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Stereoselective synthesis of α-disubstituted cyclopentanones by palladium-catalyzed rearrangement of allenylcyclobutanols with aryl halides

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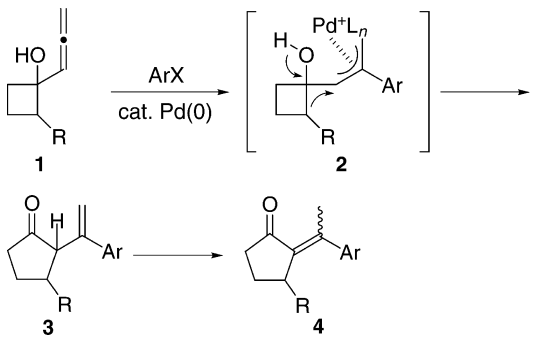
Abstract—When allenylcyclobutanols having a 1-substituted allenyl group were treated with aryl iodides in the presence of palladium(0), ring-expanded cyclopentanones possesing quaternary carbon stereocenter at the α-position were stereoselectively obtained. The reactions can be applied to various kinds of allenylcyclobutanols and aryl halides. © 2002 Elsevier Science Ltd. All rights reserved.

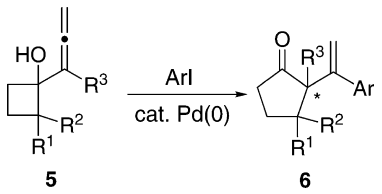
1. Introduction

There are many biologically active natural products having quaternary carbon stereocenters, and stereo- and enantioselective construction of these stereocenters is important in organic synthesis.[1] A number of methods to construct a quaternary carbon stereocenter have been developed, and the intramolecular chirality transfer reaction such as stereo- and enantiospecific rearrangement is one of the useful method to create a new quaternary carbon atom.[1]

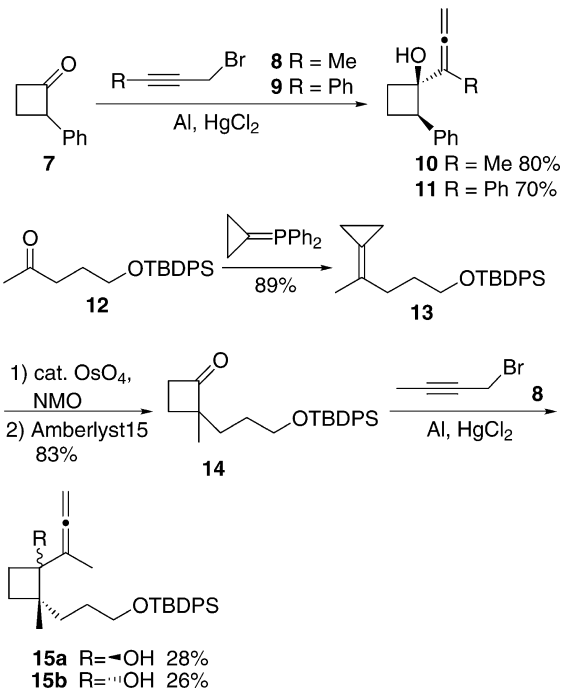
Palladium-catalyzed ring rearrangement of cyclobutanol derivatives is a valuable methodology for the construction of various substituted five-membered ring systems,[2–4] which has been successfully applied to the synthesis of natural products.[5] In recent years, we have developed a novel type of ring expansion reaction of allenylcyclobutanols



Scheme 1.



Scheme 2.



Scheme 3.

Keywords: cyclopentanones; palladium and compounds; rearrangements; ring transformations.

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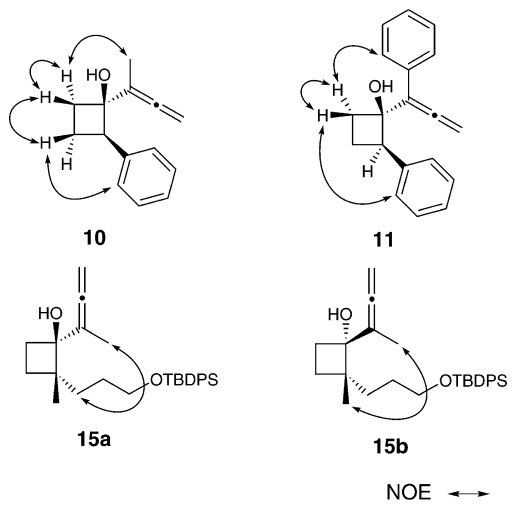


Figure 1. NOESY correlations of allenylcyclobutanols.

1 with aryl iodides (Scheme 1).[6] The reaction enables the formation of a carbon–carbon bond along with expansion of the four-membered ring system via π-allylpalladium intermediate **2** in one-pot process, and thereby constitutes a potentially useful synthetic method for the efficient synthesis of natural products. The reaction often caused double bond isomerization to give more stable α,β-unsaturated cyclopentenones **4**. But by introducing a substituent at the 1-position of the allenyl moiety, it is expected that the isomerization of the products could be suppressed and cyclopentanones **6** with quaternary carbon stereocenters could be constructed (Scheme 2). Furthermore, it is expected that stereochemical investigation would provide precise details on the mechanism of the reaction. Herein, we describe full details of the palladium-catalyzed ring expansion reaction of allenylcyclobutanols having a substituent at the 1-position of the allenyl moiety.[7]

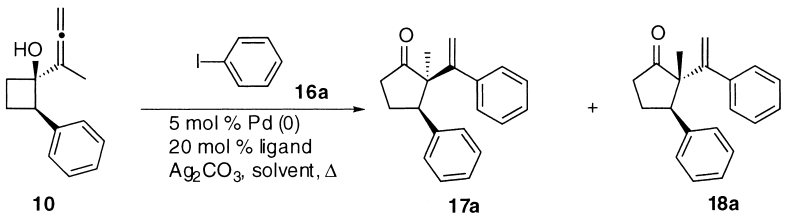
2. Results and discussion

Allenylcyclobutanols for palladium-catalyzed reaction were synthesized as follows (Scheme 3). 2-Phenylcyclobutanone **7**[8] was subjected to the reaction with propargyl aluminum reagents **8** and **9** having a methyl and a phenyl group at the terminal position to give 1-allenyl-2-phenylcyclobutanols **10** and **11** in 80 and 70% yields.[9] 2,2-Dialkylsubstituted cyclobutanone **14**, which was obtained by the Wittig cyclopropylidenation of **12** followed by the dihydroxylation and the acid-catalyzed ring rearrangement, was also converted to the allenylcyclobutanols **15a** and the **15b** in 28 and 26% yields. The stereochemistries of the obtained allenylcyclobutanols were determined by NOESY, respectively (Fig. 1).

Our initial attempt at palladium-catalyzed reaction began with allenylcyclobutanol **10** and iodobenzene **16a**. (Table 1). The reaction of **10** with **16a** in the presence of 5 mol% $Pd_2(dba)_3{\cdot}CHCl_3$, 20 mol% dppe, Ag_2CO_3 in toluene at 60°C for 20 h gave the ring-expanded product **17a** and the diastereomer **18a** as a 3:2 mixture in 80% yield (Table 1, entry 1). Interestingly, the ratio of **17a** increased in accordance with an increase of the reaction temperature (entries 2 and 3), and the highest ratio was obtained when the reaction was carried out in refluxing toluene (97:3, 57% yield in entry 3). The reaction also proceeded uneventfully in the presence of various ligands (entries 4–8). The best result was obtained by employing 5 mol% of $Pd(PPh_3)_4$ at 80°C for 3 h (entry 8), and **17a** was exclusively obtained in 80% yield. The product was also successfully produced when the reaction was carried out in THF (98:2, 81% in entry 9), and a poor result was gained by the reaction in DMF (entry 10).

Reactions of **10** with various substituted aryl halides **16b–j** were then examined (Table 2). When aryl iodides having electron-donating group **16b–d** were subjected to the

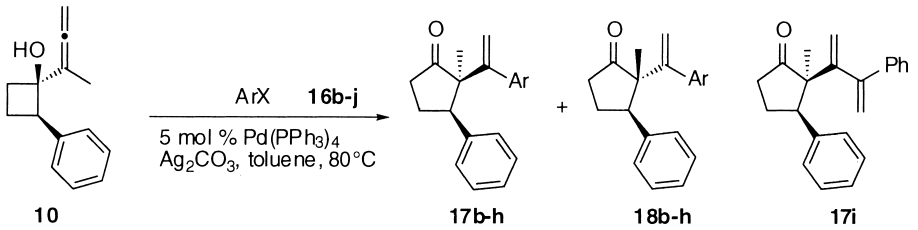
Table 1. Cascade ring expansion reaction of allenylcyclobutanol **10** with iodobenzene **16a**



Entry	Catalyst	Temperature (°C)	Solvent	Time (h)	Product	
					17a:**18a**[a]	Yield (%)
1	$Pd_2(dba)_3{\cdot}CHCl_3$, dppe	60	Toluene	20	60:40	80
2	$Pd_2(dba)_3{\cdot}CHCl_3$, dppe	80	Toluene	4	88:12	70
3	$Pd_2(dba)_3{\cdot}CHCl_3$, dppe	Reflux	Toluene	3	97:3	57
4	$Pd_2(dba)_3{\cdot}CHCl_3$, dppp	80	Toluene	2	89:11	31
5	$Pd_2(dba)_3{\cdot}CHCl_3$, dppb	80	Toluene	1	**17a** only	66
6	$Pd_2(dba)_3{\cdot}CHCl_3$, dppf	80	Toluene	24	72:28	55
7	$Pd_2(dba)_3{\cdot}CHCl_3$, P(*o*-tolyl)$_3$	80	Toluene	1.5	89:11	78
8	$Pd(PPh_3)_4$	80	Toluene	3	**17a** only	80
9	$Pd(PPh_3)_4$	Reflux	THF	3	98:2	81
10	$Pd(PPh_3)_4$	80	DMF	3	**17a** only	26

[a] The product ratios were determined by ^{1}H NMR integration of olefinic methylene signals (δ 4.87 and 5.01 for **17a**; 5.22 and 5.34 for **18a**).

Table 2. Cascade ring expansion of allenylcyclobutanol **10** with aryl halides **16b–j**



Entry	Aryl halide	Time (h)	Product	
			17:**18**[a]	Yield (%)[b]
1	**16b**: Ar=4-methodyphenyl, X=I	1.5	**17b** only	72
2	**16c**: Ar=4-methylphenyl, X=I	1	94:6	89
3	**16d**: 1-iodonaphthalene	3	84:16	79
4	**16e**: Ar=4-nitrophenyl, X=I	1.5	**17e** only	66
5	**16f**: Ar=4-acetylphenyl, X=I	4	**17f** only	77
6	**16g**: Ar=4-methodyphenyl, X=Br	30	**17b** only	37 (52)
7	**16h**: 4-bromo-1,2-(methylenedioxy)benzene	24	84:16	26
8	**16i**: α-bromostyrene	30	**17i** only	26
9[c]	**16j**: Ar=4-methoxyphenyl, X=OTf	24	**17b** only	8 (18)

[a] The product ratios were determined by ^{1}H NMR integration of olefinic methylene signals (δ 4.82 and 5.00 for **17c**; 5.18 and 5.32 for **18c**; 5.11 and 5.27 for **17d**; 4.99 and 5.06 for **18d**; 4.82 and 4.99 for **17h**; 5.15 and 5.30 for **18h**).
[b] The yield in parenthesis is based on recovered starting material.
[c] K_2CO_3 was used as a base.

reactions, the ring expansions could be smoothly performed to furnish the corresponding cyclopentanones **17b–d** with satisfactory selectivities and yields (entries 1–3). Furthermore, the reactions with electron withdrawing group **16e** and **f** also proceeded to give **17e** and **f** as a sole product in moderate yield (entries 4 and 5). When aryl bromides **16g–i** were attempted instead of aryl iodide, the reactions took longer time and the yields of the products were decreased (entries 6–8). It is interesting that the diene **17i** was obtained by the reaction with α-bromostyrene (entry 8). Aryl triflate **16j** was not effective for the ring expansion reaction (entry 9). The stereochemistries of the products **17b** and **17d** were determined by NOESY as shown in Fig. 2 and the other products were tentatively assigned by the analogy of ^{1}H NMR spectrum of **17b**.

Reactions of other allenylcyclobutanols by employing 5 mol% of $Pd(PPh_3)_4$ at 80°C were next examined (Table 3). The substrate **11** having a phenyl group at the 1-position of the allenyl moiety reacted with 4-iodoanisole **16b** to give the corresponding cyclopentanone **19** in 20% yield as a single isomer (entry 1). The low yield reflects the difficulties to construct the highly hindered triaryl compound **19**. The cyclopentanone **20** was obtained as a sole product from **15a**

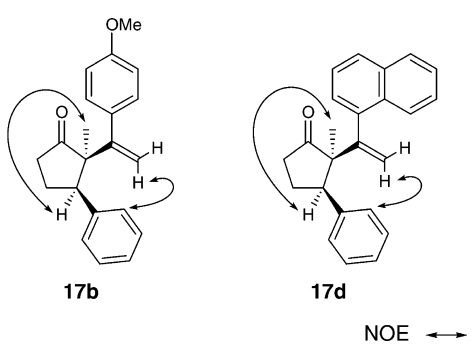
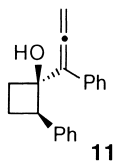
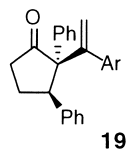
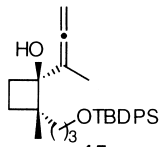
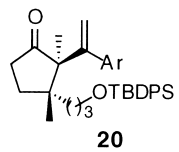
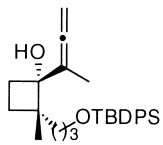
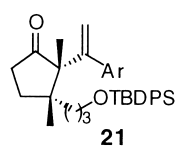


Figure 2. NOESY correlations of cyclopentanones.

(entry 2). On the other hand, the reaction of the diastereomer **15b** exclusively provided **21** (entry 3). It is ascertained from these results that the ring expansion process proceeds in a stereospecific manner. The stereochemistries of **19** and **21** were determined by NOESY, respectively (Fig. 3). The stereochemistry of **20** was also established by NOESY experiment of **22** which was obtained by the desilylation of **20** (Scheme 4, Fig. 3).

A plausible mechanism for the diastereoselectivity of the reaction is shown in Scheme 5. Stereochemistry of the

Table 3. Cascade reactions of various substituted allenylcyclobutanols with 4-iodoanisole

Entry	Substrate	Product[a]	Yield (%)
1	 **11**	 **19**	20
2	 **15a**	 **20**	81
3	 **15b**	 **21**	79

All the reactions were carried out using substrate, 4-iodoanisole **16b**, 5 mol% $Pd(PPh_3)_4$, and Ag_2CO_3 in toluene at 80°C.
[a] Ar, *p*-methoxyphenyl.

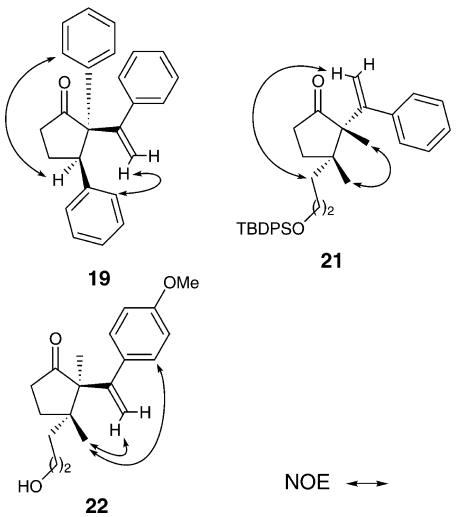
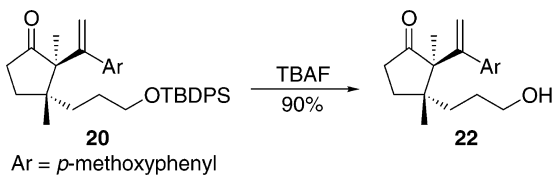


Figure 3. NOESY correlations of cyclopentanones.



Scheme 4.

product would be reflected by two transition states TS-**A** and TS-**B**, which are each formed by the insertion of two conformers **A** and **B** to the aryl palladium species followed by formation of π-allylpalladium complex.[10] At low temperature such as entries 1 and 2 in Table 1, it is expected that the rearrangement would straightly proceed from these transition states to give a mixture of **23** and **24**. On the other hand, equilibrium between TS-**A** and TS-**B**[11] at high temperature would cause the selective production of **23** by shifting the equilibrium to the more stable TS-**A**. Improvement of diastereoselectivities at the higher reaction temperature supports the equilibrium-controlled mechanism.

3. Conclusion

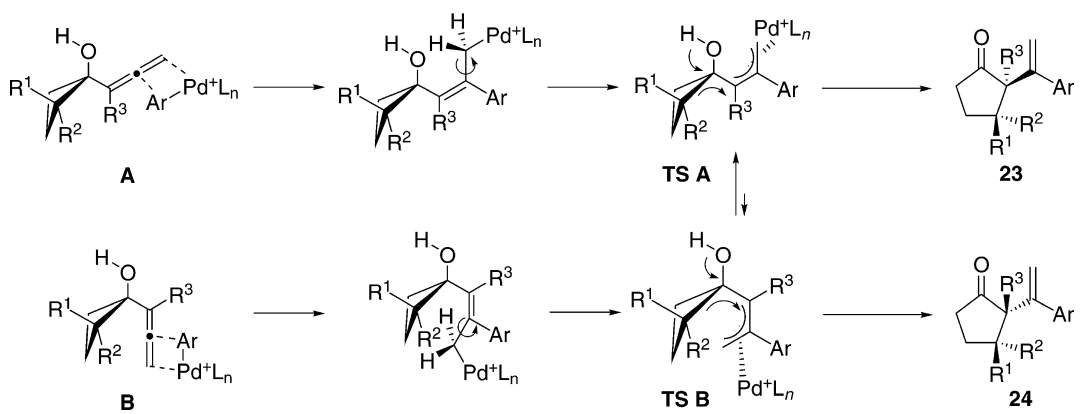
In conclusion, we have developed a novel route to the α-substituted cyclopentanones by the palladium-catalyzed ring expansion reaction of allenylcyclobutanols with aryl iodides. The reaction can be carried out using various allenylcyclobutanols and aryl halides to afford corresponding aryl-substitueted cyclopentanones. By choosing the reaction conditions, the rearrangement proceeds in a stereospecific manner to give the product having a quaternary carbon stereocenter with high diastereoselectivity. It was clear that the reaction temperature is an important factor to control the selectivity of the products. As the stereoselective construction of molecules with quaternary carbon stereocenters represents a very challenging and dynamic area in organic synthesis, our methodology would provide a new synthetic protocol in this area.

4. Experimental

4.1. General procedure

All nonaqueous reactions were carried out under a positive atmosphere of argon or nitrogen in dried glassware unless otherwise indicated. Materials were obtained from commercial suppliers and used without further purification except when otherwise noted. Solvents were dried and distilled according to standard protocols. The phrase 'residue upon workup' refers to the residue obtained when the organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. Column chromatography was performed on silica gel 60N (Merck, 100–210 mesh, 60 Å), and flash column chromatography was performed on silica gel 60 (Merck, 40–100 mesh, 60 Å) using the indicated solvent. IR spectra were measured on JASCO IR Report-100 or SHIMADZU FTIR-8300 spectrometer. NMR spectra were recorded on JEOL JNM-GX 500, JEOL AL 400 or Varian Gemini 2000 spectrometer with tetramethylsilane or chloroform as an internal standard. Mass spectra were recorded on JEOL JMS-DX-303 or JMS-AX-500 spectrometer.

4.1.1. (1*R* *,2*R* *)-1-(1-Methyl-1,2-propadienyl)-2-phenylcyclobutan-1-ol (10). A suspension of powdered aluminum (278 mg, 10.3 mmol) and mercuric chloride (112 mg, 0.414 mmol) in THF (30 mL) was refluxed for 30 min. After the mixture had been cooled to rt, 1-bromo-2-butyne **8** (1.37 g, 10.3 mmol) was added dropwise to the suspension and the mixture was stirred at the same temperature for 6 h. The above propargyl aluminum reagent was added dropwise



Scheme 5.

to a solution of the cyclobutanone **7**[8] (604 mg, 4.11 mmol) in Et_2O (40 mL) at 0°C, and the stirring was continued for 1 h. The reaction mixture was diluted with water and extracted with Et_2O. The combined extracts were washed with 10% HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (95:5 v/v) as eluent to give the allenylcyclobutanol **10** (661 mg, 80%) as a colorless oil: IR (neat) 3525, 3400, 1950 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.47 (1H, s), 1.73 (3H, t, J=3.0 Hz), 2.03–2.13 (2H, m), 2.26–2.32 (1H, m), 2.39–2.43 (1H, m), 3.81 (1H, t, J=8.5 Hz), 4.81 (1H, dq, J=10.0 and 3.0 Hz), 4.85 (1H, dq, J=10.0 and 3.0 Hz), 7.21–7.25 (2H, m), 7.29–7.35 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 20.1, 31.9, 47.9, 77.0, 78.3, 104.5, 126.8, 128.5, 128.8, 138.9, 205.3; MS m/z 200 (M^+); HRMS calcd for $C_{14}H_{16}O$ (M^+) 200.1202, found 200.1208.

4.1.2. (1*R* *,2*R* *)-1-(1-Phenyl-1,2-propadienyl)-2-phenylcyclobutan-1-ol (11). By following the same procedure described for **10**, the allenylcyclobutanol **11** was prepared from **7** and **9**: yield 70%; colorless oil; IR (neat) 3530, 3400, 1930, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.71 (1H, bs), 2.18–2.15 (1H, m), 2.38–2.54 (3H, m), 4.03–4.06 (1H, m), 5.22 (1H, d, J=11.5 Hz), 5.33 (1H, d, J=12.0 Hz), 7.20–7.41 (8H, m), 7.52 (2H, dt, J=5.1 and 0.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 34.2, 48.6, 78.1, 80.2, 111.9, 126.8, 126.9, 128.0, 128.3, 128.4, 129.0, 133.9, 138.8, 207.9; MS m/z 262 (M^+); HRMS calcd for $C_{19}H_{18}O$ (M^+) 262.1357, found 262.1349.

4.1.3. 5-*t*-Butyldiphenylsiloxy-2-cyclopropylidenepentane (13). To a stirred suspension of NaH (5.57 g, 60% of oil suspension, 139.2 mmol) in THF (200 mL) was added cyclopropyltriphenylphosphonium bromide (53.35 g, 139.2 mmol) at rt. After the mixture had been stirred for 10 h at 62°C, a solution of the siloxy ketone **12** (36.46 g, 107.1 mmol) in THF (80 mL) was added dropwise, and the stirring was continued for 3 h at the same temperature. The reaction mixture was diluted with water and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (99:1 v/v) as eluent to give the cyclopropylidene derivative **13** (36.0 g, 89%) as a colorless oil: IR 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88–1.02 (4H, m), 1.07 (9H, s), 1.76 (5H, m), 2.24 (2H, t, J=7.5 Hz), 3.70 (2H, t, J=6.8 Hz), 7.33–7.70 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.4, 2.9, 19.2, 20.7, 26.9, 30.7, 32.9, 64.0, 115.4, 124.0, 127.5, 129.7, 134.4, 135.9; MS m/z 283 (M^+-57); Anal. Calcd for $C_{24}H_{32}OSi$: C, 79.06; H, 8.85. Found C, 78.93; H, 8.98.

4.1.4. 2-(3-*t*-Butyldiphenylsiloxypropyl)-2-methylcyclobutan-1-one (14). To a stirred solution of the cyclopropylidene derivative **13** (18.0 g, 50.6 mmol), NMO (13.7 g, 101 mmol) in MeCN–H_2O–*t*-BuOH (6:1:2 v/v, 200 mL) was added a catalytic amount of OsO_4 at rt and the stirring was continued for 20 h. To the reaction mixture was added aqueous $Na_2S_2O_3$ solution and the stirring was continued for 1 h. After extraction with AcOEt, the combined extracts were washed with 1 N HCl, saturated aqueous $NaHCO_3$ and saturated aqueous NaCl. To a solution of the workup in AcOEt (150 mL) was added Amberlyst 15 (2.50 g) and the stirring was continued for 3 h. The reaction mixture was filtered through Celite and the residue upon evaporation was chromatographed on silica gel with hexane–AcOEt (85:15 v/v) as eluent to give the cyclobutanone **14** (16.4 g, 83%) as a colorless oil: IR (neat) 1770 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (9H, s), 1.18 (3H, s), 1.50–1.71 (4H, m), 1.72–1.98 (2H, m), 2.91–3.06 (2H, m), 3.67 (2H, t, J=6.8 Hz), 7.30–7.70 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 19.8, 23.5, 26.4, 31.6, 41.4, 63.3, 77.1, 127.1, 129.0, 134.2, 135.4, 213.5; MS m/z 323 (M^+−57); Anal. Calcd for $C_{24}H_{32}O_2Si$: C, 75.74; H, 8.47. Found: C, 75.64; H, 8.37.

4.1.5. [(1*R* *,2*S* *) and (1*S* *,2*S* *)]-1-(1-Methyl-1,2-propadienyl)-2-(3-*t*-butyldiphenylsiloxypropenyl)-2-methylcyclobutan-1-ol (15a and 15b). By following the same procedure described for **10**, the allenylcyclobutanols **15a** and **15b** were prepared from **14** and **8**; **15a**: yield 28%; colorless oil; IR (neat) 3447, 1956 cm^{-1}, ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (9H, s), 1.11 (3H, s), 1.25 (1H, br s), 1.33 (1H, dt, J=11.8 and 4.6 Hz), 1.39–1.46 (2H, m), 1.46–1.58 (3H, m), 1.69 (3H, t, J=3.5 Hz), 1.81 (1H, ddd, J=12.0, 9.5, 6.5 Hz), 2.32 (1H, ddd, J=12.0, 9.5, 6.5 Hz), 3.61–3.69 (2H, m), 4.69 (1H, dq, J=9.9 and 3.1 Hz), 4.74 (1H, dq, J=9.9 and 3.1 Hz), 7.35–7.43 (6H, m), 7.66 (4H, dt, J=6.5 and 1.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.7, 19.1, 19.7, 26.3, 26.8, 27.6, 30.5, 33.2, 47.4, 64.4, 75.7, 79.1, 102.0, 127.7, 129.6, 134.2, 135.7, 206.4; MS m/z 434 (M^+); HRMS calcd for $C_{28}H_{38}O_2Si$ (M^+) 434.2642, found 434.2640; **15b**: yield 26%; colorless oil; IR (neat) 3550, 3450, 1950 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.99 (3H, s), 1.06 (9H, s), 1.26 (1H, br s), 1.31 (1H, dt, J=10.7 and 4.3 Hz), 1.39–1.51 (2H, m), 1.51–1.59 (1H, m), 1.64–1.78 (3H, m), 1.66 (3H, t, J=3.0 Hz), 2.32–2.37 (1H, m), 3.66–3.68 (2H, m), 4.69 (1H, dq, J=9.8 and 3.0 Hz), 4.76 (1H, dq, J=9.8 and 3.0 Hz), 7.36–7.43 (6H, m), 7.67 (4H, d, J=7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 19.1, 21.7, 26.8, 27.5, 27.6, 29.7, 31.6, 46.7, 64.6, 75.6, 79.8, 102.2, 127.7, 129.6, 134.2, 135.7, 206.6; MS m/z 434 (M^+); HRMS calcd for $C_{28}H_{38}O_2Si$ (M^+) 434.2641, found for 434.2659.

4.2. General procedure for the palladium-catalyzed ring expansion reaction. Procedure for the reaction of 10 and 16a (entry 8 in Table 1)

To a stirred solution of the allenylcyclobutanol **10** (28.5 mg, 0.142 mmol) in toluene (5 mL) was added iodobenzene **16a** (0.024 mL, 0.213 mmol), Ag_2CO_3 (78.0 mg, 0.283 mmol) and $Pd(PPh_3)_4$ (8.1 mg, 7.0 μmol) at rt. After the stirring had been continued for 2 h at 80°C, the reaction mixture was filtered through Celite. The residue upon work up was chromatographed on silica gel with hexane–AcOEt (95:5 v/v) as eluent to give the *cis*-cyclopentanone **17a** (31.5 mg, 80%) as a colorless oil.

4.2.1. (2*R* *,3*R* *)-2-Methyl-2-(1-phenylvinyl)-3-phenylcyclopentan-1-one (17a). Colorless oil; IR (neat) 1730, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (3H, s), 2.10–2.20 (2H, m), 2.40–2.45 (2H, m), 3.22 (1H, t, J=9.0 Hz), 4.87 (1H, d, J=0.6 Hz), 5.01 (1H, s), 6.54 (2H, dt, J=7.8 and 1.2 Hz), 7.06–7.13 (3H, m), 7.22–7.24 (2H, m), 7.30–7.33 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 24.2, 37.6, 54.9, 58.8, 118.9, 126.9, 127.1, 127.5, 128.2,

128.6, 128.8, 139.9, 142.5, 149.2, 221.9; MS *m/z* 276 (M^+); Anal. Calcd for $C_{20}H_{20}O$: C, 86.92; H, 7.29. Found: C, 86.53; H, 7.16.

4.2.2. [(2*R* *,3*R* *) and (2*R* *,3*R* *)]-2-Methyl-2-(1-phenylvinyl)-3-phenylcyclopentan-1-ones (17a+18a) (ratio of 60:40). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (3H×0.4, s), 1.36 (3H×0.6, s), 2.10–2.45 (3H and 1H×0.6, m), 2.61–2.70 (1H×0.4, m), 3.22 (1H×0.6, t, *J*=9.0 Hz), 3.58 (1H×0.4, dd, *J*=11.4 and 6.9 Hz), 4.87 (1H×0.6, s), 5.01 (1H×0.6, s), 5.22 (1H×0.4, s), 5.34 (1H×0.4, s), 6.54 (2H, dt, *J*=6.9 and 1.5 Hz), 7.04–7.13 (3H, m), 7.22–7.24 (2H, m), 7.30–7.33 (3H, m).

4.2.3. (2*R* *,3*R* *)-2-Methyl-2-[1-(4-methoxyphenyl)vinyl]-3-phenylcyclopentan-1-one (17b). Colorless oil; IR (neat) 1730, 1600 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (3H, s), 2.11–2.17 (2H, m), 2.38–2.42 (2H, m), 3.18 (1H, dd, *J*=11.5 and 7.5 Hz), 3.72 (3H, s), 4.80 (1H, d, *J*=0.5 Hz), 4.96 (1H, d, *J*=0.5 Hz), 6.44 (2H, dt, *J*=5.4 and 1.5 Hz), 6.58 (2H, dt, *J*=5.4 and 1.2 Hz), 7.20–7.24 (2H, m), 7.27–7.32 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 24.3, 37.8, 55.0, 55.1, 59.0, 112.9, 118.6, 127.1, 128.3, 128.9, 129.9, 135.0, 140.0, 148.8, 158.7, 222.3; MS *m/z* 306 (M^+); HRMS calcd for $C_{21}H_{22}O_2$ (M^+) 306.1619, found 306.1601.

4.2.4. (2*R* *,3*R* *)-2-Methyl-2-[1-(4-methylphenyl)vinyl]-3-phenylcyclopentan-1-one (17c). Colorless oil; IR (neat) 1738, 1603 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, s), 2.12–2.18 (2H, m), 2.25 (3H, s), 2.39–2.44 (2H, m), 3.20 (1H, dd, *J*=11.1 and 7.8 Hz), 4.82 (1H, s), 5.00 (1H, s), 6.43 (2H, dt, *J*=6.3 and 3.3 Hz), 6.81 (2H, d, *J*=7.5 Hz), 7.22–7.26 (2H, m), 7.28–7.36 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 24.1, 24.2, 37.7, 55.0, 58.9, 118.6, 127.0, 128.1, 128.2, 128.5, 128.8, 136.6, 139.6, 139.9, 149.1, 222.1; MS *m/z* 290 (M^+); HRMS calcd for $C_{21}H_{22}O$ (M^+) 290.1671, found 290.1659.

4.2.5. [(2*R* *,3*R* *) and (2*S* *,3*R* *)]-2-Methyl-2-[1-(4-methylphenyl)vinyl]-3-phenylcyclopentan-1-ones (17c+18c) (ratio of 94:6). Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (3H×0.06, s), 1.34 (3H×0.94, s), 2.12–2.22 (2H, m), 2.25 (3H×0.94, s), 2.35 (3H×0.06, s), 2.39–2.44 (2H, m), 3.20 (1H, dd, *J*=11.1 and 7.8 Hz), 4.82 (1H×0.94, d, *J*=0.6 Hz), 5.00 (1H×0.94, d, *J*=0.6 Hz), 6.43 (2H×0.94, dt, *J*=6.3 and 3.3 Hz), 6.54 (2H×0.06, d, *J*=6.3 Hz), 6.81 (2H, d, *J*=7.5 Hz), 7.02–7.08 (2H×0.06, m), 7.11–7.17 (3H×0.06, m), 7.22–7.26 (2H×0.94, m), 7.28–7.36 (3H×0.94, m).

4.2.6. [(2*R* *,3*R* *) and (2*S* *,3*R* *)]-2-Methyl-2-[1-(1-naphthyl)vinyl]-3-phenylcyclopentan-1-ones (17d+18d) (ratio of 84:16). Colorless oil; IR (neat) 1740, 1620 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.01 (3H×0.84, s), 1.50 (3H×0.16, s), 2.10–2.24 (1H×0.16, m), 2.27–2.32 (1H×0.84, m), 2.41–2.50 (3H×0.16, m), 2.53–2.74 (3H×0.84, m), 3.27 (1H, m), 4.99 (1H×0.16, s), 5.06 (1H×0.16, s), 5.11 (1H×0.84, s), 5.22 (1H, d, *J*=7.3 Hz), 5.27 (1H×0.84, s), 6.92 (1H×0.84, t, *J*=7.3 Hz), 7.08 (1H×0.16, d, *J*=14.0 Hz), 7.25–7.47 (7H and 2H×0.16, m), 7.56 (1H×0.84, d, *J*=5.1 Hz), 7.70–7.72 (1H, m), 8.07 (1H×0.84, d, *J*=5.1 Hz); ^{1}MS *m/z* 326 (M^+); HRMS calcd for $C_{24}H_{22}O$ (M^+) 326.1671, found 326.1686.

4.2.7. (2*R* *,3*R* *)-2-Methyl-2-[1-(4-nitrophenyl)vinyl]-3-phenylcyclopentan-1-one (17e). Colorless oil; IR (neat) 1740, 1600, 1520, 1340, 860 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (3H, s), 2.23–2.39 (2H, m), 2.50–2.57 (2H, m), 3.27 (1H, dd, *J*=10.8 and 7.5 Hz), 5.09 (1H, s), 5.11 (1H, s), 6.54 (2H, dt, *J*=9.0 and 2.1 Hz), 7.18–7.21 (2H, m), 7.31–7.33 (3H, m), 7.88 (2H, dt, *J*=9.0 and 2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 24.3, 37.6, 54.7, 58.4, 120.4, 122.6, 127.5, 128.5, 128.6, 129.4, 139.5, 146.7, 148.2, 149.0, 220.9; MS *m/z* 321 (M^+); HRMS calcd for $C_{20}H_{19}NO_3$ (M^+) 321.1364, found 321.1342.

4.2.8. (2*R* *,3*R* *)-2-(4-Acetylphenylvinyl)-2-methyl-3-phenylcyclopentanone (17f). Colorless oil; IR (neat) 1736, 1682, 1604 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (3H, s), 2.21 (1H, dd, *J*=8.7 and 7.5 Hz), 2.22 (1H, dd, *J*=8.7 and 7.5 Hz), 2.45–2.51 (2H, m), 2.53 (3H, s), 3.24 (1H, dd, *J*=7.4 and 7.4 Hz), 4.98 (1H, s), 5.06 (1H, s), 6.56 (2H, dt, *J*=9.0 and 1.8 Hz), 7.19–7.24 (2H, m), 7.30–7.36 (3H, m), 7.63 (2H, *J*=9.0 and 1.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 24.3, 26.4, 37.6, 54.8, 58.6, 119.6, 127.3, 127.5, 128.4, 128.7, 128.8, 135.6, 139.7, 147.4, 148.8, 198.0, 221.4; MS *m/z* 318 (M^+); HRMS calcd for $C_{22}H_{22}O_2$ (M^+) 318.1620, found 318.1642.

4.2.9. (2*R* *,3*R* *)-2-Methyl-2-[3,4-(methylenedioxy)phenyl]-vinyl-3-phenylcyclopentan-1-one (17h). IR (neat) 1734, 1600 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (3H, s), 2.12–2.27 (2H, m), 2.42–2.52 (2H, m), 3.21 (1H, dd, *J*=12.0 and 6.8 Hz), 4.82 (1H, s), 4.99 (1H, s), 5.81–5.88 (3H, m), 6.08 (1H, dd, *J*=8.1 and 1.7 Hz), 6.51 (1H, d, *J*=7.8 Hz), 7.13–7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0, 24.3, 37.7, 54.8, 54.9, 58.9, 100.8, 107.3, 109.0, 118.8, 122.1, 122.3, 128.1, 128.6, 128.9, 136.3, 139.9, 148.8, 221.9; MS *m/z*320 (M^+); Anal. Calcd for $C_{21}H_{20}O_3$: C, 78.73; H, 6.29. Found: C, 78.42; H, 6.34.

4.2.10. [(2*R* *,3*R* *) and (2*S* *,3*R* *)]-2-Methyl-2-[3,4-(methylenedioxy)phenyl]vinyl-3-phenylcyclopentan-1-ones (17h+18h) (ratio of 84:16). IR (neat) 1730, 1600 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (3H×0.16, s), 1.32 (3H×0.84, s), 2.12–2.27 (2H, m), 2.42–2.52 (2H, m), 3.21 (1H×0.84, dd, *J*=12.0 and 6.8 Hz), 3.61 (1H×0.16, dd, *J*=11.2 and 7.3 Hz), 4.82 (1H×0.84, s), 4.99 (1H×0.84, s), 5.15 (1H×0.16, s), 5.30 (1H×0.16, s), 5.81–5.88 (3H, m), 5.93 (1H×0.16, s), 6.08 (1H×0.84, dd, *J*=8.1 and 1.7 Hz), 6.51 (1H×0.84, d, *J*=8.1 and 1.7 Hz), 6.68 (1H×0.16, m), 7.13–7.40 (5H, m); MS *m/z* 320 (M^+); HRMS calcd for $C_{21}H_{20}O_3$ (M^+) 320.1412, found 320.1418.

4.2.11. (2*R* *,3*R* *)-2-Methyl-2-(1-methylene-2-phenyl-2-propenyl)-3-phenylcyclopentan-1-one (17i). IR (neat) 1732, 1602 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24 (3H, s), 2.15–2.45 (4H, m), 3.14 (1H, dd, *J*=10.4 and 5.8 Hz), 4.16 (1H, s), 4.86 (1H, s), 5.03 (1H, s), 5.07 (1H, s), 7.20–7.36 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 37.4, 55.5, 58.3, 115.9, 116.0, 120.1, 127.3, 128.0, 128.4, 129.2, 140.1, 140.7, 148.5, 151.0, 221.0; MS *m/z*302 (M^+); HRMS calcd for $C_{22}H_{22}O$ 302.1671, found 302.1651.

4.2.12. (2*R* *,3*S* *)-2-[1-(4-Methoxyphenyl)vinyl]-2-phenyl-3-phenylcyclopentan-1-one (19) (entry 1 in Table 3). Colorless oil; IR (neat) 1730, 1600 cm^{-1}; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 2.08–2.13 (1H, m), 2.36–2.49 (2H, m), 2.57–2.64 (1H, m), 3.65 (3H, s), 4.10 (1H, t, J=5.0 Hz), 5.22 (1H, d, J=1.0 Hz), 5.70 (1H, d, J=1.0 Hz), 6.32 (2H, dt, J=9.0 and 2.0 Hz), 6.41 (2H, dt, J=9.0 and 2.0 Hz), 6.96–6.98 (2H, m), 7.12–7.13 (3H, m), 7.28 (1H, t, J=7.5 Hz), 7.37 (2H, t, J=8.0 Hz), 7.65 (2H, d, J=7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.4, 36.0, 49.9, 55.0, 66.2, 112.4, 119.1, 126.3, 127.3, 127.9, 128.4, 128.5, 129.0, 129.3, 134.6, 138.7, 142.2, 147.2, 158.2, 216.2; MS *m/z* 368 (M^+); HRMS calcd for $C_{26}H_{24}O_2$ (M^+) 368.1777, found 368.1763.

4.2.13. (2*S,3*R**)-2-Methyl-2-[1-(4-methoxyphenyl)vinyl]-3-(3-*t*-butyldiphenylsiloxypropyl)-3-methylcyclopentan-1-one (20) (entry 2 in Table 3).** Colorless oil; IR (neat) 1730, 1600 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.02 (3H, s), 1.03 (9H, s), 1.13 (3H, s), 1.14–1.34 (2H, m), 1.36–1.71 (4H, m), 2.01–2.28 (2H, m), 3.59 (2H, t, J=6.3 Hz), 3.76 (3H, s), 5.10 (1H, d, J=1.2 Hz), 5.13 (1H, d, J=1.2 Hz), 6.76 (2H, dt, J=8.7 and 3.3 Hz), 7.09 (2H, dt, J=9.0 and 3.6 Hz), 7.34–7.42 (6H, m), 7.62 (4H, dt, J=6.3 and 1.5 Hz); ^{13}C NMR δ (75 Hz, $CDCl_3$) δ 18.9, 19.2, 22.9, 26.9, 27.5, 30.1, 32.6, 35.8, 45.4, 55.2, 62.9, 64.4, 113.1, 119.8, 127.8, 129.8, 130.4, 134.1, 134.2, 135.7, 136.0, 149.4, 158.6, 222.6; MS *m/z* 540 (M^+); HRMS calcd for $C_{35}H_{44}O_3Si$ (M^+) 540.3060, found 540.3038.

4.2.14. (2*R,3*R**)-2-Methyl-2-[1-(4-methoxyphenyl)vinyl]-3-(3-*t*-butyldiphenylsiloxypropyl)-3-methylcyclopentan-1-one (21) (entry 3 in Table 3).** Colorless oil; IR (neat) 1733, 1608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.81 (3H, s), 1.02 (9H, s), 1.17 (3H, s), 1.42–1.49 (2H, m), 1.50–1.53 (2H, m), 1.56–1.61 (2H, m), 1.86 (1H, ddd, J=20.0, 9.5, 4.5 Hz), 2.11–2.18 (1H, m), 3.69–3.71 (2H, m), 3.76 (3H, s), 5.06 (1H, s), 5.14 (1H, s), 6.71 (2H, d, J=8.5 Hz), 7.04 (2H, d, 8.5 Hz), 7.36–7.43 (6H, m), 7.68 (4H, d, J=7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 19.1, 22.3, 26.8, 27.3, 31.1, 34.4, 36.2, 45.4, 55.1, 62.7, 64.6, 113.0, 119.1, 127.7, 129.7, 130.3, 134.1, 135.7, 135.9, 149.4, 158.5, 200.8; MS *m/z* 540 (M^+); HRMS calcd for $C_{35}H_{44}O_3Si$ 540.3060 (M^+), found 540.3069.

4.2.15. (2*S,3*R**)-2-Methyl-2-(4-methoxyphenylvinyl)-3-(3-hydroxypropyl)-3-methyl-cyclopentan-1-one (22).** To a stirred solution of cyclopentanone **20** (21.2 mg, 0.0392 mmol) in THF (3 mL) was added 1 M solution of TBAF in THF (0.098 mL, 0.098 mmol) at rt. After the mixture had been stirred for 2 h, it was diluted with water and extracted with AcOEt. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane–AcOEt (60:40 v/v) as eluant to give the cyclopentanone **22** (10.7 mg, 90%) as a colorless oil: IR (neat) 3421, 1733, 1607 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (3H, s), 1.15 (3H, s), 1.17–1.25 (2H, m), 1.43–1.53 (3H, m), 1.54–1.62 (1H, m), 1.69 (1H, ddd, J=13.5, 8.5, 7.0 Hz), 2.07 (1H, ddd, J=19.5, 9.5, 7.0 Hz), 2.23 (1H, ddd, J=19.5, 9.0, 6.0 Hz), 3.53–3.56 (2H, m), 3.77 (3H, s), 5.11 (1H, s), 5.12 (1H, s), 6.76 (2H, dt, J=8.5 and 2.0 Hz), 7.07 (2H, dt, J=8.5 and 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 22.8, 27.5, 30.0, 32.4, 35.7, 45.3, 55.1, 62.8, 63.4, 113.0, 119.8, 130.4, 135.9, 149.1, 158.5, 222.4; MS *m/z* 302 (M^+); HRMS calcd for $C_{19}H_{26}O_3$ (M^+) 302.1882, found 302.1908.

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10. In the ring expansion step, the palladium would be placed rear side to undergo anti attack of the migrating group.
11. It is expected that the equilibrium would be caused by conformational change and isomerization of π-allylpalladium by $\eta^3-\eta^1-\eta^3$ mechanism.