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Palladium(0)-Catalyzed Domino Cyclization-Carbonylation of Alkenyl-Allenyl-Allylic Acetate

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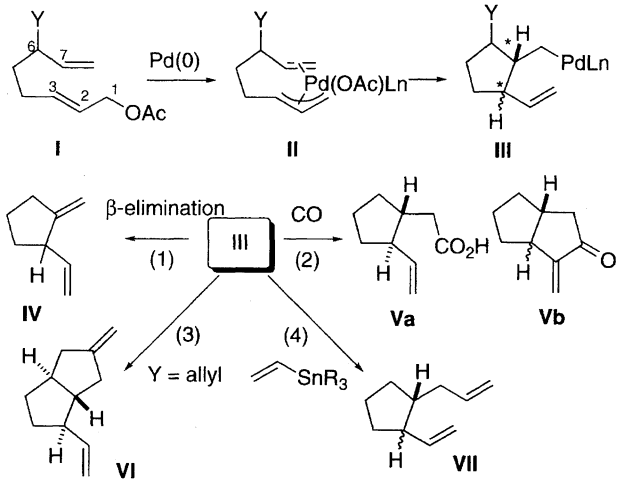
The Pd(0)-catalyzed domino cyclization-carbonylation of 5,8-dimethyl-5-(1,2-propadienyl)-2,8-nonadienyl acetate (**7**) was achieved at a rather higher temperature. The tricyclic and tetracyclic products, **15** and **16**, were produced in 77% combined yield via five and six consecutive carbon–carbon bond formations, each step proceeding in > 94% yield.

The Pd(0)-catalyzed intramolecular cyclization of 2,7-octadienyl acetate has been utilized for preparing various five-membered ring systems.[1,2] In this process (Scheme 1), a π-allylpalladium complex **II** formed from an allylic acetate **I** and a Pd(0)-catalyst undergoes either an intramolecular palladaene reaction or an intramolecular alkene insertion, leading to a cyclopentylmethylpalladium intermediate **III** that ends up with β-hydride elimination to form a methylenecyclopentane derivative **IV** (Eq. 1 in Scheme 1).[1] We focused on the utilization of the σ-alkylpalladium intermediate **III**, prior to β-elimination, to achieve domino carbon–carbon bond formation.[3] In fact, the domino carbon–carbon bond formation was carried out via Pd(0)-catalyzed cyclization-carbonylation under a carbon monoxide atmosphere, providing products **Va** and **Vb** (Eq. 2 in Scheme 1).[4] Domino cyclization with an alkene in the molecule also took place when a simple allyl group was located at the 6-position



Scheme 1.

(Y = allyl), stereoselectively generating a *trans*-fused bicyclo[3.3.0]octane system **VI** (Eq. 3 in Scheme 1).[5] The tandem carbon–carbon bond formation via transmetallation of the intermediate **III** with vinylstannane was reported by Oppolzer and Ruiz-Montes (Eq. 4 in Scheme 1).[6]

In 1996, we reported that a π-allylpalladium complex reacts intramolecularly with an allenic unit at either double bond, leading exclusively to a five-membered ring intermediate, depending on the number of carbons in the chains that tether between the reaction sites.[7] A novel domino cyclizaion-carbonylation was accomplished to give tri- and tetracyclic compounds **2** and **3** from an acyclic allylic acetate **1** (Scheme 2). In the reaction, six consecutive carbon–carbon bond formations were achieved in a one-pot operation, providing 22% of tetracyclic diketone **2** and 5% of tricyclic keto acid **3**. It is conceivable that the reaction proceeds via a regioselective allene insertion (step a) of the π-allylpalladium intermediate **A** initially formed, generating a new π-allylpalladium complex **B** that undergoes alkene insertion intramolecularly, leading to a σ-palladium complex **C** (step b). Carbonylation of **C**, leading to an acylpalladium complex **D** though β-elimination from **C**, partially occurred to give **5** (18%). Further processes are distinguished by the stereoselection in step b. When the carbopalladation leads to the β-configuration at the C8 position, the acylpalladium complex **D** does not reach intramolecularly to an alkene unit, and acid **4** is formed (12% in this particular case). On the other hand, the acylpalladium complex **D**, which has an α-configuration at the C8 position, undergoes insertion intramolecularly with an alkene unit, followed by carbonyl insertion to produce a new acylpalladium complex **E**. Then, the complex **E** undergoes insertion intramolecularly with another alkene, followed by β-elimination, leading to tetracyclic diketone **2** when the vinyl group generated in step a has the β-configuration at the C3 position. Whereas complex **E** has the vinyl group at the C3 position with the α-configuration, an acylpalladium moiety does not reach intramolecularly to the alkene and the tricyclic acid **3** is obtained. Although it was demon-

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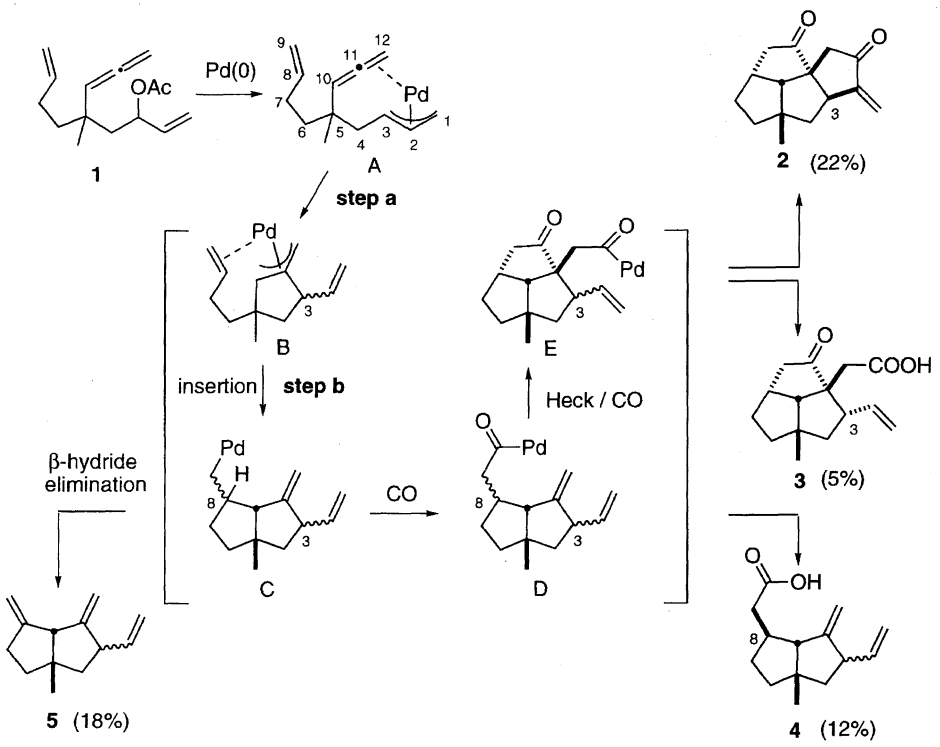
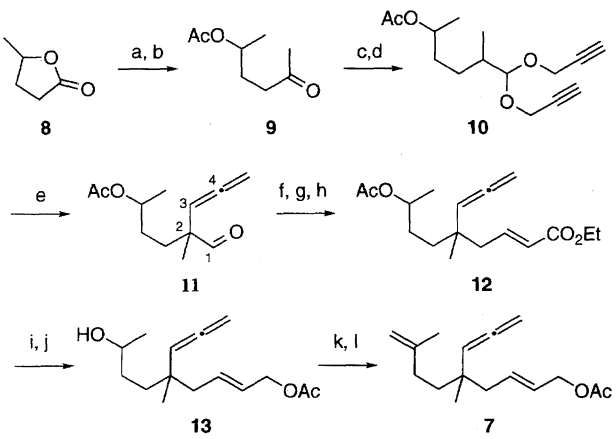


Scheme 2. Pd(0)-catalyzed domino cyclization-carbonylation of **1**.

strated that this domino cyclization is particularly powerful for synthesizing polycyclopentanones, premature products **4** (12%) and **5** (18%) were also formed in the reaction because of a β-hydride elimination of the intermediate **C** and poor stereoselectivity in the intramolecular alkene insertion (step b). We anticipated that if a methyl group is introduced at the C8 position, β-hydride elimination could be avoided and the stereoselectivity in step b could hopefully be improved. This strategy has been used in domino Heck reactions.[8,9] However, there have been few reports on the insertion of a π-allylpalladium intermediate to an 1,1-disubstituted alkene, probably because the steric hindrance of the 1,1-disubstituted alkene makes the insertion difficult, and the higher temperature could cause a β-elimination of the π-allylpalladium intermediate, itself, giving the corresponding diene.[1c,10] To overcome this problem and to make the domino cyclization efficient, the Pd(0)-catalyzed domino cyclization of 5,8-dimethyl-5-(1,2-propadienyl)-2,8-nonadienyl acetate (**7**) was examined in terms of the pressure of carbon monoxide or of the reaction temperature.



(a) MeLi, ether; (b) Ac_2O, Py, 58% (2 steps); (c) $MeOCH_2PPh_3Cl$, $KN(TMS)_2$, THF; (d) propargyl alcohol, *p*-TsOH, PhH, 64% (2 steps); (e) *p*-TsOH, *o*-dichlorobenzene, 180 °C, 85%; (f) KHMDS, $MeOCH_2PPh_3Cl$, THF; (g) HCl, THF; (h) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, 30% (3 steps); (i) DIBAL, 78%; (j) AcCl, *i*-Pr_2NEt, CH_2Cl_2, 98%; (k) $(COCl)_2$, DMSO, NEt_3, 95%; (l) CH_3PPh_3Br, $KN(TMS)_2$, 85%.

Scheme 3. The preparation of substrate **7**.

Results and Discussion

The substrate **7** was prepared according to our reported procedure described for the preparation of **1** (Scheme 3).[7] The addition of methyllithium to 4-methyl-γ-butyrolactone (**8**) and acetylation of the resulting alcohol gave 1-methyl-4-oxopentyl acetate (**9**) in 58% yield. The Wittig reaction of **9** with methoxymethylenetriphenylphosphorane, followed by acid hydrolysis, provided aldehyde, which was treated with propargyl alcohol in the presence of acid to give acetal **10** in 64%. A Claisen rearrangement of **10** was carried out by heating at 180 °C for 10 min in *o*-dichlorobenzene with a catalytic amount of *p*-toluenesulfonic acid.[11] The only product was 2,2-disubstituted-3,4-pentadienal **11**, obtained in 85% yield after column chromatography. Since it is known that 3,4-pentadienals easily isomerize to 2,4-pentadienals, the presence of a quaternary carbon at the C2 position makes sense in this preparation. The Wittig reaction with methoxymethylenetriphenylphosphorane, followed by acid hydrolysis, introduced one carbon homologated aldehyde, which underwent the Horner–Emmons reaction, leading to unsaturated ester **12** in 30% yield from **11**. The DIBAL reduction (78%) afforded diol, in which primary alcohol was selec-

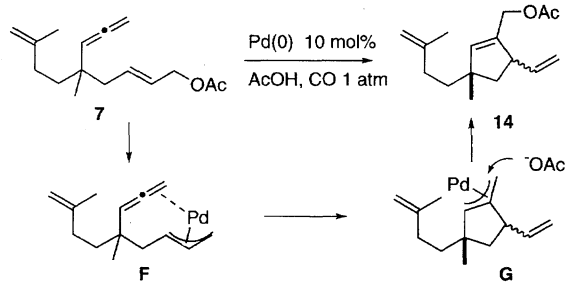
tively acetylated (98%) to give **13**. The Swern oxidation of **13**, followed by the Wittig reaction, provided the desired **7** in 83% yield from **13**.

Palladium Catalyzed Cyclization. Pd(0)-catalyzed cyclization was carried out in acetic acid at 70 °C under 1 atm of a carbon monoxide atmosphere, as shown in Table 1. The use of acetic acid as a solvent is essential to successfully perform the cyclization. The products were separated by HPLC and analyzed spectroscopically. When tetrakis(triphenylphosphine)palladium(0) (10 mol%) was used as a catalyst, only monocyclic cyclization product **14** was isolated as a 1.3 : 1.0 mixture of diastereomers in 68% combined yield. The use of $[Pd_2(dba)_3]\cdot CHCl_3$ and tri(2-furyl)phosphine also yielded a 62% of **14** with a slightly less selective diastereomeric ratio (1.2 : 1.0). It has been demonstrated that the initially formed π-allylpalladium complex **F** reacted with the rather reactive allenic unit, forming a new π-allylpalladium intermediate **G**, which did not undergo sequential alkene insertion, but the attack of an acetate ion, leading to allylic acetate **14**. It is conceivable that carbon monoxide would tightly coordinate to the π-allylpalladium intermediate **G**, so that the second alkene insertion of **G** to a rather bulky 1,1-disubstituted alkene might be prevented.[12]

We examined the cyclization-carbonylation of the allylic acetate **14** in order to optimize the reaction conditions for domino cyclization. The reactions of **14** were carried out under decreased carbon monoxide pressure, such as 1 atm of synthetic gases ($CO:N_2$ = 1 : 1, $CO:N_2$ = 1 : 4). Interestingly, the expected domino cyclization has occurred under these conditions, providing the desired tri- and tetracyclic compounds **15** and **16** isolated in moderate yields, as shown in Table 2. It is conceivable that the lower pressure of carbon monoxide could accelerate the coordination of an intramolecular alkene to the π-allylpalladium intermediate. However, the attack of an acetate ion on the disubstituted alkene also took place, providing the undesired **17**. The structure of **15** was determined by an nOe measurement, as shown in Fig. 1.

We next examined the effect of the reaction temperature in the domino reaction. When the reaction of **14** was carried out at 90 °C, no formation of **17** was observed. The results are given in Table 3. Tetrakis(triphenylphosphine)palladium(0) is more effective than the complex of $[Pd_2(dba)_3]\cdot CHCl_3$ and tri(2-furyl)phosphine. The former catalyst (20 mol%) only gave the desired compounds **15** and **16** in 34 and 29% yields, respectively, whereas the latter pre-catalysts (20 mol%) gave them in 13 and 24% yields, respectively. It is demonstrated that the second cyclization was stereoselectively proceeded to give the desired σ-alkylpalladium complex **N** (Fig. 2), which consecutively underwent carbonylation, intramolecular alkene insertion, cabonylation, intramolecular alkene insertion, and finally β-hydride elimination, leading to the exclusive formation of **15** and **16** (corresponding to the

Table 1. Pd(0)-Catalyzed Monocyclization of **7**



Catalyst	Time	Temp	Yield
$[Pd(PPh_3)_4]$	17 h	70 °C	68% (β : α = 1 : 1.3)
$[Pd_2(dba)_3]\cdot CHCl_3$ tri(2-furyl)phosphine	5 h	75 °C	62% (β : α = 1 : 1.2)

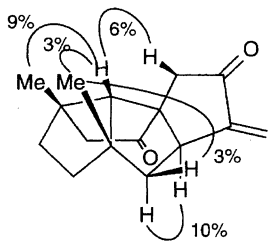
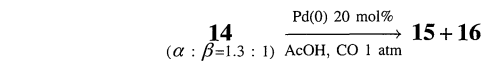


Fig. 1. nOe measurements of **15**.

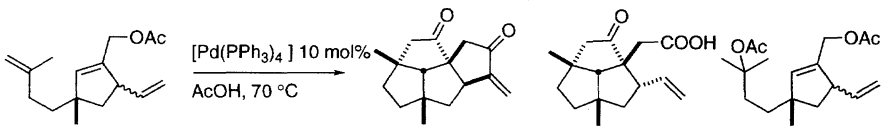
Table 3. Pd(0)-Catalyzed Domino Cyclization of **14** at 90 °C



14 (α : β=1.3 : 1)

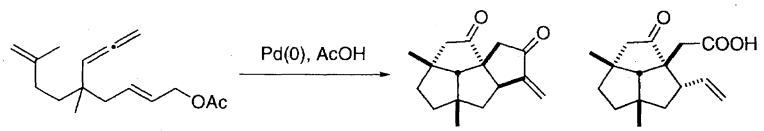
Catalyst	Time	Temp	**15**	**16**
$[Pd(PPh_3)_4]$	20 h	90 °C	34%	29%
$[Pd_2(dba)_3]\cdot CHCl_3$ tri-2-furylphosphine	20 h	90 °C	13%	24%

Table 2. Pd(0)-Catalyzed Domino Cyclization of **14** under Lower Pressure of Carbon Monoxide



14	$CO:N_2$	**15**	**16**	**17**
α : β = 1.5 : 1	1 : 4	4%	11%	19%
α : β = 1.5 : 1	1 : 1	11%	22%	8%
α only	1 : 1	—	36%	24%
β only	1 : 1	20%	—	39%

Table 4. Pd(0)-Catalyzed Domino Cyclization of **1**



7 15 16

Catalyst	CO pressure	Time	Temp	**15**	**16**
$[Pd(PPh_3)_4]$ 20 mol%	1 atm	22 h	90 °C	29%	26%
$[Pd(PPh_3)_4]$ 10 mol%	1 atm	80 h	90 °C	30%	47%
$[Pd(PPh_3)_4]$ 20 mol%	0.5 atm	24 h	90 °C	15%	30%

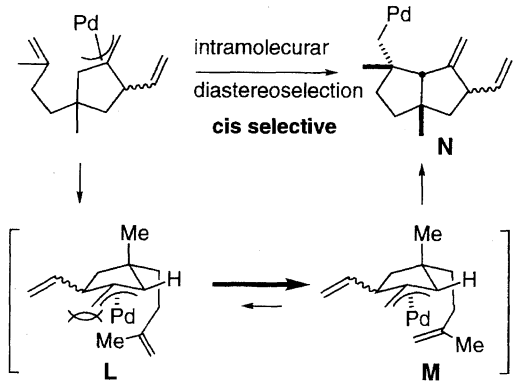


Fig. 2.

Scheme 2). This high stereoselection can be explained by the steric repulsion in transition state **L**, compared with **M**, because a methyl group of the isopropenyl moiety is covered under the 5-membered ring in transition state **L** though that in **M** is oriented outside of the ring (Fig. 2).

Domino Cyclization from Acyclic Allylic Acetate 7. We finally examined the formation of **15** and **16** via the domino cyclization of **7**. The domino cyclization of **7** was carried out under optimized reaction conditions, such as in acetic acid at 90 °C in the presence of tetrakis(triphenylphosphine)palladium(0), to give only **15** and **16**, as shown in Table 4. Under 1 atm of carbon monoxide, the reaction proceeded rather smoothly. A decrease in the amount of catalyst from 20 to 10 mol% increased the combined yield. It is conceivable that allenic dimerization was suppressed due to the lower concentration of a Pd(0) species.[7,13] As a result, it was found that five and six consecutive carbon–carbon bond formations could be successfully achieved with up to 77% combined yield (ca. > 94% per C–C bond formation).

In summary, it has been demonstrated that the Pd(0)-catalyzed domino cyclization-carbonylation of 5,8-dimethyl-5-(1,2-propadienyl)-2,8-nonadienyl acetate (**7**) can be achieved at a rather higher temperature by avoiding a β-elimination of both the π-allylpalladium **M** and the σ-palladium intermediate **N**, shown in Fig. 2.

Experimental

1-Methyl-4-oxopentyl Acetate (9). To a solution of γ-valerolactone **8** (15.8 g, 158 mmol) in dry ether (400 mL) was added 132 mL of methyllithium (173 mmol, 1.31 M in ether, 1 M = 1 mol dm^{-3}) at −78 °C. After being stirred for 15 min, the resulting mixture was poured into ether and saturated aqueous 1 M HCl. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with saturated aqueous sodium hydrogencarbonate and brine, and dried over anhydrous magnesium sulfate. After removing the solvent, the crude alcohol was used for the next reaction without further purification.

To a solution of the crude alcohol in dry CH_2Cl_2 (200 mL) was added pyridine (32.0 mL, 396 mmol) followed by acetyl chloride (17.0 mL, 239 mmol) at 0 °C. The reaction mixture was stirred for 20 min at room temperature and then diluted with ether. The etherial solution was washed with 1 M HCl and the aqueous layer was extracted with ether. The combined organic layers were washed with saturated aqueous sodium hydrogencarbonate and brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was column chromatographed on silica gel (hexane/ethyl acetate = 10) to give **9** (14.4 g, 91 mmol, 2 steps 58%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 4.89 (tq, J = 6.3, 6.6 Hz, 1H), 2.48 (t, J = 7.6 Hz, 2H), 2.15 (s, 3H), 2.03 (s, 3H), 1.9—1.8 (m, 2H), 1.23 (d, J = 6.6 Hz, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 207.9, 170.8, 70.2, 39.6, 30.0, 29.8, 21.3, 20.1; IR (neat) 2974, 2932, 1730, 1424, 1372, 1244, 1166, 1134, 1085, 1045, 1020, 949, 832, 611, 450 cm^{-1}.

1,4-Dimethyl-5,5-bis(2-propynyloxy)pentyl Acetate (10). To a solution of $MeOCH_2PPh_3Cl$ (44.22 g, 138 mmol) in dry THF (300 mL) was added 240 mL of potassium hexamethyldisilazide (120 mmol, 0.5 M in toluene) at 0 °C. After the solution was stirred for 1 h and cooled to −78 °C, ketone **9** (14.42 g, 91 mmol) was added to the dark-red solution. The reaction mixture was allowed to warm up to room temperature. After being stirred for 30 min, the resulting mixture was poured into hexane and saturated aqueous ammonium chloride. The organic layer was separated and the aqueous layer was extracted with hexane. The combined organic layers were washed with brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give crude ether, which was used for the next reaction without further purification.

To a solution of the above-mentioned ether in dry benzene (200 mL) were added a catalytic amount of *p*-TsOH and propargyl alcohol (16.1 mL, 276 mmol) at 0 °C. The reaction mixture was allowed to warm up to room temperature. After being stirred for 1 h, the reaction mixture was heated under reflux. While refluxing, water was azeotropically removed with benzene, and another portion of propargyl alcohol was added to the reaction mixture. After being stirred for 3 d, the resulting mixture was diluted with ether and poured into saturated aqueous sodium hydrogencarbonate. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with brine, and dried over anhydrous magnesium sulfate. After removal of the

solvent, the residue was column chromatographed (hexane/ethyl acetate = 10) to give **10** (15.7 g, 59 mmol, 2 steps 64%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 4.9—4.8 (m, 1H), 4.55 (d, J = 5.9 Hz, 1H), 4.3—4.2 (m, 4H), 2.45 (br, 2H), 2.03 (s, 3H), 1.8—1.7 (m, 1H), 1.7—1.4 (m, 4H), 1.22 (d, J = 6.3 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 170.8, 104.7, 79.7, 74.4, 71.3, 71.0, 54.3, 54.0, 36.0, 35.9, 33.2, 27.2, 21.4, 20.0, 14.3; IR (neat) 3296, 2970, 2930, 2866, 2114, 1728, 1450, 1371, 1249, 1100, 1047, 954, 912, 834, 735 cm^{-1}.

4-Formyl-1,4-dimethyl-5,6-heptadienyl Acetate (11). To a solution of **10** (11.0 g, 41 mmol) in 1,2-dichlorobenzene (80 mL) was added a catalytic amount of *p*-TsOH. After being stirred for 10 min at 180 °C, the reaction mixture was evaporated under reduced pressure to remove propargyl alcohol. The resulting solution was column chromatographed (hexane/ethyl acetate = 20) to give **11** (7.43 g, 35 mmol, 85%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 9.38 (s, 1H), 5.09 (t, J = 6.6 Hz, 1H), 4.89 (d, J = 6.6 Hz, 2H), 4.9—4.8 (m, 1H), 2.04 (s, 3H), 1.7—1.4 (m, 4H), 1.22 (d, J = 13.2 Hz, 3H), 1.16 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 208.5, 202.1, 202.1, 170.7, 92.2, 78.1, 70.9, 49.0, 31.1, 30.4, 21.4, 19.9, 18.9, 18.9; IR (neat) 2930, 2866, 2804, 2704, 1950, 1728, 1620, 1456, 1371, 1244, 1127, 1049, 953, 915 cm^{-1}.

Ethyl (*E*)- 8- Acetoxy- 5- methyl- 5- (1, 2- propadienyl)- 2- nonenoate (12). To a solution of $MeOCH_2PPh_3Cl$ (5.51 g, 16 mmol) in dry THF (100 mL) was added 30.0 mL of KHMDS (15 mmol, 0.5 M in toluene) at 0 °C. After the solution was stirred for 1 h and cooled to −78 °C, aldehyde **11** (2.41 g, 12 mmol) was added to the dark-red solution. The reaction mixture was allowed to warm up to room temperature. After being stirred for 15 min, the resulting mixture was poured into hexane and saturated aqueous ammonium chloride. The organic layer was separated and the aqueous layer was extracted with hexane. The combined organic layers were washed with brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was used for the next reaction without further purification.

To a solution of the crude vinyl ether in THF (200 mL) was added 1 M HCl (20 mL) at 0 °C. The solution was allowed to warm up to room temperature, stirred for 14 h, and then diluted with ether. The organic layer was washed with saturated aqueous sodium hydrogencarbonate and the aqueous layer was extracted with ether. The combined organic layers were washed with brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was used for the next reaction without further purification.

To a suspension of sodium hydride (55% in oil, 0.50 g, 11 mmol, washed with dry hexane) in dry THF (80 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (4.0 mL, 19 mmol) at 0 °C. The solution was allowed to warm up to room temperature, stirred for 30 min, and then cooled to 0 °C. A solution of the crude aldehyde was added to the colorless solution. After being stirred for 10 min, the resulting mixture was poured into 1 M HCl and ether. The organic layer was separated and the aqueous layer was extracted. The combined organic layers were washed with saturated sodium hydrogencarbonate and brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was column chromatographed (hexane/ethyl acetate = 10) to gave **12** (1.04 g, 3.6 mmol, 3 steps 30%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 6.94 (dt, J = 15.5, 7.6 Hz, 1H), 5.83 (d, J = 15.5 Hz, 1H), 4.99 (t, J = 6.6 Hz, 1H), 4.84 (q, J = 6.3 Hz, 1H), 4.78 (d, J = 6.6 Hz, 2H), 4.19 (q, J = 6.9 Hz, 2H), 2.22 (d, J = 7.6 Hz, 2H), 2.03 (s, 3H), 1.7—1.3 (m, 4H), 1.29 (t, J = 6.9 Hz, 3H), 1.21 (d, J = 6.3 Hz, 3H), 1.00 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 207.2, 170.8, 166.5, 145.7, 123.9, 98.2, 76.6, 71.3, 60.3, 43.9, 43.7, 37.3, 36.5, 30.6, 24.8, 21.1, 20.0, 14.3; IR (neat) 2970, 2866, 1952, 1720, 1650, 1593, 1500, 1460, 1370, 1314, 1245, 1185, 1095, 1042 cm^{-1}.

(*E*)-5-Methyl-5-(1,2-propadienyl)-2-nonene-1,8-diol. To a solution of **12** (0.99 g, 3.4 mmol) in dry toluene (20 mL) was added 13 mL of DIBAL (13 mmol, 1.01 M in ether) at −78 °C. The solution was warmed up to 0 °C and stirred for 15 min. Excess sodium sulfate·10 H_2O (5.7 g) was added to the mixture. The mixture was diluted with ether with vigorous stirring. The resulting mixture was dried over sodium sulfate. After removal of the solvent, the residue was chromatographed on silica gel (hexane/ethyl acetate = 2) to give (*E*)-5-methyl-5-(1,2 propadienyl)-2-nonene-1,8-diol (0.55 g, 2.6 mmol, 78%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 5.7—5.6 (m, 2H), 5.01 (t, J = 6.6 Hz, 1H), 4.74 (d, J = 6.6 Hz, 2H), 4.2—4.1 (m, 2H), 3.8—3.7 (m, 1H), 2.1—2.0 (m, 2H), 1.5—1.2 (m, 4H), 1.19 (d, J = 6.3 Hz, 3H), 0.98 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 207.1, 131.9, 129.1, 99.0, 98.9, 76.6, 68.7, 63.6, 43.9, 43.7, 37.0, 36.5, 36.5, 33.7, 24.9, 24.7, 23.6; IR (neat) 3340, 2960, 1952, 1722, 1666, 1453, 1375, 1313, 1118, 1087, 974, 845, 735 cm^{-1}.

(*E*)-8-Hydroxy-5-methyl-5-(1,2-propadienyl)-2-nonenyl Acetate (13). To a solution of (*E*)-5-methyl-5-(1,2-propadienyl)-2-nonene-1,8-diol (1.93 g, 9.2 mmol) in dry dichloromethane (40 mL) was added *N*,*N*-diisopropylethylamine (3.2 mL, 18 mmol) followed by acetyl chloride (0.78 mL, 11 mmol) at −50 °C. After being stirred for 10 min, the solution was poured into ether and water. After separation, the aqueous layer was extracted. The combined organic layers were washed with brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was column chromatographed (hexane/ethyl acetate = 10) to give **13** (2.27 g, 9.0 mmol, 98%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 5.76 (dt, J = 15.2, 7.3 Hz, 1H), 5.59 (dt, J = 15.2, 6.3 Hz, 1H), 4.99 (t, J = 6.6 Hz, 1H), 4.74 (d, J = 6.6 Hz, 2H), 4.52 (d, J = 6.3 Hz, 2H), 3.8—3.7 (m, 1H), 2.09 (d, J = 7.3 Hz, 2H), 2.06 (s, 3H), 1.5—1.2 (m, 4H), 1.19 (d, J = 5.9 Hz, 3H), 0.97 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 207.3, 171.0, 132.6, 126.7, 98.8, 68.7, 65.2, 44.4, 43.9, 37.1, 36.8, 33.9, 24.6, 23.6, 21.1; IR (neat) 3408, 2960, 1951, 1737, 1453, 1378, 1239, 1116, 1071, 1025, 973, 844, 608 cm^{-1}.

(*E*)-5-Methyl-8-oxo-5-(1,2-propadienyl)-2-nonenyl Acetate. To a solution of dimethyl sulfoxide (2.0 mL, 28 mmol) in dry dichloromethane (20 mL) was slowly added oxalyl chloride (1.2 mL, 14 mmol) at −60 °C. After being stirred for 1 h, a solution of **13** (2.27 g, 9.0 mmol) in dichloromethane (10 mL) was added dropwise. The reaction mixture was stirred for 30 min at −60 °C, and then triethylamine (6.4 mL, 46 mmol) was added. The resulting mixture was allowed to warm up to room temperature over a period of 15 min. The reaction mixture was diluted with ether and washed with 1 M HCl. The organic layer was separated and the aqueous layer was extracted. The combined organic layers were washed with saturated aqueous sodium hydrogencarbonate and brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was column chromatographed (hexane/ethyl acetate = 5) to give (*E*)-5-methyl-8-oxo-5-(1,2-propadienyl)-2-nonenyl acetate (2.14 g, 8.5 mmol, 95%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 5.75 (dt, J = 15.2, 7.3 Hz, 1H), 5.59 (dt, J = 15.2, 6.3 Hz, 1H), 4.94 (t, J = 6.6 Hz, 1H), 4.77 (d, J = 6.6 Hz, 2H), 4.52 (d, J = 6.3 Hz, 2H), 2.5—2.4 (m, 2H), 2.15 (s, 3H), 2.09 (d, J = 7.3 Hz, 2H), 2.06 (s, 3H), 1.7—1.5 (m, 2H), 0.95 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 209.1, 207.3, 170.9, 132.1, 127.1, 98.1, 76.9, 65.1, 44.2, 39.1, 37.0, 34.3, 30.1, 24.2, 21.1; IR (neat) 2958, 2924, 1951, 1736, 1715, 1443, 1362, 1231, 1166, 1024, 973, 846, 737, 608 cm^{-1}.

(*E*)-5,8-Dimethyl-5-(1,2-propadienyl)-2,8-nonadienyl Acetate (7). To a solution of Ph_3PCH_3Br (641 mg, 1.8 mmol) in dry THF

(15 mL) was added 2.8 mL of KHMDS (1.4 mmol, 0.5 M in toluene) at 0 °C. The solution was stirred for 1 h, cooled to −78 °C, and then (*E*)-5-methyl-8-oxo- 5-(1,2-propadienyl)-2-nonenyl acetate (54.8 mg, 0.22 mmol) was added to the dark-red solution. The reaction mixture was allowed to warm up to room temperature. After being stirred for 2.5 h, the resulting mixture was poured into hexane and saturated aqueous ammonium chloride. The organic layer was separated and the aqueous layer was extracted with hexane. The combined organic layers were washed with brine and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was column chromatographed (hexane/ethyl acetate = 100) to give **7** (46.4 mg, 0.19 mmol, 85%). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 5.77 (dt, J = 15.2, 7.3 Hz, 1H, −C<u>H</u>=CH−), 5.59 (dt, J = 15.2, 6.3 Hz, 1H, −CH=C<u>H</u>−), 5.00 (t, J = 6.6 Hz, 1H, −C<u>H</u>=C=CH$_2$), 4.74 (d, J = 6.6 Hz, 2H, −CH=C=C<u>H</u>$_2$) 4.7—4.6 (m, 2H, C<u>H</u>$_2$=C<), 4.53 (d, J = 6.3 Hz, 2H, −CH$_2$−O), 2.11 (d, J = 7.3 Hz, 2H, =CH−C<u>H</u>$_2$−), 2.06 (s, 3H, −OAc), 2.0—1.9 (m, 2H, =C(CH$_3$)−C<u>H</u>$_2$−), 1.72 (s, 3H, CH$_2$=C(C<u>H</u>$_3$)−), 1.5—1.4 (m, 2H, −CH$_2$−C<u>H</u>$_2$−), 0.98 (s, 3H, −C<u>H</u>$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 207.3, 170.9, 146.6, 132.7, 126.7, 109.5, 98.7, 77.1, 65.2, 43.9, 39.2, 37.3, 32.5, 24.6, 22.8, 21.1; IR (neat) 3068, 2960, 1952 (C=C=C), 1739, 1646, 1597, 1492, 1452, 1376, 1228, 1079, 1024, 972, 884 cm^{-1}; MS (EI, 70 eV) 188 (M^+ − OAc; 36%), 173 (100). HRMS (EI, 70 eV) Calcd for $C_{14}H_{20}$: (M^+ − AcOH), 188.1565. Found: *m/z* 188.1550.

Pd(0)-Catalyzed Cyclization of (*E*)-5,8-Dimethyl-5-(1,2-propadienyl)-2,8-nonadienyl Acetate (7). Preparation of (1*R,4*S**,7*R**,9*R**,13*R**)-4,7-Dimethyl-10-methylene-2,11-dioxotetracyclo[5.5.1.0^{1,9}.0^{4,13}]tridecane (15), (1*R**,4*S**,7*R**,9*R**,10*R**)-4,7-Dimethyl-2-oxo-9-vinyltricyclo[5.2.1.0^{4,10}]decan-1-yl Acetic Acid (16), 1-Acetoxymethyl-4-methyl-4-(3-methyl-3-butenyl)-2-vinyl-5-cyclopentene (14):**

General Procedure of Pd(0)-Catalyzed Cyclization (Method A). A mixture of $Pd_2(dba)_3$·$CHCl_3$ (16.6 mg, 5 mol%) and triphenylphosphine (84 mg, 100 mol%) in dry ether (2 mL) was stirred at room temperature under argon. A pale-yellow precipitate appeared rapidly. After being stirred for 4 h at the same temperature, the yellow solution was decanted. The precipitate was washed with ether (2 mL×2) by decantation. Removal of ether under reduced pressure gave tetrakis(triphenylphosphine)palladium(0).[14] To a solution of the catalyst (10 mol%) in acetic acid (0.5 mL) was added **7** (80 mg, 0.32 mmol) in acetic acid (1.5 mL) at room temperature under carbon monoxide. After being stirred for 80 h at 90 °C, the reaction mixture was passed through a short pad of florisil. Evaporation of acetic acid under reduced pressure and chromatography of the residue on silica gel gave **15** (23.5 mg, 30%) and **16** (39.9 mg, 47%).

General Procedure of Pd(0)-Cyclization (Method B). To a solution of $Pd_2(dba)_3$·$CHCl_3$ (17 mg, 5 mol%) and P(2-furyl)$_3$ (17 mg, 30 mol%)[14,15] in acetic acid (0.5 mL) was added a solution of **7** (80 mg, 0.32 mmol) in acetic acid (1.5 mL). The mixture was stirred at 75 °C under a carbon monoxide atmosphere (1 atm). After being stirred for 5 h, the solution was filtered through a short pad of florisil and the filtrate was concentrated under reduced pressure. Column chromatography of the residue provided 56 mg (70%) of **14a** (α-vinyl group) and **14b** (β-vinyl group) in a ratio of 1.2 : 1. The diastereomers were separated by HPLC.

(1*R,4*S**,7*R**,9*R**,13*R**)-4,7-Dimethyl-10-methylene-2,11-dioxotetracyclo[5.5.1.0^{1,9}.0^{4,13}]tridecane (15):** HPLC (elution with 12% ethyl acetate in hexane, 3.0 mL min^{-1}; retention time = 11—12 min). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 6.04 (dd, J = 2.6, 0.7 Hz, 1H, >C=C<u>H</u>$_2$), 5.30 (dd, J = 2.3, 0.7 Hz, 1H, >C=C<u>H</u>$_2$), 3.40 (tt, J = 7.6, 2.3 Hz, 1H, >C<u>H</u>−C=CH$_2$), 2.75 (d, J = 18.8 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.59 (d, J = 18.2 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.38 (d, J = 18.8 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.25 (d, J = 18.2 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.1—2.0 (m, 2H, −C<u>H</u>$_2$−), 2.02 (s, 1H, >C<u>H</u>−), 1.8—1.6 (m, 4H, −C<u>H</u>$_2$−), 1.23 (s, 3H, −C<u>H</u>$_3$), 1.21 (s, 3H, −C<u>H</u>$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 220.2, 204.8, 147.5, 118.8, 73.2, 63.1, 55.5, 52.7, 51.2, 48.7, 46.5, 44.6, 40.4, 39.6, 29.3, 29.2; IR ($CHCl_3$ solution) 3006, 2948, 2862, 1725, 1637, 1455, 1408, 1377, 944 cm^{-1}. Found: C, 78.25; H, 8.07%. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25%.

(1*R,4*S**,7*R**,9*R**,10*R**)-4,7-Dimethyl-2-oxo-9-vinyltricyclo[5.2.1.0^{4,10}]decane-1-yl Acetic Acid (16):** ^{1}H NMR (270 MHz, $CDCl_3$) δ = 5.72 (ddd, J = 15.6, 10.6, 8.3 Hz, 1H, −C<u>H</u>=CH$_2$), 5.1—5.0 (m, 2H, −CH=C<u>H</u>$_2$), 2.91 (d, J = 16.5 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.9—2.7 (m, 1H, >C<u>H</u>−CH=CH$_2$), 2.54 (d, J = 16.5 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.41 (d, J = 19.1 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.28 (d, J = 19.1 Hz, 1H, −C<u>H</u>$_2$−C=O), 2.12 (s, 1H, >C<u>H</u>−), 1.9—1.6 (m, 4H, −C<u>H</u>$_2$−C<u>H</u>$_2$−), 1.57 (d, J = 9.9 Hz, 2H, −C<u>H</u>$_2$−CH<), 1.22 (s, 3H, −C<u>H</u>$_3$), 1.20 (s, 3H, −C<u>H</u>$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 221.5, 177.3, 136.5, 116.0, 71.3, 62.1, 55.2, 55.1, 52.9, 44.0, 43.6, 42.0, 41.7, 38.9, 29.7, 27.6; IR (neat) 3175, 2920, 1727, 1640, 1453, 1375, 1236, 1163, 1072, 992, 914, 735, 636 cm^{-1}, Found: C, 73.21; H, 8.35%. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H 8.45%.

(2*R,4*R**)-1-Acetoxymethyl-4-methyl-4-(3-methyl-3-butenyl)-2-vinyl-5-cyclopentene (14a):** HPLC (elution with 1.5% ethyl acetate in hexane, 3.0 mL min^{-1}; retention time = 15 min). ^{1}H NMR (270 MHz, $CDCl_3$) δ = 5.65 (dt, J = 17.2, 9.5 Hz, 1H, −C<u>H</u>=CH$_2$), 5.55 (s, 1H, −C<u>H</u>=C<), 5.1—5.0 (m, 2H, −CH=C<u>H</u>$_2$), 4.68 (brs, 2H, >C=CH$_2$), 4.6—4.5 (m, 2H, −CH$_2$−O), 3.4—3.3 (m, 1H, −CH$_2$−C<u>H</u>−CH=), 2.07 (s, 3H, −OAc), 2.1—1.9 (m, 2H, CH$_2$=C(CH$_3$)−C<u>H</u>$_2$−), 1.73 (brs, 3H, CH$_2$=C(C<u>H</u>$_3$)−), 1.6—1.5 (m, 4H, −CH$_2$−C<u>H</u>$_2$−, C<u>H</u>$_2$−CH−), 1.04 (s, 3H, −C<u>H</u>$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 170.8, 146.6, 141.2, 138.1, 138.0, 115.1, 109.4, 62.1, 49.7, 47.6, 44.5, 40.2, 33.5, 26.0, 22.8, 21.0; IR ($CHCl_3$ solution) 3072, 3028, 3002, 2948, 2860, 1727, 1644, 1452, 1374, 1254, 1023, 994, 954, 919, 890 cm^{-1}; MS (EI, 70 eV) 247 ([M−1]$^+$; 0.6%), 234 (0.8), 233 (0.9), 220 (2), 219 (4), 205 (1), 167 (100). HRMS (EI, 70 eV) Calcd for $C_{16}H_{23}O_2$: ([M−1]$^+$), 247.1698. Found: *m/z* 247.1714.

(2*R,4*S**)-1-Acetoxymethyl-4-methyl-4-(3-methyl-3-butenyl)-2-vinyl-5-cyclopentene (14b):** HPLC (elution with 1.5% ethyl acetate in hexane, 3.0 mL min^{-1}; retention time = 14 min). ^{1}H NMR (270 MHz, $CDCl_3$) 5.56 (dt, J = 17.2, 9.3 Hz, 1H, −C<u>H</u>=CH$_2$), 5.52 (s, 1H, −C<u>H</u>=C<), 5.1—5.0 (m, 2H, −CH=C<u>H</u>$_2$), 4.67 (brs, 2H, >C=CH$_2$), 4.6—4.4 (m, 2H, −CH$_2$−O), 3.4—3.3 (m, 1H, −CH$_2$−C<u>H</u>−CH=), 2.2—2.1 (m, 1H, −C<u>H</u>$_2$−CH<), 2.07 (s, 3H, −OAc), 2.0—1.9 (m, 2H, CH$_2$=C(CH$_3$)−C<u>H</u>$_2$−), 1.72 (s, 3H, −C<u>H</u>$_3$), 1.6—1.4 (m, 3H, −CH$_2$−C<u>H</u>$_2$−, C<u>H</u>$_2$−CH<), 1.10 (s, 3H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 170.8, 146.6, 141.6, 138.4, 138.0, 114.9, 109.4, 62.0, 50.4, 47.6, 44.4, 39.8, 33.3, 27.8, 22.8, 21.0; IR ($CHCl_3$ solution) 3070, 3028, 3004, 2948, 2858, 1726, 1644, 1452, 1374, 1257, 1023, 994, 919, 891, 861 cm^{-1}; MS (EI, 70 eV) 247 ([M−1]$^+$; 0.7%), 234 (2), 233 (2), 220 (4), 219 (5), 205 (4), 167 (100). HRMS (EI, 70 eV) Calcd for $C_{16}H_{23}O_2$: ([M−1]$^+$), 247.1698. Found: *m/z* 247.1711.

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