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Novel Pd(0)-Catalyzed Intramolecular Reactions of Allylic Acetates with Allenic Moieties Followed by Tandem Cyclization

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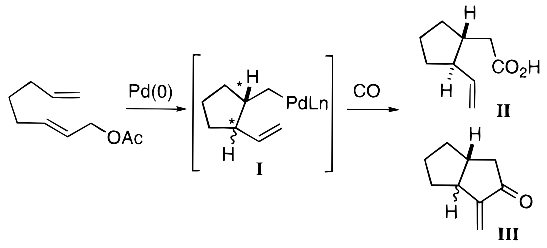
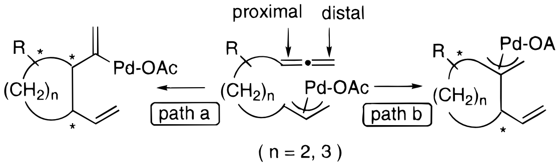
Reactions of π-allylpalladium complexes with various nucleophiles have been widely studied and used for a variety of organic syntheses.[1] Recently, we have reported that the intramolecular reactions of the π-allylpalladium complex with an alkene moiety[2] give rise effectively to five- or six-membered ring systems.[3] Moreover, tandem reactions utilizing a σ-alkylpalladium intermediate **I** formed by the alkene allylation exhibit a great advantage for the consecutive C−C bond formation, such as carbonylation **II** and the Heck reaction[4] **III**, without losing newly formed stereogenic centers (eq 1).[5−7]



(1)

Although there have been ample examples of the Heck-type carbopalladation to allenes forming a new π-allylpalladium intermediate that mostly undergoes the well known allylation with nucleophiles,[8] a few reactions of a π-allylpalladium complex with an allene moiety have been reported.[9] We wish to report, for the first time, an intramolecular version of the Pd(0)-catalyzed reaction of 2,7,8-octatrienyl acetates and 1-vinyl-4,5-hexadienyl acetates where the allene and the π-allylpalladium unit are tethered by two and three carbon chains (eq 2). The reactions hold salient features as follows: (i) regioselection (path a or path b) definitely favors the five-membered ring formation, (ii) the allene unit is more reactive toward the π-allylpalladium unit than the other alkene (R = alkenyl group), (iii) intraannular and diastereofacial stereoselectivities[10] in path a are cleanly controlled, and (iv) tandem reactions including either the newly formed σ-vinylpalladium or π-allylpalladium intermediate are developed.



(2)

The Pd(0)-catalyzed cyclization of **1a** proceeded in acetic acid at 45 °C under a carbon monoxide atmosphere to give an 82:18 mixture of **2a** and **3a** (2:1 mixture of meso-diastereomers) in 41% combined yield (Scheme 1). Presumably, the π-allylpalladium intermediate **4** formed from **1a** underwent an alkene insertion (or a pallada−ene reaction) at the proximal site of the allenic unit (path a in eq 2, $n = 3$) rather than at the other terminal alkene, and the resulting σ-vinylpalladium species **5** gave rise to **2a** and **3a** *via* carbonylation[11] followed by solvolysis.[3] To the best of our knowledge, *the regioselection of the present intramolecular carbopalladation to the allene moiety giving an alkenylpalladium intermediate is unprecedented.*[12,13] Since the intraannular diastereoselectivity[10] in the cyclization of **1a** is ambiguous because of symmetrical vinyl groups in **2a**, the reaction of **1b** that is deuterium labeled was carried out under the same reaction conditions and gave **2b**. The *trans* stereochemistry between the deuterated ($>$95%) vinyl group and the α-(hydroxycarbonyl)vinyl group was determined by a 10% NOE observation between Ha and Hb protons (Scheme 1). Therefore, the intraannular diastereoselection in the primary cyclization of **4** is shown to be predominantly *cis* ($>$88%) and the diastereofacial selectivity between the C-6 and C-3 is 82% *trans*, as indicated in **5**.[14]

The newly formed σ-vinylpalladium intermediates such as **5** could undergo not only carbonylation but also the Heck reaction shown in the reaction of **6** and **8**, respectively. Treatment of methyl-substituted analog **6** under the reaction conditions as above gave **7** and three

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(1) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer Verlag: New York, 1980. Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. Godleski, S. A. Nucleophiles with Allyl-Metal Complexes. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 585−661.

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(3) Yamamoto, K.; Terakado, M.; Murai, K.; Miyazawa, M.; Tsuji, J.; Takahashi, K.; Mikami, K. *Chem. Lett.* **1989**, 955. Terakado, M.; Murai, K.; Miyazawa, M.; Yamamoto, K. *Tetrahedron* **1994**, *50*, 5705.

(4) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379. Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146; *Org. React.* **1982**, *27*, 345.

(5) For an excellent example of stereocontroled tandem cyclization using Pd(0)-catalyzed olefin allylation followed by Heck reaction, see: Oppolzer, W.; DeVita, R. J. *J. Org. Chem.* **1991**, *56*, 6256.

(6) For tandem cyclization anion capture, see: Grigg, R.; Sukirthalingam, S.; Sridharan, V. *Tetrahedron Lett.* **1991**, *32*, 2545. Grigg, R.; Sridharan, V.; Sukirthalingam, S. *Ibid.* **1991**, *32*, 3855.

(7) Keese, R.; Guidetti-Grept, R.; Herzog, B. *Tetrahedron Lett.* **1992**, *33*, 1207.

(8) For *intermolecular* carbopalladation of allenes, see: (a) Stevens, R. R.; Shier, G. *J. Organomet. Chem.* **1970**, *21*, 495. (b) Shimizu, I.; Tsuji J. *Chem. Lett.* **1984**, 233. (c) Larock, R. C.; Varaprath, S.; Lau, H. H.; Fellows, C. A. *J. Am. Chem. Soc.* **1984**, *106*, 5274. (d) Alper, H.; Hartstock, F. W.; Despeyroux, B. *J. Chem. Soc., Chem. Commun.* **1984**, 905. (e) Ahmar, M.; Barieux, J.-J.; Cazes, B.; Gore, J. *Tetrahedron* **1987**, *43*, 513. (f) Yamamoto, Y.; Al-Masum, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 6019. (g) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, *117*, 5156. For *intramolecular* version, see: (h) Ma, S.; Negishi, E. *J. Org. Chem.* **1994** *59*, 4730. (i) Ma, S.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 6345.

(9) Only stoichiometric reactions of the π-allylpalladium complex with allenes are known; see: Hughes, R. P.; Powell, J. *J. Organomet. Chem.* **1969**, *20*, P17; **1973**, *60*, 409.

(10) Mikami, K; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021.

(11) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318.

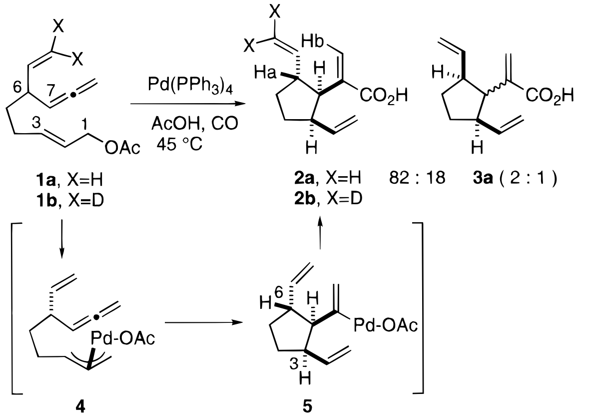
(12) In a recent example,[8f] carbopalladation to an allene with this particular regioselection had been reported. However, it was reasonably postulated as the hydropalladation mechanism with usual regioselection in ref 8g.

(13) For amino- and alkoxypalladation to allenes to generate σ-vinylpalladium intermediates, see: Alper, H.; Hartstock, F. W.; Despeyroux, B. *J. Chem. Soc., Chem. Commun.* **1984**, 905. Hegedus, L. S.; Kambe, N.; Tamaru, R.; Woodgate, P. D. *Organometallics* **1983**, *2*, 1658. Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009.

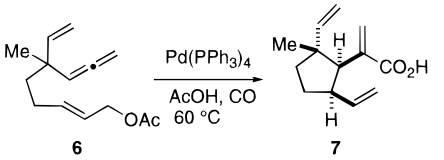
(14) Intraannluar diastereoselction of the Pd(0)-catalyzed cyclization of acyclic compounds is more or less *trans* dominant, whereas that of the Ni(0)-catalyzed cyclization is known to be exclusively *cis*: Oppolzer, W.; Keller, T. H.; Bedoya-Zurita, M.; Stone, C. *Tetrahedron Lett.* **1989**, *30*, 5883. See also refs 2 and 3.

0022-3263/96/1961-2602$12.00/0

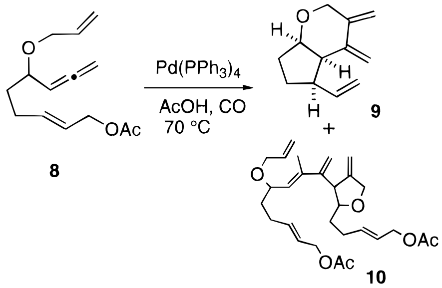
Scheme 1



diastereomers (80:14:3:3) in 28% combined yield (eq 3). The reaction of **8** under argon gave **9** in 16% yield, accompanied with a mixture of diastereomers **10** (39%), which was produced by Pd(0)-catalyzed dimerization of the allene moiety[15] and alkene allylation (eq 4). Although the yields were far from satisfactory in the cyclization of **1**, **6**, and **8**,[15] we found intramolecular carbopalladation to the allene proceeds faster than to the other terminal alkene with a novel regioselection (path a in eq 2, $n = 3$) and the resulting σ-vinylpalladium intermediates undergo further tandem reactions leading to acrylic acids **2** and **7** and the bicyclic compound **9**.



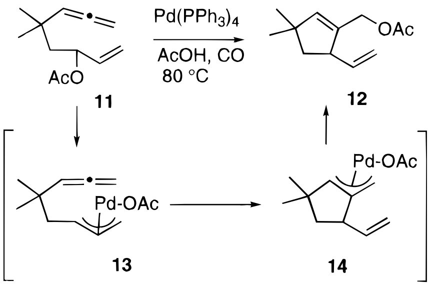
(3)



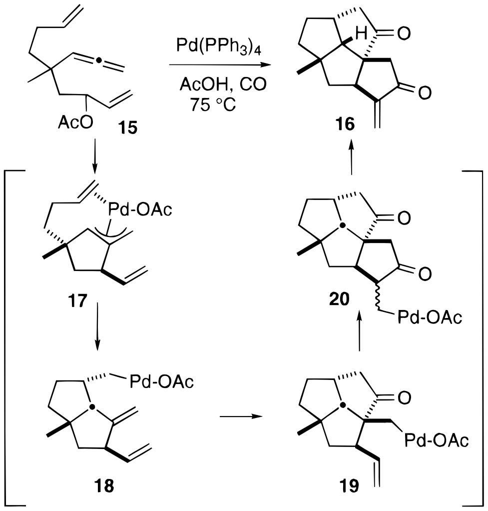
(4)

Keeping the unprecedented regioselection in the cyclizations of π-allylpalladiums with the allenes in mind, we have examined the cyclization of **11**, in which the allylic acetate and the allene are tethered by two methylene carbons. Our question is whether the π-allylpalladium intermediate can react at the proximal site of the allenic unit as shown above (path a in eq 2, $n = 2$) or can react at the distal site of that (path b in eq 2, $n = 2$), forming a five-membered ring. Treatment of **11** with Pd(PPh$_3$)$_4$ (10 mol %) in acetic acid under carbon monoxide (1 atm) provided an allylic acetate **12** in 64% yield. The initially formed π-allylpalladium complex **13** undergoes exclusively an alkene insertion at the distal site on the allenic unit (path b), resulting in a new π-allylpalladium intermediate **14**, which in turn proceeds back to the corresponding allylic acetate **12** (Scheme 2). In fact, shortening the tether by one carbon between the π-allylpalladium and the allene has caused a drastic change in the regioselection of the cyclization.[16]

Scheme 2



Scheme 3



It is thus suggested that the newly formed π-allylpalladium complex **14** could undergo further alkene allylation if another alkene moiety is located at an appropriate position. In fact, this reaction was extended to the formation of tetracyclic diketone **16** (Scheme 3). The Pd(0)-catalyzed tandem cyclization of tetraenyl acetate **15** proceeded in the presence of 10 mol % of Pd(PPh$_3$)$_4$ under carbon monoxide (in AcOH, 75 °C) to give tetracyclic compound **16** in 22% yield.[17] The stereochemistries of **16** as well as the skeleton itself were confirmed by decoupling and NOE studies in ^{1}H NMR. A proposed mechanism is shown in Scheme 3. Considering only one of the four diastereomeric intermediates, *i.e.*, **18** is topologically feasible for the formation of **16**, it is noteworthy that the six consecutive C−C bond formation involving four carbopalladation and two carbonylation insertions has taken place in one operation.

In summary, we have demonstrated that the novel intramolecular reactions of the π-allylpalladium intermediates to allene moieties gave two modes of cyclization which could be controlled by the length of a carbon tether between them, and are effective method for construction of carbocycles by tandem reactions.

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Supporting Information Available: Experimental procedures and compound characterization data (17 pages).

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[15] The low yields in the Pd(0)-catalyzed cyclization of allenes are due to the dimerization of allenes; see: Shier, G. D. *J. Organomet. Chem.* **1967**, *10*, P15. Coulson, D. R. *J. Org. Chem.* **1973**, *38*, 1483.

[16] The reaction did not proceed under argon. The presence of carbon monoxide could accelerate the reductive elimination of the intermediate **14**. See: Murahashi, S.-I.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *J. Org. Chem.* **1993**, *58*, 1538. Yamamoto, T.; Akimoto, M. Yamamoto, A. *Organometallics* **1986**, *5*, 1559.

[17] The bicyclic products were also produced in 18% yield *via* β-hydride elimination of the intermediates such as **18**.