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

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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(5*H*)-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 $NaBH_4$, and the $CuBr{\cdot}SMe_2$-catalyzed S_N2'-substitution with CH_3MgBr.

Introduction

Butenolides [2(5*H*)-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 phospholiphase A_2 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. *Allenes 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.
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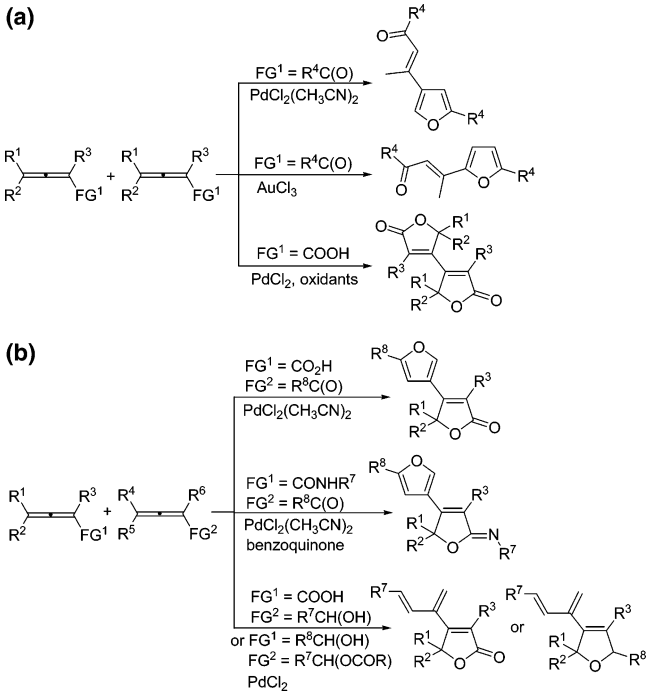
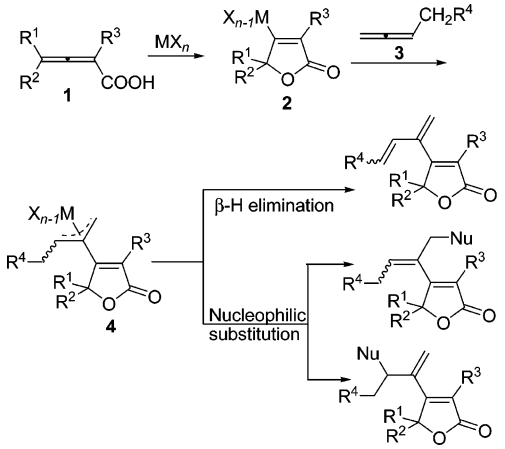
10.1021/ja072790j CCC: $37.00

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 $AuCl_3$ 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-Allenoic 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.[6e] Next, regioselective carbopalladation of simple allene **3** with **2** would give a π-allylic intermediate **4**,[14] which may undergo β-elimination[15] or nucleophilic substitution[14] 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 $LiBr{\cdot}H_2O$ 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 CH_3CN, CH_2Cl_2, 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) (a) 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.
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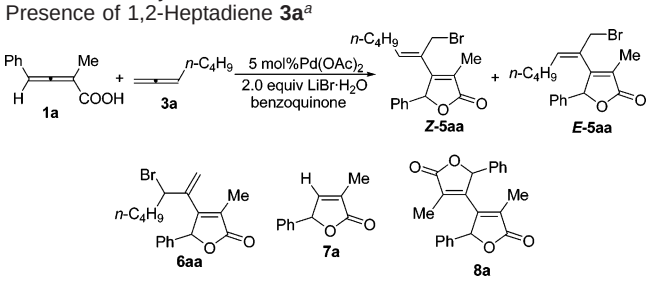
(16) (a) Grennberg, H.; Gogoll, A.; Bäckvall, J.-E. *Organmetallics* **1993**, *12*, 1790. (b) Albéniz, A. C.; Espinet, P.; Martín-Ruiz, B. *Chem.-Eur. J.* **2001**, *7*, 2481.

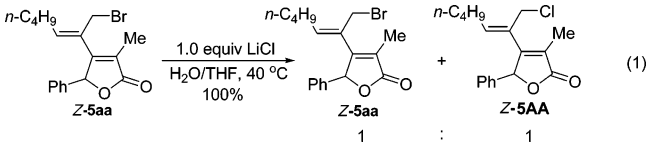
Table 1. The Cyclization Reaction of 2,3-Allenoic Acid **1a** in the Presence of 1,2-Heptadiene **3a**[a]



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_3CN	13/35	16
4[d]	1.1	CH_2Cl_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 $LiBr\cdot H_2O$, 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 $LiBr\cdot H_2O$ used contains LiCl. This problem could be solved when $LiBr\cdot H_2O$ of a higher purity[17] was used. The presence of chloride *Z*-**5AA** was confirmed by LC−MS analysis. The treatment of *Z*-**5aa** with LiCl in THF/H_2O 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.



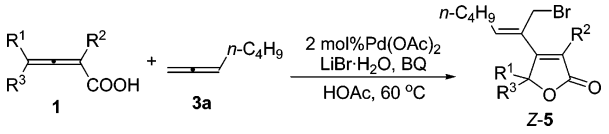
(1)

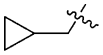
With this protocol in hand, we studied the generality of this cyclization reaction of substituted 2,3-allenoic acids in the presence of hepta-1,2-diene **3a**. With R^1 being phenyl (Table 2, entries 1−3), *p*-halophenyl (Table 2, entries 4 and 5), or α-naphthyl group (Table 2, entry 6), the reaction could afford the corresponding products smoothly. The fully substituted 2,3-allenoic 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) $LiBr\cdot H_2O$ contains less than 0.01% of chlorides.

(18) Crystal data for compound **5fa**: $C_{22}H_{23}O_2Br$, MW 399.31, monoclinic, *P*2(1)/*c*, Mo Kα, final *R* indices [$I > 2\sigma(I)$], R1 = 0.0685, wR2 = 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) Å^3, T = 293 (2) K, Z = 4, reflections collected/unique 11 159/4229 (R_{int} = 0.1412), number of observations [>2σ(*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]



	1			time	yield of *Z*-**5**
entry	R^1	R^2	R^3	(h)	(%)
1	Ph	Me	H (**1a**)	6	70 (*Z*-**5aa**)
2[b]	Ph	*n*-Pr	H (**1b**)	7	59 (*Z*-**5ba**)
3	Ph	*i*-Bu	H (**1c**)	7	44 (*Z*-**5ca**)
4	*p*BrC_6H_4	*n*-Pr	H (**1d**)	6	51 (*Z*-**5da**)
5	*p*ClC_6H_4	*n*-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 $LiBr\cdot H_2O$, 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.

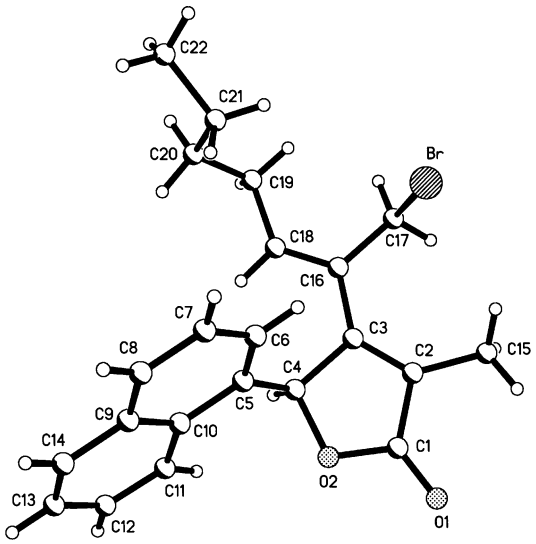


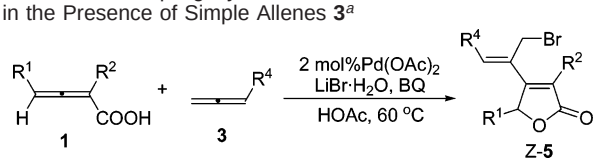
Figure 1. ORTEP representation of *Z*-**5fa**.

We also tested the reaction of 2,3-allenoic acids in the presence of other substituted alkyl- and aryl-substituted allenes; the yields are from moderate to good (Table 3). With R^4 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), acetoxyl (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-allenoic 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

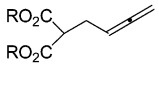
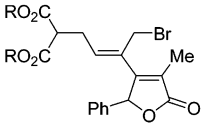
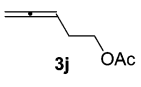
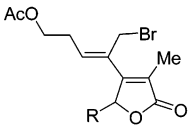
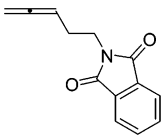
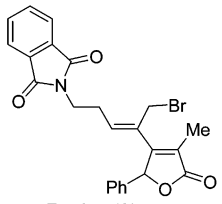
Table 3. The Coupling Cyclization Reaction of 2,3-Allenoic Acids **1** in the Presence of Simple Allenes **3**[a]



	1		3	time	yield of *Z*-**5**
entry	R^1	R^2	R^4	(h)	(%)
1	Ph	Me (**1a**)	*n*-C_6H_{13} (**3b**)	10.5	62 (*Z*-**5ab**)
2	Ph	Me (**1a**)	*n*-C_7H_{15} (**3c**)	6.5	59 (*Z*-**5ac**)
3[b]	Ph	Me (**1a**)	*n*-C_8H_{17} (**3d**)	8	60 (*Z*-**5ad**)
4	Ph	Me (**1a**)	*c*-C_6H_{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_6H_4	*n*-Pr (**1d**)	*n*-C_6H_{13} (**3b**)	6	57 (*Z*-**5db**)
8	Ph	Et (**1i**)	*n*-C_7H_{15} (**3c**)	18.5	50 (*Z*-**5ic**)
9	Ph	allyl (**1j**)	*n*-C_8H_{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**	 R = Me, **3h**	 R = Me, *Z*-**5ah**, 58%
2		R = Et, **3i**	R = Et, *Z*-**5ai**, 60%
3	**1a**	 **3j**	 R = Ph, *Z*-**5aj**, 67%
4	**1f**		R = α-Naphthyl, *Z*-**5fj**, 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 $LiBr{\cdot}H_2O$, 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]

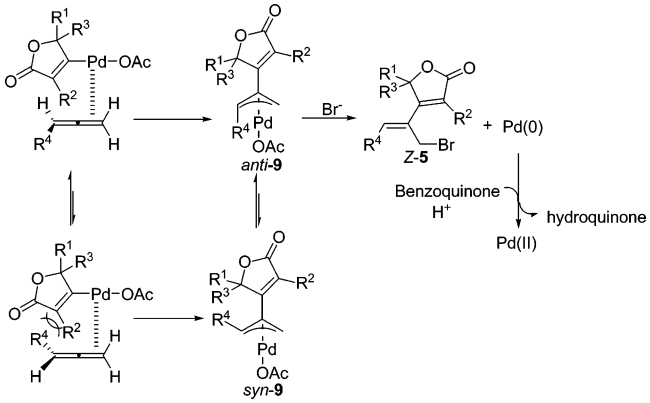
The highly selective formation of *Z*-isomer is remarkable in view of the fact that most carbopalladation reactions of monosubstituted allenes reported gave a mixture of *E* and *Z* isomeric products with low selectivity.[19] A plausible mechanism based on the face-selective coordination of allenes with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

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

		yield of *R*-(−)-*Z*-**5**	
entry	R	(%)	% ee of *Z*-**5**
1	*n*-C_4H_9 (**3a**)	63 (*R*-(−)-*Z*-**5aa**)	98
2	*n*-C_6H_{13} (**3b**)	67 (*R*-(−)-*Z*-**5ab**)	98
3	CH_2CH_2OAc (**3j**)	70 (*R*-(−)-*Z*-**5aj**)	98
4	Ph (**3f**)	80 (*R*-(−)-*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 $LiBr{\cdot}H_2O$, 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 R^4 favorably to avoid the steric congestion, which results in the formation of a π-allylpalladium species *anti*-**9** with the R^4 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(5*H*)-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 Et_2NH 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 $NaBH_4$ the C−Br bond of *Z*-**5aa** may be reduced to afford *E*-**12** in 71% yield ($E/Z \geq 22/1$) with a regioselectivity of 15/1.[22] In these cases, the substitution reaction occurred at the less-substituted

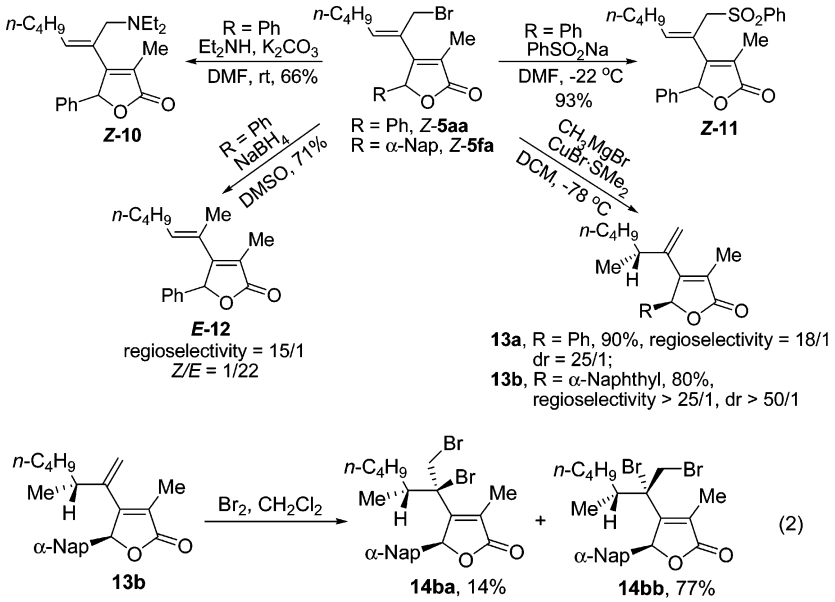
(19) For the stereoselectivity of carbometallation of allenes, see: (a) Larock, R. C.; Tu, C.; Pace, P. *J. Org. Chem.* **1998**, *63*, 6859. (b) Larock, R. C; He, Y.; Long, W. W.; Han, X.; Refvik, M. D.; Zenner, J. M. *J. Org. Chem.* **1998**, *63*, 2154. (c) Ma, S.; Negishi, E. I. *J. Am. Chem. Soc.* **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·SMe_2, the reaction of *Z*-**5aa** and *Z*-**5fa** with CH_3MgBr 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(5*H*)-one (*Z*-5aa). Typical Procedure. A mixture of **1a** (44 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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 ^{1}H NMR spectra. The residue was purified via flash chromatography on silica gel to afford *Z*-**5aa** (63 mg, 71%): oil, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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^+(^{81}Br) + 1, 0.67], 349 [M^+(^{79}Br) + 1, 0.84], 105 (100); IR (neat) 2957, 1758, 1637, 1456, 1380, 1209, 1095 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{18}H_{22}O_2Br$ [M^+(^{79}Br) + 1], 349.0798; found, 349.0808.

(2) Synthesis of 3-Propyl-4-(1′-bromohept-2′(*Z*)-en-2′-yl)-5-phenylfuran-2(5*H*)-one (*Z*-5ba). A mixture of **1b** (51 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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^+(^{81}Br) + 1], 377 [M^+(^{79}Br) + 1]; IR (neat) 2959, 1757, 1634, 1458, 1005 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{26}O_2Br$ [M^+(^{79}Br) + 1], 377.1111; found, 377.1105.

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

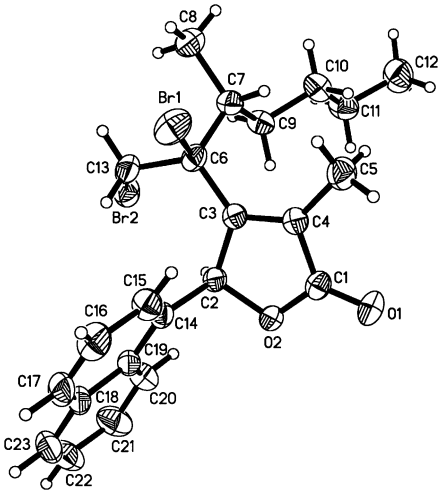


Figure 2. ORTEP representation of **14bb**.

(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**: $C_{23}H_{26}Br_2O_2$, MW 494.26, triclinic, *P*-1, Mo Kα, final *R* indices [$I > 2\sigma(I)$], R1 = 0.0603, wR2 = 0.1625, *R* indices (all data), R1 = 0.0871, wR2 = 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) Å^3, T = 293(2) K, Z = 2, reflections collected/unique 6145/4361 (R_{int} = 0.0891), number of observations [$>2\sigma(I)$] 2600, parameters 255. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC 651341.

phenylfuran-2(5*H*)-one (*Z*-5ca). A mixture of **1c** (51 mg, 0.236 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M^+(^{81}Br)$ + 1], 391[$M^+(^{79}Br)$ + 1]; IR (neat) 2957, 1759, 1667, 1456, 1009 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{21}H_{28}O_2Br$ [$M^+(^{79}Br)$ + 1], 391.1267; found, 391.1278.

(4) Synthesis of 3-Propyl-4-(1′-bromohept-2′(*Z*)-en-2′-yl)-5-(4″-bromophenyl)-furan-2(5*H*)-one (*Z*-5da). A mixture of **1d** (70 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M(^{81}Br^{81}Br)$ + Na^+], 479 [$M(^{81}Br^{79}Br)$ + Na^+], 477 [$M(^{79}Br^{79}Br)$ + Na^+], 459 [$M^+(^{81}Br^{81}Br)$ + 1], 457 [$M^+(^{81}Br^{79}Br)$ + 1], 455 [$M^+(^{79}Br^{79}Br)$ + 1]; IR (neat) 2959, 1753, 1637, 1489, 1006 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{25}O_2Br_2$ [$M^+(^{79}Br)$ + 1], 455.0216; found, 455.0216.

(5) Synthesis of 4-(1′-Bromohept-2′(*Z*)-en-2′-yl)-3-butyl-5-(4″-chlorophenyl)-furan-2(5*H*)-one (*Z*-5ea). A mixture of **1e** (63 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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, 1H), 3.89 (d, J = 10.8, 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M^+(^{37}Cl^{81}Br)$ + 1], 427 [$M^+(^{35}Cl^{81}Br + ^{37}Cl^{79}Br)$ + 1], 425 [$M^+(^{35}Cl^{79}Br)$ + 1]; IR (neat) 2957, 1758, 1493, 1084, 1010 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{21}H_{27}O_2BrCl$ [$M^+(^{35}Cl^{79}Br)$ + 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(5*H*)-one (*Z*-5fa). A mixture of **1f** (56 mg, 0.25 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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); ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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(EI) *m*/*z* (%) 400 [$M^+(^{81}Br)$ + 1, 4.96], 398 [$M^+(^{79}Br)$ + 1, 4.24], 319 (100); IR (KBr) 2957, 1753, 1635, 1458, 1097 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{22}H_{24}O_2Br$ [$M^+(^{79}Br)$ + 1], 399.0954; found, 399.0951.

(7) Synthesis of 4-(1′-Bromohept-2′(*Z*)-en-2′-yl)-3-methyl-5-ethyl-5-phenylfuran-2(5*H*)-one (*Z*-5ga). A mixture of **1g** (47 mg, 0.233 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M(^{81}Br)$ + K^+], 418 [$M(^{79}Br)$ + K^+], 396 [$M(^{81}Br)$ + NH_4^+], 394 [$M(^{79}Br)$ + NH_4^+], 379 [$M^+(^{81}Br)$ + 1], 377 [$M^+(^{79}Br)$ + 1]; IR (neat) 2928, 1757, 1448, 1210, 1079 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{25}O_2BrNa$ [$M(^{79}Br)$ + Na^+], 399.0930; found, 399.0936.

(8) Synthesis of 4-(1′-Bromohept-2′(*Z*)-en-2′-yl)-3-cyclopropylmethenyl-5-phenylfuran-2(5*H*)-one (*Z*-5ha). A mixture of **1h** (54 mg, 0.252 mmol), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M^+(^{81}Br)$ + 1, 5.34], 389 [$M^+(^{79}Br)$ + 1, 5.43], 91 (100); IR (neat) 1758, 1634, 1497, 1456, 1209, 1014 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{25}O_2Br$ [$M^+(^{79}Br)$], 388.1038; found, 388.1035.

(9) Synthesis of 4-(1′-Bromonon-2′(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5ab). A mixture of **1a** (44 mg, 0.25 mmol), **3b** (62 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$): 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M(^{81}Br)$ + NH_4^+], 394 [$M(^{79}Br)$ + NH_4^+], 379 [$M^+(^{81}Br)$ + 1], 377 [$M^+(^{79}Br)$ + 1]; IR (neat) 2927, 1757, 1637, 1456, 1096 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{26}O_2Br$ [$M^+(^{79}Br)$ + 1], 377.1111; found, 377.1107.

(10) Synthesis of 4-(1′-Bromodec-2′(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5ac). A mixture of **1a** (44 mg, 0.25 mmol), **3c** (69 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 [$M^+(^{81}Br)$ + 1, 1.39], 391 [$M^+(^{79}Br)$ + 1, 1.52], 105 (100); IR (neat) 2926, 1758, 1636, 1456, 1095 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{21}H_{28}O_2Br$ [$M^+(^{79}Br)$ + 1], 391.1267; found, 391.1280.

(11) Synthesis of 4-(1′-Bromoundec-2′(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5ad). A mixture of **1a** (44 mg, 0.25 mmol), **3d** (76 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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(EI) m/z (%) 407 [M^+(^{81}Br) + 1, 1.38], 405 [M^+(^{79}Br) + 1, 1.50], 105 (100); IR (neat) 2926, 1758, 1636, 1456, 1094 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{22}H_{30}O_2Br$ [M^+(^{79}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(5*H*)-one (*Z*-5ae). A mixture of **1a** (43 mg, 0.25 mmol), **3e** (61 mg, 0.50 mmol), LiBr·H_2O (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*-**5ae** (65 mg, 70%): oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.30 (m, 3H), 7.22−7.18 (m, 2H), 5.92 (q, J = 1.8 Hz, 1H), 5.47 (d, J = 9.9 Hz, 1H), 4.01 (d, J = 10.5 Hz, 1H), 3.95 (d, J = 10.5 Hz, 1H), 2.35−2.20 (m, 1H), 2.07 (d, J = 1.8 Hz, 3H), 1.70−1.43 (m, 5H), 1.37−0.90 (m, 5H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 10.2, 25.1, 25.5, 27.2, 31.9, 32.0, 37.3, 83.3, 124.4, 126.4, 127.4, 128.7, 129.3, 134.8, 146.9, 158.1, 174.4; MS(ESI) m/z 394 [M(^{81}Br) + NH_4^+], 392 [M(^{79}Br) + NH_4^+], 377 [M^+(^{81}Br) + 1], 375 [M^+(^{79}Br) + 1]; IR (neat) 2926, 1756, 1448, 1207, 1094 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{24}O_2Br$ [M^+(^{79}Br) + 1], 375.0954; found, 375.0968.

(13) Synthesis of 4-(1′-Bromo-3′-phenylprop-2′(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5af). A mixture of **1a** (43 mg, 0.25 mmol), **3f** (58 mg, 0.50 mmol), LiBr·H_2O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $Pd(OAc)_2$ (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, ^{1}H 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 [M(^{81}Br) + NH_4^+], 386 [M(^{79}Br) + NH_4^+], 371 [M^+(^{81}Br) + 1], 369 [M^+(^{79}Br) + 1]; IR (neat) 1754, 1622, 1496, 1455, 1091 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{18}O_2Br$ [M^+(^{79}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(5*H*)-one (*Z*-5ag). A mixture of **1a** (43 mg, 0.25 mmol), **3g** (65 mg, 0.50 mmol), LiBr·H_2O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $Pd(OAc)_2$ (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, ^{1}H 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 [M^+(^{81}Br) + 1], 383 [M^+(^{79}Br) + 1]; IR (neat) 1755, 1638, 1602, 1495, 1454, 1095, 1014 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{21}H_{20}O_2Br$ [M^+(^{79}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(5*H*)-one (*Z*-5db). A mixture of **1d** (70 mg, 0.25 mmol), **3b** (62 mg, 0.50 mmol), LiBr·H_2O (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*-**5db** (69 mg, 57%): oil, ^{1}H 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 [M(^{81}Br^{81}Br) + NH_4^+], 502 [M(^{81}Br^{79}Br) + NH_4^+], 500 [M(^{79}Br^{79}Br) + NH_4^+], 487 [M^+(^{81}Br^{81}Br) + 1], 485 [M^+(^{81}Br^{79}Br) + 1], 483 [M^+(^{79}Br^{79}Br) + 1]; IR (neat) 2928, 1758, 1634, 1489, 1207, 1006 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{22}H_{29}O_2Br_2$ [M^+(^{79}Br) + 1], 483.0529; found, 483.0535.

(16) Synthesis of 4-(1′-Bromodec-2′(*Z*)-en-2′-yl)-3-ethyl-5-phenylfuran-2(5*H*)-one (*Z*-5ic). A mixture of **1i** (47 mg, 0.25 mmol), **3c** (69 mg, 0.50 mmol), LiBr·H_2O (53 mg, 0.50 mmol), benzoquinone (41 mg, 0.375 mmol), and $Pd(OAc)_2$ (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, ^{1}H 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(EI) m/z (%) 407 [M^+(^{81}Br) + 1, 1.46], 405 [M^+(^{79}Br) + 1, 1.63], 105 (100); IR (neat) 2927, 1758, 1639, 1458, 1004 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{22}H_{30}O_2Br$ [M^+(^{79}Br) + 1], 405.1424; found, 405.1426.

(17) Synthesis of 3-Allyl-4-(1′-bromoundec-2′(*Z*)-en-2′-yl)-5-phenylfuran-2(5*H*)-one (*Z*-5jd). A mixture of **1j** (52 mg, 0.26 mmol), **3d** (76 mg, 0.50 mmol), LiBr·H_2O (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*-**5jd** (62 mg, 56%): oil, ^{1}H 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 [M^+(^{81}Br) + 1], 431 [M^+(^{79}Br) + 1]; IR (neat) 2926, 1760, 1639, 1456, 1013 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{24}H_{31}O_2BrNa$ [M(^{79}Br) + Na^+], 453.1400; found, 453.1394.

(18) Synthesis of 4-(1′-Bromo-5′,5′-dimethoxylcarbonylpenta-2′-(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5ah). A mixture of **1a** (43 mg, 0.25 mmol), **3h** (92 mg, 0.50 mmol), LiBr·H_2O (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 a mixture of *Z*-**5ah** and hydroquinone. The mixture was then dissolved in 30 mL of CH_2Cl_2, washed with water (5 mL × 3), and dried over Na_2SO_4. The solvent was evaporated to afford pure *Z*-**5ah** (63 mg, 58%): oil, ^{1}H 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 [M(^{81}Br) + Na^+], 459 [M(^{79}Br) + Na^+], 439 [M^+(^{81}Br) + 1], 437 [M^+(^{79}Br) + 1]; IR (neat) 1755, 1650, 1498, 1456, 1436, 1274, 1210, 1158, 1094, 1014 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{20}H_{22}O_6Br$ [M^+(^{79}Br) + 1], 437.0594; found, 437.0590.

(19) Synthesis of 4-(1′-Bromo-5′,5′-diethoxylcarbonylpenta-2′(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5ai). A mixture of **1a** (44 mg, 0.25 mmol), **3i** (106 mg, 0.50 mmol), LiBr·H_2O (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*-**5ai** (71 mg, 60%): oil, ^{1}H 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 [M(^{81}Br) + Na^+], 487 [M(^{79}Br) + Na^+], 467 [M^+(^{81}Br) + 1], 465 [M^+(^{79}Br) + 1]; IR (neat) 1755, 1456, 1370, 1269, 1095, 1017 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{22}H_{26}O_6Br$ [M^+(^{79}Br) + 1], 465.0907; found, 465.0898.

(20) Synthesis of 4-(1′-Bromo-5′-acetoxylpenta-2′(*Z*)-en-2′-yl)-3-methyl-5-phenylfuran-2(5*H*)-one (*Z*-5aj). A mixture of **1a** (44 mg, 0.25 mmol), **3j** (63 mg, 0.50 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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^+(^{81}Br) + 1, 1.27], 379 [M^+(^{79}Br) + 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 $C_{18}H_{19}O_4$ [M^+ − Br], 299.1283; found, 299.1280.

(21) Synthesis of 4-(1′-Bromo-5′-acetoxylpenta-2′(*Z*)-en-2′-yl)-3-methyl-5-(α-naphthyl)-furan-2(5*H*)-one (*Z*-5fj). A mixture of **1f** (56 mg, 0.25 mmol), **3j** (62 mg, 0.49 mmol), LiBr·H_2O (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, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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^+(^{81}Br) + 1], 429 [M^+(^{79}Br) + 1]; IR (neat) 1751, 1598, 1638, 1450, 1239, 1095, 1035 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{22}H_{21}O_4BrNa$ [M(^{79}Br) + 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(5*H*)-one (*Z*-5ak). A mixture of **1a** (44 mg, 0.25 mmol), **3k** (106 mg, 0.50 mmol), LiBr·H_2O (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 CH_2Cl_2, then washed with water (5 mL × 4), and dried over Na_2SO_4. The solvent was evaporated, and the residue was purified via flash chromatography on silica gel to afford *Z*-**5ak** (87 mg, 74%): oil, ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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(^{81}Br) + K^+], 504 [M(^{79}Br) + K^+], 490 [M(^{81}Br) + Na^+], 488 [M(^{79}Br) + Na^+], 468 [M^+(^{81}Br) + 1], 466 [M^+(^{79}Br) + 1]; IR (neat) 1755, 1710, 1396, 1361, 1097, 1007 cm^{-1}; HRMS (MALDI/DHB) calcd for $C_{24}H_{21}NO_4$-Br [M^+(^{79}Br) + 1], 466.0649; found, 466.0645.

Typical Procedure for the Cyclization of Optically Active 2,3-Allenoic 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(5*H*)-one (*R*-(−)-*Z*-5aa). A mixture of *R*-(−)-**1a** (44 mg, 0.25 mmol, 98%ee), **3a** (48 mg, 0.50 mmol), LiBr·H_2O (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. $[\alpha]_D^{20}$ = −215° (c = 0.590, $CHCl_3$).

(2) Synthesis of *R*-(−)-3-Methyl-4-(1′-bromonon-2′(*Z*)-en-2′-yl)-5-phenylfuran-2(5*H*)-one (*R*-(−)-5ab). A mixture of *R*-(−)-**1a** (43 mg, 0.25 mmol, 98%ee), **3b** (62 mg, 0.50 mmol), LiBr·H_2O (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. $[\alpha]_D^{20}$ = −166° (c = 0.900, $CHCl_3$).

(3) Synthesis of *R*-(−)-3-Methyl-4-(1′-bromo-5′-acetoxylpenta-2′(*Z*)-en-2′-yl)-5-phenylfuran-2(5*H*)-one (*R*-(−)-*Z*-5aj). A mixture of *R*-(−)-**1a** (43 mg, 0.25 mmol, 98%ee), **3j** (63 mg, 0.50 mmol), LiBr·H_2O (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. $[\alpha]_D^{20}$ = −187° (c = 1.300, $CHCl_3$).

(4) Synthesis of *R*-(−)-3-Methyl-4-(1′-bromo-3′-phenylprop-2′-(*Z*)-en-2′-yl)-5-phenylfuran-2(5*H*)-one (*R*-(−)-*Z*-5af). A mixture of *R*-(−)-**1a** (44 mg, 0.25 mmol, 98%ee), **3f** (58 mg, 0.50 mmol), LiBr·H_2O (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. $[\alpha]_D^{20}$ = −487° (c = 0.710, $CHCl_3$).

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 H_2O (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(5*H*)-one (*Z*-10). Under an argon atmosphere, a mixture of ***Z*-5aa** (59 mg, 0.17 mmol), Et_2NH (25 mg, 0.34 mmol), K_2CO_3 (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 H_2O (5 mL) and extracted with 50 mL of ether. The organic layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated, and the crude product was analyzed by ^{1}H NMR spectra. The residue was purified via flash chromatography on silica gel to afford *Z*-**10** (38 mg, 66%): ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 $C_{22}H_{31}NO_2$ [M^+], 341.2355; found, 341.2362.

(2) Synthesis of 3-Methyl-4-(1′-phenylsulfonylhepta-2′(*Z*)-en-2′-yl)-5-phenyl-furan-2(5*H*)-one (*Z*-11). Under an argon atmosphere, a mixture of ***Z*-5aa** (54 mg, 0.15 mmol), $PhSO_2Na$·$2H_2O$ (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 H_2O and brine. The organic layer was dried over Na_2SO_4. The solvent was evaporated, and the crude product was analyzed by ^{1}H NMR spectra. The residue was purified via flash chromatography on silica gel to afford *Z*-**11** (59 mg, 93%): ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 $C_{24}H_{26}O_4S$ [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), $NaBH_4$ (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 H_2O and brine. The organic layer was dried over Na_2SO_4. The solvent was evaporated, and the crude product was analyzed by ^{1}H NMR spectra (regiolectivity: 1/15, $E/Z \geq 22/1$). The residue was purified via flash chromatography on silica gel to afford pure *E*-**12** (38 mg, 71%): ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 $C_{18}H_{22}O_2$ [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·SMe_2 (2 mg, 0.01 mmol), and DCM (4 mL) was cooled to −78 °C. A solution of CH_3MgBr [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 H_2O 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 ^{1}H NMR spectra (regioselectivity = 18/1, dr = 25/1). The residue was purified via flash chromatography on silica gel to afford **13a** (51 mg, 90%): ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 $C_{19}H_{24}O_2$ [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·SMe_2 (1 mg, 0.005 mmol) in DCM (3 mL) was added CH_3MgBr (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 H_2O 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 ^{1}H NMR spectra (regioselectivity >25/1, dr >50/1). The residue was purified via flash chromatography on silica gel to afford **13b** (36 mg, 80%): ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 $C_{23}H_{26}O_2$ [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 CH_2Cl_2 was added Br_2 (0.36 mL, 0.50 mol/L in CH_2Cl_2), 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 $Na_2S_2O_3$ was added until the disappearance of the deep color of the excess Br_2. The mixture was extracted with 30 mL of CH_2Cl_2, and the organic layer was dried over anhydrous Na_2SO_4. 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, ^{1}H NMR (300 MHz, $CDCl_3$) 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 × ^{81}Br) + NH_4^+], 512 [M(2 × ^{79}Br^{81}Br) + NH_4^+], 510 [M(2 × ^{79}Br) + NH_4^+], 497 [M(2 × ^{81}Br)$^+$ + 1], 495 [M(2 × ^{79}Br^{81}Br)$^+$ + 1], 493 [M(2 × ^{79}Br)$^+$ + 1]; IR (neat) 1762, 1512, 1459, 1379, 1313, 1100, 1020 cm^{-1}; HRMS calcd for $C_{23}H_{26}O_2Br_2Na$ [M(2 × ^{79}Br) + Na^+], 515.0192; found, 515.0187. **14bb**: solid, mp 107−109 °C (ethyl acetate/ether/petroleum ether), ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75.4 MHz, $CDCl_3$) 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 × ^{81}Br) + NH_4^+], 512 [M(2 × ^{79}Br^{81}Br) + NH_4^+], 510 [M(2 × ^{79}Br) + NH_4^+], 497 [M(2 × ^{81}Br)$^+$ + 1], 495 [M(2 × ^{79}Br^{81}Br)$^+$ + 1], 493 [M(2 × ^{79}Br)$^+$ + 1]; IR (neat) 1759, 1512, 1464, 1380, 1312, 1100, 1018 cm^{-1}; HRMS calcd for $C_{23}H_{26}O_2Br_2Na$ [M(2 × ^{79}Br) + Na^+], 515.0192; found, 515.0189.

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Supporting Information Available: ^{1}H/^{13}C 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.

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