Pergamon

Tetrahedron 57 (2001) 1723–1729

TETRAHEDRON

Regio- and stereoselectivity in palladium-catalyzed cycloreductions of 1,6-enynes in the presence of formic acid or triethylsilane

Chang Ho Oh,* Hyung Hoon Jung, Hye Rhyan Sung and Jung Duk Kim

Department of Chemistry, Hanyang University, Haengdang-17, Sungdong-Gu, Seoul 133-791, South Korea

Received 30 October 2000; accepted 15 December 2000

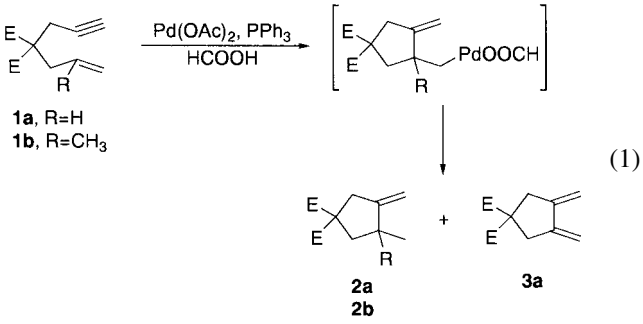
Abstract—Palladium catalyzed 1,6-enyne cycloreductions in the presence of 1.2 equiv. of formic acid (method A) would involve cycloalkylpalladium formates which proceed via two consecutive steps: β-elimination of alkylpalladium intermediates and then reduction at the less hindered olefins regio- and stereoselectivity. Triethylsilane, however, directly reduced the alkylpalladium intermediates to give the corresponding cycloreduced products (method B). © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Since functionalized carbocycles are very common structural subunits in many biologically active natural compounds, their preparation becomes of paramount interest in organic synthesis.[1] Of particular significance are the palladium-catalyzed cycloisomerizations of enediynes, dienynes, enynes and diynes.[2] In the pioneering work from the Trost group, various enynes were transformed to the corresponding σ-palladium species via hydropalladation of the terminal triple bond and subsequent intramolecular carbopalladation.[3] Iterative trapping of the σ-palladium species with tethered olefins allows for tandem cycloisomerizations.[4] Direct reduction of the σ-bonded alkylpalladium intermediates by excess external hydrogen donors such as triethylsilane or polymethylhydrosiloxane (PMHS) would represent an useful process particularly.[5] Although this method was highly valuable with diverse enyne substrates, one critical disadvantage is the requirement of a large excess of trialkylsilane, which should cause purification of the products to be problematic. An alternative method, developed by the Stork group, involves two-step processes: radical cyclization initiated by tributyltin radical and destannylation over silica gel.[6] We have long been interested in palladium-catalyzed cycloreductions of enediynes and enynes, which could offer new or alternative methodologies for constructing diverse carbocycles. Recently, we reported a new variation of palladium-catalyzed enediyne cyclization in which enediynes under palladium catalysis selectively gave either [m,6,n]- or [m,5,n]-tricyclic compounds depending on how much formic acid was used.[7] We have noted that even the alkylpalladium formates possessing a β-hydrogen also underwent carbopalladation rather than β-elimination. Based on these observations, we could postulate that use of an equivalent of formic acid played a dual role in initiating the catalytic reaction and also in reducing the alkylpalladium intermediate at the end of the catalytic cycle.[8] In this paper, we report our results demonstrating the scope and limitations of palladium-catalyzed enyne cycloreductions in the presence of formic acid or triethylsilane.

2. Results and discussion

Diethyl allylpropargylmalonate (**1a**) as an enyne substrate was examined as shown in Eq. (1). Our initial hypothesis was as follows. (1) The initially formed H–Pd–OOCH adds to the terminal triple bond regioselectively, and adds to the double bond to form an alkylpalladium intermediate. (2) The alkylpalladium formate could undergo reductive cleavage by the formate ligand more rapidly than β-elimination. In fact, treatment of enyne **1a** with 5 mol% $Pd(OAc)_2$, 10 mol% PPh_3, and 2.5 equiv. of HCOOH in



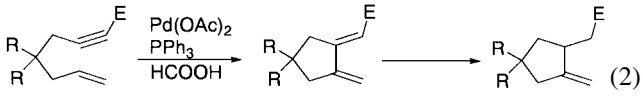
(1)

Keywords: formic acid; triethylsilane; cycloreductions.

* Corresponding author. Tel.: +82-2-2290-0932; fax: +82-2-2299-0762; e-mail: changho@email.hanyang.ac.kr

PII: S0040-4020(01)00008-4

toluene or 1,4-dioxane mainly furnished the cycloreduced product **2a** in 60–75% isolated yield along with a trace of the diene **3a**. This hypothesis was further supported from the reaction of enyne **1b**, since the alkylpalladium intermediate derived from the enyne **1b** under our conditions could not undergo β-elimination due to the lack of β-hydrogen to the alkylpalladium intermediate. The formation of cycloreduced product **2b** implied that direct reduction of the alkylpalladium intermediates could occur rapidly.[9] During the course of extension of this palladium-catalyzed cycloreduction methodology, we found that the enynes **4** conjugated with a carbonyl group (E) initially formed the dienes **5** via β-elimination of the alkylpalladium intermediates. The dienes **5** underwent reduction to the γ, δ-unsaturated carbonyl compounds **6** for a prolonged period of reaction time (Eq. (2)).[10]

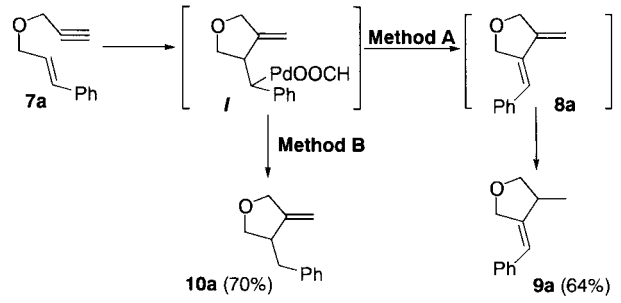


(2)

4, R = CH_2OMe
E = electron withdrawing group

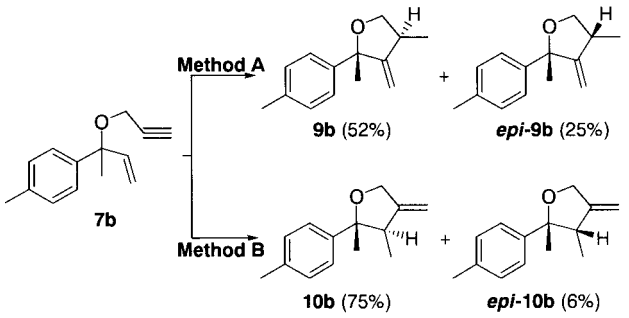
5 **6**

Formation of the dienes **5** prompted us to reinvestigate Pd-catalyzed cycloreductions of a variety of enynes and to revise our proposed mechanism.[11] When the enyne **7a** was heated at 60°C with 5 mol% $Pd(OAc)_2$, 10 mol% PPh_3, and 1.2 equiv. of HCOOH in toluene (method A), we obtained the compound **9a** in 64% isolated yield along with a trace of the isomer **10a** (Scheme 1). We should understand how the product **9a** was formed in order to search an asymmetric version of this method and its application to natural product syntheses.[12] Thus, when only 10 mol% of formic acid was employed in method A, the enyne **7a** was exclusively transformed to the diene **8a**, that was further reduced to the product **9a** by adding one equivalent of formic acid. Next, we subjected enyne **7a** to method B, a modified Trost method.[13] When the enyne **7a** was heated at 60°C with 5 mol% $Pd(dppe)Cl_2$, 1.2 equiv. of HCOOH, and 1.2 equiv. of triethylsilane in toluene, we obtained the product **10a** in 70% isolated yield. Exclusive formation of the product **10a** implied that direct reduction of σ-alkylpalladium intermediate *I* has predominantly occurred. These experiments showed the possibility that palladium-catalyzed enyne cycloreductions provide one of two expected regioisomers selectively depending on the reaction conditions. Then, the two methods (A and B) were applied to several structurally diverse enynes.



Method A: 5 mol% $Pd(OAc)_2$, 10 mol% PPh_3, 1.2 eq HCOOH, toluene
Method B: 5 mol% $Pd(dppe)Cl_2$, 1.2 eq HCOOH, 1.2 eq Et_3SiH, toluene

Scheme 1.



Scheme 2.

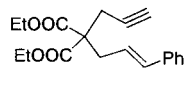
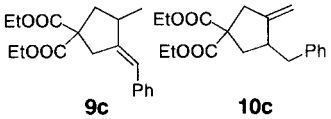
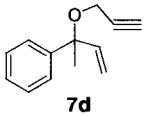
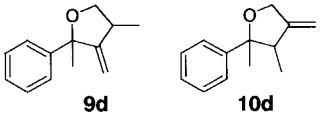
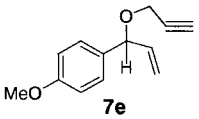
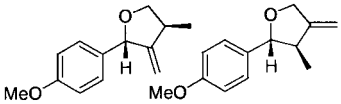
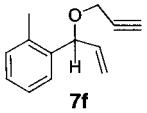
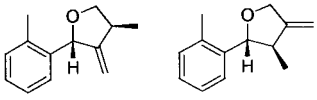
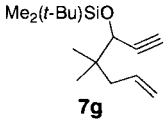
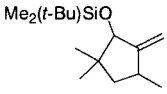
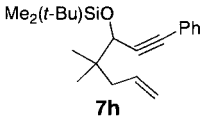
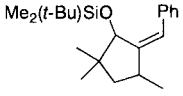
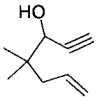
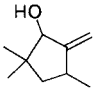
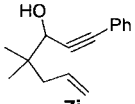
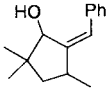
The enyne **7b** was tested as a second substrate, since it is a good model substrate for the natural product laurene and we should revise and confirm structural assignments for its cycloreduced products (Scheme 2).[14] The enyne **7b** under **method A** was converted to the product **9b** and its stereoisomer *epi*-**9b** in 52 and 25% isolated yields, respectively. The enyne **7b** under method B was converted to the product **10b** and its stereoisomer *epi*-**10b** in 75 and 6% isolated yields, respectively.[15] With these products in hand, we then determined their relative stereochemistries by analyzing a series of NMR data including NOESY data. ^1H, ^{13}C-NMR, DEPT, COSY, TOCSY, HETCOR experiments enabled us to accomplish complete ^1H and ^{13}C NMR signal assignments of compounds **9b**, *epi*-**9b**, and **10b** and to confirm the relative configurations of each compound. Coupling constants given by DQF–COSY experiment were analyzed to identify the orientation of *J*-coupled proton networks and to observe possible five-membered ring puckering. In addition, temperature-dependent(−20–25°C) and variable mixing times (τm=50, 100, 250, 500 ms) of NOESY experiments were carried out to observe the direct NOE connectivities exhibiting the orientation of side chains.[16]

Then, we prepared structurally similar enynes **7c–j** and applied them to the present two methods. These results are summarized in Table 1. Methods A and B worked well for the substrates **7c–7f** to afford the corresponding cycloreduced products **9c–f** (70–77% yields) and the products **10c–f** (60–85% yields), respectively. Like substrate **7b**, enyne **7d** was cycloreduced to **9d** (1:4) and to **10d** (1:9) as mixtures of diastereomers under the two different conditions, respectively. The enynes **7e** and **7f** for both methods did exhibit great stereoselectivities, up to a 99:1 ratio, respectively. When the enynes **7g** and **7h** were cyclized under method A, the products **10g** and **10h** were isolated in 81 and 41% yields, respectively. The enynes **7g** and **7h** under method B, however, were not cyclized at all. When the enynes having a hydroxyl functionality (**7i** and **7h**) were applied to the two methods, the corresponding products were formed with opposite relative stereochemistry, indicating that the different mechanisms might be operating.

2.1. Proposed mechanism

While sterically bulky groups of the enynes seemed to be associated with the regioselectivities of cycloreductions in method A, those did not in method B. For example, the

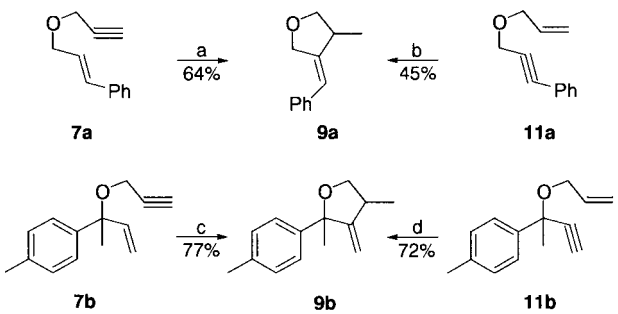
Table 1. Palladium-catalyzed enyne cycloreductions under two methods

Substrates	Method solvent	Temp(°C) Time(h)	Products	% Yield
 **7c**	**A**, toluene **B**, *p*-dioxane	60, 2 60, 2	 **9c** **10c**	**9c** (77%) **10c** (85%)
 **7d**	**A**, toluene **B**, toluene	70, 4 70, 10	 **9d** **10d**	**9d** (72%, 1:4)[a] **10d** (81%, 1:9)[a]
 **7e**	**A**, toluene **B**, toluene	70, 2 60, 2	 **9e** **10e**	**9e** (75%) **10e** (60%)
 **7f**	**A**, *p*-dioxane **B**, toluene	70, 1 80, 3	 **9f** **10f**	**9f** (70%) **10f** (88%)
 **7g**	**A**, toluene **B**, toluene	60, 2 60, 2	 **10g**	**10g** (81%, 3:1)[a] no reaction
 **7h**	**A**, toluene **B**, toluene	60, 2 60, 2	 **10h**	**10h** (41%, 9:1)[a] no reaction
 **7i**	**A**, *p*-dioxane **B**, toluene	70, 2 70, 2	 **10i**	**10i** (74%, 3:1)[a] **10i** (78%, 1:2)[a]
 **7j**	**A**, toluene **B**, *p*-dioxane	80, 2 100, 20	 **10j**	**10j** (40%, 9:1)[a] **10j** (55%, 1:9)[a]

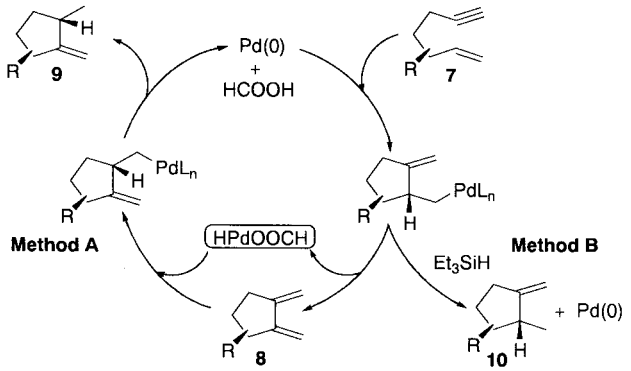
[a] Ratios mean *trans*:*cis* relations between substituents such as Me and Me, Me and $OSiMe_2(t\text{-Bu})$, or Me and OH.
Method A: 5 mol% $Pd(OAc)_2$, 10 mol% PPh_3, 1.2 equiv. HCOOH. *Method B*: 5 mol% $Pd(dppe)Cl_2$, 1.2 equiv. HCOOH, 1.2 equiv. Et_3SiH.

enynes **7a–e** under method B were cycloreduced to the products **10a–e**, which could be formed via direct reduction of the alkylpalladium intermediates by triethylsilane. Those enynes under method A, however, initially formed the dienes. When these dienes were reduced by HPdOOCH under the similar reaction conditions, we obtained the products **9a–e** in high yields, respectively. Such regioselectivity could be confirmed by control experiments with the enynes **11a** and **11b**, which are regioisomers of enynes **7a** and **7b**, respectively (Scheme 3). When the enyne **11a** was applied to method A, the reaction was sluggish to give the expected product **9a** in 45% yield. The enyne **11a** under method B did not give any cyclized products but reduced the triple bond to the double bond.[17]

In contrast to the enyne **11a**, the enyne **11b** under method A was cleanly transformed to the expected product **9b** as a 3:1 mixture of diastereomers. The method B did give the same product **9b** but in a different ratio of isomers (2:1). These experiments showed that cyclizations of the enynes **7a–j** and **11a–b** under method A should involve the diene intermediacy. Finally, a distinct stereochemical outcome has been observed from cycloreductions of the enynes **7i** and



Scheme 3. All reactions were carried out by method A under the following conditions. (a) toluene, 60°C, 2 h; (b) toluene, 60°C, 1 h; (c) 1,4-dioxane, 40°C, 3 h; (d) toluene, 50°C, 4 h.



Scheme 4.

7j. The method A afforded the predominant formation of the *trans* isomer, since HPdOOCH could coordinate with the –OH functionality and therefore H-transfer occurred at the same face of the hydroxy group. The method B mainly produced the *cis* isomer for both enynes. Such *cis*-relationship might be understood by chelation effect of the vinylpalladium species with the pendant –OH group, so that the subsequent carbopalladation should occur at the same face of –OH group.

Following is a summary for the present two methods. First, all enynes under both methods were hydro- and subsequently carbopalladated to the corresponding alkylpalladium intermediates. While triethylsilane could directly reduce the intermediates to lead to the corresponding cyclereduced products (method B), formic acid could not (method A). In method A, the intermediates readily underwent β-elimination to the dienes **8**, which were reduced to give the cyclereduced product **9** in excellent yields and in excellent regio- and stereoselectivities. Second, the regioselectivity in method A seemed to arise from the steric factors of the dienes **8**. The coordination of the palladium catalyst with the dienes **8** at the sterically less hindered double bond yielded the products as shown in Scheme 4. In method B, the initially formed vinylpalladium intermediates were carbopalladated to give the more stable alkylpalladium intermediates, which were reduced by triethylsilane to yield the products **10**. The hydroxy functionality in the enynes **7i** and **7j** might coordinate with the palladium catalyst to control the regio- and stereoselectivities in both methods. We believe that the present study will provide easy access to the regio- and stereoselective syntheses of exomethylenecyclopentane derivatives.

3. Experimental

3.1. General procedure

All reactions were carried out under an atmosphere of dry argon. Commercial reagents were used as received without further purification. All products were purified by flash chromatography using silica gel 60 (70–230 mesh, Merck) and/or by a Young-Lin M 930 HPLC employing a Nova-Pak silica preparative column and a UV detector. The purified products were identified with ^{1}H and ^{13}C NMR spectral data obtained from a Varian Mercury 400 MHz NMR spectrometer using tetramethylsilane as an internal standard.

3.2. Compound 9a. General procedure for method A

To a mixture of PPh_3 (15.2 mg, 0.058 mmol) and $Pd(OAc)_2$ (6.5 mg, 0.029 mmol) in a 5 mL test tube was added a solution of enyne **7a** (100 mg, 0.58 mmol) in dry toluene (1 mL). The mixture was stirred for 10 min under argon atmosphere and then treated with formic acid (27 μL, 0.69 mmol) via a gastight syringe. The mixture was stirred for 2 h at 60°C in a preheated oil bath. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. Silica gel chromatography (1:9 EtOAc/hexane) of the residue gave the product **9a** (64.6 mg, 64%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (t, *J*=7.6 Hz, 2H), 7.22 (t, *J*=7.2 Hz, 1H), 7.15 (d, *J*=7.6 Hz, 2H), 6.30 (d, *J*=2.0 Hz, 1H), 4.67 (ABq, Δδ=33.6 Hz, *J*=14.0 Hz, 2H), 4.08 (dd, *J*=7.6, 8.0 Hz, 1H), 3.39 (dd, *J*=8.0, 8.0 Hz, 1H), 2.92 (m, 1H), 1.22 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.31, 137.22, 128.37, 127.74, 126.36, 119.78, 74.28, 70.31, 39.87, 16.51; FT-IR (neat, cm^{-1}): 3055, 3025, 2964, 2842, 1662, 1492, 1447, 1374, 1081, 1063; HRMS calcd for $C_{12}H_{14}O$ (M^+) 174.1044, found 174.1046.

3.2.1. Compound 9b and *epi*-9b. 9b ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J*=8.0 Hz, 2H), 7.11 (d, *J*=8.0 Hz, 2H), 5.06 (d, *J*=2.8 Hz, 1H), 4.99 (d, *J*=2.8 Hz, 1H), 4.05 (dd, *J*=8.0, 8.0 Hz, 1H), 3.47 (dd, *J*=8.0, 8.0 Hz, 1H), 2.72 (m, 1H), 2.32 (s, 3H), 1.59 (s, 3H), 1.13 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.11, 142.77, 136.20, 128.62, 124.67, 104.53, 85.34, 71.86, 37.71, 28.25, 21.16, 16.33; FT-IR (neat, cm^{-1}): 3079, 3024, 2971, 2928, 2870, 1664, 1508, 1450, 1368, 1084, 1033; HRMS calcd for $C_{14}H_{18}O$ (M^+) 202.1357, found 202.1360.; *epi*-**9b** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J*=8.4 Hz, 2H), 7.13 (d, *J*=8.4 Hz, 2H), 5.10 (d, *J*=2.0 Hz, 1H), 5.03 (d, *J*=2.0 Hz, 1H), 4.10 (dd, *J*=8.8, 8.8 Hz, 1H), 3.27 (dd, *J*=8.8, 8.8 Hz, 1H), 2.94 (m, 1H), 2.33 (s, 3H), 1.59 (s, 3H), 1.02 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.03, 142.01, 136.26, 128.66, 125.39, 105.71, 85.46, 71.82, 38.93, 29.55, 21.12, 17.27; FT-IR (neat, cm^{-1}): 2973, 2928, 2870, 1662, 1508, 1450, 1373, 1182, 1137, 1103, 1033, 1020.

3.2.2. Compound 9c. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.29 (m, 4H), 7.19 (m, 1H), 6.22 (d, *J*=2.8 Hz, 1H), 4.18 (m, 4H), 3.29 (ABq, Δδ=68.4 Hz, *J*=17.6 Hz, 2H), 2.78 (m, 1H), 2.59 (ddd, *J*=12.4, 7.2, 1.2 Hz, 1H), 1.75 (dd, *J*=12.4, 11.6 Hz, 1H), 1.25 (t, *J*=7.2 Hz, 3H), 1.23 (t, *J*=7.2 Hz, 3H), 1.22 (d, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.76, 171.72, 146.23, 137.83, 128.19, 128.17, 126.06, 121.30, 61.56, 59.04, 41.36, 39.09, 38.88, 18.33, 14.07, 14.05; FT-IR (neat, cm^{-1}): 3023, 2979, 2933, 2870, 1730, 1492, 1447, 1299, 1276, 1250, 1177, 1152, 1060, 1029; HRMS calcd for $C_{19}H_{24}O_4$ (M^+) 316.1674, found 316.1669.

3.2.3. Compound 9d and *epi*-9d. 9d ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J*=6.8 Hz, 2H), 7.31 (t, *J*=6.8 Hz, 2H), 7.22 (t, *J*=6.8 Hz, 1H), 5.08 (d, *J*=2.8 Hz, 1H), 5.01 (d, *J*=2.4 Hz, 1H), 4.07 (dd, *J*=8.6, 8.6 Hz, 1H), 3.48 (dd,

J=8.6, 8.6 Hz, 1H), 2.72 (m, 1H), 1.60 (s, 3H), 1.14 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.02, 145.72, 127.97, 126.65, 124.77, 104.71, 85.43, 71.91, 37.65, 28.21, 16.23; FT-IR (neat, cm^{-1}): 3081, 2970, 2929, 2870, 1663, 1560, 1491, 1446, 1369, 1215, 1066, 1028; HRMS calcd for $C_{13}H_{16}O$ (M^+) 188.1201, found 188.1205; *epi*-**9d** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J=8.0 Hz, 2H), 7.31 (t, J=8.0 Hz, 2H), 7.22 (t, J=8.0 Hz, 1H), 5.11 (d, J=2.4 Hz, 1H), 5.03 (d, J=2.4 Hz, 1H), 4.11 (dd, J=8.4, 8.4 Hz, 1H), 3.28 (dd, J=8.4, 8.4 Hz, 1H), 2.94 (m, 1H), 1.60 (s, 3H), 1.01 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.03, 145.05, 128.03, 126.78, 125.50, 105.94, 85.54, 71.87, 38.86, 29.44, 17.24; FT-IR (neat, cm^{-1}): 3059, 2961, 2926, 2854, 1738, 1490, 1447, 1373, 1137, 1071, 1026.

3.2.4. Compound 9e. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, J=8.8 Hz, 2H), 6.88 (d, J=8.8 Hz, 2H), 5.20 (d, J=2.0 Hz, 1H), 4.96 (dd, J=2.8, 2.8 Hz, 1H), 4.76 (dd, J=2.8, 3.2 Hz, 1H), 4.30 (dd, J=8.4, 8.0 Hz, 1H), 3.80 (s, 3H), 3.41 (dd, J=8.4, 9.6 Hz, 1H), 2.90 (m, 1H), 1.16 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.98, 156.90, 133.93, 128.17, 113.62, 105.38, 83.46, 74.53, 55.29, 38.69, 15.37; FT-IR (neat, cm^{-1}): 3076, 2963, 2931, 2871, 2837, 1667, 1612, 1586, 1513, 1463, 1303, 1248, 1172; HRMS calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1138.

3.2.5. Compound 9f. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (m, 1H), 7.18 (m, 3H), 5.48 (d, J=2.0 Hz, 1H), 4.97 (dd, J=2.8, 2.8 Hz, 1H), 4.72 (dd, J=2.4, 2.8 Hz, 1H), 4.32 (dd, J=8.0, 8.0 Hz, 1H), 3.43 (dd, J=9.6, 8.0 Hz, 1H), 2.96 (m, 1H), 2.42 (s, 3H), 1.19 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.28, 139.24, 136.14, 130.47, 127.64, 127.53, 125.97, 105.25, 81.17, 74.58, 38.93, 19.54, 15.70; FT-IR (neat, cm^{-1}): 3075, 3024, 2964, 2929, 2870, 1665, 1491, 1461, 1288, 1062, 1033; HRMS calcd for $C_{13}H_{16}O$ (M^+) 188.1201, found 188.1197.

3.2.6. Compound *trans*-10g[18]**.** ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.95 (dd, J=0.8, 1.2 Hz, 1H), 4.86 (dd, J=0.8, 1.2 Hz, 1H), 3.96 (td, J=2.4, 2.4 Hz, 1H), 2.54 (m, 1H), 1.69 (dd, J=12.6, 8.8 Hz, 1H), 1.07 (d, J=7.2 Hz, 3H), 1.00 (dd, J=12.8, 9.6 Hz, 1H), 0.98 (s, 3H), 0.93 (s, 9H), 0.77 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.24, 105.85, 82.19, 44.89, 41.21, 33.15, 27.16, 26.09, 21.92, 20.27, 18.34, −4.01, −4.23; FT-IR (neat, cm^{-1}): 2958, 2930, 2858, 1664, 1472, 1463, 1385, 1366, 1257, 1116; HRMS calcd for $C_{15}H_{30}OSi$ (M^+) 254.2066, found 254.2083.

3.2.7. Compound *trans*-10h and *cis*-10h. *trans*-**10h** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.30 (m, 4H), 7.19 (t, J=7.6 Hz, 1H), 6.37 (d, J=1.6 Hz, 1H), 3.80 (s, 1H), 3.09 (m, 1H), 1.76 (dd, J=12.2, 8.4 Hz, 1H), 1.58 (dd, J=13.4, 7.2 Hz, 1H), 1.15 (d, J=6.8 Hz, 3H), 1.01 (s, 3H), 0.91 (s, 9H), 0.85 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.67, 137.48, 128.25, 128.09, 126.15, 124.64, 87.33, 46.60, 41.60, 32.88, 26.23, 26.02, 22.98, 22.79, 21.05, 18.37, −3.49, −4.44; FT-IR (neat, cm^{-1}): 3059, 3026, 2957, 2930, 2859, 2365, 1602, 1494, 1471, 1385, 1362, 1251, 1170, 1158, 1142, 1071, 1051; HRMS calcd for $C_{21}H_{34}OSi$(M^+) 330.2379, found 330.2365; *cis*-**10h** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.19 (m, 5H), 4.97 (d, J=2.0 Hz, 1H), 4.92 (d, J=2.0 Hz, 1H), 4.37 (s, 2H), 3.86 (dd, J=8.8, 6.4 Hz, 1H), 3.60 (dd, J=8.8, 6.0 Hz, 1H), 2.95 (m, 1H), 2.94 (dd, J=15.2, 5.2 Hz, 1H), 2.63 (dd, J=15.2, 11.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.09, 139.83, 128.64, 128.28, 126.06, 104.01, 73.52, 71.62, 45.31, 38.82; FT-IR (neat, cm^{-1}): 3062, 3026, 2938, 2848, 1665, 1495, 1453, 1182, 1063.

3.2.8. Compound *trans*-10i and *cis*-10i. *trans*-**10i** ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.10 (dd, J=2.8, 2.4 Hz, 1H), 4.97 (dd, J=2.8, 2.0 Hz, 1H), 3.99 (dq, J=8.8, 2.8 Hz, 1H), 2.56 (m, 1H), 1.73 (dd, J=12.6, 8.4 Hz, 1H), 1.33 (d, J=8.4 Hz, 1H), 1.09 (d, J=7.2 Hz, 3H), 1.07 (s, 3H), 1.04 (dd, J=12.6, 10.0 Hz, 1H), 0.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.71, 106.35, 82.27, 44.87, 40.91, 33.31, 26.47, 21.32, 19.42; FT-IR (neat, cm^{-1}): 3382, 2956, 2926, 2868, 1660, 1462, 1383, 1366, 1153, 1083, 1052; HRMS calcd for $C_9H_{16}O$ (M^+) 140.1201, found 140.1209.; *cis*-**10i** ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.15 (dd, J=2.0, 2.0 Hz, 1H), 4.96 (dd, J=2.0, 2.0 Hz, 1H), 3.92 (d, J=6.4 Hz, 1H), 2.54 (m, 1H), 1.73 (dd, J=12.6, 9.4 Hz, 1H), 1.31 (dd, J=12.6, 7.2 Hz, 1H), 1.29 (d, J=6.4 Hz, 1H), 1.14 (d, J=6.8 Hz, 3H), 0.98 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.37, 106.59, 82.79, 44.77, 40.31, 32.82, 26.57, 21.97, 20.74; FT-IR (neat, cm^{-1}): 3408, 2958, 2929, 2869, 1659, 1460, 1365, 1279, 1175, 1106, 1076, 1028.

3.2.9. Compound *trans*-10j and *cis*-10j. *trans*-**10j** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, J=7.6 Hz, 2H), 7.31 (t, J=7.6 Hz, 2H), 7.19 (t, J=7.6 Hz, 1H), 6.38 (t, J=2.0 Hz, 1H), 4.44 (dt, J=5.2, 2.0 Hz, 1H), 2.84 (m, 1H), 1.89 (dd, J=12.4, 8.8 Hz, 1H), 1.59 (d, J=5.2 Hz, 1H), 1.24 (d, J=6.8 Hz, 3H), 1.12 (dd, J=12.4, 8.8 Hz, 1H), 1.00 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.03, 137.11, 128.47, 128.27, 126.57, 124.76, 80.81, 45.15, 41.67, 35.84, 27.60, 21.53, 20.64; FT-IR (neat, cm^{-1}): 3584, 3436, 3057, 3024, 2956, 2868, 1598, 1494, 1447, 1382, 1074, 1045; HRMS calcd for $C_{15}H_{20}O$ (M^+) 216.1514, found 216.1509; *cis*-**10j** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J=7.2 Hz, 2H), 7.33 (t, J=7.2 Hz, 2H), 7.22 (tt, J=7.2, 2.0 Hz, 1H), 6.47 (d, J=1.6 Hz, 1H), 4.13 (d, J=4.4 Hz, 1H), 2.77 (m, 1H), 1.66 (dd, J=12.2, 7.2 Hz, 1H), 1.48 (dd, J=12.2, 11.2 Hz, 1H), 1.47 (d, J=4.4 Hz, 1H), 1.25 (d, J=6.8 Hz, 3H), 1.12 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.98, 137.29, 128.29, 128.26, 127.73, 126.69, 79.82, 44.83, 42.57, 37.14, 25.84, 22.61, 22.50; FT-IR (neat, cm^{-1}): 3583, 3469, 3057, 3025, 2956, 2928, 2868, 1598, 1494, 1449, 1383, 1232, 1064, 1018.

3.3. Compound 10a. General procedure for method B

To a mixture of $Pd(dppe)Cl_2$ (9.9 mg, 0.017 mmol) in a 5 mL test tube was added a solution of enyne **7a** (96.5 mg, 0.56 mmol) in dry toluene (1 mL). The mixture was stirred for 10 min under argon atmosphere and then treated with Et_3SiH (110 μL, 0.69 mmol) and formic acid (26 μL, 0.67 mmol) via gastight syringes. The mixture was stirred for 3 h at 60°C in a preheated oil bath. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. Silica gel chromatography (1:9

EtOAc/hexane) of the residue gave the product **10a** (68.2 mg, 70%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.19 (m, 5H), 4.97 (d, J=2.0 Hz, 1H), 4.92 (d, J=2.0 Hz, 1H), 4.37 (s, 2H), 3.86 (dd, J=8.8, 6.4 Hz, 1H), 3.60 (dd, J=8.8, 6.0 Hz, 1H), 2.95 (m, 1H), 2.94 (dd, J=15.2, 5.2 Hz, 1H), 2.63 (dd, J=15.2, 11.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.09, 139.83, 128.64, 128.28, 126.06, 104.01, 73.52, 71.62, 45.31, 38.82; FT-IR (neat, cm^{-1}): 3062, 3026, 2938, 2848, 1665, 1495, 1453, 1182, 1063; HRMS calcd for $C_{12}H_{14}O$ (M^+) 174.1044, found 174.1040.

3.3.1. Compound 10b. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J=8.0 Hz, 2H), 7.16 (d, J=8.0 Hz, 2H), 4.92 (d, J=2.4 Hz, 1H), 4.87 (d, J=2.4 Hz, 1H), 4.52 (ABq, $\Delta\delta$=50.4 Hz, J=13.2 Hz, 2H), 2.67 (m, 1H), 2.34 (s, 3H), 1.32 (s, 3H), 1.09 (d, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.28, 143.19, 136.26, 128.71, 124.71, 103.11, 85.92, 69.03, 48.95, 21.14, 20.57, 12.73; FT-IR (neat, cm^{-1}): 2971, 2924, 2858, 2361, 2342, 1669, 1514, 1459, 1376, 1306, 1240, 1186, 1078, 1037; HRMS calcd for $C_{14}H_{18}O$ (M^+) 202.1357, found 202.1362.

3.3.2. Compound 10c. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.19 (m, 5H), 4.99 (d, J=2.4 Hz, 1H), 4.88 (d, J=2.4 Hz, 1H), 4.37 (s, 2H), 4.16 (m, 4H), 3.03 (dd, J=13.6, 5.2 Hz, 1H), 3.01 (ABq, $\Delta\delta$=29.4 Hz, J=16.8 Hz, 2H), 2.87 (m, 1H), 2.50 (dd, J=13.6, 10.4 Hz, 1H), 2.36 (dd, J=13.0, 7.6 Hz, 1H), 1.85 (dd, J=13.0, 10.4 Hz, 1H), 1.23 (t, J=7.2 Hz, 3H), 1.21 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.56, 171.53, 151.36, 140.19, 128.71, 128.19, 125.87, 106.52, 61.54, 61.47, 53.24, 43.80, 41.05, 40.34, 39.62, 14.16, 14.13; FT-IR (neat, cm^{-1}): 2983, 2932, 1731, 1657, 1451, 1367, 1254, 1181, 1072, 1019; HRMS calcd for $C_{19}H_{24}O_4$ (M^+) 316.1674, found 316.1677.

3.3.3. Compound 10d. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J=7.2 Hz, 2H), 7.35 (t, J=7.2 Hz, 2H), 7.26 (t, J=7.2 Hz, 1H), 4.93 (d, J=2.0 Hz, 1H), 4.88 (d, J=2.0 Hz, 1H), 4.53 (ABq, $\Delta\delta$=50.2 Hz, J=13.2 Hz, 2H), 2.68 (m, 1H), 1.34 (s, 3H), 1.10 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.25, 146.23, 128.10, 126.79, 124.84, 103.25, 86.00, 69.07, 48.91, 20.45, 12.62; FT-IR (neat, cm^{-1}): 3060, 2972, 2857, 1667, 1494, 1446, 1377, 1304, 1073, 1037; HRMS calcd for $C_{13}H_{16}O$ (M^+) 188.1201, found 188.1208.

3.3.4. Compound 10e. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, J=8.4 Hz, 2H), 6.90 (d, J=8.8 Hz, 2H), 4.97 (d, J=2.8 Hz, 1H), 4.90 (d, J=2.4 Hz, 1H), 4.55 (ABq, $\Delta\delta$=107.6 Hz, J=13.2 Hz, 2H), 4.22 (d, J=9.6 Hz, 1H), 3.82 (s, 3H), 2.49 (m, 1H), 1.06 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.11, 153.06, 132.36, 127.71, 113.64, 102.85, 87.89, 71.17, 55.31, 46.37, 13.49; FT-IR (neat, cm^{-1}): 2961, 2836, 1666, 1613, 1515, 1462, 1374, 1303, 1248, 1173, 1059, 1035; HRMS calcd for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1143.

3.3.5. Compound 10f. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J=7.2 Hz, 1H), 7.20 (m, 3H), 4.98 (d, J=2.4 Hz, 1H), 4.91 (d, J=2.4 Hz, 1H), 4.62 (d, J=9.6 Hz, 1H), 4.58 (ABq, $\Delta\delta$=97.4 Hz, J=13.6 Hz, 2H), 2.65 (m, 1H), 2.38 (s, 3H), 1.11 (d, J=6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.23, 138.36, 135.99, 130.36, 127.56, 126.23, 126.15, 102.98, 84.43, 71.16, 46.12, 19.49, 14.08; FT-IR (neat, cm^{-1}): 3075, 3026, 2962, 2930, 1668, 1492, 1461, 1375, 1057, 1039; HRMS calcd for $C_{13}H_{16}O$ (M^+) 188.1201, found 188.1193.

Acknowledgements

We wish to acknowledge the financial support of KOSEF (1999-1-123-001-5), Korea, made in the program year of 1999.

References

1. Widenhoefer, R. A.; Stengone, C. N. *J. Org. Chem.* **1999**, *64*, 8681–8692.
2. For reviews, see: (a) Trost, B. M. *Science* **1991**, *254*, 1471–1477. (b) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34–42. (c) Trost, B. M.; Krische, M. J. *Synlett* **1998**, 1–16. (d) Lu, X.; Zhu, G.; Wang, Z.; Ma, S.; Ji, J.; Zhang, Z. *Pure Appl. Chem.* **1997**, *69*, 553–558.
3. Trost, B. M.; Li, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6625–6633.
4. (a) Yamada, H.; Aoyagi, S.; Kibayashi, C. *Tetrahedron Lett.* **1997**, *38*, 3027–3030. (b) Trost, B. M.; Lautens, M.; Chan, C.; Jebaratnam, D. J.; Mueller, T. *J. Am. Chem. Soc.* **1991**, *113*, 636–644. (c) Grigg, R.; Loganathan, V.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T. *Tetrahedron* **1996**, *35*, 11479–11502.
5. (a) Trost, B. M.; Fleitz, F. J.; Watkins, W. J. *J. Am. Chem. Soc.* **1996**, *118*, 5146–5147. (b) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580.
6. (a) Stork, G.; Mook, Jr., R. *J. Am. Chem. Soc.* **1987**, *109*, 2829–2831. (b) Stork, G.; Mook, Jr., R. *J. Am. Chem. Soc.* **1983**, *105*, 3720–3722. For extended works, see: (c) Beckwith, A. L. J.; O'Shea, D. M. *Tetrahedron Lett.* **1986**, *27*, 4525–4528. (d) Clive, D. L. J.; Magnuson, S. R.; Manning, H. W.; Mayhew, D. L. *J. Org. Chem.* **1996**, *61*, 2095–2108.
7. Oh, C. H.; Kim, A.; Rhim, C. Y.; Kang, J. H.; Park, B. S. *Bull. Koran Chem. Soc.* **1996**, *17*, 879–881.
8. For the use of formic acid or formates as a hydrogen equivalent in palladium-mediated reactions, see: (a) Tsuji, J. *Palladium Reagents and Catalysts*, Wiley: Chichester, England, 1995. (b) Tsuji, J.; Mandai, T. *Synthesis* **1996**, 1–24.
9. (a) Oh, C. H.; Rhim, C. Y.; Kang, J. H.; Kim, A.; Park, B. S.; Seo, Y. *Tetrahedron Lett.* **1996**, *37*, 8875–8878. (b) Oh, C. H.; Jung, H. H. *Tetrahedron Lett.* **1999**, *40*, 1535–1538.
10. Oh, C. H.; Jung, H. H.; Kim, J. S.; Cho, S. W. *Angew. Chem. Int., Ed. Engl.* **2000**, *39*, 752–755.
11. Trost, B. M.; Edstrom, E. D.; Carter-Petillo, M. B. *J. Org. Chem.* **1989**, *54*, 4489–4490.
12. (a) Wratten, S. J.; Faulkner, D. J. *J. Org. Chem.* **1977**, *42*, 3343–3349. (b) Irie, T.; Yasunari, Y.; Suzuki, T.; Imai, N.; Kurosawa, E.; Masamune, T. *Tetrahedron Lett.* **1965**, *6*, 3619–3624. (c) Irie, T.; Suzuki, T.; Yasunari, Y.; Kurosawa, E.; Masamune, T. *Tetrahedron* **1969**, *25*, 459–468. (d) Bailey, W. F.; Jiang, X.-L.; McLeod, C. E. *J. Org. Chem.* **1995**, *60*, 7791–7795.
13. Trost, B. M.; Rise, F. *J. Am. Chem. Soc.* **1987**, *109*, 3161–3163.

14. (a) Wratten, S. J.; Faulkner, D. J. *J. Org. Chem.* **1977**, *42*, 3343–3349. (b) Hall, J. G.; Reiss, J. A. *Aus. J. Chem.* **1986**, *39*, 1401–1409.
15. *epi*-**10** Was not fully characterized due to a limited amount of the isolated product.
16. Oh, C. H.; Han, J. W.; Kim, J. S.; Um, S. Y.; Jung, H. H.; Jang, W. H.; Won, H. S. *Tetrahedron Lett.* **2000**, *53*, 8365–8369.
17. Yamada, H.; Aoyagi, S.; Kibayashi, C. *Tetrahedron Lett.* **1996**, *37*, 8787–8790.
18. Full characterization of *cis*-**10g** has not been accomplished, since the desilylated product of *cis*-**10g** and the *cis*-**10i** were identical in their ^{1}H NMR spectra except some peaks corresponding to impurities.