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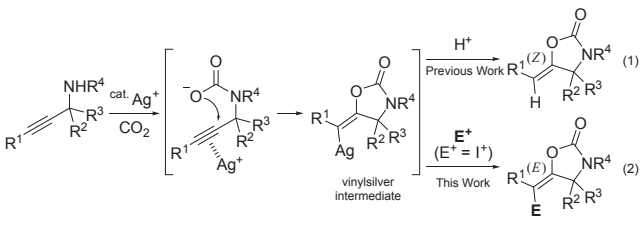
Silver-catalyzed Three-component Reaction of Propargylic Amines, Carbon Dioxide, and *N*-Iodosuccinimide for Stereoselective Preparation of (*E*)-Iodovinyloxazolidinones

Kohei Sekine, Ryo Kobayashi, and Tohru Yamada*
Department of Chemistry, Keio University, Hiyoshi, Kohoku-ku, Yokohama, Kanagawa 223-8522

(E-mail: yamada@chem.keio.ac.jp)

The silver-catalyzed three-component reaction of propargylic amines, carbon dioxide, and *N*-iodosuccinimide for the stereoselective synthesis of (*E*)-iodovinyloxazolidinones was developed. The silver-catalytic system could be applied to various propargylic amines to afford the corresponding iodovinyloxazolidinones in high yields. The structure of the oxazolidinone was confirmed by X-ray structure analysis to be the *E*-isomer for the geometry of the *exo*-olefin. The silver-catalyzed cyclization and replacement of silver with the iodine group in the intermediate were thought to be crucial steps.

Carbon dioxide is one of the most attractive carbon sources due to its low toxicity, ease of handling, and abundance to displace toxic reagents such as phosgene and carbon monoxide. For the incorporation of carbon dioxide in fine chemicals, much effort has been actively made;[1] three- or four-component reactions using aryne,[2] allene,[3] alkyne,[4] or others[5] have been recently developed to afford diverse building blocks such as carboxylic acid, lactone, carbonate, and carbamate derivatives. Sequential reactions in a one-pot operation would provide promising methods to form various important frameworks in the pharmaceutical and material science fields. Our group has reported that carbon dioxide incorporation into propargylic amines was effectively catalyzed by silver salts under mild conditions to selectively afford (*Z*)-alkenyloxazolidinones (Scheme 1, eq 1).[6] Through the reaction, a vinylsilver intermediate was expected to be stereoselectively generated as a result of the anti-addition of carbamate to the C–C triple bond activated by silver salts. This assumption was supported by DFT calculations of the silver-catalyzed carbon dioxide incorporation into propargylic alcohols.[6b] It is reasonable to assume that the silver ion in the intermediate would be stereospecifically replaced by a proton to produce (*Z*)-alkenyloxazolidinone and regenerate the silver catalyst. This plausible mechanism suggested that in the presence of appropriate electrophiles (E^+), the C(vinyl)–Ag bond could be stereospecifically trapped by the electrophiles instead of the proton to afford the corresponding oxazolidinones containing the C(vinyl)–E bond with high geometry control (Scheme 1, eq 2). The exchange reaction of silver with electrophiles would be persuasive evidence for the vinylsilver intermediates in the present silver-catalytic systems.[6] In recent publications, the transformation of the C(vinyl)–Ag bond following the silver-catalyzed cyclization of allenylamine, *o*-alkynylaniline or alkynyl silyl enol ether has been developed to form the C(vinyl)–Cl bond,[7a] C(vinyl)–F bond,[7b,7c] C(vinyl)–I bond,[7d] and C(vinyl)–$SnBu_3$ bond.[7e]

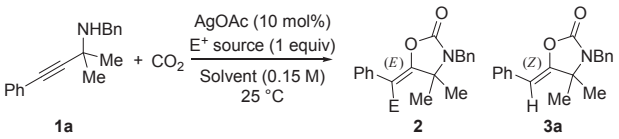


Scheme 1. Incorporation of carbon dioxide into propargylic amines.

The halovinyl component is one of the most reliable structures for metal-catalyzed coupling reactions to form new carbon frameworks. Thus, the successive introduction of carbon dioxide and a halogen group into propargylic amines was investigated to afford oxazolidinones bearing (*E*)-halovinyl moieties. As an example for the sequential introduction of carbon dioxide and a halogen group, the iodo-cyclization of primary propargylic amines and carbon dioxide with *t*-BuOI was reported,[8] but the yields of the products and variations of the substituents at the terminal position are not sufficient. According to previous studies,[6] it was expected that the silver-catalytic system could be applied to various propargylic amines bearing internal alkynes at around room temperature. In this communication, we report the silver-catalyzed three-component reaction of propargylic amine, carbon dioxide, and halonium ions to provide the corresponding oxazolidinone derivatives with an (*E*)-halovinyl group.

For the initial screening, the propargylic amine **1a** was employed as the starting material using 10 mol % AgOAc in DMSO under a 2.0 MPa CO_2 atmosphere (Table 1, Entries 1–3). The halonium ions were first examined using the corresponding

Table 1. Examination of halonium ion sources as electrophile

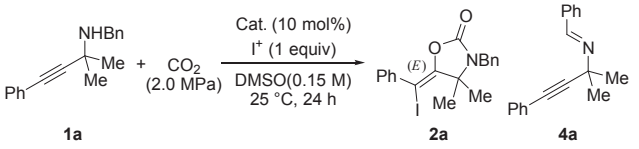


1a 2 3a

Entry	E^+ source	Solvent	CO_2 pressure /MPa	Time /h	Yield[a] **2** /%
1	NCS	DMSO	2.0	24	0[b]
2	NBS	DMSO	2.0	24	0
3	NIS	DMSO	2.0	24	92(**2a**)
4	I_2	DMSO	2.0	24	trace
5	I-Cl	DMSO	2.0	24	0
6	I^+[c]	DMSO	2.0	24	0
7	NIS	DMSO	1.0	60	92(**2a**)
8	NIS	DMF	2.0	24	71(**2a**)
9	NIS	CH_3CN	2.0	24	57(**2a**)
10	NIS	CH_2Cl_2	2.0	24	3(**2a**)
11	NIS	Toluene	2.0	24	trace

[a]Isolated yield. [b]The corresponding oxazolidinone **3a** was obtained in 15% yield. [c]Bis(2,4,6-trimethylpyridine)iodonium hexafluorophosphate was employed.

Table 2. Comparative experiments



1a 2a 4a

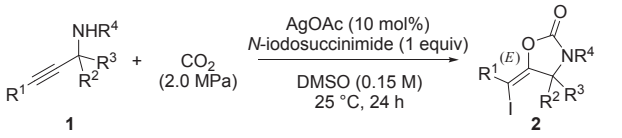
Entry	Cat.	I^+ source	Yield[a] **2a**/%	**4a**/%	**1a**/%
1	AgOAc	NIS	92	trace	0
2	none	NIS	10	20	26
3	none	I_2	0	5	71

[a]Isolated yield.

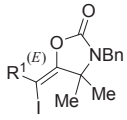
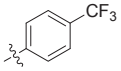
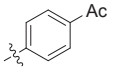
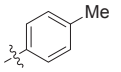
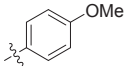
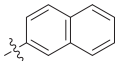
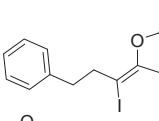
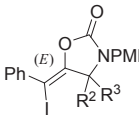
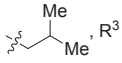
succinimides. In the case of *N*-chlorosuccinimide and *N*-bromosuccinimide, the corresponding oxazolidinone **2** was not obtained (Table 1, Entries 1 and 2). On the other hand, when *N*-iodosuccinimide (NIS) was employed, the propargylic amine **1a** was completely consumed in 24 h to produce the oxazolidinone **2a** bearing the iodovinyl group in 92% yield (Table 1, Entry 3). According to the ^{1}H NMR spectroscopic analysis, the oxazolidinone **2a** was obtained as the sole isomer. The structure of the oxazolidinone **2a** was confirmed by X-ray analysis, and the geometry of the *exo*-olefin in **2a** was suggested to be the *E*-isomer (Figure S1). To our surprise, the oxazolidinone **3a** was not observed at all, which suggested that the silver ion was effectively replaced with the iodonium ion prior to the proton derived from the amino group. Several iodine sources were then examined to determine variations in the effective iodonium sources. It was revealed that iodine, iodine monochloride, or bis(2,4,6-trimethylpyridine)iodonium hexafluorophosphate were not effective (Table 1, Entries 4–6). When the carbon dioxide pressure was reduced to 1.0 MPa, the corresponding iodovinyl derivative **2a** was produced in 92% yield, though a longer reaction time was required (Table 1, Entry 7). After evaluation of the solvents (Table 1, Entries 8–11), aprotic polar solvents, such as CH_3CN, DMF, and DMSO, turned out to be suitable to produce the oxazolidinone **2a** in good yields.

For a detailed study of the reaction, some comparative experiments were carried out (Table 2). The halonium ion is typically employed as an activator for alkenes and alkynes for halocyclization, such as halolactonization.[9] Therefore, it was a concern that, without silver catalysts, NIS itself promoted the cyclization to afford the oxazolidinone **2a**. In the absence of AgOAc, the oxazolidinone **2a** was obtained in 10% yield along with a 20% yield of the imine **4a**. The imine **4a** was supposed to be produced by the oxidation of benzylamine by the iodonium ion (Table 2, Entry 2).[10] When iodine was employed instead of NIS, the reaction did not afford the oxazolidinone **2a** at all (Table 2, Entry 3). It was assumed that the iodo-cyclization pathway was not dominant in the present silver-catalyzed reaction and that the vinylsilver intermediate could be trapped by the iodonium ion to stereoselectively afford corresponding (*E*)-oxazolidinones. In addition, it was notable that the silver catalysts were necessary to promote the cyclization reaction prior to oxidation of benzylamine by the iodonium ion. Next, the oxazolidinone **3a**, which was synthesized under the previous conditions,[6] was exposed to the reaction conditions in order to confirm whether the oxazolidinone **3a** was transformed into the iodine-introduced **2a** (Scheme S1). As a result, the vinyl iodine **2a** was not detected at all and the starting oxazolidinone **3a** was

Table 3. Three-component reaction for secondary propargylic amines



1 2

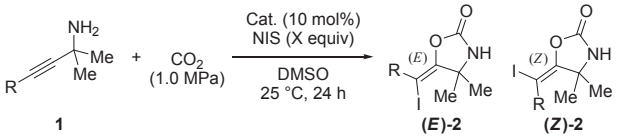
Entry	Product		Yield[a]/%
1		R^1 = Ph (**2a**)	92
2		R^1 =  (**2b**)	89
3		R^1 =  (**2c**)	82
4[b]		R^1 =  (**2d**)	91
5[b]		R^1 =  (**2e**)	91
6		R^1 =  (**2f**)	96
7[b]		R^1 =  (**2g**)	95
8		R^1 =  (**2h**)	90
9[b]		(**2i**)	86
10[b,c]		R^2 = Me, R^3 = Me (**2j**)	92
11		R^2 =  , R^3 = H (**2k**)	92

[a]Isolated yield. *E*-Isomer was selectively obtained in every case. [b]The reaction was carried out for 48 h. [c]The reaction was carried out under 1.0 MPa CO_2.

recovered in 99% yield, which suggested that the iodovinyl moiety did not form through the oxazolidinone **3a**.

The scope of the substrates was investigated under the optimized reaction conditions (Table 3). First, substituents on the aromatics were evaluated using secondary propargylic amines. In the case of the substrates **1b** (*p*-CF_3) and **1c** (*p*-Ac) bearing electron-withdrawing groups, the corresponding (*E*)-oxazolidinones **2b** and **2c** were obtained in 89% and 82% yields, respectively. Propargylic amines **1d** (*p*-Me) and **1e** (*p*-OMe) were transformed into the corresponding oxazolidinones **2d** and **2e** in 91% and 91% yields, respectively. The reaction of the propargylic amines **1f** and **1g** having a 1-naphthyl or 2-naphthyl group proceeded to give the oxazolidinones **2f** and **2g** in high yields, respectively. The 2-thienyl- and alkyl-substituted alkynes substrates **1h** and **1i** were also suitable for the reaction to furnish the corresponding products **2h** and **2i** in 90% and 86% yields, respectively. The *p*-methoxybenzyl propargylic amines **1j–1l** were found to be good substrates. Substrates **1j** and **1k** were converted to oxazolidinones **2j** and **2k** in 92% yields,

Table 4. Evaluation of primary amine derivatives



Entry	R	Cat.	*X* /equiv	Conc. /M	Yield[a] /%	*E*:*Z*[b]
1	Ph (**1l**)	AgOAc	1.2	0.30	86	58:42
2	Ph (**1l**)	none	1.2	0.30	79[c]	22:78
3	Ph (**1l**)	AgOAc	1.0	0.15	95	83:17
4	Ph (**1l**)	$AgSbF_6$	1.0	0.15	95	88:12
5	Ph (**1l**)	$AgNO_3$	1.0	0.15	90	91:9
6	Ph (**1l**)	$AgNO_3$	1.0	0.05	94	95:5
7	4-MeC_6H_4 (**1m**)	$AgNO_3$	1.0	0.05	91	96:4
8[d]	4-$CF_3C_6H_4$ (**1n**)	$AgNO_3$	1.0	0.05	98	97:3

[a]Isolated yield. [b]Determined by ^{1}H NMR. [c]Undesired and unseparated compound was detected by ^{1}H NMR. [d]2.0 MPa CO_2 pressure.

respectively. In every case, the *E*-isomer was selectively obtained as the sole isomer.[11]

The optimized reaction system was also applied to primary amine derivatives. The reaction of substrate **1l** smoothly proceeded, but unfortunately, the *E* and *Z* isomers of the oxazolidinones were obtained with the *E*/*Z* ratio 58:42 (Table 4, Entry 1). Though the iodonium ion was not effective for secondary propargylic amines as shown in Table 2, according to a previous report,[8] it was considered that the iodo-cyclization of primary propargylic amines and carbon dioxide occurred as a background reaction. Actually, the reaction conditions without AgOAc gave the corresponding oxazolidinone. Interestingly, the oxazolidinone **(*Z*)-2l** was obtained as a major product (Table 4, Entry 2), which should be caused by the equilibration in the iodonium intermediate.[12] The background reaction could cause the poor stereoselectivity for the *E*-isomer in Table 4, Entry 1. It was found that a low concentration depressed the background reaction (Table 4, Entry 3). If the silver-catalyzed cyclization proceeded prior to the background iodo-cyclization, the oxazolidinone **2l** was supposed to be obtained with high *E*-selectivity. After examination of the several counter anions of silver salts to promote the cyclization step, $AgNO_3$ turned out to be suitable for the high *E*-selective synthesis of oxazolizinones (Table 4, Entries 3–5). Finally, when the concentration was reduced to 0.05 M, the oxazolidinones **(*E*)-2l** and **(*Z*)-2l** were produced in 94% yield with the ratios of 95:5 (Table 4, Entry 6). Substrates containing an electron-donating group **1m** (*p*-Me) and an electron-withdrawing group **1n** (*p*-CF_3) on the aromatics were transformed into corresponding the oxazolidinones **2m** and **2n** in high yields with the ratios of 96:4 and 97:3, respectively (Table 4, Entries 7 and 8).

In conclusion, the silver-catalyzed three-component reaction of propargylic amines, carbon dioxide, and NIS for the stereoselective synthesis of (*E*)-iodovinyloxazolidinones was developed. The silver-catalytic system could be applied to various secondary propargylic amines to afford the corresponding iodovinyloxazolidinones in high yields. It should be noted that prior to the other possibility of oxidation and protodeauration, silver catalysts could control the reaction to selectively afford (*E*)-iodovinyloxazolidinones. In the case of primary amines, a low concentration was found to be suitable for the highly *E*-selective synthesis. The structure of the oxazolidinone **2a** was confirmed by an X-ray structure analysis to be the *E*-isomer for the geometry of the *exo*-olefin. The silver-catalyzed cyclization and replacement of silver with the iodine group in the intermediate were supposed to be crucial steps. The transformation should provide persuasive evidence for the vinylsilver intermediates for the previously reported silver-catalytic incorporation of carbon dioxide.

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Supporting Information is available electronically on J-STAGE.

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