Communication

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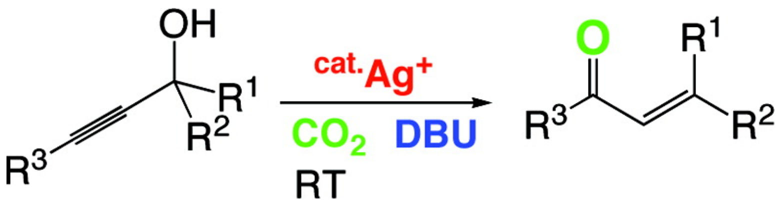

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Carbon Dioxide-Mediated Catalytic Rearrangement of Propargyl Alcohols into α,β-Unsaturated Ketones

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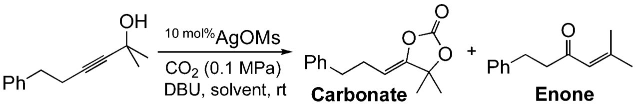
Propargyl alcohols are readily prepared by a conventional addition reaction of the corresponding acetylides to carbonyl compounds and have been employed as starting compounds in various transformation reactions. The Meyer−Schuster reaction reported in 1922[1] is the rearrangement reaction of propargyl alcohol into the corresponding α,β-unsaturated carbonyl compounds. This reaction consists of two key steps: (1) effective enhancement of the leaving ability of the hydroxy group to generate the carbocation intermediate and (2) nucleophilic addition of hydroxide equivalent to activated alkyne to afford the resulting enone. For a tertiary propargyl alcohol, a protic acid was used as a simple reagent to drive this reaction though the Rupe rearrangement via an enyne intermediate, which afforded the undesired α,β-unsaturated carbonyl compounds as byproducts. To suppress such byproduct formation during this textbook[2] reaction, oxo-metallic reagents[3,4] have been examined to remove the hydroxy group concomitantly with the [3,3]-sigmatropic rearrangement involving the nucleophilic addition to an alkyne; however, high temperature was required to drive these reactions toward completion.[5] The high affinity of late transition-metals such as gold[6] for acetylenic π-bonds was used to activate propargyl alcohols under mild conditions, although their applicable substrates were limited. For example, a ruthenium complex catalyst[7] was employed for the activation of an alkyne via a vinylidene−ruthenium intermediate derived from terminal alkynes.

It has been reported that propargyl alcohols also react with carbon dioxide to afford the corresponding cyclic carbonates using various metal salts or phosphines as a catalyst;[8] however, this approach requires high CO_2 pressure and/or high temperature, and is limited to terminal alkynes. In a previous Communication, we reported that the combined use of a catalytic amount of silver acetate and DBU efficiently catalyzed the incorporation of CO_2 under mild reaction conditions for a wide range of propargyl alcohols to afford the corresponding cyclic carbonates in high-to-excellent yields.[9] In this reaction, the corresponding α,β-unsaturated carbonyl compounds generated via a Meyer−Schuster type reaction were detected in some polar solvents. In this Communication, we report that various tertiary and secondary propargyl alcohols are efficiently converted into the corresponding α,β-unsaturated carbonyl compounds in high yield using a catalytic amount of a silver salt with DBU and carbon dioxide under mild reaction conditions.

In a toluene solution, the silver-catalyzed reaction of propargyl alcohol with carbon dioxide selectively afforded the corresponding cyclic carbonate, while in dichloromethane and chlorobenzene the corresponding α,β-unsaturated carbonyl compounds generated via a Meyer−Schuster type reaction were obtained along with the cyclic carbonate (entries 1−3, Table 1). We propose the following reaction mechanism for incorporating CO_2 into propargyl alcohol using this approach: the carbonate intermediate would be generated from propargyl alcohol and CO_2, then an intramolecular ring-closing reaction would proceed at the α-carbon of the propargyl alcohol, which was activated by the silver salt, to afford the cyclic carbonate (path A in Scheme 1). The β-carbon of the propargyl alcohol would be alternatively attacked to promote the [3,3]-sigmatropic rearrangement into the allene-enolate. The α,β-unsaturated carbonyl compounds would result from the release of CO_2 (path B in Scheme 1). It is reasonable to assume that the polarized structure with an elongated C−O bond in the carbonate intermediate would be stabilized in a polar solvent, enhancing the attack on the β-carbon in the activated propargyl alcohol. In fact, DMF and DMA solvents improved the selectivity toward the enone (entries 4−6). It was found that formamide was the best choice to selectively obtain the corresponding enone (entry 7).

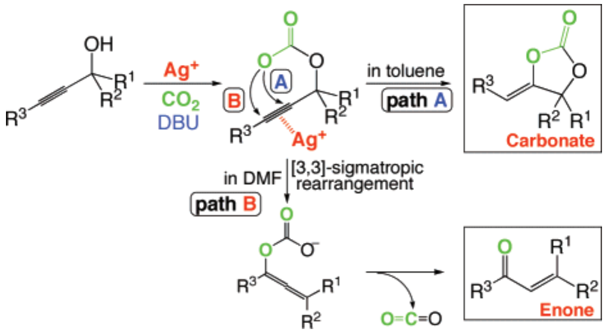
Table 1. Examination of Various Solvents



entry[a]	solvent	time/day	yield (%)[b]	
			carbonate	enone
1	toluene	1	74	trace
2	CH_2Cl_2	1	45	39
3	PhCl	1	79	11
4	DMF	3	trace	39
5[c]	DMF	0.5	7	73
6[c]	DMA	0.5	16	63
7[c]	formamide	0.5	6	86

[a] Reaction conditions: The reaction was carried out in 0.5 mL of solvent using 10 mol % silver methanesulfonate, 0.25 mmol of substrate and 0.25 mmol of DBU under atmospheric CO_2 pressure at room temperture. [b] Isolated yield. [c] The reaction was carried out under 1.0 MPa CO_2 pressure.

Scheme 1. Reaction Mechanism of Propargyl Alcohol with CO_2



The proposed mechanism is supported by results from an isotopic experiment using $C^{18}O_2$. The reaction was carried out under a carbon dioxide atmosphere to afford the α,β-unsaturated ketone with a MW of 188 when regular CO_2 was used, and an α,β-unsaturated ketone with a MW of 190 when $C^{18}O_2$ was used. As shown in Figure 1, no cross-product containing ^{16}O could be

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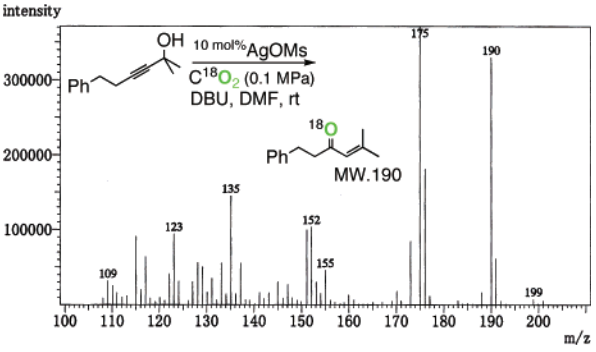


Figure 1. MS spectrum of the enone obtained from the labeled CO_2.

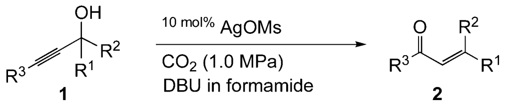
detected by GC−MS analysis. No reaction proceeded under a nitrogen atmosphere. These observations suggest that the present reaction should be promoted by carbon dioxide and that the rearrangement step should proceed in an intramolecular [3,3]-sigmatropic manner, and not by the intermolecular addition of H_2O or carbonate anion.

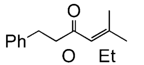
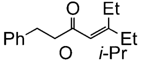
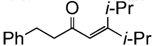
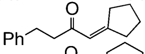
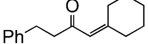
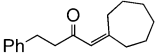
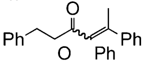
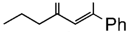
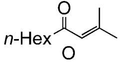
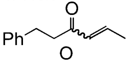
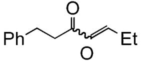
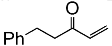
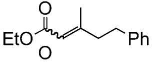
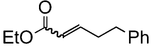
Various bases along with the use of a silver catalyst were examined. In the presence of a stoichiometric amount of pyridine, no reaction proceeded, while DBU, DBN, and diisopropylethylamine drove the reaction of the propargyl alcohol **1e** at room temperature to afford the α,β-unsaturated ketone **2e** in high yield. The amount of base could be reduced to a catalytic concentration. For the reaction of propargyl alcohol **1a**, 0.2 equiv of diisopropylethylamine afforded product **2a** in 59% yield at room temperature, while at 60 °C, the yield was improved to 81%. By using 0.2 equiv of DBU at 60 °C, the reaction rate was also improved, and the product was obtained in 89% yield after 8 h.

The optimized system was successfully applied to various propargyl alcohols (Table 2). In the presence of 10 mol % silver methanesulfonate and 0.2 equiv of DBU under 1.0 MPa CO_2 at 60 °C, alkyl-substituted tertiary propargyl alcohols **1a** and **1b** were smoothly converted into the corresponding α,β-unsaturated ketones **2a** and **2b** in high yield (entries 1 and 2). Propargyl alcohol **1c**, which possesses bulky substituents, was converted into corresponding enone **2c** in high yield at 60 °C (entry 3) when 3.0 equiv of DBU was employed. For propargyl alcohols **1d**−**f**, which have five-to-seven-membered rings, the reactions smoothly proceeded under mild conditions using 1.0 equiv of diisopropylethylamine to afford rearranged products **2d**−**f** with cycloalkylidene groups in 93%, 90%, and 94% yields, respectively, without any isomerization of the C−C double bond. Propargyl alcohols **1g**−**h** with a phenyl group at the propargylic position, reacted with CO_2 to afford the corresponding enones **2g** in 98% yield (entry 7) and **2h** in 80% yield (in DMF, entry 8). The present catalytic system could be applied to various tertiary and secondary propargyl alcohols to afford products **2j** and **2k** in high yield at room temperature (entries 10 and 11), even though it has been reported that secondary propargyl alcohols are difficult to convert into the corresponding α,β-unsaturated ketones under mild conditions.[10] However, propargyl alcohol **1l** was less reactive, and the corresponding monosubstituted enone **2l** was obtained in 29% yield (entry 12). The ethoxy-substituted propargylic alcohols[6c,d] **1m** and **1n** were good substrates that afforded the corresponding ethyl ester of the α,β-unsaturated carboxylic acids **2m** and **2n** in high yield (entries 13 and 14).

It is noted that in the presence of a catalytic amount of a silver salt with DBU, the Meyer−Schuster reaction of various tertiary and secondary propargyl alcohols were efficiently promoted by carbon dioxide to afford the corresponding α,β-unsaturated carbonyl compounds in high yield.

Table 2. Transformation of Various Propargyl Alcohols into the Enones



entry[a]	enone		time (h)	yield (%)[b]
1[c]		**2a**	8	89
2[c]		**2b**	24	74
3[d]		**2c**	25	70
4[e]		**2d**	24	93
5[e]		**2e**	48	90
6[e]		**2f**	40	94
7[e]		**2g**	47	98 (46 / 54)[g]
8[f]		**2h**	96	80
9[f]		**2i**	19	84
10		**2j**	48	93 (75 / 25)[g]
11		**2k**	48	84 (76 / 24)[g]
12		**2l**	72	29
13[e]		**2m**	19	87 (46 / 54)[g]
14[e]		**2n**	54	70 (79 / 21)[g]

[a] Reaction conditions: The reaction was carried out in 0.5 mL of formamide with 10 mol % silver mathanesulfonate, 0.25 mmol of substrate and 1.0 equiv of DBU under 1.0 MPa CO_2 pressure at room temperature. [b] Isolated yield. [c] Reaction run using 0.2 equiv of DBU at 60 °C. [d] Reaction run using 3.0 equiv of DBU at 60 °C. [e] i-Pr_2NEt was used as a base. [f] The reaction was carried out in DMF. [g] E/Z ratio was provided in parenthesis.

Supporting Information Available: Experimental procedure and spectra data of the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Meyer, K. H.; Schuster, K. *Chem. Ber.* **1922**, *55*, 819−823.
(2) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th ed; John Wiley & Sons: New York, 2001; pp 423.
(3) Vanadium: (a) Ernan, M. B.; Aul'chenko, I. S.; Kheifits, L. A.; Dulova, V. G.; Novikov, J. N.; Vol'pin, M. E. *Tetrahedron Lett.* **1976**, *34*, 2981−2984. (b) Choudary, B. M.; Durga Prasad, A.; Valli, V. L. K. *Tetrahedron Lett.* **1990**, *31*, 7521−7522. (c) Chabardes, P.; Kuntz, E.; Varagnat, J. *Tetrahedron* **1977**, *33*, 1775−1783. Molybdenum: (d) Lorber, C. Y.; Osborn, J. A. *Tetrahedron Lett.* **1996**, *37*, 853−856.
(4) Titanium alkoxide: Chabardes, P. *Tetrahedron Lett.* **1988**, *29*, 6253−6256.
(5) Under mild reaction conditions using a rhenium salt: Narasaka, K.; Kusama, H.; Hayashi, Y. *Chem. Lett.* **1991**, 1413−1416.
(6) (a) Fukuda, Y.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2013−2015. (b) Georgy, M.; Boucard, V.; Campagne, J. *J. Am. Chem. Soc.* **2005**, *127*, 14180−14181. (c) Engel, D. A.; Dudley, G. B. *Org. Lett.* **2006**, *8*, 4027−4029. (d) Lopez, S. S.; Engel, D. A.; Dudley, G. B. *Synlett* **2007**, *6*, 949−953. (e) Yu, M.; Li, G.; Wang, S.; Zhang, L. *Adv. Synth. Catal.* **2007**, *349*, 871−875.
(7) (a) Picquet, M.; Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1997**, 1201−1202. (b) Picquet, M.; Fernández, A.; Bruneau, C.; Dixneuf, P. H. *Eur. J. Org. Chem.* **2000**, 2361−2366. (c) Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Tetrahedron Lett.* **2002**, *43*, 7531−7533. (d) Cadierno, V.; Diez, J.; Garcia-Garrido, S. E.; Gimeno, J. *Chem. Commun.* **2004**, 2716−2717. (e) Cadierno, V.; Garcia-Garrido, S. E.; Gimeno, J. *Adv. Synth. Catal.* **2006**, *348*, 101−110.
(8) Kayaki, Y.; Yamamoto, M.; Ikariya, T. *J. Org. Chem.* **2007**, *72*, 647−649 and references cited therein.
(9) Yamada, W.; Sugawara, Y.; Cheng, H.-M.; Ikeno, T.; Yamada, T. *Eur. J. Org. Chem.* **2007**, 2604−2607.
(10) A high reaction temperature was required to complete the reaction of the secondary propargyl alcohol (see refs 3b, 3d, 5, 6a, 7c, and 7e).

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