

Pd-catalyzed Suzuki coupling reaction of chloroalkylidene- β -lactones with LB-Phos as the ligand†Cite this: *Org. Biomol. Chem.*, 2013, **11**, 98

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In this paper, LB-Phos-HBF₄ salt has been applied for the Pd-catalysed Suzuki coupling reactions of optically active (Z)- α -chloroalkylidene- β -lactones. Aryl, vinyl, alkyl and heteroaromatic boronic acids may be coupled with optically active β -lactones affording corresponding optically active products highly selectively and efficiently.

Introduction

Much progress has been achieved with C–Cl bond activation reactions in past years thanks to the development of new phosphine ligands.¹ Recently, we have developed a new type of monophosphine ligand, which could be used in palladium-catalyzed Suzuki coupling reactions² and aminations³ of organic chlorides. In the Suzuki coupling of optically active chlorinated 2-(5*H*)-furanones, LB-Phos showed advantages over some other known ligands by affording the coupling products, *i.e.* optically active β -substituted butenolides, within 5–10 min without racemization.⁴ In this paper, we wish to report our recent results on the Suzuki coupling reaction of optically active α -chloroalkylidene- β -lactones derivatives of high ee.

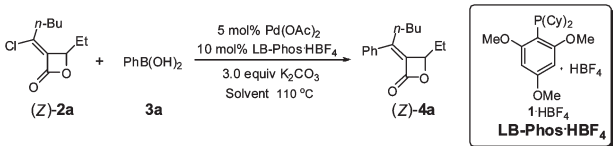
Results and discussion

At the beginning, (Z)- α -(1-chloropentylidene)- β -ethyl- β -lactone ((Z)-**2a**),⁵ which was prepared by the PdCl₂-catalyzed cyclocarbonylation of propargyl alcohols with CuCl₂ developed in this group, and phenyl boronic acid (**3a**) (1.5 equiv) were used to test the catalytic activity of Pd/LB-Phos-HBF₄. We found that the Suzuki coupling product (Z)-**4a** would be formed in 100% yield using 3.0 equiv of K₂CO₃ at 110 °C in toluene (Table 1, entry 1). Other solvents such as dioxane, DMSO and DMF would lead to lower yields (Table 1, entries 2–4). Reducing the

amount of **3a** to 1.2 equiv. had a slight negative effect on the yield of (Z)-**4a** (Table 1, entry 5). However, reducing the loading of Pd(OAc)₂, LB-Phos-HBF₄, or K₂CO₃, respectively, would all decrease the yield of (Z)-**4a** (Table 1, entries 5–8). This problem was circumvented by using 2.0 equiv of K₃PO₄·3H₂O as the base affording (Z)-**4a** in 95% yield (Table 1, entry 9).

Optically active coupling product (S,Z)-**4a** could also be produced from (S,Z)-**2a** under our optimized reaction conditions in 98% yield with no racemization (eqn (1)). Thus, it is concluded that even such strained allylic C–O bonds may also be kept untouched.⁴

Table 1 Suzuki coupling reactions of (Z)-**2a** with PhB(OH)₂**3a**

					
Entry	3a (equiv)	Solvent	Time (h)	Yield of (Z)- 4a ^a (%)	Recovery of (Z)- 2a ^a (%)
1	1.5	Toluene	1.0	100	—
2	1.5	Dioxane	1.0	58	39
3	1.5	DMF	1.5	—	—
4	1.5	DMSO	3.2	—	—
5	1.2	Toluene	2.6	94	—
6 ^b	1.2	Toluene	1.2	77	23
7 ^c	1.2	Toluene	1.0	86	14
8 ^d	1.2	Toluene	1.7	88	—
9 ^{d,e}	1.2	Toluene	0.7	95	—

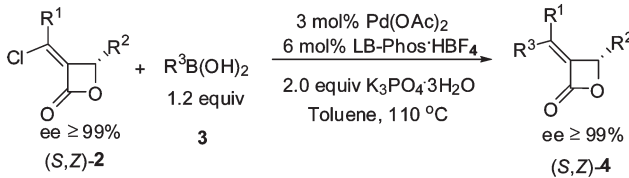
^a Determined by ¹H NMR analysis using methylene bromide as the internal standard. ^b K₂CO₃ (2.0 equiv) was used. ^c LB-Phos-HBF₄ (5 mol %) was used. ^d Pd(OAc)₂ (3 mol %) and LB-Phos-HBF₄ (6 mol %) were used. ^e K₃PO₄·3H₂O (2.0 equiv) was used.

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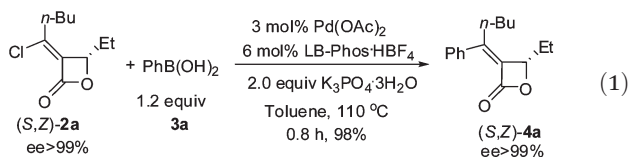
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† Electronic supplementary information (ESI) available. CCDC 888344, 888345. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob26365c

Table 2 Suzuki coupling reactions of (*S,Z*)-**2** with organoboronic acids^a

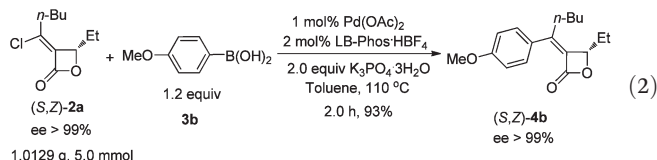
					
		3			
Entry	(<i>S,Z</i>)- 2	R ¹	R ²	R ³	Time (h) Yield ^b (%)
1	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	Ph (3a)	0.8 98 ((<i>S,Z</i>)- 4a)
2	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	4-MeOC ₆ H ₄ (3b)	2.0 84 ((<i>S,Z</i>)- 4b)
3	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	3-MeOC ₆ H ₄ (3c)	1.0 77 ((<i>S,Z</i>)- 4c)
4	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	2-MeOC ₆ H ₄ (3d)	3.7 69 ((<i>S,Z</i>)- 4d)
5	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	(<i>E</i>)-Styryl (3e)	2.8 91 ((<i>S,Z,E</i>)- 4e)
6	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	4-MeC ₆ H ₄ (3f)	1.0 93 ((<i>S,Z</i>)- 4f)
7	(<i>S,Z</i>)- 2b	<i>n</i> -Bu	Me	4-MeC ₆ H ₄ (3f)	1.0 71 ((<i>S,Z</i>)- 4g)
8	(<i>S,Z</i>)- 2a	<i>n</i> -Bu	Et	2-Naphthyl (3g)	1.0 86 ((<i>S,Z</i>)- 4h)
9	(<i>S,Z</i>)- 2c	<i>n</i> -Bu	<i>i</i> -Pr	Ph (3a)	1.5 94 ((<i>S,Z</i>)- 4i)
10	(<i>S,Z</i>)- 2d	Ph	Et	4-MeOC ₆ H ₄ (3b)	1.5 93 ((<i>S,Z</i>)- 4j)
11	(<i>S,Z</i>)- 2d	Ph	Et	(<i>E</i>)-1-Pentenyl (3h)	0.8 95 ((<i>S,E,E</i>)- 4k)

^a Standard conditions A: a mixture of 1.0 equiv of (*S,Z*)-**2** (0.2 mmol or 0.4 mmol), 1.2 equiv of **3**, 2.0 equiv of K₃PO₄·3H₂O, 0.03 equiv of Pd(OAc)₂ and 0.06 equiv of LB-Phos-HBF₄ was stirred in toluene (0.1 M) at 110 °C. ^b Isolated yield.



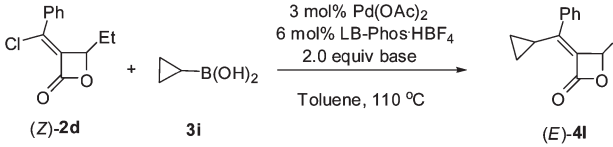
Encouraged by these results, a series of optically active α-chloroalkylidene-β-lactones⁶ were tested under the optimized conditions (Table 2). Aromatic (Table 2, entries 1–4 and 6–10) and vinylic boronic acids (Table 2, entries 5 and 11) could all be coupled with the starting β-lactones to afford the products within 0.8–3.7 h. Increasing the steric hindrance in the *ortho*-position of aryl boronic acid led to longer reaction times and lower yields (Table 2, compare entries 1 and 4). 2-Naphthyl boronic acid (**3g**) was also used to couple with (*S,Z*)-**2a** affording (*S,Z*)-**4h** in 86% yield (Table 2, entry 8).

One 5.0 mmol-scale reaction was carried out affording (*S,Z*)-**4b** with a relatively higher yield (eqn (2)) vs. entry 2, Table 2) within 2.0 h when 1 mol% Pd(OAc)₂ together with 2 mol% LB-Phos-HBF₄ was used as the catalyst (eqn (2)).



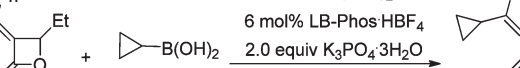
However, when cyclopropylboronic acid **3i** and (*Z*)-**2d** were coupled under the optimized conditions, the yield of product (*E*)-**4l** was only 23% (Table 3, entry 1).⁶ A higher loading of boronic acid **3i** did not help to give a higher yield (Table 3, entries 2–3). The base-sensitive β-lactone (*Z*)-**2d** would

Table 3 Suzuki coupling reactions of (*Z*)-**2d** with cyclopropyl acid **3i**

					
		3i			
Entry	3i (equiv)	Base	Time (h)	Yield of (<i>E</i>)- 4l ^a (%)	Recovery of (<i>Z</i>)- 2d ^a (%)
1	1.2	K ₃ PO ₄ ·3H ₂ O	1.0	23	0
2	1.5	K ₃ PO ₄ ·3H ₂ O	1.8	17	0
3	3.0	K ₃ PO ₄ ·3H ₂ O	1.5	12	<4
4 ^b	0.0	K ₃ PO ₄ ·3H ₂ O	1.5	0	21
5 ^c	1.2	K ₃ PO ₄ ·3H ₂ O	5.0	19	0
6	1.2	Cs ₂ CO ₃	1.3	12	27
7	1.2	CsF	1.1	0	83
8	1.2	K ₂ HPO ₄ ·3H ₂ O	6.0	0	97

^a Determined by ¹H NMR analysis. ^b Neither Pd(OAc)₂ nor ligand was added here. ^c Pd₂(dba)₃·CHCl₃ was used to replace Pd(OAc)₂.

Table 4 Suzuki coupling reactions of (*Z*)-**2d** with cyclopropylboronic acid **3i** using toluene and water as the solvent



Reaction scheme showing the conversion of (Z)-**2d** and **3i** to (E)-**4l**. The reaction conditions are: 3 mol% Pd(OAc)₂, 6 mol% LB-Phos-HBF₄, 2.0 equiv K₃PO₄·3H₂O, Toluene / H₂O, 110 °C.

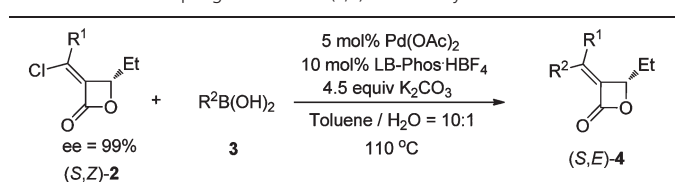
Entry	Toluene : H ₂ O	Time (h)	Yield of (E)- 4l ^a (%)	Recovery of (Z)- 2d ^a (%)
1	5 : 1	8.0	29	50
2	10 : 1	3.0	54	0
3	20 : 1	0.7	24	0

^a Determined by ¹H NMR analysis.

decompose quickly even in absence of Pd(OAc)₂ and LB-Phos-HBF₄ (Table 3, entry 5). Using weaker base such as CsF and K₂HPO₄·3H₂O gave no expected product but recovery of (*Z*)-**2d** (Table 3, entries 7 and 8).

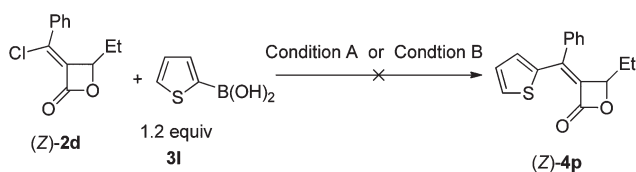
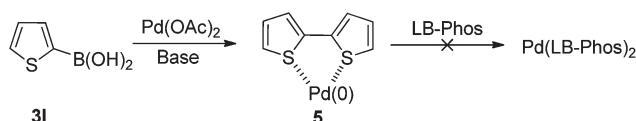
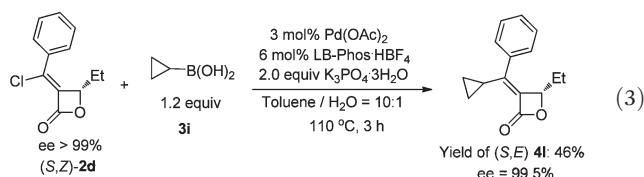
Further screening led to the observation that when toluene-water (v/v = 5 : 1) was used as the mixed solvent, (*E*)-**4l** was obtained in 29% yield with 50% of (*Z*)-**2d** being recovered (Table 4, entry 1). Decreasing the amount of water to 1 : 10 ratio (water/toluene (v/v)) would lead to 54% yield (Table 4, entry 2). Further decreasing the amount of water did not improve the yield of (*E*)-**4l** (Table 4, entry 3).

Under the newly optimized conditions (Table 4, entry 2), cyclopropylboronic acid could couple with optically active (*S,Z*)-**2d** affording (*S,E*)-**4l** in 46% yield (eqn (3)). However, the coupling of *n*-butylboronic acid with (*S,Z*)-**2d** did not afford the desired coupling product (*S,E*)-**4m**. Increasing the loading of K₂CO₃ to 4.5 equiv solved the problem (Table 5, entry 1). Under the same conditions (standard conditions B), *n*-hexylboronic acid could easily couple with (*S,Z*)-**2d** affording (*S,E*)-**4n** in 72% yield (Table 5 entry 2).

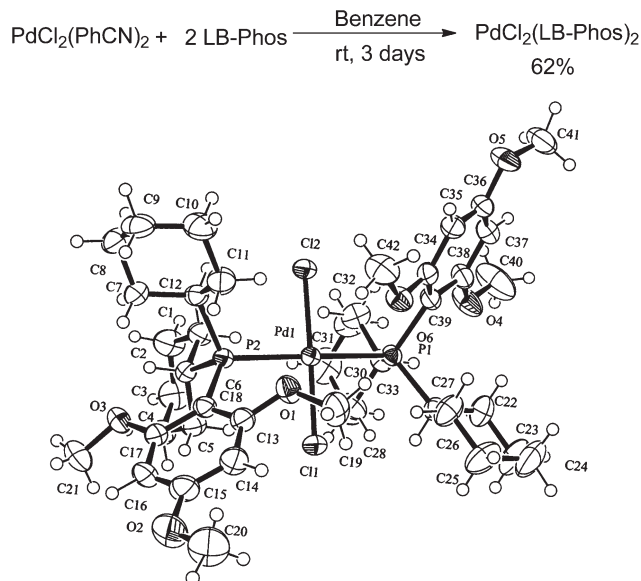
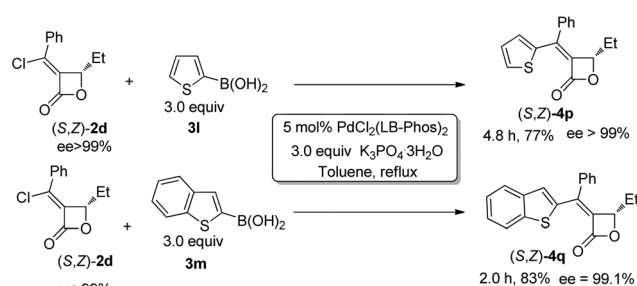
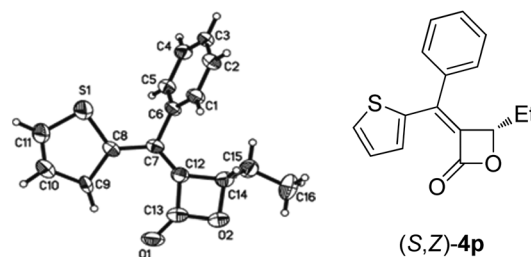
Table 5 Suzuki coupling reactions of (*S,Z*)-**2** with alkyl boronic acid^a

Entry	(<i>S,Z</i>)- 2 R ¹	3 (equiv)	R ²	Time (h)	Yield ^b (%)	ee%
1	Ph (<i>S,Z</i>)- 2d	2.0	<i>n</i> -Bu (3j)	3.0	73 ((<i>S,E</i>)- 4m)	99.3
2	Ph (<i>S,Z</i>)- 2d	2.0	<i>n</i> -Hex (3k)	6.0	72 ((<i>S,E</i>)- 4n)	>99
3	<i>n</i> -Bu (<i>Z</i>)- 2a	2.0	<i>n</i> -Bu (3j)	8.0	23 (4o)	—
4 ^c	<i>n</i> -Bu (<i>S,Z</i>)- 2a	3.0	<i>n</i> -Bu (3j)	3.0	55 ((<i>S</i>)- 4o)	99.4

^a Standard conditions B: a mixture of 1.0 equiv of (*S,Z*)-**2**, 2.0 equiv of **3**, 4.5 equiv of K₂CO₃, 0.05 equiv of Pd(OAc)₂ and 0.10 equiv of LB-Phos·HBF₄ were stirred in toluene–H₂O = 10 : 1 at 110 °C. ^b Isolated yield. ^c PdCl₂(LB-Phos)₂ (5 mol%) was used as catalyst.

**Scheme 1****Scheme 2**

Furthermore, we found that 2-thienylboronic acid **3l** failed to couple with (*Z*)-**2d** under the standard conditions A or B (Scheme 1). We reasoned that the formation of Pd–S complex **5** was too stable to prevent the formation of P–Pd species (Scheme 2). Then we synthesized complex PdCl₂(LB-Phos)₂⁷ by stirring PdCl₂(PhCN)₂ with LB-Phos in benzene for 3 days at room temperature. Indeed, this problem was also conquered by using PdCl₂(LB-Phos)₂ (Scheme 3) as the catalyst. (*S,Z*)-**4p**⁸ and (*S,Z*)-**4q** could be prepared in 77% and 83% yields, respectively, under these conditions (Scheme 4). The absolute configuration of (*S,Z*)-**4p** was further confirmed by X-ray diffraction studies (Fig. 1). It is interesting to note that by using 5 mol% PdCl₂(LB-Phos)₂ and 3.0 equiv of *n*-butylboronic acid,

**Scheme 3** Synthesis and ORTEP representation of *trans*-PdCl₂(LB-Phos)₂.**Scheme 4****Fig. 1** ORTEP representation of (*S,Z*)-**4p**.⁸

the yield of *S*-**4o** was also improved to 55% (Table 5, entry 4) as compared with the results presented in entry 3 of Table 5.

Conclusions

We have prepared a series of optically active α -alkylidene- β -lactones of high ee *via* the Suzuki coupling reaction of aryl, vinylic boronic acid with optically active α -chloroalkylidene- β -lactones using LB-Phos as ligand.⁹ When a mixture of toluene and H₂O in 10 : 1 in volume was used, alkyl boronic acid could also be coupled to afford the products in a moderate yields. 2-Benzothienylboronic acid and 2-thienylboronic acid could also be coupled easily in presence of the pre-formed PdCl₂(LB-Phos)₂. Further studies in this area are being conducted in our laboratory.

Experimental section

General information

¹H and ¹³C NMR spectra were recorded on the instruments operated at 300 and 75 MHz, respectively, in CDCl₃. Chemical shifts (δ) are given in parts per million (ppm) with the residual peak of CHCl₃ at 7.260 ppm or TMS at 0.000 ppm as the internal standard. Infrared spectra were recorded from thin films of pure samples on sodium chloride plates for liquid or in the form of KBr discs for the solid samples. Mass and HRMS spectra were carried out in EI mode. Thin layer chromatography was performed on pre-coated glass-back plates and visualized with UV light at 254 nm. Anhydrous CuCl₂ (96%) was purchased from Energy Chemical and heated at 200 °C under vacuum (<1 mmHg) to remove residual water before use. Flash column chromatography was performed on silica gel (10–40 μ). Dioxane and toluene used was refluxed in the presence of sodium wire using diphenyl ketone as indicator and distilled right before use. All the boronic acids were purchased from Alfa Aesar, Aldrich, or J&K chemical LTD.

1. SYNTHESIS OF STARTING MATERIAL. (*S,Z*)-**2a–2b** and racemic compounds (*Z*)-**2a–2c** are known compounds and prepared according to our published procedure.⁵

(1) *Synthesis of (S,Z)- α -(1-chloropentylidene)- β -isopropyl-lactone ((S,Z)-2c). Typical procedure.* In a flame-dried flask, a solution of (*S*)-2-methylnon-4-yn-3-ol (282 mg, 1.8 mmol, ee = 99%) and anhydrous CuCl₂ (1.2252 g, 9 mmol) in 20 mL of dry THF was stirred for about 5 min at room temperature followed by the addition of PdCl₂ (32.7 mg, 0.18 mmol). Then the flask was transferred to a Parr pressure reactor and charged with 20 atm of CO gas. After the mixture was stirred for 4.3 h at 40 °C, the gas was carefully ventilated, and the residue was diluted with Et₂O. Filtration through a short column of silica gel (eluent: Et₂O 2 \times 70 mL), evaporation, and flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 100/1) afforded 237.6 mg (60%) of (*S,Z*)-**2c** as a colorless liquid in 99% ee, as determined by HPLC (Chiralpak AS-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, λ = 230 nm, *t*_R = 8.4 min (major), 10.2 min (minor)): [α]_D²⁰ = -45.9 (*c* = 1.14, CHCl₃), ¹H NMR (300 MHz, CDCl₃) δ 4.89 (d, *J* = 3.6 Hz, 1H, OCH), 2.34 (t, *J* = 7.7 Hz, 2H, CH₂), 2.24–2.07 (m, 1H, CH), 1.79–1.49 (m, 2H, CH₂), 1.44–1.26 (m, 2H, CH₂), 1.09 (d, *J* = 6.9 Hz, 3H, CH₃),

0.99 (d, *J* = 6.9 Hz, 3H, CH₃), 0.93 (t, *J* = 7.2 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 161.5, 138.9, 131.9, 83.5, 36.2, 30.9, 28.8, 22.0, 18.4, 15.6, 13.7; IR (neat) ν (cm⁻¹) 2965, 2934, 2876, 1814, 1702, 1467, 1429, 1389, 1370, 1344, 1287, 1216, 1191, 1166, 1109, 1081, 1058; MS (70 ev, EI) *m/z* (%): 218 (M⁺(³⁷Cl), 0.33), 216 (M⁺(³⁵Cl), 0.99), 173 (100); Anal. Calcd For C₁₁H₁₇ClO₂: C, 60.97; H, 7.91. Found: C, 61.09; H, 7.97.

The following compounds were prepared according to this procedure.

(2) (*S,Z*)- α -(1-Chlorobenzylidene)- β -ethyl- β -lactone ((*S,Z*)-**2d**). The mixture of (*S*)-1-phenylpent-1-yn-3-ol (805.4 mg, 5.0 mmol, ee > 99%) and anhydrous CuCl₂ (3.3611 g, 25.0 mmol) were stirred in 50 mL of dry THF at room temperature for about 10 min followed by the addition of PdCl₂ (88.3 mg, 0.50 mmol). Then the mixture was stirred for 4.2 h under 20 atm of CO atmosphere at 40 °C to afford (*S,Z*)-**2d** (723.3 mg, 65%) (eluent: petroleum ether/ethyl acetate = 8/1, then recrystallization in *n*-hexane and ethyl acetate): ee > 99% as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, λ = 230 nm, *t*_R = 14.0 min (major)): [α]_D²⁰ = -96.1 (*c* = 1.14, CHCl₃); white solid, m.p. 83–84 °C (*n*-hexane/ethyl acetate); ¹H NMR (300 MHz, CDCl₃) δ 7.58–7.51 (m, 2H, Ar-H), 7.51–7.42 (m, 3H, Ar-H), 5.35 (dd, *J*₁ = 7.5 Hz, *J*₂ = 3.0 Hz, 1H, OCH), 1.95–1.78 (m, 1H, one proton in CH₂), 1.72–1.52 (m, 1H, one proton in CH₂), 0.92 (t, *J* = 7.4 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 161.6, 134.2, 133.5, 132.8, 131.4, 128.9, 128.0, 81.2, 24.4, 8.2; IR (KBr) ν (cm⁻¹) 3063, 2976, 2922, 2871, 1806, 1675, 1588, 1579, 1495, 1461, 1445, 1309, 1267, 1236, 1184, 1151, 1129, 1077, 1060, 1024; MS (70 ev, EI) *m/z* (%): 224 (M⁺(³⁷Cl), 12.73), 222 (M⁺(³⁵Cl), 38.89), 221 (100); Anal. Calcd for C₁₂H₁₁ClO₂: C, 64.73; H, 4.98. Found: C, 64.75; H, 4.95.

(3) (*Z*)- α -(1-Chlorobenzylidene)- β -ethyl- β -lactone ((*Z*)-**2d**). The mixture of 1-phenylpent-1-yn-3-ol (799.4 mg, 5.0 mmol) and anhydrous CuCl₂ (3.3629 g, 25.0 mmol) were stirred in 50 mL of dry THF at room temperature for about 10 min followed by the addition of PdCl₂ (88.5 mg, 0.50 mmol). Then the mixture was stirred for 4.0 h under 20 atm CO atmosphere at 40 °C afforded (*Z*)-**2d** (658.5 mg, 59%) (eluent: petroleum ether/ethyl acetate = 100/1, then recrystallization in *n*-hexane and ethyl acetate): a white solid: m.p. 54–55 °C (*n*-hexane/ethyl acetate); ¹H NMR (300 MHz, CDCl₃) δ 7.58–7.51 (m, 2H, Ar-H), 7.51–7.42 (m, 3H, Ar-H), 5.35 (dd, *J*₁ = 7.5 Hz, *J*₂ = 3.0 Hz, 1H, OCH), 1.95–1.80 (m, 1H, one proton in CH₂), 1.72–1.54 (m, 1H, one proton in CH₂), 0.92 (t, *J* = 7.4 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 161.7, 134.2, 133.5, 132.7, 131.4, 128.9, 128.0, 81.2, 24.3, 8.3; IR (KBr) ν (cm⁻¹) 2967, 2936, 2920, 2877, 1797, 1675, 1493, 1447, 1436, 1389, 1311, 1269, 1236, 1161, 1134, 1065; MS (70 ev, EI) *m/z* (%): 224 (M⁺(³⁷Cl), 12.73), 222 (M⁺(³⁵Cl), 39.49), 221 (100); Anal. Calcd for C₁₂H₁₁ClO₂: C, 64.73; H, 4.98. Found: C, 64.82; H, 4.97.

2. SYNTHESIS OF PdCl₂(LB-Phos)₂. A solution of PdCl₂(PhCN)₂ (0.9650 g, 2.51 mmol) and LB-Phos^{2,4} (1.8299 g, 5.03 mmol) in 10 mL of dry benzene was stirred for 3 days. Then filtration with petroleum ether (3 \times 10 mL) afforded a yellow solid of PdCl₂(LB-Phos)₂ (1.4124 g, 62%): m.p. 218–219 °C (ether : ethyl

acetate); ^1H NMR (300 MHz, CDCl_3) δ 6.12 (s, 4H, Ar-H), 3.89 (s, 12H, $4 \times \text{OCH}_3$), 3.83 (s, 6H, $2 \times \text{OCH}_3$), 2.96–2.77 (m, 4H, $2 \times \text{CH}_2$), 2.24–2.00 (m, 4H, $2 \times \text{CH}_2$), 1.90–1.08 (m, 36H, $16 \times \text{CH}_2$ and $4 \times \text{CH}$); ^{13}C NMR (75 MHz, CDCl_3) δ 164.4, 163.2, 94.5 (t, $J = 19.4$ Hz), 91.0, 55.8, 55.1, 33.4, 29.7, 28.6, 27.5 (t, $J = 5.0$ Hz), 27.3 (t, $J = 7.1$ Hz), 26.5; ^{31}P NMR (121 MHz, CDCl_3) δ 17.6; IR (KBr) ν (cm^{-1}) 2925, 2848, 1598, 1580, 1465, 1454, 1405, 1331, 1287, 1266, 1225, 1206, 1180, 1160, 1121, 1089, 1034, 1003. MS (ESI-TOF) 871 ($\text{C}_{42}\text{H}_{66}^{37}\text{ClO}_6\text{P}_2\text{Pd}^+$, 100), 869 ($\text{C}_{42}\text{H}_{66}^{35}\text{ClO}_6\text{P}_2\text{Pd}^+$, 99.11); Anal. Calcd For $\text{C}_{42}\text{H}_{66}\text{Cl}_2\text{-O}_6\text{P}_2\text{Pd}$: C, 55.66; H, 7.34. Found: C, 55.75; H, 7.44.

3. Pd-CATALYSED SUZUKI COUPLING OF α -CHLOROALKYLIDENE- β -LACTONES WITH ARYL AND VINYL BORONIC ACID

(1) *Synthesis of (S,Z)- α -(1-butylbenzylidene)- β -ethyl- β -lactone ((S,Z)-4a). Typical procedure (condition A).* A rubber-capped Schlenk vessel was dried with flame under vacuum and back-filled with nitrogen for three times. Then $\text{Pd}(\text{OAc})_2$ (1.3 mg, 0.006 mmol), LB-Phos-HBF_4 (5.3 mg, 0.012 mmol), $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (107.1 mg, 0.40 mmol), phenylboronic acid (29.4 mg, 0.24 mmol), and 1 mL of toluene were added into the Schlenk vessel sequentially. After being stirred for about 10 min at room temperature, (S,Z)-2a (40.7 mg, 0.20 mmol, ee > 99%) and 1 mL of toluene were added sequentially to the vessel. The resulting mixture was heated at 110 °C with a pre-heated oil bath. After 45 min, the reaction was complete as monitored by TLC. Then the reaction mixture was cooled to room temperature and diluted by 10 mL of Et_2O and filtered through a short column of silica gel (eluent: 2×10 mL of Et_2O). Evaporation and purification by chromatography (eluent: petroleum ether/ethyl acetate = 60/1) on silica gel afforded (S,Z)-4a (48.4 mg, 98%) as a liquid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min $^{-1}$, $\lambda = 230$ nm, $t_R = 9.9$ min (major)): $[\alpha]_D^{20} = -26.1$ ($c = 1.56$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 7.57–7.47 (m, 2H, Ar-H), 7.46–7.34 (m, 3H, Ar-H), 5.03 (dd, $J_1 = 7.5$ Hz, $J_2 = 3.0$ Hz, 1H, OCH), 2.60–2.36 (m, 2H, CH_2), 2.20–2.04 (m, 1H, one proton in CH_2), 1.96–1.78 (m, 1H, one proton in CH_2), 1.44–1.24 (m, 4H, $2 \times \text{CH}_2$), 1.11 (t, $J = 7.4$ Hz, 3H, CH_3), 0.87 (t, $J = 7.2$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 163.3, 148.5, 134.8, 132.1, 129.5, 128.3, 128.0, 79.0, 33.0, 30.0, 26.3, 22.5, 13.7, 8.6; IR (neat) ν (cm^{-1}) 3056, 3028, 2955, 2936, 2873, 1799, 1683, 1577, 1496, 1459, 1446, 1380, 1367, 1312, 1291, 1240, 1159, 1106, 1049, 1014; MS (70 ev, EI) m/z (%): 245 ($\text{M}^+ + 1$, 6.32), 244 (M^+ , 42.33), 145 (100); HRMS Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$ (M^+): 244.1463. Found 244.1457.

The following compounds were prepared according to these procedures.

(2) *(Z)- α -(1-Butylbenzylidene)- β -ethyl- β -lactone ((Z)-4a).* The reaction of (Z)-2a (40.5 mg, 0.20 mmol), phenyl boronic acid 3a (29.5 mg, 0.24 mmol), $\text{Pd}(\text{OAc})_2$ (1.2 mg, 0.006 mmol), LB-Phos-HBF_4 (5.4 mg, 0.012 mmol), and $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (106.9 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (Z)-4a (43.6 mg, 89%) (eluent: petroleum ether/ethyl acetate = 60/1) as a liquid. ^1H NMR (300 MHz, CDCl_3) δ 7.57–7.48 (m, 2H, Ar-H), 7.46–7.36 (m, 3H, Ar-H), 5.03 (dd, $J_1 = 7.7$ Hz, $J_2 = 3.2$ Hz, 1H, OCH), 2.60–2.36 (m, 2H,

CH_2), 2.20–2.06 (m, 1H, one proton in CH_2), 1.96–1.77 (m, 1H, one proton in CH_2), 1.44–1.27 (m, 4H, $2 \times \text{CH}_2$), 1.11 (t, $J = 7.4$ Hz, 3H, CH_3), 0.86 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR δ 163.3, 148.6, 134.9, 132.1, 129.6, 128.3, 128.0, 79.0, 33.0, 30.1, 26.3, 22.6, 13.8, 8.6; IR (neat) ν (cm^{-1}) 3063, 2959, 2931, 2873, 1801, 1683, 1496, 1461, 1446, 1380, 1312, 1240, 1159, 1128, 1104, 1049; MS (70 ev, EI) m/z (%): 245 ($\text{M}^+ + 1$, 4.69), 244 (M^+ , 30.31), 145 (100); HRMS Calcd for $\text{C}_{16}\text{H}_{20}\text{O}_2$ (M^+): 244.1463. Found: 244.1460.

(3) *(S,Z)- α -(1-Butyl-(4'-methoxyl)benzylidene)- β -ethyl- β -lactone ((S,Z)-4b).* The reaction of (S,Z)-2a (39.1 mg, 0.19 mmol, ee > 99%), 4-methoxyphenylboronic acid 3b (37.4 mg, 0.25 mmol), $\text{Pd}(\text{OAc})_2$ (1.3 mg, 0.006 mmol), LB-Phos-HBF_4 (5.4 mg, 0.012 mmol), and $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (108.6 mg, 0.41 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (S,Z)-4b (44.7 mg, 84%) (eluent: 30–60 °C petroleum ether/ethyl acetate = 20/1) as a liquid in ee = 99.7%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 97 : 3, 1.0 mL min $^{-1}$, 230 nm, $t_R = 14.9$ min (major), 25.8 (minor)); $[\alpha]_D^{20} = +5.6$ ($c = 1.01$, CHCl_3); ^1H NMR (300 MHz, CDCl_3) δ 7.56 (d, $J = 9.0$ Hz, 2H, Ar-H), 6.93 (d, $J = 9.0$ Hz, 2H, Ar-H), 5.00 (dd, $J_1 = 7.7$ Hz, $J_2 = 3.2$ Hz, 1H, OCH), 3.83 (s, 3H, OCH_3), 2.58–2.29 (m, 2H, CH_2), 2.17–2.02 (m, 1H, one proton in CH_2), 1.94–1.75 (m, 1H, one proton in CH_2), 1.45–1.20 (m, 4H, $2 \times \text{CH}_2$), 1.09 (t, $J = 7.4$ Hz, 3H, CH_3), 0.87 (t, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 163.6, 160.7, 148.1, 130.4, 129.7, 127.0, 113.7, 78.9, 55.2, 32.7, 30.4, 26.4, 22.6, 13.8, 8.6; IR (neat) ν (cm^{-1}) 2958, 2933, 2870, 2838, 1789, 1674, 1605, 1574, 1514, 1463, 1443, 1380, 1301, 1255, 1182, 1157, 1127, 1097, 1040; MS (70 ev, EI) m/z (%): 275 ($\text{M}^+ + 1$, 12.52), 274 (M^+ , 62.30), 175 (100); HRMS Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_3$ (M^+): 274.1569. Found 274.1577.

(4) *(Z)- α -(1-Butyl-(4'-methoxyl)benzylidene)- β -ethyl- β -lactone ((Z)-4b).* The reaction of (Z)-2a (40.6 mg, 0.20 mmol), 4-methoxyphenyl boronic acid 3b (36.8 mg, 0.24 mmol), $\text{Pd}(\text{OAc})_2$ (1.3 mg, 0.006 mmol), LB-Phos-HBF_4 (5.3 mg, 0.012 mmol), and $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (107.1 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (Z)-4b (50.2 mg, 91%) (eluent: petroleum ether/ethyl acetate = 60/1) as a liquid: ^1H NMR (300 MHz, CDCl_3) δ 7.56 (d, $J = 8.7$ Hz, 2H, Ar-H), 6.93 (d, $J = 8.7$ Hz, 2H, Ar-H), 5.00 (dd, $J_1 = 7.7$ Hz, $J_2 = 3.2$ Hz, 1H, OCH), 3.83 (s, 3H, OCH_3), 2.57–2.30 (m, 2H, CH_2), 2.17–2.03 (m, 1H, one proton in CH_2), 1.94–1.76 (m, 1H, one proton in CH_2), 1.47–1.23 (m, 4H, $2 \times \text{CH}_2$), 1.10 (t, $J = 7.4$ Hz, 3H, CH_3), 0.87 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 163.7, 160.7, 148.1, 130.4, 129.7, 127.1, 113.7, 78.9, 55.2, 32.7, 30.4, 26.4, 22.6, 13.8, 8.6; IR (neat) ν (cm^{-1}) 2959, 2934, 2873, 2840, 1795, 1676, 1605, 1574, 1514, 1462, 1377, 1301, 1256, 1183, 1157, 1127, 1097, 1040; MS (70 ev, EI) m/z (%): 275 ($\text{M}^+ + 1$, 13.42), 274 (M^+ , 70.85), 175 (100); HRMS Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_3$ (M^+): 274.1569. Found: 274.1574.

(5) *(S,Z)- α -(1-Butyl-(3'-methoxyl)benzylidene)- β -ethyl- β -lactone ((S,Z)-4c).* The reaction of (S,Z)-2a (80.8 mg, 0.40 mmol, ee > 99%), 3-methoxyphenyl boronic acid 3c (73.4 mg, 0.48 mmol), $\text{Pd}(\text{OAc})_2$ (2.7 mg, 0.012 mmol), LB-Phos-HBF_4 (10.8 mg, 0.024 mmol), and $\text{K}_3\text{PO}_4 \cdot 3\text{H}_2\text{O}$ (212.0 mg, 0.80 mmol) in 4 mL of toluene at 110 °C under nitrogen afforded (S,Z)-4c (83.9 mg,

77%) (eluent: petroleum ether/ethyl acetate = 50/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 97:3, 0.8 mL min⁻¹, 230 nm, *t*_R = 10.0 min (major)): [α]_D²⁰ = -25.8 (*c* = 0.89, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.31 (t, *J* = 8.1 Hz, 1H, Ar-H), 7.15 (s, 1H, Ar-H), 7.08 (d, *J* = 3.9 Hz, 1H, Ar-H), 6.97–6.89 (m, 1H, Ar-H), 5.01 (dd, *J*₁ = 7.8 Hz, *J*₂ = 2.7 Hz, 1H, OCH), 3.84 (s, 3H, OCH₃), 2.58–2.33 (m, 2H, CH₂), 2.21–2.02 (m, 1H, one proton in CH₂), 1.97–1.77 (m, 1H, one proton in CH₂), 1.50–1.23 (m, 4H, 2 × CH₂), 1.10 (t, *J* = 7.4 Hz, 3H, CH₃), 0.87 (t, *J* = 6.6 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 159.3, 148.3, 136.1, 132.1, 129.3, 120.1, 115.4, 113.7, 79.0, 55.3, 33.0, 30.1, 26.3, 22.6, 13.8, 8.6; IR (neat) ν (cm⁻¹) 2959, 2930, 2873, 2838, 1801, 1684, 1599, 1579, 1489, 1464, 1430, 1374, 1319, 1290, 1235, 1181, 1153, 1106, 1050; MS (70 ev, EI) *m/z* (%): 275 (*M*⁺ + 1, 18.18), 274 (*M*⁺, 100); HRMS Calcd for C₁₇H₂₂O₃ (*M*⁺): 274.1569. Found 274.1565.

(6) (*Z*)- α -(1-Butyl-(3'-methoxy)benzylidene)- β -ethyl- β -lactone ((*Z*)-**4c**). The reaction of (*Z*)-**2a** (40.4 mg, 0.20 mmol), 3-methoxyphenyl boronic acid **3c** (36.5 mg, 0.24 mmol), Pd(OAc)₂ (1.2 mg, 0.006 mmol), LB-Phos-HBF₄ (5.3 mg, 0.012 mmol), and K₃PO₄·3H₂O (107.2 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4c** (43.8 mg, 80%) (eluent: petroleum ether/ethyl acetate = 50/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.31 (t, *J* = 6.0 Hz, 1H, Ar-H), 7.15 (t, *J* = 2.0 Hz, 1H, Ar-H), 7.08 (d, *J* = 3.9 Hz, 1H, Ar-H), 6.97–6.87 (m, 1H, Ar-H), 5.02 (dd, *J*₁ = 7.8 Hz, *J*₂ = 3.0 Hz, 1H, OCH), 3.84 (s, 3H, OCH₃), 2.57–2.33 (m, 2H, CH₂), 2.20–2.03 (m, 1H, one proton in CH₂), 1.96–1.77 (m, 1H, one proton in CH₂), 1.46–1.23 (m, 4H, 2 × CH₂), 1.11 (t, *J* = 7.4 Hz, 3H, CH₃), 0.87 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 159.4, 148.3, 136.1, 132.2, 129.3, 120.1, 115.5, 113.7, 79.0, 55.3, 33.0, 30.2, 26.3, 22.6, 13.8, 8.6; IR (neat) ν (cm⁻¹) 2959, 2935, 2873, 2837, 1801, 1685, 1599, 1579, 1489, 1464, 1430, 1380, 1319, 1289, 1234, 1181, 1153, 1127, 1106, 1049; MS (70 ev, EI) *m/z* (%): 275 (*M*⁺ + 1, 17.84), 274 (*M*⁺, 100); HRMS Calcd for C₁₇H₂₂O₃ (*M*⁺): 274.1569. Found: 274.1569.

(7) (*S,Z*)- α -(1-Butyl-(2'-methoxy)benzylidene)- β -ethyl- β -lactone ((*S,Z*)-**4d**). The reaction of (*S,Z*)-**2a** (81.1 mg, 0.40 mmol, ee > 99%), 2-methoxyphenyl boronic acid **3d** (73.3 mg, 0.48 mmol), Pd(OAc)₂ (2.7 mg, 0.012 mmol), LB-Phos-HBF₄ (10.9 mg, 0.024 mmol), and K₃PO₄·3H₂O (212.9 mg, 0.80 mmol) in 4 mL of toluene at 110 °C under nitrogen afforded (*S,Z*)-**4d** (90.5 mg, 82%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid in ee = 99.6%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98:2, 0.8 mL min⁻¹, 214 nm, *t*_R = 12.4 min (major), *t*_R = 15.6 min (major)); [α]_D²⁰ = -16.9 (*c* = 1.04, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.27 (m, 1H, Ar-H), 7.16 (dd, *J*₁ = 7.5 Hz, *J*₂ = 1.8 Hz, 1H, Ar-H), 7.02–6.87 (m, 2H, Ar-H), 5.07 (dd, *J*₁ = 7.5 Hz, *J*₂ = 3.0 Hz, 1H, OCH), 3.80 (s, 3H, OCH₃), 2.57–2.35 (m, 2H, CH₂), 2.20–2.04 (m, 1H, one proton in CH₂), 1.97–1.80 (m, 1H, one proton in CH₂), 1.36–1.22 (m, 4H, 2 × CH₂), 1.11 (t, *J* = 7.4 Hz, 3H, CH₃), 0.84 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 156.3, 147.0, 133.2, 130.1, 130.0, 124.8, 120.3, 110.9, 79.4, 55.4, 33.2, 29.5, 26.2, 22.5, 13.8, 8.4; IR (neat) ν

(cm⁻¹) 2955, 2935, 2873, 1806, 1698, 1599, 1580, 1491, 1463, 1435, 1380, 1294, 1243, 1161, 1124, 1093, 1050; MS (70 ev, EI) *m/z* (%): 275 (*M*⁺ + 1, 19.03), 274 (*M*⁺, 100); HRMS Calcd for C₁₇H₂₂O₃ (*M*⁺): 274.1569. Found: 274.1577.

(8) (*Z*)- α -(1-Butyl-(2'-methoxy)benzylidene)- β -ethyl- β -lactone ((*Z*)-**4d**). The reaction of (*Z*)-**2a** (40.2 mg, 0.20 mmol), 2-methoxyphenyl boronic acid **3d** (36.7 mg, 0.48 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.5 mg, 0.012 mmol), and K₃PO₄·3H₂O (107.0 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4d** (35.7 mg, 65%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.28 (m, 1H, Ar-H), 7.15 (dd, *J*₁ = 7.5 Hz, *J*₂ = 1.8 Hz, 1H, Ar-H), 7.02–6.86 (m, 2H, Ar-H), 5.07 (dd, *J*₁ = 7.4 Hz, *J*₂ = 3.2 Hz, 1H, OCH), 3.80 (s, 3H, OCH₃), 2.58–2.35 (m, 2H, CH₂), 2.20–2.04 (m, 1H, one proton in CH₂), 1.97–1.80 (m, 1H, one proton in CH₂), 1.36–1.20 (m, 4H, 2 × CH₂), 1.11 (t, *J* = 7.5 Hz, 3H, CH₃), 0.84 (t, *J* = 6.9 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 156.3, 147.0, 133.1, 130.1, 130.0, 124.8, 120.3, 110.8, 79.4, 55.4, 33.2, 29.5, 26.2, 22.5, 13.8, 8.4; IR (neat) ν (cm⁻¹) 2955, 2935, 2873, 1806, 1699, 1599, 1580, 1491, 1463, 1435, 1380, 1294, 1267, 1243, 1181, 1161, 1124, 1093, 1050; MS (70 ev, EI) *m/z* (%): 275 (*M*⁺ + 1, 18.92), 274 (*M*⁺, 100); HRMS Calcd for C₁₇H₂₂O₃ (*M*⁺): 274.1569. Found: 274.1569.

(9) (*S*)- α -(1(*Z*)-(2'(E)-Phenylethenyl)pentylidene)- β -ethyl- β -lactone ((*S,Z,E*)-**4e**). The reaction of (*S,Z*)-**2a** (80.4 mg, 0.40 mmol, ee > 99%), *E*-phenylethenyl boronic acid **3e** (71.2 mg, 0.48 mmol), Pd(OAc)₂ (2.7 mg, 0.012 mmol), LB-Phos-HBF₄ (10.8 mg, 0.024 mmol) and K₃PO₄·3H₂O (212.7 mg, 0.8 mmol) in 4 mL of toluene at 110 °C under nitrogen afforded (*S,Z,E*)-**4e** (97.3 mg, 91%) (eluent: petroleum ether/ethyl acetate = 60/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak AD-H, *n*-hexane-*i*-PrOH = 98:2, 0.8 mL min⁻¹, 230 nm, *t*_R = 10.4 min (major)); [α]_D²⁰ = -17.0 (*c* = 0.88, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.61 (d, *J* = 16.5 Hz, 1H, C=CH), 7.57–7.47 (m, 2H, Ar-H), 7.43–7.27 (m, 3H, Ar-H), 6.90 (d, *J* = 16.5 Hz, 1H, C=CH), 5.01 (dd, *J*₁ = 7.8 Hz, *J*₂ = 3.3 Hz, 1H, OCH), 2.43–2.26 (m, 2H, CH₂), 2.15–1.97 (m, 1H, one proton in CH₂), 1.92–1.73 (m, 1H, one proton in CH₂), 1.69–1.32 (m, 4H, 2 × CH₂), 1.08 (t, *J* = 7.4 Hz, 3H, CH₃), 0.96 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.1, 144.9, 135.9, 134.5, 133.1, 129.0, 128.7, 127.3, 123.5, 79.6, 31.5, 28.6, 26.3, 23.0, 13.8, 8.7; IR (neat) ν (cm⁻¹) 3079, 3056, 3037, 3018, 2959, 2933, 2873, 1793, 1670, 1627, 1573, 1492, 1464, 1449, 1378, 1366, 1321, 1295, 1236, 1148, 1125, 1054; MS (70 ev, EI) *m/z* (%): 271 (*M*⁺ + 1, 4.69), 270 (*M*⁺, 16.98), 213 (100); HRMS Calcd for C₁₈H₂₂O₂ (*M*⁺): 270.1620. Found 270.1627.

(10) α -(1(*Z*)-(2'(E)-Phenylethenyl)pentylidene)- β -ethyl- β -lactone ((*Z,E*)-**4e**). The reaction of (*Z*)-**2a** (40.6 mg, 0.20 mmol), *E*-phenylethenyl boronic acid **3e** (35.6 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), 1-HBF₄ (5.4 mg, 0.012 mmol), and K₃PO₄·3H₂O (107.1 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z,E*)-**4e**⁹ (43.7 mg, 81%) (eluent: petroleum ether/ethyl acetate = 60/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.61 (d, *J* = 16.5 Hz, 1H, C=CH), 7.57–7.50 (m, 2H, Ar-H), 7.43–7.27 (m, 3H, Ar-H), 6.90 (d, *J* =

16.5 Hz, 1H, C=CH), 5.01 (dd, $J_1 = 7.8$ Hz, $J_2 = 3.3$ Hz, 1H, OCH), 2.44–2.25 (m, 2H, CH₂), 2.16–1.97 (m, 1H, one proton in CH₂), 1.91–1.73 (m, 1H, one proton in CH₂), 1.69–1.34 (m, 4H, 2 × CH₂), 1.08 (t, $J = 7.4$ Hz, 3H, CH₃), 0.97 (t, $J = 7.2$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.1, 144.9, 135.9, 134.4, 133.1, 129.0, 128.7, 127.3, 123.4, 79.6, 31.4, 28.6, 26.3, 22.9, 13.8, 8.7; IR (neat) ν (cm⁻¹) 3082, 3060, 3044, 3028, 2959, 2933, 2873, 1791, 1669, 1622, 1576, 1496, 1449, 1374, 1317, 1295, 1236, 1148, 1125, 1094, 1054; MS (70 ev, EI) m/z (%): 271 ($M^+ + 1$, 5.52), 270 (M^+ , 27.71), 213 (100).

(11) (*S,Z*)- α -(1-Butyl-(4'-methyl)benzylidene)- β -ethyl- β -lactone ((*S,Z*)-**4f**). The reaction of (*S,Z*)-**2a** (40.4 mg, 0.20 mmol, ee > 99%), 4-methylphenyl boronic acid **3f** (32.6 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), and K₃PO₄·3H₂O (106.7 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*S,Z*)-**4f**⁹ (48.1 mg, 93%) (eluent: petroleum ether/ethyl acetate = 50/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, 230 nm, t_R = 9.3 min (major)); [α]_D²⁰ = -10.8 ($c = 0.72$, CHCl₃, Lit. [α]_D²⁰ = -10.1 ($c = 1.0$, CHCl₃, ee = 99.9%)⁹); ¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.22 (d, $J = 8.1$ Hz, 2H, Ar-H), 5.01 (dd, $J_1 = 7.7$ Hz, $J_2 = 2.9$ Hz, 1H, OCH), 2.61–2.31 (m, 5H, CH₃ and CH₂), 2.20–2.04 (m, 1H, one proton in CH₂), 1.95–1.77 (m, 1H, one proton in CH₂), 1.45–1.24 (m, 4H, 2 × CH₂), 1.11 (t, $J = 7.4$ Hz, 3H, CH₃), 0.87 (t, $J = 7.1$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.4, 148.6, 139.7, 131.9, 131.3, 129.0, 127.9, 79.0, 32.9, 30.2, 26.3, 22.6, 21.3, 13.7, 8.5; IR (neat) ν (cm⁻¹) 3028, 2959, 2926, 2873, 1798, 1681, 1610, 1564, 1513, 1460, 1380, 1312, 1291, 1239, 1158, 1128, 1095, 1048, 1020; MS (70 ev, EI) m/z (%): 259 ($M^+ + 1$, 5.06), 258 (M^+ , 28.77), 159 (100).

(12) (*Z*)- α -(1-Butyl-(4'-methyl)benzylidene)- β -ethyl- β -lactone ((*Z*)-**4f**). The reaction of (*Z*)-**2a** (40.6 mg, 0.20 mmol), 4-methylphenyl boronic acid **3f** (33.2 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), and K₃PO₄·3H₂O (106.4 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4f**⁹ (50.1 mg, 97%) (eluent: petroleum ether/ethyl acetate = 50/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, $J = 8.4$ Hz, 2H, Ar-H), 7.22 (d, $J = 7.8$ Hz, 2H, Ar-H), 5.01 (dd, $J_1 = 7.7$ Hz, $J_2 = 3.2$ Hz, 1H, OCH), 2.60–2.26 (m, 5H, CH₃ and CH₂), 2.20–2.03 (m, 1H, one proton in CH₂), 1.95–1.77 (m, 1H, one proton in CH₂), 1.45–1.24 (m, 4H, 2 × CH₂), 1.11 (t, $J = 7.4$ Hz, 3H, CH₃), 0.87 (t, $J = 7.1$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.4, 148.6, 139.8, 131.9, 131.3, 129.0, 127.9, 79.0, 32.9, 30.2, 26.3, 22.6, 21.3, 13.8, 8.5; IR (neat) ν (cm⁻¹) 3025, 2959, 2930, 2873, 1798, 1681, 1610, 1564, 1513, 1460, 1380, 1312, 1291, 1239, 1158, 1128, 1095, 1048, 1020; MS (70 ev, EI) m/z (%): 259 ($M^+ + 1$, 5.05), 258 (M^+ , 27.60), 159 (100).

(13) (*S,Z*)- α -(1-Butyl-(4'-methyl)benzylidene)- β -methyl- β -lactone ((*S,Z*)-**4g**). The reaction of (*S,Z*)-**2b** (36.8 mg, 0.20 mmol, ee > 99%), 4-methylphenyl boronic acid **3f** (33.0 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), K₃PO₄·3H₂O (106.6 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*S,Z*)-**4g** (34.1 mg,

71%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, 230 nm, t_R = 9.0 min (major)); [α]_D²⁰ = +9.5 ($c = 0.97$, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.46 (d, $J = 8.1$ Hz, 2H, Ar-H), 7.22 (d, $J = 8.1$ Hz, 2H, Ar-H), 5.12 (q, $J = 6.3$ Hz, 1H, OCH), 2.60–2.31 (m, 5H, CH₃ and CH₂), 1.67 (d, $J = 6.0$ Hz, 3H, CH₃), 1.44–1.24 (m, 4H, 2 × CH₂), 0.87 (t, $J = 7.1$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.3, 148.4, 139.8, 133.0, 131.8, 129.0, 127.9, 74.2, 32.5, 30.2, 22.5, 21.3, 19.5, 13.7; IR (neat) ν (cm⁻¹) 3021, 2957, 2930, 2869, 1798, 1680, 1610, 1513, 1454, 1378, 1339, 1258, 1157, 1107, 1086, 1061, 1014; MS (70 ev, EI) m/z (%): 245 ($M^+ + 1$, 4.22), 244 (M^+ , 23.54), 143 (100); HRMS Calcd for C₁₆H₂₀O₂ (M^+): 244.1463. Found 244.1459.

(14) (*Z*)- α -(1-Butyl-(4'-methyl)benzylidene)- β -methyl- β -lactone ((*Z*)-**4g**). The reaction of (*Z*)-**2b** (38.0 mg, 0.20 mmol), 4-methylphenyl boronic acid **3f** (33.2 mg, 0.24 mmol), Pd(OAc)₂ (1.4 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), and K₃PO₄·3H₂O (107.2 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4g** (37.9 mg, 77%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.51–7.42 (m, 2H, Ar-H), 7.22 (d, $J = 7.8$ Hz, 2H, Ar-H), 5.12 (q, $J = 6.2$ Hz, 1H, OCH), 2.60–2.33 (m, 5H, CH₃ and CH₂), 1.67 (d, $J = 6.3$ Hz, 3H, CH₃), 1.46–1.22 (m, 4H, 2 × CH₂), 0.87 (t, $J = 7.1$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 148.4, 139.8, 133.0, 131.8, 129.1, 127.9, 74.2, 32.5, 30.2, 22.5, 21.3, 19.5, 13.7; IR (neat) ν (cm⁻¹) 3031, 2957, 2931, 2869, 1798, 1679, 1610, 1513, 1454, 1378, 1339, 1258, 1157, 1107, 1090, 1061, 1014; MS (70 ev, EI) m/z (%): 245 ($M^+ + 1$, 4.54), 244 (M^+ , 26.94), 143 (100); HRMS Calcd for C₁₆H₂₀O₂ (M^+): 244.1463. Found: 244.1466.

(15) (*S,Z*)- α -(1-(2'-Naphthyl)butylidene)- β -ethyl- β -lactone ((*S,Z*)-**4h**). The reaction of (*S,Z*)-**2a** (80.6 mg, 0.40 mmol, ee > 99%), 2-naphthyl boronic acid **3g** (82.7 mg, 0.48 mmol), Pd(OAc)₂ (2.8 mg, 0.012 mmol), LB-Phos-HBF₄ (10.9 mg, 0.024 mmol), and K₃PO₄·3H₂O (212.9 mg, 0.80 mmol) in 4 mL of toluene 110 °C under nitrogen afforded (*S,Z*)-**4h** (101.0 mg, 86%) (eluent: petroleum ether/methylene dichloride = 2/1) as a solid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, 230 nm, t_R = 12.8 min (major)); [α]_D²⁰ = -5.1 ($c = 2.26$, CHCl₃); m.p. 83–84 °C (*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 8.03 (s, 1H, Ar-H), 7.97–7.78 (m, 3H, Ar-H), 7.73–7.61 (m, 1H, Ar-H), 7.59–7.43 (m, 2H, Ar-H), 5.08 (dd, $J_1 = 7.7$ Hz, $J_2 = 3.2$ Hz, 1H, OCH), 2.74–2.43 (m, 2H, CH₂), 2.27–2.05 (m, 1H, one proton in CH₂), 2.04–1.80 (m, 1H, one proton in CH₂), 1.53–1.23 (m, 4H, 2 × CH₂), 1.16 (t, $J = 7.4$ Hz, 3H, CH₃), 0.87 (t, $J = 6.9$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.3, 148.5, 133.7, 132.8, 132.3, 128.5, 128.0, 127.8, 127.6, 126.8, 126.3, 125.4, 79.1, 33.0, 30.1, 26.3, 22.5, 13.7, 8.6; IR (KBr) ν (cm⁻¹) 3057, 2959, 2933, 2872, 1797, 1681, 1597, 1504, 1461, 1380, 1311, 1239, 1155, 1123, 1097, 1048, 1017; MS (70 ev, EI) m/z (%): 295 ($M^+ + 1$, 10.17), 294 (M^+ , 47.97), 237 (100); Anal. Calcd for C₂₀H₂₂O₂: C, 81.60; H, 7.53. Found: C, 81.82; H, 7.58.

(16) (*Z*)- α -(1-(2'-Naphthyl)butylidene)- β -ethyl- β -lactone ((*Z*)-**4h**). The reaction of (*Z*)-**2a** (40.7 mg, 0.20 mmol), 2-

naphthylboronic acid **3g** (41.6 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), K₃PO₄·3H₂O (106.4 mg, 0.4 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4h** (52.7 mg, 89%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 8.03 (d, *J* = 1.2 Hz, 1H, Ar-H), 7.94–7.79 (m, 3H, Ar-H), 7.71–7.61 (m, 1H, Ar-H), 7.57–7.46 (m, 2H, Ar-H), 5.08 (dd, *J*₁ = 7.8 Hz, *J*₂ = 3.0 Hz, 1H, OCH), 2.72–2.45 (m, 2H, CH₂), 2.25–2.06 (m, 1H, one proton in CH₂), 2.01–1.82 (m, 1H, one proton in CH₂), 1.50–1.24 (m, 4H, 2 × CH₂), 1.15 (t, *J* = 7.4 Hz, 3H, CH₃), 0.87 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.3, 148.5, 133.7, 132.9, 132.4, 132.3, 128.6, 128.0, 127.8, 127.6, 126.9, 126.3, 125.4, 79.1, 33.0, 30.2, 26.4, 22.6, 13.8, 8.6; IR (neat) ν (cm⁻¹) 3057, 2959, 2933, 2873, 1798, 1681, 1600, 1501, 1461, 1374, 1308, 1239, 1155, 1123, 1097, 1048, 1014; MS (70 ev, EI) *m/z* (%): 295 (*M*⁺ + 1, 10.23), 294 (*M*⁺, 47.88), 237 (100); HRMS Calcd for C₂₀H₂₂O₂ (*M*⁺): 294.1620. Found: 294.1615.

(17) (*S,Z*)-α-(1-Butylbenzylidene)-β-isopropyl-β-lactone ((*S,Z*)-**4i**). The reaction of (*S,Z*)-**2c** (86.6 mg, 0.40 mmol, ee = 99%), phenyl boronic acid **3a** (59.1 mg, 0.48 mmol), Pd(OAc)₂ (2.8 mg, 0.012 mmol), LB-Phos-HBF₄ (10.9 mg, 0.024 mmol), K₃PO₄·3H₂O (213.6 mg, 0.80 mmol) in 4 mL of toluene at 110 °C under nitrogen afforded (*S,Z*)-**4i** (97.1 mg, 94%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, 230 nm, *t*_R = 8.1 min (major)): [*α*]_D²⁰ = -6.8 (*c* = 1.02, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.58–7.47 (m, 2H, Ar-H), 7.46–7.32 (m, 3H, Ar-H), 4.98 (d, *J* = 2.7 Hz, 1H, OCH), 2.63–2.49 (m, 1H, one proton in CH₂), 2.49–2.36 (m, 1H, one proton in CH₂), 2.36–2.18 (m, 1H, CH), 1.47–1.23 (m, 4H, 2 × CH₂), 1.17 (d, *J* = 7.2 Hz, 3H, CH₃), 1.05 (d, *J* = 6.9 Hz, 3H, CH₃), 0.87 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.3, 148.6, 134.9, 131.3, 129.4, 128.2, 127.9, 82.3, 33.2, 30.6, 29.8, 22.5, 18.7, 14.9, 13.6; IR (neat) ν (cm⁻¹) 3059, 3022, 2963, 2932, 2873, 1801, 1682, 1573, 1494, 1466, 1445, 1387, 1375, 1341, 1296, 1244, 1187, 1148, 1105, 1072, 1038; MS (70 ev, EI) *m/z* (%): 259 (*M*⁺ + 1, 3.06), 258 (*M*⁺, 21.03), 145 (100); HRMS Calcd for C₁₇H₂₂O₂ (*M*⁺): 258.1620. Found: 258.1609.

(18) (*Z*)-α-(1-Butylbenzylidene)-β-isopropyl-β-lactone ((*Z*)-**4i**). The reaction of (*Z*)-**2c** (43.5 mg, 0.20 mmol), phenylboronic acid **3a** (30.1 mg, 0.25 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), K₃PO₄·3H₂O (107.1 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4i** (45.0 mg, 87%) (eluent: petroleum ether/ethyl acetate = 50/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.55–7.46 (m, 2H, Ar-H), 7.46–7.35 (m, 3H, Ar-H), 4.97 (d, *J* = 3.0 Hz, 1H, OCH), 2.63–2.34 (m, 2H, CH₂), 2.34–2.16 (m, 1H, CH), 1.44–1.23 (m, 4H, 2 × CH₂), 1.16 (d, *J* = 6.9 Hz, 3H, CH₃), 1.04 (d, *J* = 6.9 Hz, 3H, CH₃), 0.86 (t, *J* = 7.1 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.4, 148.7, 135.0, 131.4, 129.5, 128.3, 128.0, 82.4, 33.4, 30.7, 29.9, 22.6, 18.8, 15.0, 13.7; IR (neat) ν (cm⁻¹) 2963, 2932, 2873, 1801, 1682, 1489, 1465, 1445, 1383, 1338, 1244, 1185, 1147, 1105, 1068, 1038; MS (70 ev, EI)

m/z (%): 259 (*M*⁺ + 1, 3.42), 258 (*M*⁺, 21.00), 145 (100); HRMS Calcd for C₁₇H₂₂O₂ (*M*⁺): 258.1620. Found: 258.1612.

(19) (*S,Z*)-α-(1-(4'-Methoxyphenyl)benzylidene)-β-ethyl-β-lactone ((*S,Z*)-**4j**). The reaction of (*S,Z*)-**2d** (88.9 mg, 0.40 mmol, ee > 99%), 4-methoxyphenyl boronic acid **3a** (73.4 mg, 0.48 mmol), Pd(OAc)₂ (2.7 mg, 0.012 mmol), LB-Phos-HBF₄ (10.8 mg, 0.024 mmol), K₃PO₄·3H₂O (212.8 mg, 0.80 mmol) in 4 mL of toluene at 110 °C under nitrogen afforded (*S,Z*)-**4j** (109.2 mg, 93%) (eluent: petroleum ether/ethyl acetate = 20/1) as a solid in ee > 99%, as determined by HPLC (Chiralpak OJ-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, 230 nm, *t*_R = 35.8 min (major)): [*α*]_D²⁰ = +65.1 (*c* = 1.08, CHCl₃); m.p. 68–69 °C (*n*-hexane/ethyl acetate); ¹H NMR (300 MHz, CDCl₃) δ 7.55–7.47 (m, 2H, Ar-H), 7.45–7.35 (m, 3H, Ar-H), 7.29–7.18 (m, 2H, Ar-H), 6.94–6.85 (m, 2H, Ar-H), 5.17 (dd, *J*₁ = 7.2 Hz, *J*₂ = 3.3 Hz, 1H, OCH), 3.84 (s, 3H, OCH₃), 1.64–1.47 (m, 1H, one proton in CH₂), 1.46–1.30 (m, 1H, one proton in CH₂), 0.85 (t, *J* = 7.4 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.8, 161.1, 146.7, 137.7, 131.8, 130.8, 129.3, 129.2, 128.6, 128.2, 113.6, 79.6, 55.3, 24.7, 8.1; IR (KBr) ν (cm⁻¹) 3053, 2971, 2931, 2908, 2876, 2841, 1783, 1650, 1604, 1513, 1493, 1459, 1445, 1297, 1257, 1174, 1161, 1128, 1077, 1064, 1023; MS (70 ev, EI) *m/z* (%): 295 (*M*⁺ + 1, 18.33), 294 (*M*⁺, 90.71), 265 (100); HRMS Calcd for C₁₉H₁₈O₃ (*M*⁺): 294.1256. Found: 294.1255.

(20) (*Z*)-α-(1-(4'-Methoxyphenyl)benzylidene)-β-ethyl-β-lactone ((*Z*)-**4j**). The reaction of (*Z*)-**2d** (44.7 mg, 0.20 mmol), 4-methoxyphenyl boronic acid **3a** (36.9 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), K₃PO₄·3H₂O (106.8 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*Z*)-**4j** (57.7 mg, 97%) (eluent: petroleum ether/ethyl acetate = 40/1) as a solid: m.p. 97–98 °C (*n*-hexane/ethyl acetate); ¹H NMR (300 MHz, CDCl₃) δ 7.56–7.47 (m, 2H, Ar-H), 7.45–7.35 (m, 3H, Ar-H), 7.29–7.19 (m, 2H, Ar-H), 6.94–6.85 (m, 2H, Ar-H), 5.17 (dd, *J*₁ = 7.2 Hz, *J*₂ = 3.6 Hz, 1H, OCH), 3.84 (s, 3H, OCH₃), 1.64–1.48 (m, 1H, one proton in CH₂), 1.48–1.30 (m, 1H, one proton in CH₂), 0.85 (t, *J* = 7.4 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 163.8, 161.1, 146.7, 137.7, 131.8, 130.8, 129.3, 129.2, 128.6, 128.2, 113.6, 79.5, 55.3, 24.7, 8.1; IR (KBr) ν (cm⁻¹) 2996, 2968, 2962, 2932, 2873, 2834, 1802, 1670, 1606, 1514, 1456, 1441, 1389, 1320, 1272, 1250, 1182, 1161, 1125, 1077, 1053, 1029; MS (70 ev, EI) *m/z* (%): 295 (*M*⁺ + 1, 19.56), 294 (*M*⁺, 92.91), 265 (100); Anal. Calcd for C₁₉H₁₈O₃ (*M*⁺): C: 77.53, H: 6.16. Found: C: 77.44, H: 5.99.

(21) (*S*)-α-(1(*E*)-(Pent-1'*E*)-enyl)benzylidene)-β-ethyl-β-lactone ((*S,E,E*)-**4k**). The reaction of (*S,Z*)-**2d** (88.5 mg, 0.40 mmol, ee > 99%), (1*E*)-pentenyl boronic acid **3h** (55.3 mg, 0.48 mmol), Pd(OAc)₂ (2.7 mg, 0.012 mmol), LB-Phos-HBF₄ (10.7 mg, 0.024 mmol), K₃PO₄·3H₂O (213.5 mg, 0.80 mmol) in 4 mL of toluene at 110 °C under nitrogen afforded (*S,E,E*)-**4k** (96.6 mg, 95%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak AD-H, *n*-hexane-*i*-PrOH = 98 : 2, 0.8 mL min⁻¹, 230 nm, *t*_R = 8.0 min (major), 8.5 min (minor)): [*α*]_D²⁰ = -120.7 (*c* = 1.04, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.45–7.32 (m, 3H, Ar-H), 7.25–7.15 (m, 2H, Ar-H), 7.10 (d, *J* = 15.9 Hz, 1H, C=CH), 5.84

(dt, $J_1 = 15.9$ Hz, $J_2 = 7.4$ Hz, 1H, C=CH), 4.97 (dd, $J_1 = 7.1$ Hz, $J_2 = 3.5$ Hz, 1H, OCH), 2.18 (q, $J = 7.3$ Hz, 2H, CH₂), 1.59–1.21 (m, 4H, 2 × CH₂), 0.89 (t, $J = 7.4$ Hz, 3H, CH₃), 0.78 (t, $J = 7.5$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.1, 145.0, 143.2, 134.6, 131.3, 128.8, 128.5, 126.7, 79.9, 35.1, 25.3, 22.0, 13.7, 8.2; IR (neat) ν (cm⁻¹), 2964, 2932, 2874, 1795, 1664, 1462, 1444, 1322, 1310, 1301, 1236, 1163, 1106, 1054; MS (70 ev, EI) m/z (%): 257 ($M^+ + 1$, 2.24), 256 (M^+ , 11.22), 185 (100); HRMS Calcd for C₁₇H₂₀O₂ (M^+): 256.1463. Found: 256.1458.

(22) α -(1(*E*)-(Pent-1'(*E*)-enyl)benzylidene)- β -ethyl- β -lactone ((*E*, *E*)-**4k**). The reaction of (*Z*)-**2d** (45.1 mg, 0.40 mmol), (1*E*)-pentenylboronic acid **3h** (27.9 mg, 0.24 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol), LB-Phos-HBF₄ (5.4 mg, 0.012 mmol), K₃PO₄·3H₂O (107.6 mg, 0.40 mmol) in 2 mL of toluene at 110 °C under nitrogen afforded (*E*,*E*)-**4k** (48.1 mg, 92%) (eluent: petroleum ether/ethyl acetate = 40/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.52–7.32 (m, 3H, Ar-H), 7.25–7.15 (m, 2H, Ar-H), 7.10 (d, $J = 15.6$ Hz, 1H, C=CH), 5.94–5.74 (m, 1H, C=CH), 4.97 (dd, $J_1 = 7.1$ Hz, $J_2 = 3.8$ Hz, 1H, OCH), 2.18 (q, $J = 7.1$ Hz, 2H, CH₂), 1.57–1.19 (m, 4H, 2 × CH₂), 0.89 (t, $J = 7.5$ Hz, 3H, CH₃), 0.78 (t, $J = 7.4$ Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.1, 145.0, 143.2, 134.6, 131.3, 128.8, 128.5, 126.7, 79.9, 35.1, 25.3, 22.0, 13.7, 8.3; IR (neat) ν (cm⁻¹) 2964, 2931, 2869, 1794, 1665, 1629, 1462, 1444, 1382, 1322, 1304, 1293, 1236, 1163, 1106, 1073, 1054; MS (70 ev, EI) m/z (%): 257 ($M^+ + 1$, 1.52), 256 (M^+ , 8.33), 185 (100); HRMS Calcd for C₁₇H₂₀O₂ (M^+): 256.1463. Found: 256.1469.

4. Pd-CATALYSED SUZUKI COUPLING OF α -CHLOROALKYLIDENE- β -LACTONES WITH CYCLOPROPYL BORONIC ACID

(1) *Synthesis of (S,E)- α -(1-cyclopropylbenzylidene)- β -ethyl- β -lactone ((S,E)-**4l**). Typical procedure* A rubber-capped Schlenk vessel was dried with flame under vacuum and backfilled with nitrogen for three times. Then Pd(OAc)₂ (2.6 mg, 0.012 mmol), LB-Phos-HBF₄ (10.9 mg, 0.024 mmol), K₃PO₄·3H₂O (212.8 mg, 0.80 mmol), cyclopropylboronic acid **3i** (41.4 mg, 0.48 mmol), 2 mL of toluene and 0.4 mL of H₂O were added into the Schlenk vessel sequentially. Then (*S*,*Z*)-**2d** (89.1 mg, 0.40 mmol, ee > 99%) and 2 mL of toluene were added sequentially to the vessel. The resulting mixture was heated at 110 °C with a preheated oil bath. After 3.0 h, the reaction was complete as monitored by TLC. Then the reaction mixture was diluted by 10 mL of Et₂O and filtered through a short column of silica gel (eluent: 2 × 10 mL of Et₂O). Evaporation and purification by chromatography (eluent: petroleum ether/ethyl acetate = 30/1) on silica gel and recrystallization (8 mL of *n*-hexane) afforded (*S*,*E*)-**4l** (42.4 mg, 46%) as a solid in 99.5% ee, as determined by HPLC (Chiralpak OJ-H, *n*-hexane-*i*-PrOH = 98:2, 0.8 mL min⁻¹, $\lambda = 230$ nm, $t_R = 16.6$ min (major), 15.6 min (minor)); [α]_D²⁰ = -29.0 ($c = 1.02$, CHCl₃); m.p. 87–88 °C (*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.42–7.29 (m, 3H, Ar-H), 7.14–7.00 (m, 2H, Ar-H), 4.78 (dd, $J_1 = 7.2$ Hz, $J_2 = 3.6$ Hz, 1H, OCH), 2.66–2.48 (m, 1H, CH), 1.53–1.21 (m, 2H, CH₂), 0.99–0.84 (m, 2H, CH₂), 0.84–0.63 (m, 4H, CH₃ and one proton in CH₂), 0.53–0.37 (m, 1H, one proton in CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 164.8, 151.7, 133.5, 131.9, 128.5, 128.3, 127.8, 79.9, 25.5, 14.9, 8.3, 6.9, 6.2; IR (KBr) ν (cm⁻¹)

3087, 3012, 2987, 2963, 2940, 2922, 2878, 1792, 1697, 1489, 1463, 1441, 1420, 1306, 1235, 1194, 1168, 1119, 1055, 1011; MS (70 ev, EI) m/z (%): 229 ($M^+ + 1$, 2.36), 228 (M^+ , 14.38), 153 (100); Anal. Calcd for C₁₅H₁₆O₂: C, 78.92; H, 7.06. Found: C, 79.08; H, 7.36.

The following compounds were prepared according to this procedure.

(2) (*E*)- α -(1-Cyclopropylbenzylidene)- β -ethyl- β -lactone ((*E*)-**4l**). The reaction of (*Z*)-**2d** (90.1 mg, 0.41 mmol), *n*-butyl boronic acid **3i** (41.6 mg, 0.48 mmol), Pd(OAc)₂ (2.6 mg, 0.012 mmol), LB-Phos-HBF₄ (10.8 mg, 0.024 mmol), K₃PO₄·3H₂O (213.2 mg, 0.80 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H₂O at 110 °C under nitrogen afforded (*E*)-**4l** (22.6 mg, 24%) (eluent: petroleum ether/ethyl acetate = 30/1, then recrystallization in 8 mL *n*-hexane) as a solid: m.p. 68–69 °C (*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.42–7.28 (m, 3H, Ar-H), 7.14–6.98 (m, 2H, Ar-H), 4.78 (dd, $J_1 = 7.2$ Hz, $J_2 = 3.9$ Hz, 1H, OCH), 2.66–2.49 (m, 1H, CH), 1.53–1.18 (m, 2H, CH₂), 0.99–0.83 (m, 2H, CH₂), 0.83–0.63 (m, 4H, CH₃ and one proton in CH₂), 0.53–0.35 (m, 1H, one proton in CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 164.8, 151.7, 133.5, 131.9, 128.5, 128.3, 127.8, 79.9, 25.5, 14.9, 8.3, 6.9, 6.2; IR (KBr) ν (cm⁻¹) 3009, 2965, 2940, 2917, 2873, 1790, 1695, 1603, 1496, 1461, 1435, 1312, 1261, 1235, 1194, 1169, 1119, 1094, 1056, 1042, 1012; MS (70 ev, EI) m/z (%): 229 ($M^+ + 1$, 2.15), 228 (M^+ , 13.49), 153 (100); Anal. Calcd for C₁₅H₁₆O₂: C, 78.92. H, 7.06. Found: C, 78.94; H, 7.14.

5. Pd-CATALYSED SUZUKI COUPLING OF α -CHLOROALKYLIDENE- β -LACTONES WITH ALKYL BORONIC ACID

(1) *Synthesis of (S,E)- α -(1-butylbenzylidene)- β -ethyl- β -lactone ((S,E)-**4m**). Typical procedure (condition B).* A rubber-capped Schlenk vessel was dried with flame under vacuum and backfilled with nitrogen for three times. Then Pd(OAc)₂ (2.2 mg, 0.01 mmol), LB-Phos-HBF₄ (9.1 mg, 0.02 mmol), K₂CO₃ (124.1 mg, 0.90 mmol), *n*-butylboronic acid **3j** (40.8 mg, 0.40 mmol), 1 mL of toluene and 0.2 mL of H₂O were added into the Schlenk vessel sequentially and stirred. Then (*S*,*Z*)-**2d** (44.3 mg, 0.20 mmol, ee > 99%) and 1 mL of toluene were added sequentially to the vessel. The resulting mixture was heated at 110 °C with a preheated oil bath. After 3.0 h, the reaction was complete as monitored by TLC. Then the reaction mixture was diluted by 10 mL of Et₂O and filtered through a short column of silica gel (eluent: 2 × 10 mL of Et₂O). Evaporation and purification by chromatography ((eluent: *n*-hexane-CH₂Cl₂ = 2:1 (300 mL), then *n*-hexane/ethyl acetate = 100/1)) afforded (*S*,*E*)-**4m** (35.5 mg, 73%) as a liquid in ee 99.3%, as determined by HPLC (Chiralpak AD-H, *n*-hexane-*i*-PrOH = 98:2, 0.8 mL min⁻¹, 230 nm, $t_R = 10.7$ min (major)); [α]_D²⁰ = +23.4 ($c = 0.94$, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.47–7.35 (m, 3H, Ar-H), 7.34–7.24 (m, 2H, Ar-H), 5.20 (dd, $J_1 = 7.2$ Hz, $J_2 = 3.3$ Hz, 1H, OCH), 3.28–3.07 (m, 1H, one proton in CH₂), 2.82–2.65 (m, 1H, one proton in CH₂), 1.78–1.57 (m, 1H, one proton in CH₂), 1.56–1.24 (m, 5H, 2 × CH₂ and one proton in CH₂), 0.94–0.71 (m, 6H, 2 × CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.7, 149.1, 136.3, 132.4, 129.3, 128.8, 127.2, 80.5, 31.5, 30.5, 24.7, 22.2, 13.7, 8.3; IR (neat) ν (cm⁻¹) 2960, 2930, 2870, 2860,

1797, 1687, 1459, 1442, 1378, 1309, 1239, 1161, 1131, 1088, 1054; MS (70 ev, EI) m/z (%): 245 ($M^+ + 1$, 2.76), 244 (M^+ , 20.81), 129 (100); HRMS Calcd for $C_{16}H_{20}O_2$ (M^+): 244.1463. Found: 244.1458.

The following compounds were prepared according to these procedure.

(2) (*E*)- α -(1-Butylbenzylidene)- β -ethyl- β -lactone ((*E*)-**4m**). The reaction of (*Z*)-**2d** (89.6 mg, 0.40 mmol), *n*-butylboronic acid **3j** (81.7 mg, 0.80 mmol), $Pd(OAc)_2$ (4.6 mg, 0.02 mmol), LB-Phos-HBF₄ (18.0 mg, 0.04 mmol), K₂CO₃ (248.4 mg, 1.80 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H₂O at 110 °C under nitrogen afforded (*E*)-**4m** (73.9 mg, containing 0.5% 1,3,5-trimethoxybenzene as determined by ¹H NMR analysis, yield 75%) (eluent: 30–60 °C petroleum ether/CH₂Cl₂ = 2/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.47–7.35 (m, 3H, Ar-H), 7.34–7.22 (m, 2H, Ar-H), 5.20 (dd, $J_1 = 7.1$ Hz, $J_2 = 3.2$ Hz, 1H, OCH), 3.26–3.09 (m, 1H, one proton in CH₂), 2.81–2.65 (m, 1H, one proton in CH₂), 1.78–1.58 (m, 1H, one proton in CH₂), 1.56–1.24 (m, 5H, 2 \times CH₂ and one proton in CH₂), 0.93–0.75 (m, 6H, 2 \times CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.7, 149.1, 136.3, 132.4, 129.4, 128.8, 127.2, 80.5, 31.6, 30.5, 24.7, 22.2, 13.7, 8.3; IR (neat) ν (cm⁻¹) 2960, 2930, 2870, 2860, 1797, 1688, 1460, 1442, 1309, 1239, 1161, 1131, 1088, 1054; MS (70 ev, EI) m/z (%): 245 ($M^+ + 1$, 2.59), 244 (M^+ , 19.19), 129 (100); HRMS Calcd for $C_{16}H_{20}O_2$ (M^+): 244.1463. Found 244.1464.

(3) (*S,E*)- α -(1-Hexylbenzylidene)- β -ethyl- β -lactone ((*S,E*)-**4n**). The reaction of (*S,Z*)-**2d** (44.6 mg, 0.20 mmol, ee > 99%), *n*-hexylboronic acid **3k** (51.4 mg, 0.40 mmol), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol), LB-Phos-HBF₄ (9.0 mg, 0.02 mmol), and K₂CO₃ (125.0 mg, 0.90 mmol) in the mixture solvent of 2 mL of toluene and 0.2 mL of H₂O at 110 °C under nitrogen afforded (*S,E*)-**4n** (39.9 mg, containing 0.8% 1,3,5-trimethoxybenzene as determined by ¹H NMR analysis, yield 72%) (eluent: petroleum ether/ethyl acetate = 100/1) as a liquid in ee > 99%, as determined by HPLC (Chiralpak AS-H, *n*-hexane-*i*-PrOH = 98:2, 0.8 mL min⁻¹, 230 nm, $t_R = 7.2$ min (major)): [α]_D²⁰ = +20.6 ($c = 1.18$, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.48–7.36 (m, 3H, Ar-H), 7.35–7.24 (m, 2H, Ar-H), 5.20 (dd, $J_1 = 7.1$ Hz, $J_2 = 3.5$ Hz, 1H, OCH), 3.25–3.09 (m, 1H, one proton in CH₂), 2.83–2.66 (m, 1H, one proton in CH₂), 1.77–1.58 (m, 1H, one proton in CH₂), 1.53–1.14 (m, 9H, 4 \times CH₂ and one proton in CH₂), 0.93–0.77 (m, 6H, 2 \times CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.7, 149.1, 136.3, 132.4, 129.3, 128.8, 127.2, 80.5, 31.8, 31.4, 28.7, 28.4, 24.7, 22.4, 14.0, 8.3; IR (neat) ν (cm⁻¹) 3059, 2957, 2929, 2858, 1798, 1688, 1603, 1578, 1495, 1461, 1445, 1379, 1309, 1239, 1160, 1130, 1090, 1055; MS (70 ev, EI) m/z (%): 273 ($M^+ + 1$, 1.33), 272 (M^+ , 8.97), 143 (100); HRMS Calcd for $C_{18}H_{24}O_2$ (M^+): 272.1776. Found: 272.1777.

(4) (*E*)- α -(1-Hexylbenzylidene)- β -ethyl- β -lactone ((*E*)-**4n**). The reaction of (*Z*)-**2d** (88.3 mg, 0.40 mmol), *n*-hexylboronic acid **3k** (104.3 mg, 0.80 mmol), $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), LB-Phos-HBF₄ (10.8 mg, 0.024 mmol), and K₂CO₃ (244.4 mg, 1.77 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H₂O at 110 °C under nitrogen afforded (*E*)-**4n** (87.0 mg, containing 1.0% 1,3,5-trimethoxybenzene as

determined by ¹H NMR analysis, yield 80%) (eluent: petroleum ether/ethyl acetate = 80/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 7.48–7.35 (m, 3H, Ar-H), 7.34–7.24 (m, 2H, Ar-H), 5.20 (dd, $J_1 = 7.4$ Hz, $J_2 = 3.5$ Hz, 1H, OCH), 3.25–3.08 (m, 1H, one proton in CH₂), 2.82–2.65 (m, 1H, one proton in CH₂), 1.78–1.58 (m, 1H, one proton in CH₂), 1.54–1.12 (m, 9H, 4 \times CH₂ and one proton in CH₂), 0.96–0.72 (m, 6H, 2 \times CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.7, 149.1, 136.3, 132.4, 129.3, 128.8, 127.2, 80.5, 31.8, 31.4, 28.7, 28.4, 24.7, 22.4, 14.0, 8.3; IR (neat) ν (cm⁻¹) 3059, 2957, 2929, 2858, 1798, 1688, 1492, 1460, 1445, 1382, 1309, 1239, 1160, 1131, 1090, 1055; MS (70 ev, EI) m/z (%): 273 ($M^+ + 1$, 3.93), 272 (M^+ , 21.87), 143 (100); HRMS Calcd for $C_{18}H_{24}O_2$ (M^+): 272.1776. Found: 272.1776.

(5) (*S*)- α -(5-Nonylidene)- β -ethyl- β -lactone ((*S*)-**4o**). The reaction of (*S,Z*)-**2a** (80.1 mg, 0.40 mmol, ee > 99%), *n*-butylboronic acid **3j** (123.4 mg, 1.21 mmol), $PdCl_2(LB-Phos)_2$ (18.3 mg, 0.02 mmol), and K₂CO₃ (248.4 mg, 1.80 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H₂O at 110 °C under nitrogen afforded (*S*)-**4o** (48.7 mg, 55%) (eluent: 30–60 °C petroleum ether/CH₂Cl₂ = 2/1) as a liquid in ee = 99.4%, as determined by HPLC (Chiralpak AS-H, *n*-hexane-*i*-PrOH = 98:2, 0.8 mL min⁻¹, 230 nm, $t_R = 6.3$ min (major), 8.4 min (minor)): [α]_D²⁰ = -64.5 ($c = 1.21$, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 4.89 (dd, $J_1 = 7.5$ Hz, $J_2 = 3.3$ Hz, 1H, OCH), 2.60–2.39 (m, 2H, CH₂), 2.14–1.90 (m, 3H, CH₂ and one proton in CH₂), 1.84–1.64 (m, 1H, one proton in CH₂), 1.56–1.18 (m, 8H, 4 \times CH₂), 1.03 (t, $J = 7.4$ Hz, 3H, CH₃), 0.97–0.79 (m, 6H, 2 \times CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.6, 152.0, 131.4, 79.5, 31.7, 30.7, 30.1, 29.5, 26.3, 22.7, 22.4, 13.8, 8.6; IR (neat) ν (cm⁻¹) 2959, 2933, 2874, 2861, 1800, 1709, 1462, 1380, 1310, 1243, 1147, 1123, 1095, 1053, 1013; MS (70 ev, EI) m/z (%): 224 (M^+ , 2.75), 195 (100); HRMS Calcd for $C_{14}H_{24}O_2$ (M^+): 224.1776. Found: 224.1780.

(6) α -(5-Nonylidene)- β -ethyl- β -lactone (**4o**). The reaction of (*Z*)-**2a** (40.4 mg, 0.20 mmol), *n*-butylboronic acid **3j** (61.0 mg, 0.60 mmol), $PdCl_2(LB-Phos)_2$ (9.2 mg, 0.01 mmol), and K₂CO₃ (125.5 mg, 0.91 mmol) in the mixture solvent of 2 mL of toluene and 0.2 mL of H₂O at 110 °C under nitrogen afforded **4o** (25.3 mg, 56%) (eluent: 30–60 °C petroleum ether/CH₂Cl₂ = 2/1) as a liquid: ¹H NMR (300 MHz, CDCl₃) δ 4.89 (dd, $J_1 = 7.5$ Hz, $J_2 = 3.0$ Hz, 1H, OCH), 2.60–2.39 (m, 2H, CH₂), 2.14–1.90 (m, 3H, CH₂ and one proton in CH₂), 1.84–1.64 (m, 1H, one proton in CH₂), 1.56–1.17 (m, 8H, 4 \times CH₂), 1.02 (t, $J = 7.5$ Hz, 3H, CH₃), 0.97–0.79 (m, 6H, 2 \times CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 164.6, 152.1, 131.4, 79.5, 31.7, 30.7, 30.1, 29.4, 26.3, 22.7, 22.4, 13.8, 8.6; IR (neat) ν (cm⁻¹) 2959, 2932, 2874, 2860, 1799, 1709, 1463, 1380, 1310, 1257, 1243, 1147, 1123, 1095, 1053, 1013; MS (70 ev, EI) m/z (%): 224 (M^+ , 2.58), 195 (100); HRMS Calcd for $C_{14}H_{24}O_2$ (M^+): 224.1776. Found: 224.1777.

6. Pd-CATALYSED SUZUKI COUPLING OF α -CHLOROALKYLIDENE- β -LACTONES WITH HETEROAROMATIC BORONIC ACID

(1) *Synthesis of (S,Z)- α -(1-(2'-thienyl)benzylidene)- β -ethyl- β -lactone ((S,Z)-**4p**)*. Typical procedure. A rubber-capped Schlenk vessel was dried with flame under vacuum and back-filled with nitrogen for three times. Then $PdCl_2(LB-Phos)_2$

(18.2 mg, 0.02 mmol), $K_3PO_4 \cdot 3H_2O$ (319.1 mg, 1.20 mmol), 2-thienylboronic acid **3l** (153.6 mg, 1.20 mmol), and 2 mL of toluene were added into the Schlenk vessel sequentially and stirred. Then (*S,Z*)-**2d** (88.7 mg, 0.40 mmol, ee > 99%) and 2 mL of toluene were added sequentially to the vessel. The resulting mixture was heated to reflux with a preheated oil bath. After 4.8 h, the reaction was complete as monitored by TLC. Then the reaction mixture was cooled and diluted by 10 mL of Et_2O and filtered through a short column of silica gel (eluent: 2 \times 10 mL of Et_2O). Evaporation and purification by chromatography (petroleum ether/ethyl acetate = 30/1) afforded (*S,Z*)-**4p** (83.3 mg, 77%) as a yellow solid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 98 : 2, 1.0 mL min⁻¹, 230 nm, t_R = 10.0 min (major), 14.7 min (minor)); $[\alpha]_D^{20}$ = -104.6 (c = 1.02, $CHCl_3$); m.p. 72–73 °C (*n*-hexane and ethyl acetate); ¹H NMR (300 MHz, $CDCl_3$) δ 7.89 (dd, J_1 = 3.8 Hz, J_2 = 0.8 Hz, 1H, Ar-H), 7.53–7.39 (m, 4H, Ar-H), 7.39–7.30 (m, 2H, Ar-H), 7.16–7.08 (m, 1H, Ar-H), 5.00 (dd, J_1 = 7.2 Hz, J_2 = 3.6 Hz, 1H, OCH), 1.54–1.20 (m, 2H, CH_2), 0.83 (t, J = 7.4 Hz, 3H, CH_3); ¹³C NMR (75 MHz, $CDCl_3$) δ 163.2, 139.5, 139.1, 136.9, 132.2, 130.4, 129.8, 129.4, 128.65, 128.62, 128.1, 79.2, 25.0, 8.1; IR (KBr) ν (cm⁻¹) 2969, 2936, 2871, 1787, 1650, 1462, 1441, 1415, 1374, 1293, 1226, 1154, 1125, 1101, 1052; MS (70 ev, EI) m/z (%): 271 (M^+ + 1, 12.60), 270 (M^+ , 65.41), 240 (100); Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22. Found: C, 70.62; H, 5.16.

The following compounds were prepared according to this procedure.

(2) (*Z*)- α -(1-(2'-Thienyl)benzylidene)- β -ethyl- β -lactone ((*Z*)-**4p**). The reaction of (*Z*)-**2d** (44.4 mg, 0.20 mmol), 2-thienylboronic acid **3k** (76.7 mg, 0.60 mmol), $PdCl_2(LB-Phos)_2$ (9.1 mg, 0.01 mmol), $K_3PO_4 \cdot 3H_2O$ (159.2 mg, 0.60 mmol) in 2 mL of toluene afford (*Z*)-**4p** (41.1 mg, 76%) (eluent: petroleum ether/ethyl acetate = 30/1) as a yellow solid: m.p. 75–76 °C (*n*-hexane and ethyl acetate); ¹H NMR (300 MHz, $CDCl_3$) δ 7.90 (dd, J_1 = 3.8 Hz, J_2 = 1.1 Hz, 1H, Ar-H), 7.52–7.39 (m, 4H, Ar-H), 7.39–7.31 (m, 2H, Ar-H), 7.14–7.07 (m, 1H, Ar-H), 4.99 (dd, J_1 = 7.1 Hz, J_2 = 3.5 Hz, 1H, OCH), 1.53–1.18 (m, 2H, CH_2), 0.82 (t, J = 7.4 Hz, 3H, CH_3); ¹³C NMR (75 MHz, $CDCl_3$) δ 163.2, 139.4, 139.1, 136.9, 132.2, 130.4, 129.7, 129.4, 128.61, 128.59, 128.1, 79.2, 24.9, 8.1; IR (KBr) ν (cm⁻¹) 3097, 2969, 2936, 2878, 1789, 1650, 1489, 1460, 1444, 1415, 1368, 1299, 1244, 1227, 1154, 1125, 1100, 1052; MS (70 ev, EI) m/z (%): 271 (M^+ + 1, 13.24), 270 (M^+ , 13.24), 241 (100). Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22. Found: C, 71.03; H, 5.19.

(3) (*S,Z*)- α -(1-(2'-Benzothienyl)benzylidene)- β -ethyl- β -lactone ((*S,Z*)-**4q**). The reaction of (*S,Z*)-**2d** (89.2 mg, 0.40 mmol, ee > 99%), 2-benzothienylboronic acid **3m** (214.4 mg, 1.20 mmol), $PdCl_2(LB-Phos)_2$ (18.2 mg, 0.02 mmol), and $K_3PO_4 \cdot 3H_2O$ (319.6 mg, 1.20 mmol) in 4 mL of toluene under nitrogen afforded (*S,Z*)-**4q** (106.3 mg, 83%) (eluent: petroleum ether/ethyl acetate = 50/1) as a yellow solid in 99.1% ee, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 90 : 10, 1.0 mL min⁻¹, 230 nm, t_R = 9.16 min (major), 17.9 min (minor)); $[\alpha]_D^{20}$ = -13.7 (c = 1.12, $CHCl_3$); m.p. 102–103 °C (*n*-hexane and ethyl acetate); ¹H NMR (300 MHz, $CDCl_3$) δ 7.94 (s,

1H, Ar-H), 7.84–7.74 (m, 2H, Ar-H), 7.54–7.43 (m, 3H, Ar-H), 7.43–7.33 (m, 4H, Ar-H), 5.05 (dd, J_1 = 7.2 Hz, J_2 = 3.3 Hz, 1H, OCH), 1.58–1.18 (m, 2H, CH_2), 0.86 (t, J = 7.4 Hz, 3H, CH_3); ¹³C NMR (75 MHz, $CDCl_3$) δ 162.8, 141.7, 139.5, 139.2, 138.8, 136.5, 132.3, 129.6, 129.3, 128.7, 126.0, 124.8, 124.7, 122.1, 79.4, 24.9, 8.2; IR (KBr) ν (cm⁻¹) 3058, 3027, 2970, 2937, 2877, 1790, 1651, 1594, 1504, 1457, 1443, 1431, 1343, 1299, 1264, 1239, 1192, 1145, 1120, 1099, 1057, 1030; MS (70 ev, EI) m/z (%): 321 (M^+ + 1, 20.28), 320 (M^+ , 100); Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 74.77; H, 5.01.

(4) (*Z*)- α -(1-(2'-Benzothienyl)benzylidene)- β -ethyl- β -lactone ((*Z*)-**4q**). The reaction of (*Z*)-**2d** (44.8 mg, 0.20 mmol), 2-benzothienylboronic acid **3m** (106.8 mg, 0.60 mmol), $PdCl_2(LB-Phos)_2$ (9.2 mg, 0.01 mmol), and $K_3PO_4 \cdot 3H_2O$ (159.5 mg, 0.60 mmol) in 2 mL of toluene under nitrogen afforded (*Z*)-**4q** (59.3 mg, 92%) (eluent: petroleum ether/ethyl acetate = 30/1) as a yellow solid: m.p. 145–146 °C (*n*-hexane and ethyl acetate); ¹H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 1H, Ar-H), 7.85–7.71 (m, 2H, Ar-H), 7.55–7.42 (m, 3H, Ar-H), 7.42–7.33 (m, 4H, Ar-H), 5.04 (dd, J_1 = 7.1 Hz, J_2 = 3.5 Hz, 1H, OCH), 1.60–1.20 (m, 2H, CH_2), 0.86 (t, J = 7.4 Hz, 3H, CH_3); ¹³C NMR (75 MHz, $CDCl_3$) δ 162.8, 141.7, 139.5, 139.2, 138.8, 136.6, 132.3, 129.6, 129.3, 128.7, 126.0, 124.8, 124.7, 122.2, 79.4, 24.9, 8.1; IR (KBr) ν (cm⁻¹) 2964, 2928, 1793, 1651, 1590, 1501, 1455, 1443, 1378, 1365, 1300, 1253, 1237, 1190, 1160, 1146, 1118, 1075, 1058, 1029; MS (70 ev, EI) m/z (%): 321 (M^+ + 1, 31.86), 320 (M^+ , 100). Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 74.73; H, 5.04.

7. (*S,Z*)- α -(1-BUTYL-(4'-METHOXYL)BENZYLIDENE)- β -ETHYL- β -LACTONE ((*S,Z*)-**4b**) on a 5 mmol scale. The $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), $LB-Phos \cdot HBF_4$ (45.5 mg, 0.10 mmol), $K_3PO_4 \cdot 3H_2O$ (2.6608 g, 10.0 mmol), 4-methoxyphenylboronic acid (913.7 mg, 6.0 mmol), and 20 mL of toluene were added into a rubber-capped Schlenk vessel under nitrogen sequentially. After being stirred for about 5 min at room temperature, (*S,Z*)-**2a** (1.0129 g, 5.0 mmol, ee > 99%) and 30 mL of toluene were added sequentially to the vessel. The resulting mixture was heated at 110 °C with a preheated oil bath. After 2.0 h, the reaction was complete as monitored by TLC. Then the reaction mixture was filtered through a short column of silica gel (eluent: 3 \times 20 mL of Et_2O). Evaporation and purification by chromatography (petroleum ether/ethyl acetate = 40/1 (400 mL), then petroleum ether/ethyl acetate = 20/1) on silica gel afforded (*S,Z*)-**4b** (1.2754 g, 93%) as a liquid in ee > 99%, as determined by HPLC (Chiralpak OD-H, *n*-hexane-*i*-PrOH = 95 : 5, 1.0 mL min⁻¹, λ = 230 nm, t_R = 9.7 min (major)); $[\alpha]_D^{20}$ = +6.5 (c = 0.99, $CHCl_3$); ¹H NMR (300 MHz, $CDCl_3$) δ 7.62–7.46 (m, 2H, Ar-H), 6.97–6.83 (m, 2H, Ar-H), 5.00 (dd, J_1 = 7.7 Hz, J_2 = 2.9 Hz, 1H, OCH), 3.83 (s, 3H, OCH_3), 2.58–2.29 (m, 2H, CH_2), 2.17–2.02 (m, 1H, one proton in CH_2), 1.94–1.75 (m, 1H, one proton in CH_2), 1.45–1.20 (m, 4H, 2 \times CH_2), 1.09 (t, J = 7.4 Hz, 3H, CH_3), 0.87 (t, J = 6.8 Hz, 3H, CH_3); ¹³C NMR (75 MHz, $CDCl_3$) δ 163.7, 160.7, 148.1, 130.4, 129.7, 127.0, 113.7, 78.9, 55.2, 32.7, 30.4, 26.4, 22.6, 13.8, 8.6.

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