

# A Novel Methodology for the Synthesis of Cyclic Carbonates Based on the Palladium-Catalyzed Cascade Reaction of 4-Methoxycarbonyloxy-2-butyn-1-ols with Phenols, Involving a Novel Carbon Dioxide Elimination-Fixation Process

Masahiro Yoshida,\* Mika Fujita, Toru Ishii, and Masataka Ihara\*

Contribution from the Department of Organic Chemistry, Graduate School of Pharmaceutical Sciences, Tohoku University, Aobayama, Sendai 980-8578, Japan

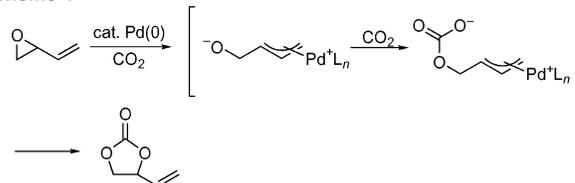
Received January 8, 2003; E-mail: mihara@mail.pharm.tohoku.ac.jp

**Abstract:** A palladium-catalyzed CO<sub>2</sub>-recycling reaction has been developed. Reaction of 4-methoxycarbonyloxy-2-butyn-1-ols with phenols, carried out in the presence of a palladium catalyst, produces phenoxy-substituted cyclic carbonates by way of a pathway involving a CO<sub>2</sub> elimination-fixation. A variety of propargylic alcohols and phenols participate in these reactions which yield cyclic carbonates with high efficiencies. Stereoselective construction of *trans*-cyclic carbonates is achieved by using nonsymmetric substrates. Highly enantioselective reactions occur when (*S*)-BINAP is used as a ligand. Reaction of 4-phenoxy-carbonyloxy-2-butyn-1-ol in the presence of the palladium catalyst yields the corresponding cyclic carbonates via a three-component decomposition-reconstruction process.

## Introduction

The chemistry of CO<sub>2</sub> has received much attention recently because of its potential use as an abundant carbon source and its indirect role as an environmental pollutant. The transformation of CO<sub>2</sub> into organic substances represents an attractive area of study in both organic and green chemistry.<sup>1</sup> Transition metal-mediated reactions are among the most common methods to convert CO<sub>2</sub> into organic compounds.<sup>2</sup> An example of a process of this type is the palladium-catalyzed reaction of vinyl epoxides and CO<sub>2</sub> to afford cyclic carbonates (Scheme 1), reported independently by Fujinami and Trost and their co-workers.<sup>3,4</sup>

## Scheme 1



This reaction proceeds via the formation of the π-allylpalladium complex followed by the incorporation of carbon dioxide.

In contrast, decarboxylation is a familiar process in organic chemistry, and many reactions are known in which elimination of CO<sub>2</sub> is the driving force.<sup>5</sup> For example, allylic and propargylic carbonates undergo facile palladium-catalyzed decarboxylation to generate π-allyl- and allenylpalladium complexes. These complexes react with nucleophiles to give substitution products (Scheme 2).<sup>6,7</sup> In these decarboxylation reactions, the eliminated CO<sub>2</sub> is a byproduct. Importantly, no examples exist in which the eliminated CO<sub>2</sub> is incorporated into the product molecule.

We have recently devised a new reaction, termed “recycling of CO<sub>2</sub>” (Figure 1), in which a substrate bearing a CO<sub>2</sub> component undergoes initial catalyst promoted decarboxylation

- (1) Arakawa, H.; Aresta, M.; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; DuBois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, D. W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nicholas, K. M.; Periana, R.; Que, L.; Rostrup-Nielsen, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P. C.; Stults, B. R. *Chem. Rev.* **2001**, *101*, 953.
- (2) (a) Vol'pin, M. E.; Kolominkov, I. S. *Pure Appl. Chem.* **1973**, *33*, 567. (b) Eisenberg R.; Hendriksen, D. E. *Adv. Catal.* **1979**, *28*, 79. (c) Ibers, J. A. *Chem. Soc. Rev.* **1982**, *11*, 57. (d) Haruki, E.; Ito, T.; Yamamoto, A.; Yamazaki, N.; Higashi, F.; Inoue, S. In *Organic and Bioorganic Chemistry of Carbon Dioxide*; Inoue, S., Yamazaki, N., Eds.; Kodansha: Tokyo, 1982; p 199. (e) Behr, A. In *Catalysis in C<sub>1</sub> Chemistry*; Keim, W., Ed.; D. Reidel Publ. Co.: Dordrecht, Holland, 1983; p 169. (f) Walther, D. *Coord. Chem. Rev.* **1987**, *79*, 135. (g) Braunstein, P.; Matt, D.; Nobel, D. *Chem. Rev.* **1988**, *88*, 747. (h) Cutler, A. R.; Hanna, P. K.; Vites, J. C. *Chem. Rev.* **1988**, *88*, 1363. (i) Behr, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 661. (j) Behr, A. *Carbon Dioxide Activation by Metal Complexes*; VCH: Weinheim, 1988; p 91. (k) Miller, J. D. In *Reactions of Coordinated Ligands*; Braterman, P. S., Ed.; Plenum Press: New York, 1989; Vol. 2, p 1. (l) Halmann, M. M. *Chemical Fixation of Carbon Dioxide. Methods for Recycling CO<sub>2</sub> into Useful Products*; CRC Press: Boca Raton, FL, 1993. (m) Creutz, C. In *Electrochemical and Electrocatalytic Reactions of Carbon Dioxide*; Sullivan, B. P., Krist, K., Guard, H. E., Eds.; Elsevier: Amsterdam, 1993; Chapter 2. (n) Aresta, M.; Quaranta, E.; Tommasi, I. *New J. Chem.* **1994**, *18*, 133. (o) Leitner, W. *Coord. Chem. Rev.* **1996**, *153*, 127. (p) Gibson, D. H. *Chem. Rev.* **1996**, *96*, 2063. (q) Yin, X.; Moss, J. R. *Coord. Chem. Rev.* **1999**, *181*, 27. (r) Walther, D.; Ruben, M.; Rau, S. *Coord. Chem. Rev.* **1999**, *182*, 67.

- (3) (a) Fujinami, T.; Suzuki, T.; Kamiya, M.; Fukuzawa, S.; Sakai, S. *Chem. Lett.* **1985**, 199. (b) Trost, B. M.; Angle, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 6123. (c) Trost, B. M.; Lynch, J. K.; Angle, S. R. *Tetrahedron Lett.* **1987**, *28*, 375. (d) Wershofen, S.; Scharf, H. D. *Synthesis* **1988**, 854. (e) Suzuki, S.; Fujita, Y.; Kobayashi, Y.; Sato, F. *Tetrahedron Lett.* **1989**, *30*, 3487.
- (4) Palladium-catalyzed CO<sub>2</sub> fixation of alkydienols with aryl halides via π-allylpalladium complex is also known: Uemura, K.; Shiraishi, D.; Noziri, M.; Inoue, Y. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1063.
- (5) For examples of decarboxylation, see: (a) Krapcho, A. P. *Synthesis* **1982**, 805. (b) Schäfer, H. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, p 633. (c) Crich, D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 7, p 717.

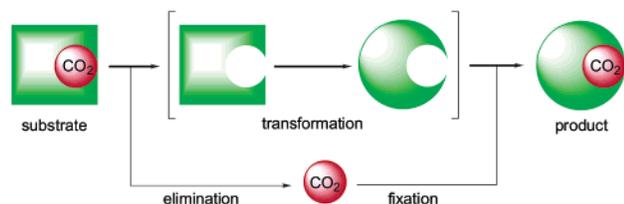
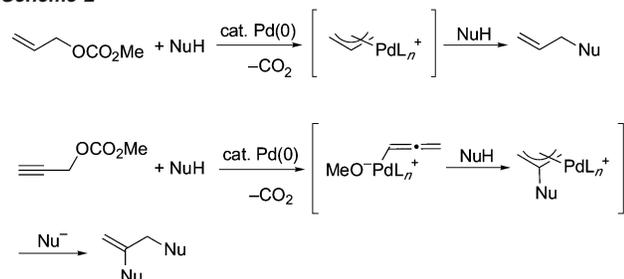
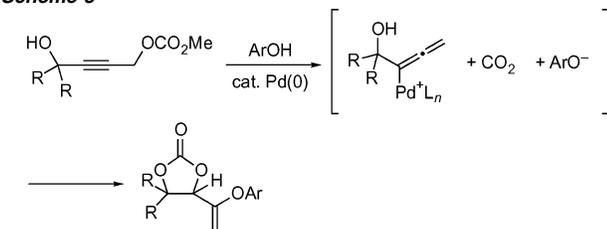


Figure 1. Concept of "recycling of CO<sub>2</sub>".

### Scheme 2



### Scheme 3



to give an intermediate and CO<sub>2</sub>. Reaction of the intermediate is then followed by CO<sub>2</sub> incorporation to afford a CO<sub>2</sub>-containing product. This concept has been used to develop a new CO<sub>2</sub>-recycling process as part of a novel methodology for the synthesis of cyclic carbonates, involving the palladium-catalyzed cascade reaction of 4-methoxycarbonyloxy-2-butyne-1-ols with phenols (Scheme 3).<sup>8</sup> In this reaction, palladium-induced decarboxylation of the substrate is followed by fixation of the resulting CO<sub>2</sub>. The results of a thorough investigation of this process are presented below.

## Results and Discussion

Initial investigations of the novel CO<sub>2</sub>-recycling reaction were carried out with the substrates 1-(3-methoxycarbonyloxy-2-propynyl)cyclopentanol (**1a**) and 4-methoxyphenol (**2a**). Reaction of **1a** and **2a** in the presence of 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> and 20 mol % dppe in dioxane at 80 °C in a sealed tube for 2 h yields the cyclic carbonate **3aa** (53%) along with the dihydrofuran **4aa** (12%) (Table 1, entry 1). The yield of **3aa**

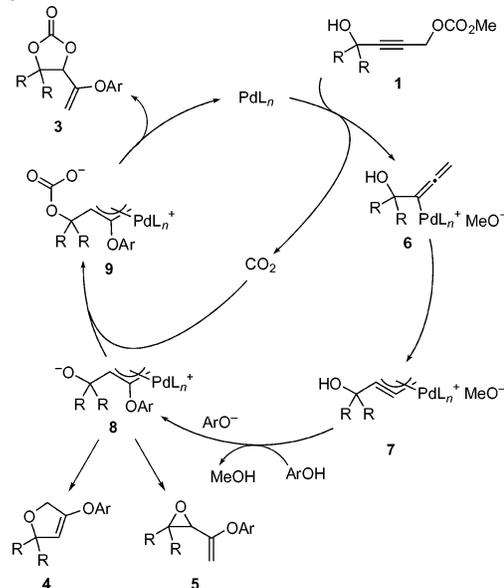
Table 1. Formation of Cyclic Carbonate **3aa** by the CO<sub>2</sub> Refixation Reaction of Propargylic Carbonate **1a** with *p*-Methoxyphenol

Reaction conditions for Table 1: 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub>, 20 mol % ligand, dioxane, under argon atmosphere in sealed tube, 1–4 h.

entry	ligand	temp (°C)	yields of products (%) <sup>a</sup>		
			3aa	4aa	5aa
1	dppe	80	53	12	
2	dppe	100	40	15	23
3	dppe	50	85	5	trace
4	dppe	rt	89	5	
5	dppp	50	80	6	
6 <sup>b</sup>	dppb	rt	83	5	
7	dppf	50	70	9	
8	PPh <sub>3</sub> <sup>c</sup>	50	82	9	
9	P(O <sup>i</sup> Pr) <sub>3</sub>	80	33	22	17

<sup>a</sup> Isolated yields. <sup>b</sup> The reaction was carried out for 7 h. <sup>c</sup> 40 mol % PPh<sub>3</sub> was used.

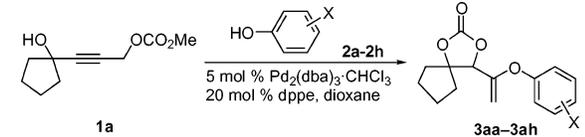
### Scheme 4



decreases to 40%, and epoxide **5aa** is produced in 23% yield along with **4aa** (15%) when the reaction is carried out at 100 °C (entry 2). Lowering the reaction temperature (entries 3 and 4) results in increased yields of **3aa**, an optimal yield of **3aa** of 89% being obtained in the reaction of **1a** and **2a** at room temperature (entry 4). When other bidentate and monodentate phosphine ligands (e.g., dppp, dppb, dppf, and PPh<sub>3</sub>) are employed, **3aa** is produced in high yields (entries 5–9). Large amounts of **4aa** and **5aa** are formed in the reaction at 80 °C, in which P(O<sup>i</sup>Pr)<sub>3</sub> is used as the ligand (entry 9).

A plausible mechanism for the formation of products **3**–**5** is shown in Scheme 4. In this process, the palladium catalyst promotes decarboxylation of the propargylic carbonate **1** to generate the allenylpalladium methoxide **6** and CO<sub>2</sub>. Reacting as a π-propargylpalladium complex **7**, **6** undergoes nucleophilic attack by phenoxide to produce the π-allylpalladium intermedi-

- (6) For reviews of palladium-catalyzed reactions of allylic compounds: (a) Tsuji, J. *Acc. Chem. Res.* **1969**, *2*, 144. (b) Tsuji, J. *Pure Appl. Chem.* **1982**, *54*, 197. (c) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, p 799. (d) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. (e) Tsuji, J. *J. Organomet. Chem.* **1986**, *300*, 281. (f) Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140. (g) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: New York, 1990. (h) Godleski, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon: Oxford, 1991; Vol. 4, p 585. (i) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley and Sons: Chichester, 1995.
- (7) For reviews of palladium-catalyzed reactions of propargylic carbonates: (a) Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140. (b) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361. (c) Tsuji, J.; Mandai, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2589.
- (8) The results of our preliminary studies have been published: Yoshida, M.; Ihara, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 616.

**Table 2.** Reactions of Propargylic Carbonate **1a** with Phenols **2a–h**


entry	X	temp (°C)	time (h)	product	yield (%)
1	<b>2a</b> : 4-OMe	50	2	<b>3aa</b>	85
2	<b>2b</b> : 2-OMe	rt	3	<b>3ab</b>	90
3	<b>2c</b> : 4-Me	rt	5	<b>3ac</b>	87
4	<b>2d</b> : H	rt	9	<b>3ad</b>	81
5	<b>2e</b> : 1-naphthol	rt	4	<b>3ae</b>	74
6	<b>2f</b> : 4-Cl	50	2	<b>3af</b>	70
7	<b>2g</b> : 4-F	50	2	<b>3ag</b>	54
8	<b>2h</b> : 4-acetyl	50	5	<b>3ah</b>	36

ate **8**,<sup>10</sup> which re-adds CO<sub>2</sub> to afford the carbonate **9**. Subsequent cyclization of **9** gives the phenoxy-substituted cyclic carbonate **3**. Dihydrofuran **4** and epoxide **5** result from direct cyclization of  $\pi$ -allylpalladium intermediate **8**.<sup>11</sup> To the best of our knowledge, the pathway leading to cyclic carbonate **3** represents the first example of an efficient CO<sub>2</sub> elimination-fixation process as part of a decarboxylation reaction.<sup>12</sup>

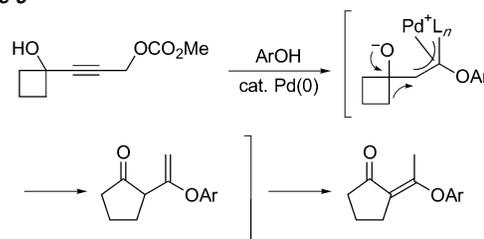
To examine the scope of this reaction, various substituted phenols were used as substrate. The corresponding cyclic carbonates **3aa–3ac** are formed in high yields when phenols bearing an electron-donating group **2a–2c** are used (Table 2, entries 1–3). Reactions of phenol (**2d**) and 1-naphthol (**2e**) also form the respective carbonates **3ad** and **3ae** in good yields (entries 4 and 5). In contrast, carbonates **3af–3ah** are produced in lower yet still acceptable yields in reactions employing electron-withdrawing-group-substituted phenols **2f–2h** (entries 6–8).

The results of reactions of propargylic carbonates, containing cycloalkanol moieties of various ring sizes, with phenol **2a** are summarized in Table 3. Reactions of substrates **1b–1d**, which possess six- to eight-membered rings, provide the corresponding cyclic carbonates **3ba–3da** in high yields (entries 2–4). When the cyclobutyl-substituted substrate **1e** is subjected to the palladium-catalyzed reaction at room temperature, cyclic carbonate **3ea** is formed in 63% yield along with the cyclopentanone **10** in 6% yield (entry 5). The byproduct **10** is likely produced by ring expansion of the four-membered ring of the  $\pi$ -allylpalladium intermediate followed by the double bond isomerization (Scheme 5).<sup>9c</sup> Interestingly, the ratio of **3ea** to **10** can be dramatically changed by altering the reaction temperature (entries 6 and 7). Accordingly, the yield of **3ea**

**Table 3.** Cascade Reactions of Propargyl Carbonate with *p*-Methoxyphenol: Part 1<sup>a</sup>

entry	substrate	temp. (°C)	product	yield (%)
1	<b>1a</b>	50	<b>3aa</b>	85
2	<b>1b</b>	rt	<b>3ba</b>	92
3	<b>1c</b>	rt	<b>3ca</b>	89
4	<b>1d</b>	rt	<b>3da</b>	80
5	<b>1e</b>	rt	<b>3ea</b>	63
			<b>10</b>	6
6	<b>1e</b>	50	<b>3ea</b>	49
			<b>10</b>	22
7	<b>1e</b>	80	<b>3ea</b>	trace
			<b>10</b>	81

<sup>a</sup> Reactions were carried out in the presence of 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub>, 20 mol % dppe, and 1.1 equiv of *p*-methoxyphenol in dioxane under an argon atmosphere in a sealed tube for 2–5 h.

**Scheme 5**

decreases to 49%, and that of **10** increases to 22% yield in the reaction at 50 °C (entry 6), while **10** is the exclusive product (81%) of the reaction conducted at 80 °C (entry 7).

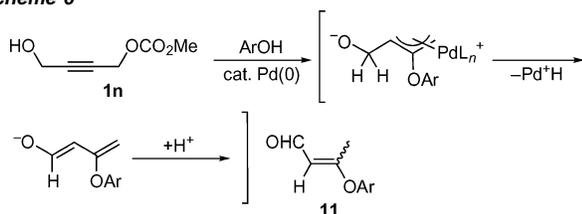
Various acyclic substrates were also subjected to the palladium-catalyzed reaction conditions described above. The substrate **1f** with dimethyl substitution undergoes reaction with phenol **2a** under an argon atmosphere to give cyclic carbonate **3fa** in 83% yield (Table 4, entry 1). Reaction of diethyl-substituted substrate **1g** also affords cyclic carbonate **3ga** (entry 3). Substrates **1h**, **1i**, and **1j**, which contain dipropyl, dipentyl, and diisopropyl groups, are transformed to the corresponding products **3ha**, **3ia**, and **3ja** in moderate yields (entries 5, 7, 9). It is clear that bulky side chain substituents, as in **1k–1m**, decrease the reactivity of the substrates, presumably a result of steric effects which decrease the rate of the CO<sub>2</sub> fixation step (entries 11, 13, 15). The yields of the cyclic carbonate forming reactions dramatically improve when the processes are conducted under a CO<sub>2</sub> atmosphere (entries 2, 4, 6, 8, 10, 12, 14, 16). Finally, the reaction of **1n**, which has no substituents at the propargylic position, does not lead to formation of a cyclic carbonate. Rather, the  $\alpha,\beta$ -unsaturated aldehyde **11** is formed as a mixture of geometric isomers in 49% yield (entry 17). In this case,  $\beta$ -elimination of palladium from the intermediate

- (9) Tsutsumi, K.; Ogoshi, S.; Nishiguchi, S.; Kurosawa, H. *J. Am. Chem. Soc.* **1998**, *120*, 1938. (b) Tsutsumi, K.; Kawase, T.; Kakiuchi, K.; Ogoshi, S.; Okada, Y.; Kurosawa, H. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2687.
- (10) For other examples of similar palladium-catalyzed reactions of propargyl carbonates with nucleophiles, see: (a) Minami, I.; Yuhara, M.; Watanabe, H.; Tsuji, J. *J. Organomet. Chem.* **1987**, *334*, 225. (b) Fournier-Ngouefack, C.; Lhoste, P.; Sinou, D. *Synlett* **1996**, 553. (c) Yoshida, M.; Nemoto, H.; Ihara, M. *Tetrahedron Lett.* **1999**, *40*, 8583. (d) Labrosse, J. R.; Lhoste, P.; Sinou, D. *Tetrahedron Lett.* **1999**, *40*, 9025. (e) Labrosse, J. R.; Lhoste, P.; Sinou, D. *Org. Lett.* **2000**, *2*, 527. (f) Kozawa, Y.; Mori, M. *Tetrahedron Lett.* **2001**, *42*, 4869. (g) Kozawa, Y.; Mori, M. *Tetrahedron Lett.* **2002**, *43*, 1499.
- (11) For examples of similar reactions that form dihydrofurans and epoxides via  $\pi$ -allylpalladium complexes, see: (a) Ma, S.; Shi, Z. *J. Org. Chem.* **1998**, *63*, 6387. (b) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **1999**, *121*, 7943.
- (12) Bäckvall et al. reported that a palladium-catalyzed reaction of an allylic carbonate in the presence of an amine leads to allylic carbamates as a byproduct. The reaction proceeds via nucleophilic attack on the  $\pi$ -allylpalladium intermediate by R<sub>2</sub>NCOO<sup>-</sup>, which is generated in situ from CO<sub>2</sub> and the amine. Bäckvall, J. E.; Granberg, K. L.; Heumann, A. *Isr. J. Chem.* **1991**, *31*, 17.

**Table 4.** Cascade Reactions of Propargylic Carbonate with *p*-Methoxyphenol: Part 2<sup>a</sup>

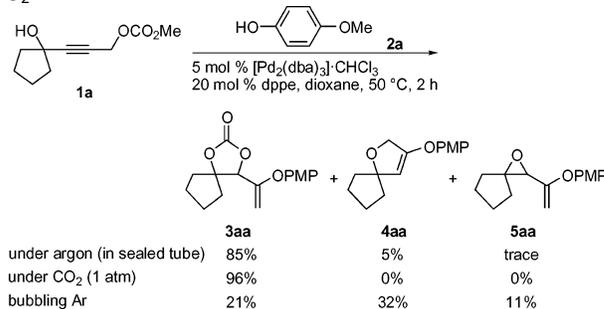
entry	substrate	atmosphere	product	yield
1		argon		83
2	<b>1f</b>	CO <sub>2</sub>	<b>3fa</b>	96
3		argon		42
4	<b>1g</b>	CO <sub>2</sub>	<b>3ga</b>	97
5		argon		69
6	<b>1h</b>	CO <sub>2</sub>	<b>3ha</b>	87
7		argon		61
8	<b>1i</b>	CO <sub>2</sub>	<b>3ia</b>	82
9		argon		61
10	<b>1j</b>	CO <sub>2</sub>	<b>3ja</b>	72
11		argon		42
12	<b>1k</b>	CO <sub>2</sub>	<b>3ka</b>	85
13		argon		16(22) <sup>b</sup>
14	<b>1l</b>	CO <sub>2</sub>	<b>3la</b>	90
15		argon		trace
16	<b>1m</b>	CO <sub>2</sub>	<b>3ma</b>	32 <sup>c</sup>
17	<b>1n</b>	CO <sub>2</sub>	<b>11</b>	49 <sup>d</sup>

<sup>a</sup> Reactions were carried out in the presence of 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub>, 20 mol % dppe, and 1.1 equiv of *p*-methoxyphenol in dioxane for 2–5 h. <sup>b</sup> The yield in parentheses is based on recovered starting material. <sup>c</sup> The reaction was carried out under 5 atm of CO<sub>2</sub>. <sup>d</sup> A mixture of two geometric isomers (*E:Z* = 4.3:1) was obtained.

**Scheme 6**

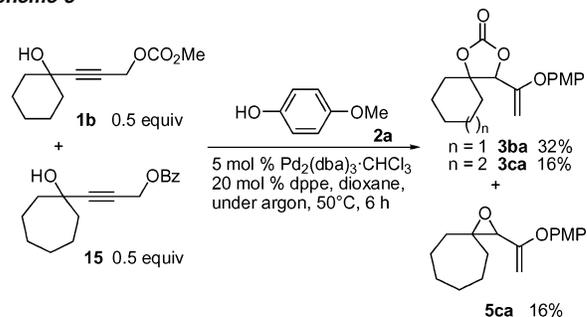
$\pi$ -allylpalladium complex occurs to give **11** prior to the CO<sub>2</sub> fixation step (Scheme 6).

**Mechanistic Studies.** As shown in Scheme 4, the mechanism proposed for cyclic carbonate formation involves sequential CO<sub>2</sub> elimination and fixation. Another pathway for this process, in which intramolecular CO<sub>2</sub>-transfer takes place via coordination to palladium, is possible. To examine whether CO<sub>2</sub> dissociates from the substrate in this reaction, we conducted the reactions in both the presence and the absence of added CO<sub>2</sub> (Scheme 7). While the reaction of **1a** and **2a** under argon atmosphere gives cyclic carbonate **3aa** in 85% yield, the process carried out under 1 atm of CO<sub>2</sub> leads to a 96% yield of **3aa**. In addition, when the reaction is run under bubbling argon to remove the

**Scheme 7.** Reactions “in the Presence” and “in the Absence” of CO<sub>2</sub>**Table 5.** Reactions of Propargylic Compounds with *p*-Methoxyphenol under a CO<sub>2</sub> Atmosphere

entry	R	time (h)	yield (%) <sup>a</sup>
1	<b>12</b> : Ms	24	53
2	<b>13</b> : Ac	30	28 (58)
3	<b>14</b> : Bz	6	82

<sup>a</sup> The yields in parentheses are based on recovered starting material.

**Scheme 8**

resulting CO<sub>2</sub>, **3aa** is formed in only 21% yield together with **4aa** (32%) and **5aa** (11%). The results suggest that the process proceeds through a pathway involving decarboxylation-followed fixation of the liberated CO<sub>2</sub>.

Reactions of propargylic compounds **12–14**, which contain non-CO<sub>2</sub> liberating leaving groups, under a CO<sub>2</sub> atmosphere were examined next. Interestingly, propargylic mesylate **12** reacts with phenol **2a**, under an atmosphere of CO<sub>2</sub> in the presence of DBU, to afford cyclic carbonate **1ga** (Table 5, entry 1). The propargylic acetate **13** and benzoate **14** are also transformed efficiently to carbonate **1ga** (entries 2 and 3). The results indicate that cyclic carbonates are formed by a route in which CO<sub>2</sub> is incorporated from an external source.

We next performed a crossover experiment with the propargylic carbonate **1b** and propargylic benzoate **15** (Scheme 8). Reaction of an equimolar mixture of **1b** and **15** with phenol **2a** in a sealed tube results in production of the cyclic carbonate **3ca** (16%), derived from **15**, along with the **1b**-derived cyclic carbonate **3ba** and the epoxide **5ca**. It is clear that **3ca** arises by reaction of in situ generated CO<sub>2</sub> formed by decarboxylation of **1b**.

**Application to the Stereoselective Formation of Cyclic Carbonates.** Palladium-catalyzed reactions of unsymmetric

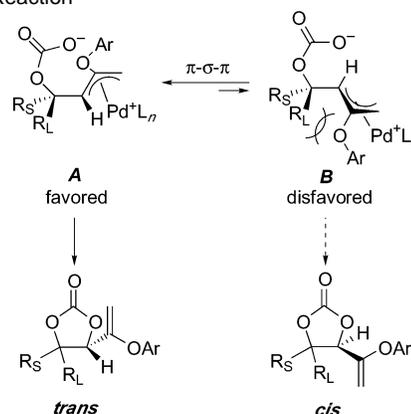
**Table 6.** Diastereoselective Reactions Using Unsymmetrical Substrates with *p*-Methoxyphenol<sup>a</sup>

entry	substrate	atmosphere	product <sup>b</sup>	yield (%) ( <i>trans</i> : <i>cis</i> )
1		argon		58
2	<b>1o</b>	CO <sub>2</sub>	<b>3oa<sup>c</sup></b>	92
3		argon		59 (18.5:1)
4	<b>1p</b>	CO <sub>2</sub>	<b>3pa<sup>d</sup></b>	93 (13.3:1)
5		argon		<b>5qa</b> 82
6	<b>1q</b>	CO <sub>2</sub>		<b>5qa</b> 47 <b>3qa</b> 42
7		argon		87
8	<b>1r</b>	CO <sub>2</sub>		<b>5ra<sup>c</sup></b> 85

<sup>a</sup> Reactions were carried out in the presence of 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub>, 20 mol % dppe, and 1.1 equiv of *p*-methoxyphenol in dioxane for 4–24 h at 50 °C in a sealed tube. <sup>b</sup> Ar = *p*-methoxyphenyl. <sup>c</sup> The stereochemistry of the *trans*-product was determined by <sup>1</sup>H–NOESY. <sup>d</sup> The stereochemistry of the products were tentatively assigned by analogy with the <sup>1</sup>H NMR spectrum of the other product.

propargylic carbonates were examined next. The substrate **1o**, having a  $\beta$ -phenylcyclohexyl group, reacts with phenol **2a** to form **3oa** as a single diastereomer in 58% yield (Table 6, entry 1). The yield of **3oa** increases to 92% when reaction of **1o** and **2a** is conducted under a CO<sub>2</sub> atmosphere (entry 2). The menthone-derived substrate **1p** is also stereoselectively converted to *trans*-carbonate **3pa** (entries 3 and 4). On the other hand, reactions of the estrone- and camphor-derived propargylic carbonates, **1q** and **1r**, afford predominantly epoxides **5qa** and **5ra** instead of the corresponding cyclic carbonates (entries 5 and 7). The cyclic carbonate **3qa** was produced together with epoxide **5qa** from reaction of **1q** under a CO<sub>2</sub> atmosphere, but no cyclic carbonate was generated from **1r** under these reaction conditions (entry 8). In these cases, it appears that steric crowding of the hydroxyl groups prevents refluxation of CO<sub>2</sub>. The high diastereoselectivities observed in these reactions are likely the result of steric factors which influence the relative energies of the competing transition states for cyclization of the interconverting, isomeric  $\pi$ -allylpalladium intermediates, **A** and **B** (Scheme 9). Equilibration between **A** and **B** occurs by  $\pi$ – $\sigma$ – $\pi$  isomerization.<sup>13</sup> It is expected that the transition state for cyclization **A**, forming the *trans*-product, would be of lower energy because of the absence of the A<sub>1,3</sub>-strain that is present in the transition state derived from **B**.

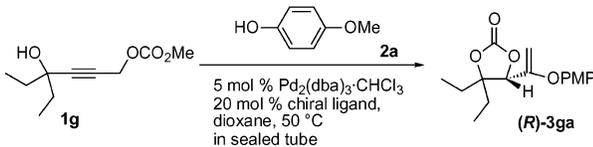
**Enantioselective Formation of Cyclic Carbonates.** Although a large number of asymmetric reactions of allylic compounds with nucleophiles are known, only a few asymmetric palladium-catalyzed nucleophilic substitution reactions of propargylic substrates have been reported.<sup>10e</sup> In the reaction described above, a new asymmetric center is formed by cyclization of the  $\pi$ -allylpalladium intermediate. We anticipated that the absolute configuration of the newly formed stereogenic center could be controlled by using chiral palladium catalysts.<sup>14</sup> Indeed, reaction of **1g** with **2a** in the presence of 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> and 20 mol % (*S*)-BINAP (**16**) in THF leads to

**Scheme 9.** Proposed Transition States for the Diastereoselective Cascade Reaction

generation of the chiral cyclic carbonate (*R*)-**3ga** in 31% yield with a 62% ee (Table 7, entry 1).<sup>15,16</sup> Superior results are obtained by employing dioxane as solvent (entry 2) and when 4 Å MS is used as an additive (entry 3). Yields are dramatically improved by carrying out the reaction under a CO<sub>2</sub> atmosphere (75% yield with 71% ee, entry 4), but the % ee decreases slightly when the reaction is run under 5 atm of CO<sub>2</sub> (entry 5). The use of (*S*)-TolBINAP (**17**)<sup>17</sup> in place of (*S*)-BINAP results in the formation of (*R*)-**3ga** in 88% yield with a 67% ee (entry 6). Reactions using other chiral phosphine ligands (e.g., **18**,<sup>18</sup> **19**,<sup>19</sup> **20**,<sup>20</sup> and **21**)<sup>21</sup> do not result in the production of the cyclic carbonate (entries 7–10).

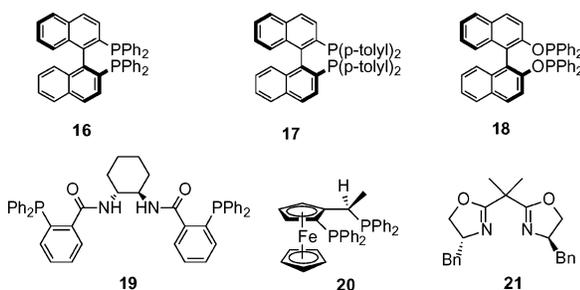
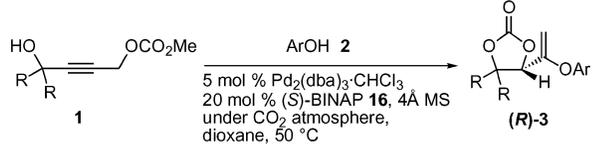
We next evaluated the scope of the (*S*)-BINAP-promoted asymmetric reaction by using various propargylic carbonates. Treatment of the five-to-eight-membered ring substrates **1a–1d** with phenol **2a** leads to production of the cyclic carbonates (*R*)-**3aa–3da** in moderate yields and enantiomeric puri-

- (13) (a) Cuvigny, T.; Julia, M.; Rolande, C. *J. Organomet. Chem.* **1985**, 285, 395. (b) Åkermark, B.; Krakenberger, B.; Hansson, S.; Vitagliano, A. *Organometallics* **1987**, 6, 620. (c) Åkermark, B.; Zetterberg, K.; Hansson, S.; Krakenberger, B.; Vitagliano, A. *J. Organomet. Chem.* **1987**, 335, 133. (d) Åkermark, B.; Hansson, S.; Vigagliano, A. *J. Am. Chem. Soc.* **1990**, 112, 4587. (e) Sjögren, M.; Hansson, S.; Norrby, P.-O.; Åkermark, B.; Cucciolito, M. E.; Vitagliano, A. *Organometallics* **1992**, 11, 3954. (f) Sjögren, M. P. T.; Hansson, S.; Åkermark, B.; Vitagliano, A. *Organometallics* **1994**, 13, 1963.
- (14) Examples about palladium-catalyzed asymmetric intramolecular cyclizations via  $\pi$ -allylpalladium species, see: (a) Yamamoto, K.; Tsuji, J. *Tetrahedron Lett.* **1982**, 23, 3089. (b) Genêt, J. P.; Grisoni, S. *Tetrahedron Lett.* **1989**, 29, 4543. (c) Takemoto, T.; Nishikimi, M.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1992**, 33, 3531. (d) Koch, G.; Pfaltz, A. *Tetrahedron: Asymmetry* **1996**, 7, 2213. (e) Trost, B. M.; Krische, M. J.; Radinov, R.; Zaroni, G. *J. Am. Chem. Soc.* **1996**, 118, 6297. (f) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, 60, 482. (g) Zenner, J. M.; Larock, R. C. *J. Org. Chem.* **1999**, 64, 7312.
- (15) (a) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, 102, 7932. (b) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, 23, 345.
- (16) For reports of enantioselective reactions via  $\pi$ -allylpalladium intermediate using BINAP, see: (a) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, 4, 1113. (b) Yamaguchi, M.; Shima, T.; Yamagishi, T.; Hida, M. *Tetrahedron Lett.* **1990**, 31, 5049. (c) Yamaguchi, M.; Shima, T.; Yamagishi, T.; Hida, M. *Tetrahedron: Asymmetry* **1991**, 2, 663. (d) Kuwano, R.; Ito, Y. *J. Am. Chem. Soc.* **1999**, 121, 3236. (e) Kuwano, R.; Nishino, R.; Ito, Y. *Org. Lett.* **1999**, 1, 837. (f) Braun, M.; Laicher, F.; Meier, T. *Angew. Chem., Int. Ed.* **2000**, 39, 3494.
- (17) (a) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Kaketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, 51, 629. (b) Larok, C.; Alper, H. *J. Am. Chem. Soc.* **1997**, 119, 3709.
- (18) Yoshizaki, H.; Satoh, H.; Sato, Y.; Nukui, S.; Shibasaki, M.; Mori, M. *J. Org. Chem.* **1995**, 60, 2016.
- (19) Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, 114, 9327.
- (20) (a) Muller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, 74, 232. (b) Lautens, M.; Fagnou, K.; Rovis, T. *J. Am. Chem. Soc.* **2000**, 122, 5650.
- (21) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, 60, 482.

**Table 7.** Enantioselective Reactions of **1g** with **2a** by Using Chiral Phosphine Ligands **16–21**<sup>a,b</sup>


entry	ligand	solvent	additive	atmosphere	yield (%)	ee (%) <sup>c</sup>
1	<b>16</b>	THF		argon	31	62
2	<b>16</b>	dioxane		argon	30	71
3	<b>16</b>	dioxane	4 Å MS	argon	34	72
4	<b>16</b>	dioxane	4 Å MS	CO <sub>2</sub>	75	71
5	<b>16</b>	dioxane	4 Å MS	CO <sub>2</sub> <sup>d</sup>	79	62
6	<b>17</b>	dioxane	4 Å MS	CO <sub>2</sub>	88	67
7	<b>18</b>	dioxane	4 Å MS	CO <sub>2</sub>	N.R.	
8	<b>19</b>	dioxane	4 Å MS	CO <sub>2</sub>	N.R.	
9	<b>20</b>	dioxane	4 Å MS	CO <sub>2</sub>	N.R.	
10	<b>21</b>	dioxane	4 Å MS	CO <sub>2</sub>	N.R.	

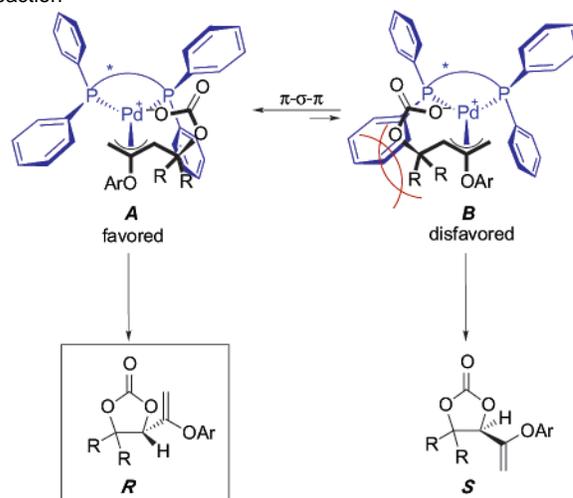
<sup>a</sup> All reactions are carried out in a sealed tube. <sup>b</sup> Absolute configurations of **3ga** were determined by using Kusumi's MTPA ester procedure. The details were described in the Supporting Information. <sup>c</sup> Enantiomeric excesses are determined by chiral HPLC (CHIRALPAK AS). <sup>d</sup> The reaction is carried out under 5 atm of CO<sub>2</sub>.

**Table 8.** Enantioselective Reactions of Various Propargylic Carbonates<sup>a,b</sup>


entry	substrate	ArOH	product	yield (%)	ee (%) <sup>c</sup>
1	<b>1a</b> : R + R = (CH <sub>2</sub> ) <sub>4</sub>	<b>2a</b>	<b>3aa</b> <sup>d</sup>	81	23
2	<b>1b</b> : R + R = (CH <sub>2</sub> ) <sub>5</sub>	<b>2a</b>	<b>3ba</b> <sup>d</sup>	84	39
3	<b>1c</b> : R + R = (CH <sub>2</sub> ) <sub>6</sub>	<b>2a</b>	<b>3ca</b> <sup>d</sup>	74	30
4	<b>1d</b> : R + R = (CH <sub>2</sub> ) <sub>7</sub>	<b>2a</b>	<b>3da</b> <sup>d</sup>	48	53
5	<b>1f</b> : R = Me	<b>2a</b>	<b>3fa</b> <sup>d</sup>	94	40
6	<b>1j</b> : R = <sup>i</sup> Pr	<b>2a</b>	<b>3ja</b> <sup>d</sup>	79	63
7	<b>1h</b> : R = Pr	<b>2a</b>	<b>3ha</b> <sup>d</sup>	83	66
8	<b>1i</b> : R = Pen	<b>2a</b>	<b>3ia</b> <sup>d</sup>	66	71
9	<b>1k</b> : R = β-phenethyl	<b>2a</b>	<b>3ka</b> <sup>d</sup>	79	78
10	<b>1l</b> : R = β-cyclohexylethyl	<b>2a</b>	<b>3la</b> <sup>d</sup>	80	85
11 <sup>e</sup>	<b>1l</b>	<b>2a</b>	<b>3la</b> <sup>d</sup>	55	89
12	<b>1l</b>	<b>2b</b>	<b>3lb</b> <sup>f</sup>	83	91
13	<b>1l</b>	<b>2e</b>	<b>3le</b> <sup>g</sup>	68	93

<sup>a</sup> All reactions are carried out in a sealed tube. <sup>b</sup> The absolute configurations of the products were tentatively assigned by analogy with the optical rotatory power of (*R*)-**3ga**. <sup>c</sup> Enantiomeric excesses are determined by chiral HPLC (CHIRALPAK AS or AD or OD-H). <sup>d</sup> Ar = *p*-methoxyphenyl. <sup>e</sup> Reactions are carried out by using 5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub>, 10 mol % (*S*)-BINAP (Pd:L\* = 1:1). <sup>f</sup> Ar = 2-methoxyphenyl. <sup>g</sup> Ar = 1-naphthyl.

ties (Table 8, entries 1–4). Reactions of the acyclic substrates **1f**, **1h–1l** were also investigated (entries 5–10). Reaction of the dimethyl-substituted propargylic carbonate **1f** with **2a** affords

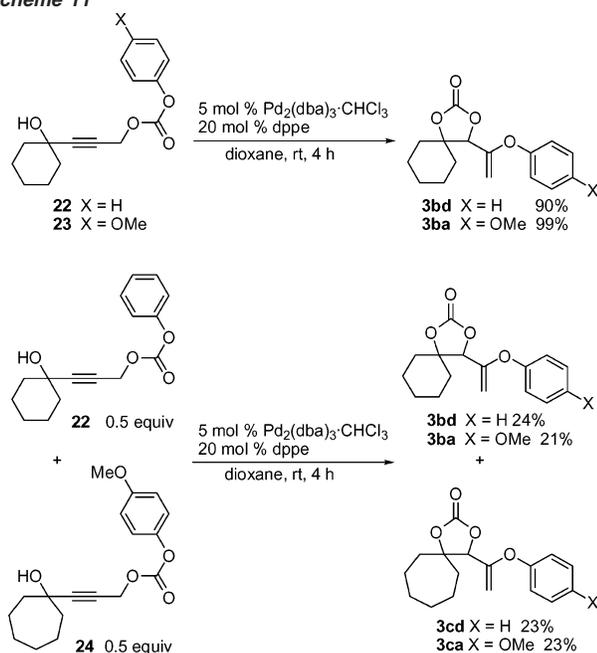
**Scheme 10.** Proposed Transition States for the Enantioselective Reaction

the cyclic carbonate **3fa** in 94% yield and 40% ee (entry 5). These results show that reactions of the longer chain substrates give cyclic carbonates in higher enantiomeric purities (>63% ee) (entries 6–10). Thus, bulky substituents at the β-position of the alkyl side chain result in increased enantioselectivities. The best results are observed for the reaction of the bis-β-cyclohexylethyl derivative **1l**, which yields **3la** in 85% ee (entry 10). The enantiomeric purity of **3la** rises to 89% ee when the mole ratio of palladium catalyst (5 mol %) and (*S*)-BINAP is changed to 1:2, even though the yield of the process decreases to 55% (entry 11). Furthermore, reactions of **1l** with 2-methoxyphenol **2b** and 1-naphthol **2e** give the corresponding products **3lb** and **3le** with high % ee, the highest (93% ee) being observed in the reaction of **2e** (entry 13).

A proposed rationale for the absolute configurational outcome of the process is based on a consideration of transition state models. Absolute stereochemistry in this process is determined in the step involving cyclization of the π-allylpalladium intermediate, for which there are two possible transition states **A** and **B**, depicted in Scheme 10. Inspection of the models shows that severe steric repulsion exists between the R-substituent of the substrate and a benzene ring of the BINAP ligand in transition state **B**. Therefore, reaction should take place preferentially via the more stable transition state **A** to provide the (*R*)-product.

**A Three-Component Decomposition-Reconstruction Reaction.** 4-Aryloxy-carbonyloxy-2-butyn-1-ols, **22** and **23**, contain latent nucleophilic phenolic moieties as part of the carbonate leaving groups (Scheme 11). As a result, sequential palladium-induced elimination of the carbonate group in these substrates followed by decarboxylation should produce phenoxide nucleophiles, capable of adding to the intermediate palladium complex. Interestingly, reactions of **22** and **23** with the palladium catalyst afford the corresponding cyclic carbonates **3bd** and **3ba** in high yields (**3ba** nearly quantitative). In this process, the substrate decomposes to yield three components, allenylpalladium, phenoxide, and CO<sub>2</sub>, which then recombine to form cyclic carbonate. Crossover experiments were conducted to confirm that the pathway proposed for this three-component decomposition-reconstruction process is actually followed. Treatment of an equimolar mixture of the propargylic carbonates **22** and **24** with the palladium catalyst leads to formation of a mixture containing

Scheme 11



equal amounts of the four cyclic carbonates **3bd**, **3ba**, **3cd**, and **3ca**. This result demonstrates that the phenoxide ion completely dissociates from the propargylic moiety in this process.

## Conclusion

The studies described above have resulted in the development of a novel CO<sub>2</sub>-recycling process involving a palladium-catalyzed cascade reaction between 4-methoxycarbonyloxy-2-butyne-1-ols and phenols. The cyclic carbonates, formed in this manner, can be viewed as equivalents of  $\alpha,\beta$ -dihydroxyketones, and, as a result, this process should serve as a useful synthetic methodology. *trans*-Cyclic carbonates are generated with a high degree of stereochemical control in reactions of unsymmetric substrates. By using the chiral phosphine BINAP, we found that asymmetric reactions occur to produce chiral products with high enantioselectivities. Finally, a three-component decomposition-reconstruction reaction of phenoxy-substituted propargylic carbonates has been developed. This process efficiently transforms substrates into structurally isomeric products without the concomitant formation of byproducts. Beyond its mechanistic and synthetic interest, this CO<sub>2</sub>-recycling reaction should gain the attention of scientists searching for new eco-friendly chemical transformations.

## Experimental Section

**General Procedure for the Palladium-Catalyzed Cascade Reaction of 4-Methoxycarbonyloxy-2-butyne-1-ol with Phenols. Reaction of **1a** with **2a**.** To a stirred solution of the propargylic carbonate **1a** (45.2 mg, 0.228 mmol) in dioxane (4 mL) were added *p*-methoxyphenol (31.1 mg, 0.251 mmol), Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (11.8 mg, 0.0114 mmol), and dppe (18.2 mg, 0.0456 mmol) in a sealed tube at room temperature. After stirring was continued for 2 h at 50 °C, the reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (90:10 v/v) as eluent to give the cyclic carbonate **3aa** (56.3 mg, 85%), dihydrofuran **4aa** (2.8 mg, 5%), and a trace amount of epoxide **5aa** as a colorless oil.

**General Procedure for the Palladium-Catalyzed Reaction of Propargylic Compounds with *p*-Methoxyphenol under CO<sub>2</sub> Atmo-**

**sphere.** To a stirred solution of the propargylic benzoate **14** (52.0 mg, 0.210 mmol) in dioxane (3 mL) were added *p*-methoxyphenol **2a** (29.0 mg, 0.230 mmol), Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (11.0 mg, 0.011 mmol), dppe (17.0 mg, 0.042 mmol), and DBU (47.0  $\mu$ L, 0.320 mmol) at room temperature. After stirring was continued under CO<sub>2</sub> atmosphere for 6 h at 50 °C, the reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (92:8 v/v) as eluent to give the cyclic carbonate **1ga** (50.6 mg, 82%) as a colorless oil.

**Crossover Experiment of **1b** and **15**.** To a stirred solution of the propargylic carbonate **1b** (50.0 mg, 0.236 mmol) and propargylic benzoate **15** (64.0 mg, 0.236 mmol) in dioxane (4 mL) were added *p*-methoxyphenol **2a** (64.0 mg, 0.519 mmol), Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (24.0 mg, 0.0236 mmol), dppe (38.0 mg, 0.0944 mmol), and DBU (53.0  $\mu$ L, 0.354 mmol) in a sealed tube at room temperature. After stirring was continued for 6 h at 50 °C, the reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (92:8 v/v) as eluent to give the cyclic carbonate **3ba** (24.0 mg, 32%), **3ca** (45.0 mg, 16%), and epoxide **5ca** (21.0 mg, 16%) as a colorless oil.

**General Procedure for the Diastereoselective Palladium-Catalyzed Reaction.** To a stirred solution of the propargylic carbonate **1o** (30.8 mg, 0.107 mmol) in dioxane (2 mL) were added *p*-methoxyphenol **2a** (14.6 mg, 0.118 mmol), Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (5.5 mg, 5.3  $\mu$ mol), and dppe (8.5 mg, 0.0214 mmol) in a sealed tube under 1 atm of CO<sub>2</sub> at room temperature. After stirring was continued for 16 h at 50 °C, the reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (92:8 v/v) as eluent to give the cyclic carbonate **3oa** (37.5 mg, 92%) as colorless prisms.

**General Procedure for the Enantioselective Palladium-Catalyzed Reaction.** To a stirred solution of Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (10.4 mg, 10.0  $\mu$ mol) in dioxane (1.4 mL) was added (*S*)-BINAP **16** (24.9 mg, 40.0  $\mu$ mol) in a sealed tube at room temperature. After stirring was continued for 30 min at 50 °C, a solution of the propargylic carbonate **1g** (40.0 mg, 0.20 mmol), *p*-methoxyphenol (27.3 mg, 0.22 mmol) in dioxane (1.3 mL), and 4 Å MS (80 mg, activated powder) was added to this reaction mixture, and the mixture was stirred for 3.5 h at 50 °C under 1 atm of CO<sub>2</sub>. The reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (92:8 v/v) as eluent to give the cyclic carbonate (*R*)-**3ga** (43.2 mg, 75%, 71% ee) as a colorless oil.

**General Procedure for the Palladium-Catalyzed Reaction of 4-Aryloxy-carbonyloxy-2-butyne-1-ol: The Reaction of **23**.** To a stirred solution of the propargylic carbonate **23** (42.1 mg, 0.138 mmol) in dioxane (3 mL) were added Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (7.1 mg, 6.9  $\mu$ mol) and dppe (10.9 mg, 0.0274 mmol) in a sealed tube at room temperature. After stirring was continued for 2 h at the same temperature, the reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (90:10 v/v) as eluent to give the cyclic carbonate **3ba** (41.8 mg, 99%) as colorless needles.

**Crossover Reaction of **22** and **24** (Scheme 11).** To a stirred solution of the propargylic carbonate **22** (20.4 mg, 0.074 mmol) and **24** (23.5 mg, 0.074 mmol) in dioxane (2 mL) in a sealed tube were added Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (7.2 mg, 0.007 mmol) and dppe (11.1 mg, 0.0278 mmol) at room temperature. After stirring was continued for 4 h at room temperature, the reaction mixture was concentrated, and the residue was chromatographed on silica gel with hexane–AcOEt (92:8 v/v) as eluent to give the cyclic carbonates **3bd** (9.7 mg, 24%), **3ba** (9.5 mg, 21%), **3cd** (9.8 mg, 23%), and **3ca** (10.8 mg, 23%) as a colorless oil.

**Acknowledgment.** This work was supported in part by the Research Fellowships of the Japan Society for the Promotion of Science (JSPS) for Young Scientists (M.Y.) and Scientific

Research on Priority Areas (A) "Exploitation of Multi Element Cyclic Molecules" from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

**Supporting Information Available:** Characterization data of all new compounds, synthetic procedures of substrates **1a–1r**,

**12–15**, and **22–24**. NOESY correlations of **3oa** and **5ra**. Procedure and characterization data for the determination of the absolute configuration of **3ga** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA0340681