EurJOC
European Journal of Organic Chemistry

DOI: 10.1002/ejoc.201200350

Application of LB-Phos·HBF$_4$ in the Suzuki Coupling Reaction of 2-Bromoalken-3-ols with Alkylboronic Acids

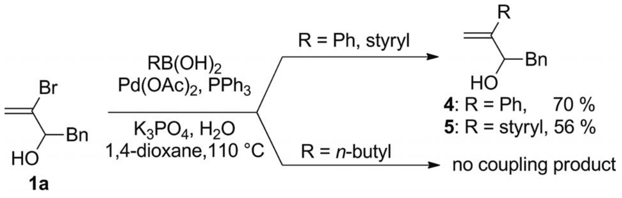
Binjie Guo,[a] Chunling Fu,[a] and Shengming Ma*[a]

Keywords: Suzuki coupling / Alkylboronic acid / Cross-coupling / Homogeneous catalysis / Palladium

LB-Phos·HBF$_4$ was used in the Suzuki coupling reaction of 2-bromoalken-3-ols with alkylboronic acids to give the coupling products in moderate to good yields. Substituents such as benzyl, phenyl, allyl, and alkyl are tolerated at the 1- and 3-positions of the 2-bromoalken-3-ols. The reactions of both primary and secondary alkylboronic acids proceed smoothly.

Introduction

Among cross-coupling reactions, Suzuki reactions have been widely studied due to the commercial availability of a broad array of functionalized boronic acids, which are stable to air and moisture. Much attention has been paid to this area, and different metal sources and ligands have been developed.[1] The efficiency of several catalysts for the reaction of aryl or alkenyl halides with aryl or alkenylboronic acid derivatives has been studied in detail.[1] However, the Suzuki coupling reaction with alkylboronic acids has attracted less attention.[2] Miyaura and co-workers reported the alkylation of bromocyclohexenones or bromoacrylates with functionalized alkylboron derivatives by using PdCl$_2$(dppf) as catalyst and Tl$_2$CO$_3$ as base.[3] Bellina and co-workers described the alkylations of alkenyl bromides by using a dibromofuranone and alkylboronic acids such as *n*-butyl or *n*-octylboronic acids with PdCl$_2$(MeCN)$_2$ (5 mol-%) together with AsPh$_3$ (20 mol-%) and Ag$_2$O as additives to afford the monoalkylated products in 69–79 % yields.[4] Ag$_2$O has also been used for the coupling of alkenyl iodides with functionalized primary alkylboronic acids to afford the corresponding *Z*-alkenes in good yields.[5,6] Reactions of alkenyl halides with alkyltrifluoroborates with PdCl$_2$(dppf)·CH$_2$Cl$_2$ as catalyst and Cs$_2$CO$_3$ as base have proceeded in a similar way.[7] Coupling reactions of alkenyl triflates with primary alkylboronic acids by using PdCl$_2$(dppf)·CH$_2$Cl$_2$ as catalyst have also been reported.[8] Recently, Santelli and co-workers reported the coupling of alkenyl bromides and chlorides with primary alkylboronic acids by using PdCl(C$_3$H$_5$)(dppb) as catalyst and expensive Cs$_2$CO$_3$ as base, affording the coupling products in moderate yields (40–71 %).[9] Over the last few years, Fu and co-workers have made significant contributions to the development of Suzuki coupling reactions between alkyl boron reagents and alkyl halides or sulfonates[10c] by using Pd[10a–10c] or Ni[10d–10i] catalysts. Air-sensitive electron-rich and bulky phosphane ligands have also been used in such couplings. For example, the alkylation of tetrahydroiodopyridines with tri-*n*-butylboroxine was achieved by using Pd(*t*Bu$_3$P)$_2$ as the catalyst.[11] Recently, the Suzuki coupling of (*Z*)-α-(1-chlorobenzylidene)-β-cyclohexyl-β-lactone by using SPhos [2-(dicyclohexylphosphanyl)-2′,6′-dimethoxybiphenyl] has been described by our group.[12] In summary, the discovery of more effective catalytic systems with less toxic and/or less expensive bases for the Suzuki coupling is still highly desirable. Recently, we observed that 2-bromoalken-3-ols may be prepared from the reaction of simple allenes with NBS.[13] As an application, the vinylic bromide could be substituted by phenyl and styryl (sp^2-hybridized) groups from boronic acids by Suzuki coupling.[13] However, when an sp^3-hybridized alkyl boronic acid was subjected to conditions [RB(OH)$_2$ (2.0 equiv.), Pd(OAc)$_2$ (3 mol-%), PPh$_3$ (6 mol-%), K$_3$PO$_4$ (3.5 equiv.), H$_2$O (3.0 equiv.), 1,4-dioxane, 110 °C] that were successful for the corresponding cross-coupling of phenyl- or styrylboronic acids with 3-bromo-1-phenylbut-3-en-2-ol (**1a**), none of the coupling product was obtained (Scheme 1). In this paper, we wish to describe the use of LB-Phos·HBF$_4$[14] (Figure 1) as the ligand in the Pd-catalyzed cross-coupling of 2-bromoalken-3-ols with alkylboronic acids.



Scheme 1.

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[a] Laboratory of Molecular Recognition and Synthesis,
Department of Chemistry, Zhejiang University,
Hangzhou 310027, Zhejiang, P. R. China
Fax: +86-216-260-9305
E-mail: masm@sioc.ac.cn

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201200350.

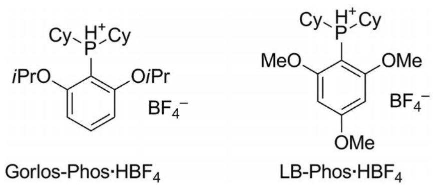


Figure 1. Ligands used in this work.

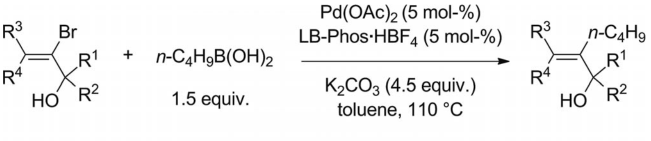
Results and Discussion

Initially, we chose *n*-butylboronic acid (**2a**) and 3-bromo-1-phenylbut-3-en-2-ol (**1a**) as model substrates to optimize the reaction conditions. Because PPh_3 was ineffective both in 1,4-dioxane with K_3PO_4 and in toluene with K_2CO_3 (Table 1, Entries 1 and 4), Gorlos-Phos·HBF_4[15] (Figure 1) was tested instead. To our delight, product **3a** was obtained, albeit in low yield (20%; Table 1, Entry 2). The conditions developed in our group by using LB-Phos·HBF_4 as ligand were also tested,[14a] but only a 9% yield of the product was obtained, and 58% of **1a** was recovered unreacted (Table 1, Entry 3). To our delight, when K_2CO_3 was added and LB-Phos·HBF_4 was used as the ligand, a 76% isolated yield of **3a** was obtained (Table 1, Entry 5). When the amount of *n*-butylboronic acid was reduced to 1.5 equiv., **3a** was formed in 80% yield (Table 1, Entry 6).

Thus, 1.5 equiv. of alkylboronic acid, 5 mol-% of $Pd(OAc)_2$, 5 mol-% of LB-Phos·HBF_4, and 4.5 equiv. of K_2CO_3 in toluene at 110 °C (Table 1, Entry 6) were found to be the optimized reaction conditions.

With these standard reaction conditions established, we investigated the scope of the substrates, and the results are summarized in Table 2. The secondary or tertiary allylic alcohols reacted with *n*-butylboronic acid to give the coupling products in moderate to good yields (63 to 80%) (Table 2, Entries 1–10 and 12). For secondary alcohols (R^2 = H), R^1 could be benzyl (80%; Table 2, Entry 1), alkyl (68 to 80%; Table 2, Entries 2–6), or phenyl (63%; Table 2, Entry 7). Tertiary alcohols could also be used (70 to 76%; Table 2, Entries 8–10 and 12). The low yield of **3k** may arise from its instability at the high reaction temperature. Primary alcohols with additional substituents on the alkene moiety (i.e., **1m–p**) also reacted smoothly to afford the corresponding coupling products (i.e., **3m–p**) in moderate to good yields (Table 2, Entries 13–16). It is worth noting that when more substituted substrate **1q** was used, product **3q** was still obtained in 56% yield (Table 2, Entry 17).

Table 2. Suzuki coupling reaction of **1** with *n*-butylboronic acid using LB-Phos·HBF_4 as the ligand.[a]

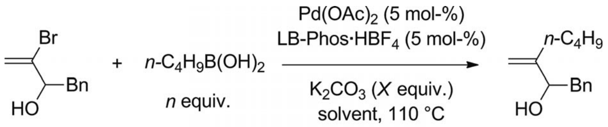


1 **2a** **3**

Entry	1				*T* [h]	Yield of **3** [%][b]
	R^1	R^2	R^3	R^4		
1[c]	Bn	H	H	H (**1a**)	5.7	80 (**3a**)
2[d]	*n*-C_6H_{13}	H	H	H (**1b**)	4.3	80 (**3b**)
3	*n*-C_7H_{15}	H	H	H (**1c**)	6	80 (**3c**)
4	*n*-C_8H_{17}	H	H	H (**1d**)	5.5	77 (**3d**)
5	*n*-$C_{10}H_{21}$	H	H	H(**1e**)	4.3	68 (**3e**)
6	*c*-C_6H_{11}	H	H	H (**1f**)	3.3	69 (**3f**)
7	Ph	H	H	H (**1g**)	4.5	63 (**3g**)
8	Ph	Et	H	H (**1h**)	8.5	72 (**3h**)
9	Ph	*n*Bu	H	H (**1i**)	23	70 (**3i**)
10	Ph	*n*-C_6H_{13}	H	H (**1j**)	7	76 (**3j**)
11	Ph	allyl	H	H (**1k**)	3	25 (**3k**)
12	*n*Bu	*n*Bu	H	H (**1l**)	7.5	71 (**3l**)
13	H	H	Ph	H (**1m**)	14	79 (**3m**)
14	H	H	Bn	H (**1n**)	20	64 (**3n**)
15	H	H	*n*Bu	*n*Bu (**1o**)	4	56 (**3o**)
16	H	H	Ph	*n*-C_6H_{13} (**1p**)	13.7	60 (**3p**)
17	Me	H	Ph	Ph (**1q**)	7.5	56 (**3q**)

[a] The reaction was carried out by using **1** (0.3 mmol), **2a** (1.5 equiv.), $Pd(OAc)_2$ (5 mol-%), LB-Phos·HBF_4 (5 mol-%), and K_2CO_3 (4.5 equiv.) in toluene (2 mL) at 110 °C under a nitrogen atmosphere. [b] Isolated yield. [c] 0.2 mmol of **1a** was used. [d] 2.0 equiv. of **2a** was used.

Table 1. Optimization of the reaction conditions for the Suzuki coupling reaction of 3-bromo-1-phenylbut-3-en-2-ol (**1a**) with *n*-butylboronic acid (**2a**).



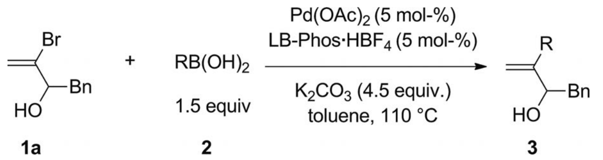
1a **2a** **3a**

Entry	*n*	X	Solvent	*T* [h]	Yield of **3a** [%][a]	Recovery of **1a** [%][a]
1[b]	2.0	–	1,4-dioxane	23	0	0
2[c]	3.0	–	1,4-dioxane	46.5	20	0
3[d]	2.0	–	1,4-dioxane	11	9	58
4[e]	2.0	4.5	toluene	6	0	0
5	2.0	4.5	toluene	24	(76)[f]	0
6	1.5	4.5	toluene	5.7	79 (80)[f]	0

[a] Determined by ^1H NMR spectroscopy by using CH_2Br_2 as internal standard. [b] $Pd(OAc)_2$ (3 mol-%) was added, with PPh_3 (6 mol-%) as the ligand and K_3PO_4 (3.5 equiv.) as the base, together with H_2O (3.0 equiv.). [c] Gorlos-Phos·HBF_4 (10 mol-%) was used as the ligand with K_3PO_4 (3.5 equiv.) as the base, and H_2O (3.0 equiv.) was added. [d] K_3PO_4 (3.5 equiv.) was used instead of K_2CO_3 as the base, together with H_2O (3.0 equiv.). [e] PPh_3 (10 mol-%) was used as the ligand instead of LB-Phos·HBF_4. [f] Isolated yield.

The optimized conditions could also be extended to the Suzuki coupling of 2-bromoalken-3-ols with other alkylboronic acids (Table 3). Isobutylboronic acid reacted with **1a** to give **3r** in 41% yield (Table 3, Entry 1). When cyclopropyl boronic acid was used, a higher yield of 86% of coupling product **3s** was obtained (Table 3, Entry 2). With *n*-pentyl, *n*-hexyl, and *n*-decyl boronic acids, products **3t**, **3u**, and **3v**, respectively, were obtained in good yields (Table 3, Entries 3–5). However, when benzyl boronic acid was used, product **3w** was only formed in a low yield of 24% (Table 3, Entry 6), probably due to the instability of the boronic acid, as 3-phenylpropyl boronic acid afforded **3x** in 77% yield (Table 3, Entry 7).

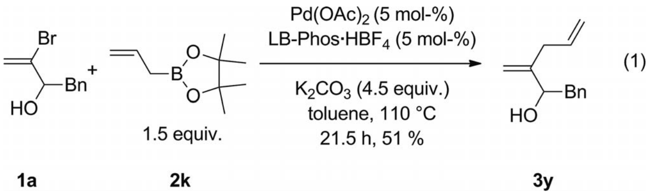
Table 3. Suzuki coupling reaction of **1a** with different alkylboronic acids by using LB-Phos·HBF_4 as the ligand.[a]



Entry	R	*T* [h]	Yield of **3** [%][b]
1	isobutyl (**2b**)	17	41 (**3r**)
2	*c*-propyl (**2c**)	22.5	86 (**3s**)
3	*n*-pentyl (**2d**)	3	80 (**3t**)
4	*n*-hexyl (**2e**)	2.3	84 (**3u**)
5	*n*-decyl (**2f**)	3	70 (**3v**)
6	Bn (**2g**)	27	24 (**3w**)
7	3-phenylpropyl (**2h**)	16.8	77 (**3x**)

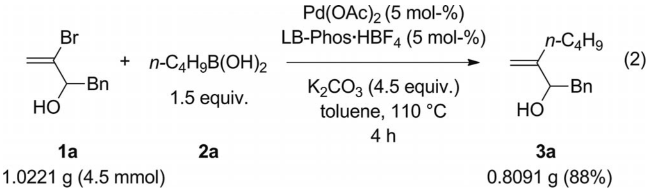
[a] The reaction was carried out using **1a** (0.3 mmol), **2** (1.5 equiv.), $Pd(OAc)_2$ (5 mol-%), LB-Phos·HBF_4 (5 mol-%), and K_2CO_3 (4.5 equiv.) in toluene (2 mL) at 110 °C under a nitrogen atmosphere. [b] Isolated yield.

Allylboronic acid pinacol ester (**2k**) also reacted with **1a** to afford allylation product **3y** in a yield of 51% [Equation (1)].

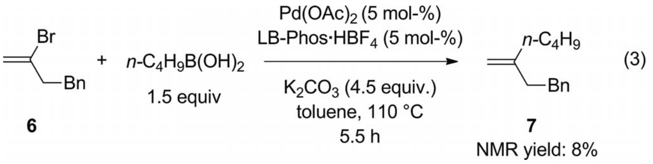


In our previous report,[13] product **4** was obtained by coupling between **1a** and $PhB(OH)_2$ in a yield of 70%, but the newly established conditions in this report allow a higher yield (86%) of this product to be obtained (Scheme 2), which indicates that LB-Phos·HBF_4 is a more effective ligand than PPh_3. The reaction of styrylboronic acid with **1a** afforded almost the same yield of coupling product **5**.

To demonstrate the practicality of the procedure, the reaction of **1a** (1.0221 g, 4.5 mmol) with *n*-butylboronic acid afforded coupling product **3a** in 88% isolated yield [Equation (2)].

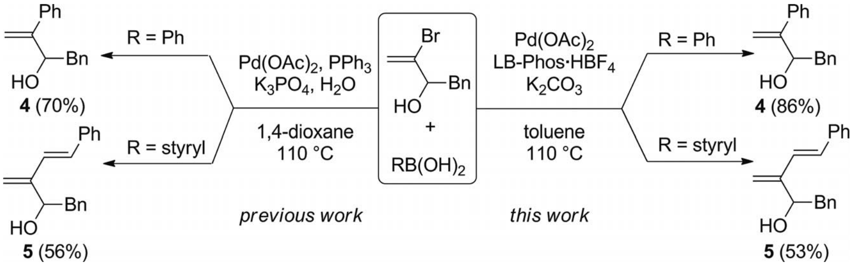


As a comparison, the reaction of 4-phenyl-2-bromobut-1-ene with *n*-butylboronic acid was conducted under the same reaction conditions, but coupling product **7** was formed in only 8% yield with complete consumption of the starting bromide, as determined by ^1H NMR spectroscopy. This indicates the importance of the hydroxy group in substrates **1a**–**q** [Equation (3)].



Conclusions

In conclusion, we have successfully used the ligand LB-Phos·HBF_4 in the Suzuki coupling of 2-bromoalken-3-ols with different alkylboronic acids to afford the coupling products in moderate to good yields. Different substituents such as benzyl, phenyl, allyl, and alkyl can be connected to the 1- and 3-positions of the 2-bromoalken-3-ols. Further-



Scheme 2.

more, the reactions of both primary and secondary alkylboronic acids also proceed smoothly. Further studies with this ligand are being conducted in our laboratory.

Experimental Section

General Methods: ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM 300 MHz spectrometer. IR spectra were recorded with a Perkin–Elmer 983G instrument. Elemental analyses were recorded with a Carlo–Erba EA1110 elemental analysis instrument. Mass spectrometry was performed with an HP 5989A system. High-resolution mass spectrometry was determined with a Finnigan MAT 8430 or Bruker APEXIII instrument. The 2-bromoalken-3-ols used in this study were prepared according to the reported method from this group.[13] Compounds **2d**–**h** was prepared according to the literature. Toluene was distilled from Na/benzophenone before use. Unless otherwise indicated, chemicals and solvents were purchased from commercial suppliers.

Typical Procedure for the Suzuki Coupling

3-Methylene-1-phenyl-2-heptanol (3a): K_2CO_3 (124.6 mg, 0.9 mmol) was added to a rubber-capped Schlenk vessel. This equipment was flame-dried under vacuum and backfilled with nitrogen three times. $Pd(OAc)_2$ (2.4 mg, 0.01 mmol), butyl boronic acid (**2a**) (30.5 mg, 0.3 mmol), toluene (1 mL), **1a** (45.9 mg, 0.2 mmol), toluene (1 mL), and LB-Phos·HBF_4 (4.5 mg, 0.01 mmol) were added sequentially to the Schlenk vessel at room temperature. The resulting mixture was stirred at 110 °C in a pre-heated oil bath. After 5.7 h, the reaction was complete, as monitored by TLC. The reaction mixture was then cooled and filtered through a short column of silica gel (ethyl acetate). Evaporation and purification by chromatography (petroleum ether/ethyl acetate = 20:1) on silica gel afforded **3a** (32.9 mg, 80%) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30–7.12 (m, 5 H, ArH), 4.98 (s, 1 H, one proton of $=CH_2$), 4.81 (d, J = 1.2 Hz, 1 H, one proton of $=CH_2$), 4.21 (dd, J = 8.9, 4.1 Hz, 1 H, CH-O), 2.87 (dd, J = 13.7, 4.1 Hz, 1 H, one proton of $ArCH_2$), 2.67 (dd, J = 13.7, 8.9 Hz, 1 H, one proton of $ArCH_2$), 2.20–1.90 (m, 2 H, CH_2), 1.53 (s, 1 H, OH), 1.48–1.36 (m, 2 H, CH_2), 1.36–1.23 (m, 2 H, CH_2), 0.86 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.4, 138.4, 129.4, 128.5, 126.5, 109.5, 75.9, 42.7, 31.7, 30.2, 22.6, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3418, 3028, 2956, 2927, 2869, 1645, 1597, 1495, 1454, 1377, 1046 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 204 (1.45) $[M]^+$, 92 (100). HRMS: calcd for $C_{14}H_{20}O$ $[M]^+$ 204.1514; found 204.1517.

A Large Scale Reaction for the Synthesis of 3a: The reaction of K_2CO_3 (2.7945 g, 20.25 mmol), $Pd(OAc)_2$ (50.7 mg, 0.225 mmol), **2a** (0.6889 g, 6.75 mmol), **1a** (1.0221 g, 4.5 mmol), toluene (30 mL), and LB-Phos·HBF_4 (101.6 mg, 0.225 mmol) at 110 °C for 4 h afforded **3a** (0.8091 g, 88%) after purification by chromatography (petroleum ether/ethyl acetate = 40:1 to 30:1) as a liquid.

The following compounds **3b**–**y** were prepared according to the typical procedure.

5-Methylene-6-dodecanol (3b): The reaction of K_2CO_3 (186.4 mg, 1.35 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), **2a** (61.1 mg, 0.6 mmol), **1b** (66.6 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 4.3 h afforded **3b** (47.7 mg, 80%) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.99 (s, 1 H, one proton of $=CH_2$), 4.82 (d, J = 1.5 Hz, 1 H, one proton of $=CH_2$), 4.05 (t, J = 6.3 Hz, 1 H, CH-O), 2.13–1.87 (m, 2 H, CH_2), 1.68 (s, 1 H, OH), 1.62–1.15 (m, 14 H, 7 CH_2), 0.95–0.77 (m, 6 H, 2 CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3, 109.0, 75.5, 35.5, 31.8, 31.0, 30.2, 29.2, 25.6, 22.63, 22.59, 14.03, 13.97 ppm. IR (neat): $\tilde{\nu}$ = 3354, 3081, 2957, 2929, 2859, 1646, 1467, 1378, 1122, 1037 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 198 (0.62) $[M]^+$, 71 (100). HRMS: calcd for $C_{13}H_{26}O$ $[M]^+$ 198.1984; found 198.1975.

5-Methylenetridecan-6-ol (3c): The reaction of K_2CO_3 (186.0 mg, 1.35 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), **2a** (45.9 mg, 0.45 mmol), **1c** (70.4 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 6 h afforded **3c** (50.7 mg, 80%) after purification by chromatography (petroleum to petroleum ether/ethyl acetate = 50:1 to 30:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.00 (s, 1 H, one proton of $=CH_2$), 4.83 (d, J = 1.5 Hz, 1 H, one proton of $=CH_2$), 4.06 (t, J = 6.3 Hz, 1 H, CH-O), 2.15–1.85 (m, 2 H, CH_2), 1.64 (s, 1 H, OH), 1.60–1.17 (m, 16 H, 8 CH_2), 0.95–0.80 (m, 6 H, 2 CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3, 109.0, 75.5, 35.5, 31.8, 31.0, 30.2, 29.5, 29.3, 25.7, 22.6, 14.06, 13.98 ppm. IR (neat): $\tilde{\nu}$ = 3362, 3081, 2957, 2928, 2858, 1642, 1466, 1378, 1119, 1047, 1020 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 212 (0.74) $[M]^+$, 71 (100). HRMS: calcd for $C_{14}H_{28}O$ $[M]^+$ 212.2140; found 212.2147.

5-Methylenetetradecan-6-ol (3d): The reaction of K_2CO_3 (186.9 mg, 1.35 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), **2a** (61.3 mg, 0.6 mmol), **1d** (74.4 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.7 mg, 0.015 mmol) at 110 °C for 5.5 h afforded **3d**[16] (52.3 mg, 77%) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.99 (s, 1 H, one proton of $=CH_2$), 4.82 (d, J = 1.5 Hz, 1 H, one proton of $=CH_2$), 4.04 (t, J = 6.3 Hz, 1 H, CH-O), 2.15–1.87 (m, 2 H, CH_2), 1.67 (s, 1 H, OH), 1.60–1.15 (m, 18 H, 9 CH_2), 0.95–0.80 (m, 6 H, 2 CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3, 109.0, 75.5, 35.5, 31.9, 31.0, 30.2, 29.6, 29.5, 29.3, 25.7, 22.6, 14.06, 13.98 ppm. IR (neat): $\tilde{\nu}$ = 3361, 3081, 2955, 2927, 2857, 1647, 1464, 1378, 1134, 1056 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 226 (0.51) $[M]^+$, 71 (100).

5-Methylenehexadecan-6-ol (3e): The reaction of K_2CO_3 (186.5 mg, 1.35 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), **2a** (45.9 mg, 0.45 mmol), **1e** (83.0 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 4.3 h afforded **3e** (51.5 mg, 68%) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.00 (s, 1 H, =CH), 4.83 (d, J = 1.2 Hz, 1 H, =CH), 4.06 (t, J = 6.2 Hz, 1 H, CH-O), 2.15–1.85 (m, 2 H, CH_2), 1.65 (s, 1 H, OH), 1.60–1.17 (m, 22 H, 11 CH_2), 0.97–0.82 (m, 6 H, 2 CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3, 109.0, 75.5, 35.5, 31.9, 31.0, 30.2, 29.60, 29.59, 29.3, 25.7, 22.7, 22.6, 14.1, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3356, 3081, 2956, 2926, 2855, 1645, 1466, 1378, 1066, 1024 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 254 (0.86) $[M]^+$, 71 (100). HRMS: calcd for $C_{17}H_{34}O$ $[M]^+$ 254.2610; found 254.2617.

1-Cyclohexyl-2-methylenehexan-1-ol (3f): The reaction of K_2CO_3 (186.5 mg, 1.35 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), **2a** (45.6 mg, 0.45 mmol), **1f** (65.4 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 3.3 h afforded **3f**[17] (40.1 mg, 69%) after purification by chromatography (petroleum ether/ethyl acetate = 50:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.95 (s, 1 H, one proton of $=CH_2$), 4.87 (d, J = 1.2 Hz, 1 H, one proton of $=CH_2$), 4.77 (d, J = 6.6 Hz, 1 H, CH-O), 2.15–2.00 (m, 1 H, CH), 2.00–1.83 (m, 2 H, CH_2), 1.83–1.60 (m, 3 H), 1.60–0.96 (m, 12 H, 6 CH_2), 0.92 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.9, 110.3, 80.6, 40.9, 30.8, 30.1, 29.9, 28.1, 26.4, 26.2, 26.0, 22.7, 14.0 ppm. IR (neat): $\tilde{\nu}$ =

3406, 3079, 2926, 2853, 1645, 1450, 1377, 1260, 1107, 1080, 1020 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 196 (4.54) [M]$^+$, 71 (100).

2-Methylene-1-phenylhexan-1-ol (3g): The reaction of K_2CO_3 (186.5 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (46.2 mg, 0.45 mmol), **1g** (64.1 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 4.5 h afforded **3g**[16] (36.1 mg, 63 %) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 5 H, ArH), 5.24 (s, 1 H, one proton of =CH$_2$), 5.12 (s, 1 H, CH-O), 4.96 (s, 1 H, one proton of =CH$_2$), 2.14 (s, 1 H, OH), 2.00–1.74 (m, 2 H, CH$_2$), 1.44–1.32 (m, 2 H, CH$_2$), 1.32–1.18 (m, 2 H, CH$_2$), 0.84 (t, *J* = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.1, 142.2, 128.4, 127.6, 126.7, 109.6, 77.3, 31.5, 30.0, 22.4, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 3374, 3086, 3063, 3029, 2957, 2929, 2872, 2858, 1647, 1493, 1454, 1379, 1239, 1189, 1037, 1025 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 190 (16.86) [M]$^+$, 133 (100).

4-Methylene-3-phenyloctan-3-ol (3h): The reaction of K_2CO_3 (186.6 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (45.8 mg, 0.45 mmol), **1h** (73.2 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 8.5 h afforded **3h** (47.8 mg, 72 %) after purification by chromatography (petroleum ether/ethyl acetate = 50:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.35 (m, 2 H, ArH), 7.35–7.25 (m, 2 H, ArH), 7.25–7.16 (m, 1 H, ArH), 5.31 (s, 1 H, one proton of =CH$_2$), 5.01 (s, 1 H, one proton of =CH$_2$), 2.15–1.95 (m, 2 H, CH$_2$), 1.92–1.70 (m, 3 H), 1.38–1.24 (m, 2 H, CH$_2$), 1.24–1.10 (m, 2 H, CH$_2$), 0.89–0.73 (m, 6 H, 2 CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.3, 145.0, 127.9, 126.6, 125.8, 108.8, 79.4, 31.8, 30.8, 30.5, 22.5, 13.9, 7.8 ppm. IR (neat): $\tilde{\nu}$ = 3481, 3087, 3059, 3026, 2958, 2931, 2872, 1639, 1493, 1447, 1378, 1128 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 218 (0.78) [M]$^+$, 189 (100). HRMS: calcd for $C_{15}H_{22}O$ [M]$^+$ 218.1671; found 218.1665.

6-Methylene-5-phenyldecan-5-ol (3i): The reaction of K_2CO_3 (186.5 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (45.9 mg, 0.45 mmol), **1i** (81.2 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 23 h afforded **3i** (52.3 mg, 70 %) after purification by chromatography (petroleum to petroleum ether/ethyl acetate = 50:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.36 (m, 2 H, ArH), 7.36–7.27 (m, 2 H, ArH), 7.27–7.18 (m, 1 H, ArH), 5.31 (d, *J* = 0.9 Hz, 1 H, one proton of =CH$_2$), 5.00 (d, *J* = 0.9 Hz, 1 H, one proton of =CH$_2$), 2.08–1.93 (m, 2 H, CH$_2$), 1.93–1.68 (m, 3 H, OH, CH$_2$), 1.38–1.05 (m, 8 H, 4 CH$_2$), 0.88 (t, *J* = 7.1 Hz, 3 H, CH$_3$), 0.80 (t, *J* = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.6, 145.3, 127.9, 126.6, 125.7, 108.7, 79.2, 39.2, 30.8, 30.5, 25.6, 23.1, 22.5, 14.1, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 3478, 3088, 3060, 3026, 2956, 2931, 2871, 1639, 1601, 1494, 1467, 1447, 1378, 1341, 1255, 1214, 1166, 1131, 1052, 1031 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 246 (1.05) [M]$^+$, 189 (100). HRMS: calcd for $C_{17}H_{26}O$ [M]$^+$ 246.1984; found 246.1980.

5-Methylene-6-phenyldodecan-6-ol (3j): The reaction of K_2CO_3 (186.7 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (46.0 mg, 0.45 mmol), **1j** (88.8 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 7 h afforded **3j** (62.2 mg, 76 %) after purification by chromatography (petroleum ether/ethyl acetate = 50:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.36 (m, 2 H, ArH), 7.36–7.27 (m, 2 H, ArH), 7.27–7.17 (m, 1 H, ArH), 5.31 (s, 1 H, one proton of =CH$_2$), 4.99 (s, 1 H, one proton of =CH$_2$), 2.08–1.93 (m, 2 H, CH$_2$), 1.91–1.70 (m, 3 H, OH, CH$_2$), 1.40–1.08 (m, 12 H, 6 CH$_2$), 0.86 (t, *J* = 6.3 Hz, 3 H, CH$_3$), 0.79 (t, *J* = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.5, 145.2, 127.9, 126.6, 125.7, 108.6, 79.2, 39.4, 31.8, 30.7, 30.5, 29.7, 23.4, 22.6, 22.5, 14.1, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3483, 3088, 3060, 3026, 2956, 2929, 2859, 1636, 1597, 1493, 1466, 1447, 1378, 1341, 1188, 1161, 1131, 1047, 1029 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 274 (0.86) [M]$^+$, 189 (100). HRMS: calcd for $C_{19}H_{30}O$ [M]$^+$ 274.2297; found 274.2290.

5-Methylene-4-phenylnon-1-en-4-ol (3k): The reaction of K_2CO_3 (186.6 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (46.2 mg, 0.45 mmol), **1k** (76.4 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 3 h afforded **3k** (17.6 mg, 25 %) after purification by chromatography (petroleum ether/ethyl acetate = 50:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.38 (m, 2 H, ArH), 7.37–7.28 (m, 2 H, ArH), 7.28–7.15 (m, 1 H, ArH), 5.75–5.57 (m, 1 H, =CH), 5.29 (s, 1 H, one proton of =CH$_2$), 5.25–5.09 (m, 2 H, =CH$_2$), 5.01 (s, 1 H, one proton of =CH$_2$), 2.92–2.73 (m, 2 H, CH$_2$), 2.21 (s, 1 H, OH), 2.00–1.75 (m, 2 H, CH$_2$), 1.39–1.10 (m, 4 H, 2 CH$_2$), 0.80 (t, *J* = 7.2 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.1 144.7, 133.6, 128.0, 126.8, 125.7, 120.0, 109.0, 77.8, 44.4, 30.7, 30.4, 22.5, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3558, 3479, 3077, 3060, 3026, 2956, 2930, 2871, 2858, 1639, 1600, 1493, 1447, 1378, 1342, 1247, 1170, 1132, 1055, 1020 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 230 (6.72) [M]$^+$, 105 (100). HRMS: calcd for $C_{16}H_{22}O$ [M]$^+$ 230.1671; found 230.1678.

5-Butyl-6-methylenedecan-5-ol (3l): The reaction of K_2CO_3 (186.2 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (46.1 mg, 0.45 mmol), **1l** (74.5 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 7.5 h afforded **3l** (47.7 mg, 71 %) after purification by chromatography (*n*-hexane/ethyl acetate = 50:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.04 (d, *J* = 0.9 Hz, 1 H, =CH), 4.89 (d, *J* = 0.9 Hz, 1 H, =CH), 1.88 (t, *J* = 7.7 Hz, 2 H, CH$_2$), 1.63–1.39 (m, 7 H), 1.39–1.20 (m, 8 H, 4 CH$_2$), 1.17–1.02 (m, 2 H, CH$_2$), 0.98–0.82 (m, 9 H, 3 CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.8, 108.0, 78.0, 39.5, 30.9, 30.3, 25.4, 23.1, 22.8, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 3487, 3093, 2957, 2929, 2872, 2863, 1637, 1467, 1379, 1343, 1284, 1257, 1147, 1037 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 226 (1.41) [M]$^+$, 169 (100). HRMS: calcd for $C_{15}H_{30}O$ [M]$^+$ 226.2297; found 226.2301.

(*E*)-2-Benzylidenehexan-1-ol (3m): The reaction of K_2CO_3 (186.3 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (45.9 mg, 0.45 mmol), **1m** (63.7 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 14 h afforded **3m**[18] (44.7 mg, 79 %) after purification by chromatography (petroleum ether/ethyl acetate = 20:1 to 15:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.18 (m, 5 H, ArH), 6.52 (s, 1 H, =CH), 4.21 (s, 2 H, CH$_2$-O), 2.29 (t, *J* = 8.0 Hz, 2 H, CH$_2$), 1.88 (s, 1 H, OH), 1.58–1.40 (m, 2 H, CH$_2$), 1.40–1.20 (m, 2 H,CH$_2$), 0.88 (t, *J* = 7.4 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.3, 137.5, 128.6, 128.1, 126.4, 125.2, 66.9, 30.5, 28.5, 22.9, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 3323, 3056, 3023, 2957, 2928, 2860, 1654, 1597, 1493, 1462, 1446, 1374, 1086, 1031 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 190 (24.07) [M]$^+$, 133 (100).

(*E*)-2-(2-Phenylethylidene)hexan-1-ol (3n): The reaction of K_2CO_3 (186.5 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2a** (46.2 mg, 0.45 mmol), **1n** (67.6 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 20 h afforded **3n** (39.1 mg, 64 %) after purification by chromatography (petroleum ether/ethyl acetate = 30:1 to 20:1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.10 (m, 5 H, ArH), 5.59 (t, *J* = 7.2 Hz, 1 H, =CH), 4.06 (s, 2 H, CH$_2$-O), 3.41 (d, *J* = 7.2 Hz, 2 H, ArCH$_2$), 2.30–2.12 (m, 2 H, CH$_2$), 1.58–1.23 (m, 5 H, OH and 2 CH$_2$), 0.93 (t, *J* = 6.9 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =

141.0, 140.1, 128.4, 128.3, 125.9, 124.9, 66.9, 33.7, 30.8, 27.8, 22.9, 14.0 ppm. IR (neat): ṽ = 3327, 3085, 3062, 3027, 2956, 2931, 2860, 1604, 1494, 1453, 1378, 1221, 1159, 1103, 1058, 1030, 1000 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 204 (18.17) $[\text{M}]^+$, 173 (91.91) $[\text{M} - \text{CH}_2\text{OH}]^+$, 117 (100). HRMS: calcd for $\text{C}_{14}\text{H}_{20}\text{O}$ $[\text{M}]^+$ 204.1514; found 204.1513.

2,3-Dibutylhept-2-en-1-ol (3o): The reaction of K_2CO_3 (187.0 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2a** (46.3 mg, 0.45 mmol), **1o** (75.0 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 4 h afforded 3**o** (36.7 mg, 54%) after purification by chromatography [petroleum ether (30–60 °C)/ethyl acetate = 30:1] as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 4.10 (s, 2 H, CH_2-O), 2.18–1.93 (m, 6 H, 3 CH_2), 1.46–1.23 (m, 12 H, 6 CH_2), 1.18 (br. s, 1 H), 1.02–0.83 (m, 9 H, 3 CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 139.1, 132.9, 61.7, 32.1, 31.7, 31.6, 31.4, 31.2, 29.9, 23.05, 22.98, 22.9, 14.0 ppm. IR (neat): ṽ = 3322, 2957, 2929, 2872, 2860, 1466, 1378, 1150, 1105, 1084, 1022 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 226 (16.99) $[\text{M}]^+$, 208 (14.61) $[\text{M} - \text{H}_2\text{O}]^+$, 169 (100). HRMS: calcd for $\text{C}_{15}\text{H}_{30}\text{O}$ $[\text{M}]^+$ 226.2297; found 226.2293.

(*Z*)-2-Butyl-3-phenylnon-2-en-1-ol (3p): The reaction of K_2CO_3 (186.5 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2a** (46.2 mg, 0.45 mmol), **1p** (89.4 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 13.7 h afforded **3p** (49.8 mg, 60%) after purification by chromatography [petroleum ether (30–60 °C)/ethyl acetate = 30:1] as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 7.40–7.18 (m, 3 H, ArH), 7.17–7.00 (m, 2 H, ArH), 3.87 (s, 2 H, CH_2-O), 2.40–2.21 (m, 4 H, 2 CH_2), 1.55–1.30 (m, 4 H, 2 CH_2), 1.30–1.05 (m, 9 H), 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.84 (t, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 142.5, 140.5, 135.1, 128.5, 128.0, 126.3, 62.9, 34.1, 31.7, 31.3, 29.4, 29.3, 28.0, 23.0, 22.6, 14.1, 14.0 ppm. IR (neat): ṽ = 3322, 3075, 3056, 3015, 2926, 2858, 1596, 1491, 1466, 1444, 1378, 1233, 1185, 1099, 1069, 1028 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 274 (45.49) $[\text{M}]^+$, 217 (57.61) $[\text{M} - \text{C}_4\text{H}_9]^+$, 91 (100). HRMS: calcd for $\text{C}_{19}\text{H}_{30}\text{O}$ $[\text{M}]^+$ 274.2297; found 274.2294.

3-(Diphenylmethylene)heptan-2-ol (3q): The reaction of K_2CO_3 (186.4 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2a** (46.1 mg, 0.45 mmol), **1q** (90.7 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 7.5 h afforded **3q** (47.1 mg, 56%) after purification by chromatography [petroleum ether (30–60 °C)/ethyl acetate = 30:1] as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 7.35–7.22 (m, 4 H, ArH), 7.22–7.10 (m, 6 H, ArH), 4.65 (q, *J* = 6.5 Hz, 1 H, CH-O), 2.28–2.09 (m, 2 H, CH_2), 1.50–1.22 (m, 6 H, OH, CH_2, CH_3), 1.22–1.07 (m, 2 H, CH_2), 0.72 (t, *J* = 7.4 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 142.6, 142.3, 141.4, 140.2, 128.9, 128.8, 128.2, 128.1, 126.5, 126.4, 68.5, 32.8, 27.2, 23.1, 22.0, 13.7 ppm. IR (neat): ṽ = 3389, 3077, 3055, 3020, 2957, 2930, 2871, 1597, 1490, 1463, 1443, 1367, 1285, 1100, 1073, 1053, 1031, 1002 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 280 (1.87) $[\text{M}]^+$, 223 (79.04) $[\text{M} - \text{C}_4\text{H}_9]^+$, 167 (100). HRMS: calcd for $\text{C}_{20}\text{H}_{24}\text{O}$ $[\text{M}]^+$ 280.1827; found 280.1830.

5-Methyl-3-methylene-1-phenylheptan-2-ol (3r): The reaction of K_2CO_3 (186.7 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2b** (46.0 mg, 0.45 mmol), **1a** (68.7 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 17 h afforded **3r** (25.2 mg, 41%) after purification by chromatography [petroleum ether (30–60 °C)/ethyl acetate = 30:1] as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 7.37–7.28 (m, 2 H, ArH), 7.28–7.18 (m, 3 H, ArH), 5.12 (s, 1 H, one proton of =CH_2), 4.87 (d, *J* = 0.9 Hz, 1 H, one proton of =CH_2), 4.29–4.19 (m, 1 H, CH-O), 2.95 (dd, *J* = 13.8, 6.9 Hz, 1 H, one proton of ArCH_2), 2.71 (dd, *J* = 13.8, 8.9 Hz, 1 H, one proton of ArCH_2), 2.08–1.91 (m, 2 H, CH_2), 1.91–1.78 (m, 1 H, CH), 1.60 (d, *J* = 3.0 Hz, 1 H, OH), 0.97–0.88 (m, 6 H, 2 CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 149.9, 138.4, 129.4, 128.4, 126.5, 110.7, 75.4, 42.7, 42.2, 26.5, 22.8, 22.4 ppm. IR (neat): ṽ = 3420, 3086, 3063, 3028, 2954, 2924, 2868, 1647, 1599, 1496, 1454, 1384, 1366, 1168, 1099, 1077, 1050, 1031 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 204 (1.24) $[\text{M}]^+$, 92 (100). HRMS: calcd for $\text{C}_{14}\text{H}_{20}\text{O}$ $[\text{M}]^+$ 204.1514; found 204.1511.

3-Cyclopropyl-1-phenylbut-3-en-2-ol (3s): The reaction of K_2CO_3 (186.2 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2b** (39.1 mg, 0.45 mmol), **1a** (68.3 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 22.5 h afforded **3s** (48.4 mg, 86%) after purification by chromatography (*n*-hexane/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 7.39–7.17 (m, 5 H, ArH), 4.87 (s, 1 H, one proton of =CH_2), 4.62 (s, 1 H, one proton of =CH_2), 4.37 (dd, *J* = 8.4, 3.9 Hz, 1 H, CH-O), 3.05 (dd, *J* = 13.8, 4.5 Hz, 1 H, one proton in ArCH_2), 2.83 (dd, *J* = 13.5, 8.7 Hz, 1 H, one proton in ArCH_2), 1.84 (s, 1 H, OH), 1.45–1.33 (m, 1 H, CH), 0.82–0.67 (m, 2 H, CH_2), 0.58–0.43 (m, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 152.7, 138.4, 129.4, 128.3, 126.4, 106.0, 42.8, 12.1, 7.1 ppm. IR (neat): ṽ = 3420, 3083, 3060, 3028, 3000, 2922, 2852, 1644, 1602, 1496, 1454, 1423, 1391, 1269, 1081, 1043, 1020 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 188 (3.05) $[\text{M}]^+$, 92 (100). HRMS: calcd for $\text{C}_{13}\text{H}_{16}\text{O}$ $[\text{M}]^+$ 188.1201; found 188.1204.

3-Methylene-1-phenyloctan-2-ol (3t): The reaction of K_2CO_3 (185.5 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2d** (52.8 mg, 0.45 mmol), **1a** (67.6 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 3 h afforded **3t** (51.7 mg, 80%) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 7.36–7.26 (m, 2 H, ArH), 7.26–7.16 (m, 3 H, ArH), 5.04 (s, 1 H, one proton of =CH_2), 4.87 (d, *J* = 0.9 Hz, 1 H, one proton of =CH_2), 4.26 (dd, *J* = 8.9, 3.8 Hz, 1 H, CH-O), 2.93 (dd, *J* = 13.8, 4.2 Hz, 1 H, one proton in ArCH_2), 2.73 (dd, *J* = 13.8, 8.7 Hz, 1 H, one proton in ArCH_2), 2.21–1.98 (m, 2 H, CH_2), 1.69 (s, 1 H, OH), 1.56–1.40 (m, 2 H, CH_2), 1.40–1.26 (m, 4 H, 2 CH_2), 0.91 (t, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 151.4, 138.4, 129.3, 128.4, 126.4, 109.4, 75.8, 42.7, 31.9, 31.7, 27.6, 22.5, 14.0 ppm. IR (neat): ṽ = 3417, 3085, 3063, 3028, 2955, 2928, 2859, 1646, 1603, 1496, 1455, 1378, 1078, 1031 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 218 (1.18) $[\text{M}]^+$, 92 (100). HRMS: calcd for $\text{C}_{15}\text{H}_{22}\text{O}$ $[\text{M}]^+$ 218.1671; found 218.1672.

3-Methylene-1-phenylnonan-2-ol (3u): The reaction of K_2CO_3 (186.2 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2e** (58.7 mg, 0.45 mmol), **1a** (68.2 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF_4 (6.8 mg, 0.015 mmol) at 110 °C for 2.3 h afforded **3u** (58.3 mg, 84%) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, CDCl_3): δ = 7.38–7.28 (m, 2 H, ArH), 7.28–7.17 (m, 3 H, ArH), 5.05 (s, 1 H, one proton of =CH_2), 4.88 (d, *J* = 1.2 Hz, 1 H, one proton of =CH_2), 4.27 (dd, *J* = 8.7, 3.9 Hz, 1 H, CH-O), 2.93 (dd, *J* = 13.7, 4.1 Hz, 1 H, one proton of ArCH_2), 2.73 (dd, *J* = 13.7, 8.9 Hz, 1 H, one proton of ArCH_2), 2.22–1.97 (m, 2 H, CH_2), 1.65 (s, 1 H, OH), 1.57–1.42 (m, 2 H, CH_2), 1.42–1.22 (m, 6 H, 3 CH_2), 0.90 (t, *J* = 6.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ = 151.4, 138.5, 129.3, 128.4, 126.5, 109.4, 75.9, 42.7, 32.0, 31.7, 29.2, 27.9, 22.6, 14.1 ppm. IR (neat): ṽ = 3407, 3085, 3063, 3028, 2956, 2927, 2857, 1647, 1603, 1496, 1454, 1378, 1108, 1078, 1049, 1031 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 232 (0.75) $[\text{M}]^+$, 92 (100). HRMS: calcd for $\text{C}_{16}\text{H}_{24}\text{O}$ $[\text{M}]^+$ 232.1827; found 232.1834.

3-Methylene-1-phenyltridecan-2-ol (3v): The reaction of K_2CO_3 (186.6 mg, 1.35 mmol), Pd(OAc)_2 (3.4 mg, 0.015 mmol), **2f**

(84.0 mg, 0.45 mmol), **1a** (68.6 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 3 h afforded **3v** (61.0 mg, 70 %) after purification by chromatography (petroleum ether/ethyl acetate = 30:1) as a liquid. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.35–7.26 (m, 2 H, ArH), 7.26–7.17 (m, 3 H, ArH), 5.04 (s, 1 H, one proton of =CH$_2$), 4.87 (d, J = 0.9 Hz, 1 H, one proton of =CH$_2$), 4.27 (dd, J = 8.7, 3.9 Hz, 1 H, CH-O), 2.93 (dd, J = 13.5, 4.2 Hz, 1 H, one proton of ArCH$_2$), 2.73 (dd, J = 13.8, 8.7 Hz, 1 H, one proton of ArCH$_2$), 2.22–1.97 (m, 2 H, CH$_2$), 1.67 (s, 1 H, OH), 1.57–1.40 (m, 2 H, CH$_2$), 1.40–1.18 (m, 14 H, 7 CH$_2$), 0.89 (t, J = 6.3 Hz, 3 H, CH$_3$) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 151.4, 138.5, 129.3, 128.4, 126.4, 109.4, 75.8, 42.7, 32.0, 31.9, 29.6, 29.5, 29.3, 28.0, 22.7, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 3418, 3085, 3063, 3028, 2956, 2924, 2854, 1647, 1603, 1496, 1455, 1378, 1079, 1031 cm^{-1}. MS (EI, 70 eV): m/z (%) = 288 (0.64) [M]$^+$, 92 (100). C$_{20}$H$_{32}$O (288.47): calcd. C 83.27, H 11.18; found C 83.01, H 11.17.

3-Benzyl-1-phenylbut-3-en-2-ol (3w): The reaction of K$_2$CO$_3$ (186.8 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2g** (61.5 mg, 0.45 mmol), **1a** (68.6 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 27 h afforded **3w** (17.4 mg, 24 %) after purification by chromatography (petroleum ether/ethyl acetate = 30:1 to 20:1) as a liquid. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.39–7.23 (m, 4 H, ArH), 7.22–7.14 (m, 6 H, ArH), 5.17 (s, 1 H, one proton of =CH$_2$), 4.81 (d, J = 1.2 Hz, 1 H, one proton of =CH$_2$), 4.32–4.23 (m, 1 H, CH-O), 3.51 (d, J = 15.3 Hz, 1 H, one proton of ArCH$_2$), 3.38 (d, J = 15.6 Hz, 1 H, one proton of ArCH$_2$), 2.94 (dd, J = 13.8, 4.5 Hz, 1 H, one proton of ArCH$_2$), 2.75 (dd, J = 13.5, 9.0 Hz, 1 H, one proton of ArCH$_2$), 1.64 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 150.6, 139.2, 138.2, 129.3, 129.2, 128.5, 128.4, 126.5, 126.2, 112.3, 75.0, 42.7, 39.3 ppm. IR (neat): $\tilde{\nu}$ = 3562, 3425, 3084, 3061, 3027, 2919, 2850, 1646, 1602, 1495, 1454, 1434, 1077, 1050, 1030 cm^{-1}. MS (EI, 70 eV): m/z (%) = 238 (1.58) [M]$^+$, 146 (66.41) [M – Bn]$^+$, 129 (100). HRMS: calcd for C$_{17}$H$_{18}$O [M]$^+$ 238.1358; found 238.1363.

3-Methylene-1,6-diphenylhexan-2-ol (3x): The reaction of K$_2$CO$_3$ (187.3 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2h** (74.3 mg, 0.45 mmol), **1a** (68.2 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 16.8 h afforded **3x** (61.7 mg, 77 %) after purification by chromatography (petroleum ether/ethyl acetate = 30:1 to 20:1) as a liquid. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.35–7.23 (m, 4 H, ArH), 7.23–7.10 (m, 6 H, ArH), 5.05 (s, 1 H, one proton of =CH$_2$), 4.88 (s, 1 H, one proton of =CH$_2$), 4.24 (dd, J = 8.3, 3.8 Hz, 1 H, CH-O), 2.88 (dd, J = 13.7, 4.1 Hz, 1 H, one proton of ArCH$_2$), 2.78–2.54 (m, 3 H, one proton of ArCH$_2$ and CH$_2$), 2.25–2.00 (m, 2 H, CH$_2$), 1.90–1.75 (m, 2 H, CH$_2$), 1.70 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 150.8, 142.2, 138.3, 129.3, 128.38, 128.35, 128.2, 126.4, 125.7, 109.8, 75.8, 42.6, 35.6, 31.4, 29.6 ppm. IR (neat): $\tilde{\nu}$ = 3444, 3084, 3060, 3026, 2932, 2858, 1939, 1867, 1802, 1645, 1603, 1584, 1495, 1455, 1274, 1079, 1030 cm^{-1}. MS (EI, 70 eV): m/z (%) = 266 (0.49) [M]$^+$, 174 (41.06) [M – Bn]$^+$, 91 (100). C$_{19}$H$_{22}$O (266.38): calcd. C 85.67, H 8.32; found C 85.64, H 8.42.

3-Methylene-1-phenylhex-5-en-2-ol (3y): The reaction of K$_2$CO$_3$ (186.5 mg, 1.35 mmol), Pd(OAc)$_2$ (3.4 mg, 0.015 mmol), **2k** (76.0 mg, 0.45 mmol), **1a** (68.5 mg, 0.3 mmol), toluene (2 mL), and LB-Phos·HBF$_4$ (6.8 mg, 0.015 mmol) at 110 °C for 21.5 h afforded **3y** (29.2 mg, 51 %) after purification by chromatography [petroleum ether (30–60 °C)/ethyl acetate = 30:1] as a liquid. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.37–7.25 (m, 2 H, ArH), 7.25–7.16 (m, 3 H, ArH), 5.93–5.75 (m, 1 H, =CH), 5.17–5.02 (m, 3 H, =CH and =CH$_2$), 4.89 (d, J = 0.9 Hz, 1 H, one proton of =CH$_2$), 4.27 (dd, J = 8.4, 3.9 Hz, 1 H, CH-O), 3.01–2.64 (m, 4 H, CH$_2$ and ArCH$_2$), 1.86 (s, 1 H, OH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 149.3, 138.2, 136.0, 129.3, 128.4, 126.4, 116.6, 111.2, 75.5, 42.4, 36.6 ppm. IR (neat): $\tilde{\nu}$ = 3421, 3084, 3060, 3028, 2980, 2923, 2855, 1641, 1602, 1496, 1454, 1426, 1272, 1078, 1055, 1031 cm^{-1}. MS (EI, 70 eV): m/z (%) = 188 (0.29) [M]$^+$, 92 (100). C$_{13}$H$_{16}$O (188.27): calcd. C 82.94, H 8.57; found C 82.52, H 8.74.

2-(2-Phenylethyl)-1-hexene (7): The reaction of K$_2$CO$_3$ (621.8 mg, 4.5 mmol), Pd(OAc)$_2$ (11.3 mg, 0.05 mmol), **2a** (153.2 mg, 1.5 mmol), **6**[19] (211.7 mg, 1.0 mmol), toluene (6.7 mL), and LB-Phos·HBF$_4$ (22.7 mg, 0.05 mmol) at 110 °C for 5.5 h afforded **7**[20] (8 %, determined by NMR spectroscopy), with complete consumption of the starting bromide as determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR spectra of all key intermediates and final compounds.

Acknowledgments

Financial support from the National Basic Research Program of China (2009CB825300) and the National Natural Science Foundation of China (21172192) is greatly appreciated. S. M. is a Qiu Shi Adjunct Professor at Zhejiang University. We thank Mr. Jinxian Liu in this group for reproducing the results presented in Table 2 (Entries 10 and 15) and Table 3 (Entry 4).

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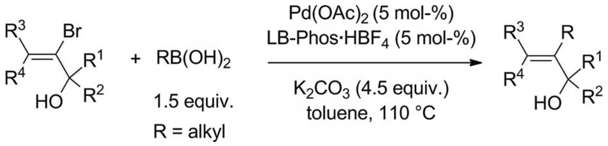
Received: March 20, 2012

Cross-Coupling



LB-Phos·HBF$_4$ was used in the Suzuki coupling reaction of 2-bromoalken-3-ols with alkylboronic acids to afford the coupling products in moderate to good yields. Substituents such as benzyl, phenyl, allyl, and alkyl are tolerated at the 1- and 3-positions of the 2-bromoalken-3-ols.

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Application of LB-Phos·HBF$_4$ in the Suzuki Coupling Reaction of 2-Bromoalken-3-ols with Alkylboronic Acids

Keywords: Suzuki coupling / Alkylboronic acid / Cross-coupling / Homogeneous catalysis / Palladium