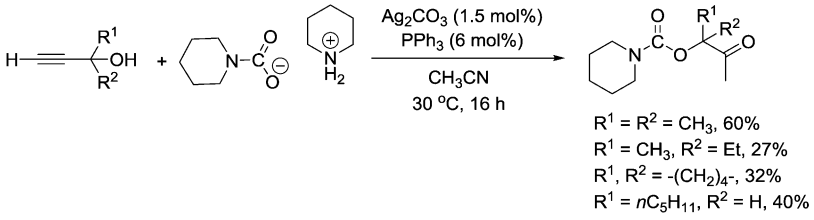
Scheme 2. The synthesis of various β-oxopropylcarbamates.

To further explore the efficient synthesis of β-oxopropylcarbamates directly from propargylic alcohols, secondary amines, and CO_2,[21] we became interested in developing a general effective methodology for the quantitative conversion of CO_2. Considering the economic attractiveness, we disclose herein the first example of utilizing ammonium carbamate (amine-CO_2), one of CO_2's derivatives, in lieu of free CO_2 to perform carboxylative cyclization with propargylic alcohols (Scheme 2b). This offers an alternative route to β-oxopropylcarbamates by utilizing the ammonium carbamate as both CO_2 and amine source, and thus could offer a cost-effective and convenient way for CO_2 utilization.

The initial reaction is based on the silver-catalyzed three-component reaction of propargylic alcohols, secondary amines, and CO_2 we reported earlier.[21b] An ammonium carbamate, for example, piperidin-1-ium piperidine-1-carboxylate **2a** (PIPC, "CO_2-piperidine" adduct) as a carboxylating reagent could be more convenient for storage, transportation and application than gaseous CO_2. We envisioned that the silver complex, with well-defined structure, might be a worthwhile catalyst for the PIPC transformation reaction.[21,22] Therefore, we herein expand the potential applications of the silver(I) catalyst system to the two-component reaction of propargylic alcohols and PIPC as indicated in Scheme 3. In this protocol, β-oxopropylcarbamates were obtained in 27–60% isolated yields at ambient conditions.

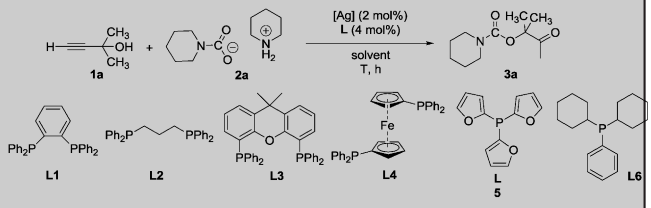
We thus are motivated to examine the utilization of CO_2 surrogates in chemical transformations, aiming at extending an alternative CO_2 recycling strategy into the existing synthetic routes. We started by exploring the silver-catalyzed β-oxopropylcarbamates synthesis from 2-methylbut-3-yn-2-ol (**1a**) with PIPC (Table 1). A variety of phosphine ligands including monophosphine and bidentate phosphine ligands were screened in the presence of AgOAc (entries 1–7). AgOAc/PPh_3 gave the most promising result, with a 52% yield of **3a** (entry 7). Among a set of representative silver compounds such as Ag_2O, Ag_2CO_3, $AgNO_3$, $AgBF_4$, and AgCl (entries 7–12), the most efficient catalysis was accomplished with Ag_2O in conjunction with PPh_3 (entry 8). With further detailed exploration (entries 13–16), an excellent result was obtained (entry 16).

With a good catalytic system in hand, we next explored the scope of the two-component reaction as shown in Scheme 4. In the beginning, a wide range of terminal tertiary propargylic alcohols (**1a**–**g**) was employed, affording the corresponding β-



Scheme 3. Synthesis of β-oxopropylcarbamates from propargylic alcohols and PIPC.

Table 1. Optimization of the Ag^{I}-catalyzed reaction of propargylic alcohols and PIPC.[a]



Entry	Catalyst	Ligand	Yield [%][b]
1	AgOAc	**L1**	9
2	AgOAc	**L2**	18
3	AgOAc	**L3**	18
4	AgOAc	**L4**	49
5	AgOAc	**L5**	5
6	AgOAc	**L6**	27
7	AgOAc	PPh_3	52
8	Ag_2O	PPh_3	66
9	Ag_2CO_3	PPh_3	58
10	$AgNO_3$	PPh_3	55
11	$AgBF_4$	PPh_3	39
12	AgCl	PPh_3	31
13[c]	Ag_2O	PPh_3	70
14[d]	Ag_2O	PPh_3	70
15[d,e]	Ag_2O	PPh_3	87
16[e,f]	Ag_2O	PPh_3	91

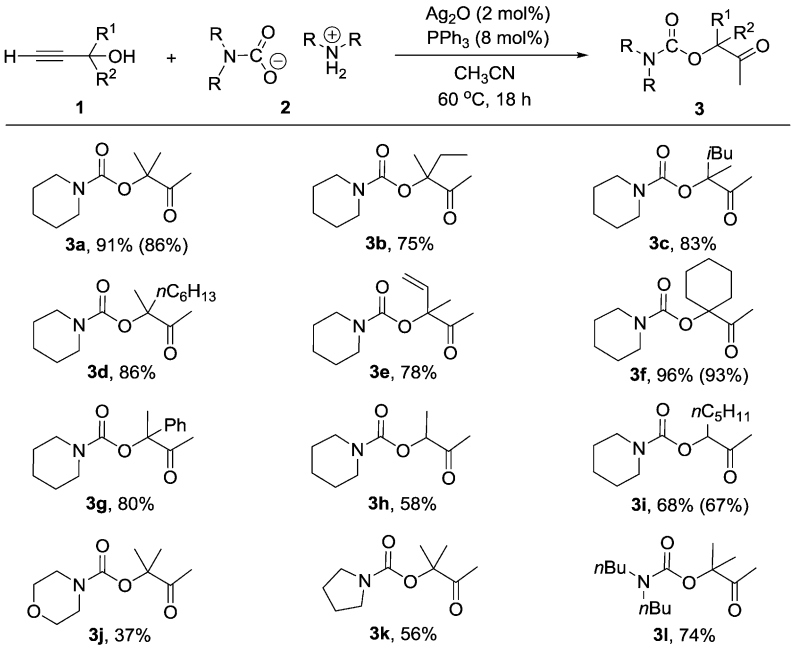
[a] Unless otherwise specified, all reactions were performed with **1a** (84.1 mg, 1.0 mmol), PIPC (0.2142 g, 1.0 mmol), Cat. (2 mol%), Ligand (4 mol%), CH_3CN (1 mL), 60 °C, 12 h. [b] Determined by NMR with 1,1,2,2-tetracholoroethane as the internal standard. [c] 24 h. [d] 8 mol% PPh_3. [e] PIPC (0.3213 g, 1.5 mmol). [f] 18 h.

oxopropylcarbamates (**3a**–**g**) in good yields. The protocol is also suitable for the secondary propargylic alcohols **1h**, **1i** in 58% and 68% yields, respectively. We also examined the scope of the carbon and nitrogen donors from different ammonium carbamates. Secondary aliphatic amines can also be used in this cascade reaction, to give the desired products (**3a**, **3j**–**l**).

To confirm the catalytic conversion of CO_2 surrogate as carbon resource, we performed the reaction with $^{13}CO_2$-labeled PIPC. As shown in Scheme 5a, the production of $^{13}C_{carbonyl}$-labeled **3a′** verifies successful conversion. $^{13}C_{carbonyl}$-labeled α-alkylidene cyclic carbonate reacted with PIPC to produce the piperidine incorporated **3a′** in 75% isolated yield (Scheme 5b). The result indicated that the reaction went through the α-alkylidene cyclic carbonate pathway. In addition, the equilibrium shift between PIPC and CO_2 (and piperidine) leads to a change of the linear conformation and charge distribution of the CO_2 molecule (Scheme 5b), which improves the reactivity of gaseous CO_2.[23] As a result, PIPC displayed excellent properties as a valuable and favorable feedstock in place of gaseous CO_2.

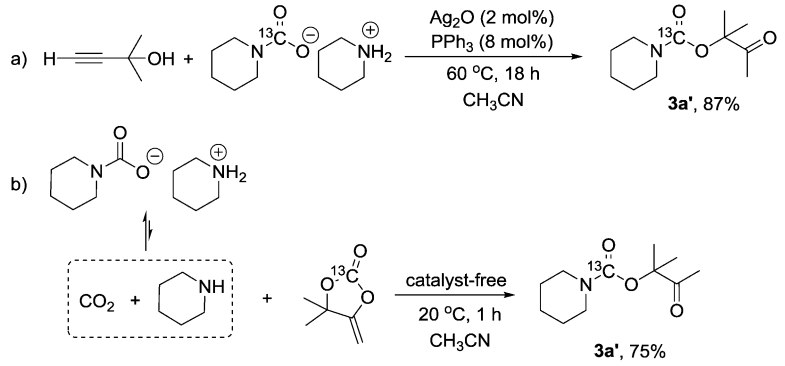
To gain further insights into the mechanism, we conducted the two-component reaction of 3,3-dimethylbut-1-yne or pent-4-yn-2-ol, and PIPC under the optimized reaction conditions. No corresponding carbamate products were obtained, along with the full recovery of the alkyne and alcohol substrates (Scheme 6), indicating that the C≡C bond involved in the reaction should not be susceptible to attack by a nucleophilic ammonium carbamate species, even though it was activated by the silver complex.

A plausible reaction mechanism is proposed as shown in Scheme 7 on the basis of the above data and results published

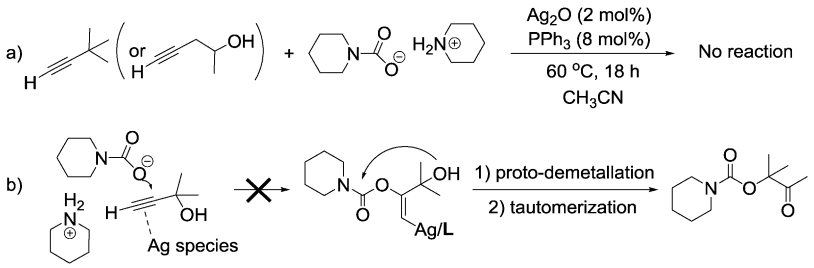


Reaction conditions: **1** (1.0 mmol), ammonium carbamate (1.5 equiv., 1.5 mmol), Ag_2O (4.6 mg, 2 mol%), PPh_3 (21.0 mg, 8 mol%), CH_3CN (1 mL), 60 °C, 18 h. NMR yield with 1,1,2,2-tetracholoroethane as the internal standard, isolated yield in the parenthese.

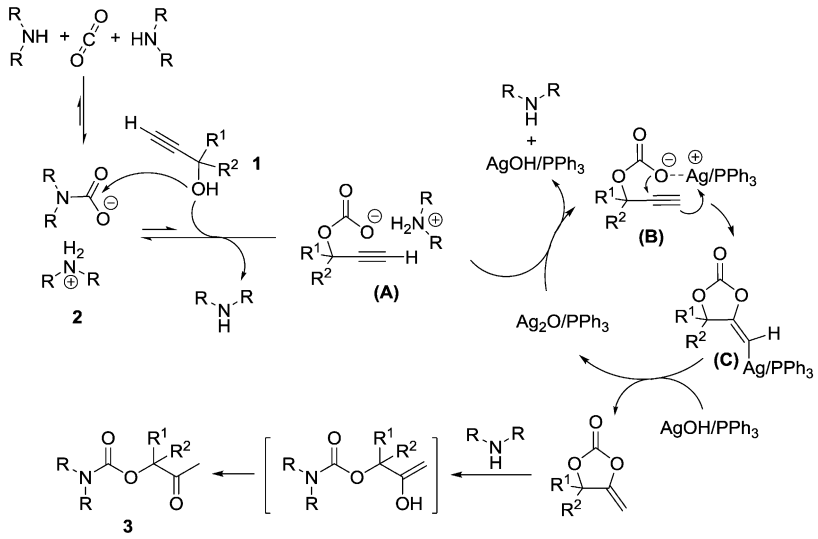
Scheme 4. Scope of the reaction of propargylic alcohols with ammonium carbamates.



Scheme 5. Isotope labeling experiments.

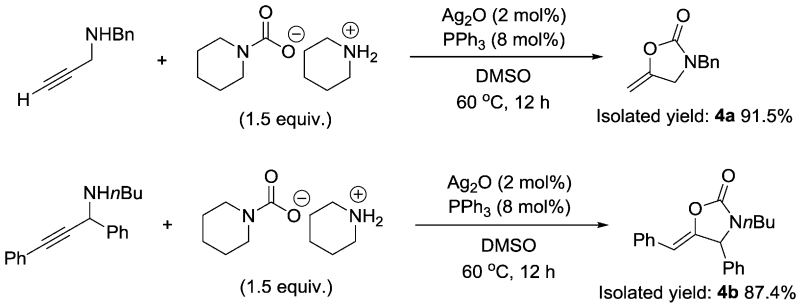


Scheme 6. Mechanistic counterevidence experiments.



Scheme 7. Plausible mechanism.

in the literature.[14,19–21] Ammonium carbamates are reversibly formed from amine and CO_2 molecule which can act as valuable carbon and nitrogen source as well as a potentially activated form of CO_2 gas. The initial step is the formation of a propargylic carbonate intermediate **A** through the reaction of propargylic alcohol with ammonium carbamate with the transfer of a proton (H^+) to amine, followed by interchanging with silver(I) catalyst to form the silver propargylic carbonates **B**. Then, intramolecular 5-*exo*-cyclization would then proceed through the activated C≡C bond by the active silver species to give intermediate **C** via an anti addition mode, followed by proto-demetallation to release the α-alkylidene cyclic carbonate (*Z*-isomer. For detailed experimental data and data published in the literature, see the Supporting Information),[24,25] which is subsequently attacked by a secondary amine to generate the carbamate species. Finally, the corresponding β-oxopropylcarbamate **3** is obtained via tautomerization.



Scheme 8. Reaction of propargylic amines with PIPC.

The successful transformation of propargylic alcohols and ammonium carbamates into β-oxopropylcarbamates under mild conditions prompted us to expand the potential application of this catalytic strategy to the reaction of propargylic amines with ammonium carbamates. In addition, α-alkylidene cyclic carbamates synthesized from propargylamines and CO_2 were apt to afford products with *Z*-isomers on the stereoselectivity with a thermodynamic controlled result.[25] To our delight, under standard reaction conditions as listed in Scheme 8 the corresponding 2-oxazolidinones **4a** and **4b** (single *Z*-isomer) were afforded in excellent yields, which extends the application scope in the quantitative fixation of CO_2.

In summary, we establish the first successful protocol of silver-catalyzed two-component reaction of propargylic alcohols and ammonium carbamates for expeditious quantitative chemical fixation of CO_2 to prepare carbamate motifs at mild conditions. The method is straightforward, efficient, and offers high atom-economy. In addition, this approach does not require a large excess of CO_2 or high reaction pressures and temperatures. A broad substrate and reaction application scope under mild reaction conditions is been demonstrated. Further studies to develop more, related transformations and elucidate the mechanism are underway.

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Keywords: carbon dioxide chemistry · homogeneous catalysis · nitrogen heterocycles · silver · synthetic methods

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