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Palladium(0)-Catalyzed Cyclization-Carbonylation of 2,7-Octadienyl Acetate and Analogs

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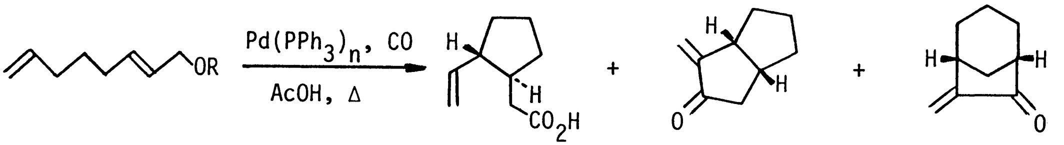
The palladium(0)-catalyzed carbonylation of 2,7-octadienyl acetate and analogs via π-allylic intermediates can be preceded by their intramolecular olefin insertion, in acetic acid, affording 2-vinylcyclopentylacetic acid and derivatives therefrom.

Despite ample examples of the palladium-catalyzed allylation of soft carbon nucleophiles, there have been few reports that indicate possible insertion of an olefin into π-allylic palladium compounds or intermediates. Recently, an intramolecular version of such reactions has been communicated as the first example of the allylation process.$^{1)}$

Oppolzer et al. have extensively been studying$^{2)}$ the Pd(0)-catalyzed cyclization of dimethyl allyl(4-acetoxy-2-butenyl)malonate into 2-vinyl-methylenecyclopentane derivative in AcOH as an effective solvent, referring to the cyclization as a palladium-ene reaction.$^{3)}$ We now report here that the Pd(0)-catalyzed cyclization-carbonylation of 2,7-octadienyl acetate (**1a**) and carbonate (**1b**) proceeds in AcOH to give three carbonylation compounds, 2-vinylcyclopentylacetic acid (**2**) being a major product (Eq. 1).



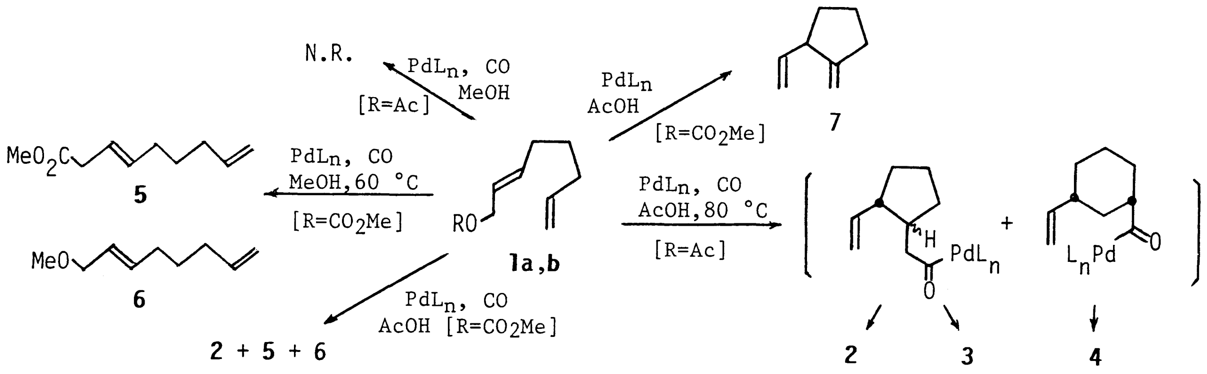
(1)

1a R = Ac
b R = CO$_2$Me

2 **3** **4**

Allylic carbonates were found to undergo a facile decarboxylation-carbonylation to give the corresponding β,γ-unsaturated esters under mild conditions.$^{4)}$ Recently, the smooth carbonylation of allylic chlorides,$^{5a,b)}$ and acetates$^{5b,c)}$ was established by modifying reaction conditions.

No carbonylation of **1a** in MeOH at 60 °C under CO (10 atm) took place. However, the carbonylation of **1b** afforded methyl 3,8-nonadienoate (**5**, 70% yield) along with 2,7-octadienyl methyl ether (**6**) under the same reaction conditions (see, Scheme 1). When **1b** was treated with CO (5 atm) in the presence of a Pd(0) catalyst in AcOH at 80 °C, 2-vinylcyclopentylacetic acid (**2**) was formed as a minor component (≈20%) in addition to **5** and **6** (40% combined yield). Without CO **1b** was



Scheme 1.

converted to 2-vinylmethylenecyclopentane (**7**)2) in 90% yield.

The crucial solvent effect of AcOH in the Pd-ene reaction was first observed by Oppolzer.2) Our results also indicate that the solvent, either MeOH or AcOH, plays a decisive role in determining the course of reaction and that the intramolecular olefin insertion to a π-allylic palladium intermediate may precede the carbonylation in AcOH. Thus, the Pd(0)-catalyzed cyclization-carbonylation of **1** was examined in detail.

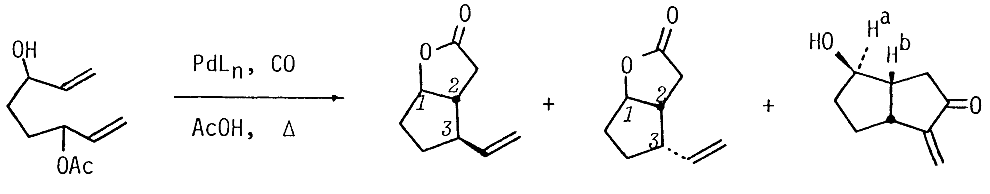
In a 50 mL microautoclave lined with a glass container were placed $Pd_2.(dba)_3.CHCl_3$ (26 mg, 0.025 mmol) and PPh_3 (39 mg, 0.15 mmol) under argon. To the mixture was added deaeronated AcOH (5 mL) and the solution was stirred magnetically for 10 min. To this solution was added 2,7-octadienyl acetate (**1a**) (168 mg, 1.0 mmol) and the autoclave was filled with CO (2 atm). The whole mixture was heated with stirring at 80 °C for 20 h. The deposited metallic palladium was collected with a short celite plug and the filtrate was concentrated by evaporation. There were three major components detected by GLC (Silicone DC-550, at 120 °C) in a ratio 12 : 25 : 60. Two minor components, obtained in 30% combined yield and separated by preparative GLC, could be assigned by ^1H and ^{13}C NMR as 2-methylene-bicyclo[3.3.0]octan-3-one (**3**)6) and 7-methylene-bicyclo[3.2.1]octan-6-one (**4**),7) respectively (the product ratio was ca. 2 : 1). The major component appeared at the longest T_R was isolated in 50% yield and assigned to be 2-vinylcyclopentylacetic acid (**2**).8) The trans-configuration of **2** was determined by its conversion into trans-2-oxabicyclo[4.3.0]nonan-3-one (**8**)9) and by comparison with the authentic cis-lactone.9,10)

Results obtained for **1a** can be explained in terms of an intramolecular insertion of a terminal olefin moiety into the π-allylpalladium intermediate prior to carbonylation of the intermediate. Such an intramolecular insertion takes place in three different directions with respect to regio- as well as stereoselection (see, Scheme 1). Carbonylation of the cis-cyclized intermediates therefrom followed by a rapid intramolecular Heck-type reaction surely gives the ketones **3** and **4**, respectively, whereas carbonylation of the major trans-cyclized one leads presumably to an acetic mixed anhydride and finally to the free acid **2** after workup.

Similarly, the Pd(0)-catalyzed carbonylation of 2,8-nonadienyl acetate (**9**) in acetic acid afforded cis-7-methylene-bicyclo[4.3.0]nonan-8-one (**10**)11) and trans-**10**11) in a ratio 3 : 1 (50% combined yield). The stereoselectivity for the Pd(0)-

catalyzed cyclizations to five- and to six-membered rings was thus inverted.

The cyclization-carbonylation sequence can also be terminated by an intramolecular esterification to give lactones (Eq. 2).$^{12)}$ Our concern in the cyclization-lactonization is the stereochemistry of three contiguous chiral centers (C_1, C_2, and C_3).$^{13)}$ The carbonylation of the allylic acetate **11**$^{14)}$ bearing an allylic alcohol unit gave the bicyclic lactones **12** in 37% combined yield along with the cis-fused bicyclooctanone **13** (16%). The lactones **12** are known compounds, which were used for the syntheses of several 11-deoxyprostaglandins.$^{15)}$ The products **12** were detected as a diastereomeric mixture (4 : 1) with respect to the C_3 stereogenic center by GLC/HPLC analyses.$^{16)}$



11 trans-**12** cis-**12** **13** (2)

Both trans and cis configurations of **12** were determined by the ^{13}C NMR analysis: 2,3-trans assignment of the major product follows from the downfield values (45.1 and 50.2 ppm) of C_2 and C_3 relative to their respective upfield values (41.2 and 46.4 ppm) of the congested cis-isomer.$^{16)}$ The ^1H NMR coupling constant of $J_{a,b}$ = 5.2 Hz$^{17,18)}$ in the bicyclooctanone **13** requires a trans arrangement of H^a and H^b, the relationship of which was confirmed by the 2-D NOESY spectrum showing a strong cross peak between the $CH_2C=O$ (2.60 ppm) and CH^aOH (4.30 ppm).

Thus, the major stereochemical outcome of the formal Pd-ene reaction, in particular, for a simple 2,3-trans-diastereoselection (in five-membered ring formation) was found to be quite different from that of the thermal-ene reaction where cis-diastereoselection has amply been observed.$^{13)}$

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6) **3**: ^{1}H NMR (90 MHz, $CDCl_3$, TMS) 1.0-2.4(m, 7H), 2.4-2.8(m, 2H), 3.2(m, 1H), 5.28(dd, *J*=2.6 and 1.1 Hz, 1H), and 6.01(dd, *J*=2.8 and 1.1 Hz, 1H). ^{13}C NMR (22.5 MHz) 25.8, 34.0, 34.5, 36.9, 44.1, 45.4, 118.0, 150.3, and 208.1.

7) **4**: ^{1}H NMR 1.0-1.7(m, 3H), 1.7-2.3(m, 6H), 2.3-2.7(m, 1H), 5.14(dd, *J*=2.6 and 1.1 Hz, 1H), and 5.86(dd, *J*=2.8 and 1.1 Hz, 1H).

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9) The *cis*-lactone **8** was prepared by an unambiguous route from bicyclo[3.3.0]-oct-2-ene: *cis*-**8**: ^{1}H NMR 1.0-3.0(m, 10H), 4.01(dd, *J*=11.5 and 6.6 Hz, 1H), and 4.29 (dd, *J*=11.5 and 4.8 Hz, 1H). IR 1745 cm^{-1}; *trans*-**8**: 1.2-2.0(m, 8H), 2.27(dd, *J*=17.8 and 12.2 Hz, 1H), 2.91(dd, *J*=17.8 and 4.9 Hz, 1H), 4.07(t, *J*=10.5 Hz, 1H), and 4.61(dd, *J*=10.5 and 4.6 Hz, 1H). IR 1720 cm^{-1}.

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14) **11**: IR(neat) 3450, 1735, 1645, 1425, 990, and 925($CH{=}CH_2$) cm^{-1}; ^{1}H NMR 1.30-2.20(m, 4H, $-C\underline{H}_2C\underline{H}_2-$), 2.04(s, 3H, $OCOC\underline{H}_3$), 4.11(dt, *J*=5.7 Hz, 1H, $C\underline{H}OH$), 5.00-5.50(m, 6H, 2 $=C\underline{H}_2$, $O\underline{H}$, and $C\underline{H}OAc$), and 5.60-6.10(m, 2H, 2 $C\underline{H}{=}CH_2$).

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16) *trans*-**12**: ^{13}C NMR 31.3, 32.0, 34.3, 45.1, 50.2, 86.1, 115.6, 139.7, and 177.6. *cis*-**12**: ^{13}C NMR 27.2, 29.8, 33.0, 41.2, 46.4, 86.2, 117.3, 137.4, and 177.6; IR(neat) 1773, 1641, 1437, 990, and 917 cm^{-1}; ^{1}H NMR 1.40-2.80(m, 8H), 4.90-5.15(m, 3H, $CH{=}C\underline{H}_2$ and $C\underline{H}OCO$), 5.70(ddd, *J*=17.8, 10.2, and 6.6 Hz, $C\underline{H}{=}CH_2$).

17) Upon irradiation at 1.80 ppm, the doublet of doublet at 4.30 ppm collapsed to the doublet (*J*=5.2 Hz). **13**: IR(neat) 3450(OH) cm^{-1}; ^{1}H NMR 1.3-2.7(m, 8H), 3.30(m, 1H, $O\underline{H}$), 4.30(m, 1H, $C\underline{H}OH$), 5.30 and 6.00(2d, *J*=2.2 Hz, 2H, $C\underline{H}_2{=}$); ^{13}C NMR 31.4, 35.4, 37.9, 42.3, 43.7, 74.9, 117.4, 130.9, and 151.5.

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