

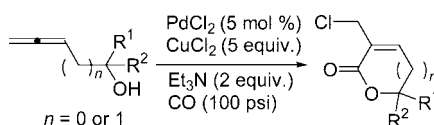
Efficient Synthesis of 3-Chloromethyl-2(5*H*)-furanones and 3-Chloromethyl- 5,6-dihydropyran-2-ones via the PdCl₂-Catalyzed Chlorocyclocarbonylation of 2,3- or 3,4-Allenols

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A mild and efficient methodology involving PdCl₂-catalyzed chlorocyclocarbonylation of 2,3- or 3,4-allenols with CuCl₂ for the synthesis of 3-chloromethyl-2(5*H*)-furanones and 3-chloromethyl-5,6-dihydropyran-2-ones was developed. This reaction proceeded in a highly regioselective manner, i.e., the chlorine atom was introduced to the terminal position of the allene moiety while the lactone linkage was formed between the center carbon atom of the allene moiety and the hydroxyl oxygen, which was established by the X-ray single crystal diffraction study of γ -lactone **3p**. The highly optically active 3-chloromethyl-2(5*H*)-furanones could be easily prepared from the readily available optically active 2,3-allenols. A mechanism for this reaction was proposed.

Introduction

2(5*H*)-Furanones and 5,6-dihydropyran-2-ones, important classes of oxygen-containing heterocyclic compounds, are common structural units in natural products¹ and important intermediates in organic synthesis.² 2(5*H*)-Furanone-containing compounds have been considered as potential insecticides, bactericides, fungicides, antibiotics, anticancer agents, antiinflammatories, allergy inhibitors, antisoriasis agents, cyclooxygenase inhibitors, phospholipase A₂ inhibitors, etc.³ Thus, much attention has been focused on the efficient and diverse synthesis

of 2(5*H*)-furanones⁴ and 5,6-dihydropyran-2-ones.⁵ Our group has also reported some methods for the synthesis of substituted 2(5*H*)-furanones based on the transition metal-promoted or

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-catalyzed cyclization reactions of 2,3-allenols.⁶ In addition, transition metal-catalyzed cyclocarbonylative cyclization reactions of (*Z*)-3-iodo-2-alkenols,⁷ 2-bromoaldehydes,⁸ (*Z*)-2-iodoalkenyl aryl or alkyl ketones,⁹ terminal or internal propargylic alcohols,¹⁰ 3-aryl-2-alkynones,¹¹ 1,6-alkynals or hex-5-ynoic acid pyridin-2-yl esters,¹² terminal alkynes/H₂O,¹³ and 4,6-di-*tert*-butylbenzofuran-2,3-dione/alkynes¹⁴ prove to be effective in constructing 2(*5H*)-furanones. However, reports concerning the synthesis of 5,6-dihydropyran-2-ones through metal-catalyzed cyclocarbonylation reactions are rare.^{15,16} In 2000, Takahashi et al.¹⁶ reported a successful cyclocarbonylation of 2,3- or 3,4-allenols to form 2(*5H*)-furanones and 5,6-dihydropyran-2-ones using a ruthenium catalyst. On the other hand, we recently described a PdCl₂-catalyzed chlorocyclocarbonylation of 2-alkynols for the efficient synthesis of (*Z*)- α -chloroalkylidene- β -lactones.¹⁷ On the basis of these results, we present here the regioselective chlorocyclocarbonylation of 2,3-

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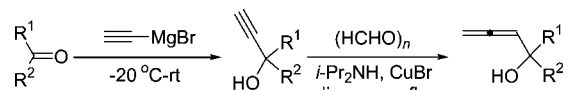
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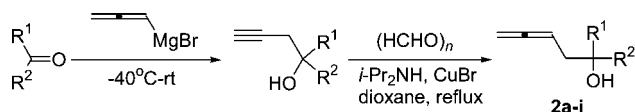
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SCHEME 1



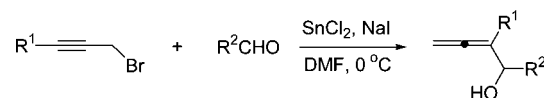
- 1a** R¹ = *n*-C₈H₁₇, R² = H (76%) **1j** R¹ = 4-ClC₆H₄, R² = H (66%)
1b R¹ = *n*-C₇H₁₅, R² = H (75%) **1k** R¹ = 4-BrC₆H₄, R² = H (65%)
1c R¹ = *n*-C₆H₁₃, R² = H (67%) **1l** R¹ = 1-naphthyl, R² = H (72%)
1d R¹ = *n*-C₅H₁₁, R² = H (69%) **1m** R¹ = 2-ClC₆H₄, R² = H (74%)
1e R¹ = PhCH₂CH₂, R² = H (68%) **1n** R¹ = 2,6-Cl₂C₆H₃, R² = H (58%)
1f R¹ = PhCH₂, R² = H (69%) **1o** R¹ = 4-EtC₆H₄, R² = H (72%)
1g R¹ = cyclohexyl, R² = H (65%) **1p** R¹, R² = (CH₂)₅ (71%)
1h R¹ = Ph, R² = H (67%) **1q** R¹, R² = (CH₂)₄ (51%)
1i R¹ = 4-FC₆H₄, R² = H (60%) **1r** R¹ = Ph, R² = Me (52%)

SCHEME 2



- 2a** R¹ = Ph, R² = H (34%)
2b R¹ = 4-EtC₆H₄, R² = H (45%)
2c R¹ = 4-ClC₆H₄, R² = H (44%)
2d R¹ = 2-ClC₆H₄, R² = H (54%)
2e R¹ = 4-BrC₆H₄, R² = H (43%)
2f R¹ = 4-PrⁱC₆H₄, R² = H (46%)
2g R¹ = 1-naphthyl, R² = H (47%)
2h R¹ = *n*-C₈H₁₇, R² = H (47%)
2i R¹ = *n*-C₅H₁₁, R² = H (47%)

SCHEME 3



- 1s** R¹ = *n*-C₆H₁₃, R² = Me
1t R¹ = *n*-C₅H₁₁, R² = 4-ClC₆H₄ (75%)

or 3,4-allenols affording 3-chloromethyl-2(*5H*)-furanones and 3-chloromethyl-5,6-dihydropyran-2-ones, respectively.

Results and Discussion

Preparation of the Starting Materials. All of the terminal 2,3- or 3,4-allenols (**1a–r** or **2a–i**) were synthesized by the Crabbé homologation of the corresponding terminal alkynols,¹⁸ which were easily obtained via the Grignard reaction of ethynyl magnesium bromide¹⁹ or allenyl magnesium bromide²⁰ with carbonyl compounds (Schemes 1 and 2). 2,3-Allenols **1s,t** were prepared from the reaction of the corresponding propargylic bromides with aldehydes in the presence of NaI and SnCl₂ (Scheme 3).²¹ 2-Methyl-4-phenylbuta-2,3-dienol (**1u**) was prepared by reduction of ethyl 2-methyl-4-phenyl-2,3-butadienoates with DIBAL-H.²²

Optically active (*R*)- or (*S*)-**1a–d** were also prepared via the Crabbé reaction of the corresponding (*R*)- or (*S*)-propargylic

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TABLE 1. PdCl₂-Catalyzed Chlorocyclocarbonylation of 1,2-Dodecadien-4-ol **1a** with CuCl₂

entry	solvent	isolated yield of 3a (%)
1	dioxane	18
2	toluene	19
3	benzene	trace
4	DMF	0
5	CH ₂ Cl ₂	57
6	THF	65
7	CH ₃ CN	66
8	THF ^a	66
9	CH ₃ CN ^a	70

^a 0.5 equiv of benzoquinone was added.

alcohols,^{18b} which are easily available from the kinetic enzymatic resolution of the corresponding racemic terminal propargylic alcohols.²³

Synthesis of 3-Chloromethyl-2(5H)-furanones via the PdCl₂-Catalyzed Chlorocyclocarbonylation of 2,3-Allenols. In our initial try, the reaction of 2,3-allenol **1a** failed to afford the chlorocarbonylative cyclization reaction under the same reaction conditions reported previously for the chlorocyclocarbonylation of 2-alkynols (10 mol % of PdCl₂ and 5 equiv of CuCl₂).¹⁷ To our delight, when 2 equiv of Et₃N were used as the base, 18% of chlorocarbonylative cyclization product 3-chloromethyl-5-octyl-2(5H)-furanone **3a** was isolated under the action of 5 mol % of PdCl₂ and 5 equiv of CuCl₂ in dioxane (entry 1, Table 1). The reaction is highly regioselective with the chlorine being introduced to the terminal position of the allene moiety and the lactone linkage being formed between the center carbon atom of the allene moiety and the hydroxyl oxygen. Further studies indicated that toluene, benzene, and DMF are poor solvents for this reaction (entries 2–4, Table 1). However, CH₂Cl₂, THF, or CH₃CN all provided the product **3a** in 57–66% yields (entries 5–7, Table 1). The addition of 0.5 equiv of benzoquinone²⁴ did not improve the yield of **3a** dramatically (entries 8 and 9, Table 1).

The effects of the loading of PdCl₂, the amount of Et₃N, and the pressure of CO were also examined (Table 2). The results indicated that 5 mol % of PdCl₂, 2 equiv of Et₃N, and 100 psi of CO are the best reaction conditions for this reaction (compare the results of Table 2 with entry 7, Table 1).

Therefore, we defined Conditions A (5 mol % of PdCl₂, 5 equiv of CuCl₂, 2 equiv of Et₃N, 100 psi of CO, CH₃CN, 30–35 °C) for the chlorocyclocarbonylation of 2,3-allenols (entry 7, Table 1). It should be noted that the reaction did not afford other cyclization products as judged from the ¹H NMR spectrum of the crude reaction mixture under the standard conditions.

To investigate the scope of the reaction, the chlorocyclocarbonylation of various 2,3-allenols **1** was conducted under Conditions A and the results are summarized in Table 3. Both secondary and tertiary alcohols afforded the products in moder-

TABLE 2. PdCl₂-Catalyzed Chlorocyclocarbonylation of 1,2-Dodecadien-4-ol **1a** with CuCl₂ in MeCN under Different Pressures of CO Using Different Amounts of PdCl₂ and Et₃N

entry	PdCl ₂ (mol %)	Et ₃ N (equiv)	CO (psi)	isolated yield of 3a (%)
1	3	2	100	60
2	10	2	100	63
3	5	2	1 atm ^a	55
4	5	2	200	61
5	5	1	100	59
6	5	3	100	52

^a This reaction was conducted with a balloon of CO.

TABLE 3. PdCl₂-Catalyzed Chlorocyclocarbonylation of Various 2,3-Allenols with CuCl₂

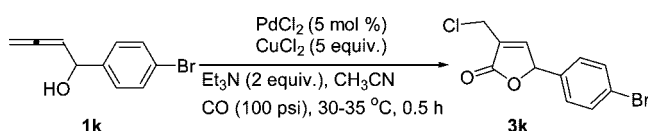
entry	substrate 1	R ¹	R ²	time (h)	isolated yield of 3 ^a (%)
1	1a	<i>n</i> -C ₈ H ₁₇	H	1	66 (3a)
2	1b	<i>n</i> -C ₇ H ₁₅	H	1	65 (3b)
3	1c	<i>n</i> -C ₆ H ₁₃	H	1	66 (3c)
4	1d	<i>n</i> -C ₅ H ₁₁	H	1	69 (3d)
5	1e	PhCH ₂ CH ₂	H	1	74 (3e)
6	1f	PhCH ₂	H	1	70 (3f)
7	1g	cyclohexyl	H	1	70 (3g)
8	1h	Ph	H	0.5	62 (3h)
9	1i	4-FC ₆ H ₄	H	0.5	66 (3i)
10	1j	4-ClC ₆ H ₄	H	0.5	67 (3j)
11	1k	4-BrC ₆ H ₄	H	0.5	69 (3k)
12	1l	1-naphthyl	H	0.5	70 (3l)
13	1m	2-ClC ₆ H ₄	H	0.5	65 (3m)
14	1n	2,6-Cl ₂ C ₆ H ₃	H	0.5	66 (3n)
15	1o	4-EtC ₆ H ₄	H	0.5	50 (3o)
16	1p	-(CH ₂) ₅ -		1	59 (3p)
17	1q	-(CH ₂) ₄ -		1	24 (3q)
18	1r	Ph	Me	1	42 (3r)

^a For entries 1–7 and 16–18 the eluent = petroleum ether and ethyl ether or ethyl acetate (10:1); for entries 8–15 the eluent = dichloromethane and petroleum ether (5:1).

ate to good yields with the 2- and 4-position substituents all being hydrogen. R¹ may be an alkyl group, benzyl, or an aryl group and R² can be hydrogen or an alkyl group. To our disappointment, under identical conditions, 2-substituted, 4-non-substituted, or 2,4-disubstituted 2,3-allenols such as **1s–u** failed to undergo this transformation although the starting materials were completely consumed. It should be pointed out that the yields of products **3h–o** with R¹ = aryl and R² = hydrogen were dramatically decreased when petroleum ether and ethyl ether or ethyl acetate (10:1) were used as the eluents for flash chromatography on silica gel. However, when a mixture of CH₂Cl₂ and petroleum ether was used as the eluent, the isolated yield of **3k** was improved (Table 4). Compounds **3a–g** and **3p–r** were isolated by using petroleum ether and ethyl ether or ethyl acetate (10:1) as the eluents for flash chromatography without any difficulty. In addition, the substrate **1o** having an electron-donating ethyl group at the para position of the aromatic ring afforded the corresponding product **3o** in somewhat lower

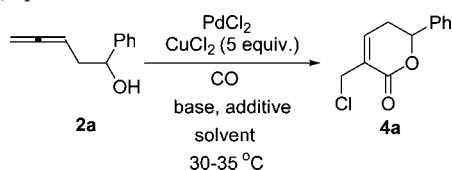
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TABLE 4. PdCl₂-Catalyzed Chlorocyclocarbonylation of **1k** with CuCl₂ Using Different Eluents for Flash Chromatography

entry	eluent for flash chromatography	isolated yield of 3k (%)
1 ^a	DCM/PE=1:1	34
2 ^b	DCM/PE=2:1	53
3 ^b	DCM/PE=3:1	64
4 ^b	DCM/PE=4:1	68
5 ^b	DCM/PE=5:1	69
6 ^b	DCM/PE=6:1	68

^a Reaction mixture was filtrated through a short column of silica gel before being subjected to flash chromatography on silica gel. ^b Reaction mixture was evaporated directly before being subjected to flash chromatography on silica gel.

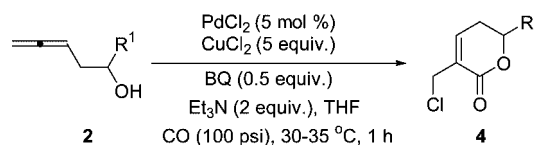
TABLE 5. PdCl₂-Catalyzed Chlorocyclocarbonylation of 1-Phenyl-3,4-pentadien-1-ol **2a** with CuCl₂

entry	PdCl ₂ (mol %)	CO (psi)	base (equiv)	additive (equiv)	solvent	time (h)	isolated yield of 4a (%)
1	10	300			THF	4	complicated
2	5	100	Et ₃ N (2)		CH ₃ CN	1	35
3	5	60	NaOAc (3)		CH ₃ CN	2	35
4	10	60	NaOAc (3)		HOAc	3	33
5 ^a	10	60	NaOAc (3)		dioxane	2	NR
6 ^b	10	60	NaOAc (3)		DMF	2	0
7 ^a	10	60			Et ₃ N	2	NR
8	5	100	Et ₃ N (2)		THF	1	48
9	5	100	Et ₃ N (2)	BQ ^c (0.1)	THF	1	50
10	5	100	Et ₃ N (2)	BQ (0.5)	THF	1	53
11	5	100	Et ₃ N (2)	BQ (1.0)	THF	1	53

^a Compound **2a** was not completely consumed. ^b No **2a** was left. ^c BQ is an abbreviation for benzoquinone.

yield (entry 15, Table 3) as compared to substrates **1h–n** (entries 8–14, Table 3). The reaction of **1q** with a five-membered ring afforded the corresponding product **3q** in 24% yield probably due to its instability. The butenolide structures of products **3** and the regioselectivity were established by the single crystal X-ray diffraction study of **3p** (see Figure S6 in the Supporting Information).²⁵

Synthesis of 3-Chloromethyl-5,6-dihydropyran-2-ones via the PdCl₂-Catalyzed Chlorocyclocarbonylation of 3,4-Allenols. Stimulated by the above successful results, we wanted to expand the current reaction from 2,3-allenols to 3,4-allenols. Again, the reaction of 3,4-allenol **2a** failed to afford the chlorocarbonylative cyclization reaction under the same reaction conditions reported previously for the chlorocyclocarbonylation of 2-alkynols (entry 1, Table 5).¹⁷ Gratifyingly, under Conditions A successfully applied for the 2,3-allenols, pyran-2-one **4a** was obtained in 35% yield (entry 2, Table 5). No improvement of yield was observed when NaOAc was used as the base instead of Et₃N (entry 3, Table 5). When HOAc was used instead of CH₃CN as the solvent, the yield dropped slightly (entry 4, Table

TABLE 6. PdCl₂-Catalyzed Chlorocyclocarbonylation of Various 3,4-Allenols with CuCl₂

entry	substrate 2	R ¹	product 4	isolated yield (%)
1	2a	Ph	4a	53
2	2b	4-EtC ₆ H ₄	4b	46
3	2c	4-ClC ₆ H ₄	4c	55
4	2d	2-ClC ₆ H ₄	4d	54
5	2e	4-BrC ₆ H ₄	4e	55
6	2f	4-Pr ^t C ₆ H ₄	4f	43
7	2g	1-naphthyl	4g	53
8	2h	<i>n</i> -C ₈ H ₁₇	4h	30
9	2i	<i>n</i> -C ₅ H ₁₁	4i	23

5). Further studies showed that dioxane, DMF, and Et₃N are all poor solvents for this reaction (entries 5–7, Table 5). When THF was used as the solvent, the yield was improved to 48% (entry 8, Table 5). When benzoquinone (0.5 equiv.), which has been extensively used for the oxidation of Pd(0) to Pd(II) under acidic conditions,²⁴ was added to the reaction mixture, the yield of product was slightly improved to 53% (compare entry 10 with entry 8, Table 5). With more benzoquinone no further improvement of the yield was observed (entry 11, Table 5). Thus, we defined Conditions B (5 mol % of PdCl₂, 5 equiv of CuCl₂, 2 equiv of Et₃N, 100 psi of CO, 0.5 equiv of benzoquinone, THF, 30–35 °C) for the chlorocyclocarbonylation of 3,4-allenols (entry 10, Table 5). It should be noted that the reaction did not afford other cyclization products as judged from the ¹H NMR spectrum of the crude reaction mixture under the standard conditions.

Some typical results for the chlorocyclocarbonylation of 3,4-allenols are listed in Table 6. Similar to the results of 2,3-allenols, 1-substituted 3,4-allenols **2a–i** underwent the cyclocarbonylation smoothly and highly regioselectively to afford 3-chloromethyl-5,6-dihydropyran-2-ones **4a–i** in moderate yields (entries 1–9, Table 6). The substrates **2h,i** having alkyl groups at the 1-position afforded the corresponding products **4h,i** in much lower yields as compared to the reaction of substrates **2a–g** with aryl groups at the same position.

Preparation of Optically Active 3-Chloromethyl-2(5*H*)-furanones. With the successful chlorocyclocarbonylation protocol for the synthesis of 3-chloromethyl-2(5*H*)-furanones in hand, further studies were conducted to see the possibility of synthesizing optically active 3-chloromethyl-2(5*H*)-furanones under the established Conditions A. Some typical results are summarized in Table 7. From Table 7, it can be concluded that racemization of the chiral center in (*R*)- or (*S*)-**3** was not observed with the yields ranging from 64% to 70%.

NMR Spectra. In the light of X-ray single crystal diffraction analysis of compound **3p**, we established the structure of the products obtained from this PdCl₂-catalyzed chlorocyclocarbonylation of 2,3- or 3,4-allenols. However, there are some noteworthy characteristics in the NMR spectra of products **3** and **4**. The related information is available in the Supporting Information.

Mechanistic Considerations. A rationale for the PdCl₂-catalyzed regioselective chlorocyclocarbonylation of 2,3- or 3,4-allenols is shown in Scheme 4. The selective coordination of the terminal double bond in **1** or **2** with PdCl₂ gives coordination

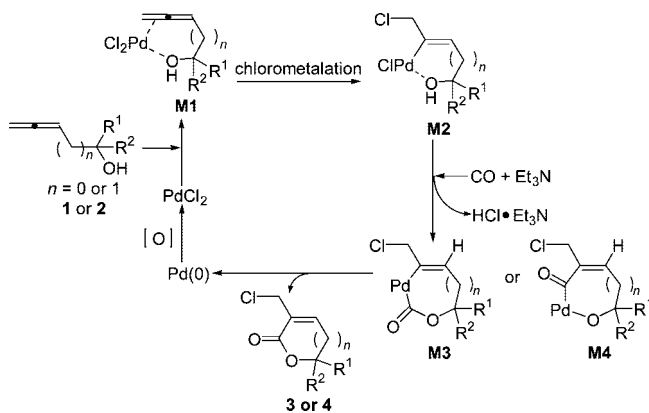
(25) For the crystal data and ORTEP representation of compound **3p**, see the Supporting Information.

TABLE 7. Synthesis of Optically Active 3-Chloromethyl-5*H*-furan-2-ones

entry	substrate	product 3	yield (%) of 3^a	ee (%) of 3^b
1			70	99
	(R)- 1a , >99% ee	(R)- 3a		
2			69	97
	(S)- 1a , 97% ee	(S)- 3a		
3			68	99
	(R)- 1b , >99% ee	(R)- 3b		
4			69	99
	(S)- 1b , 99% ee	(S)- 3b		
5			69	99
	(R)- 1c , >99% ee	(R)- 3c		
6			69	96
	(S)- 1c , 96% ee	(S)- 3c		
7 ^c			64	99
	(R)- 1d , >99% ee	(R)- 3d		
8			70	93
	(S)- 1d , 93% ee	(S)- 3d		

^a Isolated yield. ^b ee value was determined by HPLC. ^c The reaction was carried out under Conditions B.

complex **M1**, which is followed by the highly regioselective chlorometalation to give the cyclic vinylic intermediate **M2** by introducing the chlorine atom to the terminal position of the allene moiety.²⁶ Subsequent coordination and insertion of CO affords metallocyclic intermediates **M3** or **M4**. Reductive

SCHEME 4

elimination of **M3** or **M4** affords **3** or **4** and Pd(0), which is oxidized with oxidant to regenerate the catalytically active species PdCl₂.

Conclusion

In summary, we have developed a mild and efficient methodology for the regioselective synthesis of 3-chloromethyl-2(5*H*)-furanones and 3-chloromethyl-5,6-dihydropyran-2-ones in moderate to good yields. The key step of this reaction may involve the highly regioselective chlorometalation of PdCl₂ with the terminal double bond in allenols by introducing the chlorine atom to the terminal position of the allene moiety, which has similar regioselectivity as in the copper(I) chloride-mediated carbometalation of 2,3-allenols with Grignard reagents reported recently by our group.^{26c} Highly optically active 3-chloromethyl-2(5*H*)-furanones can be easily formed from the readily available optically active 2,3-allenols. Further studies in this area are being conducted in our laboratory.

Experimental Section

PdCl₂-Catalyzed Chlorocyclocarbonylation of 2,3-Allenols in the Presence of CuCl₂. Preparation of 3-Chloromethyl-2(5*H*)-furanones 3a–g and 3p–r. Typical Procedure I (Conditions A): Synthesis of 3-Chloromethyl-5-octyl-2(5*H*)-furanone (3a). 2,3-Allenol **1a** (92 mg, 0.50 mmol), anhydrous CuCl₂ (336 mg, 2.50 mmol), PdCl₂ (5 mg, 0.028 mmol), CH₃CN (6 mL), and Et₃N (102 mg, 1.01 mmol) were added sequentially to a glass vessel containing a stirring bar placed in a stainless-steel autoclave with stirring. The autoclave was flushed three times with 150 psi of CO gas. The autoclave was then charged with 100 psi of CO gas. After the mixture was stirred for 1 h at 30–35 °C (oil bath), the excess CO gas was vented, and the residue was diluted with Et₂O. Filtration through a short column of silica gel, evaporation, and flash chromatography on silica gel (eluent: petroleum ether/ethyl ether = 10:1) afforded 82 mg (66%) of **3a**: liquid; ¹H NMR (500 MHz, CDCl₃) δ 7.40 (q, *J* = 1.8 Hz, 1 H), 5.00–4.94 (m, 1 H), 4.22 (t, *J* = 1.8 Hz, 2 H), 1.80–1.69 (m, 1 H), 1.68–1.60 (m, 1 H), 1.49–1.16 (m, 12 H), 0.85 (t, *J* = 7.0 Hz, 3 H); ¹³C NMR (75.4 MHz, CDCl₃) δ 171.0, 152.0, 130.8, 81.6, 35.9, 33.0, 31.6, 29.2, 29.1, 29.0, 24.8, 22.5, 14.0; MS (EI) *m/z* (%) 246 (M⁺(³⁷Cl), 2.10), 244 (M⁺(³⁵Cl), 5.11), 57 (100); IR (neat) 2927, 1761, 1653, 1466, 1341, 1087 cm⁻¹; HRMS (EI) calcd for C₁₃H₂₁O₂³⁵Cl (M⁺) 244.1230, found 244.1232.

Preparation of 3-Chloromethyl-2(5*H*)-furanones 3h–o. Compounds **3h–o** were synthesized following typical procedure I except that the reaction time was reduced to 0.5 h, the reaction mixture was evaporated directly before being subjected to flash chroma-

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tography on silica gel, and the eluent used for flash chromatography is a 5:1 mixture of dichloromethane and petroleum ether.

PdCl₂-Catalyzed Chlorocyclocarbonylation of 3,4-Allenols in the Presence of CuCl₂. Preparation of 3-Chloromethyl-5,6-dihydropyran-2-ones 4a–i. Typical Procedure II (Conditions B): Synthesis of 3-Chloromethyl-6-(2'-chlorophenyl)-5,6-dihydropyran-2-one (4d). 3,4-Allenol **2d** (197 mg, 1.01 mmol), anhydrous CuCl₂ (672 mg, 5.00 mmol), PdCl₂ (9 mg, 0.051 mmol), benzoquinone (54 mg, 0.50 mmol), THF (12 mL), and Et₃N (202 mg, 2.00 mmol) were added sequentially to a glass vessel containing a stirring bar placed in a stainless-steel autoclave with stirring. The autoclave was flushed three times with 150 psi of CO gas. The autoclave was then charged with 100 psi of CO gas. After the mixture was stirred for 1 h at 30–35 °C (oil bath), the excess CO gas was ventilated, and the residue was diluted with Et₂O. Filtration through a short column of silica gel, evaporation, and flash chromatography on silica gel (eluent: dichloromethane/petroleum ether = 1:1) afforded 141 mg (54%) of **4d**: solid; mp 102–104 °C (petroleum ether/ethyl acetate); ¹H NMR (500 MHz, CDCl₃) δ 7.64 (dd, *J* = 7.5 and 1.5 Hz, 1 H), 7.40–7.28 (m, 3 H), 7.13–7.07 (m, 1 H), 5.84 (dd, *J* = 12.2 and 3.8 Hz, 1 H), 4.41 (dm, *J* = 13.0 Hz, 1 H), 4.34 (dm, *J* = 13.0 Hz, 1 H), 2.89 (ddd, *J* = 18.5, 6.3, and 3.8 Hz, 1 H), 2.56 (ddq, *J* = 18.5, 12.2, and 2.2 Hz, 1 H); ¹³C NMR (75.4 MHz, CDCl₃) δ 163.2, 142.4, 135.7, 131.2, 129.6, 129.5, 129.1, 127.34, 127.32, 76.0, 41.1, 30.5; MS (EI) *m/z* (%) 260 (M⁺(2

× ³⁷Cl), 0.85), 258 (M⁺(³⁷Cl, ³⁵Cl), 4.33), 256 (M⁺(2 × ³⁵Cl), 6.40), 116 (100); IR (neat) 3066, 2964, 1728, 1596, 1574, 1479, 1378, 1234, 1122 cm⁻¹. Anal. Calcd for C₁₂H₁₀O₂Cl₂: C, 56.06; H, 3.92. Found: C, 55.94; H, 3.80.

Synthesis of (5*R*)-3-Chloromethyl-5-octyl-2(5*H*)-furanone ((5*R*)-(3a)) Following Typical Procedure I. The reaction of (*R*)-**1a** (182 mg, 1.00 mmol, >99% ee), anhydrous CuCl₂ (673 mg, 5.01 mmol), PdCl₂ (9 mg, 0.051 mmol), and Et₃N (202 mg, 2.00 mmol) in 12 mL of CH₃CN afforded 172 mg (70%) of (5*R*)-**3a** with 99% ee as determined by HPLC analysis (Chiralcel OJ-H, *n*-hexane:*i*-PrOH = 90:10, 0.7 mL/min, 214 nm), *t*_r 12.5 (minor), 14.0 (major); [α]_D²⁰ -32.9 (*c* 1.05, CHCl₃).

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Supporting Information Available: General procedures and analytical data for compounds **1**, **2**, **3**, and **4**, ¹H and ¹³C NMR spectra of these compounds, and CIF file of **3p**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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