

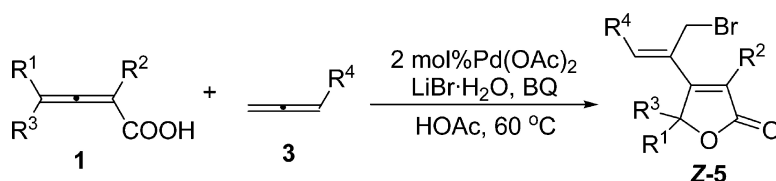
Article

Palladium Acetate-Catalyzed Cyclization Reaction of 2,3-Allenic Acids in the Presence of Simple Allenes: An Efficient Synthesis of 4-(1'-Bromoalk-2'(Z)-en-2'-yl)furan-2(5H)-one Derivatives and the Synthetic Application

Zhenhua Gu, Xinke Wang, Wei Shu, and Shengming Ma

J. Am. Chem. Soc., **2007**, 129 (35), 10948-10956 • DOI: 10.1021/ja072790j • Publication Date (Web): 11 August 2007

Downloaded from <http://pubs.acs.org> on February 15, 2009



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 15 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

[View the Full Text HTML](#)



ACS Publications
 High quality. High impact.

**Palladium Acetate-Catalyzed Cyclization Reaction of
2,3-Allenic Acids in the Presence of Simple Allenes:
An Efficient Synthesis of
4-(1'-Bromoalk-2'(Z)-en-2'-yl)furan-2(5H)-one Derivatives and
the Synthetic Application**

Zhenhua Gu, Xinke Wang, Wei Shu, and Shengming Ma*

*Contribution from the State Key Laboratory of Organometallic Chemistry, Shanghai Institute of
Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032,
People's Republic of China*

Received April 30, 2007; E-mail: masm@mail.sioc.ac.cn

Abstract: We have realized a cyclization reaction of 2,3-allenoic acids **1** in the presence of simple alkyl- or aryl-substituted allenes **3**. In this reaction, the cyclic oxypalladation of 2,3-allenoic acid with Pd(II) would afford the furanonyl palladium intermediate **2**, which could be trapped by the simple allene to afford a π -allylic intermediate *anti*-**9**. This intermediate *anti*-**9** could be nucleophilically attacked by Br⁻ to yield 4-(1'-bromoalk-2'(Z)-en-2'-yl)furan-2(5H)-one derivatives **Z-5** and Pd(0). The in-situ formed Pd(0) was efficiently converted to the catalytically active Pd(II) species by benzoquinone in HOAc. The functional groups, such as malonate, acetoxyl, and phthalic amide in allene **3**, are tolerable under the current conditions. High efficiency of chirality transfer was observed when optically active 2,3-allenoic acids were used, which reveals that the formation of the intermediates **2** was a highly stereoselective *anti*-oxypalladation process. The highly selective formation of Z-isomer may be explained by face-selective coordination of allene **3** with the palladium atom in intermediate **2**: the palladium atom coordinates to the terminal C=C double bond of allene **3** from the face opposite to the substituent group to avoid the steric congestion. The products **Z-5** could be further elaborated via the S_N2 nucleophilic substitution with amine or sodium benzenesulfinate, the reduction of the C-Br bond by NaBH₄, and the CuBr-SMe₂-catalyzed S_N2'-substitution with CH₃MgBr.

Introduction

Butenolides [2(5H)-furanones], a unit occurring in a large number of natural products,¹ have caught the attention of both organic and bioorganic chemists because many of the butenolide-containing compounds may be considered as potential insecticides, bactericides, fungicides, and phospholipase A₂ inhibitors, etc.^{2,3} Butenolides are also versatile building blocks

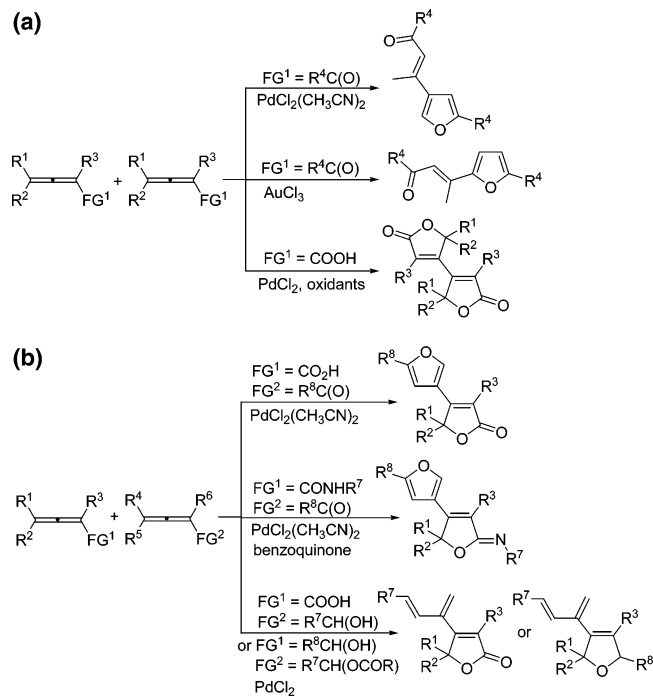
for the synthesis of a wide variety of biologically active compounds and complex natural products.⁴ Despite these achievements, the development of efficient synthetic methods leading to the formation of this class of compounds with a new structural feature readily for further elaboration is still of current interest.

On the other hand, the transition metal-catalyzed cyclization reaction of functionalized allenes has caught the attention of many synthetic chemists due to its unique reactivity and stereoselectivity.⁵⁻⁷ Recently, much attention has been paid to the reactions involving two same or different allenes (Scheme 1). Three type of reactions have been observed in the ho-

- (1) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192.
- (2) For some of the most recent examples, see: (a) Chia, Y.; Chang, F.; Wu, Y. *Tetrahedron Lett.* **1999**, *40*, 7513. (b) Evidente, A.; Sparapano, L. *J. Nat. Prod.* **1994**, *57*, 1720. (c) Damtoft, S.; Jensen, S. R. *Phytochemistry* **1995**, *40*, 157. (d) Estévez-Reyes, R.; Estévez-Braun, A.; González, A. G. *J. Nat. Prod.* **1993**, *56*, 1177. (e) Seki, T.; Satake, M.; Mackenzie, L.; Kaspar, H. F.; Yasumoto, T. *Tetrahedron Lett.* **1995**, *36*, 7093. (f) Cambie, R. C.; Bergquist, P. R.; Karuso, P. *J. Nat. Prod.* **1988**, *51*, 1014.
- (3) (a) Deshong, P.; Sidler, D. R.; Slough, G. A. *Tetrahedron Lett.* **1987**, *28*, 2233. (b) Marshall, J. A.; Wolf, M. A. *J. Org. Chem.* **1996**, *61*, 3238. (c) Xiao, W.; Alper, H. *J. Org. Chem.* **1997**, *62*, 3422. (d) Cowell, A.; Stille, J. K. *Tetrahedron Lett.* **1979**, *20*, 133. (e) Marshall, J. A.; Bartley, G. S.; Wallace, E. M. *J. Org. Chem.* **1996**, *61*, 5729. (f) Clough, J. M.; Pattenden, G.; Wight, P. G. *Tetrahedron Lett.* **1989**, *30*, 7469. (g) Yoneda, E.; Kaneko, T.; Zhang, S.; Onitsuka, K.; Takahashi, S. *Org. Lett.* **2000**, *2*, 441. (h) Renurd, M.; Ghosez, L. A. *Tetrahedron* **2001**, *57*, 2597. (i) Linclau, B.; Boydell, A. J.; Clarke, P. J.; Horan, R.; Jacquet, C. *J. Org. Chem.* **2003**, *68*, 1821. (j) Hakimelahi, G. H.; Mei, N.-W.; Moosavi-Movahedi, A. A.; Davari, H.; Hakimelahi, S.; King, K.-Y.; Ru Hwu, J.; Wen, Y.-S. *J. Med. Chem.* **2001**, *44*, 1749. (k) Marshall, J. A.; Piettre, A.; Paige, M. A.; Valeriote, F. *J. Org. Chem.* **2003**, *68*, 1780. (l) Ma, S.; Lu, L.; Lu, P. *J. Org. Chem.* **2005**, *70*, 1063. (m) Ma, S.; Gu, Z.; Deng, Y. *Chem. Commun.* **2006**, *94*. (n) Ma, S.; Duan, D.; Shi, Z. *Org. Lett.* **2000**, *2*, 1419.

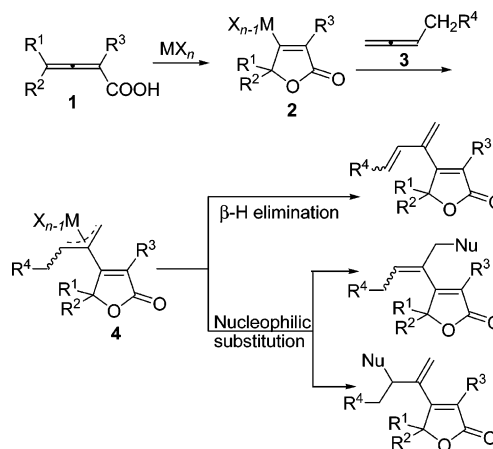
- (4) (a) Renard, M.; Ghosez, L. A. *Tetrahedron* **2001**, *57*, 2597. (b) Feringa, B. L.; de Lange, B.; Jansen, J. F. G. A.; de Jong, J. C.; Lubben, M.; Faber, W.; Schudde, E. P. *Pure Appl. Chem.* **1992**, *64*, 1865. (c) Dehoux, C.; Gorrichon, L.; Baltas, M. *Eur. J. Org. Chem.* **2001**, 1105-1113. (d) Jauch, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2764-2765. (e) Kedar, T. E.; Miller, M. W.; Hegedus, L. S. *J. Org. Chem.* **1996**, *61*, 6121.
- (5) (a) Patai, S. *The Chemistry of Ketenes, Allenes, and Related Compounds*; John Wiley & Sons: New York, 1980; Part 1. (b) Schuster, H. F.; Coppola, G. M. *Allenenes in Organic Synthesis*; John Wiley & Sons: New York, 1984. (c) Landor, S. R., Ed. *The Chemistry of the Allenes*; Academic Press: London, 1982; Vol. 1. (d) Krause, N.; Hashmi, A. S. K., Eds. *Modern Allene Chemistry*; Wiley-VCH: Weinheim, 2004; Vols. 1-2.
- (6) (a) Zimmer, R. C.; Dinesh, U.; Nandan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (b) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196. (c) Reissig, H.-U.; Schade, W.; Amombo, M. O.; Pulz, R.; Hausherr, A. *Pure Appl. Chem.* **2002**, *74*, 175. (d) Ma, S. *Chem. Rev.* **2005**, *105*, 2829 and references therein. (e) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701.

Scheme 1. The Reaction Patterns Involving Two Functionalized Allenes: (a) Intermolecular Homodimerization Reaction of Functionalized Allenes; (b) Intermolecular Heterodimerization Reaction of Functionalized Allenes



modimerization reaction of functionalized allenes (Scheme 1a): The first palladium-catalyzed homodimerization reaction of 1,2-allenyl ketones has been reported by Hashmi et al. in 1995, which led to the formation of the monocyclic 3-(3'-oxo-1'-alkenyl)-substituted furan derivatives.⁸ Interestingly, the reaction of 1,2-allenyl ketones would also afford 2-(3'-oxo-1'-alkenyl)-substituted furan derivatives when AuCl₃ was used as the catalyst.⁹ In 2003, we have reported the homodimerization of 2,3-allenoic acids affording bicyclic bibutenolides.¹⁰ In the area of heterodimerization (Scheme 1b), we have successfully realized the reactions between 2,3-allenoic acids or 2,3-allenamides and 1,2-allenyl ketones, in which both allenes were cyclized to form products with two different rings.¹¹ However, it is interesting to observe that in the palladium-catalyzed cyclization of 2,3-allenoic acids in the presence of 2,3-allenols the 2,3-allenoic acids were cyclized while 2,3-allenols formed the 1,3-dienyl units via β -hydroxide elimination.¹² Recently, Alcaide and co-workers also reported the similar cross-coupling cyclization reaction of α -allenols in the presence of 2,3-allenyl carboxylates.¹³ In these reactions involving two different classes

Scheme 2. The Proposed Reaction Pathways for the Cyclization of 2,3-Allenic Acids in the Presence of Simple Allenes



of allenes, at least one allene cyclized and the catalyst was regenerated via β -heteroatom elimination or protonolysis with the aid of the second functionalized allenes. To the best of our knowledge, there is no report on the cross-coupling cyclization reaction between a functionalized allene and a non-functionalized simple allene.

With this notion in mind, we proposed the following path to realize this type of reaction (Scheme 2). First, the interaction of 2,3-allenoic acids **1** with Pd(OAc)₂ would form intermediate **2** via cyclic oxypalladation.^{6c} Next, regioselective carbopalladation of simple allene **3** with **2** would give a π -allylic intermediate **4**,¹⁴ which may undergo β -elimination¹⁵ or nucleophilic substitution¹⁴ to yield different products and Pd(0). Thus, the challenge here would be the regeneration of the catalyst, match of the reactivities of these two very different types of allenes, and the control of regio- and stereochemistry. Herein, we report a protocol for the cyclization reaction of 2,3-allenoic acids in the presence of alkyl- or aryl-substituted allenes with the nice control of the regio- and stereoselectivity.

Results and Discussion

Our efforts in this area started with the reaction of 2,3-allenoic acid **1a** and hepta-1,2-diene **3a**. After some screening, it was observed that the reaction of **1a** with **3a** in the presence of 5 mol % Pd(OAc)₂, 110 mol % of benzoquinone (BQ),¹⁶ and 200 mol % of LiBr·H₂O in HOAc afforded **Z-5aa** in 53% yield (Table 1, entry 1). The yield dropped when only 1.5 equiv of **3a** was used (Table 1, entry 2). The reaction with 1.5 equiv of BQ gave 67% yield of **Z-5aa** (Table 1, entry 3). Other solvent, such as CH₃CN, CH₂Cl₂, or mixed solvent of trifluoroacetic acid (TFA) and HOAc, was not better than HOAc (Table 1, entries 3–5). At a higher reaction temperature, the reaction gave **Z-5aa** in relatively higher yield (compare entries 6–8, Table 1). Almost the same yield was observed when the loading of Pd(OAc)₂ was reduced to 2 mol % (Table 1, entry 9). It is important to note that a noncyclic C=C double bond in the

(7) For some of the typical reactions of allenes, see: (a) Chang, K.-J.; Rayabarapu, D. K.; Yang, F.-Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 126. (b) Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2005**, *127*, 7320. (c) Hamaguchi, H.; Kosaka, S.; Ohno, H.; Tanaka, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 1513. (d) Winkler, J. D.; Ragains, J. R. *Org. Lett.* **2006**, *8*, 4031. (e) Trost, B. M.; Xie, J. *J. Am. Chem. Soc.* **2006**, *128*, 6044. (f) Yoshino, T.; Ng, F.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 14185.
 (8) Hashmi, A. S. K. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1581. (b) Hashmi, A. S. K.; Ruppert, T. L.; Knöfel, T.; Bats, J. W. *J. Org. Chem.* **1997**, *62*, 7295.
 (9) Hashmi, A. S. K.; Schwarz, L.; Choi, J. H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285.
 (10) (a) Ma, S.; Yu, Z. *Org. Lett.* **2003**, *5*, 1507; **2003**, *5*, 2581. (b) Ma, S.; Yu, Z.; Gu, Z. *Chem.-Eur. J.* **2005**, *11*, 2351.
 (11) (a) Ma, S.; Yu, Z. *Angew. Chem., Int. Ed.* **2002**, *41*, 1775. (b) Ma, S.; Gu, Z.; Yu, Z. *J. Org. Chem.* **2005**, *70*, 6291.
 (12) Ma, S.; Gu, Z. *J. Am. Chem. Soc.* **2005**, *127*, 6182.
 (13) Alcaide, B.; Almendros, P.; Campo, T. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 4501.

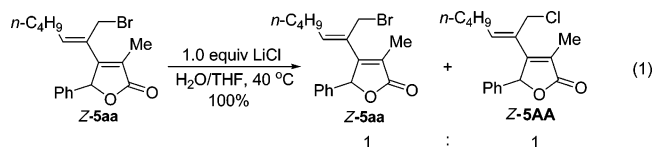
(14) (a) Shimizu, I.; Tsuji, J. *Chem. Lett.* **1984**, 233. (b) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, 28, 199.
 (15) (a) Tsuji, J.; Yamakawa, T.; Kaito, M.; Mandai, T. *Tetrahedron Lett.* **1978**, *19*, 2075. (b) Fu, C.; Ma, S. *Org. Lett.* **2005**, *9*, 1707. (c) Chang, H.-M.; Cheng, C.-H. *J. Org. Chem.* **2000**, *65*, 1767. (d) Grigg, R.; Brown, S.; Sridharan, V.; Uttley, M. D. *Tetrahedron Lett.* **1998**, *39*, 3247.
 (16) (a) Grennberg, H.; Gogoll, A.; Bäckvall, J.-E. *Organometallics* **1993**, *12*, 1790. (b) Albéniz, A. C.; Espinet, P.; Martín-Ruiz, B. *Chem.-Eur. J.* **2001**, *7*, 2481.

Table 1. The Cyclization Reaction of 2,3-Allenic Acid **1a** in the Presence of 1,2-Heptadiene **3a**^a

entry	BQ (equiv)	solvent	time/temp (h/°C)	yield of Z-5aa (%) ^b
1	1.1	HOAc	25/35	53
2 ^c	1.1	HOAc	13/35	44
3 ^d	1.1	CH ₃ CN	13/35	16
4 ^d	1.1	CH ₂ Cl ₂	10/35	trace
5	1.1	HOAc/TFA ^e	31/35	19
6	1.5	HOAc	11.5/35	67
7	1.5	HOAc	36.5/rt	43
8	1.5	HOAc	5.5/60	70
9 ^f	1.5	HOAc	6/60	70

^a The reaction was carried out using 0.25 mmol of **1a**, 0.50 mmol of **3a**, 2.0 equiv of LiBr·H₂O, 5 mol % of Pd(OAc)₂, and BQ in 2 mL of solvent in a Schlenk tube with a screw cap. ^b Isolated yields. ^c 0.375 mmol of **3a** was used. ^d 2.0 equiv of HOAc was added. ^e HOAc:trifluoroacetic acid (TFA) = 10:1. ^f 2 mol % of Pd(OAc)₂ was used.

major product was formed in its Z-form. ¹H NMR analysis of the crude mixture reveals that the Z:E ratio of **5aa** is >50:1. There exists a little amount of cycloisomerization product **7a**. No significant amounts of branched-product **6aa** and homodimeric bicyclic product **8a** were detected. The product Z-5aa may be contaminated with about 10% of the corresponding chloride when LiBr·H₂O used contains LiCl. This problem could be solved when LiBr·H₂O of a higher purity¹⁷ was used. The presence of chloride Z-5AA was confirmed by LC-MS analysis. The treatment of Z-5aa with LiCl in THF/H₂O afforded a 1:1 mixture of Z-5aa and Z-5AA in quantitative yield (eq 1), which further confirmed the presence of the chloride Z-5AA in the product.



With this protocol in hand, we studied the generality of this cyclization reaction of substituted 2,3-allenic acids in the presence of hepta-1,2-diene **3a**. With R¹ being phenyl (Table 2, entries 1–3), *p*-halophenyl (Table 2, entries 4 and 5), or α -naphthyl group (Table 2, entry 6), the reaction could afford the corresponding products smoothly. The fully substituted 2,3-allenic acid **1g** could also react with **3a** to give Z-5ga in 60% yield (Table 2, entry 7). The reaction is also tolerable for the cyclopropanyl group (Table 2, entry 8). The structure of the products was further determined by the X-ray diffraction studies of Z-5fa (Figure 1).¹⁸

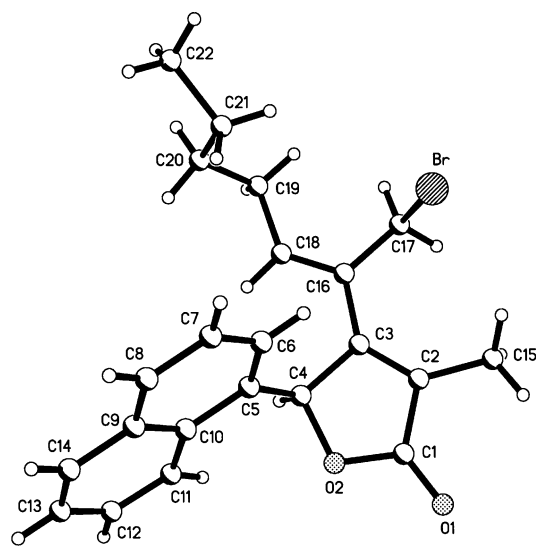
(17) LiBr·H₂O contains less than 0.01% of chlorides.

(18) Crystal data for compound **5fa**: C₂₂H₂₃O₂Br, MW 399.31, monoclinic, *P*2-(1)*c*, Mo K α , final *R* indices [*I* > 2 σ (*I*)], *R*₁ = 0.0685, *wR*₂ = 0.2031, *a* = 12.3128 (18) Å, *b* = 8.8210 (13) Å, *c* = 18.775 (13) Å, α = 90°, β = 106.790 (3)°, γ = 90°, *V* = 1952.2 (5) Å³, *T* = 293 (2) K, *Z* = 4, reflections collected/unique 11 159/4229 (*R*_{int} = 0.1412), number of observations [*>2* σ (*I*)] 1623, parameters 222. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC 626363.

Table 2. The Cross-Coupling Cyclization Reaction of **1** in the Presence of **3a**^a

entry	R ¹	R ²	R ³	time (h)	yield of Z-5 (%)
1	Ph	Me	H (1a)	6	70 (Z-5aa)
2 ^b	Ph	<i>n</i> -Pr	H (1b)	7	59 (Z-5ba)
3	Ph	<i>i</i> -Bu	H (1c)	7	44 (Z-5ca)
4	<i>p</i> BrC ₆ H ₄	<i>n</i> -Pr	H (1d)	6	51 (Z-5da)
5	<i>p</i> ClC ₆ H ₄	<i>n</i> -Bu	H (1e)	9	54 (Z-5ea)
6	α -naphthyl	Me	H (1f)	7	56 (Z-5fa)
7	Ph	Me	Et (1g)	8	60 (Z-5ga)
8	Ph		H (1h)	10	45 (Z-5ha)

^a The reaction was carried out using 0.25 mmol of **1**, 0.50 mmol of **3a**, 2 mol % of Pd(OAc)₂, 0.50 mmol of LiBr·H₂O, and 0.375 mmol of BQ in 2 mL of HOAc in a Schlenk tube with a screw cap. ^b 4 mol % of Pd(OAc)₂ was used.

**Figure 1.** ORTEP representation of Z-5fa.

We also tested the reaction of 2,3-allenic acids in the presence of other substituted alkyl- and aryl-substituted allenes; the yields are from moderate to good (Table 3). With R⁴ being 1°-alkyl (Table 3, entries 1–3, and 7–9), 2°-alkyl (Table 3, entry 4), aryl (Table 3, entry 5), and benzyl group (Table 3, entry 6), the reaction underwent smoothly to give the corresponding products.

The reaction is also tolerable for some functional groups in the simple allenes, such as malonate (Table 4, entries 1 and 2), acetoxy (Table 4, entries 3 and 4), and phthalic amide (Table 4, entry 5), which provides opportunity for further synthetic elaboration.

Furthermore, the cyclization reaction of optically active 2,3-allenic acid [*R*(-)-**1a**] in the presence of allene **3** afforded the product *R*(-)-Z-5 in high enantiopurity, where the R group may be an alkyl (Table 5, entries 1 and 2), an alkyl group with an ester functionality (Table 5, entry 3), and phenyl group (Table 4, entry 4). The high efficiency of the chirality transfer presented in Table 5 indicated that the formation of furanonyl palladium

Table 3. The Coupling Cyclization Reaction of 2,3-Allenic Acids **1** in the Presence of Simple Allenes **3**^a

entry	1		3	time (h)	yield of Z-5 (%)
	R ¹	R ²	R ⁴		
1	Ph	Me (1a)	<i>n</i> -C ₆ H ₁₃ (3b)	10.5	62 (Z-5ab)
2	Ph	Me (1a)	<i>n</i> -C ₇ H ₁₅ (3c)	6.5	59 (Z-5ac)
3 ^b	Ph	Me (1a)	<i>n</i> -C ₈ H ₁₇ (3d)	8	60 (Z-5ad)
4	Ph	Me (1a)	<i>c</i> -C ₆ H ₁₁ (3e)	7	70 (Z-5ae)
5	Ph	Me (1a)	Ph (3f)	6.5	88 (Z-5af)
6	Ph	Me (1a)	Bn (3g)	5.5	61 (Z-5ag)
7	4-BrC ₆ H ₄	<i>n</i> -Pr (1d)	<i>n</i> -C ₆ H ₁₃ (3b)	6	57 (Z-5db)
8	Ph	Et (1i)	<i>n</i> -C ₇ H ₁₅ (3c)	18.5	50 (Z-5ic)
9	Ph	allyl (1j)	<i>n</i> -C ₈ H ₁₇ (3d)	10	56 (Z-5jd)

^a For the reaction conditions, see footnote a, Table 2. ^b 4 mol % of Pd(OAc)₂ was used.

Table 4. The Coupling Cyclization Reaction of **1a** and **1f** in the Presence of Allenes **3h–k** with a Functional Group^a

Entry	1	3	Z-5
1	1a	3h	Z-5ah , 58%
2	1a	3i	Z-5ai , 60%
3	1a	3j	Z-5aj , 67%
4	1f	3k	Z-5fk , 64%
5	1a	3k	Z-5ak , 74%

^a The reaction was carried out using 0.25 mmol of **1**, 0.50 mmol of **3**, 2 mol % of Pd(OAc)₂, 0.50 mmol of LiBr·H₂O, and 0.375 mmol of BQ in 2 mL of HOAc in a Schlenk tube with a screw cap.

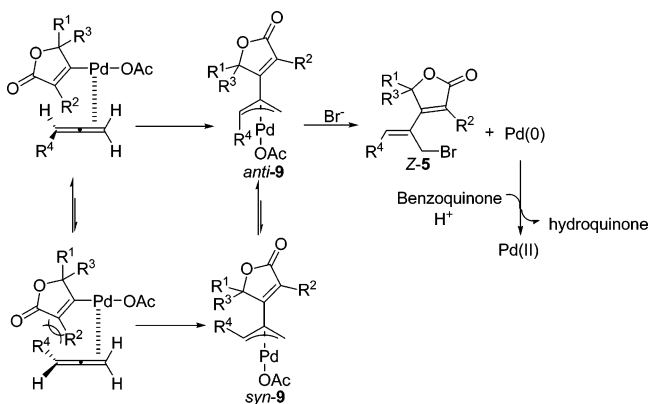
intermediate **2** in Scheme 2 is a highly stereoselective *anti*-oxypalladation process.^{6e}

The highly selective formation of *Z*-isomer is remarkable in view of the fact that most carbopalladation reactions of monosubstituted allenenes reported gave a mixture of *E* and *Z* isomeric products with low selectivity.¹⁹ A plausible mechanism based on the face-selective coordination of allenenes with the

Table 5. The Coupling Cyclization Reaction of *R*-(–)-**1a** in the Presence of Simple Allenes **3**^a

entry	R	yield of <i>R</i> -(–)-Z-5 (%)	
		yield (%)	% ee of Z-5
1	<i>n</i> -C ₄ H ₉ (3a)	63 (<i>R</i> -(–)- Z-5aa)	98
2	<i>n</i> -C ₆ H ₁₃ (3b)	67 (<i>R</i> -(–)- Z-5ab)	98
3	CH ₂ CH ₂ OAc (3j)	70 (<i>R</i> -(–)- Z-5aj)	98
4	Ph (3f)	80 (<i>R</i> -(–)- Z-5af)	97

^a The reaction was carried out using 0.25 mmol of *R*-(–)-**1a**, 0.50 mmol of **3**, 2 mol % of Pd(OAc)₂, 0.50 mmol of LiBr·H₂O, and 0.375 mmol of BQ in 2 mL of HOAc in a Schlenk tube with a screw cap.

Scheme 3. The Rationale for the Stereoselectivity

palladium atom may account for the stereoselectivity observed: the palladium atom coordinates with the terminal C=C double bond of monosubstituted allene from the face opposite to the substituent R⁴ favorably to avoid the steric congestion, which results in the formation of a π -allylpalladium species *anti*-9 with the R⁴ group *anti* to the relatively bulky furanone moiety. Furthermore, the π -allylic palladium intermediate *anti*-9 is more favorable than *syn*-9 due to the steric hindrance.^{19g,20} Further nucleophilic attack of *anti*-9 by Br[–] affords **Z-5** and Pd(0).¹⁴ BQ was acting as the oxidant to regenerate the catalytically active species Pd(II) (Scheme 3).¹⁶

The synthetic utilities of these cross-coupling products **Z-5** were demonstrated by the representative transformation of the product **Z-5aa** or **Z-5fa**. As it is known that the highly regio- and stereoselective synthesis of 4-(stereodefined multi-substituted alkenyl)-2(*5H*)-furanone derivatives is still challenging via the known methods, the chemistry presented in Scheme 4 may be of high synthetic interest. The reaction of **Z-5aa** with Et₂NH would give allylic amine **Z-10** in moderate yield. **Z-5aa** was also easily nucleophilically attacked by sodium benzenesulfinate to afford **Z-11** as the only product in excellent yield at –22 °C in DMF.²¹ Furthermore, in the presence of NaBH₄ the C–Br bond of **Z-5aa** may be reduced to afford **E-12** in 71% yield (*E/Z* ≥ 22/1) with a regioselectivity of 15/1.²² In these cases, the substitution reaction occurred at the less-substituted

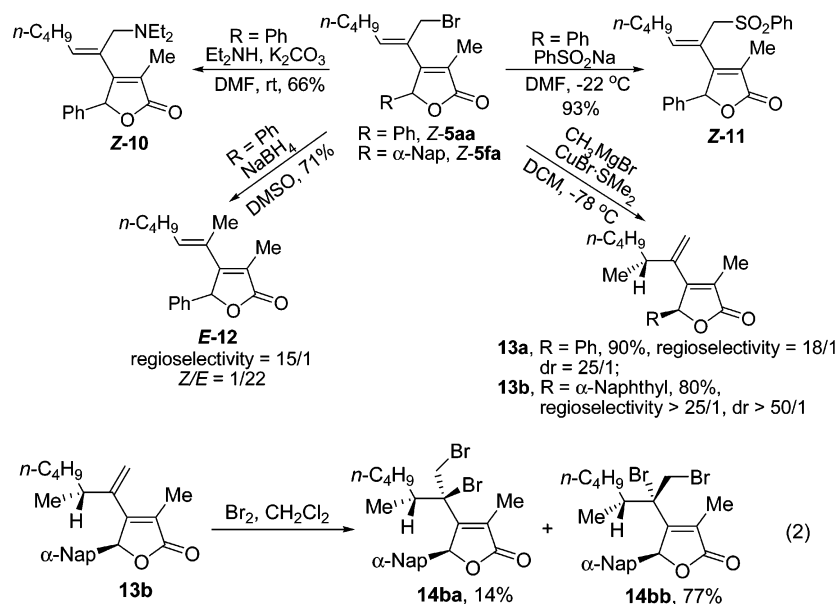
(19) For the stereoselectivity of carbometallation of allenenes, see: (a) Larock, R. C.; Tu, C.; Pace, P. *J. Org. Chem.* **1998**, *63*, 6859. (b) Larock, R. C.; He, Y.; Long, W. W.; Han, X.; Refvik, M. D.; Zenner, J. M. *J. Org. Chem.* **1998**, *63*, 2154. (c) Ma, S.; Negishi, E. I. *J. Am. Chem. Soc.* **1995**, *117*, 6345. (d) Gamez, P.; Ariente, C.; Goré, J.; Cazes, B. *Tetrahedron* **1998**, *54*, 14825. (e) Al-Masum, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 3809. (f) Jonasson, C.; Bäckvall, J.-E. *Tetrahedron Lett.* **1998**, *39*, 3601. (g) Yang, F.; Wu, M.; Cheng, C.-H. *J. Am. Chem. Soc.* **2000**, *122*, 7122. (h) Wu, M.; Rayabarapu, D. K.; Cheng, C.-H. *J. Am. Chem. Soc.* **2003**, *125*, 12426. (i) Zhao, C.; Han, L.; Tanaka, M. *Organometallics* **2000**, *19*, 4196.

(20) Aakermark, B.; Hansson, S.; Vitagliano, A. *J. Am. Chem. Soc.* **1990**, *112*, 4587.

(21) Nilsson, Y. I. M.; Andersson, P. G.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1993**, *115*, 6609.

(22) Corey, E. J.; Kirst, H. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6314.

Scheme 4. The Synthetic Utilities of Z-5



allylic terminal. However, in the presence of 5 mol % of CuBr·SMe₂, the reaction of **Z-5aa** and **Z-5fa** with CH₃MgBr led to predominant formation of branched product **13a** and **13b** with very high regioselectivity and diastereoselectivity.²³ The relative stereochemistry of the two chiral centers in **13** was determined by the single-crystal X-ray diffraction study of **14bb** (eq 2), one of the two isomeric dibromination products of **13b** (Figure 2).²⁴

Conclusion

We have developed a cyclization reaction of 2,3-allenoic acids in the presence of simple allenes, in which a lactone ring was formed from 2,3-allenoic acid and the simple allene yielded the stereodefined allylic bromide moiety, which is ready for further elaboration. A rationale was proposed to explain the stereoselectivity observed. Further studies in this area are being carried out in our laboratory.

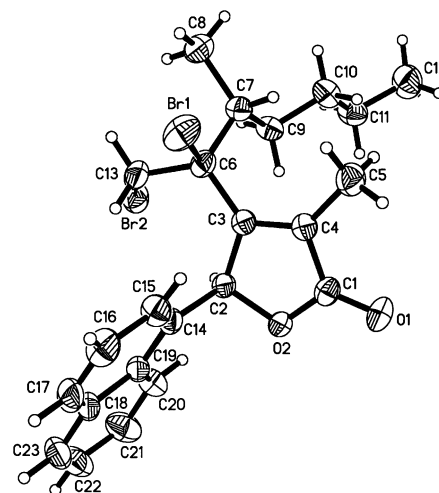
Experimental Section

Palladium-Catalyzed Cyclization of 2,3-Allenoic Acids 1 in the Presence of Simple Allenes 3. (1) Synthesis of 3-Methyl-4-(1'-bromohept-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (Z-5aa). Typical Procedure. A mixture of **1a** (44 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h in a Schlenk tube with a screw cap. After the complete consumption of the starting material as monitored by TLC, the solvent was evaporated, and the crude product was analyzed by ¹H NMR spectra. The residue was purified via flash chromatography on silica gel to afford **Z-5aa** (63 mg, 71%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.92 (q, *J* = 1.5 Hz, 1H), 5.67 (t, *J* = 7.8 Hz, 1H), 4.01 (d, *J* = 10.8 Hz, 1H), 3.93 (d, *J* = 10.8 Hz, 1H), 2.20–2.07 (m, 2H), 2.08 (d, *J* = 1.5 Hz, 3H), 1.32–

1.23 (m, 2H), 1.18–1.02 (m, 2H), 0.79 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.2, 13.7, 22.0, 26.9, 27.8, 30.7, 83.3, 124.5, 127.5, 128.5, 128.8, 129.4, 134.9, 141.9, 157.9, 174.4; MS(EI) *m/z* (%) 351 [M⁺(⁸¹Br) + 1, 0.67], 349 [M⁺(⁷⁹Br) + 1, 0.84], 105 (100); IR (neat) 2957, 1758, 1637, 1456, 1380, 1209, 1095 cm⁻¹; HRMS (MALDI/DHB) calcd for C₁₈H₂₂O₂Br [M⁺(⁷⁹Br) + 1], 349.0798; found, 349.0808.

(2) Synthesis of 3-Propyl-4-(1'-bromohept-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (Z-5ba). A mixture of **1b** (51 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (2 mg, 0.009 mmol) in 2 mL of HOAc was stirred at 60 °C for 7 h to afford **Z-5ba** (56 mg, 59%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.92 (s, 1H), 5.60 (t, *J* = 7.8 Hz, 1H), 3.96 (d, *J* = 10.8 Hz, 1H), 3.90 (d, *J* = 10.8 Hz, 1H), 2.50–2.30 (m, 2H), 2.20–2.05 (m, 2H), 1.72–1.58 (m, 2H), 1.34–1.22 (m, 2H), 1.22–1.10 (m, 2H), 1.00 (t, *J* = 7.5 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 13.7, 14.2, 21.9, 22.0, 26.7, 27.1, 27.7, 30.7, 83.3, 127.4, 128.1, 128.8, 129.2, 129.3, 134.8, 141.0, 158.9, 174.0; MS(ESI) *m/z* 379 [M⁺(⁸¹Br) + 1], 377 [M⁺(⁷⁹Br) + 1]; IR (neat) 2959, 1757, 1634, 1458, 1005 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₀H₂₆O₂Br [M⁺(⁷⁹Br) + 1], 377.1111; found, 377.1105.

(3) Synthesis of 3-Isobutyl-4-(1'-bromohept-2'(Z)-en-2'-yl)-5-

Figure 2. ORTEP representation of **14bb**.

(23) (a) Minnaard, A. J.; Feringa, B. L. *Acc. Chem. Res.* **2007**, *40*, 179. (b) López, F.; van Zijl, A. W.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2006**, 409.

(24) Crystal data for compound **14bb**: C₂₃H₂₆Br₂O₂, MW 494.26, triclinic, *P*-1, Mo K α , final *R* indices [*I* > 2 σ (*I*)], *R*₁ = 0.0603, *wR*₂ = 0.1625, *R* indices (all data), *R*₁ = 0.0871, *wR*₂ = 0.1837, *a* = 7.8406(10) Å, *b* = 11.7468(15) Å, *c* = 12.4428(16) Å, α = 76.331(2)°, β = 75.280(2)°, γ = 89.708(2)°, *V* = 1075.2(2) Å³, *T* = 293(2) K, *Z* = 2, reflections collected/unique 6145/4361 (*R*_{int} = 0.0891), number of observations > 2 σ (*I*) 2600, parameters 255. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC 651341.

phenylfuran-2(5H)-one (Z-5ca). A mixture of **1c** (51 mg, 0.236 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 7 h to afford **Z-5ca** (41 mg, 44%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.92 (s, 1H), 5.67 (t, *J* = 7.8 Hz, 1H), 3.97 (d, *J* = 10.8 Hz, 1H), 3.93 (d, *J* = 10.8 Hz, 1H), 2.40–2.28 (m, 2H), 2.20–2.06 (m, 3H), 1.32–1.24 (m, 2H), 1.20–1.12 (m, 2H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 13.7, 22.0, 22.66, 22.70, 27.3, 27.4, 27.7, 30.6, 33.4, 83.4, 127.4, 127.9, 128.3, 128.8, 129.3, 134.7, 141.0, 159.7, 174.1; MS(ESI) *m/z* 393 [M⁺(⁸¹Br) + 1], 391[M⁺(⁷⁹Br) + 1]; IR (neat) 2957, 1759, 1667, 1456, 1009 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₁H₂₈O₂Br [M⁺(⁷⁹Br) + 1], 391.1267; found, 391.1278.

(4) Synthesis of 3-Propyl-4-(1'-bromohept-2'(Z)-en-2'-yl)-5-(4'-bromophenyl)-furan-2(5H)-one (Z-5da). A mixture of **1d** (70 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **Z-5da** (58 mg, 51%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.47 (d, *J* = 6.6 Hz, 2H), 7.08 (d, *J* = 6.6 Hz, 2H), 5.88 (s, 1H), 5.57 (t, *J* = 7.8 Hz, 1H), 3.97 (d, *J* = 10.8 Hz, 1H), 3.90 (d, *J* = 10.8 Hz, 1H), 2.40 (t, *J* = 7.8 Hz, 2H), 2.20–2.05 (m, 2H), 1.78–1.56 (m, 2H), 1.38–1.22 (m, 2H), 1.22–1.10 (m, 2H), 0.98 (t, *J* = 7.5 Hz, 3H), 0.85 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 13.8, 14.2, 21.8, 22.1, 26.6, 27.0, 27.8, 30.7, 82.4, 123.4, 127.9, 129.0, 129.4, 132.0, 133.9, 141.2, 158.5, 173.7; MS(MALDI) *m/z* 481 [M⁺(⁸¹Br⁸¹Br) + Na⁺], 479 [M⁺(⁸¹Br⁷⁹Br) + Na⁺], 477 [M⁺(⁷⁹Br⁷⁹Br) + Na⁺], 459 [M⁺(⁸¹Br⁸¹Br) + 1], 457 [M⁺(⁸¹Br⁷⁹Br) + 1], 455 [M⁺(⁷⁹Br⁷⁹Br) + 1]; IR (neat) 2959, 1753, 1637, 1489, 1006 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₀H₂₅O₂Br₂ [M⁺(⁷⁹Br) + 1], 455.0216; found, 455.0216.

(5) Synthesis of 4-(1'-Bromohept-2'(Z)-en-2'-yl)-3-butyl-5-(4'-chlorophenyl)-furan-2(5H)-one (Z-5ea). A mixture of **1e** (63 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 9 h to afford **Z-5ea** (58 mg, 54%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.34–7.28 (m, 2H), 7.16–7.10 (m, 2H), 5.89 (s, 1H), 5.58 (t, *J* = 7.8 Hz, 1H), 3.97 (d, *J* = 10.8 Hz, 1H), 3.89 (d, *J* = 10.8 Hz, 1H), 2.41 (t, *J* = 8.4 Hz, 2H), 2.24–2.03 (m, 2H), 1.70–1.48 (m, 2H), 1.46–1.26 (m, 4H), 1.26–1.08 (m, 2H), 0.93 (t, *J* = 7.5 Hz, 3H), 0.84 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 13.7, 13.8, 22.1, 22.8, 24.5, 27.0, 27.8, 30.6, 30.7, 82.3, 128.0, 128.8, 129.1, 129.6, 133.4, 135.3, 141.2, 158.2, 173.7; MS(ESI) *m/z* 429 [M⁺(³⁷Cl⁸¹Br) + 1], 427 [M⁺(³⁵Cl⁸¹Br) + ³⁷Cl⁷⁹Br) + 1], 425 [M⁺(³⁵Cl⁷⁹Br) + 1]; IR (neat) 2957, 1758, 1493, 1084, 1010 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₁H₂₇O₂BrCl [M⁺(³⁵Cl⁷⁹Br) + 1], 425.0878; found, 425.0884.

(6) Synthesis of 4-(1'-Bromohept-2'(Z)-en-2'-yl)-3-methyl-5-(naphth-1'-yl)furan-2(5H)-one (Z-5fa). A mixture of **1f** (56 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 7 h to afford **Z-5fa** (56 mg, 56%): solid, mp 89–90 °C (ethyl acetate); ¹H NMR (300 MHz, CDCl₃) δ 8.19 (d, *J* = 8.1 Hz, 1H), 7.88 (t, *J* = 8.7 Hz, 2H), 7.64–7.50 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 6.3 Hz, 1H), 6.79 (q, *J* = 1.5 Hz, 1H), 5.77 (t, *J* = 7.5 Hz, 1H), 4.04 (d, *J* = 10.8 Hz, 1H), 3.87 (d, *J* = 10.8 Hz, 1H), 2.19 (d, *J* = 1.5 Hz, 3H), 2.20–2.08 (m, 2H), 1.28–1.16 (m, 2H), 1.12–1.00 (m, 2H), 0.77 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.6, 13.8, 22.2, 26.9, 28.0, 31.0, 78.9, 122.6, 125.1, 125.4, 125.7, 126.1, 127.0, 128.9, 129.1, 130.1, 130.8, 131.8, 133.8, 142.2, 157.3, 174.3; MS(ESI) *m/z* (%) 400 [M⁺(⁸¹Br) + 1, 4.96], 398 [M⁺(⁷⁹Br) + 1, 4.24], 319 (100); IR (KBr) 2957, 1753, 1635, 1458, 1097 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₂H₂₄O₂Br [M⁺(⁷⁹Br) + 1], 399.0954; found, 399.0951.

(7) Synthesis of 4-(1'-Bromohept-2'(Z)-en-2'-yl)-3-methyl-5-ethyl-5-phenylfuran-2(5H)-one (Z-5ga). A mixture of **1g** (47 mg, 0.233

mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 8 h to afford **Z-5ga** (53 mg, 60%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.40–7.20 (m, 5H), 5.31 (t, *J* = 7.5 Hz, 1H), 3.91 (d, *J* = 10.8 Hz, 1H), 3.33 (d, *J* = 10.8 Hz, 1H), 2.50–2.32 (m, 1H), 2.25–2.06 (m, 3H), 1.93 (s, 3H), 1.40–1.20 (m, 4H), 0.95–0.85 (m, 6H); ¹³C NMR (75.4 MHz, CDCl₃) δ 7.6, 9.9, 13.8, 22.3, 27.4, 27.8, 28.6, 30.7, 90.3, 125.7, 125.8, 128.0, 128.4, 128.6, 137.7, 141.0, 163.6, 174.2; MS(ESI) *m/z* 420 [M⁺(⁸¹Br) + K⁺], 418 [M⁺(⁷⁹Br) + K⁺], 396 [M⁺(⁸¹Br) + NH₄⁺], 394 [M⁺(⁷⁹Br) + NH₄⁺], 379 [M⁺(⁸¹Br) + 1], 377 [M⁺(⁷⁹Br) + 1]; IR (neat) 2928, 1757, 1448, 1210, 1079 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₀H₂₅O₂BrNa [M⁺(⁷⁹Br) + Na⁺], 399.0930; found, 399.0936.

(8) Synthesis of 4-(1'-Bromohept-2'(Z)-en-2'-yl)-3-cyclopropyl-methenyl-5-phenylfuran-2(5H)-one (Z-5ha). A mixture of **1h** (54 mg, 0.252 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 10 h to afford **Z-5ha** (44 mg, 45%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.40–7.30 (m, 3H), 7.27–7.17 (m, 2H), 5.94 (s, 1H), 5.61 (t, *J* = 7.5 Hz, 1H), 3.96 (d, *J* = 11.4 Hz, 1H), 3.93 (d, *J* = 11.4 Hz, 1H), 2.45–2.27 (m, 2H), 2.20–2.00 (m, 2H), 1.37–1.20 (m, 2H), 1.20–0.98 (m, 3H), 0.82 (t, *J* = 7.2 Hz, 3H), 0.55–0.41 (m, 2H), 0.35–0.17 (m, 2H); ¹³C NMR (75.4 MHz, CDCl₃) δ 4.7, 4.8, 10.0, 13.7, 22.0, 27.2, 27.7, 28.9, 30.6, 83.4, 127.4, 128.0, 128.8, 129.3, 134.7, 141.1, 158.9, 174.2; MS-(EI) *m/z* (%) 391 [M⁺(⁸¹Br) + 1, 5.34], 389 [M⁺(⁷⁹Br) + 1, 5.43], 91 (100); IR (neat) 1758, 1634, 1497, 1456, 1209, 1014 cm⁻¹; HRMS (EI) calcd for C₂₁H₂₅O₂Br [M⁺(⁷⁹Br)], 388.1038; found, 388.1035.

(9) Synthesis of 4-(1'-Bromonon-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ab). A mixture of **1a** (44 mg, 0.25 mmol), **3b** (62 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 10.5 h to afford **Z-5ab** (59 mg, 62%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.92 (q, *J* = 1.8 Hz, 1H), 5.67 (t, *J* = 7.5 Hz, 1H), 4.01 (d, *J* = 10.8 Hz, 1H), 3.93 (d, *J* = 10.8 Hz, 1H), 2.20–2.08 (m, 2H), 2.09 (d, *J* = 1.8 Hz, 3H), 1.36–1.04 (m, 8H), 0.84 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.2, 14.0, 22.4, 26.9, 28.0, 28.48, 28.53, 31.4, 83.2, 124.5, 127.5, 128.4, 128.8, 129.3, 134.9, 141.9, 157.8, 174.3; MS(ESI) *m/z* 396 [M⁺(⁸¹Br) + NH₄⁺], 394 [M⁺(⁷⁹Br) + NH₄⁺], 379 [M⁺(⁸¹Br) + 1], 377 [M⁺(⁷⁹Br) + 1]; IR (neat) 2927, 1757, 1637, 1456, 1096 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₀H₂₆O₂Br [M⁺(⁷⁹Br) + 1], 377.1111; found, 377.1107.

(10) Synthesis of 4-(1'-Bromodec-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ac). A mixture of **1a** (44 mg, 0.25 mmol), **3c** (69 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6.5 h to afford **Z-5ac** (58 mg, 59%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.40–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.93 (q, *J* = 1.8 Hz, 1H), 5.67 (t, *J* = 7.5 Hz, 1H), 4.01 (d, *J* = 10.8 Hz, 1H), 3.93 (d, *J* = 10.8 Hz, 1H), 2.22–2.08 (m, 2H), 2.10 (d, *J* = 1.8 Hz, 3H), 1.38–1.04 (m, 10H), 0.87 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.2, 14.0, 22.5, 26.9, 28.0, 28.5, 28.8, 28.9, 31.6, 83.2, 124.5, 127.5, 128.5, 128.8, 129.4, 134.9, 141.9, 157.8, 174.3; MS(EI) *m/z* (%) 393 [M⁺(⁸¹Br) + 1, 1.39], 391 [M⁺(⁷⁹Br) + 1, 1.52], 105 (100); IR (neat) 2926, 1758, 1636, 1456, 1095 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₁H₂₈O₂Br [M⁺(⁷⁹Br) + 1], 391.1267; found, 391.1280.

(11) Synthesis of 4-(1'-Bromoundec-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ad). A mixture of **1a** (44 mg, 0.25 mmol), **3d** (76 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (2 mg, 0.009 mmol) in 2 mL of HOAc was stirred at 60 °C for 8 h to afford **Z-5ad** (61 mg, 60%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.92 (q, *J* = 1.5 Hz, 1H), 5.67 (t, *J* = 7.8 Hz, 1H), 4.01 (d, *J* = 10.8 Hz, 1H), 3.93 (d, *J* = 10.8 Hz, 1H), 2.20–2.08 (m, 2H), 2.10 (d,

$J = 1.5$ Hz, 3H), 1.16–1.04 (m, 12H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 10.2, 14.0, 22.6, 26.9, 28.0, 28.5, 28.9, 29.1, 29.2, 31.7, 83.2, 124.5, 127.5, 128.5, 128.8, 129.4, 134.9, 141.9, 157.8, 174.3; MS(ESI) m/z (%) 407 [$\text{M}^+(\text{Br}) + 1$, 1.38], 405 [$\text{M}^+(\text{Br}) + 1$, 1.50], 105 (100); IR (neat) 2926, 1758, 1636, 1456, 1094 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 405.1424; found, 405.1441.

(12) Synthesis of 4-(1'-Bromo-3'-cyclohexylprop-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ae). A mixture of **1a** (43 mg, 0.25 mmol), **3e** (61 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 7 h to afford **Z-5ae** (65 mg, 70%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.90 (s, 1H), 5.60 (t, $J = 7.8$ Hz, 1H), 3.95 (d, $J = 10.8$ Hz, 1H), 3.89 (d, $J = 10.8$ Hz, 1H), 2.56–2.40 (m, 2H), 2.18–2.08 (m, 2H), 1.38–1.08 (m, 13H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 13.2, 14.0, 18.1, 22.6, 27.1, 28.0, 28.6, 28.87, 28.95, 31.6, 83.2, 127.4, 128.2, 128.8, 129.3, 130.6, 134.7, 141.0, 158.3, 173.8; MS(ESI) m/z (%) 407 [$\text{M}^+(\text{Br}) + 1$, 1.46], 405 [$\text{M}^+(\text{Br}) + 1$, 1.63], 105 (100); IR (neat) 2927, 1758, 1639, 1458, 1004 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 405.1424; found, 405.1426.

(13) Synthesis of 4-(1'-Bromo-3'-phenylprop-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5af). A mixture of **1a** (43 mg, 0.25 mmol), **3f** (58 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol) in 2 mL of HOAc was stirred at 60 °C for 6.5 h to afford **Z-5af** (80 mg, 88%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.42–7.22 (m, 10H), 6.69 (s, 1H), 6.07 (q, $J = 1.8$ Hz, 1H), 4.17 (d, $J = 10.8$ Hz, 1H), 4.04 (d, $J = 10.8$ Hz, 1H), 2.18 (d, $J = 1.8$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 10.5, 29.2, 83.1, 126.3, 127.5, 128.70, 128.73, 128.8, 129.0, 129.4, 129.6, 134.3, 134.5, 137.9, 157.7, 174.0; MS(ESI) m/z 388 [$\text{M}^+(\text{Br}) + \text{NH}_4^+$], 386 [$\text{M}^+(\text{Br}) + \text{NH}_4^+$], 371 [$\text{M}^+(\text{Br}) + 1$], 369 [$\text{M}^+(\text{Br}) + 1$]; IR (neat) 1754, 1622, 1496, 1455, 1091 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{20}\text{H}_{18}\text{O}_2\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 369.0485; found, 369.0483.

(14) Synthesis of 4-(1'-Bromo-4'-phenylbuta-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ag). A mixture of **1a** (43 mg, 0.25 mmol), **3g** (65 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol) in 2 mL of HOAc was stirred at 60 °C for 5.5 h to afford **Z-5ag** (58 mg, 61%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.42–7.30 (m, 3H), 7.28–7.17 (m, 5H), 6.96–6.87 (m, 2H), 5.96 (q, $J = 1.8$ Hz, 1H), 5.83 (t, $J = 7.5$ Hz, 1H), 4.11 (d, $J = 10.8$ Hz, 1H), 4.03 (d, $J = 10.8$ Hz, 1H), 3.60–3.43 (m, 2H), 2.10 (d, $J = 1.8$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3): δ 10.2, 26.6, 34.0, 83.2, 125.1, 126.6, 127.5, 128.2, 128.6, 128.9, 129.2, 129.4, 134.7, 137.7, 139.0, 157.7, 174.2; MS(ESI) m/z 385 [$\text{M}^+(\text{Br}) + 1$], 383 [$\text{M}^+(\text{Br}) + 1$]; IR (neat) 1755, 1638, 1602, 1495, 1454, 1095, 1014 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{21}\text{H}_{20}\text{O}_2\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 383.0641; found, 383.0654.

(15) Synthesis of 4-(1'-Bromonon-2'(Z)-en-2'-yl)-5-(4'-bromophenyl)-3-propyl-furan-2(5H)-one (Z-5db). A mixture of **1d** (70 mg, 0.25 mmol), **3b** (62 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **Z-5db** (69 mg, 57%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.46 (d, $J = 8.7$ Hz, 2H), 7.07 (d, $J = 8.7$ Hz, 2H), 5.88 (s, 1H), 5.57 (t, $J = 7.8$ Hz, 1H), 3.97 (d, $J = 10.8$ Hz, 1H), 3.90 (d, $J = 10.8$ Hz, 1H), 2.40 (t, $J = 7.5$ Hz, 2H), 2.20–2.04 (m, 2H), 2.72–1.54 (m, 2H), 1.38–1.04 (m, 8H), 0.97 (t, $J = 7.5$ Hz, 3H), 0.85 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 14.0, 14.2, 21.8, 22.5, 26.6, 27.0, 28.0, 28.5, 28.6, 31.4, 82.3, 123.4, 127.9, 129.0, 129.3, 132.0, 133.9, 141.2, 158.4, 173.6; MS(ESI) m/z 504 [$\text{M}^+(\text{Br}) + \text{NH}_4^+$], 502 [$\text{M}^+(\text{Br}) + \text{NH}_4^+$], 500 [$\text{M}^+(\text{Br}) + \text{NH}_4^+$], 487 [$\text{M}^+(\text{Br}) + 1$], 485 [$\text{M}^+(\text{Br}) + 1$]; IR (neat) 2928, 1758,

1634, 1489, 1207, 1006 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{22}\text{H}_{29}\text{O}_2\text{Br}_2$ [$\text{M}^+(\text{Br}) + 1$], 483.0529; found, 483.0535.

(16) Synthesis of 4-(1'-Bromodec-2'(Z)-en-2'-yl)-3-ethyl-5-phenylfuran-2(5H)-one (Z-5ic). A mixture of **1i** (47 mg, 0.25 mmol), **3c** (69 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol) in 2 mL of HOAc was stirred at 60 °C for 18.5 h to afford **Z-5ic** (50 mg, 50%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 5.90 (s, 1H), 5.60 (t, $J = 7.8$ Hz, 1H), 3.95 (d, $J = 10.8$ Hz, 1H), 3.89 (d, $J = 10.8$ Hz, 1H), 2.56–2.40 (m, 2H), 2.18–2.08 (m, 2H), 1.38–1.08 (m, 13H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 13.2, 14.0, 18.1, 22.6, 27.1, 28.0, 28.6, 28.87, 28.95, 31.6, 83.2, 127.4, 128.2, 128.8, 129.3, 130.6, 134.7, 141.0, 158.3, 173.8; MS(ESI) m/z (%) 407 [$\text{M}^+(\text{Br}) + 1$, 1.46], 405 [$\text{M}^+(\text{Br}) + 1$, 1.63], 105 (100); IR (neat) 2927, 1758, 1639, 1458, 1004 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{22}\text{H}_{30}\text{O}_2\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 405.1424; found, 405.1426.

(17) Synthesis of 3-Allyl-4-(1'-bromoundec-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (Z-5jd). A mixture of **1j** (52 mg, 0.26 mmol), **3d** (76 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 10 h to afford **Z-5jd** (62 mg, 56%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.38–7.30 (m, 3H), 7.22–7.18 (m, 2H), 6.03–5.90 (m, 2H), 5.71 (t, $J = 7.5$ Hz, 1H), 5.16 (s, 1H), 5.14–5.10 (m, 1H), 3.99 (d, $J = 10.8$ Hz, 1H), 3.92 (d, $J = 10.8$ Hz, 1H), 3.27–3.23 (m, 2H), 2.20–2.04 (m, 2H), 1.38–1.08 (m, 12H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 14.0, 22.6, 26.9, 28.1, 28.5, 28.8, 28.9, 29.1, 29.2, 31.7, 83.3, 116.5, 126.5, 127.5, 128.0, 128.9, 129.4, 133.9, 134.7, 142.0, 159.6, 173.6; MS(ESI) m/z 433 [$\text{M}^+(\text{Br}) + 1$], 431 [$\text{M}^+(\text{Br}) + 1$]; IR (neat) 2926, 1760, 1639, 1456, 1013 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{24}\text{H}_{31}\text{O}_2\text{BrNa}$ [$\text{M}^+(\text{Br}) + \text{Na}^+$], 453.1400; found, 453.1394.

(18) Synthesis of 4-(1'-Bromo-5',5'-dimethoxycarbonylpenta-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ah). A mixture of **1a** (43 mg, 0.25 mmol), **3h** (92 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford a mixture of **Z-5ah** and hydroquinone. The mixture was then dissolved in 30 mL of CH_2Cl_2 , washed with water (5 mL \times 3), and dried over Na_2SO_4 . The solvent was evaporated to afford pure **Z-5ah** (63 mg, 58%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.39–7.30 (m, 3H), 7.22–7.13 (m, 2H), 5.89 (q, $J = 1.8$ Hz, 1H), 5.60 (t, $J = 7.5$ Hz, 1H), 4.01 (d, $J = 11.1$ Hz, 1H), 3.90 (d, $J = 11.1$ Hz, 1H), 3.66 (s, 3H), 3.61 (s, 3H), 3.38 (t, $J = 7.2$ Hz, 1H), 2.72 (dd, $J = 7.8, 7.8$ Hz, 2H), 2.03 (d, $J = 1.8$ Hz, 3H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 10.1, 26.1, 27.2, 50.2, 52.7, 52.8, 83.1, 125.7, 127.4, 128.8, 129.4, 131.2, 134.4, 135.1, 157.4, 168.4, 173.9; MS(ESI) m/z (%) 461 [$\text{M}^+(\text{Br}) + \text{Na}^+$], 459 [$\text{M}^+(\text{Br}) + \text{Na}^+$], 439 [$\text{M}^+(\text{Br}) + 1$], 437 [$\text{M}^+(\text{Br}) + 1$]; IR (neat) 1755, 1650, 1498, 1456, 1436, 1274, 1210, 1158, 1094, 1014 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{26}\text{H}_{22}\text{O}_6\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 437.0594; found, 437.0590.

(19) Synthesis of 4-(1'-Bromo-5',5'-diethoxycarbonylpenta-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5ai). A mixture of **1a** (44 mg, 0.25 mmol), **3i** (106 mg, 0.50 mmol), $\text{LiBr}\cdot\text{H}_2\text{O}$ (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $\text{Pd}(\text{OAc})_2$ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **Z-5ai** (71 mg, 60%): oil, ^1H NMR (300 MHz, CDCl_3) δ 7.40–7.25 (m, 3H), 7.25–7.13 (m, 2H), 5.89 (s, 1H), 5.62 (t, $J = 7.5$ Hz, 1H), 4.23–3.96 (m, 5H), 3.90 (d, $J = 10.8$ Hz, 1H), 3.33 (t, $J = 7.2$ Hz, 1H), 2.72 (t, $J = 7.5$ Hz, 2H), 2.03 (s, 3H), 1.27–1.15 (m, 6H); ^{13}C NMR (75.4 MHz, CDCl_3) δ 10.1, 13.92, 13.93, 26.2, 27.2, 50.6, 61.69, 61.75, 83.1, 125.7, 127.4, 128.8, 129.4, 131.1, 134.5, 135.4, 157.4, 168.0, 168.1, 174.0; MS(ESI) m/z 489 [$\text{M}^+(\text{Br}) + \text{Na}^+$], 487 [$\text{M}^+(\text{Br}) + \text{Na}^+$], 467 [$\text{M}^+(\text{Br}) + 1$], 465 [$\text{M}^+(\text{Br}) + 1$]; IR (neat) 1755, 1456, 1370, 1269, 1095, 1017 cm^{-1} ; HRMS (MALDI/DHB) calcd for $\text{C}_{22}\text{H}_{26}\text{O}_6\text{Br}$ [$\text{M}^+(\text{Br}) + 1$], 465.0907; found, 465.0898.

(20) Synthesis of 4-(1'-Bromo-5'-acetoxypenta-2'(Z)-en-2'-yl)-3-methyl-5-phenylfuran-2(5H)-one (Z-5aj). A mixture of **1a** (44 mg, 0.25 mmol), **3j** (63 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **Z-5aj** (64 mg, 67%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.40–7.27 (m, 3H), 7.24–7.15 (m, 2H), 5.91 (q, *J* = 1.5 Hz, 1H), 5.63 (t, *J* = 7.8 Hz, 1H), 4.02 (t, *J* = 6.0 Hz, 2H), 3.96 (d, *J* = 10.8 Hz, 1H), 3.90 (d, *J* = 10.8 Hz, 1H), 2.58–2.38 (m, 2H), 2.06 (d, *J* = 1.5 Hz, 3H), 1.92 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.1, 20.7, 26.4, 27.5, 62.1, 83.2, 125.4, 127.4, 128.8, 129.4, 130.9, 134.6, 135.9, 157.4, 170.6, 174.0; MS(EI) *m/z* (%) 381 [M⁺(⁸¹Br) + 1], 1.27], 379 [M⁺(⁷⁹Br) + 1], 1.06], 299 (M⁺ – Br, 12.83), 43 (100); IR (neat) 1755, 1652, 1497, 1456, 1239, 1095, 1036 cm⁻¹; HRMS (EI) calcd for C₁₈H₁₉O₄ [M⁺ – Br], 299.1283; found, 299.1280.

(21) Synthesis of 4-(1'-Bromo-5'-acetoxypenta-2'(Z)-en-2'-yl)-3-methyl-5-(α-naphthyl)-furan-2(5H)-one (Z-5fj). A mixture of **1f** (56 mg, 0.25 mmol), **3j** (62 mg, 0.49 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 10 h to afford **Z-5fj** (69 mg, 64%): oil, ¹H NMR (300 MHz, CDCl₃) δ 8.17 (d, *J* = 8.1 Hz, 1H), 7.86 (t, *J* = 8.1 Hz, 2H), 7.63–7.49 (m, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 6.6 Hz, 1H), 6.78 (q, *J* = 1.8 Hz, 1H), 5.74 (t, *J* = 7.5 Hz, 1H), 4.05–3.88 (m, 3H), 3.83 (d, *J* = 11.1 Hz, 1H), 2.52–2.38 (m, 2H), 2.17 (d, *J* = 1.8 Hz, 3H), 1.82 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.5, 20.6, 26.4, 27.5, 62.0, 78.8, 122.4, 125.1, 125.6, 126.1, 126.3, 127.1, 128.9, 130.2, 130.4, 131.4, 131.6, 133.7, 136.2, 156.8, 170.6, 174.0; MS(ESI) *m/z* 431 [M⁺(⁸¹Br) + 1], 429 [M⁺(⁷⁹Br) + 1]; IR (neat) 1751, 1598, 1638, 1450, 1239, 1095, 1035 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₂H₂₁O₄BrNa [M⁺(⁷⁹Br) + Na⁺], 451.0515; found, 451.0517.

(22) Synthesis of 4-(1'-Bromo-5'-phthalamidopenta-2'(Z)-en-2'-yl)-3-methyl-5-(α-naphthyl)furan-2(5H)-one (Z-5ak). A mixture of **1a** (44 mg, 0.25 mmol), **3k** (106 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h in a Schlenk tube with a screw cap. After the complete consumption of the starting material as monitored by TLC, the solvent was evaporated, and the residue was dissolved in 50 mL of CH₂Cl₂, then washed with water (5 mL × 4), and dried over Na₂SO₄. The solvent was evaporated, and the residue was purified via flash chromatography on silica gel to afford **Z-5ak** (87 mg, 74%): oil, ¹H NMR (300 MHz, CDCl₃) δ 7.88–7.77 (m, 2H), 7.77–7.63 (m, 2H), 7.30–7.18 (m, 3H), 7.18–7.10 (m, 2H), 5.85 (s, 1H), 5.71 (t, *J* = 7.5 Hz, 1H), 3.89 (d, *J* = 10.8 Hz, 1H), 3.82 (d, *J* = 10.8 Hz, 1H), 3.80–3.61 (m, 2H), 2.69–2.47 (m, 2H), 2.02 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.1, 26.2, 27.3, 36.3, 83.1, 123.3, 125.5, 127.3, 128.8, 129.4, 131.4, 131.7, 134.1, 134.5, 136.1, 157.1, 168.1, 174.0; MS(ESI) *m/z* 506 [M(⁸¹Br) + K⁺], 504 [M(⁷⁹Br) + K⁺], 490 [M(⁸¹Br) + Na⁺], 488 [M(⁷⁹Br) + Na⁺], 468 [M⁺(⁸¹Br) + 1], 466 [M⁺(⁷⁹Br) + 1]; IR (neat) 1755, 1710, 1396, 1361, 1097, 1007 cm⁻¹; HRMS (MALDI/DHB) calcd for C₂₄H₂₁NO₄Br [M⁺(⁷⁹Br) + 1], 466.0649; found, 466.0645.

Typical Procedure for the Cyclization of Optically Active 2,3-Allenic Acids R(-)-1a in the Presence of Simple Allenes 3. (1) Synthesis of R(-)-3-Methyl-4-(1'-bromohept-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (R(-)-Z-5aa). A mixture of **R(-)-1a** (44 mg, 0.25 mmol, 98% ee), **3a** (48 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **R(-)-Z-5aa** (59 mg, 67%, 98% ee). HPLC conditions: OD-H column; rate, 0.5 mL/min; eluent, hexane/*i*-PrOH 70/30. λ = 230 nm. [α]_D²⁰ = -215° (*c* = 0.590, CHCl₃).

(2) Synthesis of R(-)-3-Methyl-4-(1'-bromonon-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (R(-)-5ab). A mixture of **R(-)-1a** (43 mg, 0.25 mmol, 98% ee), **3b** (62 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg,

0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h in a Schlenk tube with a screw cap to afford **R(-)-Z-5ab** (60 mg, 63%, 98% ee). HPLC conditions: OD-H column; rate, 0.7 mL/min; eluent, hexane/*i*-PrOH 80/20. λ = 230 nm. [α]_D²⁰ = -166° (*c* = 0.900, CHCl₃).

(3) Synthesis of R(-)-3-Methyl-4-(1'-bromo-5'-acetoxypenta-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (R(-)-Z-5aj). A mixture of **R(-)-1a** (43 mg, 0.25 mmol, 98% ee), **3j** (63 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **R(-)-Z-5aj** (66 mg, 70%, 98% ee). HPLC conditions: OD-H column; rate, 0.5 mL/min; eluent, hexane/*i*-PrOH 70/30. λ = 254 nm. [α]_D²⁰ = -187° (*c* = 1.300, CHCl₃).

(4) Synthesis of R(-)-3-Methyl-4-(1'-bromo-3'-phenylprop-2'(Z)-en-2'-yl)-5-phenylfuran-2(5H)-one (R(-)-Z-5af). A mixture of **R(-)-1a** (44 mg, 0.25 mmol, 98% ee), **3f** (58 mg, 0.50 mmol), LiBr·H₂O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and Pd(OAc)₂ (1 mg, 0.0045 mmol, 2 mol %) in 2 mL of HOAc was stirred at 60 °C for 6 h to afford **R(-)-Z-5af** (75 mg, 80%, 97% ee). HPLC conditions: ODH column; rate, 0.7 mL/min; eluent, hexane/*i*-PrOH 95/5. λ = 230 nm. [α]_D²⁰ = -487° (*c* = 0.710, CHCl₃).

The Reaction of Z-5aa with LiCl. A mixture of **Z-5aa** (100 mg, 0.29 mmol), LiCl (49 mg, 1.16 mmol), THF (4 mL), and distilled H₂O (4 mL) was stirred at 40 °C for 5.5 h to afford 101 mg of **Z-5aa** and **Z-5AA** with a ratio of 1:1.

Synthetic Application of Z-5aa. (1) Synthesis of 3-Methyl-4-(1'-diethylaminohepta-2'(Z)-en-2'-yl)-5-phenyl-furan-2(5H)-one (Z-10). Under an argon atmosphere, a mixture of **Z-5aa** (59 mg, 0.17 mmol), Et₂NH (25 mg, 0.34 mmol), K₂CO₃ (47 mg, 0.34 mmol), and DMF (2 mL) was stirred in a Schlenk tube with a screw cap at room temperature for 6 h. After the complete consumption of the starting material as monitored by TLC, the reaction mixture was quenched with H₂O (5 mL) and extracted with 50 mL of ether. The organic layer was washed with brine and dried over Na₂SO₄. The solvent was evaporated, and the crude product was analyzed by ¹H NMR spectra. The residue was purified via flash chromatography on silica gel to afford **Z-10** (38 mg, 66%): ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.28 (m, 3H), 7.25–7.15 (m, 2H), 6.15 (q, *J* = 1.5 Hz, 1H), 5.64 (t, *J* = 7.2 Hz, 1H), 3.04 (d, *J* = 14.1 Hz, 1H), 2.90 (d, *J* = 14.1 Hz, 1H), 2.58–2.41 (m, 2H), 2.31–2.18 (m, 2H), 2.18–2.00 (m, 2H), 1.99 (d, *J* = 1.5 Hz, 3H), 1.35–1.22 (m, 2H), 1.22–1.03 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 6H), 0.81 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.0, 11.5, 13.8, 22.0, 27.6, 31.4, 46.3, 51.1, 83.6, 122.6, 127.8, 128.6, 129.0, 130.9, 135.4, 138.2, 163.1, 175.2; MS(EI) *m/z* (%) 341 [M⁺, 3.84], 58 (100); IR (neat) 1756, 1654, 1455, 1090 cm⁻¹; HRMS calcd for C₂₂H₃₁NO₂ [M⁺], 341.2355; found, 341.2362.

(2) Synthesis of 3-Methyl-4-(1'-phenylsulfonyl)hepta-2'(Z)-en-2'-yl)-5-phenyl-furan-2(5H)-one (Z-11). Under an argon atmosphere, a mixture of **Z-5aa** (54 mg, 0.15 mmol), PhSO₂Na·2H₂O (60 mg, 0.30 mmol), and DMF (2 mL) was stirred at -22 °C for 2.5 h. After the complete consumption of the starting material as monitored by TLC, the mixture was diluted with 60 mL of ether and washed sequentially with H₂O and brine. The organic layer was dried over Na₂SO₄. The solvent was evaporated, and the crude product was analyzed by ¹H NMR spectra. The residue was purified via flash chromatography on silica gel to afford **Z-11** (59 mg, 93%): ¹H NMR (300 MHz, CDCl₃) δ 7.72 (d, *J* = 7.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.38–7.28 (m, 3H), 7.22–7.13 (m, 2H), 5.96 (q, *J* = 1.5 Hz, 1H), 5.81 (t, *J* = 7.5 Hz, 1H), 3.94 (d, *J* = 14.7 Hz, 1H), 3.75 (d, *J* = 14.7 Hz, 1H), 2.01 (d, *J* = 1.5 Hz, 3H), 1.80–1.67 (m, 1H), 1.66–1.50 (m, 1H), 1.11–0.89 (m, 4H), 0.71 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.7, 13.6, 21.9, 28.1, 30.3, 55.7, 83.0, 119.8, 124.1, 127.8, 128.2, 128.9, 129.2, 129.4, 134.1, 134.2, 137.9, 145.8, 158.7, 174.1; MS(EI) *m/z* (%) 410 (M⁺, 3.45), 268 (100); IR (neat) 1754, 1634, 1585, 1447, 1320, 1156, 1086, 1016 cm⁻¹; HRMS calcd for C₂₄H₂₆O₄S [M⁺], 410.1552; found, 410.1568.

(3) Synthesis of 3-Methyl-4-(hepta-2'(*E*)-en-2'-yl)-5-phenylfuran-2(5*H*)-one (*E*-12). Under an argon atmosphere, a mixture of *Z*-5aa (69 mg, 0.20 mmol), NaBH₄ (15 mg, 0.40 mmol), and DMSO (3 mL) was stirred at 18 °C for 50 min. After the complete consumption of the starting material as monitored by TLC, the mixture was diluted with 60 mL of ether and washed sequentially with H₂O and brine. The organic layer was dried over Na₂SO₄. The solvent was evaporated, and the crude product was analyzed by ¹H NMR spectra (regioselectivity: 1/15, *E/Z* ≥ 22/1). The residue was purified via flash chromatography on silica gel to afford pure *E*-12 (38 mg, 71%): ¹H NMR (300 MHz, CDCl₃) δ 7.40–7.29 (m, 3H), 7.23–7.14 (m, 2H), 5.87 (q, *J* = 1.5 Hz, 1H), 5.57 (t, *J* = 7.2 Hz, 1H), 2.13–1.92 (m, 5H), 1.72 (s, 3H), 1.35–1.19 (m, 2H), 1.19–1.03 (m, 2H), 0.80 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.4, 13.8, 15.4, 22.0, 27.7, 31.0, 83.4, 121.7, 127.3, 127.4, 128.6, 129.0, 135.6, 137.0, 161.9, 175.0; MS(EI) *m/z* (%) 271 [M⁺ + 1, 24.67], 270 [M⁺, 56.45], 105 (100); IR (neat) 1755, 1640, 1456, 1331, 1092, 1003 cm⁻¹; HRMS calcd for C₁₈H₂₂O₂ [M⁺], 270.1620; found, 270.1630.

(4) Synthesis of (5*S,3'*R**)-3-Methyl-4-(3'-methylhepta-1'-en-2'-yl)-5-phenylfuran-2(5*H*)-one (13a).** Under an argon atmosphere, a mixture of *Z*-5aa (70 mg, 0.20 mmol), CuBr·SMe₂ (2 mg, 0.01 mmol), and DCM (4 mL) was cooled to -78 °C. A solution of CH₃MgBr [0.36 mL, 1.4 mol/L in toluene/THF (75/25), 0.50 mmol] was carefully added to the mixture via a syringe at this temperature. After being stirred for 30 min at -78 °C, 0.5 mL of H₂O was added to the reaction mixture at this temperature, and then the reaction mixture was warmed to room temperature. The reaction mixture was filtered via a short column of silica gel, evaporated, and analyzed by ¹H NMR spectra (regioselectivity = 18/1, *dr* = 25/1). The residue was purified via flash chromatography on silica gel to afford 13a (51 mg, 90%): ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.27 (m, 3H), 7.21–7.12 (m, 2H), 5.85 (q, *J* = 1.8 Hz, 1H), 5.15 (s, 1H), 4.95 (s, 1H), 2.19–2.00 (m, 1H), 1.98 (d, *J* = 1.8 Hz, 3H), 1.42–1.30 (m, 1H), 1.28–0.98 (m, 5H), 0.86 (d, *J* = 7.2 Hz, 3H), 0.79 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.0, 13.9, 20.1, 22.6, 29.3, 34.2, 37.2, 83.7, 116.4, 124.1, 127.3, 128.6, 129.1, 134.7, 146.0, 162.0, 174.6; MS(EI) *m/z* (%) 285 [M⁺ + 1, 56.84], 284 [M⁺, 20.07], 91 (100); IR (neat) 1759, 1656, 1456, 1319, 1091, 1003 cm⁻¹; HRMS calcd for C₁₉H₂₄O₂ [M⁺], 284.1776; found, 284.1783.

(5) Synthesis of (5*S,3'*R**)-3-Methyl-4-(3'-methylhepta-1'-en-2'-yl)-5-(α -naphthyl)furan-2(5*H*)-one (13b).** Under an argon atmosphere, to a mixture of *Z*-5fa (54 mg, 0.135 mmol) and CuBr·SMe₂ (1 mg, 0.005 mmol) in DCM (3 mL) was added CH₃MgBr (0.24 mL, 1.4 mol/L in toluene/THF (75/25), 0.34 mmol) carefully via a syringe at -78 °C. After the mixture was stirred for 30 min at -78 °C, 0.5 mL of H₂O was added to the reaction mixture at this temperature, and then the reaction mixture was warmed to room temperature. The reaction mixture was filtered via a short column of silica gel, evaporated, and analyzed by ¹H NMR spectra (regioselectivity >25/1, *dr* >50/1). The residue was purified via flash chromatography on silica gel to afford 13b (36 mg, 80%): ¹H NMR (300 MHz, CDCl₃) δ 8.15 (d, *J* = 8.1 Hz, 1H), 7.87 (t, *J* = 8.7 Hz, 2H), 7.63–7.48 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 6.3 Hz, 1H), 6.70 (q, *J* = 1.8 Hz, 1H), 5.24 (s, 1H), 5.16 (s, 1H), 2.09 (d, *J* = 1.8 Hz, 3H), 2.00 (q, *J* = 6.9 Hz, 1H), 1.35–1.22 (m, 1H), 1.22–1.03 (m, 1H), 1.03–0.75 (m, 7H), 0.65 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 10.4, 13.8, 20.4, 22.4, 29.1, 34.3, 37.1, 79.6, 116.9, 122.7, 125.0, 125.6, 125.9, 126.0, 126.8, 128.9, 130.0,

130.5, 131.8, 133.8, 146.6, 161.3, 174.5; MS(EI) *m/z* (%) 334 (M⁺, 13.00), 141 (100); IR (neat) 1758, 1512, 1456, 1379, 1319, 1096 cm⁻¹; HRMS calcd for C₂₃H₂₆O₂ [M⁺], 334.1933; found, 334.1934.

(6) Synthesis of (5*S,2'*R**,3'*R**)-3-Methyl-4-(3'-methyl-1',2'-dibromohept-2'-yl)-5-(α -naphthyl)furan-2(5*H*)-one (14ba) and (5*S**,2'*S**,3'*R**)-3-Methyl-4-(3'-methyl-1',2'-dibromohept-2'-yl)-5-(α -naphthyl)furan-2(5*H*)-one (14bb).** To a stirred solution of 13b (30 mg, 0.09 mmol) in 2 mL of CH₂Cl₂ was added Br₂ (0.36 mL, 0.50 mol/L in CH₂Cl₂), which was followed by stirring at room temperature for 5 h. After complete consumption of the starting material as monitored by TLC, a minimal amount of aqueous saturated solution of Na₂S₂O₃ was added until the disappearance of the deep color of the excess Br₂. The mixture was extracted with 30 mL of CH₂Cl₂, and the organic layer was dried over anhydrous Na₂SO₄. After evaporation of the solvent, the residue was purified via flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1) to afford 14ba (less polar, 6 mg, 14%) and 14bb (more polar, 34 mg, 77%). **14ba:** oil, ¹H NMR (300 MHz, CDCl₃) δ 8.33 (d, *J* = 8.7 Hz, 1H), 7.98–7.88 (m, 2H), 7.66–7.40 (m, 4H), 7.14 (q, *J* = 1.5 Hz, 1H), 3.69 (d, *J* = 10.2 Hz, 1H), 3.28 (d, *J* = 10.2 Hz, 1H), 2.52–2.38 (m, 1H), 2.33 (d, *J* = 1.5 Hz, 3H), 1.58–1.22 (m, 6H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.94 (t, *J* = 7.2 Hz, 3H); MS(ESI) *m/z* (%) 514 [M(2 × ⁸¹Br) + NH₄⁺], 512 [M(2 × ⁷⁹Br⁸¹Br) + NH₄⁺], 510 [M(2 × ⁷⁹Br) + NH₄⁺], 497 [M(2 × ⁸¹Br)⁺ + 1], 495 [M(2 × ⁷⁹Br⁸¹Br)⁺ + 1], 493 [M(2 × ⁷⁹Br)⁺ + 1]; IR (neat) 1762, 1512, 1459, 1379, 1313, 1100, 1020 cm⁻¹; HRMS calcd for C₂₃H₂₆O₂Br₂Na [M(2 × ⁷⁹Br) + Na⁺], 515.0192; found, 515.0187. **14bb:** solid, mp 107–109 °C (ethyl acetate/ether/petroleum ether), ¹H NMR (300 MHz, CDCl₃) δ 8.34 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 9.0 Hz, 2H), 7.68–7.50 (m, 2H), 7.50–7.35 (m, 2H), 7.18 (bs, 1H), 3.82 (d, *J* = 11.4 Hz, 1H), 3.73 (d, *J* = 11.4 Hz, 1H), 2.48–2.20 (m, 1H), 2.29 (d, *J* = 1.8 Hz, 3H), 1.59–1.42 (m, 2H), 1.42–1.20 (m, 2H), 1.18 (d, *J* = 6.6 Hz, 3H), 1.15–0.95 (m, 2H), 0.88 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 12.5, 14.0, 15.9, 22.8, 30.7, 32.7, 43.5, 79.6, 122.7, 124.9, 125.3, 126.1, 126.9, 129.0, 130.0, 130.4, 130.6, 131.4, 134.0, 158.2, 173.6; MS(ESI) *m/z* (%) 514 [M(2 × ⁸¹Br) + NH₄⁺], 512 [M(2 × ⁷⁹Br⁸¹Br) + NH₄⁺], 510 [M(2 × ⁷⁹Br) + NH₄⁺], 497 [M(2 × ⁸¹Br)⁺ + 1], 495 [M(2 × ⁷⁹Br⁸¹Br)⁺ + 1], 493 [M(2 × ⁷⁹Br)⁺ + 1]; IR (neat) 1759, 1512, 1464, 1380, 1312, 1100, 1018 cm⁻¹; HRMS calcd for C₂₃H₂₆O₂Br₂Na [M(2 × ⁷⁹Br) + Na⁺], 515.0192; found, 515.0189.

Acknowledgment. Financial support from the National Natural Science Foundation of China (20121202, 20332060, and 20423001), the State Basic and Research Development Program (Grant No. 2006CB806105), and the Shanghai Municipal Committee of Science and Technology is greatly appreciated. We thank Mr. Jinbo Zhao for reproducing the results presented in entry 7 of Table 2, entry 7 of Table 3, entry 1 of Table 4, and 13a in Scheme 4.

Supporting Information Available: ¹H/¹³C NMR spectra of all new compounds, chiral HPLC results of the optically active compounds, and X-ray data (CIF) of *Z*-5fa and 14bb. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA072790J