Stereoselective Synthesis of α-(Chloromethylene)-γ-butyrolactone Derivatives from Acyclic Allylic 2-Alkynoates

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α-Methylene-γ-butyrolactones have been constructed by a bis(benzonitrile)palladium dichloride catalyzed cyclization reaction of the easily available acyclic 2′-alkenyl 2-alkynoates in the presence of $CuCl_2$. A mechanism involving a stereoselective chloropalladation in the presence of $CuCl_2$, followed by intramolecular insertion of a carbon–carbon double bond to the carbon–palladium bond, and subsequent $CuCl_2$-mediated formation of a new carbon–chlorine bond is briefly discussed.

Introduction

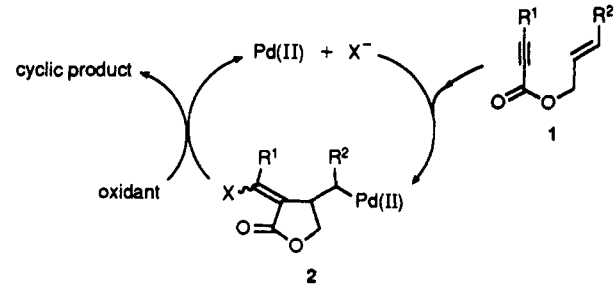
Natural products containing α-methylene-γ-butyrolactones show some important biological activities, such as cytotoxicity, antitumority, etc.; however, none are used clinically at present because of their high toxicity.[1] Thus, new methods for the synthesis of compounds containing α-methylene-γ-butyrolactone rings for screening are needed. Recently we have developed a new methodology for stereoselective synthesis of α-(*Z*)-(halomethylene)-γ-butyrolactone derivatives by divalent palladium-catalyzed cyclization of acyclic haloallylic 2-alkynoates.[2] In this reaction, the γ-butyrolactone ring is constructed by carbon–carbon bond formation, which is quite different from the other methodologies reported.[1,3] In order to regenerate the catalytic divalent palladium species by dehalopalladation, a halomethyl group is necessary in the starting material.[2] On the other hand, if the newly formed palladium intermediate **2** was terminated by another pathway which generates a zero valent palladium species, and an oxidant was used to oxidize Pd(0) to Pd(II), α-methylene-γ-butyrolactone derivatives might be synthesized from very easily available acyclic precursors, 2′-alkenyl 2-alkynoates (Scheme I).

In this paper, we wish to report our recent results on the Pd(II)-catalyzed cyclization of 2′-alkenyl 2-alkynoates in the presence of cupric chloride.

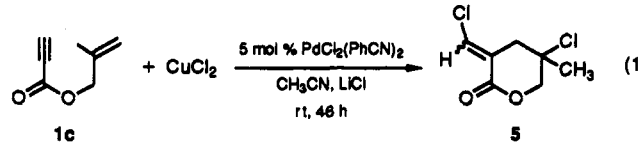
Results and Discussion

Cyclization of 2′-Alkenyl 2-Propynoates. We chose $CuCl_2$ as the oxidant to meet the requirement shown in Scheme I. While the solubility of $CuCl_2$ in most organic solvents such as THF, 1,4-dioxane, CH_3NO_2, DMF, HOAc, etc. is small, CH_3OH and CH_3CN can dissolve $CuCl_2$ by addition of LiCl. Thus, we first tried the reaction of a mixture of 3′-phenyl-2′(*E*)-propenyl 2-propynoate (**1a**), $PdCl_2(PhCN)_2$ (5 mol %), $CuCl_2$ (2.5 equiv), and LiCl (2 equiv) in CH_3CN (0.2 M) at rt. Unexpectedly, the reaction afforded two products: 3′-phenyl-2′(*E*)-propenyl 2,3-dichloro-2(*E*)-propenoate (**3a**) and α-(*E*)-(chloromethylene)-β-(1′-chlorobenzyl)-γ-butyrolactone (**4a**) in 12% and 35% yield, respectively. When the amount of $CuCl_2$ increases, the yield of **4a** increases and that of **3a** decreases. The stereochemistry of **3a** was determined by comparing the chemical shift of its vinylic proton β to the carbonyl group with its known analogous compound methyl 2,3-dichloro-2(*E*)-propenoate.[4] The configuration of the exocyclic double bond of **4a** was determined by comparing the chemical shifts of olefinic hydrogen; i.e., there is a low-field chemical shift for the *E* isomer.[2,5] The results are shown in Table I. The stereochemistry of the exo C=C bond is opposite to that reported in ref 2. Only one diastereoisomer of **4a** was detected by 200-MHz ^1H NMR spectroscopy.

Scheme I



Under similar conditions, 2′-methyl-2′-propenyl 2-propynoate (**1c**) afforded a six-membered ring, γ-chloro-γ-methyl-α-(chloromethylene)-δ-pentyrolactone (**5**) in 32% yield (eq 1). The six-membered ring structure was determined by the chemical shift of CH_2 group β to the carbonyl group. The five-membered γ-butyrolactone derivative was not detected, a result similar to that reported by Saegusa et al.[6]



(1)

(1) Hoffmann, H. M. R.; Rube, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
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(3) Grieco, P. A. *Synthesis* **1975**, 67. Petragnani, N.; Ferraz, H. M. C.; Silva, G. V. J. *Synthesis* **1986**, 157. Larock, R. C.; Harrison, L. W.; Hsu, M. H. *J. Org. Chem.* **1984**, *49*, 3662.
(4) Kobrich, G.; Flory, K. *Chem. Ber.* **1966**, *99*, 1773.
(5) Minami, T.; Niki, I.; Agawa, T. *J. Org. Chem.* **1974**, *39*, 3236. Tanaka, K.; Tamura, N.; Kaji, A. *Chem. Lett.* **1980**, 595.
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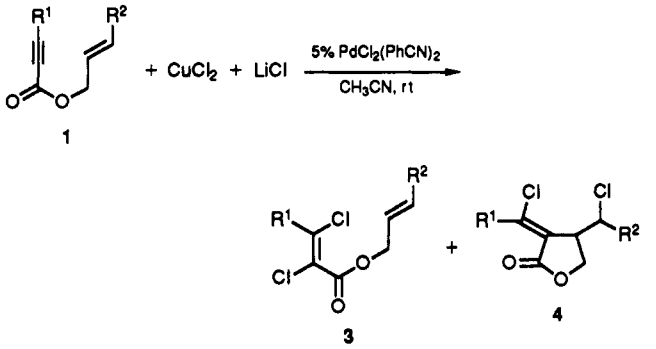
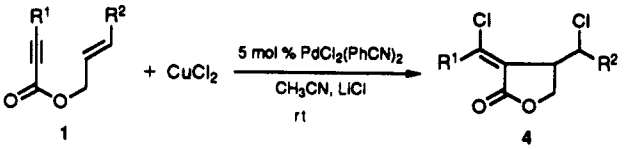
Table I. Divalent Palladium-Catalyzed $CuCl_2$-Mediated Cyclization of 2'-Alkenyl 2-Propynoates[a]



	1				yield (%)	
entry	R^1	R^2	$CuCl_2$ (equiv)	time (h)	3	4 (E/Z)[b]
1	H	Ph (1a)	2.5	42	12 (3a)	35 (88/12) (4a)
2		(1a)	5	48	4 (3a)	56 (91/9) (4a)
3		(1a)	10	48	4 (3a)	39 (91/9) (4a)
4		(1a)	5[c]	72	4 (3a)	53 (89/11) (4a)
5	H	H (1b)	2.5	48	17 (3b)	41 (100/0) (4b)
6	H	H (1b)	2.5[d]	70		30 (100/0) (4b)
7	H	H (1b)	5	61	5.5 (3b)	58 (100/0) (4b)

[a] 2 equiv of LiCl was used in all reactions. [b] The ratio of E/Z was determined by ^1H NMR spectra. [c] $CuCl_2 \cdot 2H_2O$ was used instead of anhyd $CuCl_2$. [d] CH_3OH was used as the solvent.

Table II. Cyclization of 2-Alkenyl 2-Alkynoates[a]



	1				
entry	R^1	R^2	LiCl added (equiv)	time (h)	4 yield (%) (E/Z)[b]
1	CH_3	H (1d)	2	72	94 (21.5/78.5) (4d)
2		(1d)	6	72	85 (5/95) (4d)
3	CH_3	Ph (1e)	2	43	52 (1.5/98.5) (4e)
4		(1e)	6	43	55 (0/100)[c] (4e)
5	CH_3	Ph (1e')[d]	6	43	50 (0/100) (4e')[e]
6	*n*-Bu	H (1f)	2	45	74 (31/69) (4f)
7		(1f)	6	52	81 (2.5/97.5) (4f)
8	*n*-Bu	Ph (1g)	2	46	67 (30/70)[f] (4g)
9		(1g)	6	46	69 (9.5/90.5)[g] (4g)

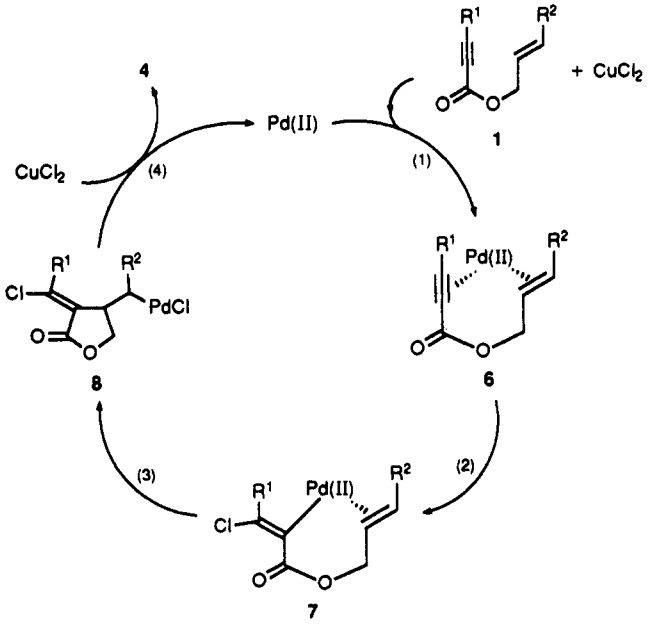
[a] 5 equiv of $CuCl_2$ was used in all the reactions. [b] The ratio of Z/E was determined by isolation. [c] 6.5% of 3-phenyl-2-propenyl chloride was isolated. [d] Z-isomer was used. [e] 7% of 4e was also isolated. [f] 8.3% of 3-phenyl-2-propenyl chloride was isolated. [g] 3.3% of 3-phenyl-2-propenyl chloride was isolated.

Cyclization of 2'-Alkenyl-Substituted 2-Alkynoates. It is quite unexpected that in the cases of substituted 2-alkynoates no chlorination products of carbon–carbon triple bond **3** were formed, and the higher preference toward the Z forms of **4** was observed. Also noteworthy are the different stereoselectivities of the cyclizations of substituted and unsubstituted 2-propynoates. The Z and E isomers can be separated by TLC, and the configuration of the exocyclic C=C bond was determined by comparing the chemical shifts of methylene protons adjacent to the C=C bond.[2,5] Increasing the amount of LiCl improved the Z stereoselectivity. Such a similar observation has also been found in the Pd(II)-catalyzed cyclization of 4'-halo-2'-alkenyl 2-alkynoates.[2] The results are shown in Table II. In Table II, it is worth noting that (i) only one diastereoisomer for **4e** and **4g** was detected by 200-MHz ^1H NMR spectra (Table II, entries 3, 4, 8, and 9) and (ii) 3-phenyl-2(E)-propenyl chloride was isolated in some cases (Table II, entries 4, 8, and 9).

Mechanism. Reaction of unsubstituted 2-alkynoate **1a**, LiCl (2 equiv), and $CuCl_2$ (5 equiv) in CH_3CN (0.2 M) in the absence of Pd(II) at rt for 6 days afforded **3a** in 60% yield as the sole product, while substituted 2-alkynoate **1d** reacted with $CuCl_2$ very slowly (10 days, <10%). Direct reaction of methyl 2-propynoate with $CuCl_2$ in CH_3CN at 50 °C for 24 h gave methyl 2,3-dichloro-2(E)-propenoate[4] in 84% yield. These results indicate that (1) the chlorination products **3a** and **3b** are formed by direct reaction of **1a** and **1b** with $CuCl_2$, respectively,[7] (2) the reactivities of unsubstituted and substituted carbon–carbon triple bonds toward $CuCl_2$ are quite different, and (3) the palladium species plays an important role in the formation of **4**. Weber et al.[8] have studied the reaction of the β-styryl palladium chloride, methyl acrylate, and $CuCl_2$ in CH_3OH, which afforded 1-phenyl-4-carbomethoxy-1,3-butadiene, an intermolecular insertion-β-H elimination product, indicating that a new intermediate with a C–Pd bond was formed. But the reaction of β-styryl palladium

(7) Castro, C. E.; Gaughan, E. J.; Owsley, D. C. *J. Org. Chem.* **1965**, *30*, 587.
(8) Weber, W. P.; Felix, R. A.; Willard, A. K.; Koenig, K. E. *Tetrahedron Lett.* **1971**, 4701.

Scheme II



chloride, ethylene, and $CuCl_2$ afforded 1-phenyl-4-chlorobut-1-ene, an intermolecular insertion C–Cl bond formation product. Thus, whether the β-H elimination can occur or not depends on the structure of the substrates. In the latter case, the reaction regenerates $PdCl_2$ before β-H elimination can occur. Thus, the mechanism of the present reaction might be similar to that of Pd(II)-catalyzed cyclization of 4′-halo-2′-alkenyl 2-alkynoates;[2] i.e., compound 1 first coordinates with Pd and/or Cu to form a metal–enyne complex 6,[9] and subsequent stereoselective chloropalladation in the presence of $CuCl_2$ (cis addition for R^1 = H, trans addition for R^1 = alkyl or aryl) affords the intermediate 7, followed by intramolecular insertion of the C=C bond into the C–Pd bond to afford 8, which through formation of a C–Cl bond[10] affords product 4 and the Pd(II) species (Scheme II).

From Tables I and II, it can be seen that cyclization of unsubstituted 2-propynoates shows *E*-stereoselectivity, which is different from our previous report,[2] while cyclization of substituted 2-alkynoates shows *Z* stereoselectivity.

In order to study further the effect of Pd(II) in this reaction, the following reaction was carried out with an equimolar amount of Pd(II). A mixture of unsubstituted 2-alkynoate **1a** (0.25 mmol), LiCl (0.5 mmol), $PdCl_2(PhCN)_2$ (0.25 mmol), and $CuCl_2$ (0.35 mmol) in CH_3CN (5 mL) at rt afforded **4a** in 24% yield with an *E*/*Z* ratio of 46/54. When substituted 2-alkynoate **1d** was used, (*Z*)-**4d** was isolated with high stereoselectivity in 24% yield. Comparing these observations with that of Tables I and II, one can see that increasing the amount of $PdCl_2(PhCN)_2$ tends to favor trans chloropalladation, which is in accordance with the previous report.[2] The different stereochemical results of unsubstituted 2-propynoates and substituted 2-alkynoates might be due to the different reaction behavior of the unsubstituted and substituted carbon–carbon triple bond to $CuCl_2$ or $CuCl_2$–$PdCl_2$ complexes; i.e., $CuCl_2$ might participate in the chloropalladation step.

The mechanism of oxidative cleavage of a C–Pd bond by $CuCl_2$ has been extensively studied, but is still unclear.[11] A radical mechanism has been postulated by Kochi et al.[12] We have used *tert*-butyl nitroxide to try to capture the possible radical intermediate. No radical signal was detected by an ESR study except the signal of $CuCl_2$.[13] Also, it is well-known that (1) only Pd(0), but not Pd(II), can initiate a radical reaction;[14] (2) the reactions of allylic compounds (halides, carbamates, acetates, etc.) with a Pd(0) complex proceed through a π-allyl palladium intermediate, rather than a radical intermediate.[14] In the present reaction, not only was a Pd(II) complex used as the catalyst but also the substrates used are allyl 2-alkynoates; thus, a radical mechanism seems unlikely.

Through the study of stereochemistry of the oxidative cleavage of a C–Pd bond by $CuCl_2$, Bäckvall et al. also concluded that the results are inconsistent with a radical mechanism but are consistent with the idea that oxidative cleavage occurs with predominate inversion in the presence of excess of free nucleophiles.[15] In our case, reaction of **1a** and LiCl (2 equiv) with an equimolar amount of $PdCl_2(PhCN)_2$ in CH_3CN was carried out at rt for 24 h at first, followed by addition of anhyd $CuCl_2$ (5 equiv), but it did not afford any lactone products, although **1a** disappeared. This implies that the formation of the C–Cl bond in step (4) (Scheme II) must be mediated by $CuCl_2$ together with palladium.[10] Using a low concentration of $CuCl_2$ or without the use of $CuCl_2$, the catalytic reaction did not occur.

As to the stereochemistry of step 4, we chose 3′-phenyl-2′(*Z*)-(or 2′(*E*))-propenyl 2-butynoate (*E* isomer, **1e**; *Z* isomer, **1e′**) as model compounds. Under the same conditions as described in Table II, **1e** and **1e′** afforded different products **4e** and **4e′**, respectively. These results are quite different from those expected if a radical cyclization reaction were involved.[16] Compounds **4e** and **4e′** showed not only the same MS molecular ion but also the same analytical data, indicating that **4e** and **4e′** might be a pair of diastereoisomers of the γ-butyrolactone products. Their ^1H NMR spectral data ($CDCl_3$, 600 MHz) are shown in Table III.

The stereochemistry of the insertion of a C=C bond into a C–Pd bond was believed to be cis;[17] thus, the relative configuration of intermediates **8e** and **8e′** are as shown in eqs 2 and 3. Unfortunately, the configurations of **4e** and **4e′** could not be exactly assigned from their ^1H NMR and ^1H 2D NOESY spectra. From Bäckvall's results,[15] the oxidative cleavage of the C–Pd bond by $CuCl_2$ occurs with inversion in the presence of excess chloride ion. So the configuration of **4e** and **4e′** might be tentatively assigned as shown in eqs 2 and 3. This might be the reason that

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(11) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds, Mechanistic Principles and Synthetic Methodology Including Biochemical Processes*; Academic Press: New York, 1981; Chapter 7.

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(13) We have used 1,4-dinitrobenzene (SET transfer inhibitor) and 1,4-dihydroxybenzene (chain-transfer inhibitor) to study the mechanism, but both these two compounds could react with $CuCl_2$ alone.

(14) Curran, D. P.; Chang, C.-T. *Tetrahedron Lett.* **1990**, *31*, 933.

(15) Bäckvall, J.-E.; Akermark, B.; Ljunggren, S. O. *J. Chem. Soc., Chem. Commun.* **1977**, 264. Bäckvall, J.-E. *Tetrahedron Lett.* **1977**, 467.

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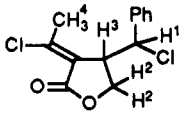
(17) Heck, R. F. *Pure Appl. Chem.* **1978**, *50*, 691. Antonsson, T.; Moberg, C.; Tottie, L.; Henmann, A. *J. Org. Chem.* **1989**, *54*, 4914.

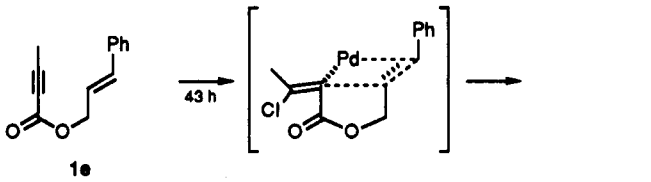
Table III. ^{1}H NMR (600 MHz, $CDCl_3$) Spectral Data of 4e and 4e′



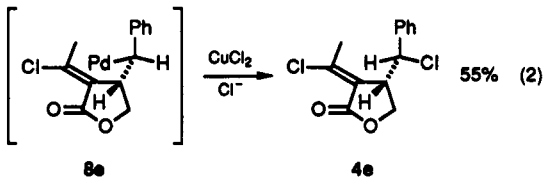
4e or 4e′

	H^{Ph}	H^1	H^2	H^3	H^4
4e	7.450–7.200 (m, 5 H)	4.994 (d, J = 7.10 Hz, 1 H)	4.226 (d, J = 9.70 Hz, 1 H), 4.146 (dd, J_1 = 7.10 Hz, J_2 = 9.70 Hz, 1 H)	3.749 (t, J = 7.10 Hz, 1 H)	2.314 (s, 3 H)
4e′	7.420–7.320 (m, 5 H)	4.875 (d, J = 8.76 Hz, 1 H)	4.675 (d, J = 9.54 Hz, 1 H), 4.253 (dd, J_1 = 6.12 Hz, J_2 = 9.54 Hz, 1 H)	3.560 (dd, J_1 = 6.12 Hz, J_2 = 8.76 Hz, 1 H)	1.600 (s, 3 H)

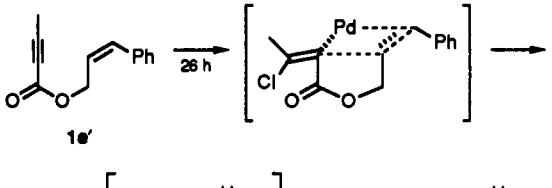
compounds **4a**, **4e**, and **4g** were obtained as a single diastereomer.



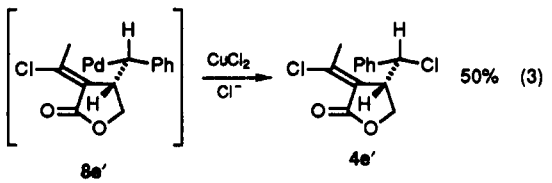
1e



8e 4e



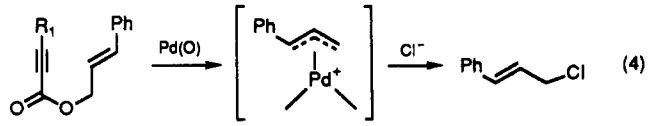
1e′



8e′ 4e′

Under the same conditions, 3-phenyl-2(*Z*)-propenol isomerized to its *E* isomer completely within 24 h. Thus, the 7% yield of **4e** formed from cyclization of **1e′** might be the cyclization product of **1e** which was in situ generated by isomerization of a *Z* C=C bond to a *E* C=C bond, i.e., **1e′** to **1e**.

It is possible that a Pd(0) species, which is further oxidized to the reactive catalytic species Pd(II) by $CuCl_2$, might be involved. Cleavage of the allylic carbon–oxygen bond of **1** by Pd(0) forms a π-allyl palladium complex,[18] which was supported by the isolation of 3-phenyl-2-propenyl chloride in entries 4, 8, and 9 in Table II as shown in eq 4.[19]



(4)

Further experiments showed that **3a** remained unchanged when it was treated with $Pd_2(dba)_3$·$CHCl_3$ (30 mol %) in CH_3CN at rt, implying that the minor *Z* isomer of **4a** might not be formed by the in-situ generated Pd(0)-catalyzed cyclization of **3a**.

In conclusion, the present methodology provides an efficient route for the synthesis of α-methylene-γ-butyrolactone derivatives via a palladium(II)-catalyzed carbon–carbon coupling reaction of acyclic 2′-alkenyl 2-alkynoates with the simultaneous formation of two C–Cl bonds. Due to its simplicity, good stereoselectivity, and good yields in certain cases, the present reaction will show its utility in organic synthesis.

Experimental Section

Materials. $PdCl_2(PhCN)_2$,[20] $Pd_2(dba)_3$ $CHCl_3$,[21] 2-butynoic acid,[22] 2-propynoic acid,[23] and allyl 2-propynoate[24] were prepared as reported. 3-Phenyl-2(*E*)-propenyl bromide was prepared from the reaction of 3-phenyl-2(*E*)-propenol with PBr_3 in ether.[25] The analytical samples were further purified by Kugelrohr distillation with the oven temperature (ot) given.

Synthesis of 3′-Phenyl-2′(*E*)-propenyl and 2′-Methyl-2′-propenyl 2-Propynoate. Typical Procedure: 3′-Phenyl-2′-(*E*)-propenyl 2-Propynoate (1a). To a solution of 2-propynoic acid (2.0 g, 28.6 mmol) and 3-phenyl-2(*E*)-propenol (3.83 g, 28.6 mmol) in ether (8 mL) was added at −20 °C dropwise a solution of DCC (6.0 g, 29.1 mmol) and DMAP (118 mg, 0.96 mmol) in ether (35 mL) with stirring. Then the reaction was stirred at 20 °C for 22 h. After the reaction was complete, the white solid was filtered off and the solvent was removed, and then the crude product was submitted to chromatography on silica gel using petroleum ether/ethyl acetate (10:1) as the eluent to afford **1a**:[26] yield 4.2 g (80%); ot 158–160 °C (3 mmHg); IR (neat) 2200, 1720, 1660, 1220 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.50–7.20 (m, 5 H, Ph), 6.70 (d, J = 16.0 Hz, 1 H, PhCH=), 6.28 (dt, J_1 = 16.0 Hz, J_2 = 7.6 Hz, 1 H, CH=), 4.85 (d, J = 7.6 Hz, 2 H, OCH_2), 2.90 (d, J = 1.3 Hz, 1 H, H-C≡); MS *m/e* 187 (M^+ + 1, 1.19), 186 (M^+, 8.58), 117 ($M^+ - C_2HCO_2$, 100.00).

2′-Methyl-2′-propenyl 2-Propynoate (1c). Obtained by distillation: yield 2.47 g (47%); bp 70–72 °C (35 mmHg); IR (neat) 2200, 1720, 1660, 1220 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ 5.00 (s, 2 H, $=CH_2$), 4.55 (s, 2 H, OCH_2), 2.77 (s, 1 H, C≡CH), 1.77 (s, 3 H, CH_3); MS *m/e* 125 (M^+ + 1, 9.48), 124 (M^+, 6.00), 72 ($M^+ + 1 - C_2HCO$, 100.00).

Synthesis of Allyl 2-Butynoate (1d). 1d was prepared as allyl 2-propynoate:[24] yield 2.62 g (74%); bp 98–100 °C/45 mmHg;

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IR (neat) 2300, 1720, 1650, 1250 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ 6.30–4.90 (m, 3 H, CH=CH_2), 4.55 (d, J = 4.6 Hz, 2 H, OCH_2), 1.93 (s, 3 H, CH_3); MS m/e 125 (M^+ + 1, 10.06), 124 (M^+, 0.09), 109 ($M^+ - CH_3$, 1.27), 68 ($M^+ - CH_3CH_2CH$=CH_2, 100.00). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found: C, 67.08; H, 6.28.

3′-Phenyl-2′(*E*)-propenyl 2-butynoate (1e) was synthesized as reported in ref 2 (solvent: HMPA): yield 1.66 g (35%); ot 155–157 °C (5 mmHg); IR (neat) 2400, 1710, 1660, 1250 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.50–7.20 (m, 5 H, Ph), 6.70 (d, J = 16.0 Hz, PhCH=), 6.30 (dt, J_1 = 16.0 Hz, J_2 = 7.80 Hz, 1 H, CH=), 4.84 (dd, J_1 = 1.8 Hz, J_2 = 7.8 Hz, 2 H, OCH_2), 2.00 (s, 3 H, CH_3); MS m/e 202 (M^+ + 2, 18.19), 201 (M^+ + 1, 2.08), 200 (M^+, 18.08). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.94; H, 6.00.

Synthesis of 3′-Phenyl-2′(*Z*)-propenyl 2-Butynoate (1e′). 1e′ was prepared as 1a by using CH_2Cl_2 instead of ether as the solvent. The starting materials added were as follows: 2-butynoic acid (1.0 g, 11.9 mmol), 3-phenyl-2(*Z*)-propenol (1.60 g, 11.9 mmol), DCC (3.70 g, 17.9 mmol), DMAP (145 mg, 10 mol %). The addition was finished at 0 °C, and then the reaction was carried out at rt for 24 h: yield 2.31 g (97%); ot 130–132 °C/2 mmHg; IR (neat) 2420, 1710, 1460, 1240, 1080 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.55–7.18 (m, 5 H, Ph), 6.72 (d, J = 11.5 Hz, 1 H, PhCH=), 5.85 (dt, J_1 = 6.4 Hz, J_2 = 11.5 Hz, 1 H), 4.95 (dd, J_1 = 2.0 Hz, J_2 = 11.5 Hz, 2 H, OCH_2), 2.00 (s, 3 H, CH_3); MS m/e 200 (M^+, 0.43), 199 (M^+ - 1, 1.21), 67 (100.00). Anal. Calcd for $C_{13}H_{12}O_3$: C, 77.98; H, 6.04. Found: C, 78.23; H, 5.51.

Cyclization Reaction of 2-Alkynoate with $CuCl_2$ under the Catalysis of $PdCl_2(PhCN)_2$. Typical Procedure. To a solution of 1a (185 mg, 1.0 mmol), $CuCl_2$ (680 mg, 5.0 mmol), and LiCl (90 mg, 2.1 mmol) in CH_3CN (5 mL) was added $PdCl_2(PhCN)_2$ (20 mg, 0.053 mmol), and the reaction was stirred and monitored by TLC (eluent: petroleum ether/ethyl acetate (10:3)). After the reaction was complete, water (5 mL) was added, and then the mixture was extracted with ether (3 × 10 mL) and dried ($MgSO_4$). Preparative TLC on silica gel (eluent: petroleum ether/ethyl acetate (10:3)) afforded the product 3a and 4a in pure form.

(*E*)-3′-Phenyl-2′-propenyl (*E*)-2,3-dichloro-2-propenoate (3a): yield 10.0 mg (4%); ot 155–157 °C (4.5 mmHg); IR (neat) 2950, 1730, 1580, 1210 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.50–7.22 (m, 5 H, Ph), 6.90 (s, 1 H, CHCl=), 6.76 (d, J = 15.8 Hz, 1 H, PhCH=), 6.34 (dt, J_1 = 15.8 Hz, J_2 = 6.0 Hz, 1 H, CH=), 4.90 (d, J = 6.0 Hz, 2 H, OCH_2); MS m/e 260 (M^+ (2 ^{37}Cl), 0.70), 258 (M^+ (^{37}Cl, ^{35}Cl), 3.38), 256 (M^+ (2 ^{35}Cl), 4.53), 107 ($^{37}ClC_2H_2CO_2^+$, 1.08), 105 ($^{35}ClC_2H_2CO_2^+$, 24.83), 83 ($C_2HCO_2CH_2^+$, 100.00); HRMS calcd for $C_{12}H_{10}C_{12}O_2$ 256.0058 (2 ^{35}Cl), 258.0027 (^{35}Cl, ^{37}Cl), found 256.0073 (2 ^{35}Cl), 258.0023 (^{35}Cl, ^{37}Cl).

α-(Chloromethylene)-β-(1′-chlorobenzyl)-γ-butyrolactone (4a): yield 144 mg (56%); mp 88–90 °C; IR (neat) 1760, 1630, 1240 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.50–7.30 (m, 5 H, Ph), [6.93 (*E* isomer), 5.86 (*Z* isomer) (d, J = 1.5 Hz, 1 H, HCCl=)], [4.89, 4.85 (d, J = 8.8 Hz, 1 H, CHClPh)], [[4.60 (dd, J_1 = 3.0 Hz, J_2 = 10.0 Hz), 4.46 (dd, J_1 = 7.2 Hz, J_2 = 10 Hz) (*Z* isomer)], [4.20 (dd, J_1 = 7.0 Hz, J_2 = 8.8 Hz), 4.02 (dd, J_1 = 3.0 Hz, J_2 = 10 Hz) (*E* isomer)] 2 H, OCH_2)], 3.70 (bt, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1 H, OCCH); MS m/e 261 (M^+ (^{37}Cl) + 1, 0.56), 260 (M^+ (2 ^{37}Cl), 0.50), 259 (M^+ (^{37}Cl, ^{35}Cl) + 1, 3.50), 258 (M^+ (^{37}Cl, ^{35}Cl), 0.78), 257 (M^+ (2 ^{35}Cl) + 1, 5.58). Anal. Calcd for $C_{12}H_{10}C_{12}O_2$: C, 56.06; H, 3.92; Cl, 27.58. Found: C, 56.05; H, 3.92; Cl, 27.50. The two isomers could be separated carefully by repeated preparative TLC on silca gel (eluent: petroleum ether–ethyl acetate (10:3)), and the assignment of ^{1}H NMR spectra was based on that of the isolated samples.

2′-Propenyl 2,3-dichloro-2(*E*)-propenoate (3b): ot 120–122 °C (5 mmHg); IR (neat) 2950, 1725, 1590, 1220; ^{1}H NMR (60 MHz, CCl_4) δ 6.90 (s, 1 H, CHCl=), 6.50–5.10 (m, 3 H, CH=CH_2), 4.75 (d, J = 8.0 Hz, 2 H, OCH_2); MS m/e 185 (M^+ (2 ^{37}Cl) + 1, 11.76), 184 (M^+ (2 ^{37}Cl), 8.05), 183 (M^+ (^{35}Cl, ^{37}Cl) + 1, 50.09), 182 (M^+ (^{35}Cl, ^{37}Cl), 28.00), 181 (M^+ (2 ^{35}Cl) + 1, 51.25), 180 (M^+ (2 ^{35}Cl), 20.55). Anal. Calcd for $C_6H_6Cl_2O_2$: C, 39.81; H, 3.34. Found: C, 39.54; H, 3.18.

α-(*E*)-(Chloromethylene)-β-(chloromethyl)-γ-butyrolactone (4b): mp 70–72 °C; IR (Nujol film) 2950, 1760, 1620, 1190 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.88 (d, J = 1.80 Hz, 1 H, CHCl=), 4.46 (dd, J_1 = 7.4 Hz, J_2 = 9.5 Hz, 1 H, OCH), 4.26 (dd, J_1 = 3.6, J_2 = 9.5 Hz, 1 H, OCH), 3.70–3.60 (m, 2 H, CH_2Cl), 3.58–3.44 (m, 1 H, ClCCH); MS m/e 185 (M^+ (2 ^{37}Cl) + 1, 8.34), 184 (M^+ (2 ^{37}Cl), 4.94), 183 (M^+ (^{35}Cl, ^{37}Cl) + 1, 50.66), 182 (M^+ (^{35}Cl, ^{37}Cl), 15.15), 181 (M^+ (2 ^{35}Cl) + 1, 78.95), 180 (M^+ (2 ^{35}Cl), 18.09), 87 (M^+ (^{35}Cl) - CH_2Cl - CO_2, 100.00). Anal. Calcd for $C_6H_6Cl_2O_2$: C, 39.81; H, 3.34; Cl, 39.17. Found: C, 39.60; H, 3.42; Cl, 39.36.

α-(1′-Chloroethylidene)-β-(chloromethyl)-γ-butyrolactone (4d). *Z* isomer: ot 130–132 °C (2.5 mmHg); IR (neat) 2950, 1760, 1660, 1220, 1140 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.32 (d, J = 3.1 Hz, 2 H, OCH_2), 3.76–3.44 (m, 3 H, $CHCH_2Cl$), 2.40 (s, 3 H, CH_3); MS m/e 198 (M^+ (2 ^{37}Cl), 2.90), 196 (M^+ (^{37}Cl, ^{35}Cl), 11.04), 194 (M^+ (2 ^{35}Cl), 18.04), 162 (M^+ (^{37}Cl) - Cl + 1, 0.55), 161 (M^+ (^{37}Cl) - Cl, 4.74), 160 (M^+ (^{35}Cl) - Cl + 1, 1.82), 159 (M^+ (^{35}Cl) - Cl, 14.20). Anal. Calcd for $C_7H_8Cl_2O_2$: C, 43.11; H, 4.13. Found: C, 43.07; H, 4.16.

***E* isomer**: oil; IR (neat) 1760, 1660, 1240 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.52–4.04 (m, 3 H, OCH_2CH), 3.92–3.52 (m, 2 H, CH_2Cl), 2.64 (s, 3 H, CH_3); MS m/e 198 (M^+ (2 ^{37}Cl), 1.07), 196 (M^+ (^{35}Cl, ^{37}Cl), 7.12), 194 (M^+ (2 ^{35}Cl), 12.03), 161 (M^+ (^{37}Cl) - Cl, 3.33), 160 (1.28), 159 (M^+ (^{35}Cl) - Cl, 10.59), 83 ($M^+ - 2ClCH_3CH_2$, 100.00); HRMS calcd for $C_7H_8Cl_2O_2$ 193.9901 (2 ^{35}Cl), 195.9871 (^{35}Cl, ^{37}Cl), found 193.9900 (2 ^{35}Cl), 195.9862 (^{35}Cl, ^{37}Cl).

α-(1′-Chloroethylidene)-β-(1″-chlorobenzyl)-γ-butyrolactone (4e). *Z* isomer: mp 119–121 °C; IR (Nujol film) 1760, 1650, 1240, 1140 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) see Table III); MS m/e 275 (M^+ (2 ^{37}Cl) + 1, 0.12), 273 (M^+ (^{35}Cl, ^{37}Cl) + 1, 0.25), 271 (M^+ (2 ^{35}Cl) + 1, 0.31). Anal. Calcd for $C_{13}H_{12}Cl_2O_2$: C, 57.59; H, 4.46. Found: C, 56.91; H, 4.28.

***E* isomer**: oil; IR (neat) 1760, 1660, 1230, 1140, 1020 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.30 (s, 5 H, Ph), 5.44 (d, J = 5.2 Hz, 1 H, CHCl), 4.64 (dd, J_1 = 10.0 Hz, J_2 = 1.2 Hz, 1 H, OCH), 4.25 (dd, J_1 = 10.0 Hz, J_2 = 6.7 Hz, 1 H, OCH), 3.94 (m, 1 H, OCCH), 2.62 (s, 3 H, CH_3); MS m/e 274 (M^+ (2 ^{37}Cl), 1.19), 272 (M^+ (^{37}Cl, ^{35}Cl), 2.79), 270 (M^+ (2 ^{35}Cl), 3.06), 237 (M^+ (^{37}Cl) - Cl, 3.83), 236 (M^+ (^{37}Cl) - Cl - 1, 17.66), 235 (M^+ (^{35}Cl) - Cl, 12.37), 234 (M^+ (^{35}Cl) - Cl - 1, 28.94), 126 ($M^+ - 1 - 2Cl - CO_2 - CH_3CH_2$, 100.00); HRMS calcd for $C_{13}H_{12}Cl_2O_2$ 270.0214 (2 ^{35}Cl), 272.0184 (^{35}Cl, ^{37}Cl), found 270.0221 (2 ^{35}Cl), 272.0208 (^{35}Cl, ^{37}Cl).

α-(*Z*)-(1′-Chloroethylene)-β-(1″-chlorobenzyl)-γ-butyrolactone (4e′): mp 134–136 °C; IR (Nujol film) 2950, 1740, 1630, 1460, 1370 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) see Table III; MS m/e 273 (M^+ (^{35}Cl, ^{37}Cl) + 1, 0.45), 271 (M^+ (2 ^{35}Cl) + 1, 0.87), 127 (^{37}ClPhCH$^+$, 30.23), 125 (^{35}ClPhCH$^+$, 100.00). Anal. Calcd for $C_{13}H_{12}Cl_2O_2$: C, 57.59; H, 4.46. Found: C, 57.55; H, 3.98.

α-(1′-Chloropentylidene)-β-(chloromethyl)-γ-butyrolactone (4f). *Z* isomer: ot 154–156 °C (2 mmHg); IR (neat) 1760, 1640, 1230, 1140 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.48–4.12 (m, 2 H, OCH_2), 3.70–3.40 (m, 3 H, $CHCH_2Cl$), 2.52 (t, J = 7.7 Hz, 2 H, CH_2CCl=), 1.90–1.10 (m, 4 H, CH_2CH_2), 0.96 (t, J = 6.4 Hz, 3 H, CH_3); MS m/e 240 (M^+ (2 ^{37}Cl), 0.34), 239 (0.65), 238 (M^+ (^{35}Cl, ^{37}Cl), 2.42), 237 (1.74), 236 (M^+ (2 ^{35}Cl), 3.82), 83 (100.00). Anal. Calcd for $C_{10}H_{14}Cl_2O_2$: C, 50.65; H, 5.95. Found: C, 50.77; H, 5.98.

***E* isomer**: ot 160–162 °C (6 mmHg); IR (neat) 1760, 1650, 1230, 1140 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.48–4.16 (m, 2 H, OCH_2), 3.84–3.48 (m, 3 H, $CHCH_2Cl$), 3.10 (bt, J = 6.4 Hz, 2 H, CH_2CCl=), 1.72–1.04 (m, 4 H, CH_2CH_2), 0.92 (t, J = 6.4 Hz, 3 H, CH_3); MS m/e 240 (M^+ (2 ^{37}Cl), 0.23), 239 (0.26), 238 (M^+ (^{37}Cl, ^{35}Cl), 1.65), 237 (0.63), 236 (M^+ (2 ^{35}Cl), 2.65). Anal. Calcd for $C_{10}H_{14}Cl_2O_2$: C, 50.65; H, 5.95. Found: C, 50.64; H, 5.99.

α-(1′-Chloropentylidene)-β-(1″-chlorobenzyl)-γ-butyrolactone (4g). *Z* isomer: ot 210 °C (1 mmHg); IR (neat) 1760, 1640, 1220, 1200, 1140 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.32 (s, 5 H, Ph), 4.92 (d, J = 7.7 Hz, 1 H, CHCl), 4.32–4.00 (m, 2 H, OCH_2), 3.72 (dt, J_1 = 7.7, J_2 = 1.8 Hz, 1 H, OCCH), 2.68–2.40 (m, 2 H, CH_2CCl=), 1.84–1.16 (m, 4 H, CH_2CH_2), 0.96 (t, J = 6.4 Hz, CH_3); MS m/e 317 (M^+ (2 ^{37}Cl) + 1, 2.15), 316 (2.20), 315 (M^+ (^{37}Cl, ^{35}Cl) + 1, 11.79), 314 (3.75), 313 (M^+ (2 ^{35}Cl) + 1, 19.23), 279 (M^+ (^{37}Cl) - Cl, 0.95), 278 (1.21), 277 (M^+ (^{35}Cl) - Cl, 2.89), 124 (*n*-BuC=CCO_2^+ - 1, 100.00). Anal. Calcd for $C_{16}H_{18}Cl_2O_2$: C, 61.35; H, 5.79. Found: C, 61.13; H, 5.79.

***E* isomer**: ot 200 °C (1.5 mmHg); IR (neat) 1760, 1650, 1230, 1140 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.50–7.20 (m, 5 H, Ph), 5.60–5.38 (m, 1 H, PhCHCl), 4.75–3.6 (m, 3 H, OCH_2CH), 3.85–3.40 (m, 2 H, C=CCH_2), 1.80–1.10 (m, 4 H, CH_2CH_2), 0.90 (t, J

= 6.80 Hz, 3 H, CH_3); MS *m/e* 316 (M^+ (2 ^{37}Cl), 0.20), 315 (1.16), 313 (0.88), 312 (M^+ (2 ^{35}Cl), 0.43), 240 (M^+ (2 ^{37}Cl) + 1 - Ph, 8.03), 238 (M^+ (^{37}Cl, ^{35}Cl) + 1 - Ph, 31.50), 236 (M^+ (2 ^{35}Cl) + 1 - Ph, 57.16). Anal. Calcd for $C_{16}H_{18}Cl_2O_2$: C, 61.35; H, 5.79. Found: C, 61.32; H, 5.73.

α-(Chloromethylene)-γ-chloro-γ-methyl-δ-pentyrolactone (5): mp 93–95 °C; IR (Nujol film) 1720, 1600, 1150 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.62 (t, *J* = 1.6 Hz, 1 H, CHCl=), 4.30 (bs, 2 H, OCH_2), 3.04–2.80 (m, 2 H, $=CCH_2$), 1.68 (s, 3 H, CH_3); MS *m/e* 199 (0.35), 198 (M^+ (2 ^{37}Cl), 3.16), 197 (2.19), 196 (M^+ (^{37}Cl, ^{35}Cl), 27.68), 194 (M^+ (2 ^{35}Cl), 29.34), 168 (M^+ (2 ^{37}Cl) - OCH_2, 9.07), 1.67 (2.68), 166 (M^+ (^{35}Cl, ^{37}Cl) - OCH_2, 53.45), 164 (M^+ (2 ^{35}Cl) - OCH_2, 71.55). Anal. Calcd for $C_7H_8Cl_2O_2$: C, 43.11; H, 4.13. Found: 43.20; H, 3.86.

Procedure for ESR Study. To a solution of **1d** (20 mg, 0.16 mmol), $CuCl_2$ (110 mg, 0.80 mmol), LiCl (15 mg, 0.33 mmol), *t*-BuN→O (25 mg, 0.29 mmol), and CH_3CN (0.5 mL) in an ESR tube was added $PdCl_2(PhCN)_2$ (20 mg, 0.05 mmol) at rt. Then the tube was placed in an ESR spectrometer for radical signal detection at rt.

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Supplementary Material Available: ^1H NMR spectra for compounds **1c**, **1d**, **1e'**, **3a**, **4d** (*E*-isomer), **4e** (*Z*-isomer), **4e** (*E*-isomer), and **4e'** (*Z*-isomer) and ^1H 2D NOESY spectra of **4e** (*Z*-isomer) and **4e'** (*Z*-isomer) (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.