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Stereoselective Formation of α-Alkylidene Cyclic Carbonates via Carboxylative Cyclization of Propargyl Alcohols in Supercritical Carbon Dioxide

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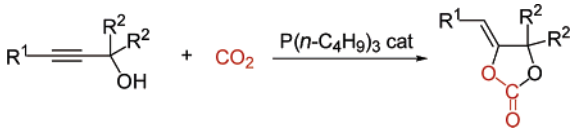
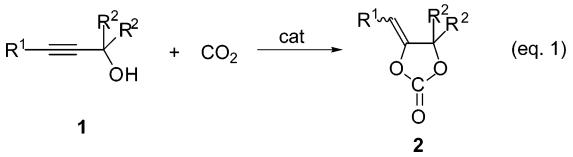


Carboxylative cyclization of propargyl alcohols in supercritical carbon dioxide ($scCO_2$) containing $P(n\text{-}C_4H_9)_3$ as a catalyst proceeded smoothly to give α-alkylidene-1,3-dioxolan-2-ones. Internal propargyl alcohols afforded *Z*-alkylidene cyclic carbonates exclusively. CO_2 incorporation was markedly promoted under supercritical conditions, possibly due to the facile formation of a putative $P(n\text{-}C_4H_9)_3{-}CO_2$ adduct as a key intermediate.

A large body of work has been devoted over the past decades to the use of CO_2 as an environmentally benign C_1 feedstock for the production of useful chemical commodities.[1] For example, the direct synthesis of carbonates[2] from the reaction of CO_2 and epoxides[3,4] or alcohols[5−7] has been widely exploited as an alternative to phosgene processes. Five-membered cyclic carbonates, 1,3-dioxolan-2-ones, are also accessible from propargyl alcohols (**1**) and CO_2 in the presence of transition metal compounds[8−10] or tertiary phosphines[11] as shown in eq 1. Although such cyclic carbonate products are versatile intermediates or precursors in organic synthesis[12] and polymer chemistry,[13] the reaction scopes remain unclear especially for the internal propargylic alcohols leading to α-alkylidene carbonates. Inoue et al. reported a facile reaction of 4-hydroxy-4-methyl-1-phenyl-2-pentyn-1-one ($R^1 = C_6H_5C(=O)$ in eq 1) with CO_2 in triethylamine without catalysts giving (*E*)-4-benzoylmethylene-5,5-dimethyl-1,3-dioxolan-2-one,[14] while the *Z*-carbonate products are obtainable in a range of 15−35% yield from conjugated alkynol having a phenyl or allenyl group under basic conditions.[7c] In addition, Dixneuf et al. reported the reaction of conjugated propargyl alcohols with CO_2 catalyzed by tri-*n*-butylphosphine, $P(n\text{-}C_4H_9)_3$, leading to cyclic carbonates without stereochemical information.[11b]



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Recently, we have found that supercritical CO_2 ($scCO_2$) effectively promotes the direct formation of cyclic urethanes

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TABLE 1. Carboxylative Cyclization of Propargyl Alcohols with $scCO_2$[a]

run	alkynol	R^1	R^2	product	yield (%)[b]
1	**1a**	H	CH_3, CH_3	**2a**	99
2	**1b**	C_6H_5	CH_3, CH_3	**2b**	76 (88)[c]
3	**1c**	4-Cl-C_6H_4	CH_3, CH_3	**2c**	80
4	**1d**	4-CH_3CO-C_6H_4	CH_3, CH_3	**2d**	82
5	**1e**	4-CN-C_6H_4	CH_3, CH_3	**2e**	86
6	**1f**	4-NO_2-C_6H_4	CH_3, CH_3	**2f**	77
7	**1g**	4-CF_3-C_6H_4	CH_3, CH_3	**2g**	87
8	**1h**	4-CH_3-C_6H_4	CH_3, CH_3	**2h**	62
9	**1i**	4-CH_3O-C_6H_4	CH_3, CH_3	**2i**	0
10	**1j**	2-naphthyl	CH_3, CH_3	**2j**	72
11	**1k**	2-pyridyl	CH_3, CH_3	**2k**	64
12	**1l**	CH_3	CH_3, CH_3	**2l**	0
13	**1m**	C_6H_5	$-(CH_2)_5-$	**2m**	74
14	**1n**	4-NO_2-C_6H_4	CH_3, H	**2o**	0
15	**1o**	4-NO_2-C_6H_4	H, H	**2p**	0

[a] Reaction conditions: **1** (5.0 mmol), P(*n*-C_4H_9)$_3$ (0.25 mmol), 10 MPa, 100 °C, 15 h. [b] Isolated yield. [c] Determined by ^{1}H NMR spectroscopy.

TABLE 2. Pressure Dependence on the Formation of 2b[a]

run	pressure (MPa)	yield (%)[b]
1	2.0	41
2	5.0	52
3	6.0	62
4	8.0	79
5	10.0	88
6	12.0	70

[a] Reaction conditions: **1b** (5.0 mmol), P(*n*-C_4H_9)$_3$ (0.25 mmol), 100 °C, 15 h. [b] Determined by ^{1}H NMR spectroscopy.

from propargylamines even in the absence of metal and base catalysts.[15] Since supercritical fluids have many potential advantages originating from their unique physicochemical properties, which are easily controlled by pressure and temperature,[16] $scCO_2$ is regarded as a promising solvent for developing efficient CO_2 fixation systems. In the present study, we explored the carboxylative cyclization of propargyl alcohols catalyzed by P(*n*-C_4H_9)$_3$ in $scCO_2$, in which internal substrates bearing aryl groups were readily converted into the *Z*-alkylidene cyclic carbonates in a stereoselective manner.

Using a catalytic amount (5 mol %) of P(*n*-C_4H_9)$_3$, we carried out the reaction of propargyl alcohols (**1**) with CO_2 for 16 h (Table 1). We have briefly reported that $scCO_2$ can be applied to the catalyst system for converting a terminal alkynol, 2-methyl-3-propyn-2-ol (**1a**) into 5-methylene-4,4-dimethyl-1,3-dioxolan-2-one (**2a**) and for enhancing catalytic activity.[17] In fact, **2a** was obtained quantitatively from **1a** under the conditions of 100 °C and 10.0 MPa (run 1). An internal alkynol, 2-methyl-4-phenyl-3-propyn-2-ol (**1b**), also reacted with CO_2 under similar conditions to give 4-benzylidene-5,5-dimethyl-1,3-dioxolan-2-one (**2b**) in 88% yield (run 2). Table 2 shows that the CO_2 pressure strongly influences the carboxylative cyclization of **2b**. When the CO_2 pressure was increased from 2.0 to 10.0 MPa, the yields obtained at 100 °C were gradually increased (runs 1−5); however, when the pressure was greater than 10.0 MPa, there was a slight decrease in the yield of the carbonate product (run 6, vide infra).

Other substrates having various aromatic groups can be converted into the corresponding cyclic carbonates in good yields as shown in Table 1. In the reactions of **1c**−**g** containing electron-withdrawing groups on the arene ring, the desired carbonates were successfully obtained in the range of 77−87%. On the other hand, the presence of an electron-donating group bound to the arene ring reduced the reactivity of the alkynes toward the carboxylative cyclization. The reaction of **1h** having a *p*-tolyl group gave the product in a slightly lower yield, and the propargyl alcohol having the *p*-methoxyphenyl group **1i** provided unsatisfactory results (runs 5 and 6). The use of 2-naphthyl and 2-pyridyl substituents at the acetylenic terminus also gave the desired cyclic carbonates (**2j** and **2k**) in good yields (runs 10 and 11), whereas an internal alkyne bound to the methyl group was inert to the cyclization (run 12). Although a spiro carbonate compound (**2m**) was also obtained by this CO_2 fixation (run 13), no carboxylation product was formed from secondary and primary alcohols (runs 14 and 15), possibly due to lack of a *gem*-dialkyl effect.[18]

The stereochemistry of the carbonate products was determined from analytical and spectral data. The ^{1}H NMR spectrum of each crude product showed signals around 5.5 ppm due to an olefinic proton of the α-alkylidene cyclic carbonate formed as a single isomer. In NOESY experiments, a correlation between the olefinic proton and the methyl protons bound to the C-4 carbon on the 1,3-dioxolan-2-one ring was detected, suggesting the formation of *Z*-trisubstituted olefins (See Supporting Information). An X-ray crystal structure determination of the product **2d** also revealed the *Z*-configuration of the alkylidene moiety, indicating that the cyclization took place in a trans addition mode to the C−C triple bond (see Supporting Information).

While the precise mechanism of the present reaction still remains an open question, the selective formation of *Z*-alkylidene carbonates suggests that the cyclization should take place through a nucleophilic attack process on the C−C triple bond of the substrates. The positive effect on the carbonate yields observed with substrates with electron-withdrawing groups seems to be consistent with the nucleophilic attack mechanism. One may propose that the reaction pathway involving alkyne activation by the phosphine catalyst generates an intermediate **A** and the subsequent intramolecular attack of the carbonate moieties is formed from the alcoholic OH group and CO_2 (Cycle I in Scheme 1). An alternative pathway might involve the formation of tri-*n*-butylphosphonioformate, $(C_4H_9)_3P^+CO_2^-$,[19] as a consequence of a CO_2 activation by P(*n*-C_4H_9)$_3$ (Cycle II). The zwitter ionic CO_2 adduct may also undergo nucleophilic attack to the C−C triple bond to give an intermediate **B** where the electrophilic carboxyl group is susceptible to attack by the alcoholic oxygen when the product carbonate and the regener-

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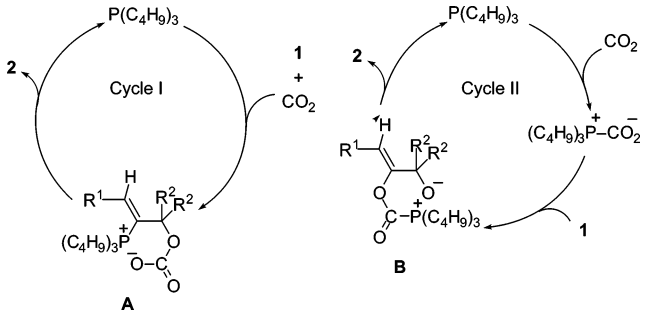
SCHEME 1. Plausible Mechanisms for Carboxylative Cyclization of Propargyl Alcohols Catalyzed by P(*n*-C_4H_9)$_3$



ated phosphine catalyst are released. Despite any direct evidence of formation of the hydrogen carbonate or the phosphine−CO_2 adduct by high-pressure NMR spectroscopy,[20] it is plausible that the supercritical conditions favorable for formation of the CO_2 adduct would allow access to the carbonate product. Possible ionic intermediates might be influenced by the phase behavior relevant to the polarity of the reaction system. In fact, the carbonate formation was slightly retarded by a large increase in the CO_2 pressure as mentioned above (Table 2, run 6). The pressure effect may be ascribable to reduction of the liquid reaction phase by enhanced mass transfer of reaction components into scCO_2. Further studies are now focused upon the full understanding of the roles of the phosphine catalyst.

In summary, we have shown that the stereo- and regioselective cyclization of propargyl alcohols with CO_2 to α-alkylidene cyclic carbonates was promoted by P(*n*-C_4H_9)$_3$ under supercritical conditions. The use of supercritical conditions facilitates efficient incorporation of the CO_2 molecule into synthetically useful organic compounds. In addition to the carboxylative cyclization mentioned earlier,[7c,11b,14] stereoselective synthesis of α-alkylidene-1,3-dioxolan-2-ones has been accomplished with the Mizoroki−Heck reaction of aryl halides with α-methylene cyclic carbonates[12] and palladium-catalyzed carboxylative coupling reactions of propargylic alcohols with organic halides under CO_2.[7b,c] The former reaction affords the *Z*-alkylidene carbonates with a small amount of the *E*-isomer, whereas the *E*-isomers can be obtained in the latter case. It should be noted that the present phosphine-catalyzed system provides an alternative procedure for synthesis of *Z*-alkylidene carbonates from internal propargyl alcohols and scCO_2 with high efficiency.

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Experimental Section

CAUTION: The experiments described here could involve risk of an explosion and were conducted using equipment and safety precautions suitable for scCO_2 studies.

Typical Procedure for the Carboxylic Cyclization. The reaction of 2-methyl-4-(4′-acetyl)phenyl-3-butyn-2-ol **1d** with scCO_2 (Table 1, run 4) was carried out in a 50-mL stainless steel autoclave equipped with a stirring bar. The autoclave containing substrate **1d** (1.011 g, 5.0 mmol) was purged with argon gas to remove oxygen. P(*n*-C_4H_9)$_3$ (50.6 mg, 0.25 mmol) was introduced into the autoclave with a syringe while the vessel was purged with argon. The vessel was charged with CO_2 to the required pressure through a cooling apparatus with an HPLC pump. After being stirred for 15 h at 100 °C, the reaction was stopped by cooling the autoclave in a dry ice/methanol bath. CO_2 was vented, and the autoclave was slowly warmed to room temperature. The reaction mixture was analyzed by ^{1}H NMR spectroscopy with durene as an internal standard. The crude products were purified by column chromatography on silica gel (hexane/ethyl acetate = 5:1) and Kugelrohr distillation to yield (*Z*)-4-(4′-acetyl)benzylidene-5,5-dimethyl-1,3-dioxolan-2-one **2d** (1.050 g, 82%). Mp 156−158 °C; ^{1}H NMR (300.5 MHz, $CDCl_3$) δ 1.70 (s, 6H, C(C*H*$_3$)$_2$), 2.59 (s, 3H, COC*H*$_3$), 5.53 (s, 1H, C=C*H*), 7.60 (A_2B_2 pattern, 2H, C$_6$*H*$_4$), 7.92 (A_2B_2 pattern, 2H, C$_6$*H*$_4$); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 26.6, 27.6, 85.7, 100.6, 128.5, 128.7, 135.7, 137.1, 150.8, 152.8, 197.4; Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.19; H, 5.69.

Crystal Structure Determination. Crystal data for **2d**: $C_{14}H_{14}O_4$, M = 246.26, monoclinic, $P2_1/c$, a = 6.576(4) Å, b = 7.356(4) Å, c = 26.19(2) Å, β = 90.0000°, V = 1266.6(13) Å^3, Z = 4, T = 193 K, D_c = 1.291 g·cm^{-3}, λ(Mo Kα) = 0.71070 Å, 9545 reflections measured, 2677 unique (R_{int} = 0.058), which were used in all calculations. The structure was solved by direct method (SIR92) and refined by the full-matrix least-squares methods on F^2 with 177 parameters. R1 = 0.057 ($I > 2\sigma(I)$) and wR2 = 0.203, GOF 0.95; max/min residual density 0.37/−0.39 e Å^{-3}. The detail of the refinement is described in the CIF file in the Supporting Information.

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Supporting Information Available: General information, characterization data for **1** and **2**, crystallographic details, copies of the NMR spectra (^{1}H, ^{13}C, and NOESY) for **2**, and X-ray crystallographic information files (CIF) for **2d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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