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Palladium(0)-Catalyzed Cycloisomerization of Enallenes

Katja Närhi, Johan Franzén, and Jan-E. Bäckvall*[a]

Abstract: A novel palladium(0)-catalyzed cycloisomerization of enallenes has been developed. This reaction, catalyzed by [Pd(dba)$_2$] (dba = dibenzylideneacetone) in acetic acid, results in the formation of cyclopentene derivatives and [*n*.3.0]bicyclic systems ($n = 3$, 4) in good to high yields. The carbon–carbon bond-forming step is highly stereoselective to give *cis*-fused bicyclic systems. The presence of acetic acid as solvent and dba as ligand for palladium(0) turned out to be essential for the reaction in order to provide good reactivity and regioselectivity.

Keywords: allenes · cycloisomerization · homogenous catalysis · palladium

Introduction

A majority of the biologically active substances, isolated from nature or produced by pharmaceutical industry, contains stereodefined ring systems. Thus, the development of efficient and stereoselective methods for the construction of carbocycles and heterocycles is of great importance in organic chemistry. Transition-metal-catalyzed carbon–carbon and carbon–heteroatom bond-formation reactions have provided useful methodology for the stereoselective construction of ring systems.[1] In particular, transition-metal-catalyzed cycloisomerization reactions, which have been studied thoroughly for enynes[2] and dienes,[3] are important synthetic reactions. Not only are these cycloisomerization reactions an efficient way of constructing carbo- and heterocycles, they are also associated with high atom economy, because there is no requirement of additional reactants and no waste products are formed in the process.[4,5] In contrast to alkenes and alkynes, allenes have received much less attention as components in transition-metal-catalyzed cycloisomerizations. However, in recent years transition-metal-catalyzed cycloisomerization reactions of allenynes with various transition metals (Ti,[6] Rh,[7] Pd,[7a] Mo,[8] Pt[9]) have been reported. Enallenes have also been used in transition-metal-catalyzed cycloisomerization reactions, for which Trost and coworkers reported the first studies with Ni/Cr[10] catalysts. More recently Kang et al.[11] and Itoh et al.[12] reported on ruthenium- and rhodium-catalyzed cycloisomerization of enallenes to give 1,3- and 1,4-dienes. However, to the best of our knowledge there is only one palladium-catalyzed cycloisomerization reaction of one single enallenic substrate previously reported.[13,14]

We have recently reported on palladium(0)-catalyzed carbocyclization reactions of allene-substituted dienes[15] and allene-substituted allylic carboxylates,[16] and on palladium(II)-catalyzed oxidative carbocyclization reactions of allene-substituted dienes[15] and enallenes[14a] in the presence of *p*-benzoquinone.[17] In connection with these studies we found that enallenes **1a–c** underwent palladium(0)-catalyzed cycloisomerization in acetic acid to give **2a–c** as the major products together with a minor isomer **3a–c** in good yields (Scheme 1).[18] We now report on the palladium(0)-catalyzed cycloisomerization of enallenes. This reaction constitutes the first protocol for efficient cycloisomerization of enallenes catalyzed by palladium(0).[19]

Results and Discussion

The requisite starting materials **1** were readily obtained from the corresponding allylic acetates (Scheme 2).[14a,20] A Pd(0)-catalyzed allylic substitution of the acetate with sodium dimethyl malonate, followed by reaction with a disubstituted bromoallene, furnished enallenes **1a–c** and **6** in good yields.

The palladium(0)-catalyzed reaction of **1a** resulted in a carbocyclization reaction to give a regioisomeric mixture of **2a** and **3a** (Table 1, entry 1). Traces (< 6%) of a third

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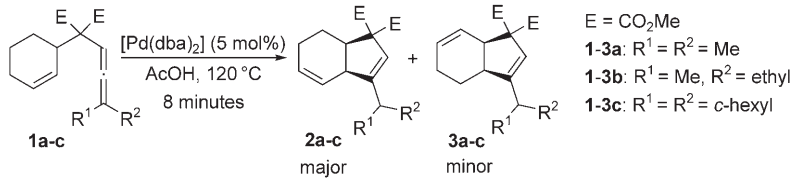
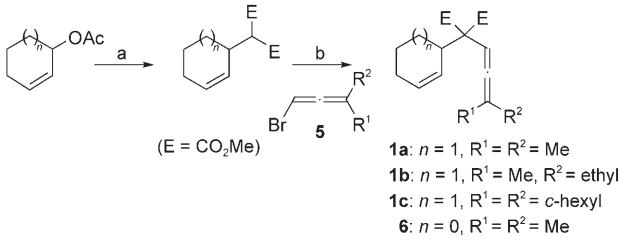


Scheme 1.

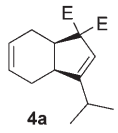


Scheme 2. a) NaH, $(MeO_2C)_2CH_2$, $[Pd(OAc)_2]$, PPh_3, THF, reflux; b) NaH, **5**, THF, reflux.

Table 1. Palladium(0)-catalyzed cycloisomerization of **1a** under different reaction conditions.[a]

Entry	Solvent	Additive (mol%)	Conv. (%)	Ratio (**2a**:**3a**)[b]
1	**AcOH**	–	**100**	**6:1**
2	CH_3CN	-	0	–
3	toluene	–	0	–
4	dichloroethane	–	0	–
5[c]	CH_3CN	AcOH (10)	90	3:1
6[d]	AcOH	LiOAc (1 M)	100	4:1
7[e]	CF_3CO_2H	–	100	complex mixture
8	Toluene	CF_3CO_2H (15)	100	complex mixture
9	AcOH	CF_3CO_2H (10)	50	5:1 (and byproducts)
10	AcOH	$H_2NC_2H_4NH_2$ (10)	100	4:1
11	AcOH	Maleic anhydride (10)	0	–
12	AcOH	PPh_3	90	complex mixture

[a] Enallene **1a** and $[Pd(dba)_2]$ (5 mol%) and additive was dissolved in the specific solvent (10 mL mmol^{-1}) and heated to 120°C (microwave heating) for 8 minutes. [b] The ratio was determined by ^{1}H NMR experiments. This mixture also contains traces of **4a**. [c] 30 minutes reaction time. [d] 15 minutes reaction time. [e] 60°C reaction temperature.

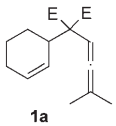
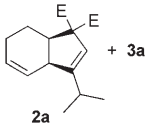
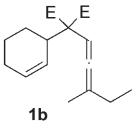
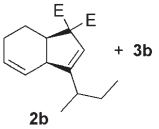
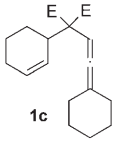
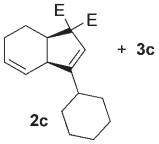
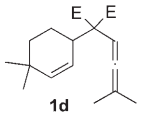
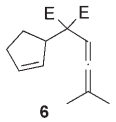
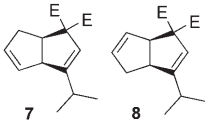
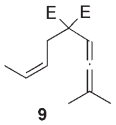
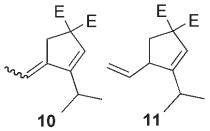
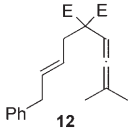
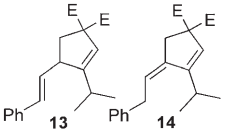
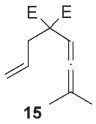
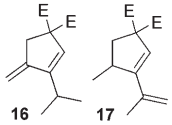


isomer (**4a**) were also detected in the product mixture. The reaction conditions were varied and it was found that the use of 5 mol% $[Pd(dba)_2]$ (dba = dibenzylideneacetone) in acetic acid at 120°C, heated by microwave irradiation, gave the best results with respect to both regioselectivity and yield. Under these reaction conditions, **2a** and **3a** were obtained in a 6:1 ratio with full conversion after eight minutes (Table 1, entry 1).[18,21] A similar result was obtained when the reaction of **1a** was carried out with thermal heating in an oil-bath, but otherwise under the same reaction conditions. The microwave flash heating was used mainly as an efficient tool to scan different reaction conditions.[22] It was found that acetic acid was essential for an efficient reaction to proceed. For example, if the solvent used in the reaction was changed to an aprotic solvent (e.g., acetonitrile, 1,2-dichloroethane, or toluene, 120°C, microwave heating) no reaction occurred and the starting material was recovered (Table 1, entries 2–4). If a catalytic amount of acetic acid was added to the reaction mixture in acetonitrile (Table 1, entry 5) 90% conversion of **1a** to **2a** and **3a** was obtained in a 3:1 ratio after 30 minutes. When the acidity was increased by the use of trifluoroacetic acid, a very fast consumption of the substrate **1a** occurred at 60°C to give a complex mixture of unidentified products (Table 1, entry 7). The same result was obtained when catalytic amounts of trifluoroacetic acid in toluene were used (entry 8). When trifluoroacetic acid (10 mol%) was used in acetic acid, this unexpectedly resulted in a decrease of the reaction rate and a less selective reaction (Table 1, entry 9). In an attempt to improve the regioselectivity of the reaction (of **1a** to **2a** and **3a**), a few different ligands for palladium(0) were added to the reaction (Table 1, entries 10–12). Electron-donating ligands, such as ethylene diamine, had no effect on substrate conversion but lowered the selectivity of the reaction giving a 4:1 ratio between **2a** and **3a**. Maleic anhydride, which can act as an electron-withdrawing ligand, inhibits the reaction under these conditions (Table 1, entry 11). Surprisingly, addition of triphenylphosphine to the palladium-catalyzed reaction of **1a** led to side reactions and only minor amounts of **2a** and **3a** could be detected together with a mixture of unidentified products.

The best reaction conditions from Table 1 (entry 1) were employed for the preparative carbocyclizaton of a number of different enallenes (Table 2). Reaction of **1a** with 5 mol% $[Pd(dba)_2]$ in AcOH, under microwave heating at 120°C for eight minutes and workup by flash chromatography gave **2a+3a** in a ratio of 88:12 and in a total yield of 83% (Table 2, entry 1).[18,23,24] Cyclization of the methyl ethyl (**1b**) and cyclohexyl derivatives (**1c**) under these reaction conditions gave **2b+3b**[25] and **2c+3c**, respectively, in a ratio of 6:1 and in a total yield of 90% in both cases (Table 2, entries 2 and 3).[18,21,26]

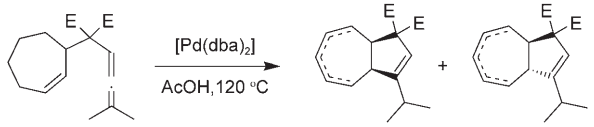
When two methyl groups were present in the allylic position (**1d**) no reaction occurred and the starting material was recovered (Table 2, entry 4). The reaction of the five-membered ring analogue **6** under the same reaction conditions

Table 2. Palladium(0)-catalyzed cycloisomerization of allene-substituted olefins **1**.[a]

Entry	Starting material	Products	Yield (%)[b] (ratio)
1	 **1a**	 **2a** + **3a**	83 (**2a**:**3a** = 88:12)[c,d,e]
2	 **1b**	 **2b** + **3b**	90 (**2b**:**3b** = 6:1)[d,f,g]
3	 **1c**	 **2c** + **3c**	90 (**2c**:**3c** = 6:1)[d,f]
4	 **1d**	–	no reaction
5	 **6**	 **7** **8**	92 (**7**:**8** = 78:22)[c]
6	 **9**	 **10** **11**	73 (**12**:**11** = 67:33)[c,h]
7	 **12**	 **13** **14**	74 (**13**:**14** = 73:27)[c,h]
8	 **15**	 **16** **17**	52(**16**:**17** = 13:3)[i,j]

[a] Unless otherwise noted; **1** and $[Pd(dba)_2]$ (5 mol%) in AcOH (6 mL mmol^{-1}) was heated to 120°C for 8 minutes by microwave irradiation. [b] Isolated yields after flash chromatography. [c] The ratio was determined by GC. [d] Traces of the corresponding regioisomer **4a–c** were also detected (<6%). [e] The isolated yield (83%) contains traces of **4a** (<6% of the total amount (determined by GC). [f] The ratio was determined by ^{1}H NMR integration. [g] Compounds **2b** and **3b** were obtained as a 1:1 mixture of their corresponding diastereoisomers. [h] Compounds **9** or **12** and $[Pd(dba)_2]$ (10 mol%) in AcOH (6 mL mmol^{-1}) were heated to 120°C for 40 minutes. [i] Compound **15** and $[Pd(dba)_2]$ (10 mol%) in AcOH (6 mL mmol^{-1}) were heated to 80°C for 10 h. [j] Compound **17** is an Alder–ene product formed by means of a thermal background reaction, see reference [27].

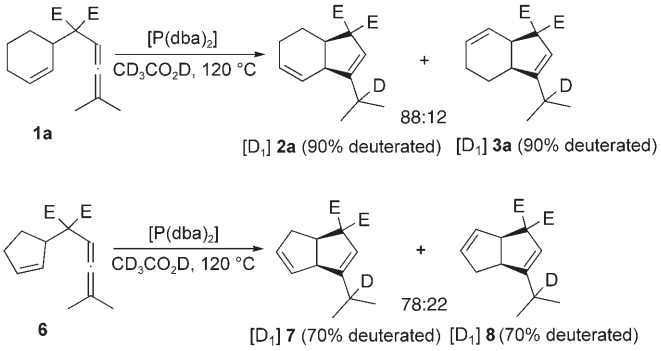
gave products **7**+**8** in a ratio of 78:22 in 92% total yield with full conversion within eight minutes (Table 2, entry 5).[23] The cyclization of **1a–c** and **6** is stereoselective in the C–C bond-forming step and gives only the *cis*-fused ring systems. In contrast to the five- and six-membered ring substrates, the reaction of the seven-membered ring analogue showed poor stereoselectivity in the carbon–carbon bond-forming step. Under the same reaction conditions as for **1a–c** a mixture of *cis*- and *trans*-fused ring systems were obtained (Scheme 3).



Scheme 3.

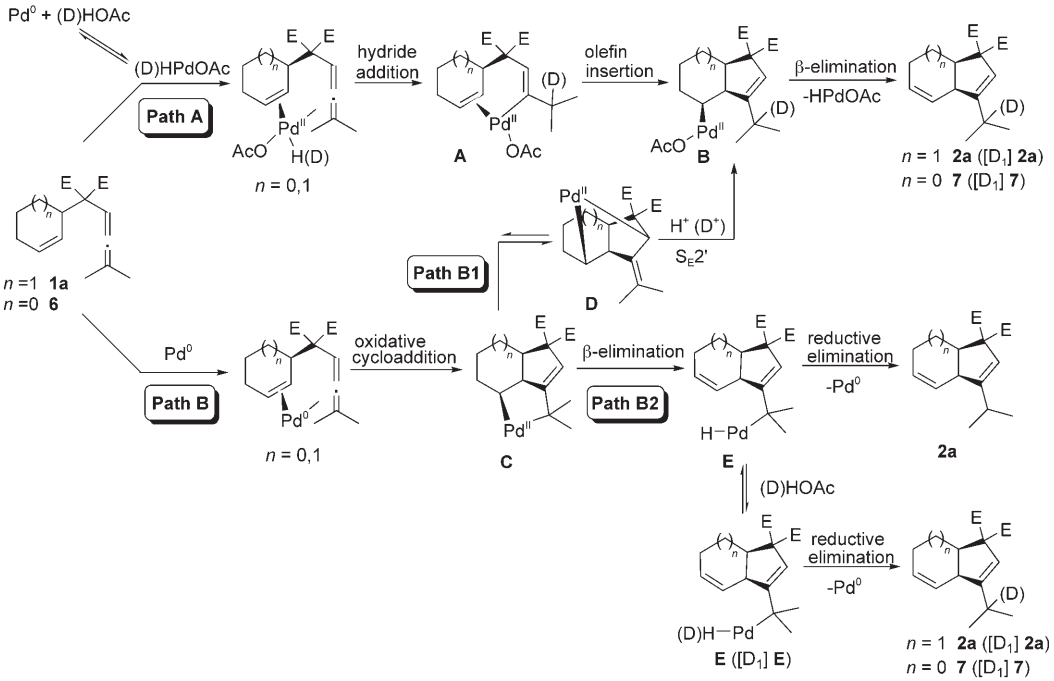
For the acyclic substrates the catalyst loading and the reaction time were increased to obtain full conversion. Palladium-catalyzed cycloisomerization of **9** and **12** (10 mol% $[Pd(dba)_2]$ in AcOH and microwave heating at 120°C for 40 minutes) produced a mixture of regioisomeric cyclopentene derivatives in good yields (entries 6 and 7). Using the same reaction conditions as above for the acyclic substrate with a terminal olefin (**15**, entry 8) resulted in the formation of only one regioisomer, but in a moderate yield (50%) and also contaminated with a thermal Alder–ene product (**17**) formed in the reaction (Table 2, entry 8).[27] To reduce the formation of the thermal product the temperature was decreased. The best result was obtained at 80°C with a reaction time of 10 h, which afforded **16** and **17** in a ratio of 13:3 in 52% yield.[27]

Mechanistic consideration: To gain further insight into the mechanism of the cycloisomerization, enallenes **1a** and **6** were treated with 5 mol% $[Pd(dba)_2]$ in deuterated acetic acid; this resulted in the formation of the monodeuterated products $[D_1]$**2a**+$[D_1]$**3a** and $[D_1]$**7**+$[D_1]$**8** (according to ^{1}H NMR spectroscopy; Scheme 4).



Scheme 4.

The $[Pd(dba)_2]$-catalyzed reaction of **1a** or **6** in acetic acid to give **2a** or **7**, respectively, can be initiated in two ways: 1) either through oxidative addition of the solvent (HOAc) to palladium(0) (Path A, Scheme 5) or 2) by means of an oxidative cycloaddition reaction (Path B, Scheme 5). The oxida-



Scheme 5.

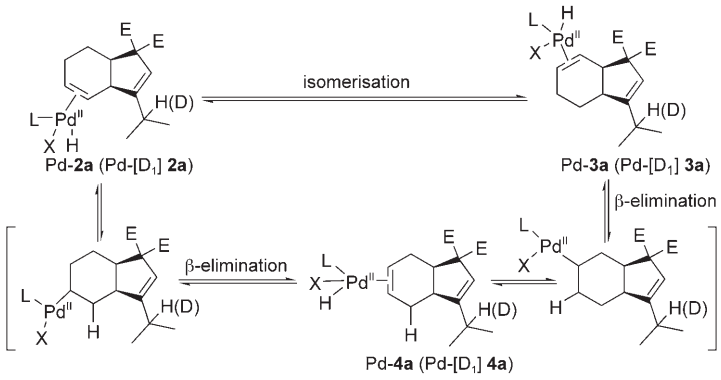
tive addition of acetic acid to $[Pd(dba)_2]$ would give a palladium(II) hydride species. This palladium(II) hydride species can then add to the terminal carbon atom of the allenic moiety resulting in a vinyl–palladium intermediate (**A**; this would account for the incorporation of deuterium in the products $[D_1]$**2a** and $[D_1]$**7** when DOAc is used). An insertion of the double bond into the palladium–carbon bond would give **B**, which subsequently would undergo a β-hydride elimination to give the product (Scheme 5, Path A). In the final step HPdOAc is formed, which initially is coordinated to the product (**2a** or **7**). Once free in solution, HPdOAc is expected to undergo relatively fast exchange with acetic acid, and with deuterated acetic acid DPdOAc would be produced. Coordinatinon of the substrate (**1a** or **6**) to the palladium(II) hydride species would close the catalytic cycle. The observation of a significant amount of non-deuterated product **2a** or **7** when DOAc is employed as solvent, can be explained by a too slow exchange of HPdOAc with DOAc, so that some HPdOAc re-enters the catalytic cycle.

The cycloisomerization can also be explained by an oxidative cycloaddition of the enallene to palladium(0), forming the (η_1-allyl)(σ-alkyl)palladium(II) intermediate **C** (Scheme 5, Path B). Similar types of (mono-σ-allyl)palladium complexes have been studied by Kurosawa et al.[28] and more recently by Szabo et al.,[29] and it has been shown that electron-donating groups, such as σ-carbon-bonded ligands, on palladium makes the allyl function rather reactive towards electrophiles. Incorporation of deuterium in the isopropyl moiety can be explained by isomerization of **C** to **D**, followed by protonation (deuteration) in an S_E2' fashion to give **B**, which then leads to the product formation by means of β-hydride elimination (Scheme 5, Path B1).

It can also be argued that intermediate **C** could undergo β-hydride elimination to give **E**, followed by a reductive hydride elimination to give **2a** or **7** (Scheme 5, Path B2). However, cyclization according to path B2 cannot explain the incorporation of deuterium when DOAc is employed, unless **E** undergoes deuterium exchange with DOAc to give $[D_1]$**E**. Subsequently $[D_1]$**E** would undergo a reductive elimination forming the deuterated product $[D_1]$**2a** or $[D_1]$**7** (Scheme 5, Path B2). However, exchange of Pd–H with DOAc is known to be a slow process when a hydrocarbon is coordinated to palladium.[30] This makes path B2 less likely.

During the optimization of the reaction it was found that the palladium(0)-catalyzed reaction of **1a** does not work with aprotic solvents (Table 1, entries 2–4). This is consistent with path A being the major pathway for the cyclization of **1a** to **2a**. Moreover, when the acetic acid concentration is decreased the reaction becomes slower (compare entries 1 and 5, Table 1). This can be interpreted as the equilibrium for the oxidative addition of palladium(0) to acetic acid is shifted to the left, leading to a decrease in the concentration of the reactive palladium hydride intermediate and consequently a slower reaction. This observation is in accordance with path A.[31] On the other hand in the presence of trifluoroacetic acid, the concentration of the palladium hydride intermediate should increase (i.e., the equilibrium would be shifted to the right); this increase is expected to lead in turn to an increased reaction rate. However, a slower reaction was observed and this is probably due to the lower stability of $HPdOOCCF_3$ (see Table 1, entry 9).

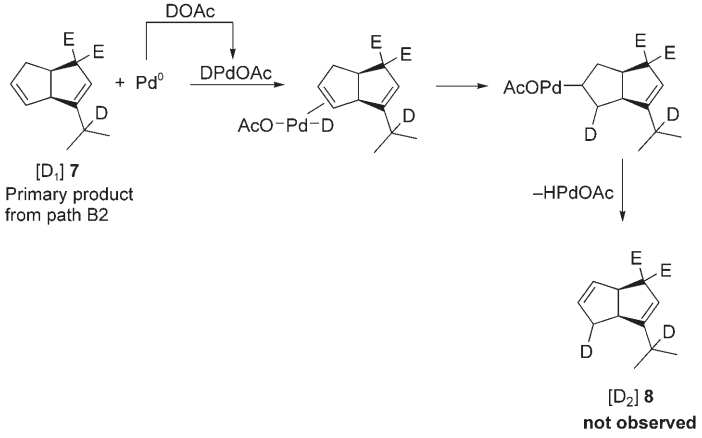
A fast reversible β-elimination/re-addition/β-elimination process would explain the formation of the regioisomeric products **3a–c** (Scheme 6). This isomerization process also



Scheme 6.

involves the formation of the third regioisomer, **4a–c** (Scheme 6), and the ratio between **2**, **3**, and **4** is most likely the thermodynamic product distribution. This was further supported by comparing the energies of the preferred conformer of each of the three isomers.[32] Unfortunately, the palladium hydride catalyzed isomerization of **2** to **3** and **4** is faster than the cyclization of **1**. Thus, inhibition of the isomerization of **2** would also lead to an inhibition of the cyclization of **1**, since the same palladium hydride intermediate is believed to be the active catalyst in both processes.

When running the reaction of enallenes **1a** and **6** in deuterated acetic acid the isomerization of the primary product of path B2 would lead to deuterium incorporation in the ring that is isomerized. This is because Pd^0 is formed in a reductive elimination in path B2, and addition of DOAc to Pd^0 would produce DPdOAc. The latter would introduce deuterium in the ring that is isomerized (shown for the product from **6**, Scheme 7). When five-membered-ring analogue **6** was treated with 5 mol% [$Pd(dba)_2$] in deuterated



Scheme 7.

acetic acid monodeuterated products [D_1]**7**+[D_1]**8** were formed, and no additional incorporation of deuterium was detected in [D_1]**8** by ^{1}H NMR spectroscopy (Scheme 4). This observation rules out pathway B2.

The lack of deuterium in the ring that is isomerized is consistent with pathways A and B1. In these pathways the palladium hydride formed from β-elimination is re-added to the coordinated double bond (cf. Scheme 6). The observation that a protic solvent is required for the reaction favors path A.

Conclusion

A novel palladium-catalyzed cycloisomerization of readably available enallenes has been developed. The reaction gives stereodefined bicyclic compounds or functionalized cyclopentene derivatives in high yield. From deuterium labeling experiments and the fact that the reaction requires a protic solvent, we propose that the cyclization involves the formation of a palladium hydride species as the active catalyst. Addition of the latter to the allene results in the formation of a vinyl–palladium species. A subsequent insertion of the olefin into the Pd–vinyl bond constitutes the carbon–carbon bond formation step.[33]

Experimental Section

Commercially available chemicals were used without further purification. The microwave heating was performed in a Smith Creator (Biotage AB, Uppsala, Sweden). The reaction mixture was stirred with a magnetic stir bar during the irradiation. The temperature, pressure, and irradiation power were monitored during the course of the reaction. Merck silica gel 60 (240–400 mesh) was used for flash column chromatography. ^{1}H NMR (400 or 300 MHz) and ^{13}C NMR (100 and 75 MHz) spectra were recorded with [D_1]chloroform ($\delta = 7.26$ ppm ^{1}H, $\delta = 77$ ppm ^{13}C) as internal standard. The preparative HPLC used was a Bischoff HPLC compact pump with a refractive index detector and column; Kromasil 100 SIL 5 μm (250×20 mm). Gas chromatography analyses were performed on a Varian 3380, CP-Sil 8 CB (30 m×0.32 mm×0.25 μm) capillary column (CHROMPACK).

Substrates 1a–g were prepared according to previously described procedure.[14a]

General procedure for the preparation of 2 and 3

*Compounds **2a** and **3a***: A solution of **1a** (0.139 g, 0.5 mmol) and [Pd(dba)$_2$] (0.014 g, 0.025 mmol) in acetic acid (3 mL) was microwave-heated at 120 °C for 8 min. Water (10 mL) was added, and the aqueous layer was extracted with Et_2O (4×20 mL). The combined organic phases were washed with saturated $NaHCO_3$ solution (3×10 mL) and dried (Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (pentane/Et_2O 6:1) to give 0.115 g (83% total yield) of **2a** and **3a** (ratio 88:12) contaminated with some of **4a**. Alternatively the crude product could be purified by preparative HPLC (pentane/ethylacetate 25:1) to give 0.099 g of **2a** and **3a** in a total yield of 71%. (free from traces of isomer **4a**). ^{1}H NMR (400 MHz, $CDCl_3$) of **2a**: $\delta = 5.82$ (m, 2H), 5.38 (dd, $J = 2.9$, 1.5 Hz, 1H), 3.73 (s, 3H), 3.69 (s, 3H), 3.44 (m, 1H), 3.13 (ddd, $J = 12.9$, 6.0, 4.3 Hz, 1H), 2.34 (heptet, $J = 6.7$ Hz, 1H), 1.98 (m, 2H), 1.34 (m, 1H), 1.25 (m, 1H), 1.11 (d, $J = 6.7$ Hz, 3H), 1.01 ppm (d, $J = 6.7$ Hz, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) of [D_1]**2a**: $\delta = 5.82$ (m, 2H), 5.38 (d, $J = 3.0$ Hz, 1H), 3.73 (s, 3H), 3.69 (s, 3H), 3.44 (m, 1H), 3.13 (ddd, $J = 12.9$, 6.0, 4.3 Hz, 1H), 1.98

(m, 2H), 1.34 (m, 1H), 1.25 (m, 1H), 1.10 (s, 3H), 1.006 ppm (s, 3H); ^{1}H NMR (400 MHz, $CDCl_3$) of **3a**: significant peaks $\delta = 5.75$ (m, 2H), 5.40 (t, $J = 1.5$ Hz, 1H), 3.71 (s, 3H), 3.68 (s, 3H), 2.98 (m, 1H), 1.13 (d, $J = 7.0$ Hz, 3H), 1.01 ppm (d, $J = 7.0$ Hz, 3H); elemental analysis calcd (%) for (**2a**/**3a**) $C_{16}H_{22}O_4$: C 69.04, H 7.97; found: C 69.03, H 7.92.

A sample of the minor isomer **4a** was obtained by preparative HPLC purification. ^{1}H NMR (400 MHz, $CDCl_3$) of **4a**: $\delta = 5.80$ (br d, $J = 10.9$ Hz), 5.60 (dddd, $J = 10.1$, 3.8, 2.0, 1.0 Hz, 1H), 5.38 (t, $J = 1.5$ Hz, 1H), 3.75 (s, 3H), 3.66 (s, 3H), 3.45 (m, 1H), 2.85 (m, 1H), 2.39 (heptet, $J = 6.9$ Hz, 1H), 1.97 (m, 3H), 1.78 (dq, $J = 13.1$, 4.6 Hz, 1H), 1.15 (d, $J = 6.9$ Hz, 3H), 1.03 ppm (d, $J = 6.9$ Hz, 3H).

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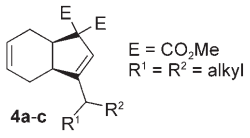

[18] Traces of the corresponding regioisomer **4a–c** were also detected.

[19] A single example of a cycloisomerization of a cyano-activated enallene catalyzed by Pd^{2+} has been reported.[13]

[20] The acyclic starting materials **9**, **12**, and **15** were obtained in the same way as the cyclic starting materials **1a–c** and **6** from there corresponding allylic acetates.

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[23] An alternative workup can be performed by preparative HPLC to give **2a** and **3a** in 71% yield without any traces of regioisomer **4a** (see the Experimental Section).

[24] The ratio was determined by GC.

[25] Compounds **2b** and **3b** were obtained as a 1:1 mixture of their corresponding diastereoisomers.

[26] The ratio could not be determined by GC, because of poor separation between all three products.

[27] During this work we found that enallenes undergo thermal Alder–ene reactions when no palladium catalyst is present at 120°C. In the reaction of **1h** the thermal Alder–ene reaction competes with the palladium-catalyzed reaction. Therefore the reaction temperature was decreased to 80°C and the reaction time was prolonged to 10 h to give **16** and **17** in a ratio of 13:3 in 52% yield. Further work on the thermal Alder–ene reaction is currently pursued in our laboratory and will be reported shortly.

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[31] Another possible mechanistic pathway that is not discussed in Scheme 5 involves, as in Path A, an oxidative addition of acetic acid to palladium(0) to give a palladium(II) hydride species (which would explain the need of a protic solvent). The palladium(II) hydride species would then undergo an oxidative cycloaddition to produce a palladium(IV) intermediate (a palladacycle similar to **C** but with Pd^{IV} hydride) followed by a reductive elimination and a β-hydride elimination forming the product. This pathway would also account for the incorporation of deuterium in the product $[D_1]$**2**. Palladium(IV) intermediates have been proposed as possible intermediates in cycloisomerization reactions.[2a]

[32] In all three isomers the carbon atoms bound to the six-membered ring have to possess an equatorial and axial position, respectively. In **2a** and **3a** energy is gained if the axial carbon is in the allylic position (pseudoaxial) and the equatorial carbon substituent is in the nonallylic position. Thus **3a** is forced to have the more sterically hindered carbon substituent $C(CO_2Me)_2$ in the allylic pseudoaxial position, whereas **2a** can have the less sterically hindered carbon atom in the allylic pseudoaxial position. For this reason **2a** is more stable than **3a**. In **4a** one of the carbon atoms has to be in a nonallylic axial position, which is the least favorable situation. Therefore **4a** is the least stable regioisomer. Simple Chem 3D calculations confirmed this conclusion.

[33] The formation of a palladium–vinyl species is not the expected reaction between a palladium hydride species and an allene. Generally one would expect the hydride to add to the middle carbon of the allene to form a palladium–allyl intermediate. However, formation of vinyl–palladium intermediates from allenes have been observed before: a) R. Zimmer, C. U. Dinesh, E. Nandanam, F. A. Khan, *Chem. Rev.* **2000**, *100*, 3067; b) Y. Yamamoto, U. Radhakrishnan, *Chem. Soc. Rev.* **1999**, *28*, 199.

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