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Synthesis of 5-Vinylideneoxazolidin-2-ones by DBU-Mediated CO_2-Fixation Reaction of 4-(Benzylamino)-2-butynyl Carbonates and Benzoates

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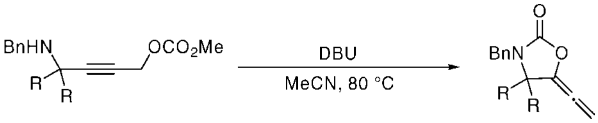
ABSTRACT



A CO_2-fixation reaction of 4-(benzylamino)-2-butynyl carbonates and benzoates, carried out in the presence of DBU, provides substituted 5-vinylideneoxazolidin-2-ones. The reaction has been successfully applied to the CO_2-recycling process and fixation of atmospheric CO_2.

A number of 5-substituted oxazolidinones are shown to have high potency as biologically active molecules and are widely used in the pharmaceutical industry.[1] Consequently, much attention and extensive study have been focused on the synthesis of oxazolidinones. The chemical fixation of CO_2 with aziridines[2] or propargylic amines[3] is one of the most useful and efficient methods. We have recently developed a palladium-catalyzed CO_2-fixation of 4-(benzylamino)-2-butenyl carbonates (Scheme 1).[4] The reaction proceeds through a pathway involving decarboxylation−fixation of liberated CO_2[5] to afford 5-vinyloxazolidinones. We expected that this process could be applied for the propargylic substrate bearing an amino group at the propargylic position. We report here a DBU-mediated CO_2-fixation reaction of 4-(benzylamino)-2-butynyl carbonates and benzoates. It is noteworthy that the reaction undergoes under palladium-free conditions to afford the 5-vinylideneoxazolidin-2-ones in good yields.

The initial reactions were carried out using a cyclohexyl-substituted propargylic carbonate **1a** in the presence of CO_2.

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Scheme 1

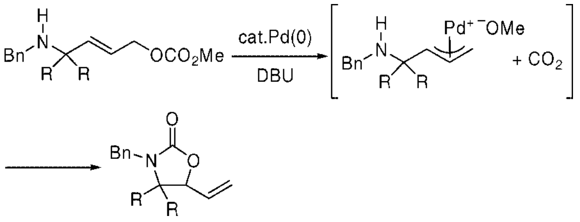
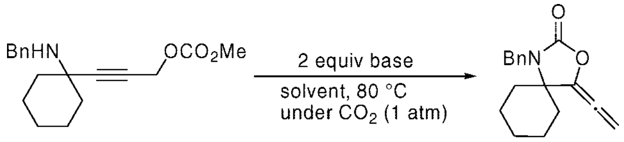


Table 1. Initial Attempts for the Base-Mediated Fixation of **1a**



1a **2a**

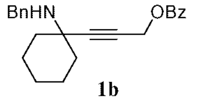
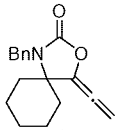
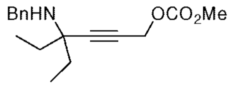
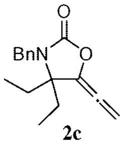
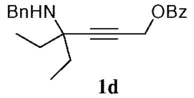
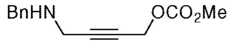
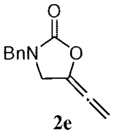
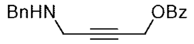
entry	base	solvent	time (h)	yield[a] (%)
1[b]	DBU	MeCN	6	51
2	DBU	MeCN	12	99
3	DBU	DMSO	9	81
4	DBU	DMF	10	86
5	DBU	THF	48	58 (80)
6	DBU	CH_2Cl_2	48	59 (92)
7	DABCO	MeCN	14	60
8	NEt_3	MeCN	48	79
9	TMEDA	MeCN	48	58 (73)
10		MeCN	48	N.R.

[a] The yields in parentheses are based on recovered starting material. [b] The reaction was carried out in the presence of 10 mol % $Pd(PPh_3)_4$.

When **1a** was subjected to the reaction with 10 mol % of $Pd(PPh_3)_4$ and 2 equiv of DBU under CO_2 (1 atm) in MeCN at 80 °C, the vinylideneoxazolidinone **2a** was produced in 51% yield (entry 1 in Table 1). Further investigations have made clear that the reaction successfully proceeded in the absence of palladium catalyst. Thus, oxazolidinone **2a** was obtained in 99% yield when only 2 equiv of DBU was employed (entry 2). The reaction using various solvents resulted in the production of **2a** in moderate to good yields (entries 3−6). Other amine bases such as DABCO, Et_3N, and TMEDA were also effective for the reaction (entries 7−9), but no reaction proceeded in the absence of base (entry 10).

The results of the reactions using various substrates **1b**−**f** are shown in Table 2. The reaction of **1b**, having a benzoyloxy group as the leaving group, with DBU under CO_2 (1 atm) yielded the vinylideneoxazolidinone **2a** in 92% yield (entry 1). Diethyl-substituted propargylic carbonate **1c** was transformed to **2c** in 90% yield (entry 2). The product **1c** was similarly yielded from the reaction of diethyl-substituted benzoate **1d** in 99% yield (entry 3). Reactions of the carbonate **1e** and benzoate **1f**, which have no substituents at the propargylic position, also afforded the corresponding oxazolidinone **2e** in 81% and 99% yields, respectively (entries 4 and 5).

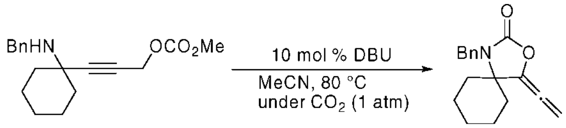
Table 2. Reactions Using Various Substituted Substrates **1b**−**f**[a]

entry	substrate	product	yield (%)
1	 **1b**	 **2a**	92
2	 **1c**	 **2c**	90
3	 **1d**	**2c**	99
4	 **1e**	 **2e**	81
5	 **1f**	**2e**	99

[a] Reactions were carried out in the presence of 2 equiv of DBU in acetonitrile under CO_2 (1 atm) at 80 °C for 0.5−12 h.

We then examined the required amount of DBU for the above CO_2-fixation reaction. As a result, it was clear that the reaction successfully proceeded even in the catalytic amount of DBU (10 mol %) to afford the product **2a** in moderate yield (Scheme 2).

Scheme 2



1a **2a** 51% yield

It is known that DBU reacts with CO_2 to form DBU−CO_2 zwitterionic carbamic complex **3**, which exhibits high activity for various CO_2-fixation reactions.[4,6] To examine the effect

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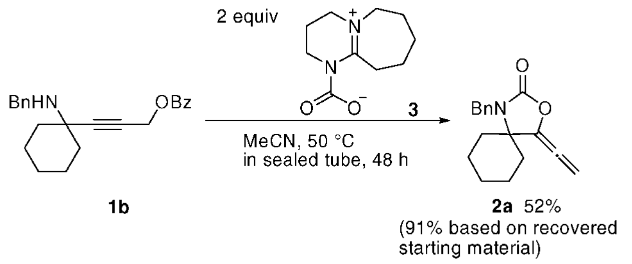
(5) For other examples about the palladium-catalyzed CO_2-recycling reactions, see:(a) Yoshida, M.; Ihara, M. *Chem. Eur. J.* **2004**, 2886. (b) Yoshida, M.; Ihara, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 616. (c) Yoshida, M.; Fujita, M.; Ishii, T.; Ihara, M. *J. Am. Chem. Soc.* **2003**, *125*, 4874. (d) Yoshida, M.; Fujita, M.; Ihara, M. *Org. Lett.* **2003**, *5*, 3325. (e) Yoshida, M.; Ohsawa, Y.; Ihara, M. *J. Org. Chem.* **2004**, *69*, 1590. (f) Yoshida, M.; Ohsawa, Y.; Ihara, M. *Tetrahedron* **2006**, *62*, 11218.

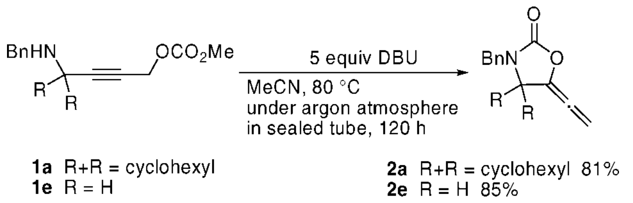
of DBU in the synthesis of vinylideneoxazolidinone, the reaction of propargylic benzoate **1b** with DBU−CO$_2$ complex **3** was attempted. When **1b** was subjected to the reaction with 2 equiv of **3** in MeCN at 50 °C, the corresponding oxazolidinone **2a** was produced in 52% yield (91% yield based on recovered starting material) (Scheme 3). This result implies that the CO$_2$-fixation process proceeds through the formation of DBU−CO$_2$ complex **3**.

Scheme 3



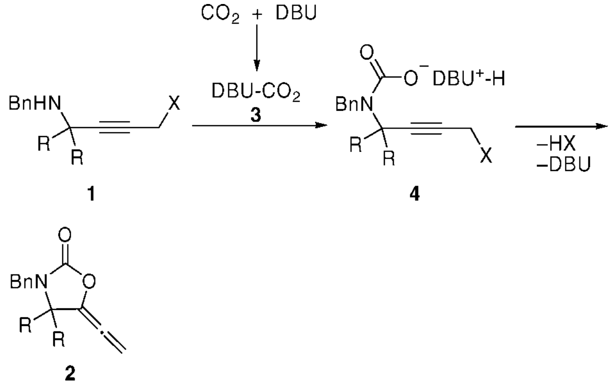
We next attempted the reaction in the absence of an external CO$_2$ source, to confirm whether a CO$_2$-recycling process[4,5] occurs under the palladium-free conditions (Scheme 4). When propargylic carbonate **1a** was subjected to the reaction with 5 equiv of DBU under argon atmosphere in a sealed tube, the desired oxazolidinone **2a** was produced in 81% yield. The substrate **1e** was also transformed to the corresponding product **2e** in 85% yield. From these results, it was clear that CO$_2$ component in the substrate was efficiently utilized as a CO$_2$ source. To the best of our knowledge, this is the first example of a CO$_2$-recycling reaction under transition metal-free conditions.

Scheme 4



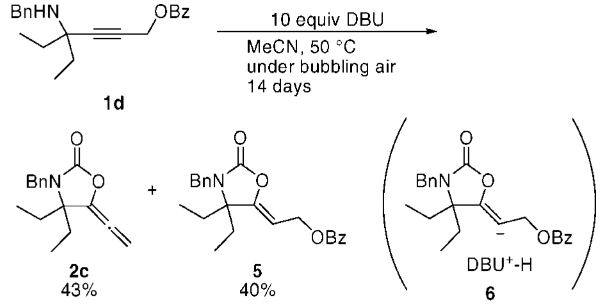
A plausible mechanism for the reaction is shown in Scheme 5. The substrate **1** reacts with DBU−CO$_2$ complex **3**, a reactive species formed from DBU and CO$_2$ in situ,[7,8] to afford the carbamate−DBU complex **4**. Intramolecular S$_N$2′ substitution of **4** produces the vinylideneoxazolidinone **2** with the regeneration of DBU.

Scheme 5



To further highlight the potential of this process, we tried the fixation of atmospheric CO$_2$ (Scheme 6). Direct fixation of air containing CO$_2$ into the organic molecules has received much attention from the viewpoint of its potential use as an abundant carbon source and global warming problems, but few examples about this methodology were reported.[9] When the reaction of propargylic benzoate **1a** was carried out under air bubbling conditions with 10 equiv DBU for 14 days, the CO$_2$-fixed vinylideneoxazolidinone **2a** was obtained along with the by-produced oxazolidinone **5**[10] in 43% and 40% yields, respectively. The product **5** would be formed by intramolecular nucleophilic attack of the carbamate anion to the alkyne in the carbamate−DBU complex **4**, followed by successive protonation of the resulting intermediate **6**.[11] Although the reaction time was too long, the result clearly indicates that air containing CO$_2$ has been incorporated into the propargylic substrate.

Scheme 6



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(6) (a) Pérez, E. R.; da Silva, M. O.; Costa, V. C.; Rodrigues-Filho, U. P.; Franco, D. W. *Tetrahedron Lett.* **2002**, *43*, 4091. (b) Pérez, E. R.; Santos, R. H. A.; Gambardella, M. T. P.; de Macedo, L. G. M.; Rodrigues-Filho, U. P.; Launay, J.-C.; Franco, D. W. *J. Org. Chem.* **2004**, *69*, 8005. (c) Dinsmore, C. J.; Mercer, S. P. *Org. Lett.* **2004**, *6*, 2885.

(7) It is expected that the corresponding carbamate complexes are formed in situ when other amines such as Et$_3$N, pyridine, and DABCO are employed.

(8) In the CO$_2$-recycling reaction (Scheme 4), it is presumed that the CO$_2$ source for the initial formation of DBU−CO$_2$ complex **3** would be derived from extremely low levels of CO$_2$ in the solvent. The related observation has been reported, see ref 6c.

(9) It is known that zinc and copper complexes can fix atmospheric CO$_2$: Sun, W. Y.; Kong, L. Y.; Zhang, Z. H.; Kawaguchi, H.; Okamura, T.; Doi, M.; Ueyama, N.; Ford, C. W *Angew. Chem., Int. Ed.* **2005**, *44*, 4352.

(10) The stereochemistry of **5** was determined unambiguously by NOE correlation, see the Supporting Information.

(11) (a) Similar cyclization reactions have been reported: Arcadi, A.; Inesi, A.; Marinelli, F.; Rossi, L.; Verdecchia, M. *Synlett* **2005**, 67. (b) Asao, N.; Iso, K.; Yodha, S. S. *Org. Lett.* **2006**, *8*4149.

In conclusion, we have developed a methodology for the synthesis of 5-vinylideneoxazolidin-2-ones by DBU-mediated CO_2-fixation reaction. Substituted oxazolidinones are attractive and important compounds in both medicinal and synthetic organic chemistry, and our methodology would provide a new protocol for the synthesis of substituted oxazolidinones. Further studies about this type of reaction and synthetic application of the resulting oxazolidinones are now in progress.

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Supporting Information Available: Starting material preparations, spectral data, and copies of ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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