

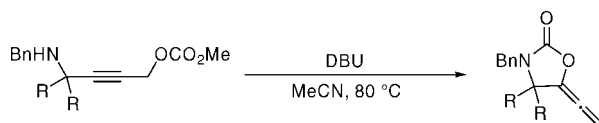
Synthesis of 5-Vinylideneoxazolidin-2-ones by DBU-Mediated CO₂-Fixation Reaction of 4-(Benzylamino)-2-butynyl Carbonates and Benzoates

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ABSTRACT



A CO₂-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 CO₂-recycling process and fixation of atmospheric CO₂.

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 CO₂ with aziridines² or propargylic amines³ is one of the most useful and efficient methods. We have recently developed a palladium-catalyzed CO₂-fixation of 4-(benzylamino)-2-butenyl carbonates (Scheme 1).⁴ The reaction proceeds through a pathway involving decarboxylation–fixation of liberated CO₂⁵ to afford 5-vinylloxazolidinones. 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 CO₂-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 CO₂.

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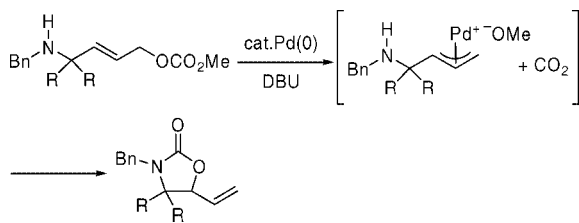
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Scheme 1



When **1a** was subjected to the reaction with 10 mol % of $\text{Pd(PPh}_3)_4$ 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

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

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 % $\text{Pd(PPh}_3)_4$.

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 benzyloxy group as the leaving group, with DBU under CO_2 (1

Table 2. Reactions Using Various Substituted Substrates **1b–f**^a

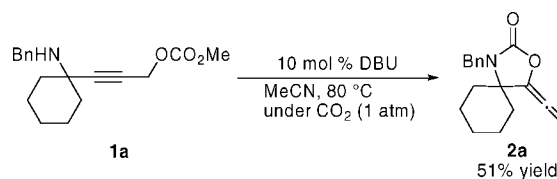
entry	substrate	product	yield (%)
1	1b	2a	92
2	1c	2c	90
3	1d	2c	99
4	1e	2e	81
5	1f	2e	99

^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.

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).

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

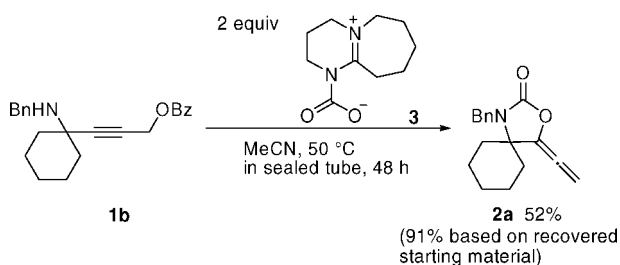


It is known that DBU reacts with CO_2 to form DBU- CO_2 zwitterionic carbamic complex **3**, which exhibits high activity for various CO_2 -fixation reactions.^{4,6} To examine the effect

(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–CO₂ 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

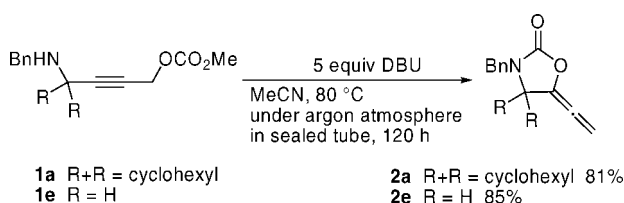
Scheme 3



implies that the CO₂-fixation process proceeds through the formation of DBU–CO₂ complex **3**.

We next attempted the reaction in the absence of an external CO₂ source, to confirm whether a CO₂-recycling process^{4,5} occurs under the palladium-free conditions (Scheme 4). When propargylic carbonate **1a** was subjected to the

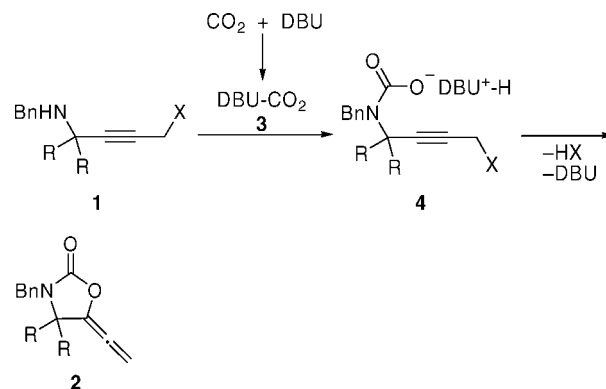
Scheme 4



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 CO₂ component in the substrate was efficiently utilized as a CO₂ source. To the best of our knowledge, this is the first example of a CO₂-recycling reaction under transition metal-free conditions.

A plausible mechanism for the reaction is shown in Scheme 5. The substrate **1** reacts with DBU–CO₂ complex **3**, a reactive species formed from DBU and CO₂ in situ,^{7,8}

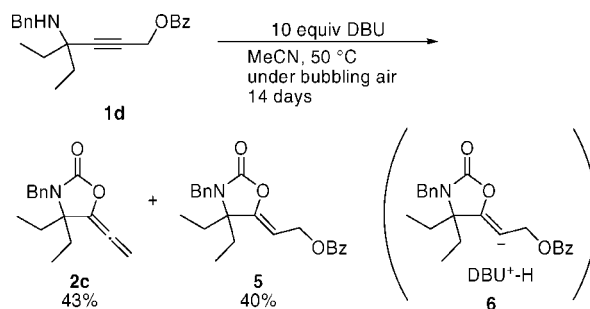
Scheme 5



to afford the carbamate–DBU complex **4**. Intramolecular S_N2' substitution of **4** produces the vinylideneoxazolidinone **2** with the regeneration of DBU.

To further highlight the potential of this process, we tried the fixation of atmospheric CO₂ (Scheme 6). Direct fixation

Scheme 6



of air containing CO₂ 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 CO₂-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 CO₂ has been incorporated into the propargylic substrate.

(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 Et₃N, pyridine, and DABCO are employed.

(8) In the CO₂-recycling reaction (Scheme 4), it is presumed that the CO₂ source for the initial formation of DBU–CO₂ complex **3** would be derived from extremely low levels of CO₂ in the solvent. The related observation has been reported, see ref 6c.

(9) It is known that zinc and copper complexes can fix atmospheric CO₂: 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**, 84149.

In conclusion, we have developed a methodology for the synthesis of 5-vinylideneoxazolidin-2-ones by DBU-mediated CO₂-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.

Acknowledgment. This study was supported in part by a Grant-in-Aid for the Encouragement of Young Scientists (B)

from the Japan Society for the Promotion of Science (JSPS) and Takeda Science Foundation. We are grateful to a reviewer for helpful suggestions about the reaction mechanism.

Supporting Information Available: Starting material preparations, spectral data, and copies of ¹H and ¹³C 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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