Pd^{II}-Catalyzed Oxidative Dimeric Cyclization–Coupling Reaction of 2,3-Allenoic Acids: An Efficient Synthesis of Bibutenolide Derivatives

Shengming Ma,* Zhanqian Yu, and Zhenhua Gu[a]

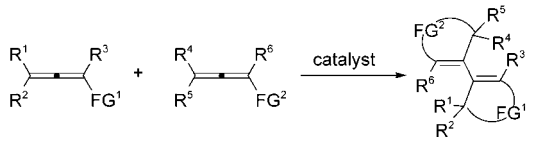
Abstract: Three sets of convenient catalytic systems have been developed for the oxidative dimeric cyclization coupling of differently substituted 2,3-allenoic acids catalyzed by Pd^{II}, affording bibutenolides that are not otherwise readily available. The advantages and disadvantages of these systems are discussed. Although the diastereoselectivity for the bicyclization of racemic 2,3-allenoic acids is low, excellent diastereoselectivity was realized in the bicyclization reaction of optically active 2,3-allenoic acids, leading to the optically active bibutenolides in high yields and *ee*. Based on a mechanistic study, it is believed that the reaction may proceed by means of a double oxypalladation and reductive elimination to yield butenolide **3** and Pd^0 species, which may be reoxidized to the catalytically active Pd^{II} species in the presence of alkyl iodide/air, metallic iodide/air, or benzoquinone.

Keywords: allenes · butenolides · homogeneous catalysis · palladium

Introduction

Allenes are three-carbon functional groups that possess two perpendicular π orbitals with great potential in organic synthesis in terms of chirality transfer and diversity, due to the existence of the axial chirality and the substituent-loading capability.[1,2] Under the catalysis of the palladium species, functionalized allene compounds have also been reported to form a variety of cyclic compounds.[3–8] Recently, we established a new area of transition-metal-catalyzed oxidative cyclization–dimerization reactions between two different functionalized allenes to give interesting bicyclic compounds in a single step (Scheme 1).[9]

In this reaction, the regeneration of catalytically active Pd^{II} is critical.[10] In a preliminary communication,[11] we disclosed an oxidative cyclization–coupling reaction of 2,3-allenoic acids catalyzed by $PdCl_2$ by applying excess of an alkyl iodide as the oxidant for the synthesis of bibutenolides, which is of current interest due to their potential biological activities and a structural unit in many natural products.[12] In this paper, we wish to present new and efficient catalytic systems; the scope and mechanism of this reaction in detail.



Scheme 1. FG = functional group.

Results and Discussion

We have developed three systems to realize this reaction. The results are listed in Table 1. When five equivalents of propyl iodide (**2a**) were added in DMA, the oxidative cyclization–coupling reaction catalyzed by $PdCl_2$ led to the formation of **3a** in 74% yield (Table 1, entry 1). The yield decreased when a smaller amount of **2a** was added (Table 1, entry 2). Furthermore the yields were also lower in other solvents (Table 1, entries 3–5). An explanation of this reaction is the possible oxidation of the in-situ formed Pd^0 to Pd^{II} with I_2, which may be formed by the aerobic oxidation of I^- released from alkyl iodide. Thus, alkyl iodide was replaced with metallic iodide. It is interesting to observe that the reaction also proceeded smoothly to yield **3a** (Table 1, entries 6–9). Furthermore, the reaction can also occur with

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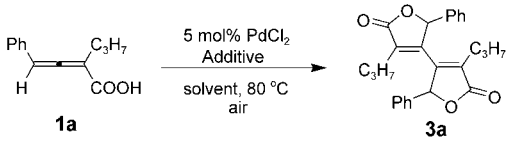
Table 1. Pd^{II}-catalyzed oxidative cyclization–coupling reaction of 4-phenyl-2-propyl-2,3-butadienoic acid (**1a**).[a]



1a **3a**

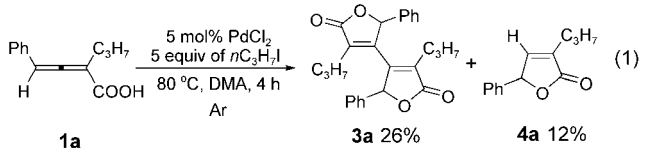
Entry	Additive (equiv)	Solvent	*T* [°C]	*t* [h]	Yield of **3a** [%][b]
1	C_3H_7I (5)	DMA	80	10	74
2	C_3H_7I (3)	DMA	80	6.5	62
3	C_3H_7I (5)	THF	reflux	46	trace
4	C_3H_7I (5)	MeCN	reflux	16	66
5	C_3H_7I (5)	EtOH	reflux	10	42
6	TBAI (1)	DMA	80	5	62
7	NaI (0.5)	DMA	80	5	68
8	KI (0.5)	DMA	80	5	74
9	KI (0.2)	DMA	80	5	64
10	BQ[c] (0.63)	DMF	80	2	92

[a] The reaction was carried out using 0.25 mmol of 2,3-allenoic acids. [b] Isolated yield. [c] BQ = benzoquinone.

20 mol% KI. The best result was obtained when 50 mol% KI was used, leading to a 74% yield of product **3a** (Table 1, entry 8). In addition, benzoquinone was reported to be a good oxidant for the transformation of Pd^0 to Pd^{II} under acidic conditions.[13] Thus, 0.63 equivalents of benzoquinone (slightly more than the required 0.5 equiv) was applied as the oxidant to afford **3a** in a much higher yield (92%; Table 1, entry 10).

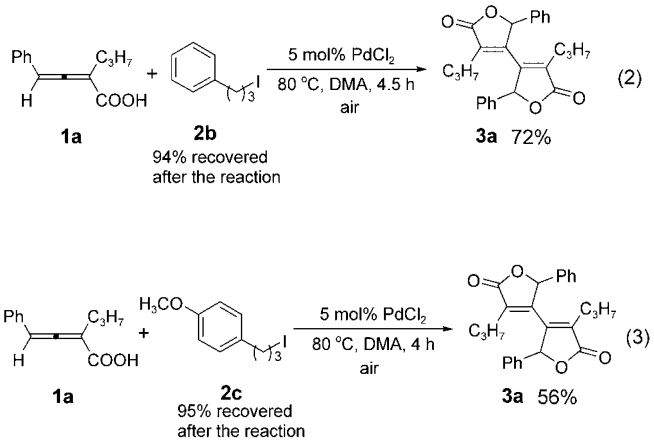
Some typical results are summarized in Table 2. It should be noted that a variety of alkyl- and aryl-substituted 2,3-allenoic acids successfully underwent cyclization–coupling reactions to afford bibutenolides in decent yields. The RI/O_2 system (method A) is the most general, although the yield may not be the highest; with R^1 being alkyl and R^2 being benzyl, alkyl, or hydrogen, the reaction did not give the corresponding product in good yields when KI (method B) was used as the additive (Table 2, entries 16, 19, 23, 27, 31, 35, and 39). Benzoquinone (methods C and D) is more suitable for the reaction of 4-aryl-2-alkyl/benzyl-substituted and 4-alkyl-substituted-2-nonsubstituted allenoic acids, affording bibutenolides **3a–e,j–l** in higher yields (Table 2, entries 3, 6, 9, 11, 14, 32, 33, 36, 37, 40, and 41).

Mechanistic study: At first, the reaction with 5 mol% $PdCl_2$ under an argon atmosphere occurred with difficulty to afford **3a** only in 26% yield, along with **4a** in a 12% yield [Eq. (1)], which indicates that the oxygen in air may participate in the catalytic cycle.



1a **3a** 26% **4a** 12%

When we used two alkyl iodides with high boiling points, that is, **2b** and **2c**, after the reaction they were recovered in 94 and 95% yields, respectively, indicating that most of the alkyl iodide was not consumed during the reaction [Eqs. (2) and (3)]. After analyzing the crude reaction mixture, no product derived from the alkyl iodide was detected.



In all the cases reported in Table 2, the distereoselectivity of the products is low, ranging from 1.0 to 2.18. However, with optically active 4-aryl-2,3-allenoic acids, which could be easily obtained by resolution of the racemic allenoic acids, only one diastereoisomer of **3** was obtained. Some typical results are listed in Table 3. In the presence of benzoquinone, the reaction gave the corresponding compounds in excellent yields, diastereoselectivity, and *ee*. The absolute configurations of two chiral centers in the product (+)-**3o** from the *S*-configuration allenoic acid (*S*)-(+)-**1o** were determined to be *S,S* by the X-ray diffraction study (Figure 1),[15] indicating that the cyclization was realized by a Pd^{II}-catalyzed oxypalladation process.[2e–g]

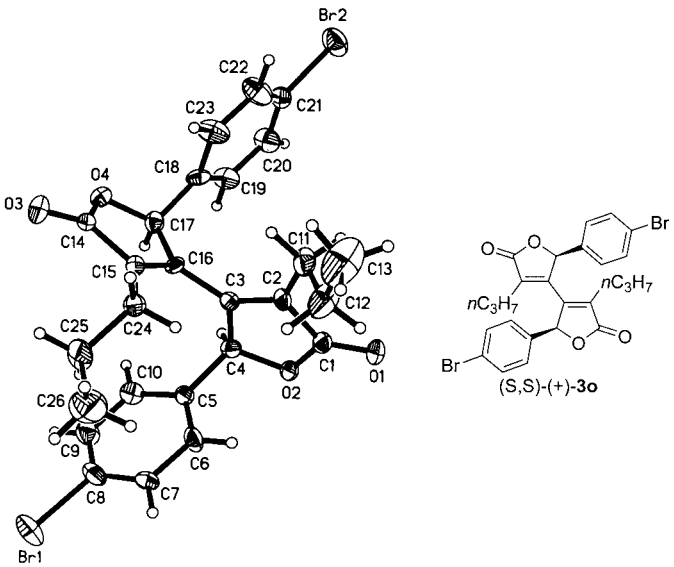
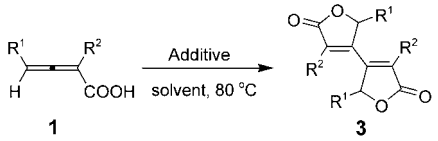


Figure 1. ORTEP representation of the product (*S,S*)-(+)-**3o**.

Table 2. Oxidative dimeric cyclizing-coupling reaction of 2,3-allenoic acids.



1 3

Entry	Substrate **1**		Method[a]	*t*	Yield	*R*S*/R*R**
	R^1	R^2		[h]	[%] of **3**	
1	Ph	*n*-C_3H_7 (**1a**)	method A	10	74 (**3a**)	1/1.87
2			method B	5	75 (**3a**)	1/2.18
3			method C	2	92 (**3a**)	1/1.65
4	Ph	CH_3 (**1b**)	method A	4	64 (**3b**)	1/1.62
5			method B	4	74 (**3b**)	1/1.66
6			method C	2	96 (**3b**)	1/2.03
7	Ph	$PhCH_2$ (**1c**)	method A	11.5	75 (**3c**)	1/1.53
8			method B	11.5	mixture	–
9			method C	2	94 (**3c**)	0.9/1
10	α-naphthyl	CH_3 (**1d**)	method A	4	71 (**3d**)	1/1.28
11			method C	2	92 (**3d**)	1/1.84
12	α-naphthyl	*n*-C_3H_7 (**1e**)	method A	4.5	64 (**3e**)	1/1.43
13			method B	6	65 (**3e**)	1/1.54
14			method C	2	67 (**3e**)	1/1.33
15	CH_3	$PhCH_2$ (**1f**)	method A	3.5	72 (**3f**)	1.04/1
16			method B	5	15 (**3f**)	–
17			method C	2	36 (**3f**)	–
18	*n*-C_6H_{13}	CH_3 (**1g**)	method A	21	47 (**3g**)	1/1.87
19			method B	17	11 (**3g**)	1.23/1
20			method C	3.5	13 (**3g**)	1/1.84
21			method D	2	[b]	–
22	CH_3	CH_3 (**1h**)	method A	20	43 (**3h**)	1/1.13
23			method B	22.5	mixture	–
24			method C	2	22 (**3h**)	1/2
25			method D	11	20 (**3h**)	1/1.62
26	*n*-C_3H_7	*n*-C_3H_7 (**1i**)	method A	17	61 (**3i**)	1/1.59
27			method B	2.5	25 (**3i**)	1/1.02
28			method C	2	[c]	–
29			method D	2.5	mixture	–
30	*n*-C_5H_{11}	H (**1j**)	method A	3	52 (**3j**)	1/1.67
31			method B	15	mixture	–
32			method C	2	46 (**3j**)	1/1.06
33			method D	2	61 (**3j**)	1.19/1
34	*n*-C_7H_{15}	H (**1k**)	method A	6	49 (**3k**)	1/1
35			method B	21	mixture	–
36			method C	2	80 (**3k**)	1.06/1
37			method D[d]	2	83 (**3k**)	1/1.05
38	*n*-C_8H_{17}	H (**1l**)	method A	3	54 (**3l**)	1/1[e]
39			method B	2	32 (**3l**)	1/1.38
40			method C	2	71 (**3l**)	1/1.06
41			method D	2	73 (**3l**)	1/1.06
42	H	Bn (**1m**)	method A	10.5	mixture	–
43	H	H (**1n**)	method C	2	NR	–

[a] See the Experimental Section for the general procedures for methods A–D. [b] 62% of cycloismerization product was isolated. [c] 8% of cycloismerization product was isolated. [d] Carried out in 0.25 mmol scale of 2,3-allenoic acid. [e] The stereochemistry of **3l** was determined by the X-ray diffraction study,[14] and the stereochemistry of **3j** and **3k** were established by the comparison with **3l**.

Based upon these experimental findings, it was proposed that the Pd^{II} species firstly coordinates with the relatively electron-rich C–C double bond in the allene moiety to form a coordination complex. Subsequently, Pd^{II}-induced double cyclic oxypalladation, which is responsible for the high efficiency of chirality transfer observed with the optically active 2,3-allenoic acids,[2e–g] would afford intermediate **5o**. Subsequent reductive elimination yields the bibutenolide (*S*,*S*)-**3o** and the Pd^0 species. Then the Pd^0 species is reoxidized by the in-situ-formed I_2, which may be produced by the reaction of alkyl iodide or KI with the oxygen in air, or benzoquinone to give the catalytically active Pd^{II} species to complete the catalytic cycle (Scheme 2).

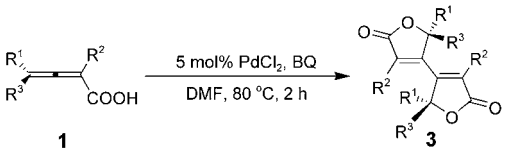
Conclusion

We have developed an oxidative dimeric cyclization–coupling reaction of 2,3-allenoic acids catalyzed by $PdCl_2$, affording bi-butenolides[16] that are not otherwise readily available, by using three oxidative systems. Although the diastereoselectivity for the bicyclization of racemic 2,3-allenoic acids is low, excellent diastereoselectivity was realized in the bicyclization reaction of optically active 2,3-allenoic acids, leading to the optically active bibutenolides in high yields and *ee*. Further studies on the application of these Pd^{II}-regenerating oxidation systems are being pursued in our laboratory.

Experimental Section

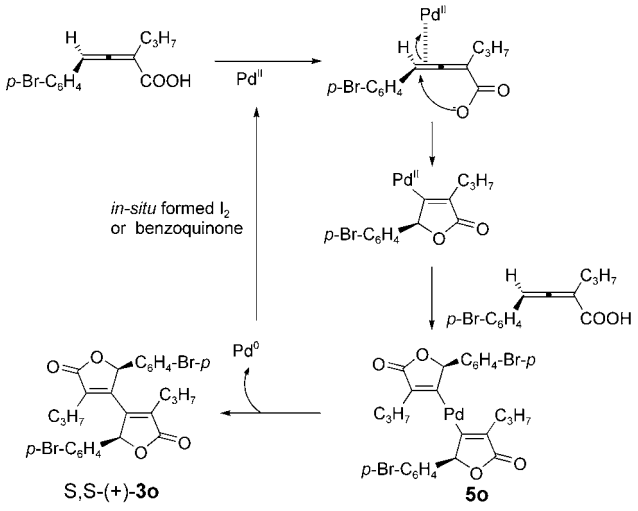
General procedures *Method A*: A solution of 2,3-allenoic acid (**1**;

Table 3. Oxidative dimeric cyclizing-coupling reaction of optical active 2,3-allenoic acids.



Entry	Allenoic acids	Equiv of BQ	Product **3**	Yield of **3** [%]	*ee* of **3** [%]	*R*R**/*R*S**[a]
1	*R*-(-)-**1a**, 97% *ee*	0.63	*R*,*R*-(-)-**3a**	88	>99	>99:1
2	*R*-(-)-**1b**, 99% *ee*	0.58	*R*,*R*-(-)-**3b**	100	99	25:1
3	*S*-(+)-**1d**, 98% *ee*	0.74	*S*,*S*-(+)-**3d**	86	>99	20:1
4	*S*-(+)-**1o**, 99% *ee*	0.67	*S*,*S*-(+)-**3o**	94	98	24:1

[a] The ratio was determined by the ^{1}H NMR spectra.



Scheme 2.

0.50 mmol), propyl iodide (**2a**; 2.50 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred in air at 80 °C for the time indicated in the tables. Then the mixture was diluted with diethyl ether, washed with water, and dried by $MgSO_4$. After evaporation, the residues were purified by flash chromatography on silica gel with petroleum ether/ethyl acetate as the eluent to afford **3**.

Method B: A solution of 2,3-allenoic acid (**1**; 0.50 mmol), KI (42 mg, 0.25 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred in air at 80 °C for the time indicated in Table 2 to afford **3**.

Method C: A solution of 2,3-allenoic acid (**1**; 0.50 mmol), benzoquinone (0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMF (2 mL) was stirred at 80 °C for the time indicated in Table 2 to afford **3**.

Method D: A solution of 2,3-allenoic acid (**1**; 0.50 mmol), benzoquinone (0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for the time indicated in Table 2 to afford **3**.

For the analytical data of **3a–f** see the Supporting Information of reference [11].

3,3′-Dimethyl-5,5′-dihexyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3g)

Method A: A solution of 2-methyldeca-2,3-dienoic acid (**1g**; 92 mg, 0.51 mmol), **2a** (428 mg, 2.50 mmol), and $PdCl_2$ (5 mg, 0.028 mmol) in DMA (5 mL) was stirred at 80 °C for 21 h to afford 43 mg (47 %) of **3g** (*R**,*S**:*R**,*R** = 1:1.87).

Method B: A solution of **1g** (91 mg, 0.50 mmol), KI (42 mg, 0.25 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (3 mL) was stirred at 80 °C for 17 h to afford 10 mg (11 %) of **3g** (*R**,*S**:*R**,*R** = 1.23:1).

Method C: A solution of **1g**; 92 mg, 0.51 mmol), benzoquinone (32 mg, 0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMF (2 mL) was stirred at 80 °C for 3.5 h to afford 12 mg (13 %) of **3g** (*R**,*S**:*R**,*R** = 1:1.84).

*R**,*R** isomer (less polar): liquid; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.04$ (br, 2H), 1.92 (s, 6H), 1.48–1.15 (m, 20H), 0.88 ppm (t, $J = 6.6$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 10.7$, 14.0, 22.4, 24.6, 28.8, 31.5, 33.1, 81.1, 129.0, 151.1, 172.5 ppm; EIMS: *m*/*z* (%): 362 (3.79) [M^+], 69 (100); IR (neat): $\tilde{\nu} = 2928$, 2858, 1755 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{35}O_4^+$ [M^++1]: 363.25299; found: 363.2552.

*R**,*S** isomer (more polar): liquid; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.00$–5.90 (m, 2H), 1.82 (d, $J = 2.1$ Hz, 6H), 1.70–1.15 (m, 20H), 0.89 ppm (t, $J = 6.6$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): $\delta = 10.0$, 14.0, 22.4, 25.3, 28.8, 31.5, 33.3, 81.9, 129.4, 152.0, 172.2 ppm; EIMS: *m*/*z* (%): 362 (4.53) [M^+], 43 (100); IR (neat): $\tilde{\nu} = 2956$, 2928, 2858, 1757 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{35}O_4^+$ [M^++1]: 363.25299; found: 363.2548.

3,3′-Dimethyl-5,5′-dimethyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3h)

Method A: A solution of 2-methylpenta-2,3-dienoic acid (**1h**; 56 mg, 0.50 mmol), **2a** (420 mg, 2.47 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 20 h to afford 24 mg (43 %) of **3h** (d.r. = 1:1.13).

Method C: A solution of **1h** (56 mg, 0.50 mmol), benzoquinone (32 mg, 0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h to afford 12 mg (22 %) of **3h** (d.r. = 1:2).

Method D: A solution of **1h** (56 mg, 0.50 mmol), benzoquinone (32 mg, 0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 11 h to afford 11 mg (20 %) of **3h** (d.r. = 1:1.62).

Solid, m.p. 153–175 °C (ethyl acetate and petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 5.25$–5.03 (2m, 2H), 1.94, 1.84 (2d, $J = 2.1$ Hz, 6H), 1.47, 1.39 ppm (2d, $J = 6.9$ Hz, 6H); EIMS: *m*/*z* (%): 222 (16.86) [M^+], 151 (100); IR (KBr): $\tilde{\nu} = 2927$, 1759 cm^{-1}; elemental analysis calcd (%) for $C_{12}H_{14}O_4$: C 64.85, H 6.35; found: C 64.54, H 6.29.

3,3′-Dipropyl-5,5′-dipropyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3i)

Method A: A solution of 2-propylhepta-2,3-dienoic acid (**1i**; 84 mg, 0.50 mmol), **2a** (425 mg, 2.50 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 17 h to afford 51 mg (61 %) of **3i** (d.r. = 1:1.59).

Method B: A solution of **1i** (85 mg, 0.51 mmol), KI (42 mg, 0.25 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 2.5 h to afford 21 mg (25 %) of **3i** (d.r. = 1:1.02).

Solid, m.p. 123–125 °C (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.05–4.83 (2m, 2H), 2.40–2.01 (2m, 4H), 1.80–1.30 (m, 12H), 1.05–0.82 ppm (m, 12H); EIMS: *m*/*z* (%): 334 (12.06) [M^+], 291 (100); IR (KBr): $\tilde{\nu}$ = 2961, 2934, 2874, 1764, 1642 cm^{-1}; elemental analysis calcd (%) for $C_{20}H_{30}O_4$: C 71.82, H 9.04; found: C 71.74, H 8.87.

5,5′-Dipentyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3j)

Method A: A solution of nona-2,3-dienoic acid (**1j**;77 mg, 0.50 mmol), **2a** (430 mg, 2.53 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 3 h to afford 40 mg (52 %) of **3j** (*R**,*S**:*R**,*R** = 1:1.67).

Method C: A solution of **1j** (78 mg, 0.50 mmol), benzoquinone (32 mg, 0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h to afford 35 mg (46 %) of **3j** (*R**,*S**:*R**,*R** = 1:1.06).

Method D: A solution of **1j** (76 mg, 0.49 mmol), benzoquinone (33 mg, 0.31 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 2 h to afford 46 mg (61 %) of **3j** (*R**,*S**:*R**,*R** = 1.19:1).

*R**,*R** isomer (less polar): solid, m.p. 160–162 °C (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.27 (d, *J* = 1.1 Hz, 2H), 5.27 (dd, *J* = 1.1, 4.8 Hz, 2H), 2.19–2.00 (m, 2H), 1.78–1.58 (m, 2H), 1.55- 1.20 (m, 12H), 0.89 ppm (t, *J* = 4.8 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 13.9, 22.4, 23.9, 31.2, 33.8, 82.7, 121.2, 155.5, 170.8 ppm; EIMS: *m*/*z* (%): 306 (2.29) [M^+], 43 (100); IR (KBr): $\tilde{\nu}$ = 2957, 2931, 2859, 1732 cm^{-1}; elemental analysis calcd (%) for $C_{18}H_{26}O_4$: C 70.56, H 8.55; found: C 70.48, H 8.46.

*R**,*S** isomer (more polar): liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.22 (d, *J* = 1.5 Hz, 2H), 5.35–5.27 (m, 2H), 2.09–1.92 (m, 2H), 1.65–1.50 (m, 2H), 1.50–1.18 (m, 12H), 1.00–0.80 ppm (m, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 13.8, 22.4, 24.0, 31.2, 33.3, 82.2, 120.8, 156.0, 170.7 ppm; EIMS: *m*/*z* (%): 306 (1.83) [M^+], 43 (100); IR (neat): $\tilde{\nu}$ = 2956, 2930, 2860, 1744 cm^{-1}; HRMS: *m*/*z* calcd for $C_{18}H_{27}O_4^+$ [M^++1]: 307.19039; found: 307.1913.

5,5′-Diheptyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3k)

Method A: A solution of undeca-2,3-dienoic acid (**1k**; 94 mg, 0.52 mmol), **2a** (425 mg, 2.50 mmol), and $PdCl_2$ (5 mg, 0.028 mmol) in DMA (2 mL) was stirred at 80 °C for 6 h to afford 46 mg (49 %) of **3k** (*R**,*S**:*R**,*R** = 1:1).

Method C: A solution of **1k** (91 mg, 0.50 mmol), benzoquinone (32 mg, 0.15 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h to afford 72 mg (80 %) of **3k** (*R**,*S**:*R**,*R** = 1.06:1).

Method D: A solution of **1k** (47 mg, 0.26 mmol), benzoquinone (16 mg, 0.15 mmol), and $PdCl_2$ (2 mg, 0.011 mmol) in DMA (2 mL) was stirred at 80 °C for 2 h to afford 39 mg (83 %) of **3k** (*R**,*S**:*R**,*R** = 1:1.05).

*R**,*R** isomer (less polar): solid, m.p. 146–147 °C (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.26 (d, *J* = 1.2 Hz, 2H), 5.26 (dd, *J* = 1.2, 6.3 Hz, 2H), 2.15–1.98 (m, 2H), 1.74–1.54 (m, 2H), 1.50–1.12 (m, 20H), 0.88 ppm (t, *J* = 6.0 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0, 22.5, 24.2, 29.0, 29.1, 31.6, 33.9, 82.7, 121.2, 155.5, 170.8 ppm; EIMS: *m*/*z* (%): 362 (9.16) [M^+], 57 (100); IR (KBr): $\tilde{\nu}$ = 2956, 2927, 2856, 1732 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{35}O_4^+$ [M^++1]: 363.25299; found: 363.2557.

*R**,*S** isomer (more polar): solid, m.p. 63–64 °C (diethyl ether and petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.21 (d, *J* = 1.2 Hz, 2H), 5.30 (bd, *J* = 6.0 Hz, 2H), 2.09–1.92 (m, 2H), 1.86–1.50 (m, 2H), 1.50–1.18 (m, 20H), 0.88 ppm (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0, 22.5, 24.3, 29.0, 29.1, 31.6, 33.3, 82.2, 120.8, 156.0, 170.7 ppm; EIMS: *m*/*z* (%): 362 (8.23) [M^+], 57 (100); IR (KBr): $\tilde{\nu}$ = 2955, 2926, 2856, 1748 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{35}O_4^+$ [M^++1]: 363.25299; found: 363.2556.

5,5′-Dioctyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3l)

Method A: A solution of dodec-2,3-dienoic acid (**1l**; 97 mg, 0.50 mmol), **2a** (425 mg, 2.50 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 3 h to afford 52 mg (54 %) of **3l** (*R**,*S**:*R**,*R** = 1:1) and cycloisomeriztion product 5-octyl-5H-furan-2-one 5 mg (5 %).

Method B: A solution of **1l** (97 mg, 0.50 mmol), KI (44 mg, 0.27 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 2 h to afford 31 mg (32 %) of **3l** (*R**,*S**:*R**,*R** = 1:1.38).

Method C: A solution of **1l** (97 mg, 0.50 mmol), benzoquinone (32 mg, 0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h to afford 68 mg (71 %) of **3l** (*R**,*S**:*R**,*R** = 1:1.06).

Method D: A solution of **1l** (96 mg, 0.49 mmol), benzoquinone (32 mg, 0.30 mmol), and $PdCl_2$ (4 mg, 0.023 mmol) in DMA (2 mL) was stirred at 80 °C for 2 h to afford 70 mg (73 %) of **3l** (*R**,*S**:*R**,*R** = 1:1.06).

*R**,*R** isomer (less polar): solid, m.p. 147–148 °C (ethyl acetate and petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.19 (d, *J* = 1.2 Hz, 2H), 5.19 (dd, *J* = 1.2, 6.0 Hz, 2H), 2.09–1.92 (m, 2H), 1.67–1.49 (m, 2H), 1.46–1.10 (m, 24H), 0.81 ppm (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0, 22.6, 24.2, 29.07, 29.10, 29.2, 31.7, 33.9, 82.7, 121.2, 155.5, 170.7 ppm; EIMS: *m*/*z* (%): 390 (16.40) [M^+], 43 (100); IR (KBr): $\tilde{\nu}$ = 2955, 2925, 2855, 1732 cm^{-1}; elemental analysis calcd (%) for $C_{24}H_{38}O_4$: C 73.81, H 9.81; found: C 73.87, H 9.92.

*R**,*S** isomer (more polar): solid, m.p. 68–70 °C (diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.16 (s, 2H), 5.24 (d, *J* = 6.9 Hz, 2H), 2.02–1.85 (m, 2H), 1.60–1.43 (m, 2H), 1.43–1.10 (m, 24H), 0.81 ppm (t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 14.0, 22.6, 24.3, 29.08, 29.10, 29.3, 31.7, 33.3, 82.2, 120.8, 156.0, 170.7 ppm; EIMS: *m*/*z* (%): 390 (13.21) [M^+], 43 (100); IR (KBr): $\tilde{\nu}$ = 2925, 2855, 1748 cm^{-1}; HRMS: *m*/*z* calcd for $C_{24}H_{38}O_4Na^+$ [M^++Na]: 413.26623; found: 413.2627. The X-ray structure of compound **3l** is shown in Figure 2.

(*R*,*R*)-(−)-3,3′-Dipropyl-5,5′-diphenyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3a)

Method C: A solution of *R*-(−)-4-phenyl-2-propyl-2,3-butadienoic acid (**1a**; 50 mg, 0.248 mmol, 97 % *ee*), benzoquinone (17 mg, 0.157 mmol), and $PdCl_2$ (2 mg, 0.011 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h

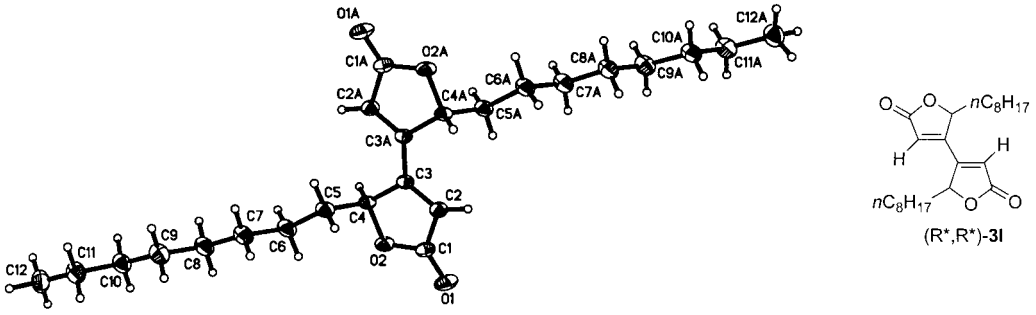


Figure 2. ORTEP representation of the product (*R**,*R**)-**3l**.

to afford 44 mg (88%, >99% *ee*) of (*R*,*R*)-(−)-**3a**. HPLC conditions: AD column; rate: 0.7 mL min^{-1}; eluent: hexane/*i*PrOH 90/10; $[\alpha]=-262$ ($c=0.76$ in $CHCl_3$).

(*R*,*R*)-(−)-3,3′-Dimethyl-5,5′-diphenyl-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3b)

Method C: A solution of *R*-(−)-2-methyl-4-phenyl-2,3-butadienoic acid (**1b**; 44 mg, 0.253 mmol, 99% *ee*), benzoquinone (16 mg, 0.148 mmol), and $PdCl_2$ (2 mg, 0.011 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h to afford 44 mg (100%, 99% *ee*) of (*R*,*R*)-(−)-**3b**. (*R**,*S**:*R**,*R**=1:25): HPLC conditions: AD column; rate: 0.7 mL min^{-1}; eluent: hexane/*i*PrOH 70/30; $[\alpha]=-325$ ($c=1.055$ in $CHCl_3$).

(*S*,*S*)-(+)-3,3′-Dimethyl-5,5′-dinaphthy-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3d) *Method C*: A solution of *S*-(+)-2-methyl-4-naphthyl-2,3-butadienoic acid (**1d**; 56 mg, 0.25 mmol, 98% *ee*), benzoquinone (20 mg, 0.189 mmol), and $PdCl_2$ (2 mg, 0.011 mmol) in DMF (2 mL) was stirred at 80 °C for 2 h to afford 48 mg (86%, >99% *ee*) of (*S*,*S*)-(+)-**3d**. (*R**,*S**:*R**,*R**=1: 20); HPLC conditions: AD column; rate: 0.7 mL min^{-1}; eluent: hexane/*i*PrOH 60/40; $[\alpha]=+210$ ($c=0.945$ in $CHCl_3$).

(*S*,*S*)-(+)-3,3′-Dipropyl-5,5′-di(4′-bromophenyl)-5H,5′H-[4,4′]bifuranyl-2,2′-dione (3o)

Method C: A solution of *S*-(+)-4-(4′-bromophenyl)-2-propyl-2,3-butadienoic acid (**1o**; 35 mg, 0.125 mmol, 99% *ee*), benzoquinone (9 mg, 0.083 mmol), and $PdCl_2$ (1 mg, 0.006 mmol) in DMF (1 mL) was stirred at 80 °C for 2 h to afford 33 mg (94%, 98% *ee*) of (*S*,*S*)-(+)-**3o**. (*R**,*S**:*R**,*R**=1: 24): HPLC conditions: AD column; rate: 0.7 mL min^{-1}; eluent: hexane/*i*PrOH 85/15; $[\alpha]=+194$ ($c=0.785$ in $CHCl_3$); m.p. 216–218 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.38$ (d, $J=8.4$ Hz, 2H), 6.82 (d, $J=8.4$ Hz, 2H), 5.81 (s, 1H), 2.33–2.21 (m, 1H), 2.14–2.00 (m, 1H), 1.59–1.42 (m, 1H), 1.31–1.14 (m, 1H), 0.85 ppm (t, $J=7.5$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz): $\delta=14.1$, 20.8, 27.3, 81.8, 123.9, 127.6, 131.9, 132.3, 133.0, 150.0, 171.6 ppm; EIMS: *m*/*z* (%): 558 (22.12) [M^+(^{79}Br)], 560 (36.58) [M^+(^{81}Br)], 323 (100); IR(KBr): $\tilde{\nu}=1745$, 1645, 1489 cm^{-1}; elemental analysis calcd (%) for $C_{26}H_{24}Br_2O_4$: C 55.74, H 4.32, found C 55.69, H 4.28.

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[15] Crystal data for compound (*S*,*S*)-(+)-**3o**. $C_{26}H_{24}Br_2O_4$, $M_r=560.27$, monoclinic, space group $P2_1$, $Mo_{K\alpha}$, final R indices [$I>2\sigma(I)$]: $R1=0.0434$, $wR2=0.1010$; unit cell: $a=9.6374(10)$, $b=12.0918(12)$, $c=10.8607(11)$ Å, $\beta=103.264(2)°$, $V=1231.9(2)$ Å^3, $T=293(2)$ K, $Z=2$, reflections collected/unique: 7582/4800 ($R_{int}=0.0719$), no observation [$I>2\sigma(I)$] 3086, parameters 300. CCDC 223809 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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