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Studies on Pd(II)-Catalyzed Synthesis of (*Z*)-α-Haloalkylidene-*β*-lactones from Cyclocarbonylation of 2-Alkynols and the Subsequent Coupling Reactions

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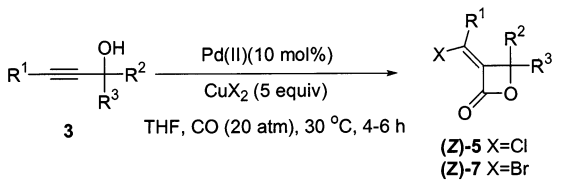

A good regio- and stereoselectivity was observed for the $PdCl_2$-catalyzed cyclocarbonylation of 2-alkynols with $CuCl_2$ affording (*Z*)-α-chloroalkylidene-*β*-lactones. The highly optically active (*Z*)-α-chloroalkylidene-*β*-lactones could be easily prepared from the readily available optically active propargylic alcohols. The Pd(II)-catalyzed cyclocarbonylation of 2-alkynols with $CuBr_2$ was also studied. Although the yields of (*Z*)-α-bromoalkylidene-*β*-lactones were low, due to the relatively higher activity of the C−Br bond, the coupling reactions of (*Z*)-α-bromoalkylidene-*β*-lactones were quite smooth to afford the corresponding products in high yields. A rationale for this reaction is discussed.

Introduction

β-Lactones, an important class of strained four-membered oxygen-containing heterocyclic compounds, can be found in many biologically active natural products.[1] For example, among the most widely studied *β*-lactones are the antibiotic F-244 (1233A) **1** (an inhibitor of HMG-CoA synthase)[2] and the antiobesity drug tetrahydrolipstatin (orlistat) **2** (an inhibitor of the serine pancreatic lipase)[3] (Figure 1).

In the family of *β*-lactones, α-alkylidene-*β*-lactones are one of the most important skeletons in some biologically active natural products[4] and are considered as useful building blocks in organic synthesis.[1b,5] These compounds

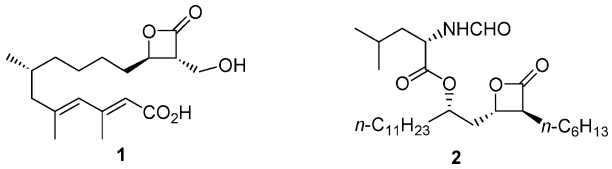

FIGURE 1. Some important inhibitors bearing a *β*-lactone moiety.

are usually prepared via [2+2] cycloaddition of ketenes with carbonyl compounds,[6] lactonization of *β*-hydroxy carboxylic acids or derivatives,[7] deoxygenation of *β*-peroxylactones,[8] Pd(0) or PdI_2/KI-catalyzed cyclocarbonyla-

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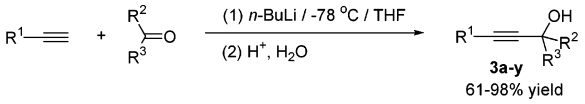
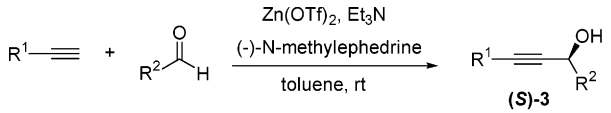
SCHEME 1



3a R^1 = *n*-C_6H_{13}, R^2 = C_2H_5, R^3 = H
3b R^1 = *n*-C_5H_{11}, R^2 = *n*-C_4H_9, R^3 = H
3c R^1 = *n*-C_3H_7, R^2 = *n*-C_4H_9, R^3 = H
3d R^1 = *n*-C_4H_9, R^2 = Me, R^3 = H
3e R^1 = *n*-C_4H_9, R^2 = *n*-C_3H_7, R^3 = H
3f R^1 = *n*-C_4H_9, R^2 = *n*-C_5H_{11}, R^3 = H
3g R^1 = *n*-C_4H_9, R^2 = *i*-Pr, R^3 = H
3h R^1 = *n*-C_4H_9, R^2 = *i*-Bu, R^3 = H
3i R^1 = *n*-C_4H_9, R^2 = cyclohexyl, R^3 = H
3j R^1 = *t*-Bu, R^2 = *n*-C_4H_9, R^3 = H
3k R^1 = Ph, R^2 = *i*-Pr, R^3 = H
3l R^1 = Ph, R^2 = *i*-Bu, R^3 = H
3m R^1 = Ph, R^2 = cyclohexyl, R^3 = H
3n R^1 = $PhCH_2CH_2$, R^2 = *i*-Pr, R^3 = H
3o R^1 = $PhCH_2CH_2$, R^2 = *i*-Bu, R^3 = H
3p R^1 = $PhCH_2CH_2$, R^2 = cyclohexyl, R^3 = H
3q R^1 = *n*-C_4H_9, R^2 = C_2H_5, R^3 = H
3r R^1 = *n*-C_4H_9, R^2, R^3 = $(CH_2)_5$
3s R^1 = *n*-C_4H_9, R^2, R^3 = $(CH_2)_4$
3t R^1 = *n*-C_4H_9, R^2, R^3 = $(CH_2)_6$
3u R^1= *n*-C_4H_9, R^2 = Me, R^3 = Me
3v R^1 = *n*-C_4H_9, R^2 = Me, R^3 = Et
3w R^1 = *n*-C_4H_9, R^2 = Et, R^3 = Et
3x R^1 = *n*-C_4H_9, R^2 = Me, R^3 = *t*-Bu
3y R^1 = *n*-C_4H_9, R^2 = Me, R^3 = Ph
3z R^1 = Ph, R^2, R^3 = $(CH_2)_5$

SCHEME 2



(*S*)-3k R^1 = Ph, R^2 = *i*-Pr	85% yield, >91% ee
(*S*)-3l R^1 = Ph, R^2 = *i*-Bu	94% yield, >83% ee
(*S*)-3m R^1 = Ph, R^2 = cyclohexyl	92% yield, 96% ee
(*S*)-3n R^1 = $PhCH_2CH_2$, R^2 = *i*-Pr	84% yield, 97% ee
(*S*)-3o R^1 = $PhCH_2CH_2$, R^2 = *i*-Bu	80% yield, 95% ee
(*S*)-3p R^1 = $PhCH_2CH_2$, R^2 = cyclohexyl	92% yield, 98% ee

tion of 2-alkynols,[9] and ruthenium-catalyzed cyclocarbonylation of 2-alkynols.[10]

In a recent communication, we described a $PdCl_2$-catalyzed cyclocarbonylation of 2-alkynols for the efficient synthesis of (*Z*)-α-chloroalkylidene-β-lactones.[11] Here we wish to present a detailed study on this reaction: the scope of the reaction, mechanism, and the subsequent coupling reactions.

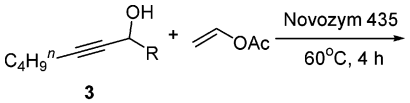
Results and Discussion

Preparation of the Starting Materials. All of the propargylic alcohols were synthesized by the application of the known procedure shown in Scheme 1.[12]

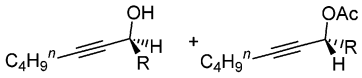
The optically active propargylic alcohols (*S*)-**3k**−**p** were prepared according to Carreira's method shown in Scheme 2.[13]

The optically active (*S*)-**3d**, (*S*)-**3q**, (*R*)-**4d**, and (*R*)-**4q** were prepared via the enzymatic resolution of racemic propargylic alcohols (Scheme 3).[14] Then (*R*)-**4d** and (*R*)-**4q** were hydrolyzed to afford the optically active propargylic alcohols (*R*)-**3d** and (*R*)-**3q** (Scheme 4).

SCHEME 3

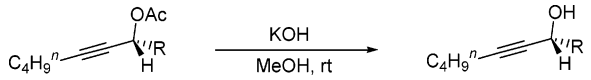


3d R = Me
3q R = C_2H_5



(*S*)-3d **(*R*)-4d**
(*S*)-3q **(*R*)-4q**

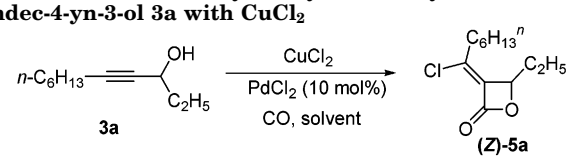
SCHEME 4



(*R*)-4d R = Me
(*R*)-4q R = C_2H_5

(*R*)-3d 84% yield, 99% ee
(*R*)-3q 90% yield, >95% ee

TABLE 1. $PdCl_2$-Catalyzed Cyclocarbonylation of Undec-4-yn-3-ol 3a with $CuCl_2$



entry	CO (atm)	$CuCl_2$ (equiv)	solvent	temp (°C)	time (h)	yield[a] (%)
1	1	3	PhH	20	18	29
2	14	3	PhH	30	16	40
3[b]	15	3	PhH	30	24	33
4[c]	15	3	PhH	20	16	–[f]
5[d]	14	3	PhH	20	24	–[f]
6[e]	15	3	PhH	18	42	19
7	15	3	THF	25	17	35
8	20	5	THF	20	4	65
9	**20**	**5**	**THF**	**30**	**4**	**86**
10	20	5	THF	40	4	71
11	20	5	THF	50	4	40
12	20	5	THF	70	4	31

[a] Isolated yield. [b] 1.1 equiv of NaOAc was added. [c] 2 equiv of Et_3N was added. [d] 2 equiv of $HC(OEt)_3$ was added. [e] 15 equiv of ^{t}BuOH was applied. [f] The reaction was complicated.

Synthesis of (*Z*)-α-Chloroalkylidene-β-lactones via the $PdCl_2$-Catalyzed Cyclocarbonylation of 2-Alkynols. The reaction of **3a**, 3 equiv of $CuCl_2$, and CO (1 atm) with $PdCl_2$ as the catalyst at 20 °C in PhH afforded (*Z*)-α-chloroalkylidene-β-lactone (*Z*)-**5a** in 29% yield (entry 1, Table 1). With the pressure of CO being 14 atm, the yield was not dramatically improved (entry 2, Table 1). Although different additives were applied, no improvement was observed (entries 3−6, Table 1). When THF was used instead of PhH, the yield was 35% (entry 7, Table 1). With 5 equiv of $CuCl_2$ and 20 atm of CO, the yield of product was improved to 65% within 4 h (entry 8, Table 1). Further study indicated that the

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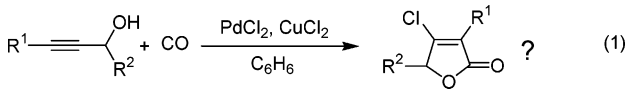
reaction temperature is also important for this reaction (entries 8−12, Table 1). The best reaction conditions are 10 mol % of $PdCl_2$, 5 equiv of $CuCl_2$, and CO (20 atm) in THF at 30 °C for 4 h (Conditions A) affording (*Z*)-**5a** in isolated 86% yield (entry 9, Table 1).

During our studies on the chemistry of functionalized allenes, we have developed some new methodologies for the efficient synthesis of butenolides starting from 2,3-allenoic acids or derivatives.[15] Although we initially envisioned that the $PdCl_2$-catalyzed cyclocarbonylation of 2-alkynols would afford butenolides (eq 1), after some



(1)

analysis, we surprisingly found the products display intense IR absorption at ν = 1813 cm^{-1}, which is the characteristic absorption of the carbonyl groups in β-lactones (ν = 1840−1810 cm^{-1}). Single-crystal X-ray diffraction of (*Z*)-**5k** and (*Z*)-**5n** established the (*Z*)-α-chloroalkylidene-β-lactone skeleton.[11]

Some amounts of (*E*)-α-chloroalkylidene-β-lactone (*E*)-**5a** and butenolides **6** were also formed in the reaction mixture with their ratio determined by the analysis of the ^1H NMR spectra of the crude product(s).

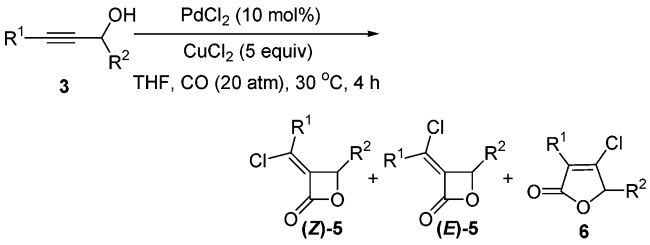
Some typical results under the established conditions A are shown in Table 2. It should be pointed out that the reaction is general with good chemo- and stereoselectivities to afford the products in moderate to excellent yields. R^1 can be an alkyl group and aryl group including ^{t}Bu while R^2 group should be an alkyl group.

The cyclocarbonylation of 1-hexynylcyclohexan-1-ol **3r** was used to optimize the reaction conditions for tertiary alcohols with the representative results listed in Table 3. Under Conditions A, the yield of (*Z*)-**5r** was only 16% (entry 1, Table 3). The reaction was complicated with a prolonged reaction time (entry 2, Table 3); the yield of reaction was slightly higher with a shorter reaction time (entry 3, Table 3); when the reaction was stopped after 1 h, the substrate was not completely consumed (entry 4, Table 3). With the addition of 1 equiv of Et_3N, the reaction did not proceed at all (entry 5, Table 3). When benzoquinone (1 equiv), which has been extensively used for the oxidation of Pd(0) to Pd(II),[16] was added to the reaction mixture, fortunately the yield of product was improved (compare entry 1 with entry 6, entry 3 with entry 7, Table 3). When 3 equiv of benzoquinone was added, the yield was improved to 86% (entry 9, Table 3). With more benzoquinone no further improvement was observed (entry 10, Table 1).

Then we investigated the effect of the relative ratio of $PdCl_2$, $CuCl_2$, and benzoquinone on the reaction (Table 4). With 10 mol % of $PdCl_2$ and 1.2 equiv of $CuCl_2$, the reaction afforded (*Z*)-**5r** in 71% (entry 7, Table 4). With 1 or 3 equiv of $CuCl_2$, the yield of (*Z*)-**5r** was somewhat lower as compared to the results with 5 equiv of $CuCl_2$ (entries 2−4, Table 4). So we established conditions B for tertiary propargylic alcohols: $PdCl_2$ (10 mol %), $CuCl_2$ (5 equiv), benzoquinone (3 equiv), CO (20 atm) in THF for 2 h.

Some typical results for the cyclocarbonylation of tertiary propargylic alcohols are listed in Table 5, which indicate that the reaction is general: R^1 can be an alkyl group or an aryl group and R^2, R^3 can be alkyl groups. The yields of products were affected by the bulkiness of

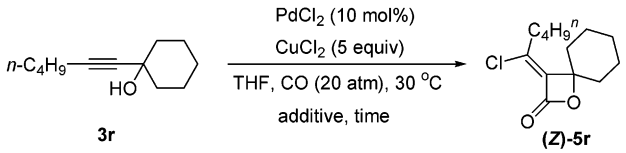
TABLE 2. $PdCl_2$-Catalyzed Cyclocarbonylation of Secondary Propargylic Alcohols with $CuCl_2$



entry	R^1	R^2	isolated yield of (*Z*)-**5** (%)	ratio of *Z*-**5**:*E*-**5**:**6** (%)[a]
1	n-C_6H_{13}	C_2H_5	86/(*Z*)-**5a**	78:12:10
2	n-C_5H_{11}	n-Bu	76/(*Z*)-**5b**	82:8:10
3	n-C_3H_7	n-Bu	74/(*Z*)-**5c**	80:10:10
4	n-Bu	Me	64/(*Z*)-**5d**	78:9:13
5	n-Bu	n-C_3H_7	72/(*Z*)-**5e**	78:10:12
6[b]	n-Bu	n-C_5H_{11}	67/(*Z*)-**5f**	81:9:10
7	n-Bu	i-Pr	71/(*Z*)-**5g**	—[c]
8	n-Bu	i-Bu	90/(*Z*)-**5h**	78:12:10
9	n-Bu	cyclohexyl	82/(*Z*)-**5i**	86:5:9
10	t-Bu	n-Bu	89/(*Z*)-**5j**	95: 0: 5
11[b]	Ph	i-Pr	91/(*Z*)-**5k**	90: 6: 4
12	Ph	i-Bu	81/(*Z*)-**5*l***	89: 8: 3
13[b]	Ph	cyclohexyl	78/(*Z*)-**5m**	89: 6: 5
14	$PhCH_2CH_2$	i-Pr	66/(*Z*)-**5n**	74:11:15
15[b]	$PhCH_2CH_2$	i-Bu	52/(*Z*)-**5o**	75:15:10
16[b]	$PhCH_2CH_2$	cyclohexyl	63/(*Z*)-**5p**	79:8:13

[a] The ratio of (*Z*)-**5**:(*E*)-**5**:**6** was determined by the analysis of the 300 MHz ^1H NMR spectra of the crude mixture. (*E*)-**5** and **6** were not fully characterized due to the difficulty met in the purification process. [b] The reaction time was 6 h. [c] The ratio could not be determined by the analysis of the ^1H NMR spectra of the crude mixture.

TABLE 3. The $PdCl_2$-Catalyzed Cyclocarbonylation of 1-Hexynylcyclohexan-1-ol 3r



entry	additive (equiv)	time (h)	isolated yield (%)
1		4	16
2		6	complicated
3		2	28
4		1	39
5	Et_3N (1)	4	trace
6	benzoquinone (1)	4	29
7	benzoquinone (1)	2	57
8	benzoquinone (2)	2	83
9	**benzoquinone (3)**	**2**	**86**
10	benzoquinone (4)	2	86

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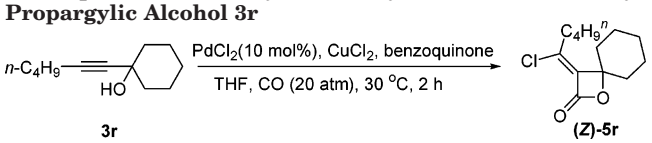
TABLE 4. The Effect of the Ratio of $PdCl_2$, $CuCl_2$, and Benzoquinone on the Cyclocarbonylation of the Tertiary Propargylic Alcohol 3r



3r (Z)-5r

entry	$CuCl_2$ (equiv)	benzoquinone (equiv)	yield of (*Z*)-**5r** (%)[a]
1	5	4	86[b]
2	5	3	86
3	3	2	79
4	1	2	79
5	0.5	2	50
6	1.2	3	75
7	1.2	2	71

[a] Isolated yield. [b] 6% (*E*)-**5r** was isolated, and (*E*)-**5r** was not formed in any other cases.

the R^2, R^3 groups (entries 5−7, Table 5). When R^3 was an aryl group, the reaction was complicated (entry 9, Table 5).

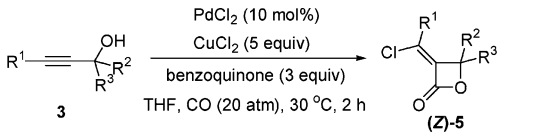
Preparation of Optically Active (*Z*)-α-Chloroalkylidene-β-lactones. With a range of optically active secondary propargylic alcohols in hand, we studied the corresponding cyclocarbonylation under the established Conditions A. Some typical results were summarized in Table 6. From Table 6, it can be concluded that racemization of the chiral center in (*R*)- or (*S*)-**3** was not observed with the yields ranging from 52% to 89%.

Synthesis of (*Z*)-α-Bromoalkylidene-β-lactones via the Pd(II)-Catalyzed Cyclocarbonylation of Propargylic Alcohols. After studying $PdCl_2$-catalyzed carbonylation of 2-alkynols with $CuCl_2$, we envisioned preparing (*Z*)-α-bromoalkylidene-β-lactones using $Pd(OAc)_2$ and $CuBr_2$ instead of $PdCl_2$ and $CuCl_2$. After a try with $Pd(OAc)_2$ and 5 equiv of $CuBr_2$, it was observed that the reaction afforded (*Z*)-**7f** in only 6% yield (entry 1, Table 7). When 3 equiv of benzoquinone was added, the yield was improved to 38% (entry 2, Table 7). When 5 equiv of LiBr was used instead of $CuBr_2$, the reaction did not occur (entries 3 and 4, Table 7). The reaction proceeded in THF, PhH, *n*-hexane, ethyl acetate, or toluene to affor (*Z*)-**7f** in low yields (entries 2 and 5−8, Table 7); no reaction was observed in DMF, CH_3CN, EtOH, and PhH/THF (10:3) (entries 9−12, Table 7). The effect of the relative ratio of $CuBr_2$ and benzoquinone on the yield of product (*Z*)-**7f** was also studied. After an enormous number of tries, we established Conditions C: $Pd(OAc)_2$ (5 mol %), $CuBr_2$ (2 equiv), benzoquinone (3 equiv), CO (20 atm) in PhH for the synthesis of (*Z*)-α-bromoalkylidene-β-lactones (entry 16, Table 7).

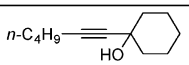
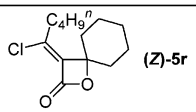
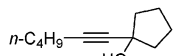
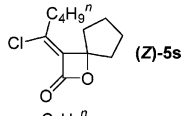
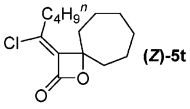
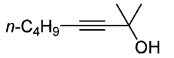
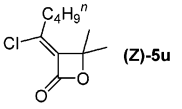
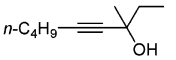
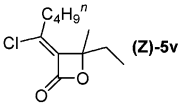
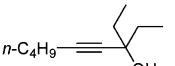
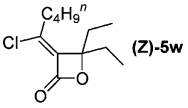
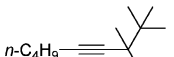
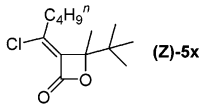
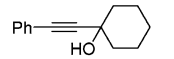
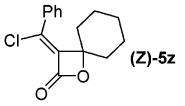
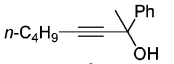
The results for Pd(II)-catalyzed cyclocarbonylation of various propargylic alcohols with $CuBr_2$ and benzoquinone are summarized in Table 8. The yields ranged from 29% to 57%, which may be attributed to the high activity of the *in situ* formed Pd(0) with the C−Br bond in (*Z*)-α-bromoalkylidene-β-lactones. The stereochemistry of these bromides was established by the X-ray diffraction study of (*Z*)-**7m**.[18] It should be noted that no (*E*)-isomers were detected during the synthesis of α-bromoalkylidene-β-lactones.

(17) (a) Ishihara, K.; Mori, A.; Arai, I.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *26*, 983. (b) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129.

TABLE 5. The $PdCl_2$-Catalyzed Cyclocarbonylation of Various Tertiary Propargylic Alcohols



3 (Z)-5

Entry	Substrate	Product	Yield (%)[a]
1	 3r	 (*Z*)-5r	86
2	 3s	 (*Z*)-5s	46
3	 3t	 (*Z*)-5t	31
4[b]	 3u	 (*Z*)-5u	50
5	 3v	 (*Z*)-5v	75
6	 3w	 (*Z*)-5w	60
7	 3x	 (*Z*)-5x	44
8	 3z	 (*Z*)-5z	71
9	 3y	-[c]	-

[a] Isolated yield. [b] The reaction was carried out under Conditions A. [c] The reaction was complicated.

Pd-Catalyzed Coupling Reactions of (*Z*)-α-Bromoalkylidene-β-lactones. The transition metal-catalyzed cross-coupling reaction has been becoming one of the most efficient methods for the formation of C−C bonds.[19] The $Pd(PPh_3)_4$-catalyzed coupling reaction of (*Z*)-**7f** with terminal alkynes or organoboronic acids afforded the coupling products **8**−**11** in high yields (Scheme 5).[20]

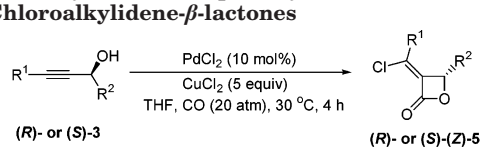
Mechanistic Considerations. A rationale for the palladium (II)-catalyzed regio- and stereoselective cyclo-

(18) Crystal data for compound (*Z*)-**7m**: $C_{16}H_{17}O_2Br$, MW = 321.21, orthorhombic, space group *P*2(1)2(1)2(1), Mo Kα, final *R* indices [$I > 2\sigma(I)$], R1 = 0.0376, *w*R2 = 0.0663, a = 8.101(6) Å, b = 9.767(7) Å, c = 18.669(13) Å, α = 90°, β = 90°, γ = 90°, V = 1477.3(18) Å^3, T = 293(2) K, Z = 4, reflections collected/unique 8726/3200 (R_{int} = 0.0779). CCDC: 249713.

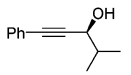
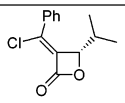
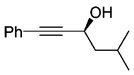
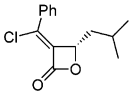
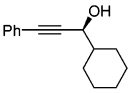
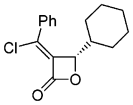
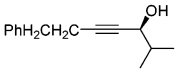
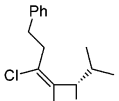
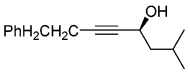
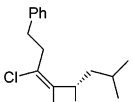
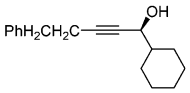
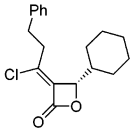
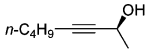
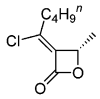
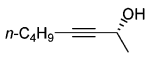
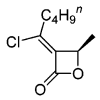
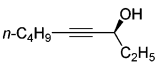
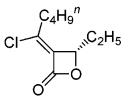
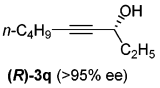
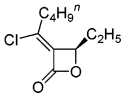
(19) *Metal-Catalyzed Cross-Coupling Reaction*; Stang, P., Diederich, F., Eds.; VCH: Weiheim, Germany, 1998.

(20) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Suzuki, A. *Pure Appl. Chem.* **1985**, *57*, 1749. (c) Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419. (d) Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213.

TABLE 6. Synthesis of Optically Active (*Z*)-α-Chloroalkylidene-*β*-lactones



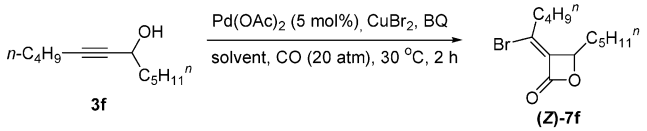
(*R*)- or (*S*)-3 → (*R*)- or (*S*)-(*Z*)-5

Entry	Substrate[a]	Product	Yield (%) of Product[b]	ee (%) of Product[c]
1[d]	 (*S*)-**3k** (>91% ee)	 (*S*)-(*Z*)-**5k**	89	92
2	 (*S*)-**3l** (>83% ee)	 (*S*)-(*Z*)-**5l**	63	85
3[d]	 (*S*)-**3m** (96% ee)	 (*S*)-(*Z*)-**5m**	83	96
4	 (*S*)-**3n** (97% ee)	 (*S*)-(*Z*)-**5n**	68	97
5	 (*S*)-**3o** (95% ee)	 (*S*)-(*Z*)-**5o**	64	92
6	 (*S*)-**3p** (98% ee)	 (*S*)-(*Z*)-**5p**	63	98
7	 (*S*)-**3d** (>99% ee)	 (*S*)-(*Z*)-**5d**	59	97
8	 (*R*)-**3d** (99% ee)	 (*R*)-(*Z*)-**5d**	52	98
9	 (*S*)-**3q** (>98% ee)	 (*S*)-(*Z*)-**5q**	59	98
10	 (*R*)-**3q** (>95% ee)	 (*R*)-(*Z*)-**5q**	58	97

[a] The absolute stereochemistry was established by comparison of the specific rotation with the literature data.[14,17] The enantiomeric excess was determined by HPLC on a chiralcel OD column. [b] Isolated yield. [c] The enantiomeric excess was determined by HPLC on a chiralcel OD-H or AS column. [d] The reaction time was 6 h.

carbonylation of propargylic alcohols is shown in Scheme 6. The coordination of the triple bond of **3** with $PdCl_2$ gave

TABLE 7. Screening of Reaction Conditions for the Pd(II)-Catalyzed Cyclocarbonylation of Dodec-5-yn-7-ol 3f with $CuBr_2$ and Benzoquinone



3f → (*Z*)-**7f**

entry	$CuBr_2$ (equiv)	BQ[a] (equiv)	additive (equiv)	solvent	isolated yield of (*Z*)-**7f** (%)
1[b]	5			toluene	6
2[c]	5	3		toluene	38
3[b]		3	LiBr (5)	toluene	NR
4[b]		3	LiBr (5)	THF	NR
5[c]	5	3		THF	31
6	**5**	**3**		**PhH**	**38**
7[c]	5	3		*n*-hexane	35
8[c]	2	3		ethyl acetate	26
9[b]	5	3		DMF	NR
10[c]	5	3		CH_3CN	0
11[b]	2	3		EtOH	NR
12[b]	2	1		PhH/THF (10:3)	trace
13[c]	5	2		PhH	31
14[c]	10	2		PhH	43
15[c]	10	1		PhH	42
16	**2**	**3**		**PhH**	**42**
17[c]	2	3	LiBr (2)	PhH	8
18[b]	1	2	LiBr (5)	PhH	trace
19[c]	2	1		PhH	38
20[c]	2	2		PhH	32
21[b]	3		O_2 (50 psi)	PhH	trace
22[c]	2	3	$K_2HPO_4 \cdot 3H_2O$ (1)	PhH	29

[a] BQ is an abbreviation for benzoquinone. [b] Compound **3f** was not completely consumed. [c] No **3f** was left.

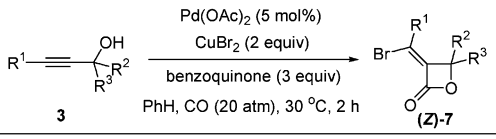
complex **M1**, which was followed by *cis*-chlorometalation to give **M2**. The subsequent coordination and insertion of CO gave metallocyclic intermediate **M3**, which was followed by reductive elimination to afford the major product (*Z*)-**5**. PdX_2 was regenerated by the oxidation reaction of the *in situ* generated Pd(0) with CuX_2 (cycle A). In cycle B, the complex **M1** undergoes *trans*-chlorometalation to give complex **M4**, which was followed by coordination and insertion of CO to afford metallocyclic intermediate **M5**. Reductive elimination of **M5** afforded the minor product (*E*)-**5**. In the cycle C, the intermediate **M6** was afforded by *trans*-chlorometalation with an opposite regioselectivity. Subsequent coordination and CO insertion gave six-membered intermediate **M7**, which yielded the other minor product **6** by reductive elimination.

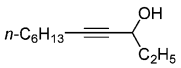
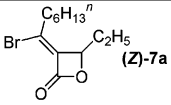
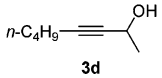
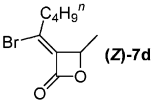
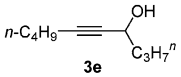
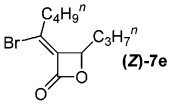
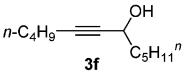
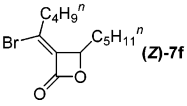
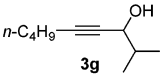
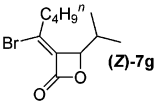
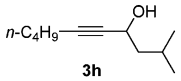
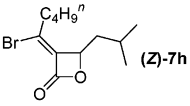
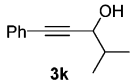
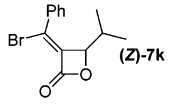
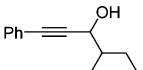
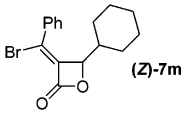
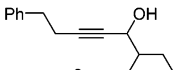
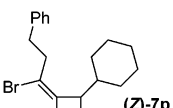
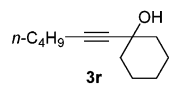
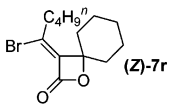
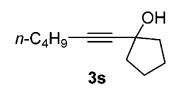
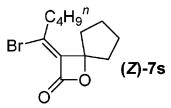
In conclusion, (1) we have developed a mild and efficient methodology for the synthesis of (*Z*)-α-chloroalkylidene-*β*-lactones in good regio- and stereoselectivity. (2) The highly optically active (*Z*)-α-chloroalkylidene-*β*-lactones could be easily formed from the readily available optically active propargylic alcohols. (3) Although the yields of (*Z*)-α-bromoalkylidene-*β*-lactones were low, due to the high activity, the coupling reactions of (*Z*)-α-bromoalkylidene-*β*-lactones were quite smooth to afford the coupling products in high yields. Further studies in this area are being conducted in our laboratory.

Experimental Section

Synthesis of Starting Material. Compounds **3a**−**y** were prepared by the reaction of the corresponding 1-alkynyllithium

TABLE 8. Pd(II)-Catalyzed Cyclocarbonylation of Various Propargylic Alcohols in the Presence of $CuBr_2$ and Benzoquinone



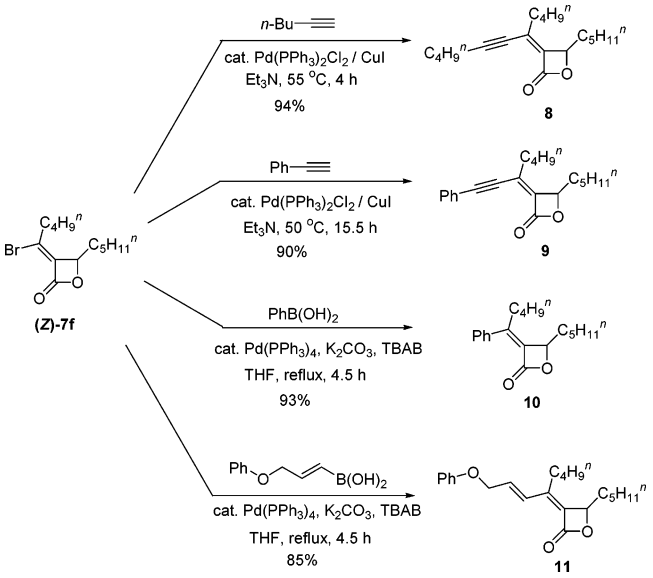
Entry	Substrate	Product	Isolated Yield (%)
1	 **3a**	 **(*Z*)-7a**	37
2	 **3d**	 **(*Z*)-7d**	26
3	 **3e**	 **(*Z*)-7e**	37
4	 **3f**	 **(*Z*)-7f**	42
5	 **3g**	 **(*Z*)-7g**	53
6	 **3h**	 **(*Z*)-7h**	40
7	 **3k**	 **(*Z*)-7k**	47
8	 **3m**	 **(*Z*)-7m**	29
9	 **3p**	 **(*Z*)-7p**	57
10	 **3r**	 **(*Z*)-7r**	41
11	 **3s**	 **(*Z*)-7s**	30

with aldehydes as reported.[12] The optically active propargylic alcohols (*S*)-**3k**−**p** were prepared according to Carreira's method.[13]

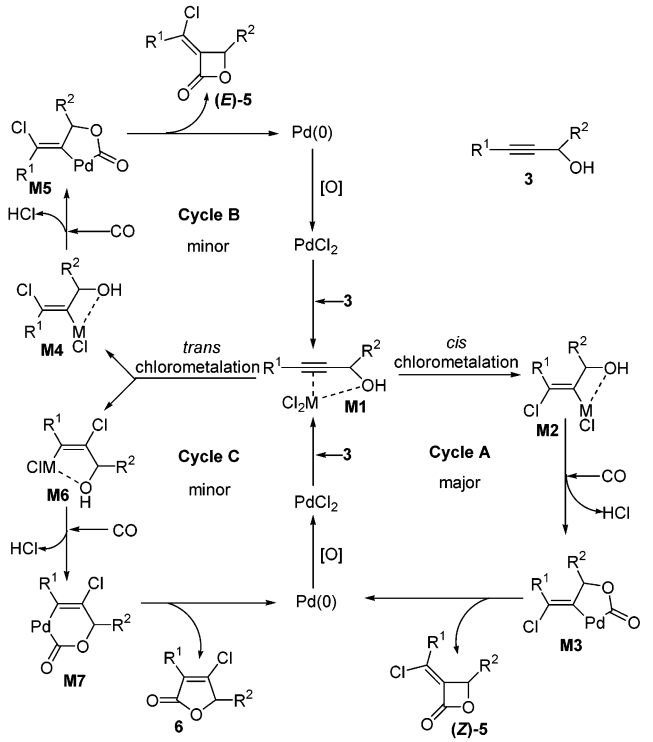
Compounds (*S*)-**3d** and (*S*)-**3q** were prepared via the kinetic resolution of racemic propargylic alcohols **3d** and **3q**.[14]

Synthesis of (*S*)-Oct-3-yn-2-ol ((*S*)-3d). Typical Procedure. To a solution of **3d** (5.072 g, 40.3 mmol) in 150 mL of vinyl acetate was added Novozym-435 (0.92 g). After being stirred at 60 °C for 28 h, the reaction mixture was worked up by filtration (ether). Evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether

SCHEME 5



SCHEME 6



= from 40/1 to 5/1) afforded (*R*)-**4d** (3.188 g, 47%) and (*S*)-**3d** (1.32 g, 26%). (*R*)-**4d**: 62% ee (GC condition: column, G-BP (20 m, 0.25 mm i.d., 0.25 μm df); carrier, N_2, 8.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 50 °C (30 min), then 1.0 °C/min to 80 °C), t_r = 44.2 (major), 44.8 (minor); $[\alpha]^{20}_D$ +78.9 (*c* 1.0, $CHCl_3$). (*S*)-**3d**: >99% ee (GC condition: column, G-BP (20 m, 0.25 mm i.d., 0.25 μm df); carrier, N_2, 10.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 70 °C (15 min)), t_r = 10.4 (major); $[\alpha]^{20}_D$ −23.5 (*c* 0.9, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.10−4.96 (m, 1 H), 2.20 (dt, J = 2.0 and 7.0 Hz, 2 H), 1.81 (br s, 1 H), 1.57−1.35 (m, 4 H), 1.43 (d, J = 6.6 Hz, 3 H), 0.91 (t, J = 6.9 Hz, 3 H).

Synthesis of (*R*)-Oct-3-yn-2-ol ((*R*)-3d). To a solution of **3d** (5.004 g, 39.7 mmol) in 150 mL of vinyl acetate was added Novozym-435 (0.9 g). After being stirred at 30 °C for 2 h, the

reaction mixture was worked up by filtration (ether). Evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether = from 40/1 to 5/1) afforded (*R*)-**4d** (2.216 g, 33%) and (*S*)-**3d** (2.498 g, 50%). (*R*)-**4d**: >99% ee (GC condition: column, Chirasil-DEX CB (25 m, 0.25 mm i.d., 0.25 μm df); carrier, N_2, 13.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 90 °C (2 min), then 1.0 °C/min to 110 °C), t_r = 14.2 (minor), 14.7 (major); $[\alpha]^{20}_D$ +138.9 (*c* 1.05, $CHCl_3$). (*S*)-**3d**: 62% ee (GC condition: column, G-BP (20 m, 0.25 mm i.d., 0.25 μm df); carrier, N_2, 10.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 70 °C (15 min)); t_r = 10.4 (major), 11.2 (minor).

To a solution of the above (*R*)-**4d** (2.176 g, 12.95 mmol, >99% ee) in 28 mL of CH_3OH was added KOH (871 mg, 15.54 mmol). After the solution was stirred at room temperature for 2 h, the solvent was removed in vacuo. The residue was extracted with 3 × 20 mL of Et_2O. The combined extracts were washed with saturated NaCl, dried with Na_2SO_4, filtered, concentrated, and purified via flash chromatography on silica gel (eluent: petroleum ether/ether = 5/1) to afford 1.363 g (84%) of (*R*)-**3d** with 99% ee as determined by GC analysis (column, G-BP (20 m, 0.25 mm i.d., 0.25 μm df); carrier,: N_2, 10.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 70 °C (15 min)); t_r = 10.4 (minor), 11.2 (major); $[\alpha]^{20}_D$ +23.8 (*c* 1.15, $CHCl_3$).

Synthesis of (*S*)-non-4-yn-3-ol ((*S*)-3q). To a solution of **3q** (5.003 g, 35.7 mmol) in 150 mL of vinyl acetate was added Novozym-435 (0.9 g). After being stirred at 60 °C for 24 h, the reaction mixture was worked up by filtration (ether). Evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether = from 30/1 to 5/1) afforded (*R*)-**4q** (3.447 g, 53%) and (*S*)-**3q** (2.007 g, 40%). (*R*)-**4q**: 79% ee (GC condition: column, Chirasil-DEX CB (25 m, 0.25 mm i.d. , 0.25 μm df); carrier, N_2, 13.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 90 °C (2 min), then 1 °C/min to 110 °C)); t_r = 19.5 (minor), 20.3 (major). (*S*)-**3q**: 98% ee (GC condition: column, Rt-βDEXcst-TM (30 m, 0.25 mm i.d. , 0.25 μm df); carrier, N_2, 13.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 95 °C (20 min), then 1 °C/min to 120 °C)); t_r = 31.6 (minor), 32.1 (major); $[\alpha]^{20}_D$ −3.1 (*c* 1.05, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.40−4.25 (m, 1 H), 2.22 (t, *J* = 6.3 Hz, 2 H), 1.81−1.60 (m, 3 H), 1.58−1.32 (m, 4 H), 1.00 (t, *J* = 7.5 Hz, 3 H), 0.91 (t, *J* = 7.2 Hz, 3 H).

Synthesis of (*R*)-Non-4-yn-3-ol ((*R*)-3q). To a solution of **3q** (3.003 g, 21.4 mmol) in 75 mL of vinyl acetate was added Novozym-435 (0.54 g). After being stirred at 30 °C for 6 h, the reaction mixture was worked up by filtration (ether). Evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether = from 40/1 to 5/1) afforded (*R*)-**4q** (1.336 g, 34%) and (*S*)-**3q** (1.605 g, 53%). (*R*)-**4q**: 99% ee (GC condition: column, Chirasil-DEX CB (25 m, 0.25 mm i.d. , 0.25 μm df); carrier, N_2, 13.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 90 °C (2 min), then 1 °C/min to 110 °C)); t_r = 19.6 (minor), 20.4 (major); $[\alpha]^{20}_D$ +108.4 (*c* 0.95, $CHCl_3$). (*S*)-**3q**: 61% ee (GC condition: column, Rt-βDEXcst-TM (30 m, 0.25 mm i.d. , 0.25 μm df); carrier, N_2, 13.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 95 °C (20 min), then 1 °C/min to 120 °C)); t_r = 31.3 (minor), 31.8 (major).

To a solution of the above (*R*)-**4q** (1.256 g, 6.9 mmol, 99% ee) in 15 mL of CH_3OH was added KOH (414 mg, 7.4 mmol). After the solution was stirred at room temperature for 10 min, the solvent was removed in vacuo. The residue was extrated with 3 × 20 mL of Et_2O. The combined extracts were washed with saturated NaCl, dried with Na_2SO_4, filtered, concentrated, and purified via flash chromatography on silica gel (eluent: petroleum ether/ether = 5/1) to afford 0.873 g (90%) of (*R*)-**3q** with >95% ee as determined by GC analysis (column, Rt-βDEXcst-TM (30 m, 0.25 mm i.d. , 0.25 μm df); carrier, N_2, 13.0 psi; injector, 250 °C; detector (FID, H_2, 0.218 Mpa), 250 °C; oven temperature, 95 °C (20 min), then 1 °C/min to 120 °C)); t_r = 31.2 (major), 32.4 (minor); $[\alpha]^{20}_D$ +4.6 (*c* 1.05, $CHCl_3$).

$PdCl_2$-Catalyzed Cyclocarbonylation of Secondary Propargylic Alcohols in the Presence of $CuCl_2$. Typical Procedure I. In a flame-dried argon-flushed flask, a solution of **3a** (157 mg, 0.93 mmol) and anhydrous $CuCl_2$ (635 mg, 4.7 mmol) in 9.3 mL of dry THF was stirred for 5 min at room temperature followed by the addition of $PdCl_2$ (16.5 mg, 0.093 mmol). Then the flask was transferred to a Parr pressure reactor. The Parr reactor was charged with 20 atm of CO gas. After the mixture was stirred for 4 h at 30 °C, the gas was ventilated, and the residue was diluted with Et_2O. Filtration through a short column of silica gel, evaporation, and flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 40/1) afforded 184 mg (86%) of (*Z*)-**5a**.

For the data of compounds (*Z*)-**5a**−**p**, (*Z*)-**5u**, and (*S*)-(*Z*)-**5k**−**p** see the Supporting Information of ref 11.

$PdCl_2$-Catalyzed Cyclocarbonylation of Various Tertiary Propargylic Alcohols in the Presence of $CuCl_2$. Typical Procedure II. Synthesis of (*Z*)-3-(1-Chloropentylidene)-1-oxaspiro[3.5]nonan-2-one ((*Z*)-5r). In a flame-dried argon-flushed flask, a solution of **3r** (180 mg, 1.0 mmol) and anhydrous $CuCl_2$ (675 mg, 5.0 mmol) in 10 mL of dry THF was stirred for 5 min at room temperature followed by the addition of $PdCl_2$ (17.7 mg, 0.1 mmol) and benzoquinone (324 mg, 3.0 mmol). Then the flask was transferred to a Parr pressure reactor. The Parr reactor was charged with 20 atm of CO gas. After the mixture was stirred at 30 °C for 2 h, the gas was ventilated, and the residue was diluted with CH_2Cl_2. Filtration through a short column of silica gel, evaporation, and flash chromatography on silica gel (eluent: petroleum ether/ether = 20/1) afforded 202 mg (86%) of (*Z*)-**5r** as a liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (t, *J* = 7.5 Hz, 2 H), 1.99 (dd, *J* = 1.8 and 12.9 Hz, 2 H), 1.90−1.55 (m, 9 H), 1.45−1.18 (m, 3 H), 0.96 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 161.6, 138.0, 136.5, 87.0, 35.4, 33.8, 28.9, 24.3, 21.8, 21.7, 13.7; MS (EI) *m/z* (%) 244 (M^+(^{37}Cl), 2.74), 242 (M^+(^{35}Cl), 6.85), 41 (100); IR (neat) 2934, 2862, 1813, 1700 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{19}{}^{35}ClO_2$ 242.1074, found 242.1077.

For the data of compounds (*S*)-(*Z*)-**5q** and (*R*)-(*Z*)-**5q** see the Supporting Information of ref 11.

Synthesis of (*Z*)-α-Bromoalkylidene-β-lactones via the Pd(II)-Catalyzed Cyclocarbonylation of Propargylic Alcohols in the Presence of $CuBr_2$. Typical Procedure III. Synthesis of (*Z*)-α-(1-Bromopentylidene)-β-(*n*-pentyl)-β-lactone ((*Z*)-7f). In a flame-dried argon-flushed flask, a solution of **3f** (179 mg, 0.98 mmol) and anhydrous $CuBr_2$ (452 mg, 2.02 mmol) in 10 mL of dry PhH was stirred for 5 min at room temperature followed by the addition of $Pd(OAc)_2$ (11 mg, 0.049 mmol) and benzoquinone (323 mg, 2.99 mmol). Then the flask was transferred to a Parr pressure reactor. The Parr reactor was charged with 20 atm of CO gas. After the mixture was stirred at 30 °C for 2 h, the gas was ventilated, and the residue was diluted with CH_2Cl_2. Filtration through a short column of silica gel, evaporation, and flash chromatography on silica gel (eluent: petroleum ether/ether = 30/1) afforded 118 mg (42%) of (*Z*)-**7f**. liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.00 (dd, *J* = 3.5 and 8.6 Hz, 1 H), 2.44 (t, *J* = 7.4 Hz, 2 H), 2.03−1.88 (m, 1 H), 1.88−1.25 (m, 11 H), 0.95 (t, *J* = 7.2 Hz, 3 H), 0.91 (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.0, 135.7, 129.6, 80.5, 37.6, 32.9, 31.3, 29.6, 24.0, 22.3, 21.7, 13.8, 13.7; MS (EI) *m/z* (%) 291 (M^+ + 1(^{81}Br), 3.24), 289 (M^+ + 1(^{79}Br), 3.89), 41 (100); IR (neat) 1813, 1698 cm^{-1}; HRMS (EI) calcd for $C_8H_{10}BrO_2$ (M^+ − C_5H_{11}) 216.9864, found 216.9848.

(*Z*)-α-(1-Hexynylpentylidene)-β-(*n*-pentyl)-β-lactone (8). A mixture of (*Z*)-**7f** (78 mg, 0.27 mmol), 1-hexyne (46 mg, 0.56 mmol), $Pd(PPh_3)_2Cl_2$ (1.8 mg, 0.0026 mmol), CuI (1.0 mg, 0.0052 mmol), and Et_3N (1.5 mL) was stirred at 55 °C for 4 h under nitrogen. After the reaction mixture was cooled to room

temperature, evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether = 30/1) afforded 73 mg (94%) of compound **8**. liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.97 (dd, J = 2.9 and 8.3 Hz, 1 H), 2.44 (t, J = 6.9 Hz, 2 H), 2.10 (t, J = 7.5 Hz, 2 H), 2.00−1.85 (m, 1 H), 1.83−1.65 (m, 1 H), 1.64−1.41 (m, 8 H), 1.41−1.24 (m, 6 H), 0.93 (m, 9 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.7, 139.2, 128.8, 102.2, 78.9, 76.5, 33.4, 33.1, 31.4, 30.3, 29.6, 24.2, 22.4, 22.1, 21.8, 19.4, 13.8, 13.7, 13.5; MS (EI) *m/z* (%) 290 (M^+, 0.70), 219 (100); IR (neat) 2218, 1809, 1681 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{30}O_2$ 290.2246, found 290.2239.

(*Z*)-α-(Phenylethynylpentylidene)-β-(*n*-pentyl)-β-lactone (9). A mixture of (*Z*)-**7f** (72 mg, 0.25 mmol), phenylacetylene (56 mg, 0.55 mmol), $Pd(PPh_3)_2Cl_2$ (1.7 mg, 0.0024 mmol), CuI (1.5 mg, 0.0079 mmol), and Et_3N (1.5 mL) was stirred at 50 °C for 15.5 h under nitrogen. After the reaction mixture was cooled to room temperature, evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether = 30/1) afforded 69 mg (90%) of compound **9** as a liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70−7.50 (m, 2 H), 7.50−7.25 (m, 3 H), 5.03 (dd, J = 3.6 and 8.1 Hz, 1 H), 2.21 (t, J = 7.4 Hz, 2 H), 2.07−1.89 (m, 1 H), 1.89−1.20 (m, 11 H), 0.96 (t, J = 7.4 Hz, 3 H), 0.91 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.4, 140.1, 132.1, 129.3, 128.3, 127.80, 122.0, 99.4, 85.0, 79.0, 33.1, 32.9, 31.4, 29.7, 24.2, 22.4, 22.2, 13.9, 13.8; MS (EI) *m/z* (%) 310 (M^+, 26.03), 239 (100); IR (neat) 2200, 1808, 1677 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{26}O_2$ 310.1933, found 310.1907.

(*Z*)-α-(1-Phenylpentylidene)-β-(*n*-pentyl)-β-lactone (10). A mixture of (*Z*)-**7f** (62 mg, 0.21 mmol), $PhB(OH)_2$ (33 mg, 0.27 mmol), $Pd(PPh_3)_4$ (11 mg, 0.0095 mmol), Bu_4NBr (5 mg, 0.016 mmol), and K_2CO_3 (87 mg, 0.63 mmol) in H_2O (0.3 mL) and THF (1.5 mL) was stirred under reflux for 4.5 h under nitrogen. After the reaction mixture was cooled to room temperature, it was extracted with Et_2O, washed with saturated NaCl, and dried over Na_2SO_4. Evaporation and purification by flash chromatography on silica gel (eluent: petroleum ether/ether = 30/1) afforded 57 mg (93%) of compound **10** as a liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62−7.48 (m, 2 H), 7.48−7.30 (m, 3 H), 5.04 (dd, J = 2.9 and 8.3 Hz, 1 H), 2.64−2.35 (m, 2 H), 2.14−1.96 (m, 1 H), 1.95−1.75 (m, 1 H), 1.73−1.48 (m, 2 H), 1.48−1.20 (m, 8 H), 0.91 (t, J = 7.1 Hz, 3 H), 0.86 (t, J = 6.9 Hz, 3 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 163.3, 148.3, 134.8, 132.5, 129.5, 128.3, 127.9, 78.2, 33.2, 32.9, 31.4, 30.0, 24.1, 22.5, 22.4, 13.9, 13.7; MS (EI) *m/z* (%) 286 (M^+, 15.33), 129 (100); IR (neat) 1802, 1682 cm^{-1}; HRMS (EI) calcd for $C_{19}H_{26}O_2$ 286.1933, found 286.1807.

(*Z*)-α-(1-(3-Phenoxy-1-(*E*)-propenyl)pentylidene)-β-(*n*-pentyl)-β-lactone (11). A mixture of (*Z*)-**7f** (61 mg, 0.21 mmol), $PhOCH_2CH{=}CHB(OH)_2$ (*E*-isomer) (48 mg, 0.27 mmol), $Pd(PPh_3)_4$ (11 mg, 0.0095 mmol), Bu_4NBr (5 mg, 0.016 mmol), K_2CO_3 (82 mg, 0.59 mmol) in H_2O (0.3 mL), and THF (1.5 mL) afforded 61 mg (85%) of compound **11** as a liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.25 (m, 2 H), 7.16 (dt, J = 1.3 and 16.2 Hz, 1 H), 7.02−6.88 (m, 3 H), 6.29 (dt, J = 5.9 and 16.2 Hz, 1 H), 4.99 (dd, J = 3.0 and 8.4 Hz, 1 H), 4.68 (dd, J = 1.3 and 5.6 Hz, 2 H), 2.24 (t, J = 7.7 Hz, 2 H), 2.04−1.88 (m, 1 H), 1.85−1.66 (m, 1 H), 1.62−1.17 (m, 10 H), 0.93 (t, J = 7.5 Hz, 6 H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 163.8, 158.2, 143.6, 134.2, 131.5, 129.4, 127.3, 121.0, 114.6, 78.6, 68.0, 33.0, 31.4, 31.2, 28.7, 24.2, 22.9, 22.4, 13.9, 13.7; MS (EI) *m/z* (%) 342 (M^+, 4.12), 55 (100); IR (neat) 1798, 1680 cm^{-1}; HRMS (EI) calcd for $C_{22}H_{30}O_3$ 342.2195, found 342.2183.

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Supporting Information Available: Typical experimental procedure and analytical data for all products not listed in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

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