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Cyclizative Atmospheric CO_2 Fixation by Unsaturated Amines with *t*-BuOI Leading to Cyclic Carbamates

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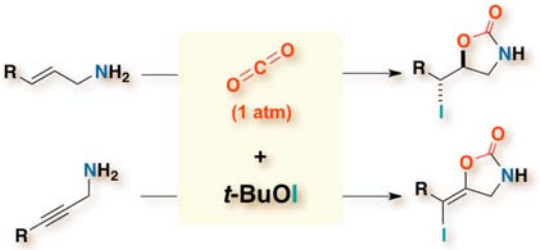
ABSTRACT



A cyclizative atmospheric CO_2 fixation by unsaturated amines such as allyl and propargyl amines under mild reaction conditions, efficiently leading to cyclic carbamates bearing a iodomethyl group, have been developed utilizing *tert*-butyl hypoiodite (*t*-BuOI).

Control of the concentration level of carbon dioxide, a notorious greenhouse gas, in the atmosphere has been a worldwide issue to be solved urgently.[1] To address the issue, there are two main types of approaches: CO_2 capture and storage/sequestration (CCS); CO_2 capture and its utilization (CCU).[2] The former approach is based on the idea of capturing CO_2 into adsorbents such as solid, liquid, and membranes.[3] On the other hand, the CCU approach would allow for not only consuming CO_2 but also producing value-added chemicals by synthetic methods from abundant and environmentally friendly C_1 feedstock. Nevertheless, the biggest obstacle to this approach lies in the thermodynamic stability of CO_2, which is at the highest oxidation state of carbon. To activate CO_2, harsh reaction conditions such as the use of external strong acids/bases, or high pressures, have been utilized.[2,4] Therefore, the development of chemical transformation methods of CO_2 without energy-consuming processes is desired. In this regard, we have developed an atmospheric CO_2 fixation method by allyl alcohols under mild reaction conditions utilizing *tert*-butyl hypoiodite (*t*-BuOI).[5] The key to success was the use of a powerful iodinating reagent (*t*-BuOI),[6,7] which readily reacts with carbonic acid monoalkyl esters ((allyl)OC(O)OH)) generated from the reaction of CO_2 and allyl alcohols, thereby exchanging the acidic proton with iodine leading to cyclic carbonate products. The only

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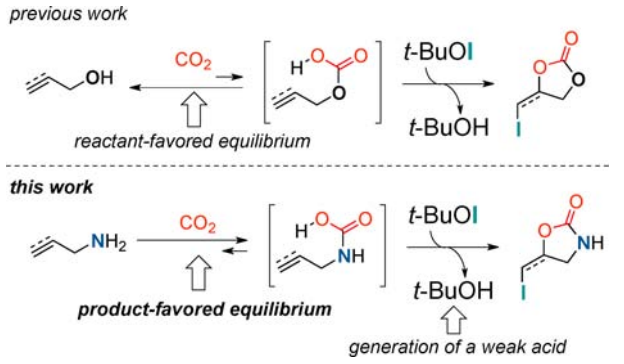
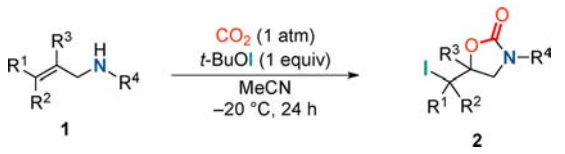
byproduct formed in this reaction is nontoxic alcohol (*t*-BuOH), which would not interfere with the progression of the reaction. However, due to the existence of a highly reactant-favored equilibrium between two systems of CO_2/allyl alcohols and carbonic acid monoalkyl esters (Scheme 1), 2 equiv of *t*-BuOI were required to obtain products in high yields. Contrary to the system, amines including allyl amines have been known to be good capturing agents for CO_2 to form carbamic acids or ammonium carbamates owing to their higher nucleophilicities than alcohols.[8] Utilization of the thermodynamically favored process in two cyclizative atmospheric CO_2 fixation methods by allyl amines leading to cyclic carbamates, which constitute an important class of heterocyclic compounds serving as synthetic intermediates for complex molecules[9] or as biologically active agents,[10] has been reported.[11] Both reactions require the concomitant use of stoichiometric amounts of I_2 and an external strong base (TMG[11a] or Cs_2CO_3[11b]), which would trap the liberated strong acid (HI), to gain high yields of product. As related reactions, metal-catalyzed cyclizative CO_2 fixations by propargyl amines under pressurized conditions or supercritical CO_2 have also been developed.[12] With these backgrounds in mind, we envisaged that an efficient cyclizative atmospheric fixation of CO_2 by allyl amines utilizing *t*-BuOI under mild conditions would be feasible without the use of external strong bases or metal catalysts (Scheme 1).

Scheme 1. Cyclizative CO_2 Fixation under Neutral Conditions



To verify the hypothesis, we treated the simplest allyl amine (**1a**) with an equimolar amount of *t*-BuOI, which

Table 1. Substrate Scope of Allyl Amines[a]



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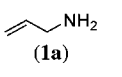
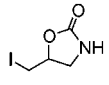
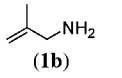
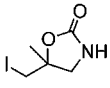
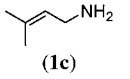
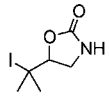
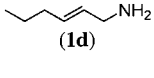
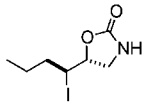
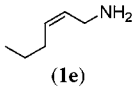
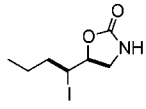
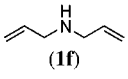
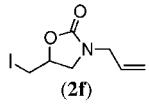
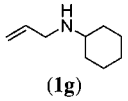
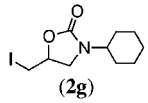
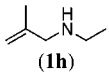
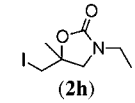
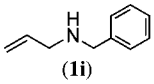
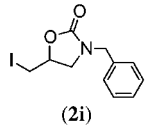
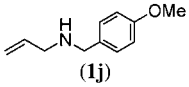
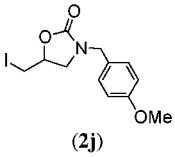
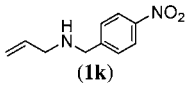
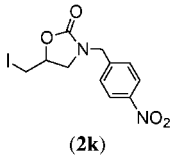
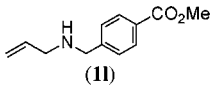
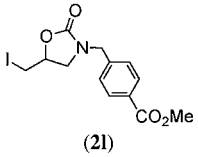
1	 (**1a**)	 (**2a**)	91
2	 (**1b**)	 (**2b**)	58
3	 (**1c**)	 (**2c**)	61
4	 (**1d**)	 (**2d**)	81[c]
5	 (**1e**)	 (**2e**)	81
6	 (**1f**)	 (**2f**)	66[d]
7	 (**1g**)	 (**2g**)	79[d]
8	 (**1h**)	 (**2h**)	78
9	 (**1i**)	 (**2i**)	87
10	 (**1j**)	 (**2j**)	77
11	 (**1k**)	 (**2k**)	94
12	 (**1l**)	 (**2l**)	89

[a] Reaction conditions: CO_2 (1 atm), allyl amine (0.5 mmol), NaI (0.5 mmol), *t*-BuOCl (0.5 mmol), and MeCN (3 mL). [b] Isolated yield. [c] Reaction was conducted at 0 °C. [d] CH_2Cl_2 was used as a solvent.

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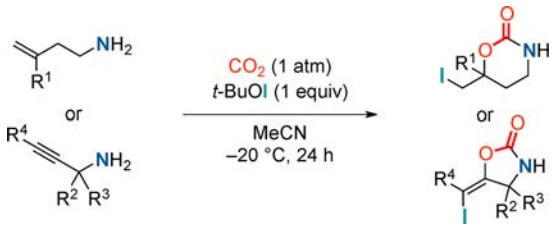
Table 2. Substrate Scope of Homoallyl and Propargyl Amines[a]



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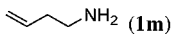
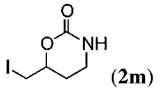
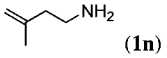
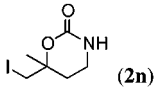
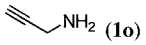
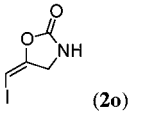
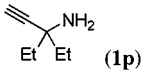
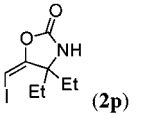
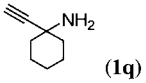
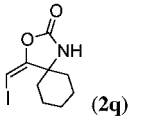
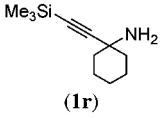
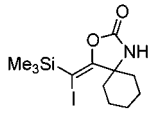
1	 (**1m**)	 (**2m**)	62
2	 (**1n**)	 (**2n**)	54
3	 (**1o**)	 (**2o**)	0
4	 (**1p**)	 (**2p**)	80
5	 (**1q**)	 (**2q**)	68
6	 (**1r**)	 (**2r**)	56

[a] Reaction conditions: CO_2 (1 atm), homoallyl or propargyl amine (0.5 mmol), NaI (0.5 mmol), *t*-BuOCl (0.5 mmol), and MeCN (3 mL). [b] Isolated yield.

was generated *in situ* from NaI and *t*-BuOCl,[6,7] under the atmospheric pressure (1 atm) of CO_2 in acetonitrile at room temperature. Gratifyingly, the expected 4-iodomethyl-2-oxazolidinone (**2a**) was successfully produced and isolated in 47% yield. To improve the efficiency of the reaction, reaction parameters such as solvents and temperatures were scrutinized (Table S1). As a result, the reaction at a lower temperature (−20 °C) in acetonitrile was found to give the desired carbamate **2a** in the highest yield of 91% (entry 1, Table 1). The reactions with other iodinating reagents such as IPy_2BF_4 (BPIT) and *N*-iodosuccinimide (NIS) resulted in rather low yields of **2a**.[13] The employment of I_2 alone or the concomitant use of I_2/Et_3N gave very poor yields. The reason why *t*-BuOI is the most suitable iodinating reagent in the reaction system could be due to the liberation of only a weak acid (*t*-BuOH) instead of HI that should be trapped by an external base in similar reaction systems.[9]

Having optimized the reaction conditions, the substrate scope was then explored (Table 1). β-Branched allyl amine **1b** was transformed into the corresponding carbamate **2b** in moderate yield (entry 2). An allyl amine having a γ-disubstituent **1c** was also applicable to the reaction (entry 3). When structurally defined geometric isomers **1d** and **1e** were employed as substrates, the reaction proceeded stereospecifically to afford **2d** and **2e** as single stereoisomers in both cases (entries 4 and 5).[14] Moreover, *N,N*-diallyl amine (**1f**) was successfully transformed into the corresponding carbamate **2f** while keeping the other allylic moiety intact (entry 6). *N*-Substitution with alkyl groups did not significantly retard reaction efficiencies (entries 7−9). Various functionalities showed good compatibility with the reaction conditions, leading to the corresponding cyclic carbamates **2j**−**2l** in good to high yields (entries 10−12).

The successful results in the transformation of allyl amines into five-membered cyclic carbamates through the CO_2 fixation prompted us to further investigate the use of homoallyl and propargyl amines as substrates (Table 2). When homoallyl amine **1m** was subjected to the reaction conditions, six-membered carbamate **2m** was obtained in moderate yield (entry 1), while γ-branched homoallyl amine **1n** was also converted to the corresponding carbamate **2n** in moderate yield (entry 2). Unfortunately, the reaction using the simplest propargyl amine (**1o**) failed to provide the desired product **2o** (entry 3). In sharp contrast, amines bearing a *gem*-disubstituent at the propargylic position gave cyclic carbamates **2p** and **2q** in good yields as sole constitutional isomers with an *E*-configuration (entries 4 and 5).[14] This significant discrepancy in these reaction outcomes would be explained in terms of the "Thorpe−Ingold effect"[15] through the intramolecular cyclization process from the intermediately generated iodonium intermediates (*vide infra*). It is noted that the silyl group on the acetylenic carbon of **1r** survived the reaction conditions in which "I^+" species coexist, leading to **2r** having a tetra-substituted olefinic moiety in moderate yield (entry 6).

The oxazolidinones that were obtained by our method would serve as useful building blocks, because an iodo-functionality attached to sp^3- or sp^2-hybridized carbon

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(13) For details, see the Supporting Information.

(14) The determination of their stereochemistry is described in the Supporting Information.

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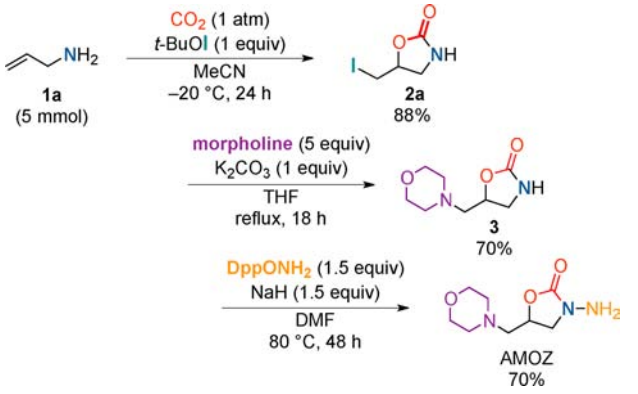
Scheme 2. Facile Synthesis of AMOZ Starting from **1a**



atoms can be transformed into other functional groups.[16] To demonstrate a synthetic application of the present reaction, a three-step preparation of 3-amino-5-morpholinomethyl-2-oxazolidinone (AMOZ),[17] which is a synthetic intermediate of moxnidazole (antiparasite drug)[18] and furaltadone (antibacterial drug),[18a,19] was efficiently accomplished starting from allyl amine **1a** (Scheme 2). The CO_2 fixation by **1a** was applicable to a gram scale operation, producing **2a** in 88% yield. The iodo functionality of **2a** was then substituted with a morpholino group, leading to oxazolidinone **3** in good yield. The treatment of **3** with *O*-(diphenylphosphinyl)hydroxylamine ($DppONH_2$)[20] and NaH in DMF afforded AMOZ in 70% yield. The fact that the conventional synthetic route to AMOZ requires as many as six steps starting from (2,2-dimethyl-1,3-dioxolan-4-yl)methanol as a starting material[21] demonstrates the utility of our reaction.

For a deeper understanding of the reaction mechanism, several experiments were conducted. In situ monitoring of a CD_3CN solution of a mixture of allyl amine (**1a**) and *t*-BuOI under a N_2 atmosphere using the ^1H NMR technique revealed that no change in the ^1H NMR spectrum of allyl amine occurred. On the other hand, under a CO_2 atmosphere similar monitoring (^1H, ^{13}C NMR, and FT-IR) of a CD_3CN solution of **1a** without *t*-BuOI indicated quantitative formation of allylammonium allylcarbamate.[8,13] Furthermore, gradual formation of

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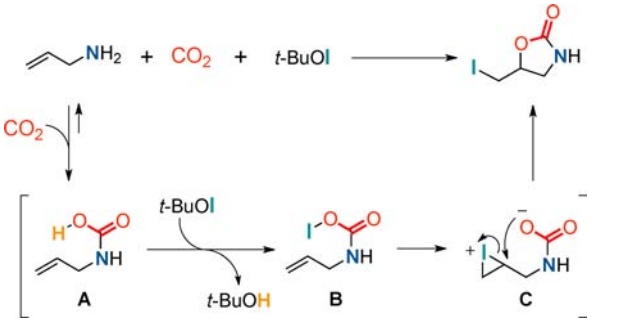
Scheme 3. Pausible Reaction Mechanism



cyclic carbamate **2a** in the solution was identified upon successive addition of *t*-BuOI to the solution.[22] Based on the experimental results, the most likely reaction mechanism is illustrated in Scheme 3: (1) allyl carbamic acid **A** is generated as a result of the product-favored equilibrium of allyl amine and CO_2;[8] (2) the resulting carbamic acid **A** reacts with *t*-BuOI to undergo proton−iodine exchange, leading to an *O*-iodinated species **B**; (3) the intermediate **B** would serve as an iodonium source to form cyclic iodonium intermediate **C**; (4) intramolecular cyclization from **C** would give a cyclic carbamate product, with the process being possibly supported by the stereospecific production of **2d** and **2e**.

In conclusion, we have developed an efficient, metal/base-free, and nonpressurized CO_2 fixation by allyl amines, leading to cyclic carbamates utilizing *t*-BuOI. The method was applicable to a wide range of unsaturated amines under mild conditions.

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Supporting Information Available. General procedures, spectral data for new compounds, and NMR experiments results. This material is available free of charge via the Internet of http://pubs.acs.org.

(22) Together with **2a**, the formation of an intermediate having an unknown structure was also observed, which was too unstable to be isolated.

The authors declare no competing financial interest.The authors declare no competing financial interest.