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Pd-catalyzed Suzuki coupling reaction of chloroalkylidene-β-lactones with LB-Phos as the ligand†

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In this paper, LB-Phos·HBF_4 salt has been applied for the Pd-catalysed Suzuki coupling reactions of optically active (*Z*)-α-choroalkylidene-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

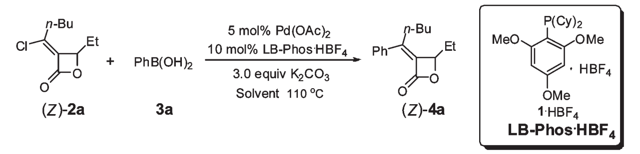
Much progress has been achieved with C–Cl bond activation reactions in past years thanks to the development of new phosphine ligands.[1] Recently, we have developed a new type of monophosphine ligand, which could be used in palladium-catalyzed Suzuki coupling reactions[2] and aminations[3] of organic 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 $PdCl_2$-catalyzed cyclocarbonylation of propargyl alcohols with $CuCl_2$ developed in this group, and phenyl boronic acid (**3a**) (1.5 equiv) were used to test the catalytic activity of Pd/LB-Phos·HBF_4. We found that the Suzuki coupling product (*Z*)-**4a** would be formed in 100% yield using 3.0 equiv of K_2CO_3 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·HBF_4, or K_2CO_3, respectively, would all decrease the yield of (*Z*)-**4a** (Table 1, entries 5–8). This problem was circumvented by using 2.0 equiv of $K_3PO_4·3H_2O$ 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] K_2CO_3 (2.0 equiv) was used. [c] LB-Phos·HBF_4 (5 mol %) was used. [d] $Pd(OAc)_2$ (3 mol%) and LB-Phos·HBF_4 (6 mol%) were used. [e] $K_3PO_4·3H_2O$ (2.0 equiv) was used.

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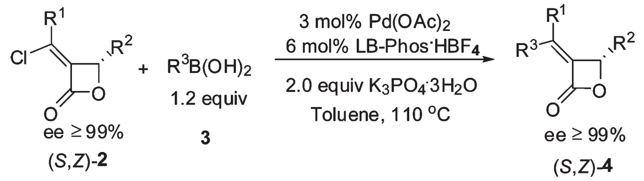
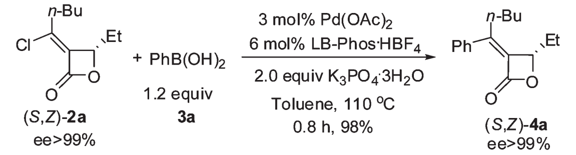
Table 2 Suzuki coupling reactions of (S,Z)-**2** with organoboronic acids[a]



Entry	(S,Z)-**2**			**3**	Time (h)	Yield[b] (%)
		R^1	R^2	R^3		
1	(S,Z)-**2a**	*n*-Bu	Et	Ph (**3a**)	0.8	98 ((S,Z)-**4a**)
2	(S,Z)-**2a**	*n*-Bu	Et	4-$MeOC_6H_4$ (**3b**)	2.0	84 ((S,Z)-**4b**)
3	(S,Z)-**2a**	*n*-Bu	Et	3-$MeOC_6H_4$ (**3c**)	1.0	77 ((S,Z)-**4c**)
4	(S,Z)-**2a**	*n*-Bu	Et	2-$MeOC_6H_4$ (**3d**)	3.7	69 ((S,Z)-**4d**)
5	(S,Z)-**2a**	*n*-Bu	Et	(E)-Styryl (**3e**)	2.8	91 ((S,Z,E)-**4e**)
6	(S,Z)-**2a**	*n*-Bu	Et	4-MeC_6H_4 (**3f**)	1.0	93 ((S,Z)-**4f**)
7	(S,Z)-**2b**	*n*-Bu	Me	4-MeC_6H_4 (**3f**)	1.0	71 ((S,Z)-**4g**)
8	(S,Z)-**2a**	*n*-Bu	Et	2-Naphthyl (**3g**)	1.0	86 ((S,Z)-**4h**)
9	(S,Z)-**2c**	*n*-Bu	i-Pr	Ph (**3a**)	1.5	94 ((S,Z)-**4i**)
10	(S,Z)-**2d**	Ph	Et	4-$MeOC_6H_4$ (**3b**)	1.5	93 ((S,Z)-**4j**)
11	(S,Z)-**2d**	Ph	Et	(E)-1-Pentenyl (**3h**)	0.8	95 ((S,E,E)-**4k**)

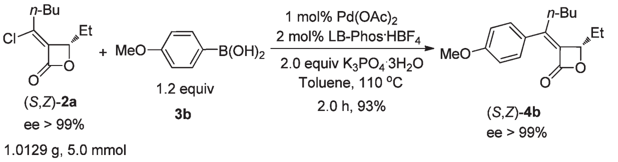
[a] Standard conditions A: a mixture of 1.0 equiv of (S,Z)-2 (0.2 mmol or 0.4 mmol), 1.2 equiv of **3**, 2.0 equiv of $K_3PO_4\cdot 3H_2O$, 0.03 equiv of Pd $(OAc)_2$ and 0.06 equiv of LB-Phos·HBF_4 was stirred in toluene (0.1 M) at 110 °C. [b] Isolated yield.



(1)

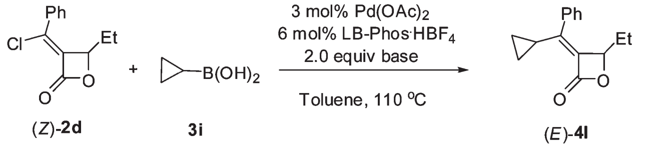
Encouraged by these results, a series of optically active α-chloroalkylidene-β-lactones[6] were tested under the optimized conditions (Table 2). Aromatic (Table 2, entries 1–4 and 6–10) and vinylic boronic acids (Table 2, entries 5 and 11) could all be coupled with the starting β-lactones to afford the 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·HBF_4 was used as the catalyst (eqn (2)).



(2)

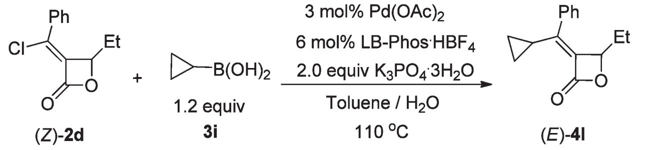
Table 3 Suzuki coupling reactions of (Z)-**2d** with cyclopropyl acid **3i**



Entry	**3i** (equiv)	Base	Time (h)	Yield of (E)-**4l**[a] (%)	Recovery of (Z)-**2d**[a] (%)
1	1.2	$K_3PO_4\cdot 3H_2O$	1.0	23	0
2	1.5	$K_3PO_4\cdot 3H_2O$	1.8	17	0
3	3.0	$K_3PO_4\cdot 3H_2O$	1.5	12	<4
4[b]	0.0	$K_3PO_4\cdot 3H_2O$	1.5	0	21
5[c]	1.2	$K_3PO_4\cdot 3H_2O$	5.0	19	0
6	1.2	Cs_2CO_3	1.3	12	27
7	1.2	CsF	1.1	0	83
8	1.2	$K_2HPO_4\cdot 3H_2O$	6.0	0	97

[a] Determined by ^1H NMR analysis. [b] Neither $Pd(OAc)_2$ nor ligand was added here. [c] $Pd_2(dba)_3\cdot CHCl_3$ 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



Entry	Toluene : H_2O	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

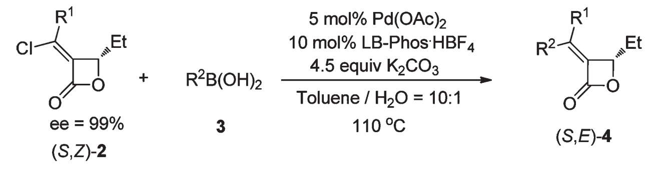
[a] Determined by ^1H NMR analysis.

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 decompose quickly even in absence of $Pd(OAc)_2$ and LB-Phos·HBF_4 (Table 3, entry 5). Using weaker base such as CsF and $K_2HPO_4\cdot 3H_2O$ 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).

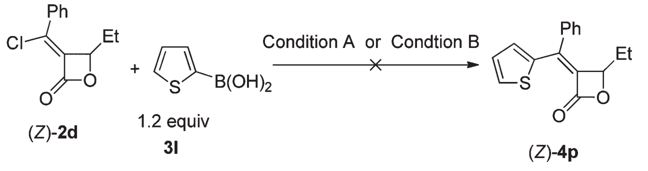
Under the newly optimized conditions (Table 4, entry 2), cyclopropylboronic acid could couple with optically active (S,Z)-**2d** affording (S,E)-**4l** in 46% yield (eqn (3)). However, the coupling of *n*-butylboronic acid with (S,Z)-**2d** did not afford the desired coupling product (S,E)-**4m**. Increasing the loading of K_2CO_3 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]

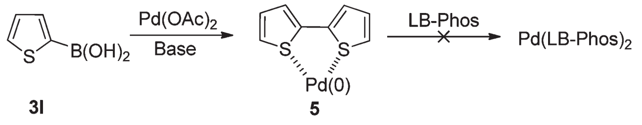


Entry	(*S*,*Z*)-**2** R^1	**3** (equiv)	**3** R^2	Time (h)	**4** Yield[b] (%)	**4** ee%
1	Ph (*S*,*Z*)-**2d**	2.0	*n*-Bu (**3j**)	3.0	73 ((*S*,*E*)-**4m**)	99.3
2	Ph (*S*,*Z*)-**2d**	2.0	*n*-Hex (**3k**)	6.0	72 ((*S*,*E*)-**4n**)	>99
3	*n*-Bu (*Z*)-**2a**	2.0	*n*-Bu (**3j**)	8.0	23 (**4o**)	—
4[c]	*n*-Bu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

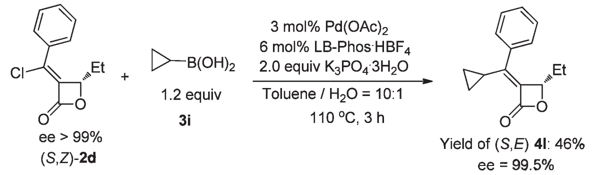
[a] Standard conditions B: a mixture of 1.0 equiv of (*S*,*Z*)-**2**, 2.0 equiv of **3**, 4.5 equiv of K_2CO_3, 0.05 equiv of $Pd(OAc)_2$ and 0.10 equiv of LB-Phos·HBF_4 were stirred in toluene–H_2O = 10 : 1 at 110 °C. [b] Isolated yield. [c] $PdCl_2(LB\text{-}Phos)_2$ (5 mol%) was used as catalyst.



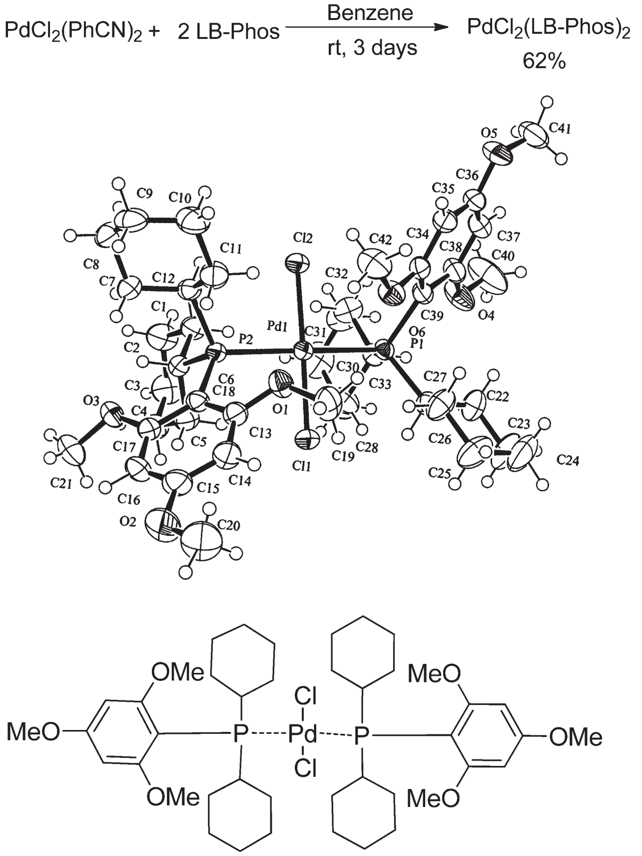
Scheme 1



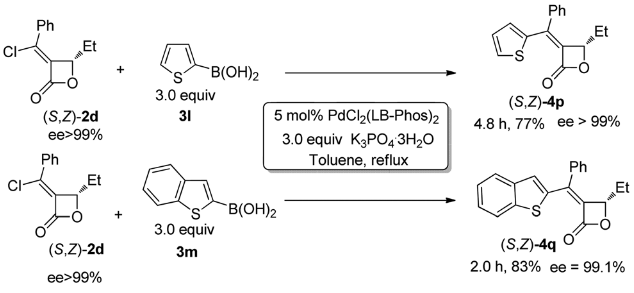
Scheme 2

 (3)

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 $PdCl_2(LB\text{-}Phos)_2$[7] by stirring $PdCl_2(PhCN)_2$ with LB-Phos in benzene for 3 days at room temperature. Indeed, this problem was also conquered by using $PdCl_2(LB\text{-}Phos)_2$ (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% $PdCl_2(LB\text{-}Phos)_2$ and 3.0 equiv of *n*-butylboronic acid, 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.



Scheme 3 Synthesis and ORTEP representation of *trans*-$PdCl_2(LB\text{-}Phos)_2$.



Scheme 4

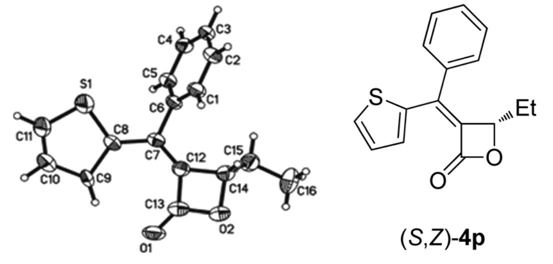


Fig. 1 ORTEP representation of (*S*,*Z*)-**4p**.[8]

Conclusions

We have prepared a series of optically active α-alkylidene-β-lactones of high ee *via* the Suzuki coupling reaction of arylic, vinylic boronic acid with optically active α-chloroalkylidene-β-lactones using LB-Phos as ligand.[9] When a mixture of toluene and H_2O 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 preformed $PdCl_2(LB\text{-}Phos)_2$. Further studies in this area are being conducted in our laboratory.

Experimental section

General information

^1H and ^{13}C NMR spectra were recorded on the instruments operated at 300 and 75 MHz, respectively, in $CDCl_3$. Chemical shifts (δ) are given in parts per million (ppm) with the residual peak of $CHCl_3$ 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 $CuCl_2$ (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-β-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 $CuCl_2$ (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 $PdCl_2$ (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 Et_2O. Filtration through a short column of silica gel (eluent: Et_2O 2 × 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)): $[\alpha]_D^{20}$ = −45.9 (c = 1.14, $CHCl_3$), ^1H NMR (300 MHz, $CDCl_3$) δ 4.89 (d, J = 3.6 Hz, 1H, OCH), 2.34 (t, J = 7.7 Hz, 2H, CH_2), 2.24–2.07 (m, 1H, CH), 1.79–1.49 (m, 2H, CH_2), 1.44–1.26 (m, 2H, CH_2), 1.09 (d, J = 6.9 Hz, 3H, CH_3), 0.99 (d, J = 6.9 Hz, 3H, CH_3), 0.93 (t, J = 7.2 Hz, 3H. CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 ($M^+(^{37}Cl)$, 0.33), 216 ($M^+(^{35}Cl)$, 0.99), 173 (100); Anal. Calcd For $C_{11}H_{17}ClO_2$: 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 $CuCl_2$ (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 $PdCl_2$ (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)): $[\alpha]_D^{20}$ = −96.1 (c = 1.14, $CHCl_3$); white solid, m.p. 83–84 °C (*n*-hexane/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) 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 CH_2), 1.72–1.52 (m, 1H, one proton in CH_2), 0.92 (t, J = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 ($M^+(^{37}Cl)$, 12.73), 222 ($M^+(^{35}Cl)$, 38.89), 221 (100); Anal. Calcd for $C_{12}H_{11}ClO_2$: 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 $CuCl_2$ (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 $PdCl_2$ (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, $CDCl_3$) 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 CH_2), 1.72–1.54 (m, 1H, one proton in CH_2), 0.92 (t, J = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 ($M^+(^{37}Cl)$, 12.73), 222 ($M^+(^{35}Cl)$, 39.49), 221 (100); Anal. Calcd for $C_{12}H_{11}ClO_2$: C, 64.73; H, 4.98. Found: C, 64.82; H, 4.97.

2. SYNTHESIS OF $PdCl_2(LB\text{-}PHOS)_2$. A solution of $PdCl_2(PhCN)_2$ (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 × 10 mL) afforded a yellow solid of $PdCl_2(LB\text{-}Phos)_2$ (1.4124 g, 62%): m.p. 218–219 °C (ether : ethyl

acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (s, 4H, Ar–H), 3.89 (s, 12H, 4 × OCH_3), 3.83 (s, 6H, 2 × OCH_3), 2.96–2.77 (m, 4H, 2 × CH_2), 2.24–2.00 (m, 4H, 2 × CH_2), 1.90–1.08 (m, 36H, 16 × CH_2 and 4 × 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 ($C_{42}H_{66}{}^{37}ClO_6P_2Pd^+$, 100), 869 ($C_{42}H_{66}{}^{35}ClO_6P_2Pd^+$, 99.11); Anal. Calcd For $C_{42}H_{66}Cl_2O_6P_2Pd$: 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 backfilled with nitrogen for three times. Then $Pd(OAc)_2$ (1.3 mg, 0.006 mmol), LB-Phos·HBF_4 (5.3 mg, 0.012 mmol), $K_3PO_4 \cdot 3H_2O$ (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 preheated 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}, λ = 230 nm, t_R = 9.9 min (major)): $[\alpha]_D^{20}$ = −26.1 (c = 1.56, $CHCl_3$); ^{1}H 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 × 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 (M^+ + 1, 6.32), 244 (M^+, 42.33), 145 (100); HRMS Calcd for $C_{16}H_{20}O_2$ (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), $Pd(OAc)_2$ (1.2 mg, 0.006 mmol), LB-Phos·HBF_4 (5.4 mg, 0.012 mmol), and $K_3PO_4 \cdot 3H_2O$ (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. ^{1}H 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 × 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 (M^+ + 1, 4.69), 244 (M^+, 30.31), 145 (100); HRMS Calcd for $C_{16}H_{20}O_2$ (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-methoxylphenylboronic acid **3b** (37.4 mg, 0.25 mmol), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol), LB-Phos·HBF_4 (5.4 mg, 0.012 mmol), and $K_3PO_4 \cdot 3H_2O$ (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, $CHCl_3$); ^{1}H 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 × 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 (M^+ + 1, 12.52), 274 (M^+, 62.30), 175 (100); HRMS Calcd for $C_{17}H_{22}O_3$ (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-methoxylphenyl boronic acid **3b** (36.8 mg, 0.24 mmol), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol), LB-Phos·HBF_4 (5.3 mg, 0.012 mmol), and $K_3PO_4 \cdot 3H_2O$ (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: ^{1}H 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 × 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 (M^+ + 1, 13.42), 274 (M^+, 70.85), 175 (100); HRMS Calcd for $C_{17}H_{22}O_3$ (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-methoxylphenyl boronic acid **3c** (73.4 mg, 0.48 mmol), $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), LB-Phos·HBF_4 (10.8 mg, 0.024 mmol), and $K_3PO_4 \cdot 3H_2O$ (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)): $[\alpha]_D^{20}$ = −25.8 (c = 0.89, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 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, OCH_3), 2.58–2.33 (m, 2H, CH_2), 2.21–2.02 (m, 1H, one proton in CH_2), 1.97–1.77 (m, 1H, one proton in CH_2), 1.50–1.23 (m, 4H, 2 × CH_2), 1.10 (t, J = 7.4 Hz, 3H, CH_3), 0.87 (t, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{17}H_{22}O_3$ (M^+): 274.1569. Found 274.1565.

*(6) (*Z*)-α-(1-Butyl-(3′-methoxyl)benzylidene)-β-ethyl-β-lactone ((*Z*)-**4c**).* The reaction of (*Z*)-**2a** (40.4 mg, 0.20 mmol), 3-methoxylphenyl boronic acid **3c** (36.5 mg, 0.24 mmol), $Pd(OAc)_2$ (1.2 mg, 0.006 mmol), LB-Phos·HBF_4 (5.3 mg, 0.012 mmol), and $K_3PO_4 \cdot 3H_2O$ (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: ^{1}H NMR (300 MHz, $CDCl_3$) 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, OCH_3), 2.57–2.33 (m, 2H, CH_2), 2.20–2.03 (m, 1H, one proton in CH_2), 1.96–1.77 (m, 1H, one proton in CH_2), 1.46–1.23 (m, 4H, 2 × CH_2), 1.11 (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 163.2, 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 $C_{17}H_{22}O_3$ (M^+): 274.1569. Found: 274.1569.

*(7) (*S*,*Z*)-α-(1-Butyl-(2′-methoxyl)benzylidene)-β-ethyl-β-lactone ((*S*,*Z*)-**4d**).* The reaction of (*S*,*Z*)-**2a** (81.1 mg, 0.40 mmol, ee > 99%), 2-methoxylphenyl boronic acid **3d** (73.3 mg, 0.48 mmol), $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), LB-Phos·HBF_4 (10.9 mg, 0.024 mmol), and $K_3PO_4 \cdot 3H_2O$ (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)); $[\alpha]_D^{20}$ = −16.9 (c = 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 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, OCH_3), 2.57–2.35 (m, 2H, CH_2), 2.20–2.04 (m, 1H, one proton in CH_2), 1.97–1.80 (m, 1H, one proton in CH_2), 1.36–1.22 (m, 4H, 2 × CH_2), 1.11 (t, J = 7.4 Hz, 3H, CH_3), 0.84 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{17}H_{22}O_3$ (M^+): 274.1569. Found: 274.1577.

*(8) (*Z*)-α-(1-Butyl-(2′-methoxyl)benzylidene)-β-ethyl-β-lactone ((*Z*)-**4d**).* The reaction of (*Z*)-**2a** (40.2 mg, 0.20 mmol), 2-methoxylphenyl boronic acid **3d** (36.7 mg, 0.48 mmol), $Pd(OAc)_2$ (1.3 mg, 0.006 mmol), LB-Phos·HBF_4 (5.5 mg, 0.012 mmol), and $K_3PO_4 \cdot 3H_2O$ (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: ^{1}H NMR (300 MHz, $CDCl_3$) 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, OCH_3), 2.58–2.35 (m, 2H, CH_2), 2.20–2.04 (m, 1H, one proton in CH_2), 1.97–1.80 (m, 1H, one proton in CH_2), 1.36–1.20 (m, 4H, 2 × CH_2), 1.11 (t, J = 7.5 Hz, 3H, CH_3), 0.84 (t, J = 6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{17}H_{22}O_3$ (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·HBF_4 (10.8 mg, 0.024 mmol) and $K_3PO_4 \cdot 3H_2O$ (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)); $[\alpha]_D^{20}$ = −17.0 (c = 0.88, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_2), 2.15–1.97 (m, 1H, one proton in CH_2), 1.92–1.73 (m, 1H, one proton in CH_2), 1.69–1.32 (m, 4H, 2 × CH_2), 1.08 (t, J = 7.4 Hz, 3H, CH_3), 0.96 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{18}H_{22}O_2$ (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**·HBF_4 (5.4 mg, 0.012 mmol), and $K_3PO_4 \cdot 3H_2O$ (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: ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_2), 2.16–1.97 (m, 1H, one proton in CH_2), 1.91–1.73 (m, 1H, one proton in CH_2), 1.69–1.34 (m, 4H, 2 × CH_2), 1.08 (t, J = 7.4 Hz, 3H, CH_3), 0.97 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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·HBF_4 (5.4 mg, 0.012 mmol), and $K_3PO_4·3H_2O$ (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)); $[\alpha]_D^{20}$ = −10.8 (c = 0.72, $CHCl_3$, Lit. $[\alpha]_D^{20}$ = −10.1 (c = 1.0, $CHCl_3$, ee = 99.9%)[9]): ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_3 and CH_2), 2.20–2.04 (m, 1H, one proton in CH_2), 1.95–1.77 (m, 1H, one proton in CH_2), 1.45–1.24 (m, 4H, 2 × CH_2), 1.11 (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 163.4, 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·HBF_4 (5.4 mg, 0.012 mmol), and $K_3PO_4·3H_2O$ (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: ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_3 and CH_2), 2.20–2.03 (m, 1H, one proton in CH_2), 1.95–1.77 (m, 1H, one proton in CH_2), 1.45–1.24 (m, 4H, 2 × CH_2), 1.11 (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 163.4, 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·HBF_4 (5.4 mg, 0.012 mmol), $K_3PO_4·3H_2O$ (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)); $[\alpha]_D^{20}$ = +9.5 (c = 0.97, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_3 and CH_2), 1.67 (d, J = 6.0 Hz, 3H, CH_3), 1.44–1.24 (m, 4H, 2 × CH_2), 0.87 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{16}H_{20}O_2$ (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·HBF_4 (5.4 mg, 0.012 mmol), and $K_3PO_4·3H_2O$ (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: ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_3 and CH_2), 1.67 (d, J = 6.3 Hz, 3H, CH_3), 1.46–1.22 (m, 4H, 2 × CH_2), 0.87 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{16}H_{20}O_2$ (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·HBF_4 (10.9 mg, 0.024 mmol), and $K_3PO_4·3H_2O$ (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)); $[\alpha]_D^{20}$ = −5.1 (c = 2.26, $CHCl_3$); m.p. 83–84 °C (*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_2), 2.27–2.05 (m, 1H, one proton in CH_2), 2.04–1.80 (m, 1H, one proton in CH_2), 1.53–1.23 (m, 4H, 2 × CH_2), 1.16, (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 163.3, 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 $C_{20}H_{22}O_2$: 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·HBF$_4$ (5.4 mg, 0.012 mmol), $K_3PO_4·3H_2O$ (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: ^{1}H NMR (300 MHz, CDCl$_3$) 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, CH$_2$), 2.25–2.06 (m, 1H, one proton in CH$_2$), 2.01–1.82 (m, 1H, one proton in CH$_2$), 1.50–1.24 (m, 4H, 2 × CH$_2$), 1.15 (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 163.3, 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 $C_{20}H_{22}O_2$ (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·HBF$_4$ (10.9 mg, 0.024 mmol), $K_3PO_4·3H_2O$ (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)): $[\alpha]_D^{20}$ = −6.8 (*c* = 1.02, CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$) 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 CH$_2$), 2.49–2.36 (m, 1H, one proton in CH$_2$), 2.36–2.18 (m, 1H, CH), 1.47–1.23 (m, 4H, 2 × CH$_2$), 1.17 (d, J = 7.2 Hz, 3H, CH$_3$), 1.05 (d, J = 6.9 Hz, 3H, CH$_3$), 0.87 (t, J = 7.1 Hz, 3H, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) 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 $C_{17}H_{22}O_2$ (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·HBF$_4$ (5.4 mg, 0.012 mmol), $K_3PO_4·3H_2O$ (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: ^{1}H NMR (300 MHz, CDCl$_3$) 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, CH$_2$), 2.34–2.16 (m, 1H, CH), 1.44–1.23 (m, 4H, 2 × CH$_2$), 1.16 (d, J = 6.9 Hz, 3H, CH$_3$), 1.04 (d, J = 6.9 Hz, 3H, CH$_3$), 0.86 (t, J = 7.1 Hz, 3H, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) 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 $C_{17}H_{22}O_2$ (M$^+$): 258.1620. Found: 258.1612.

*(19) (S,Z)-α-(1-(4′-Methoxylphenyl)benzylidene)-β-ethyl-β-lactone ((S,Z)-**4j**).* The reaction of (*S*,*Z*)-**2d** (88.9 mg, 0.40 mmol, ee > 99%), 4-methoxylphenyl boronic acid **3a** (73.4 mg, 0.48 mmol), Pd(OAc)$_2$ (2.7 mg, 0.012 mmol), LB-Phos·HBF$_4$ (10.8 mg, 0.024 mmol), $K_3PO_4·3H_2O$ (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)): $[\alpha]_D^{20}$ = +65.1 (*c* = 1.08, CHCl$_3$); m.p. 68–69 °C (*n*-hexane/ethyl acetate); ^{1}H NMR (300 MHz, CDCl$_3$) 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, OCH$_3$), 1.64–1.47 (m, 1H, one proton in CH$_2$), 1.46–1.30 (m, 1H, one proton in CH$_2$), 0.85 (t, J = 7.4 Hz, 3H, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) 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 $C_{19}H_{18}O_3$ (M$^+$): 294.1256. Found: 294.1255.

*(20) (Z)-α-(1-(4′-Methoxylphenyl)benzylidene)-β-ethyl-β-lactone ((Z)-**4j**).* The reaction of (*Z*)-**2d** (44.7 mg, 0.20 mmol), 4-methoxylphenyl boronic acid **3a** (36.9 mg, 0.24 mmol), Pd(OAc)$_2$ (1.3 mg, 0.006 mmol), LB-Phos·HBF$_4$ (5.4 mg, 0.012 mmol), $K_3PO_4·3H_2O$ (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); ^{1}H NMR (300 MHz, CDCl$_3$) 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, OCH$_3$), 1.64–1.48 (m, 1H, one proton in CH$_2$) 1.48–1.30 (m, 1H, one proton in CH$_2$), 0.85 (t, J = 7.4 Hz, 3H, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) 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 $C_{19}H_{18}O_3$ (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·HBF$_4$ (10.7 mg, 0.024 mmol), $K_3PO_4·3H_2O$ (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)): $[\alpha]_D^{20}$ = −120.7 (*c* = 1.04, CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$) 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, CH_2), 1.59–1.21 (m, 4H, 2 × CH_2), 0.89 (t, J = 7.4 Hz, 3H, CH_3), 0.78 (t, J = 7.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_2$ (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·HBF_4 (5.4 mg, 0.012 mmol), $K_3PO_4·3H_2O$ (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: ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_2), 1.57–1.19 (m, 4H, 2 × CH_2), 0.89 (t, J = 7.5 Hz, 3H, CH_3), 0.78 (t, J = 7.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_2$ (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·HBF_4 (10.9 mg, 0.024 mmol), $K_3PO_4·3H_2O$ (212.8 mg, 0.80 mmol), cyclopropylboronic acid **3i** (41.4 mg, 0.48 mmol), 2 mL of toluene and 0.4 mL of H_2O 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 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 = 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}, λ = 230 nm, t_R = 16.6 min (major), 15.6 min (minor)); $[\alpha]_D^{20}$ = −29.0 (c = 1.02, $CHCl_3$): m.p. 87–88 °C (*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_2), 0.99–0.84 (m, 2H, CH_2), 0.84–0.63 (m, 4H, CH_3 and one proton in CH_2), 0.53–0.37 (m, 1H, one proton in CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{15}H_{16}O_2$: 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·HBF_4 (10.8 mg, 0.024 mmol), $K_3PO_4·3H_2O$ (213.2 mg, 0.80 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H_2O 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); ^{1}H NMR (300 MHz, $CDCl_3$) 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, CH_2), 0.99–0.83 (m, 2H, CH_2), 0.83–0.63 (m, 4H, CH_3 and one proton in CH_2), 0.53–0.35 (m, 1H, one proton in CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{15}H_{16}O_2$: 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·HBF_4 (9.1 mg, 0.02 mmol), K_2CO_3 (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 H_2O 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 Et_2O and filtered through a short column of silica gel (eluent: 2 × 10 mL of Et_2O). Evaporation and purification by chromatography ((eluent: *n*-hexane–CH_2Cl_2 = 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)): $[\alpha]_D^{20}$ = +23.4 (c = 0.94, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 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 CH_2), 2.82–2.65 (m, 1H, one proton in CH_2), 1.78–1.57 (m, 1H, one proton in CH_2), 1.56–1.24 (m, 5H, 2 × CH_2 and one proton in CH_2), 0.94–0.71 (m, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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·HBF_4 (18.0 mg, 0.04 mmol), K_2CO_3 (248.4 mg, 1.80 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H_2O at 110 °C under nitrogen afforded (*E*)-**4m** (73.9 mg, containing 0.5% 1,3,5-trimethoxylbenzene as determined by ^1H NMR analysis, yield 75%) (eluent: 30–60 °C petroleum ether/CH_2Cl_2 = 2/1) as a liquid: ^1H NMR (300 MHz, $CDCl_3$) 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 CH_2), 2.81–2.65 (m, 1H, one proton in CH_2), 1.78–1.58 (m, 1H, one proton in CH_2), 1.56–1.24 (m, 5H, 2 × CH_2 and one proton in CH_2), 0.93–0.75 (m, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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·HBF_4 (9.0 mg, 0.02 mmol), and K_2CO_3 (125.0 mg, 0.90 mmol) in the mixture solvent of 2 mL of toluene and 0.2 mL of H_2O at 110 °C under nitrogen afforded (*S*,*E*)-**4n** (39.9 mg, containing 0.8% 1,3,5-trimethoxylbenzene 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)): $[\alpha]_D^{20}$ = +20.6 (*c* = 1.18, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) 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 CH_2), 2.83–2.66 (m, 1H, one proton in CH_2), 1.77–1.58 (m, 1H, one proton in CH_2), 1.53–1.14 (m, 9H, 4 × CH_2 and one proton in CH_2), 0.93–0.77 (m, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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·HBF_4 (10.8 mg, 0.024 mmol), and K_2CO_3 (244.4 mg, 1.77 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H_2O at 110 °C under nitrogen afforded (*E*)-**4n** (87.0 mg, containing 1.0% 1,3,5-trimethoxylbenzene as determined by ^1H NMR analysis, yield 80%) (eluent: petroleum ether/ethyl acetate = 80/1) as a liquid: ^1H NMR (300 MHz, $CDCl_3$) 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 CH_2), 2.82–2.65 (m, 1H, one proton in CH_2), 1.78–1.58 (m, 1H, one proton in CH_2), 1.54–1.12 (m, 9H, 4 × CH_2 and one proton in CH_2), 0.96–0.72 (m, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$), 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 K_2CO_3 (248.4 mg, 1.80 mmol) in the mixture solvent of 4 mL of toluene and 0.4 mL of H_2O at 110 °C under nitrogen afforded (*S*)-**4o** (48.7 mg, 55%) (eluent: 30–60 °C petroleum ether/CH_2Cl_2 = 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)): $[\alpha]_D^{20}$ = −64.5 (*c* = 1.21, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 4.89 (dd, J_1 = 7.5 Hz, J_2 = 3.3 Hz, 1H, OCH), 2.60–2.39 (m, 2H, CH_2), 2.14–1.90 (m, 3H, CH_2 and one proton in CH_2), 1.84–1.64 (m, 1H, one proton in CH_2), 1.56–1.18 (m, 8H, 4 × CH_2), 1.03 (t, *J* = 7.4 Hz, 3H, CH_3), 0.97–0.79 (m, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 K_2CO_3 (125.5 mg, 0.91 mmol) in the mixture solvent of 2 mL of toluene and 0.2 mL of H_2O at 110 °C under nitrogen afforded **4o** (25.3 mg, 56%) (eluent: 30–60 °C petroleum ether/CH_2Cl_2 = 2/1) as a liquid: ^1H NMR (300 MHz, $CDCl_3$) δ 4.89 (dd, J_1 = 7.5 Hz, J_2 = 3.0 Hz, 1H, OCH), 2.60–2.39 (m, 2H, CH_2), 2.14–1.90 (m, 3H, CH_2 and one proton in CH_2), 1.84–1.64 (m, 1H, one proton in CH_2), 1.56–1.17 (m, 8H, 4 × CH_2), 1.02 (t, *J* = 7.5 Hz, 3H, CH_3), 0.97–0.79 (m, 6H, 2 × CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 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 backfilled with nitrogen for three times. Then $PdCl_2$(LB-Phos)$_2$

(18.2 mg, 0.02 mmol), $K_3PO_4·3H_2O$ (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 × 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); ^{13}C 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), $PdCl_2(LB\text{-}Phos)_2$ (9.1 mg, 0.01 mmol), $K_3PO_4·3H_2O$ (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); ^{13}C 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), $PdCl_2(LB\text{-}Phos)_2$ (18.2 mg, 0.02 mmol), and $K_3PO_4·3H_2O$ (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); ^{13}C 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), $PdCl_2(LB\text{-}Phos)_2$ (9.2 mg, 0.01 mmol), and $K_3PO_4·3H_2O$ (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); ^{13}C 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·HBF_4 (45.5 mg, 0.10 mmol), $K_3PO_4·3H_2O$ (2.6608 g, 10.0 mmol), 4-methoxylphenylboronic 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 × 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 × CH_2), 1.09 (t, *J* = 7.4 Hz, 3H, CH_3), 0.87 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C 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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7 Crystal data for compound *trans*-PdCl$_2$(LB-Phos)$_2$: $C_{46}H_{76}Cl_2O_7P_2Pd$, M_W = 980.31, triclinic, space group $P\bar{1}$, final R indices [$I > 2\sigma(I)$], R_1 = 0.0290, wR_2 = 0.0839; R indices (all data), R_1 = 0.0323, wR_2 = 0.0881; a = 12.8490(5) Å, b = 13.1603(5) Å, c = 17.5483(6) Å, α = 73.847(1)°, β = 68.570(1)°, γ = 65.921(1)°, V = 2492.57(16) Å^3. T = 296 K, wavelength: 0.71073 Å, Z = 2, reflections collected/unique: 29003/8738. (R_{int} = 0.0178); number of observations [$>2\sigma(I)$] 8018, parameters: 526. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, CCDC: 888344.

8 Crystal data for compound (*S*,*Z*)-4p: $C_{16}H_{14}O_2S$, M_W = 270.33, monoclinic, space group P 21, final R indices [$I > 2\sigma(I)$], R_1 = 0.0685, wR_2 = 0.1807; R indices (all data), R_1 = 0.0880, wR_2 = 0.2043; a = 9.3629(6) Å, b = 16.6080(8) Å, c = 9.8929(5) Å, α = 90°, β = 115.250 (7)°, γ = 90°, V = 1391.37(17) Å^3. T = 293 K, wavelength: 1.54184 Å, Z = 4, reflections collected/unique: 13412/4948 (R_{int} = 0.0516); number of observations [$>2\sigma(I)$] 3803, parameters: 346. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, CCDC: 888345.

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