Allenes as Carbon Nucleophiles in Intramolecular Attack on (π-1,3-Diene)-palladium Complexes: Evidence for *trans* Carbopalladation of the 1,3-Diene

Ismet Dorange, Joakim Löfstedt, Katja Närhi, Johan Franzén, and Jan-E. Bäckvall*[a]

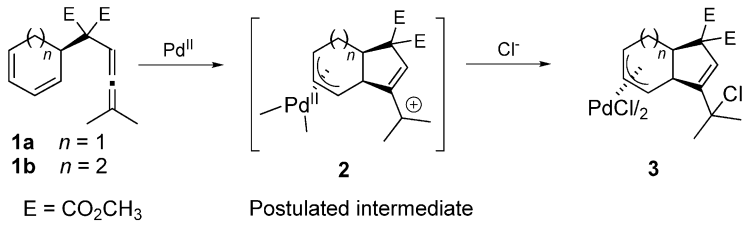
Abstract: Reaction of allene-substituted cyclohexa- and cyclohepta-1,3-dienes with $[PdCl_2(PhCN)_2]$ gave η^3-(1,2,3)-cyclohexenyl- and η^3-(1,2,3)-cycloheptenylpalladium complexes, respectively, in which C–C bond formation between the allene and the 1,3-diene has occurred. Analysis of the (π-allyl)palladium complexes by NMR spectroscopy, using reporter ligands, shows that the C–C bond formation has occurred by a *trans* carbopalladation involving nucleophilic attack by the middle carbon atom of the allene on a (π-diene)palladium(II) complex. The stereochemistry of the (π-allyl)palladium complexes was confirmed by benzoquinone-induced stereoselective transformations to allylic acetates.

Keywords: C-C coupling · carbopalladation · palladium · reaction mechanisms

Introduction

Palladium(II)-catalyzed oxidations of unsaturated hydrocarbons are of importance in organic chemistry.[1–3] These reactions involve nucleophilic addition to carbon–carbon double bonds coordinated to palladium(II) centers, and recently they have been extended to enantioselective versions.[4, 5] An important point regarding the nucleophilic addition is the stereochemistry of the process.[6, 7] The nucleophile can coordinate to the metal center and then migrate to the coordinated double bond (insertion of olefinic bond into the palladium-nucleophile bond) or the nucleophile may attack the coordinated olefin on the face opposite to that of the metal (*trans* attack).[6, 8]

We recently reported on an intramolecular palladium(II)-catalyzed reaction of allenic conjugated dienes involving carbon–carbon bond formation between the allene and diene moieties.[9] Several mechanisms were proposed as likely pathways and one of the mechanisms considered involves *trans* nucleophilic attack by the allene on a (π-diene)palladium(II) complex. Such *trans* attack by π-nucleophiles on coordinated carbon–carbon double bonds is rare and the only established example is allylsilane attack on a (π-diene)palladium complex.[10, 11] We now report on a *trans* nucleophilic addition of an allene to a (π-1,3-diene)palladium complex, which leads to a *trans* carbopalladation of the double bond of the conjugated diene (Scheme 1).[12]



Scheme 1. Carbopalladation of 1,3-diene.

Results and Discussion

Recent studies in our laboratories, carried out with the explicit purpose of gaining further insight into the mechanism of the palladium(0)-catalyzed carbocyclization of allenic allylic ester derivatives, indicated that the allene moiety can act as a π-nucleophile on a (π-allyl)palladium complex under certain conditions.[13] In the palladium(II)-catalyzed reaction of **1a** using benzoquinone as the oxidant, allylic acetate **4a** was obtained as the product (Scheme 2). There are three possible mechanisms for the formation of **4a**; 1) attack by the allene on the (π-diene)palladium intermediate followed by benzoquinone-induced acetate migration;[14] 2) nucleophilic attack by the allene on the Pd^{II} center, followed by insertion of the olefin into the C_{vinyl}–Pd bond; and 3) acetoxypalladation of the 1,3-diene and subsequent insertion of the allene into the

[a] Prof. Dr. J.-E. Bäckvall, Dr. I. Dorange, Dr. J. Löfstedt, K. Närhi, J. Franzén
Department of Organic Chemistry, Arrhenius Laboratory
Stockholm University, 10691 Stockholm (Sweden)
Fax: (+46) 8-154908
E-mail: jeb@organ.su.se

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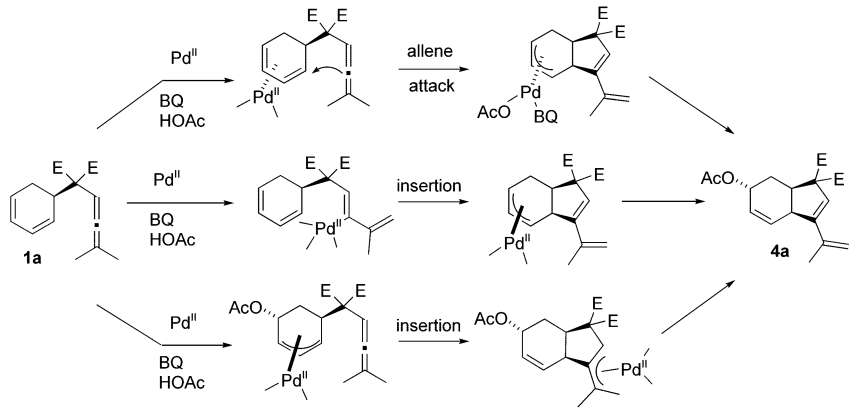
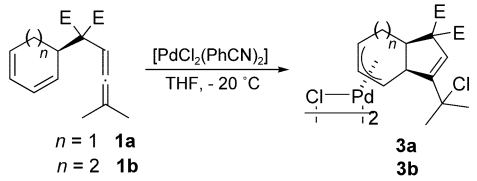


Scheme 2. Allene attack versus insertion mechanism for the formation of **4a**. BQ = 1,4-benzoquinone, E = CO_2CH_3.

C_{allyl}–Pd bond (Scheme 2).[15] In all three pathways the Pd^0 center generated is reoxidized to Pd^{II} by benzoquinone.

Synthesis of complexes 3: To obtain evidence for a possible pathway through attack by the allenic subunit on the (π-diene)palladium(II) complex from the opposite face of the metal, we focused on the isolation of possible (π-allyl)palladium complexes from the reaction of **1** with Pd^{II} (Schemes 1 and 2). In previous studies carried out in our laboratories, bicyclic (π-allyl)palladium complexes were isolated from intramolecular attack by heteroatom and carbon nucleophiles on the 1,3-diene in the presence of stoichoimetric amounts of palladium(II).[10, 16, 17]

The same reaction conditions were tested with the allenic 1,3-dienes, and the best conditions were found to involve the use of $[PdCl_2(PhCN)_2]$ at low temperature [Eq. (1)]. Reaction of allenic diene **1a** with $[PdCl_2(PhCN)_2]$ in anhydrous THF at −20 °C afforded (π-allyl)complex **3a** in quantitative yield. The same reaction conditions were successfully applied to the seven-membered analogue **1b**, which afforded π-allyl complex **3b**.

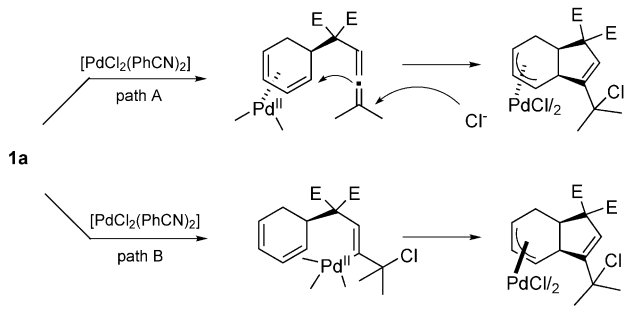


(1)

E = CO_2CH_3

Without knowing the stereochemistry of π-allyl complexes **3a** and **3b**, two pathways are possible for their formation. They may be formed by nucleophilic attack by the central carbon atom of the pendant allene on the Pd^{II}-activated 1,3-diene or they may be formed by chloropalladation of the allene followed by insertion of the 1,3-diene into the C_{vinyl}–Pd bond (Scheme 3). In the former pathway (path A in Scheme 3) the allenic carbocation formed would be trapped by a chloride ion. Stereochemical assignments of the π-allyl complexes **3a** and **3b** would differentiate between these pathways since the former pathway proceeds by *trans* carbopalladation of the 1,3-diene, while the latter pathway involves *cis* carbopalladation of the 1,3-diene.

Stereochemical assignment of complexes 3: The stereochemistry of **3b** was assigned by the use of the reporter ligand technique.[10, 13, 18, 19] Complex **3b** was transformed into its analogous bipyridine complex **5**, using a modified literature procedure (Scheme 4).[20] Irradiation of the bridgehead proton H_a' in **5** resulted in a 10% NOE enhancement for the other bridgehead proton H_a and a 5% NOE enhancement for the signal of the 2-protons of the bipyridine moiety (H_b). The former NOE proves the *cis* stereochemistry of the ring junction, and the latter NOE

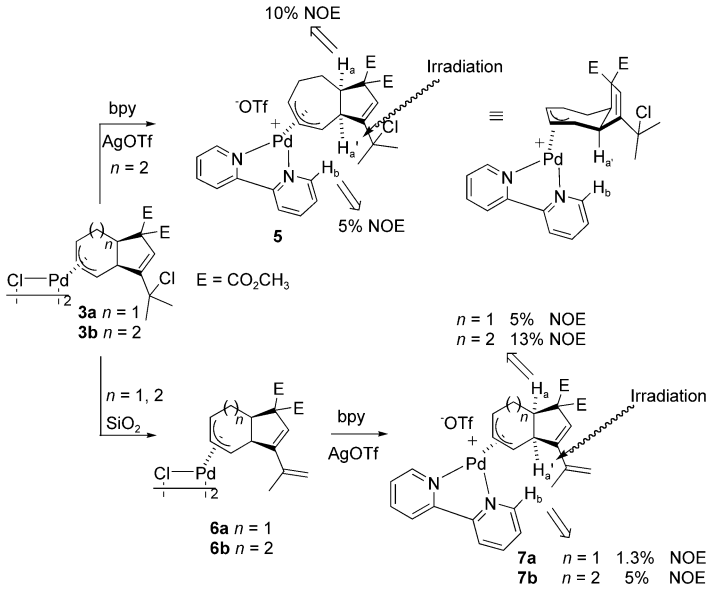


Scheme 3. Two possible pathways for the formation of π-allyl complex.

shows that the metal is located on the same face of the ring as the bridgehead protons and hence *trans* to the carbon atom that has added to the diene. This establishes that nucleophilic attack by the central carbon atom of the allene group on the coordinated diene has occurred on the face opposite to that of the palladium atom (*trans* carbopalladation). Therefore, the insertion pathway, in which the metal and the nucleophilic carbon atom would have been located on the same side of the bicycle, can be ruled out.

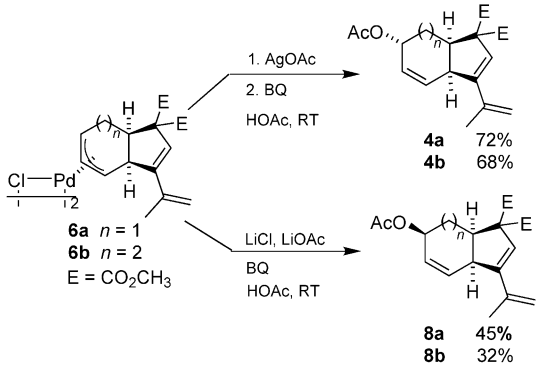
For a comparison with our previous results,[9] complexes **3a** and **3b** were transformed to their isoprenyl analogues **6a** and **6b**, respectively, by treatment with silica gel (Scheme 4). Treatment of complexes **3a** and **3b** with silica in CH_2Cl_2 at room temperature overnight afforded complexes **6a** and **6b**, respectively. Complexes **6a** and **6b** were subsequently allowed to react with 2,2′-bipyridine in the presence of AgOTf to give complexes **7a** and **7b**. NOE difference experiments analogous to those carried out on complex **5** confirmed that the palladium center is *trans* to the carbon atoms in the fused five-membered ring.

The stereochemical assignment of complexes **6a** and **6b** was confirmed by their transformation to allylic acetate



Scheme 4. Assignments of the stereochemistry by using reporter ligand technique.

products **4a**/**8a** and **4b**/**8b**,[21] respectively. Treatment of complex **6a** with AgOAc to give the (π-allyl)PdOAc complex followed by addition of *p*-benzoquinone (BQ) afforded (via acetate migration) the known compound **4a** in 72% yield (Scheme 5).[14, 22] Reaction of **6a** in the presence of LiCl,



Scheme 5. Stereoselective transformations of complexes **6a** and **6b**.

LiOAc, and BQ, conditions known to give external acetate attack,[14] produced allylic acetate **8a** in 45% yield as a 2:1 mixture of **8a**:**4a**.[23] The stereochemistry of these two products (**4a** and **8a**) requires that the palladium center and the five-membered ring are *trans* to one another in **6a**. The analogous *cis* and *trans* acetoxylation reactions were also carried out on the seven-membered ring complex **6b** to give **4b** (68% yield) and **8b**[21] (32% yield, as a 3:1 mixture of **8b**:**4b**), respectively, which confirms the stereochemical assignment made by NOE difference experiments.

Mechanistic considerations: A general picture regarding the π-nucleophilicity of allenes is emerging. In the present study, we have shown that a pendant allene can attack a (π-1,3-diene)palladium complex to give *trans* carbopalladation of the diene, and in previous work[13] we demonstrated that an allene can attack a (π-allyl)-palladium complex *trans* to the metal center in an intramolecular reaction. Thus, the allene can function as a nucleophile in attack on unsaturated hydrocarbon ligands coordinated to palladium center in analogy with other π-nucleophiles such as enol ethers[24] and allylsilanes.[10, 25] An interesting question is whether the allene requires activation by a nucleophilic center to act as a π-nucleophile. In our previous study,[13] in which Pd^0 catalyzed the reaction, we considered a pathway that involved formation of a carbonium ion, which is trapped by Pd^0. Alternatively, a nucleophilic Pd^0 center could activate the allene and trigger the attack. In the present study an analogous nucleophilic activation, in this case by chloride ion, may trigger the nucleophilic attack by the allene (see Scheme 3, path A). Support for activation of the allene by a chloride ion is provided with the fact that no *trans* carbopalladation occurred when $[PdCl_2(PhCN)_2]$ was replaced by $Pd(OAc)_2$.

Conclusion

This study constitutes the first established example of nucleophilic attack of an allene on a (π-1,3-diene)palladium complex. The reaction is stereospecific, affording (π-allyl)-palladium complexes of bicyclo[5.3.0] or bicyclo[4.3.0] systems having a *cis*-ring junction. These π-allyl complexes can subsequently undergo a second nucleophilic attack. The stereochemical outcome of the second nucleophilic attack can be controlled by using different reaction conditions, making this methodology a valuable tool in organic chemistry. Studies to further explore the synthetic utility of this novel reaction are in progress.

Experimental Section

All reactions were carried out under inert atmosphere of dry argon unless otherwise noted. All glassware used was oven-dried (120 °C) or flame-dried. Organic solvents/reagents were purified prior to use as follows: THF and diethyl ether were freshly distilled from Na/benzophenone, CH_2Cl_2 was distilled from CaH_2. Column chromatography was performed on flash-grade silica gel. Eluting solvents are reported as v/v % mixture. Preparative thin-layer chromatography was performed on Merck silica gel 60 F_{254} 0.25 mm plates. ^1H NMR (400 or 300 MHz) and ^{13}C NMR (100 or 75 MHz) spectra were recorded by using $[D_1]$chloroform or $[D_3]$acetonitrile as internal standard. Starting material **1a/1b** were synthesized as described in ref. [9].

General procedure for the preparation of (π-Allyl)palladium complexes, as exemplified with the preparation of complex 3b: A flame-dried round bottom flask was charged with $[PdCl_2(PhCN)_2]$ (90.8 mg, 1 equiv) under argon. The flask was then cooled down to $-18\,^{\circ}C$ and a solution of **1b** (102 mg, 0.35 mmol) in anhydrous THF (4 mL) was added by syringe. The brown solution was then stirred at $-18\,^{\circ}C$ overnight under an inert atmosphere of argon. The solvent was evaporated in vacuo to give a brown oil, which was then dissolved in CH_2Cl_2. The solution was washed with H_2O and the aqueous phases were combined and back extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered, and concentrated to yield **3b** (150 mg, quantitative yield) as a yellowish oil. ^1H NMR: (300 MHz, $CDCl_3$): $\delta = 5.75$ (d, $J = 3$ Hz, 1H; H8), 5.51 (m, 1H), 5.12 (m, 1H), 4.92 (m, 1H), 3.98 (m, 1H), 3.72 (s, 3H; CH_3), 3.71 (m, 4H; CH_3 and H10), 2.04 (4H; H4, H4′, H5, H5′), 1.85 (s, 3H; CH_3), 1.82 ppm (s, 3H; CH_3).

(π-Allyl)palladium complex 3a: The same procedure as above was followed: reaction of $[PdCl_2(PhCN)_2]$ with **1a** (146 mg) afforded complex **3a** (210 mg; 95% yield), which was used without purification for the preparation of complex **6a**.

(π-Allyl)palladium complex 6a: Complex **3a** (200 mg) was dissolved in CH_2Cl_2 (100 mL) and silica gel (7 g) was added. The yellow slurry was stirred at room temperature overnight. Ethyl acetate (150 mL) was then added and the mixture was stirred for 1 h, then filtered and concentrated in vacuo to give **6a** (138.6 mg; 75% yield). Complex **6a** was further purified by preparative TLC (multiple development technique) to give a pure sample. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.64$ (s, 1H; H7), 5.33 (s, 1H; isoprenyl H11), 5.24 (ap. t, $J = 6.4$ Hz, 1H; H2), 5.19 (s, 1H; isoprenyl H11′), 5.05 (m, 1H; H3), 4.93 (d, $J = 6.4$ Hz, 1H; H1), 3.72 (s, 3H; CH_3), 3.68 (s, 3H; CH_3), 3.46 (d, $J = 7.8$ Hz, 1H; H9), 3.20 (t, $J = 7.8$ Hz, 1H; H5), 2.40 (dd, $J = 19.8$, 7.2 Hz, 1H; H4), 2.27 (dd, $J = 19.8$, 7.4 Hz, 1H; H4′), 1.94 ppm (s, 3H; CH_3 vinylic).

(π-Allyl)palladium complex 6b: The above protocol was followed with complex **3b** (150 mg), which afforded **6b** (106.5 mg; 77% yield). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 5.70$ (s, 1H; H8), 5.37 (s, 1H; isoprenyl H12), 5.21 (s, 1H; isoprenyl H12′), 5.05–4.76 (3H; H1, H2 and H3), 3.80 (m, 1H; overlap with CH_3, H10) 3.73 (s, 3H; CH_3), 3.69 (s, 3H; CH_3), 3.31 (m, 1H; H6), 2.30 (m, 1H; H4), 2.19–1.99 (3H; H4′, H5, H5′), 1.94 (s, 3H; CH_3 vinylic).

General procedure for the preparation of bipyridine(π-Allyl)palladium complex, as shown for complex 7a: An oven-dried NMR tube was charged with 2,2′-bipyridine (5.31 mg, 1 equiv). A solution of **6a** (14.1 mg, 0.017 mmol) in CD_3CN (0.5 mL) was added, and the tube was shaken until 2,2′-bipyridine was completely dissolved. AgOTf (8.73 mg, 1 equiv) was then added and immediate precipitation of a white solid was observed. The suspension was then filtered through a short pad of Celite and the filtrate concentrated. Complex **7a** could be further purified as follows: flash-grade silica gel was added to a solution of **7a** in CH_3CN and the solvent evaporated. The powder obtained was then added to a short column, eluted with Et_2O, and then with CH_3CN, which afforded after evaporation **7a**. ^1H NMR (300 MHz, CD_3CN): $\delta = 8.89$ (d, $J = 4.8$ Hz, 1H; bipyridine), 8.70 (d, $J = 4.8$ Hz, 1H; bipyridine), 8.41 (d, $J = 8.1$ Hz, 1H; bipyridine), 8.32 (d, $J = 8.1$ Hz, 1H; bipyridine), 8.25 (ap dt, $J = 7.8$, 1.5 Hz, 1H; bipyridine), 8.10 (appt, $J = 7.5$ Hz, 1H; bipyridine), 7.74 (appt, $J = 5.4$ Hz, 1H; bipyridine), 7.62 (appt, $J = 3.9$ Hz, 1H; bipyridine), 5.81 (t, $J = 6.6$ Hz, 1H; H2), 5.80 (s, 1H; H7), 5.38 (s, 1H; isoprenyl H11), 5.35 (s, 1H; isoprenyl H11′), 5.23 (appt, $J = 6.3$ Hz, 1H; H3), 5.10 (dd, $J = 6.9$, 0.9 Hz, 1H; H1), 3.76 (s, 3H; CH_3), 3.70 (s, 3H; CH_3), 3.53 (d, $J = 7.8$ Hz, 1H; H9), 3.19 (appt, $J = 7.8$ Hz, 1H; H5), 2.62 (ddd, $J = 19.0$, 6.0, 1.8 Hz, 1H; H4), 2.24 (dd, $J = 19.0$, 7.8 Hz, 1H; H4′), 2.18 ppm (s, 3H; CH_3). NOE experiment (300 MHz, CD_3CN): irradiation of H10 resulted in a 1.3% NOE enhancement for the *ortho*-bipyridyl proton ($\delta = 8.89$ and 8.70 ppm), 5% NOE for H11/H11′, 7% NOE for H1, and 5% NOE for H6 (other bridgehead proton).

(π-Allyl)palladium complex 5: Complex **5** was obtained by using the above procedure. ^1H NMR (400 MHz, CD_3CN): $\delta = 8.85$ (br s, 1H; bipyridine), 8.66 (br s, 1H; bipyridine), 8.45–8.26 (4H; bipyridine), 7.78–7.62 (2H), 5.84 (d, $J = 3.2$ Hz, 1H; H8), 5.70 (dd, $J = 8.8$, 4.0 Hz, 1H; H1), 5.44 (appt, $J = 8.4$ Hz, 1H; H2), 5.37 (appt, $J = 7.2$ Hz, 1H; H3), 4.09 (dd, $J = 8.0$, 4.3 Hz, 1H; H10), 3.66 (s, 3H; CH_3), 3.55 (s, 3H; CH_3), 3.23 (dd, $J = 11.2$, 4.3 Hz, 1H; H6), 2.46 (m, 1H; H4), 2.04 (m, 1H; H4′), 1.97 (s, 3H; CH_3), 1.96 (s, 3H; CH_3), 1.43–1.16 (2H, H5; H5′). NOE experiment (400 MHz, CD_3CN): irradiation of H10 resulted in a 5% NOE enhancement for the *ortho*-bipyridyl proton ($\delta = 8.85$ ppm), 7% NOE for H1, and 10% NOE for H6 (other bridgehead proton).

(π-Allyl)palladium complex 7b: Complex **7b** was obtained by using the general procedure. ^1H NMR: (400 MHz, CD_3CN): $\delta = 8.86$ (d, $J = 4.4$ Hz, 1H; bipyridine), 8.72 (d, $J = 4.4$ Hz, 1H; bipyridine), 8.43 (d, $J = 8.2$ Hz, 1H; bipyridine), 8.38 (d, $J = 8.0$ Hz, 1H; bipyridine), 8.29 (m, 1H; bipyridine), 8.09 (appt, $J = 7.6$ Hz, 1H; bipyridine), 7.76 (m, 1H; bipyridine), 7.63 (m, 1H; bipyridine), 5.82 (d, $J = 2.4$ Hz, 1H; H8), 5.45 (m, 1H; H1), 5.34–5.22 (4H; H2, H3, H12, H12′), 3.95 (ap dt, $J = 6.4$, 2 Hz, 1H; H10), 3.70 (s, 3H), 3.62 (s, 3H), 3.21 (m, 1H; H6), 2.20–2.07 (m, 2H; H4, H4′), 2.05 (s, 3H; CH_3 vinylic), 1.73–1.64 ppm (m, 2H; H5, H5′). NOE experiment (400 MHz, CD_3CN): irradiation of H10 resulted in a 2.5% NOE enhancement for the *ortho*-bipyridyl proton ($\delta = 8.86$ ppm), 2.9% NOE enhancement for the ortho-bipyridyl proton and $\delta = 8.72$ ppm), 9% NOE for the protons at $\delta = 5.34$–5.22 ppm, and 9% NOE for H6 (other bridgehead proton).

Allylic acetate 4a: To a stirred solution of (π-allyl)palladium complex **6a** (140 mg, 0.16 mmol) in acetic acid (0.65 mL) was added a suspension of AgOAc (58.8 mg, 1.1 equiv) in acetic acid (1 mL) at room temperature. The mixture was stirred for 20 min and a solution of 1,4-benzoquinone (70.3 mg, 2 equiv) in acetic acid (1 mL) was added. The reaction mixture turned black, and was allowed to stir at room temperature for 8 h. Brine (4 mL) was added and the was mixture filtered to remove all precipitates. The aqueous phase was extracted with Et_2O. The combined organic phases were washed with H_2O, a saturated aqueous solution of $NaHCO_3$, and 1M NaOH, and then dried (Na_2SO_4). Concentration in vacuo yielded **4a** as a brown oil. Flash chromatography (hexane/AcOEt, 6:4) afforded **4a** (80.6 mg; 72%). Spectral data were identical to those reported in ref. [9].

Allylic acetate 4b: The same procedure as for **4a** was followed: complex **6b** (140 mg) afforded **4b** (77.1 mg; 68%). ^1H NMR (300 MHz, $CDCl_3$): $\delta =$ 5.80 (s, 1H; H8), 5.60 (dd, $J = 11.7$, 3.5 Hz, 1H; H1), 5.51 (m, 1H; H2), 5.28 (m, 1H; H3), 5.13 (s, 1H; H12), 5.03 (s, 1H; H12′), 3.99 (m, 1H; H10), 3.77 (s, 3H; CH_3), 3.66 (s, 3H; CH_3), 3.24 (ddd, $J = 12.6$, 9.3, 6.4 Hz, 1H; H6), 2.22–2.08 (2H; H4, H5), 2.05 (s, 3H; CH_3), 1.95 (s, 3H; CH_3), 1.75–1.63 (m, 1H; H4′), 1.15–1.07 ppm (m, 1H; H5′); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 171.3$, 170.7, 170.6, 151.3, 137.9, 133.7, 125.8, 124.5, 117.0, 72.6, 69.1, 52.9, 52.5, 48.5, 44.8, 28.2, 22.0, 21.5, 20.7 ppm.

Allylic acetate 8a: To a stirred solution of (π-allyl)palladium complex **6a** (40 mg, 0.048 mmol) in acetic acid (2 mL) was added a solution of $LiOAc \cdot 2H_2O$ (97.8 mg, 10 equiv), LiCl (5.3 mg, 1.3 equiv), 1,4-benzoquinone (20.6 mg, 2 equiv) in acetic acid (4.2 mL). The mixture was stirred at room temperature for 4 h. The reaction mixture was diluted with a saturated aqueous solution of NaCl and extracted with a solution of pentane/diethyl ether (9:1). The combined organic phases were washed with H_2O and a saturated aqueous solution of Na_2CO_3 and dried (Na_2SO_4). Evaporation of the solvent afforded a 2:1 mixture of **8a**:**4a** (14.4 mg; 45% overall yield). The yield was determined from the ^1H NMR spectrum by using 1,2-dimethoxybenzene as internal standard. The ^1H NMR data were obtained by comparison of the crude ^1H NMR spectrum with the spectrum of compound **4a**. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.11$ (ddd, $J = 10.3$, 4.2, 2.1 Hz, 1H), 5.72 (2H), 5.07 (m, 1H; overlap with H11 and H11′), 5.08 (s, 1H; H11), 5.02 (s, 1H; H11′), 3.77–3.70 (7H, overlapping peaks in which s at 3.76 and 3.70), 3.55 (ddd, $J = 12.2$, 6.3, 3.9 Hz, 1H), 1.93 (s, 3H), 1.69 (m, 1H), 1.38 ppm (m, 1H).

Allylic acetate 8b: The same protocol as above was followed: complex **6b** (22 mg) afforded a 3:1 mixture of **8b** and **4b** (5.7 mg; 32% yield). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 5.77$ (s, 1H; H8), 5.67 (m, 1H; H3), 5.45 (2H; H2, H1), 5.12 (s, 1H; H12), 5.00 (s, 1H; H12′), 3.76 (4H, H10; CH_3), 3.69 (s, 3H; CH_3), 3.07 (ddd, $J = 14.4$, 9.2, 4.8 Hz, 1H; H6), 2.06 (4H; H4, CH_3), 2.02 (m, 1H; H4′), 1.88 (m, 1H; H5), 1.68 (m, 1H; H4′), 1.47 ppm (m, 1H; H5′). NOE experiment (400 MHz, $CDCl_3$): irradiation of H3 (geminal to the acetoxy moiety) resulted in a 4% NOE enhancement for the allylic bridgehead proton.

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