Cobalt-Catalyzed Sequential Cyclization/Cross-Coupling Reactions of 6-Halo-1-hexene Derivatives with Grignard Reagents and Their Application to the Synthesis of 1,3-Diols

Hidenori Someya, Hirohisa Ohmiya, Hideki Yorimitsu*, and Koichiro Oshima*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University, Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

Fax: +81-75-383-2438

E-mail:yori@orgrxn.mbox.media.kyoto-u.ac.jp, oshima@orgrxn.mbox.media.kyoto-u.ac.jp

Dedicated to Professor Hisashi Yamamoto

Abstract: Cobalt/*N*-heterocyclic carbene system or cobalt/diamine combination effectively catalyzes sequential cyclization/cross-coupling reactions of 6-halo-1-hexene derivatives with trialkylsilylmethyl, 1-alkynyl, and aryl Grignard reagents. The sequential cyclization/cross-coupling reactions are applied to the synthesis of 1,3-diols starting from siloxy-tethered 6-halo-1-hexene derivatives.

Keywords: Cross-coupling reaction, Cobalt, *N*-Heterocyclic carbene, Grignard reagent, 1,3-Diols

Introduction

Transition metal-catalyzed cross-coupling reactions are very powerful tools for carbon-carbon bond formation in organic synthesis. The cross-coupling reactions of alkyl halides having *β*-hydrogen with organometallic reagents are difficult because of

slow oxidative addition of alkyl halides to low valent transition metal and *β*-hydride elimination from alkyl-transition metal intermediates. During the past decade, the development of cross-coupling reactions of alkyl halides has made remarkable progress.[1] We have been interested in cobalt-catalyzed cross-coupling reactions of alkyl halides with Grignard reagents,[2,3] and reported sequential cyclization/cross-coupling reactions of 6-halo-1-hexene derivatives with trialkylsilylmethyl and 1-alkynyl Grignard reagents, which proceed only with the aid of *N*-heterocyclic carbene (NHC) ligands. Herein we present the full details of the reactions, including its scope, the curious effects of NHC ligands,[4] and a new approach to 1,3-diols starting from silicon-tethered 6-iodo-1-hexene derivatives.[5]

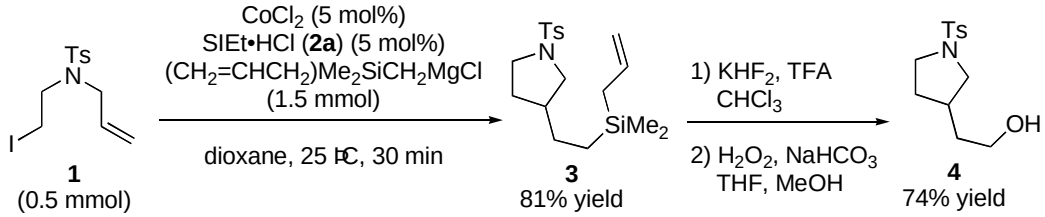
Results and discussions

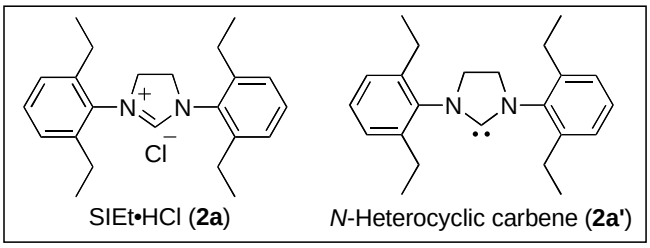
(1) Sequential cyclization/cross-coupling reactions of 6-halo-1-hexene derivatives with trialkylsilylmethyl and 1-alkynyl Grignard reagents in the presence of cobalt/*N*-heterocyclic carbene catalyst

In light of the importance of silyl groups as a hydroxy equivalent, cobalt-catalyzed sequential cyclization/cross-coupling reaction with allyldimethylsilylmethylmagnesium chloride was investigated at first. Imidazolium salt (SIEt·HCl, **2a**, Table 1, 0.025 mmol), a 4-aza-6-iodo-1-hexene derivative **1** (0.5 mmol), and $CoCl_2$ (0.025 mmol) were mixed in dioxane (2 mL). Allyldimethylsilylmethylmagnesium chloride (1.5 mmol, 1 M ether solution) was then added over 5 s at 25 ˚C, to cause an exothermic reaction. The mixture was stirred at 25 ˚C for 30 min to provide the corresponding cyclization/coupling product **3** in 81% yield (Scheme 1). The 3-(2-silylethyl)pyrrolidine derivative **3** underwent deallylative fluorination followed

by Tamao–Fleming oxidation to furnish the corresponding alcohol **4**.[6] This reaction would proceed as follows:[3] 1) generation of the corresponding carbon-centered radical from **1** by single electron transfer from an electron-rich cobalt complex, 2) radical cyclization, 3) capture of the 3-pyrrolidinylmethyl radical by a cobalt complex, and 4) reductive elimination. The electron-rich cobalt species that is active for this coupling reaction could be a Co(0) or Co(I) ate complex. [3a,b]

Scheme 1.

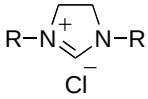
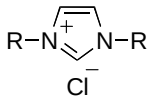
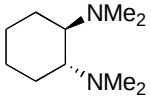




N-Heterocyclic carbene (**2a'**) was the best ligand among many ligands we tested (Table 1).[7,8] Other NHC ligands were less effective. For example, the use of 1,3-di(*tert*-butyl)-substituted imidazolium salt **2c** afforded less than 5% yield of **3** (entry 3), and a significant amount of 1-toluenesulfonyl-3-methylenepyrrolidine was formed via β-elimination. On the other hand, 1,3-dimesityl-substituted derivative IMes·HCl (**2d**) showed modest activity (entry 4), and the use of SIMes·HCl (**2b**), the dihydro analogue of **2d**, further improved the yield of **3** up to 54% (entry 2). Diisopropylphenyl-substituted imidazolium salt (IPr·HCl, **2e**) which bears larger aryl groups than IMes·HCl (**2d**) provided none of the coupling product, leaving most of the starting material (entry 5). The use of other ligands such as phosphines (PPh_3 and P^tBu_3) and

N,N,N',N'-tetramethyl-1,2-cyclohexanediamine (CD)[3g] resulted in much lower yields (entries 6–8). The carbene ligand (**2a'**) may promote facile oxidative addition through a single electron transfer mechanism and fast reductive elimination from an alkylcobalt intermediate without suffering from β-elimination. The choice of solvent had a significant effect on the yields of the coupling product. Dioxane proved to be the best solvent. Other solvents such as THF and ether gave much lower yields of the coupling product (30–40%).

Table 1. Ligand effect[a]

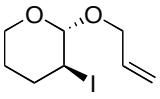
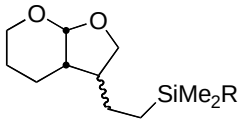
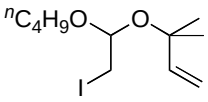
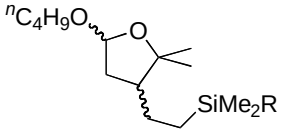
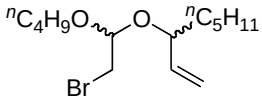
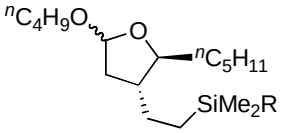
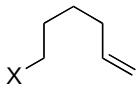
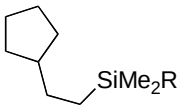
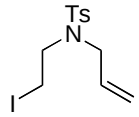
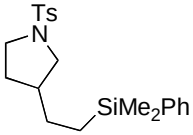
entry	ligand		yield (%)
1		R = 2,6-diethylphenyl (SIEt•HCl, **2a**)	81
2		R = Mesityl (SIMes•HCl, **2b**)	54
3		R = *tert*-butyl (**2c**)	<5
4		R = Mesityl (IMes•HCl, **2d**)	36
5		R = 2,6-diisopropylphenyl (IPr•HCl, **2e**)	<1
6	PPh_3		<1
7	P^tBu_3		<1
8		racemic CD	10

[a] The reaction conditions are described in Scheme 1.

The reactions of various substrates are summarized in Table 2. Haloacetals bearing a terminal alkene moiety underwent the cyclization/coupling reactions to give the corresponding silylethyl-substit uted tetrahydrofuran derivatives in good yields (entries 1–3). Carbocycle **13** was obtained in the reaction of iodoalkene, 6-iodo-1-hexene (**8**) in 67% yield (entry 4), whereas the bromo analogue **9**

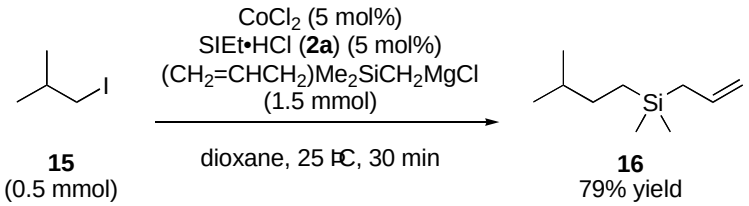
was much less reactive (entry 5). Dimethylphenylsilylmethylmagnesium chloride was also effective f or this reaction (entry 6). The cobalt/NHC system could be also employed for direct cross-coupling reactions of primary alkyl halides without a cyclization process. For instance, treatment of isobutyl iodide (**15**, 0.5 mmol) with allyldimethylsilylmethylmagnesium chloride (1.5 mmol, 1 M ether solution) in dioxane (2 mL) in the presence of $CoCl_2$ (0.025 mmol) and SIEt·HCl (**2a**, 0.025 mmol) for 30 min at 25 ˚C afforded the corresponding coupling product **16** in 79% yield (Scheme 2). Unfortunately, the reactions of secondary alkyl halides resulted in failure and gave mixtures of alkane and alkene which could be generated by protonation and β-elimination from alkylcobalt intermediate.

Table 2. Cobalt/NHC-catalyzed sequential cyclization/cross-coupling reaction with allyldimethylsilylmethylmagnesium reagents.[a]

entry	substrate		product (R = Allyl)		yield (%)
1		**5**		**10**	72 (85/15)
2		**6**		**11**	81 (67/33)
3		**7**[b]		**12**	78 (54/46)
4		**8** (X = I)		**13**	67 (X = I)
5		**9** (X = Br)			18 (X =Br)
6[c]		**1**		**14**	78

[a] The reaction conditions are described in Scheme 1. [b] 1:1 mixture of diastereomers. [c] Dimethylphenylsilylmethylmagnesium chloride was employed.

Scheme 2.



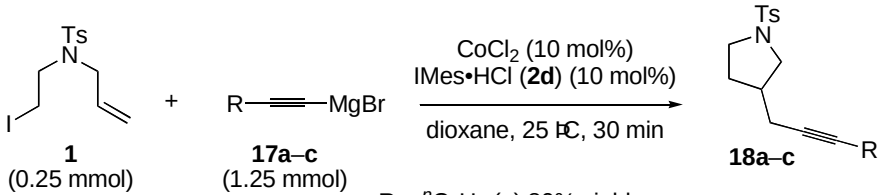
15 (0.5 mmol)

16 79% yield

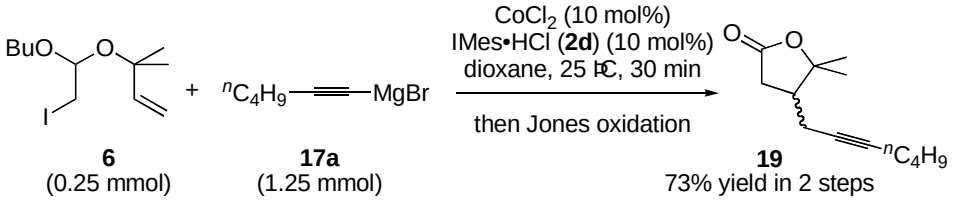
Next we turned our attention to the sequential cyclization/cross-coupling reactions of 6-halo-1-hexene derivatives with 1-alkynyl Grignard reagents (Schemes 3 and 4). The use of NHC ligand was essential for the successful reaction as in the case of the reaction with trialkylsilylmethyl Grignard reagents. For example, treatment of **1** with 1-hexynylmagnesium bromide (**17a**) in the presence of IMes·HCl (**2d**) and $CoCl_2$ provided alkynylated products **18a** in 80% yield. The use of the 1,3-dimesityl-substituted imidazolium salt (**2d**)

was crucial to attain satisfactory results. The reactions with the aid of other NHC ligands such as SIEt·HCl (**2a**), SIMes·HCl (**2b**), and IPr·HCl (**2e**) yielded none of coupling product, and most of the starting material **1** was recovered. Other ligands such as phosphines and diamines were also ineffective. Various alkynylmagnesium reagents were examined. The magnesium acetylides **17b** and **17c**, bearing a sterically bulky group and a siloxy group, respectively, reacted smoothly. However, 2-trimethylsilylethynyl[3h] or phenylethynyl Grignard reagent provided none of the expected product and gave a mixture of the nonalkynylated cyclic product and starting material **1**. Treatment of **6** provided lactone **19** in 73% yield through cyclization/alkynylation followed by Jones oxidation (Scheme 4).

Scheme 3.



Scheme 4.

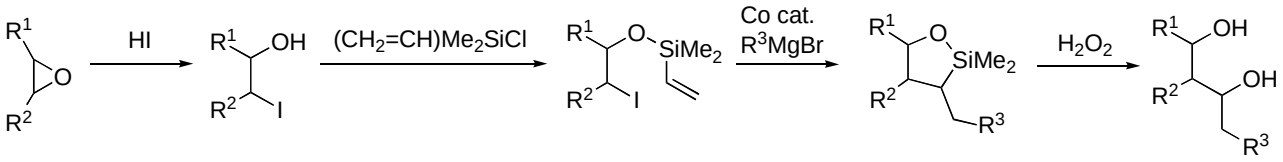


(2) Application of cobalt-catalyzed sequential cyclization/cross-coupling reaction to the synthesis of 1,3-diols using siloxy-tethered 6-iodo-1-hexene derivatives

1,3-Diol units are often observed in biologically active compounds, and can be oxidized

into 1,3-diketones or naturally occurring polyketides. The synthesis of 1,3-diols is thus well explored.[9] The significant importance of 1,3-diols prompted us to apply the sequential cyclization/cross-coupling reactions to the synthesis of 1,3-diols. Our approach to 1,3-diols starting from epoxides is outlined in Scheme 5. Ring-opening of epoxides with hydrogen iodide followed by silylation with chlorodimethylvinylsilane would provide siloxy-tethered[10] 6-iodo-1-hexene derivatives. Then, cobalt-catalyzed sequential cyclization/cross-coupling protocol would yield oxasilacyclopentanes. Finally, Tamao-Fleming oxidation[6] would afford 1,3-diols with the substituent R^3 from the Grignard reagent employed.

Scheme 5.

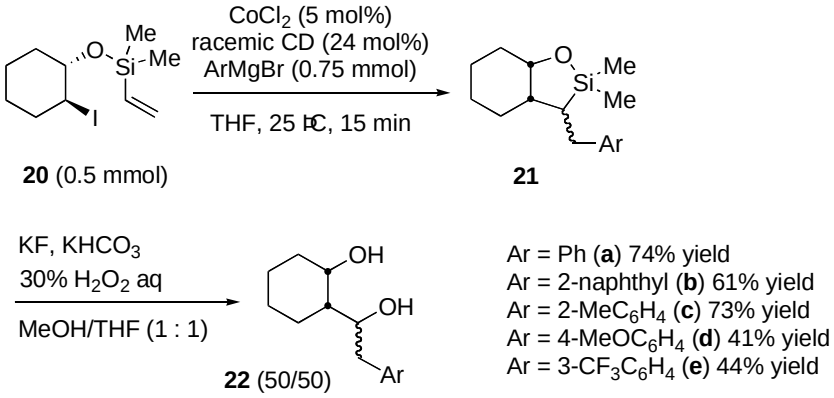


We chose cyclohexene oxide as a starting material. Cyclohexene oxide underwent ring-opening by the action of lithium iodide and acetic acid in THF to give 2-iodo-1-cyclohexanol.[11] Treatment of the crude *vic*-iodohydrin with chlorodimethylvinylsilane in the presence of triethylamine in dichloromethane provided siloxy-tethered substrate **20** quantitatively.

The silicon-tethered 6-iodo-1-hexene derivative **20** was employed for the reaction with aryl Grignard reagent in the presence of cobalt and diamine catalyst (Scheme 6).[5] *N,N,N',N'*-Tetramethyl-1,2-cyclohexanediamine (racemic CD, 0.12 mmol) was added to a suspension of $CoCl_2$ (0.025 mmol) in THF (1 mL) to form a clear-blue solution. Substrate (**20**, 0.5 mmol) was injected and then phenyl Grignard reagent (0.75 mmol, 1 M THF solution) was added over 5 s at

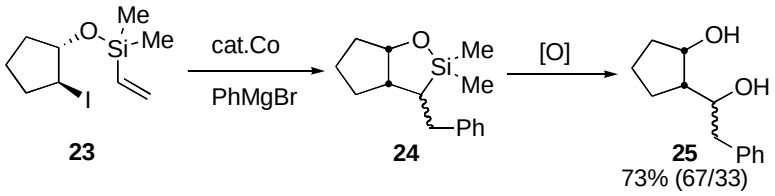
25 ˚C. An exothermic reaction immediately took place. After the mixture was stirred at 25 ˚C for 15 min, usual work-up followed by silica gel column purification afforded the corresponding benzylated cyclic product **21a** in good yield. The oxasilacyclopentane **21a** was converted to 4-aryl-1,3-butanediol efficiently upon treatment with hydrogen peroxide in the presence of potassium fluoride and potassium hydrogencarbonate.

Scheme 6.

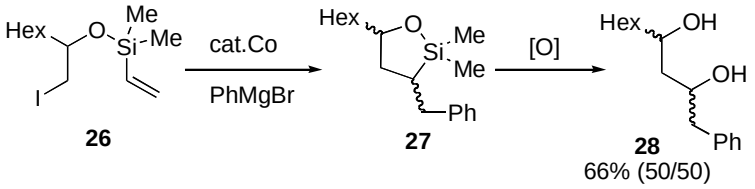


A series of aryl Grignard reagents were examined. All of the corresponding products were subjected to oxidation with alkaline hydrogen peroxide to yield diols in good yields. Not only phenylmagnesium bromide but also *o*-tolylmagnesium bromide, 4-methoxyphenyl- and 3-trifluoromethylphenylmagnesium bromides could participate in the reaction efficiently. The cyclization/arylation with 2-naphthyl Grignard reagent also proceeded smoothly. Methyl substitution at the 2-position did not retard the reaction. However, mesityl Grignard reagent could not be applicable. The products **21a–21e** were always 1:1 mixtures of diastereomers, which originate from the relationship between the *cis*-fused bicyclic system and arylmethyl group. This arylation–oxidation sequence could be effectively applied to the iodides **23** and **26**, and the corresponding diols **25** and **28** were obtained in good yields. (Schemes 7 and 8).

Scheme 7.

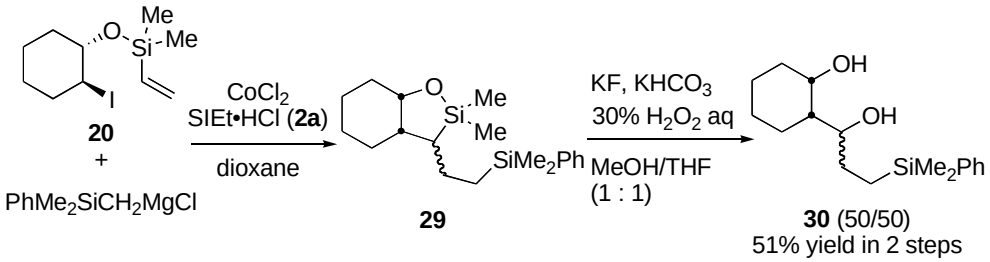


Scheme 8.

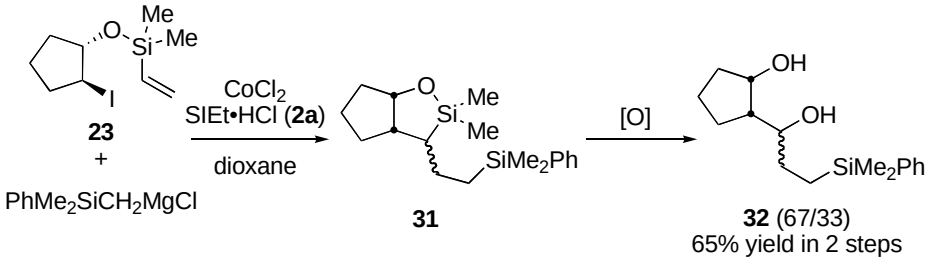


Next, the cyclization/cross-coupling reaction of the siloxy-tethered substrates with dimethylphenylsilylmethylmagnesium chloride has been examined. The cobalt/NHC-catalyzed reaction of **20** with dimethylphenylsilylmethylmagnesium chloride afforded the corresponding cyclization/coupling produc t **29**, which could be easily transformed into the 5-silyl-1,3-pentanediol **30** upon treatment with alkaline hydrogen peroxide (Scheme 9). Other siloxy-tethered substrates **23** and **26**, prepared from the corresponding epoxides in a similar fashion, were examined. The reaction of iodide **23** having five-membered ring afforded **31** with slight diastereoselectivity (Scheme 10). The primary alkyl iodide **26** served as a substrate to provide the diol **34** in 54% overall yield (Scheme 11). These products **30, 32,** and **34** could be precursors of 1,3,5-triol and related compounds.

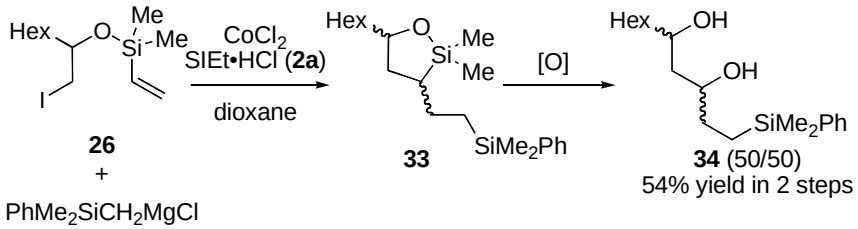
Scheme 9.



Scheme 10.



Scheme 11.



Conclusion

In summary, we have developed new and useful variants of sequential cyclization/coupling reactions of 6-halo-1-hexene derivatives with trialkylsilylmethyl, 1-alkynyl, and aryl Grignard reagents. The cross-coupling reactions proceeded only with the aid of NHC ligands in the case of trialkylsilylmethyl and 1-alkynyl Grignard reagents. Moreover, the cobalt-catalyzed sequential cyclization/cross-coupling reaction could be applied effectively to the construction of 1,3-diol units by using siloxy-tethered strategy.

Experimental section

General

^{1}H NMR (300 and 500 MHz) and ^{13}C NMR (125.7 MHz) spectra were taken on Varian Mercury 300 and UNITY INOVA 500 spectrometers and were recorded in $CDCl_3$ or C_6D_6. Chemical shifts (δ) are in parts per million relative to $CHCl_3$ at 7.26 ppm or C_6H_6 at 7.16 ppm for ^{1}H

and relative to $CDCl_3$ at 77.2 ppm or C_6D_6 at 128.4 ppm for ^{13}C unless otherwise noted. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Anhydrous $CoCl_2$ was purchased from Wako Pure Chemicals and was used after removal of water. Specifically, in each experiment, $CoCl_2$ was dried in a reaction flask carefully under reduced pressure (0.5 torr) by heating with a hair dryer for 2 min immediately before use. SIEt·HCl (**2a**) and SIMes·HCl (**2b**) were prepared according to the literature.[12] Imidazolium salt **2c**, IMes·HCl (**2d**) and IPr·HCl (**2e**) were purchased from Strem Chemicals. Trialkylsilylmethylmagnesium chloride was prepared from m agnesium metal and the corresponding (chloromethyl)trialkylsilane in diethyl ether. Diethyl ether was purchased from Kanto Chemical Co., stored under nitrogen, and used as it is. Racemic CD was prepared according to the literature (Table 1, entry 8).[3g] Arylmagnesium bromide was prepared from magnesium metal and the corresponding bromoarene in THF. THF was purchased from Kanto Chemical Co., stored under nitrogen, and used as it is. Dioxane was dried over slices of sodium. All reactions were carried out under argon atmosphere.

Typical procedure for cobalt/NHC-catalyzed coupling reaction of 6-halo-1-hexene derivative with trialkylsilylmethylmagnesium chloride

The reaction of **1** with allyldimethylsilylmethylmagnesium chloride (Scheme 1)

is representative. Anhydrous cobalt(II) chloride (3.2 mg, 0.025 mmol) was placed in a 20-mL reaction flask and was heated with a hair dryer in vacuo for 2 min. After the color of the cobalt salt became blue, anhydrous dioxane (2 mL), SIEt·HCl (**2a**, 9.3 mg, 0.025 mmol) and substrate **1** (182 mg, 0.50 mmol) were sequentially added under argon. Allyldimethylsilylmethylmagnesium chloride (1.0 M diethyl ether solution, 1.5 mL, 1.5 mmol) was then added over 5 s to the reaction mixture at 25 ˚C. While the Grignard reagent was being added, the mixture turned brown. After being stirred for 30 min at 25 ˚C, the reaction mixture was poured into saturated ammonium chloride solution. The products were extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated. Silica gel column purification (hexane/ethyl acetate = 10:1) of the crude product provided the corresponding cyclization/coupling product **3** (140 mg, 0.40 mmol) in 81% isolated yield.

Cyclization/coupling product **3** was subjected to Tamao-Fleming oxidation. A solution of **3** (88 mg, 0.25 mmol) in $CHCl_3$ (5 mL) was placed in a 30-mL flask. Potassium hydrogen fluoride (82 mg, 1.05 mmol) and trifluoroacetic acid (0.09 mL, 1.25 mmol) were sequentially added to the reaction mixture. After being stirred for 18 h at room temperature, the solvent was evaporated under a reduced pressure to give a yellow oil. The crude product was dissolved in methanol-THF (8 mL, 1:1 mixture). Potassium hydrogencarbonate (115 mg, 1.15 mmol) and 30% H_2O_2 aq (0.52 mL) were successively added. After being stirred at room temperature for 18 h, the reaction mixture was poured into saturated sodium thiosulfate solution. The product was extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated. Purification by silica gel column chromatography (hexane/ethyl acetate = 1:1) provided the alcohol **4**

(50 mg, 0.18 mmol) in 74% yield.

General procedure for cobalt/NHC-catalyzed coupling reaction of 6-halo-1-hexene derivative with 1-alkynyl Grignard reagent

The reaction of **1** with 1-hexynylmagnesium bromide (Scheme 3) is representative. Alkynylmagnesium bromide was prepared from isopropylmagnesium bromide and t he corresponding alkyne. Isopropylmagnesium bromide (1.0 M diethyl ether solution, 1.25 mL, 1.25 mmol) was placed in a 30-mL reaction flask under argon. 1-Hexyne (134 mg, 1.63 mmol) was added, and the reaction mixture was stirred for 2 h at room temperature.

Anhydrous cobalt(II) chloride (3.2 mg, 0.025 mmol) was placed in a 20-mL reaction flask and was heated with a hair dryer in vacuo for 2 min. After the color of the cobalt salt became blue, anhydrous dioxane (1 mL) and IMes·HCl (**2d**, 8.5 mg, 0.025 mmol) were sequentially added under argon. Substrate **1** (91 mg, 0.25 mmol) was added. 1-Hexynylmagnesium bromide (1.0 M diethyl ether solution, 1.25 mL, 1.25 mmol) was then added over 5 s to the reaction mixture at 25 ˚C. While the Grignard reagent was being added, the mixture turned brown. After being stirred for 30 min at 25 ˚C, the reaction mixture was poured into saturated ammonium chloride solution. The products were extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated to provide a yellow oil. Silica gel column purification (hexane/ethyl acetate = 10:1) furnished **18a** (64 mg, 0.20 mmol) in 80% yield.

General procedure for sequential cyclization/arylation of 6-iodo-4-oxa-3-sila-1-hexene derivative

The reaction of **20** with phenylmagnesium bromide (Scheme 6) is representative. Anhydrous cobalt(II) chloride (3.2 mg, 0.025 mmol) was placed in a

20-mL reaction flask and was heated with a hair dryer in vacuo for 2 min. After the color of the cobalt salt became blue, anhydrous THF (3 mL) and racemic CD (20 mg, 0.12 mmol) were sequentially added under argon. The mixture was stirred for 3 min. 6-Halo-4-oxa-3-sila-1-hexene derivative **20** (155 mg, 0.5 mmol) was added. Phenylmagnesium bromide (1.0 M THF solution, 0.75 mL, 0.75 mmol) was then added over 5 s to the reaction mixture at 25 ˚C. While the Grignard reagent was being added, the mixture turned brown. After being stirred for 15 min at 25 ˚C, the reaction mixture was poured into saturated ammonium chloride solution. The products were extracted with hexane (20 mL × 2). The combined organic layer was dried over Na_2SO_4 and concentrated to provide a yellow oil. The ^1H NMR analysis with dibromomethane as an internal standard indicated formation of the desired oxasilacyclopentane **21a** in 93% yield. Potassium fluoride (58 mg, 1.0 mmol) and potassium hydrogencarbonate (100 mg, 1.0 mmol) were dissolved in methanol-THF (5 mL, 1:1 mixture). The crude product and 30% H_2O_2 aq (0.52 mL) were successively added. After being stirred at room temperature for 12 h, the reaction mixture was poured into saturated sodium thiosulfate solution. The product was extracted with ethyl acetate (20 mL × 2). The combined organic layer was dried over Na_2SO_4 and concentrated. Purification by silica gel column chromatography (hexane/ethyl acetate = 2:1) provided the 4-phenyl-1,3-butanediol **22a** (81 mg, 0.37 mmol) in 74% isolated yield.

Typical procedure for cobalt/NHC-catalyzed coupling reaction of 6-iodo-4-oxa-3-sila-1-hexene derivative with dimethylphenylsilylmethylmagnesium chloride

The reaction of **20** with dimethylphenylsilylmethylmagnesium chloride (Scheme 9) is representative. Anhydrous cobalt(II) chloride (3.2 mg, 0.025 mmol) was placed in a

20-mL reaction flask and was heated with a hair dryer in vacuo for 2 min. After the color of the cobalt salt became blue, anhydrous dioxane (2 mL), SIEt·HCl (**2a**, 9.3 mg, 0.025 mmol) and substrate **20** (155 mg, 0.50 mmol) were sequentially added under argon. Dimethylphenylsilylmethylmagnesium chloride (1.0 M diethyl ether solution, 1.5 mL, 1.5 mmol) was then added over 5 s to the reaction mixture at 25 ˚C. While the Grignard reagent was being added, the mixture turned brown. After being stirred for 30 min at 25 ˚C, the reaction mixture was poured into saturated ammonium chloride solution. The products were extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over Na_2SO_4 and concentrated to provide a crude oil. The ^{1}H NMR analysis of this oil indicated the formation of the desired oxasilacyclopentane **29**. Potassium fluoride (58 mg, 1.0 mmol) and potassium hydrogencarbonate (100 mg, 1.0 mmol) were dissolved in methanol-THF (5 mL, 1:1 mixture). The crude product and 30% H_2O_2 aq (0.52 mL) were successively added. After being stirred at room temperature for 12 h, the reaction mixture was poured into saturated sodium thiosulfate solution. The product was extracted with ethyl acetate (20 mL × 2). The combined organic layer was dried over Na_2SO_4 and concentrated. Silica gel column purification (hexane/ethyl acetate = 2:1) of the crude product provided the diol **30** (74 mg, 0.25 mmol) in 51% isolated yield.

Characterization Data:

The substrates **1, 5, 6, 7, 8** and **9** were prepared according to the literature.[3a,b,g,13] The elemental analyses of **22c–e** are not described here. The elemental analyses of **22c–e** were carried out after converting them to the corresponding diacetates. To obtain the diacetates, the diols were subjected to the standard acetylation conditions (Ac_2O, pyridine, DMAP).

1-(*p*-Toluenesulfonyl)-3-[2-(allyldimethylsilyl)ethyl]pyrrolidine (3): oil. IR (neat) 663, 1099, 1162, 1248, 1346, 2916, 2952 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ –0.06 (s, 6H), 0.37–0.47 (m, 2H), 1.13–1.25 (m, 2H), 1.39 (m, 1H), 1.42–1.48 (dm, *J* = 8.0 Hz, 2H), 1.89–1.99 (m, 2H), 2.44 (s, 3H), 2.80 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.20 (ddd, *J* = 10.0, 8.5, 7.5 Hz, 1H), 3.32 (ddd, *J* = 10.0, 8.5, 4.5 Hz, 1H), 3.43 (dd, *J* = 10.0, 7.5 Hz, 1H), 4.79–4.84 (m, 2H), 5.73 (dddd, *J* = 17.5, 13.5, 9.5, 8.0 Hz, 1H), 7.32–7.34 (dm, *J* = 8.5 Hz, 2H) , 7.71–7.73 (dm, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.7 (× 2C), 13.4, 21.7, 23.2, 27.5, 31.3, 42.2, 47.8, 53.3, 113.1, 127.8, 129.8, 134.3, 135.0, 143.5; Found: C, 61.21; H, 8.09. Calcd for $C_{18}H_{29}NO_2SSi$: C, 61.49; H, 8.31.

2-[1-(*p*-Toluenesulfonyl)-3-pyrrolidinyl]ethanol (4): oil. IR (neat) 1043, 1160, 1340, 2880, 2930, 3566 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.41 (m, 1H), 1.52 (q, *J* = 6.5 Hz, 2H), 1.62 (brs, 1H), 1.96 (m, 1H), 2.16 (septet, *J* = 8.0 Hz, 1H), 2.43 (s, 3H), 2.83 (t, *J* = 9.0 Hz, 1H), 3.17 (m, 1H), 3.36 (m, 1H), 3.46 (dd, *J* = 10.0, 8.5 Hz, 1H), 3.56–3.64 (m, 2H), 7.31–7.33 (dm, *J* = 8.5 Hz, 2 H), 7.70–7.72 (dm, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 21.7, 31.7, 35.9 (×2C), 47.6, 53.4, 61.4, 127.7, 129.8, 134.0, 143.6; Found: C, 58.12; H, 7.30. Calcd for $C_{13}H_{19}NO_3S$: C, 57.97; H, 7.11.

Allyl{2-(2,9-dioxa-4-bicyclo[4.3.0]nonanyl)ethyl}dimethylsilane (10, Major isomer): oil. IR (neat) 898, 1147, 1251, 1629, 1773, 2877, 2921 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ –0.01 (s, 6H), 0.41–0.54 (m, 2H), 1.28 (m, 1H), 1.34–1.40 (m, 2H), 1.51–1.53 (dm, *J* = 8.5 Hz, 2H), 1.50–1.63 (m, 3H), 1.97 (m, 1H), 2.73 (m, 1H), 3.62 (dd, *J* = 10.5, 8.0 Hz, 1H), 3.65 (m, 1H), 3.75 (m, 1H), 3.95 (t, *J* = 8.0 Hz, 1H), 4.81–4.86 (m, 2H), 5.28 (d, *J* = 4.0 Hz, 1H), 5.76 (dddd, *J* =18.5, 16.5, 10.5, 8.5 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.7 (× 2C), 13.6, 19.3, 21.3, 23.3, 23.5, 36.5, 44.6, 61.2, 70.2, 102.3, 113.1, 135.1; Found: C, 66.11; H, 10.51. Calcd for $C_{14}H_{26}O_2Si$: C, 66.09; H, 10.30.

Allyl[2-(4-butoxy-2,2-dimethyl-3-oxacyclopentyl)ethyl]dimethylsilane (11) (67:33 mixture of

diastereomers): oil. IR (neat) 893, 1097, 1250, 1558, 2932, 2960 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.01 (s, 6H), 0.40–0.60 (m, 2H), 0.91 (t, *J* = 7.0 Hz, 3H), 1.01 (s, 0.67×3H), 1.13 (s, 0.33×3H), 1.14–1.21 (m, 1H), 1.23 (s, 0.33×3H), 1.32 (s, 0.67×3H), 1.33–1.41 (m, 4H), 1.49–1.64 (m, 4H), 1.72 (m, 0.33×1H), 2.04–2.11 (m, 0.67×2H), 2.45 (ddd, *J* = 13.0, 8.0, 6.0 Hz, 0.33×1H), 3.30–3.37 (m, 1H), 3.64–3.72 (m, 1H), 4.81–4.85 (m, 2H), 4.95 (d, *J* = 4.5 Hz, 0.67×1H), 5.04 (dd, *J* = 6.0, 4.5 Hz, 0.33×1H), 5.77 (dddd, *J* = 18.0, 16.5, 10.0, 8.0, Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.6 (× 2C), 14.1 (× 2C), 14.2, 14.3, 19.6, 19.7, 23.3 (× 3C), 23.4 (× 2C), 23.8, 24.2, 24.4, 28.5, 30.3, 32.1, 32.2, 39.3, 39.5, 49.2, 52.0, 66.7, 67.9, 82.9, 83.6, 102.0, 103.2, 113.0 (× 2C), 135.2 (× 2C) ; Found: C, 68.31; H, 11.45. Calcd for $C_{17}H_{34}O_2Si$: C, 68.39; H, 11.48.

Allyl[2-(4-butoxy-2-pentyl-3-oxacyclopentyl)ethyl]dimethylsilane (12) (54:46 mixture of diastereomers): oil. IR (neat) 893, 1097, 1250, 1458, 1631, 2957 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.01 (s, 6H), 0.43–0.58 (m, 2H), 0.89–0.94 (m, 6H), 1.19 (m, 0.54×1H), 1.26–1.65 (m, 17H), 1.99 (m, 0.46×1H), 2.11 (dd, *J* = 17.5, 7.5 Hz, 0.54×1H), 2.27 (ddd, *J* = 13.0, 9.5, 5.5 Hz, 0.46×1H), 3.31–3.39 (m, 1H), 3.56–3.62 (m, 1H), 3.65–3.70 (m, 1H), 4.81–4.86 (m, 2H), 5.02 (d, *J* = 5.0 Hz, 0.54×1H), 5.07 (dd, *J* = 5.0, 2.5 Hz, 0.46×1H), 5.73–5.81 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.6 (× 4C),13.5, 13.6, 14.1 (× 2C), 14.3 (× 2C), 19.7 (× 2C), 22.9 (× 2C), 23.3, 23.4, 26.3, 26.5, 27.4, 27.8, 32.1, 32.2 (× 2C), 32.3, 34.9, 37.3, 39.3, 40.0, 45.9, 47.0, 66.9, 67.3, 82.9, 85.6, 103.6, 103.7, 113.0 (× 2C), 135.2, 135.3; Found: C, 70.54; H, 11.93. Calcd for $C_{20}H_{40}O_2Si$: C, 70.52; H, 11.84.

Allyl(2-cyclopentylethyl)dimethylsilane (13): oil. IR (neat) 893, 1150, 1250, 1630, 2910, 2952 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.02 (s, 6H), 0.50–0.55 (m, 2H), 1.03–1.10 (m, 2H), 1.25–1.31 (m, 2H), 1.46–1.62 (m, 6H), 1.67–1.78 (m, 3H), 4.80–4.86 (m, 2H), 5.79 (dddd, *J* = 18.0, 16.5, 10.0,

8.0 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.6, 13.9, 23.4, 25.5, 30.2, 32.6, 43.6, 112.7, 135.6; Found: C, 73.38; H, 12.32. Calcd for $C_{12}H_{24}Si$: C, 73.21; H, 12.16.

1-(*p*-Toluenesulfonyl)-3-[2-(dimethylphenylsilyl)ethyl]pyrrolidine (14): oil. IR (neat) 815, 1113, 1163, 1345, 2919, 2953 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.22 (s, 6H), 0.61–0.69 (m, 2H), 1.17–1.27 (m, 2H), 1.35 (m, 1H), 1.89–1.98 (m, 2H), 2.44 (s, 3H), 2.77 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.18 (ddd, *J* = 10.0, 8.5, 7.5 Hz, 1H), 3.31 (ddd, *J* = 10.0, 8.5, 4.0 Hz, 1H), 3.42 (dd, *J* = 10.0, 7.5 Hz, 1H), 7.31–7.33 (dm, *J* = 8.5 Hz, 2H), 7.34–7.37 (m, 3H), 7.45–7.47 (m, 2H), 7.70–7.72 (dm, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.1 (× 2C), 14.3, 21.7, 27.5, 31.1, 42.1, 47.8, 53.2, 127.7, 128.0, 129.2, 129.8, 133.6, 134.0, 139.0, 143.4; Found: C, 65.08; H, 7.39. Calcd for $C_{21}H_{29}SNO_2Si$: C, 65.07; H, 7.39.

Allyl(3-methylbutyl)dimethylsilane (16): oil. IR (neat) 412, 1507, 1559, 2956, 3650, 3854 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ –0.03 (s, 6H), 0.47–0.51 (m, 2H), 0.86 (d, *J* = 11.5 Hz, 6H), 1.13–1.18 (m, 2H), 1.44 (m, 1H), 1.51 (td, *J* = 8.0, 1.0 Hz, 2H), 4.80–4.85 (m, 2H), 5.78 (ddt, *J* = 17.0, 10.0, 8.0 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.6 (× 2C), 12.4, 22.4 (× 2C), 23.4, 31.2, 33.0, 112.7, 135.6; HRMS (DI-EI$^+$) (*m/z*) Observed: 170.1490 (Δ= –0.7 ppm). Calcd for $C_{10}H_{22}Si$ [M+]: 170.1491.

1-(*p*-Toluenesulfonyl)-3-(2-heptynyl)pyrrolidine (18a): oil. IR (neat) 664, 1039, 1094, 1162, 1346, 2872, 2957 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.5 Hz, 3H), 1.32–1.44 (m, 4H), 1.57 (m, 1H), 1.92 (m, 1H), 2.05–2.12 (m, 4H), 2.22 (septet, *J* = 7.0 Hz, 1H), 2.43 (s, 3H), 2.98 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.23 (dt, *J* = 10.0, 8.5 Hz, 1H), 3.31 (m, 1H), 3.42 (dd, *J* = 10.0, 7.5 Hz, 1H), 7.31–7.33 (dm, *J* = 8.5 Hz, 2H), 7.71–7.73 (dm, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.8, 18.4, 21.7, 22.1, 22.2, 30.6, 31.2, 38.2, 47.6, 52.6, 77.1, 82.0, 127.7, 129.8, 133.8, 143.5; Found: C,

67.78; H, 8.06. Calcd for $C_{18}H_{25}NO_2S$: C, 67.67; H, 7.89.

1-(*p*-Toluenesulfonyl)-3-(4,4-dimethyl-2-pentynyl)pyrrolidine (18b): white solid. IR (nujol) 665, 1160, 1340, 2854, 2923 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.12 (s, 9H), 1.57 (m, 1H), 1.90 (m, 1H), 2.05 (dd, *J* = 16.5, 7.0 Hz, 1H), 2.10 (dd, *J* = 16.5, 6.0 Hz, 1H), 2.22 (septet, *J* = 7.0 Hz, 1H), 2.43 (s, 3H), 2.94 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.22–3.30 (m, 2H), 3.42 (dd, *J* = 10.0, 7.5 Hz, 1H), 7.31–7.33 (dm, *J* = 8.5 Hz, 2H), 7.71–7.72 (dm, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 21.7, 22.0, 27.5, 30.5, 31.4, 38.2, 47.7, 52.5, 75.5, 90.8, 127.8, 129.8, 134.0, 143.5; Found: C, 67.38; H, 7.82. Calcd for $C_{18}H_{25}NO_2S$: C, 67.67; H, 7.89. m.p. 76–80 ˚C.

1-(*p*-Toluenesulfonyl)-3-[7-(trimethylsilyloxy)-2-heptynyl]pyrrolidine (18c): oil. IR (neat) 664, 842, 1094, 1162, 1251, 1346, 2866, 2952 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.11 (s, 9H), 1.46–1.60 (m, 5H), 1.91 (m, 1H), 2.05–2.12 (m, 4H), 2.22 (septet, *J* = 7.0 Hz, 1H), 2.43 (s, 3H), 2.97 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.22 (dt, *J* = 10.0, 7.5 Hz, 1H), 3.31 (m, 1H), 3.41 (dd, *J* = 10.0, 7.5 Hz, 1H), 3.58 (t, *J* = 6.0 Hz, 2H), 7.31–7.33 (dm, *J* = 8.5 Hz, 2H), 7.70–7.72 (dm, *J* = 8.5 Hz, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –0.3, 18.7, 21.7, 22.3, 25.6, 30.7, 32.1, 38.3, 47.6, 52.7, 62.3, 77.5, 81.7, 127.8, 129.8, 134.1, 143.5; Found: C, 62.15; H, 8.22. Calcd for $C_{21}H_{33}NO_3SSi$: C, 61.87; H, 8.16.

4-(2-Heptynyl)-4,5-dihydro-5,5-dimethyl-2(3*H*)-furanone (19): oil. IR (neat) 960, 1123, 1272, 1388, 1773, 2959 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.5 Hz, 3H), 1.33 (s, 3H), 1.35–1.48 (m, 4H), 1.50 (s, 3H), 2.12–2.17 (m, 2H), 2.29 (dt, *J* = 6.5, 2.5 Hz, 2H), 2.39–2.46 (m, 2H), 2.71 (q, *J* = 9.5 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 13.8, 18.5, 19.8, 22.1, 22.2, 28.4, 31.1, 35.2, 44.6, 76.7, 82.8, 86.5, 175.3; Found: C, 74.70; H, 9.60. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68.

(2-Iodocyclohexyloxy)dimethylvinylsilane (20): oil. IR (neat) 785, 837, 877, 973, 1109, 1250, 2936 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 0.26 (s, 3H), 0.28 (s, 3H), 0.76–1.20 (m, 4H), 1.48 (m, 1H), 1.74

(m, 1H), 1.87 (dm, 1H), 2.14 (dm, 1H), 3.86 (td, *J* = 8.7, 3.9 Hz, 1H), 3.87 (m, 1H), 5.78 (dd, *J* = 20.1, 3.9 Hz, 1H), 5.95 (dd, *J* = 15.0, 3.9 Hz, 1H), 6.26 (dd, *J* = 20.1, 15.0 Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6) δ –1.1, –0.9, 24.1, 27.4, 35.3, 38.1, 39.7, 76.5, 133.4, 138.1; Found: C, 38.83; H, 6.10. Calcd for $C_{10}H_{19}OSiI$: C, 38.71; H, 6.17.

2-(1-Hydroxy-2-phenylethyl)cyclohexanol (22a) (50:50 mixture of diastereomers): white solid. IR (nujol) 743, 973, 2924, 3345 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21–1.32 (m, 1H), 1.32–1.52 (m, 0.5×7H), 1.56–1.87 (m, 0.5×9H), 2.23–2.29 (brs, 2H), 2.71–2.94 (m, 2H), 3.86 (m, 0.5×1H), 4.04–4.08 (m, 1H), 4.40 (m, 0.5×1H), 7.20–7.35 (m, 5H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.6, 20.0, 20.4, 25.0, 25.8, 25.9, 33.2, 33.9, 41.4, 42.0, 44.2, 44.8, 67.4, 72.4, 76.6, 77.6, 126.7, 126.8, 128.8, 128.9, 129.4, 129.5, 138.8(× 2C). Found: C, 76.13; H, 9.24. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. m.p. 69–72 ˚C.

2-[1-Hydroxy-2-(2-naphthyl)ethyl]cyclohexanol (22b) (50:50 mixture of diastereomers): white solid. IR (nujol) 823, 972, 1520, 1600, 3340 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20–1.32 (m, 1H), 1.37–1.52 (m, 0.5×7H), 1.61–1.89 (m, 0.5×9H), 2.58 (brs, 0.5×1H), 2.85 (brs, 0.5×1H), 2.94 (s, 0.5×1H), 3.00 (brs, 0.5×1H), 2.88–3.08 (m, 2H), 3.94 (m, 0.5×1H), 4.06 (m, 0.5×1H), 4.13 (m, 0.5×1H), 4.42 (m, 0.5×1H), 7.34–7.37 (m, 1H), 7.42–7.49 (m, 2H), 7.66 (s, 0.5×1H), 7.68 (s, 0.5×1H), 7.79–7.82 (m, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.7, 20.0, 20.4, 25.0, 25.8, 25.9, 33.2, 33.9, 41.5, 42.2, 44.3, 44.8, 67.5, 72.4, 77.4, 77.5, 125.7 (× 2C), 126.3 (× 2C), 127.7 (× 2C), 127.8 (× 4C), 127.9, 128.0, 128.5 (× 2C), 132.4, 132.5, 133.8, (× 2C), 136.4, 136.5. Found: C, 79.72; H, 8.26. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. m.p. 84.6–87.8 ˚C.

2-[1-Hydroxy-2-(2-methylphenyl)ethyl]cyclohexanol (22c) (50:50 mixture of diastereomers): oil. IR (neat) 743, 1456, 2859, 2929, 3380 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32–2.00 (m, 9H),

2.44 (m, 3H), 2.67 (brs, 2H), 2.84–3.06 (m, 2H), 3.94 (m, 0.5×1H), 4.15 (m, 0.5×1H), 4.18 (m, 0.5×1H), 4.53 (m, 0.5×1H), 7.24–7.28 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.8, 19.8, 19.9, 20.0, 20.4, 25.1, 25.9 (× 2C), 33.2, 33.8, 38.5, 39.2, 44.6, 45.3, 67.4, 72.4, 75.3, 76.3, 126.3 (× 2C), 126.8, 126.9, 130.2, 130.3, 130.7, 130.8, 136.9 (× 2C), 137.0, 137.1.

Diacetate of 22c (50:50 mixture of diastereomers): oil. IR (neat) 1020, 1244, 1363, 1734, 2390, 2863, 2936 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20–2.03 (m, 9H), 1.77 (s, 0.5×3H), 1.82 (s, 0.5×3H), 1.99 (s, 0.5×3H), 2.11 (s, 0.5×3H), 2.28 (s, 0.5×3H), 2.32 (s, 0.5×3H), 2.63 (dd, *J* = 14.5, 10.0 Hz, 1H), 3.02 (dd, *J* = 14.0, 3.5 Hz, 0.5×1H), 3.06 (dd, *J* = 14.5, 3.5 Hz, 0.5×1H), 5.04–5.12 (m, 1H), 5.16 (dm, *J* = 2.0 Hz, 0.5×1H), 5.24 (dm, *J* = 2.5 Hz, 0.5×1H), 7.03–7.11 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 19.5, 19.7, 20.3, 20.5, 20.8, 20.9, 21.5 (× 2C), 23.7, 24.2, 25.4 (× 2C), 30.2, 30.4, 36.1, 36.5, 44.6, 44.7, 68.2, 70.4, 73.3, 74.4, 125.8 (× 2C), 126.8 (× 2C), 130.4 (× 2C), 130.5, 130.6, 136.0 (× 2C), 136.6, 136.7, 170.0, 170.2, 170.8, 171.0; Found: C, 71.39; H, 8.31. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23.

2-[1-Hydroxy-2-(4-methoxyphenyl)ethyl]cyclohexanol (22d) (50:50 mixture of diastereomers): oil. IR (neat) 811, 1039, 1244, 1512, 2857, 2927, 3391 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22–1.88 (m, 9H), 2.52 (brs, 2H), 2.66–2.89 (m, 2H), 3.81 (s, 3H), 3.82 (m, 0.5×1H), 4.02 (m, 0.5×1H), 4.09 (m, 0.5×1H), 4.39 (m, 0.5×1H), 6.85–6.89 (m, 2H), 7.12–7.17 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.6, 20.0, 20.4, 25.0, 25.8, 25.9, 33.2, 33.8, 40.4, 41.0, 44.1, 44.6, 55.5 (× 2C), 67.4, 72.4, 76.6, 77.8, 114.2, 114.3, 130.4, 130.5, 130.7, 130.8, 158.4, 158.5.

Diacetate of 22d (50:50 mixture of diastereomers): oil. IR (neat) 1023, 1247, 1363, 1513, 1734, 2936 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20–1.48 (m, 5H), 1.59–1.98 (m, 4H), 1.89 (s, 0.5×3H), 1.94 (s, 0.5×3H), 2.00 (s, 0.5×3H), 2.10 (s, 0.5×3H), 2.63 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.95 (td, *J* = 15.0,

4.0 Hz, 1H), 3.77 (s, 0.5×3H), 3.78 (s, 0.5×3H), 4.96–5.00 (m, 1H), 5.12 (dm, *J* = 1.5 Hz, 0.5×1H), 5.23 (dm, *J* = 2.0 Hz, 0.5×1H), 6.78–6.82 (m, 2H), 7.05–7.07 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 20.2, 20.4, 21.1, 21.2, 21.4, 21.5, 23.5, 24.0, 25.3, 25.4, 30.1, 30.4, 37.3, 37.4, 43.2, 43.5, 55.4 (× 2C), 68.2, 70.1, 74.0, 75.7, 113.8, 113.9, 129.4, 129.7, 130.6, 130.7, 158.4 (× 2C), 170.3, 170.5, 170.8, 170.9; Found: C, 68.07; H, 8.08. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84.

2-{1-Hydroxy-2-[3-(trifluoromethyl)phenyl]ethyl}cyclohexanol (22e) (50:50 mixture of diastereomers): oil. IR (neat) 702, 800, 1075, 2862, 2931, 3229 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24–1.90 (m, 9H), 2.28 (brs, 2H), 2.77–2.97 (m, 2H), 3.87 (m, 0.5×1H), 4.08 (m, 0.5×1H), 4.12 (m, 0.5×1H), 4.41 (m, 0.5×1H), 7.44–7.45 (m, 2H), 7.50–7.55 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 18.7, 19.9, 20.3, 24.9, 25.7, 25.8, 33.4, 34.1, 41.1, 41.8, 44.7, 44.9, 67.6 (× 2C), 72.5, 76.2, 123.3, 123.5 (q, *J* = 3.9 Hz, × 2C), 124.4 (q, *J* = 272.1 Hz, × 2C), 126.1 (q, *J* = 3.9 Hz), 126.2 (q, *J* = 3.9 Hz), 129.1 (× 2C), 131.0 (q, *J* = 31.7 Hz, × 2C), 132.9, 133.0, 140.2, 140.3.

Diacetate of 22e (50:50 mixture of diastereomers): oil. IR (neat) 658, 705, 1023, 1074, 1124, 1163, 1201, 1245, 1329, 1363, 1448, 1734, 2938 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.22–1.96 (m, 9H), 1.86 (s, 0.5×3H), 1.91 (s, 0.5×3H), 2.00 (s, 0.5×3H), 2.11 (s, 0.5×3H), 2.73 (dd, *J* = 14.0, 8.5 Hz, 1H), 3.08 (dd, *J* = 14.0, 3.5 Hz, 1H), 4.96–5.04 (m, 1H), 5.12 (dm, *J* = 2.0 Hz, 0.5×1H), 5.26 (dm, *J* = 2.0 Hz, 0.5×1H), 7.32–7.41 (m, 3H), 7.45–7.48 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 20.2, 20.4, 20.8, 20.9, 21.4, 21.5, 23.6, 24.1, 25.3 (× 2C), 30.1, 30.5, 38.2, 38.4, 43.7, 44.1, 68.1, 69.8, 73.5, 75.2, 123.6 (q, *J* = 3.9 Hz, × 2C), 125.3 (q, *J* = 272.1 Hz, × 2C), 126.5 (q, *J* = 3.9 Hz), 126.7 (q, *J* = 3.9 Hz), 128.9, 129.0, 130.7 (q, *J* = 32.1 Hz, × 2C), 132.9, 133.1, 170.2, 170.3, 170.8, 170.9; Found: C, 61.53; H, 6.30. Calcd for $C_{19}H_{23}F_3O_4$: C, 61.28; H, 6.23.

(2-Iodocyclopentyloxy)dimethylvinylsilane (23): oil. IR (neat) 698, 787, 836, 884, 959, 1017, 1074,

1252, 1407, 2958 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 0.14 (s, 3H), 0.15 (s, 3H), 1.38–1.57 (m, 3H), 1.78–1.95 (m, 2H), 2.08 (m, 1H), 3.96 (m, 1H), 4.43 (m, 1H), 5.71 (dd, *J* = 20.1, 3.9 Hz, 1H), 5.91 (dd, *J* = 14.7, 3.9 Hz, 1H), 6.12 (dd, *J* = 20.1, 3.9 Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6) δ –1.2 (× 2C), 22.8, 32.8, 34.9, 36.4, 83.2, 133.8, 138.1; Found: C, 36.27; H, 5.48. Calcd for $C_9H_{17}OSiI$: C, 36.49; H, 5.78.

2-(1-Hydroxy-2-phenylethyl)cyclopentanol (25) (67:33 mixture of diastereomers): white solid. IR (nujol) 3334 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.60–2.05 (m, 7H), 2.72–3.01 (m, 4H), 3.98 (td, *J* = 8.1, 3.9 Hz, 0.33×1H), 4.32 (m, 0.67×1H), 4.28–4.38 (m, 0.67×1H), 4.50 (m, 0.33×1H), 7.23–7.38 (m, 5H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 21.5, 22.1, 22.7, 26.7, 35.2, 36.2, 43.0, 43.3, 47.5, 50.2, 73.1, 73.9, 74.4, 77.2, 126.6, 126.7, 128.7, 128.8, 129.4, 129.6, 138.6, 138.8. Found: C, 75.40; H, 8.76. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79.

[1-(Iodomethyl)hexyloxy]dimethylvinylsilane (26): oil. IR (neat) 786, 813, 837, 959, 1010, 1045, 1251, 2929 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 0.18 (s, 3H), 0.19 (s, 3H), 0.89 (t, *J* = 7.0 Hz, 3H), 1.16–1.27 (m, 8H), 1.47–1.49 (m, 2H), 2.96 (d, *J* = 5.5 Hz, 2H), 3.45 (m, 1H), 5.73 (dd, *J* = 20.5, 4.0 Hz, 1H), 5.91 (dd, *J* = 15.0, 4.0 Hz, 1H), 6.16 (dd, *J* = 20.0, 4.5 Hz, 1H); ^{13}C NMR (125.7 MHz, C_6D_6) δ –0.9 (× 2C), 14.3, 14.7, 23.4, 25.9, 29.9, 32.5, 37.6, 72.7, 133.7, 138.4; Found: C, 42.17; H, 7.38. Calcd for $C_{12}H_{25}OSiI$: C, 42.35; H, 7.40.

1-Phenyldecane-2,4-diol (28) (50:50 mixture of diastereomers): white solid. IR (nujol) 3391 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88–0.92 (m, 3H), 1.29–1.60 (m, 10H), 1.66–1.72 (m, 2H), 2.42 (brs, 2H), 2.76–2.82 (m, 2H), 3.84 (m, 0.5×1H), 3.98 (m, 0.5×1H), 4.11 (m, 0.5×1H), 4.19 (m, 0.5×1H), 7.21–7.35 (m, 5H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 14.3 (× 2C), 22.8 (× 2C), 25.5, 25.9, 29.5 (× 2C), 32.0 (× 2C), 37.6, 38.3, 42.0, 42.5, 44.2, 44.8, 69.5, 70.4, 73.1, 74.2, 126.8 (× 2C), 128.8 (× 2C),

129.6 (× 2C), 138.1, 138.5. Found: C, 76.49; H, 10.23. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47.

2-{3-(Dimethylphenylsilyl)-1-hydroxypropyl}cyclohexanol (30) (50:50 mixture of diastereomers): oil. IR (neat) 700, 837, 1114, 1248, 1427, 2859, 2931, 3337 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.27 (s, 3H), 0.28 (s, 3H), 0.61–0.69 (m, 1H), 0.83 (td, *J* = 13.0, 4.5 Hz, 0.5×1H), 0.91 (m, 0.5×1H), 1.16–1.89 (m, 11H), 2.50 (brs, 0.5×1H), 2.67 (brs, 0.5×1H), 2.74 (brs, 0.5×1H), 2.81 (brs, 0.5×1H), 3.50 (brs, 0.5×1H), 3.70 (m, 0.5×1H), 4.05 (brs, 0.5×1H), 4.22 (brs, 0.5×1H), 7.35–7.36 (m, 3H), 7.49–7.52 (m, 2H) ; ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.0 (× 2C), –2.9 (× 2C), 11.9, 12.0, 18.2, 20.0, 20.4, 25.1, 25.9, 26.0, 29.0, 29.4, 33.4, 34.1, 44.0, 44.2, 67.5, 72.7, 78.0, 79.1, 128.0 (× 2C), 129.2 (× 2C), 133.7 (× 2C), 139.2 (× 2C); Found: C, 69.81; H, 9.84. Calcd for $C_{17}H_{28}O_2Si$: C, 69.81; H, 9.65.

2-{3-(Dimethylphenylsilyl)-1-hydroxypropyl}cyclopentanol (32) (Major isomer): oil. IR (neat) 700, 838, 1114, 1248, 1427, 2955, 3337 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.28 (s, 6H), 0.67 (ddd, *J* = 14.0, 13.0, 4.5 Hz, 1H), 0.88 (ddd, *J* = 14.0, 13.0, 4.5 Hz, 1H), 1.40–1.88 (m, 9H), 2.44 (brs, 1H), 2.83 (brs, 1H), 3.97 (m, 1H), 4.30 (m, 1H), 7.34–7.36 (m, 3H), 7.50–7.52 (m, 2H); ^{13}C NMR (125.7 MHz, C_6D_6) δ –3.0, –2.9, 12.0, 21.2, 22.1, 30.8, 36.2, 48.0, 74.4, 77.4, 128.0, 129.1, 133.8, 139.3; Found: C, 69.13; H, 9.28%. Calcd for $C_{16}H_{26}O_2Si$: C, 69.01; H, 9.41%. **(Minor isomer):** ^1H NMR (500 MHz, C_6D_6) δ 0.28 (s, 6H), 0.72 (ddd, *J* = 14.0, 13.0, 4.5 Hz, 1H), 0.97 (ddd, *J* = 14.0, 13.0, 4.5 Hz, 1H), 1.45–1.86 (m, 9H), 2.19 (brs, 1H), 2.24 (brs, 1H), 3.64 (m, 1H), 4.40 (m, 1H), 7.34–7.36 (m, 3H), 7.50–7.52 (m, 2H); ^{13}C NMR (125.7 MHz, C_6D_6) δ –2.9 (× 2C), 11.4, 22.7, 26.6, 30.8, 35.4, 50.1, 74.5, 75.1, 128.0, 129.2, 133.8, 139.3.

1-[Dimethylphenylsilyl]undecane-3,5-diol (34) (50:50 mixture of diastereomers): oil. IR (neat) 700, 837, 1114, 1248, 1427, 2856, 2928, 3347 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.28 (s, 6H),

0.64–0.72 (m, 1H), 0.81–0.89 (m, 4H), 1.28–1.63 (m, 14H), 2.18 (brs, 1H), 2.26 (brs, 1H), 3.75 (m, 0.5×1H), 3.79–3.84 (m, 1H), 3.89 (m, 0.5×1H), 7.33–7.39 (m, 3H), 7.49–7.52 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ –3.0 (× 3C), –2.9, 11.3, 11.7, 14.3 (× 2C), 22.8 (× 2C), 25.5, 26.0, 29.5 (× 2C), 31.8, 32.0 (× 2C), 32.5, 37.7, 38.5, 41.9, 42.4, 69.7, 71.9, 73.4, 75.6, 128.0 (× 2C), 129.2 (× 2C), 133.8 (× 2C), 139.2 (× 2C); Found: C, 70.93; H, 10.89. Calcd for $C_{19}H_{34}O_2Si$: C, 70.75; H, 10.62.

Acknowledgment

This work was supported by Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Government of Japan. H.O. acknowledges JSPS for financial support.

References and notes

1) For reviews: a) Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674–688; b) Terao, J.; Kambe, N. *J. Synth. Org. Chem. Jpn.* **2004**, *62*, 1192–1204; c) Netherton, M. R.; Fu, G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525–1532; d) Fürstner, A.; Martin, R. *Chem. Lett.* **2005**, *34*, 624–629.

2) For recent reports on cobalt-catalyzed coupling reactions, see: (a) Cahiez, G.; Avedissian, H. *Tetrahedron Lett.* **1998**, 39, 6159–6162. (b) Avedissian, H.; Bérillon, L.; Cahiez, G.; Knochel, P. *Tetrahedron Lett.* **1998**, 39, 6163–6166. (c) Nishii, Y.; Wakasugi, K.; Tanabe, Y. *Synlett* **1998**, 67–69. (d) Korn, T. J.; Knochel, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 2947–2951. (e) Gomes, P.; Gosmini, C.; Périchon, J. *Org. Lett.* **2003**, *5*, 1043–1045. (f) Amatore, M.; Gosmini, C.; Périchon, J. *Eur. J. Org. Chem.* **2005**, 989–992.

3) (a) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374–5375. (b) Ohmiya, H.; Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 2207–2213. (c) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Chem. Lett.* **2004**, *33*, 1240–1241. (d) Mizutani, K.; Yorimitsu, H.; Oshima, K. *Chem. Lett.* **2004**, *33*, 832–833. (e) Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 4137–4139. (f) Ohmiya, H.; Tsuji, T.; Yorimitsu, H.; Oshima, K. *Chem. Eur. J.* **2004**, *10*, 5640–5648. (g) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc*. **2006**, *128*, 1886–1889. (h) Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett*. **2006**, *7*, 3093–3096. (i) Yorimitsu, H.; Oshima, K. *Pure Appl. Chem*. **2006**, *78*, 441–449.

4) A part of this work was communicated: Someya, H.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Org. Lett*. **2007**, *9*, 1565–1567.

5) We have recently reported an approach to 4-aryl-1,3-butanediols by cobalt-catalyzed sequential radical cyclization/arylation reaction of silicon-tethered 6-iodo-1-hexene derivatives: Someya, H.; Kondoh, A.; Sato, A.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Synlett* **2006**, *18*, 3061–3064.

6) (a) Tamao, K.; Nakajima, T.; Kumada, M. *Organometallics* **1984**, *3*, 1655–1660. (b) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29–31. (c) Klos, A. M.; Heintzelman, G. R.; Weinreb, S. M. *J. Org. Chem.* **1997**, *62*, 3758–3761. For review on carbon–silicon bond oxidation, see: (d) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662.

7) (a) *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Glorius, F., Ed.; *Topics in Organometallic Chemistry*, Vol. 21; Springer: Heidelberg, **2007**. (b) *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, **2006**. (c) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309. (d) Bourissou, D.; Guerret, O.; Gabbaï, F.

P.; Bertrand, G. *Chem. Rev*. **2000**, *100*, 39–91.

8) Several groups reported the use of NHC ligands in the palladium- and iron-catalyzed cross-coupling reactions of alkyl halides with organometallic reagents, see: (a) Frisch, A. C.; Rataboul, F.; Zapf, A.; Beller, M. *J. Organomet. Chem.* **2003**, *687*, 403–409. (b) Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc*. **2003**, *125*, 13642–13643. (c) Arentsen, K.; Caddick, S.; Cloke, F. G. N.; Herring, A. P.; Hitchcock, P. B. *Tetrahedron Lett.* **2004**, 45, 3511–3515. (d) Hadei, N.; Kantchev, E. A. B.; O'Brien, C. J.; Organ, M. G. *Org. Lett.* **2005**, *7*, 3805–3807. (e) Bedford, R. B.; Betham, M.; Bruce, D. W.; Danopoulos, A. A.; Frost, R. M.; Hird, M. *J. Org. Chem.* **2006**, *71*, 1104–1110. (f) Altenhoff, G.; Würtz, S.; Glorius, F. *Tetrahedron Lett*. **2006**, *47*, 2925–2928.

9) (a) Bode, S. E.; Wolberg, M.; Müller, M. *Synthesis* **2006**, 557–588. (b) Oishi, T.; Nakata, T. *Synthesis* **1990**, 635–645. (c) Schneider, C. *Angew. Chem. Int. Ed.* **1998**, *37*, 1375–1378. (d) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev*. **1993**, *93*, 1307–1370. (e) Hoffmann, R. W. *Angew. Chem. Int. Ed*. **2000**, *39*, 2054–2070. (f) Rychnovsky, R. D. *Chem. Rev*. **1995**, *95*, 2021–2040. (g) Norcross, R. D.; Paterson, I. *Chem. Rev*. **1995**, *95*, 2041–2114.

10) (a) Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, *95*, 1253–1277. (b) Gauthier, D. R., Jr.; Zandi, K. S.; Shea, K. J. *Tetrahedron* **1998**, *54*, 2289–2338. (c) Fensterbank, L.; Malacria, M.; Sieburth, S. M. *Synthesis* **1997**, 813–854.

11) Bajwa, J. S.; Anderson, R. C. *Tetrahedron Lett.* **1991**, *32*, 3021–3024.

12) Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729–7737.

13) Inoue, R.; Nakao, J.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2039–2049.

Table of Contents Graphics

Cobalt-Catalyzed Sequential Cyclization/Cross-Coupling Reactions of 6-Halo-1-hexene Derivatives with Grignard Reagents and Their Application to the Synthesis of 1,3-Diols

Hidenori Someya, Hirohisa Ohmiya, Hideki Yorimitsu,* and Koichiro Oshima*