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Palladium-catalyzed reactions of vinylidenecyclopropanes with acetic acid

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Abstract—$Pd(PPh_3)_4$-catalyzed reactions of vinylidenecyclopropanes **1** with acetic acid proceeded smoothly at 80 °C in toluene to give the corresponding acetylated dienes **2** in moderate to good yields in the presence of DPEphos ligand. The plausible mechanism is proposed on the basis of the control and deuterium labeling experiments.

1. Introduction

Vinylidenecyclopropanes **1**[1] are one of the most remarkable organic compounds known. They have an allene moiety connected by a cyclopropane ring and yet they are thermally stable and reactive substances. Thermal and photochemical skeletal conversions of vinylidenecyclopropanes **1** have attracted much attention from mechanistic, theoretical, spectroscopic and synthetic viewpoints.[2,3] Vinylidenecyclopropanes **1** also undergo a variety of unique addition reactions with electrophiles to give novel products sometimes along with the formation of cyclopropane ring-opened products.[4] Previously, we reported the palladium-catalyzed isomerization of a variety of methylenecyclopropanes (MCPs), another kind of molecules having surprising stability along with a high level of strain, in acetic acid to give the corresponding 1-substituted or 1,1-disubstituted dienes in good yields.[5] However, to the best of our knowledge, there has been no report on the palladium-catalyzed reactions of vinylidenecyclopropanes **1** until now. In this context, we wish to disclose the first example of palladium-catalyzed reactions of vinylidenecyclopropanes with acetic acid to give the corresponding acetylated dienes **2** in moderate to good yields.

2. Results and discussion

As an initial examination, the reaction of vinylidenecyclopropane **1a** with acetic acid (2.0 equiv) was carried out with a variety of catalysts in toluene at 80 °C. The results are summarized in Table 1. As shown in Table 1, $Pd(PPh_3)_4$ can catalyze the reaction of vinylidenecyclopropane **1a** with acetic acid in toluene to produce **2a** in moderate yields as mixtures of *E*- and *Z*-isomers (Table 1). The structure of product **2a** was determined by ^1H and ^{13}C NMR spectroscopic data, HRMS and NOESY analytic data (Supplementary data). The NOESY of **2a** is shown in Figure 1, which clearly indicates that the major isomer has *E*-configuration. Other palladium catalysts, such as $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, $PdCl_2(dppf)$ and $Pd(dba)_2$, did not catalyze the reaction under identical conditions (Table 1, entries 5, 8–10). A variety of phosphine ligands, such as PPh_3, $AsPh_3$, tri-2-furylphosphine (TFP), bis[(2-diphenylphosphino)phenyl]ether (DPEphos), 1,4-bis(diphenylphosphino)butane (dppb) and 1,3-bis(diphenylphosphino)propane (dppp), were also examined for this reaction to improve the yield of **2a**. We found that when $Pd(PPh_3)_4$ (10 mol %) and DPEphos (40 mol %) were utilized in this reaction, **2a** can be obtained in 58% yield as mixtures of *E*- and *Z*-isomers (*E*:*Z*=6:1) (Table 1, entry 16). Using $Pd(OAc)_2$ or $Pd(dba)_2$ as a catalyst, **2a** was still obtained in lower yield even in the presence of $AsPh_3$ or DPEphos ligand (Table 1, entries 6, 11 and 12).

Using $Pd(PPh_3)_4$ (10 mol %) and DPEphos (40 mol %) as the catalyst, solvent effects were also examined upon heating or under reflux. The results are summarized in Table 1 as entries 16–20. As can be seen from these experiments, toluene is the best solvent for this reaction at 80 °C (Table 1, entries 16–20). We found that the employed amount of DPEphos slightly affected the yield of product **2a** in toluene at 80 °C (Table 1, entries 21–23). When $Pd(PPh_3)_4$ (10 mol %) and DPEphos (20 mol %) were used, **2a** was obtained in 64% yield, which is the highest yield in this reaction (Table 1, entry 22).

Keywords: Palladium catalyst; Vinylidenecyclopropanes; Acetic acid; Acetylated dienes; Deuterium labeling experiment.
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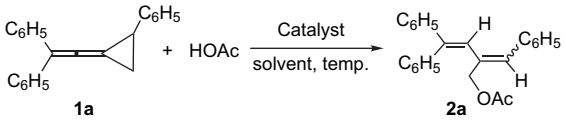
Table 1. Optimization of the reaction condition of **1a** with acetic acid



Entry[a]	Catalyst/ligand/mol %	Solvent	Temp/°C	Time/h	**2a** Yield[b]/% (*E*:*Z*)[c]
1	—	Toluene	80	48	N.R
2	$Pd(PPh_3)_4$ (10)	Toluene	80	5	44 (6:1)
3	$Pd(PPh_3)_4/PPh_3$ (10/40)	Toluene	80	6	37 (6:1)
4	$Pd(PPh_3)_4/AsPh_3$ (10/40)	Toluene	80	6	50 (6:1)
5	$Pd(OAc)_2$	Toluene	80	12	Complex
6	$Pd(OAc)_2/AsPh_3$ (10/40)	Toluene	80	18	14 (9:1)
7	$Pd(PPh_3)_4$/TFP (10/40)	Toluene	80	6	38 (6:1)
8	$PdCl_2(PPh_3)_2/PPh_3$ (10/40)	Toluene	80	20	N.R
9	$PdCl_2$(dppf)/dppf (10/20)	Toluene	80	24	N.R
10	$Pd(dba)_2$ (10)	Toluene	80	9	Complex
11	$Pd(dba)_2$/DPEphos (10/20)	Toluene	80	18	42 (8:1)
12	$Pd(OAc)_2$/DPEphos (10/20)	Toluene	80	18	36 (7:1)
13	$Pd(PPh_3)_4$/dppp (10/40)	Toluene	80	33	34 (11:1)
14	$Pd(PPh_3)_4$/dppb (10/40)	Toluene	80	33	32 (5:1)
15	$Pd(PPh_3)_4/(o\text{-}CH_3C_6H_4)_3P$ (10/40)	Toluene	80	17	36 (6:1)
16	$Pd(PPh_3)_4$/DPEphos (10/40)	Toluene	80	20	58 (6:1)
17	$Pd(PPh_3)_4$/DPEphos (10/40)	Toluene	110	11	26 (9:1)
18	$Pd(PPh_3)_4$/DPEphos (10/40)	Dioxane	100	9	10 (11:1)
19	$Pd(PPh_3)_4$/DPEphos (10/40)	CH_3CN	80	9	21 (9:1)
20	$Pd(PPh_3)_4$/DPEphos (10/40)	THF	66	33	14 (12:1)
21	$Pd(PPh_3)_4$/DPEphos (20/60)	Toluene	80	36	36 (>40:1)
22	$Pd(PPh_3)_4$/DPEphos (10/20)	Toluene	80	18	64 (7:1)
23	$Pd(PPh_3)_4$/DPEphos (10/10)	Toluene	80	12	60 (8:1)

[a] All reactions were carried out using **1a** (0.3 mmol), AcOH (0.6 mmol) and catalysts in a variety of solvents (2.0 mL).
[b] Isolated yields.
[c] Determined from ^{1}H NMR spectroscopic data and NOESY.

Under these optimized conditions, we next examined a variety of vinylidenecyclopropanes **1** with acetic acid for the reaction generality. The results are summarized in Table 2. With respect to the electron-rich and electron-poor arylvinylidenecyclopropanes **1** (R^1, R^2=aryl), they reacted with acetic acid smoothly to provide the corresponding acetylated dienes **2** in moderate to good yields (Table 2, entries 1–7). For arylvinylidenecyclopropane **1c** (R^1=C_6H_5 and R^2=*p*-ClC_6H_4), the corresponding *E*- and *Z*-isomers can be separated by silica gel chromatograph. In other cases, the corresponding *E*- and *Z*-isomers are inseparable. For alkylvinylidenecyclopropanes **1i** and **1j** (R^1=alkyl, R^2=aryl), the corresponding acetylated dienes **2i** and **2j** were also formed in 36 and 61% yields, respectively (Table 2, entries 8 and 9).

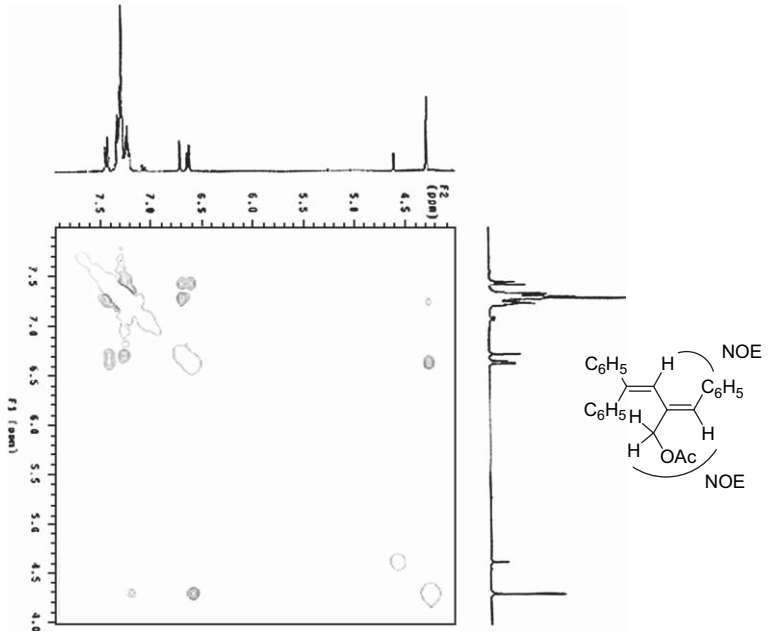
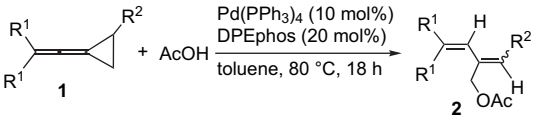


Figure 1.

Table 2. Palladium-catalyzed reactions of vinylidenecyclopropanes **1** with acetic acid in toluene

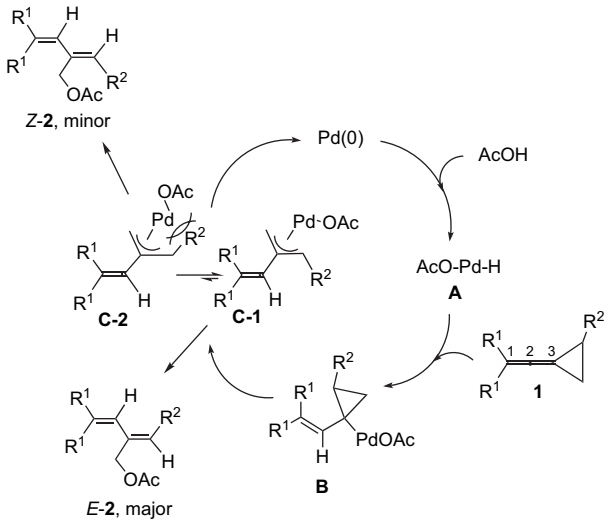


Entry[a]	**1** (R^1/R^2)	**2** Yield[b]/% (*E*:*Z*)[c]
1	**1b** (C_6H_5/*p*-MeC_6H_4)	**2b**, 67 (8:1)
2	**1c** (C_6H_5/*p*-ClC_6H_4)	**2c**, 67 (7:1)
3	**1d** (C_6H_5/*p*-$MeOC_6H_4$)	**2d**, 78 (19:1)
4	**1e** (*p*-MeC_6H_4/C_6H_5)	**2e**, 75 (8:1)
5	**1f** (*p*-FC_6H_4/C_6H_5)	**2f**, 67 (11:1)
6	**1g** (*p*-$MeOC_6H_4$/C_6H_5)	**2g**, 70 (14:1)
7	**1h** (*p*-ClC_6H_4/C_6H_5)	**2h**, 65 (8:1)
8	**1i** (^{n}Bu/C_6H_5)	**2i**, 36 (5:1)
9	**1j** (CH_3/C_6H_5)	**2j**, 61 (5:1)

[a] All reactions were carried out using **1** (0.3 mmol), AcOH (0.6 mmol), $Pd(PPh_3)_4$ (10 mol %) and DPEphos (20 mol %) in toluene (2.0 mL).
[b] Isolated yields.
[c] Determined from ^{1}H NMR spectroscopic data and NOESY.

It should be noted that for alkylvinylidenecyclopropanes **1i** and **1j**, other complicated products were also formed presumably due to the β-hydride elimination from aliphatic R^1 group. In addition, we found that vinylidenecyclopropanes **1** are labile under the reaction conditions, partially leading to the formation of **2** in moderate yields.

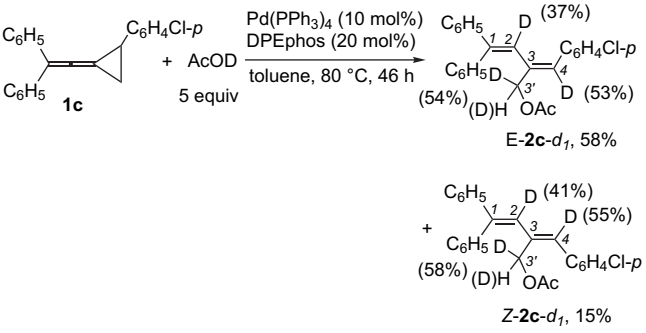
A plausible mechanism for the formation of acetylated dienes **2** is outlined in Scheme 1 on the basis of previous investigations.[5,6] The initial step is a regioselective hydropalladation of vinylidenecyclopropane **1** with hydridopalladium species **A**, generated from oxidative addition of Pd(0) with acetic acid, to afford intermediate **B**, which undergoes β-carbon elimination to give two π-allyl-palladium intermediates **C-1** and **C-2**. Intermediate **C-1** should be the major conformer because of the steric repulsion between R^2 group and palladium metal center in intermediate **C-2**. Reductive elimination of intermediates **C-1** and **C-2** gives the corresponding product **2** as mixtures of *E*- and *Z*-isomers, leading to the formation of *E*-**2** as major product from intermediate



Scheme 1. Plausible mechanism for the reactions of vinylidenecyclopropanes **1** with acetic acid in the presence of palladium(0) catalyst.

C-1, along with the regeneration of palladium(0) catalyst. Previously, Yamamoto and co-workers reported that alkynes can be allylated by carbon pronucleophiles in the presence of palladium/acetic acid catalyst via a π-allyl-palladium intermediate.[7] However, we found that no such allylation occurred in our system when malononitrile [$CH_2(CN)_2$] (2.0 equiv) and diethyl malonate [$CH_2(COOEt)_2$] (2.0 equiv) were used as the carbon pronucleophiles in the presence of $Pd(PPh_3)_4$ (10 mol %)/DPEphos (20 mol %)/AcOH (20 mol %). This result suggests that the reaction mechanism is not involved in the nucleophilic attack of AcOH to π-allyl intermediates **C-1** and **C-2** to produce **2**. In addition, it should also be noted here that when formic acid was used instead of acetic acid in this case, many unidentified products were formed.[8]

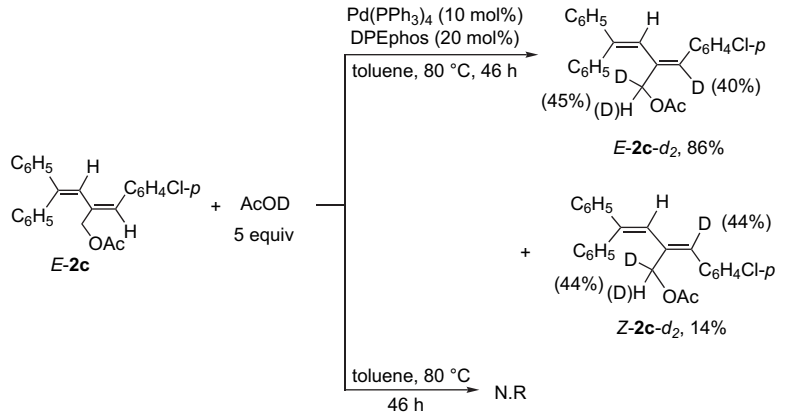
In order to clarify the mechanism of this reaction, the reaction of **1c** in deuterated acetic acid AcOD (D content 99%) was carried out under identical conditions (Scheme 2).[5] Based on the observed ^{1}H NMR spectral data, we confirmed that besides the olefinic protons at C_2 (D content: 37% in *E*-**2c**-d_1 and 41% in *Z*-**2c**-d_1), deuterium incorporation also occurred at the olefinic protons of C_4 (D content 53% in *E*-**2c**-d_1 and 55% in *Z*-**2c**-d_1) and at the allylic protons of $C_{3'}$ (D content: 54% in *E*-**2c**-d_1 and 58% in *Z*-**2c**-d_1). The 37% D content at C_2 is due to the generation of AcO–Pd–H species via β-hydride elimination during the reaction, which can initiate the same reaction to give the acetylated diene **2c** without deuterium incorporation even in AcOD (Scheme 1).[5,9]



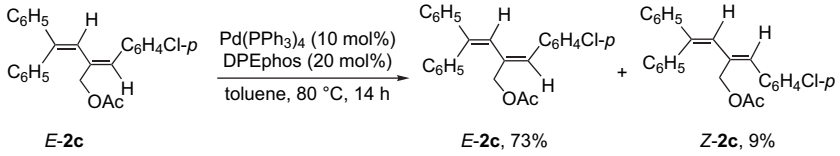
Scheme 2. Reaction of vinylidenecyclopropane **1c** with AcOD (5.0 equiv) under these optical conditions.

The control experiment confirmed that deuterium incorporation at the olefinic protons of C_4 and the allylic protons of $C_{3'}$ is derived from the scrambling of *E*-**2c** with AcOD catalyzed by Pd(0) as shown in Scheme 3 because similar D contents at C_4 and $C_{3'}$ were observed in the reaction of *E*-**2c** with AcOD in the presence of Pd(0) catalyst and no reaction occurred in the absence of Pd(0) catalyst as in the previously reported example.[5]

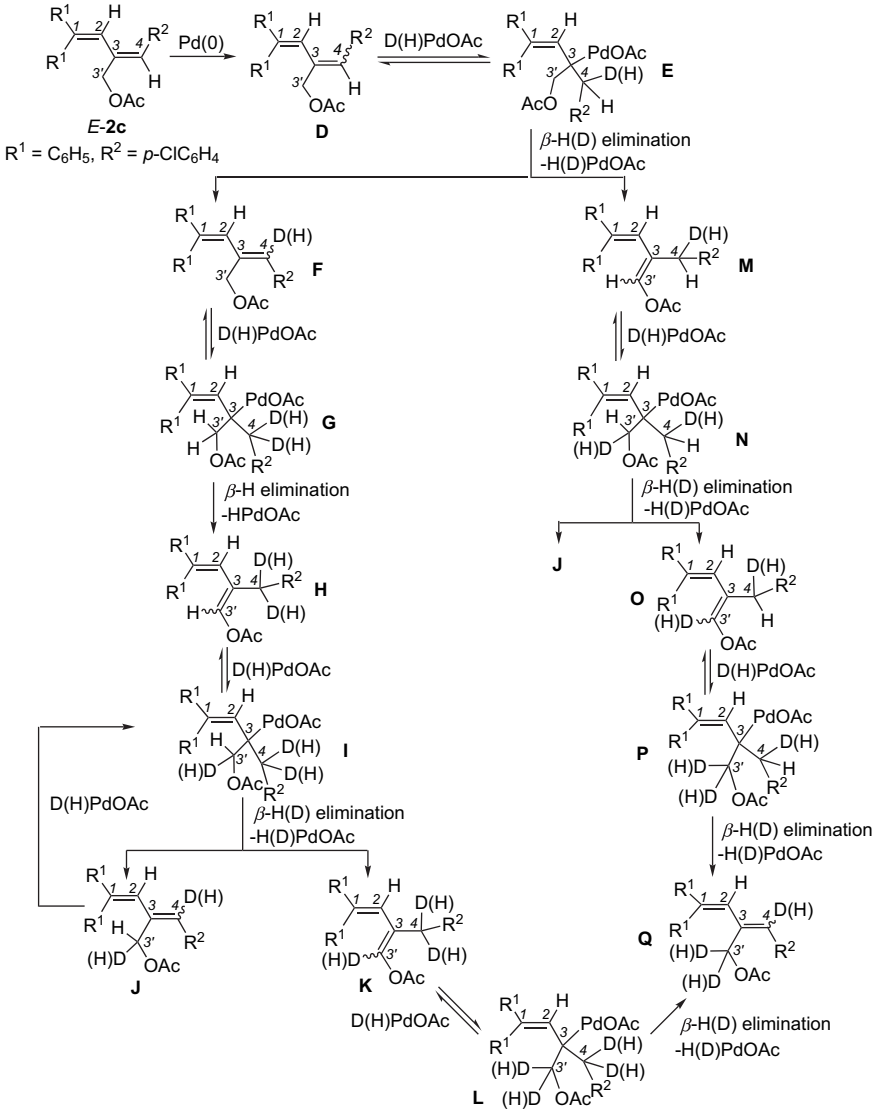
The control experiment of the transformation of *E*-**2c** to *E*- and *Z*-regioisomers in the presence of Pd(0) catalyst was also examined under the standard conditions. The result is shown in Scheme 4, which clearly indicates that *E*- and *Z*-isomerization independently takes place through the corresponding π-allyl intermediates **C-1** and **C-2** and it is not related with HOAc in the reaction system. A plausible mechanism for the formation of *E*-**2c**-d_2 and *Z*-**2c**-d_2 is shown in Scheme 5. The initial step is a palladium-catalyzed



Scheme 3. Reactions of *E*-**2c** with AcOD (5 equiv).

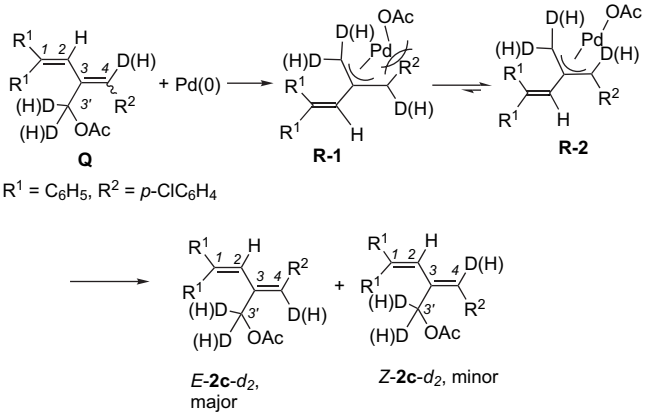


Scheme 4. Isomerization of *E*-**2c** in the presence of Pd(0).



Scheme 5. Plausible mechanism for the formation of *E*-**2c**-*d* and *Z*-**2c**-*d* in the presence of palladium(0) catalyst.

isomerization of *E*-**2c** to produce intermediate **D** as mixtures of *E*- and *Z*-isomers. Regioselective deuteropalladation or hydropalladation of **D** with deuteropalladium species or hydridopalladium species, generated from the oxidative addition of Pd(0) with deuterated acetic acid (AcOD) and β-hydride elimination during the reaction, respectively, to afford intermediate **E**.[5] Intermediate **E** undergoes β-hydride (β-H) or β-deuterium (β-D) elimination to give intermediates **F** and **M**. Intermediate **F** undergoes the same processes (deuteropalladation or hydropalladation, β-hydride or β-deuterium elimination and the repeated processes) to afford intermediates **J** and **Q** via intermediates **G**, **H**, **I**, **K** and **L**, successively. Regioselective deuteropalladation or hydropalladation of **J** regenerates intermediate **I**. From the same processes (deuteropalladation or hydropalladation, β-hydride or β-deuterium elimination and the repeated processes), intermediates **J** and **Q** would be also formed from intermediate **M** via intermediates **N**, **O** and **P**, respectively (Scheme 5). Then, palladium-catalyzed isomerization of intermediate **Q** gives the corresponding *E*-isomer as the major product because of the different steric effect between intermediates **R-1** and **R-2** as that described above (Scheme 6).



Scheme 6. Isomerization of intermediate **Q** to form *E*-**2c**-d_2 and *Z*-**2c**-d_2.

Overall, on the basis of the control and deuterium labeling experiments, the initial step of this reaction should indeed proceed through the hydropalladation of the C_1 and C_2 olefinic moieties of **1** via the hydridopalladium species as shown in Scheme 1. The repeated deuteropalladation or hydropalladation and β-hydride or β-deuterium elimination between the C_3 and C_4 olefinic moieties in **2** catalyzed by Pd(0) in AcOD caused the scrambling at C_4 protons and at the allylic protons of $C_{3'}$ as shown in Scheme 2.

3. Conclusion

We have disclosed the first example of palladium(0)-catalyzed reactions of vinylidenecyclopropanes **1** with acetic acid to give the corresponding acetylated dienes **2** under mild conditions. On the basis of the control and deuterium labeling experiments, we found that this reaction process is involved in the regioselective hydropalladation of vinylidenecyclopropanes **1** with AcO–Pd–H as shown in Scheme 1. Efforts are underway to elucidate the mechanistic details of this reaction and to disclose its scope and limitations. Work along this line is currently in progress.

4. Experimental

4.1. General methods

^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Mass spectra were recorded by EI and MALDI methods, and HRMS was measured on Kratos Analytical Concept mass spectrometer (EI), Bruker FT mass spectrometer (ESI), and IonSpec 4.7 Tesla FTMS (MALDI). Organic solvents used were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Yinlong GF254 silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure.

4.2. General procedure for palladium-catalyzed reaction of vinylidenecyclopropanes with acetic acid

Under an argon atmosphere, vinylidenecyclopropanes **1** (0.3 mmol), $Pd(PPh_3)_4$ (10 mol %), DPEphos (20 mol %), toluene (2.0 mL) and acetic acid (0.6 mmol) were added into a Schlenk tube. The mixture was stirred at 80 °C for 18 h. Then the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography.

4.2.1. Compound 2a. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.99 (s, 3H, CH_3), 4.29 (s, 2H, CH_2), 6.62 (s, 1H), 6.71 (d, J=1.2 Hz, 1H), 7.19–7.32 (m, 13H, Ar), 7.41–7.44 (m, 2H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.99 (s, 3H, CH_3), 4.61 (s, 2H, CH_2), 6.64 (s, 2H), 7.05–7.08 (m, 2H, Ar), 7.19–7.32 (m, 13H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 66.8, 124.9, 127.5, 127.65, 127.67, 128.0, 128.1, 128.19, 128.24, 129.3, 129.7, 132.6, 133.5, 136.7, 140.1, 142.5, 144.9, 170.7. IR (CH_2Cl_2) ν 3056, 3024, 2922, 2850, 1739, 1597, 1493, 1444, 1373, 1232, 1075, 1030, 763, 699 cm^{-1}. MS (%) *m*/*z* 354 (M^+, 2), 294 (100), 293 (40), 43 (27), 352 (26), 295 (25), 203 (22), 217 (20), 91 (20). HRMS (MALDI) calcd for $C_{25}H_{22}O_2Na$: 377.1512, found: 377.1522 ($M+Na^+$).

4.2.2. Compound 2b. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.98 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.27 (s, 2H, CH_2), 6.60 (s, 1H), 6.72 (s, 1H), 7.09 (d, J=8.1 Hz, 2H, Ar), 7.19–7.34 (m, 12H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.98 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.60 (s, 2H, CH_2), 6.63 (s, 1H), 6.64 (s, 1H), 6.97 (d, J=8.1 Hz, 2H, Ar), 7.19–7.34 (m, 12H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 21.2, 66.8, 125.1, 127.6, 127.90, 127.92, 128.1, 128.2, 129.0, 129.3, 129.8, 132.7, 132.8, 133.9, 137.4, 140.1, 142.5, 144.4, 170.4. IR (CH_2Cl_2) ν 3054, 3023, 2962, 2920, 2850, 1738, 1597, 1509, 1493, 1444, 1374, 1260, 1229, 1029, 868, 806, 758, 699 cm^{-1}. MS (%) *m*/*z* 368 (M^+, 1), 43 (100), 308 (43), 293 (32), 330 (33), 91 (29), 105 (29), 57 (28), 215 (19). HRMS (MALDI) calcd for $C_{26}H_{24}O_2Na$: 391.1669, found: 391.1674 ($M+Na^+$).

4.2.3. Compound 2c. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.01 (s, 3H, CH_3), 4.31 (s, 2H, CH_2), 6.53 (s, 1H), 6.62 (d, J=1.5 Hz, 1H), 7.16–7.34 (m,

14H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.01 (s, 3H, CH_3), 4.57 (s, 2H, CH_2), 6.55 (s, 1H), 6.62 (d, J=0.9 Hz, 1H), 6.99 (d, J=9.0 Hz, 2H, Ar), 7.24–7.35 (m, 12H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 66.6, 124.3, 127.85, 127.93, 128.0, 128.18, 128.20, 128.4, 129.7, 130.4, 130.9, 133.1, 134.3, 135.2, 139.8, 142.3, 145.5, 170.4. (*Z*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 21.0, 62.1, 127.6, 127.7, 128.19, 128.24, 128.44, 128.47, 128.7, 129.9, 130.2, 133.3, 134.1, 134.7, 135.4, 140.1, 142.9, 143.9, 170.6. (*E*-isomer): IR (CH_2Cl_2) ν 3056, 3025, 2962, 2846, 1740, 1594, 1498, 1444, 1372, 1228, 1091, 1030, 1013, 868, 763, 699 cm^{-1}. (*Z*-isomer): IR (CH_2Cl_2) ν 3056, 3025, 2961, 2920, 1740, 1597, 1489, 1444, 1374, 1232, 1092, 1028, 1014, 970, 829, 807, 763, 700 cm^{-1}. (*E*-isomer): MS (%) *m*/*z* 388 (M^+, 1), 43 (100), 328 (73), 293 (62), 215 (35), 330 (25), 202 (24), 329 (23), 292 (22). (*Z*-isomer): MS (%) *m*/*z* 388 (M^+, 3), 43 (100), 293 (63), 328 (43), 215 (35), 91 (27), 57 (26), 292 (20), 202 (20). (*E*-isomer): HRMS (MALDI) calcd for $C_{25}H_{21}O_2ClNa$: 411.1122, found: 411.1140 (M+Na^+). (*Z*-isomer): HRMS (MALDI) calcd for $C_{25}H_{21}O_2ClNa$: 411.1122, found: 411.1133 (M+Na^+).

4.2.4. Compound 2d. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.97 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 4.26 (s, 2H, CH_2), 6.57 (s, 1H), 6.71 (d, J=1.5 Hz, 1H), 6.80–6.83 (m, 2H, Ar), 7.21–7.39 (m, 12H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.99 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 4.60 (s, 2H, CH_2), 6.62 (s, 1H), 6.64 (s, 1H), 7.02 (d, J=8.7 Hz, 4H, Ar), 7.21–7.39 (m, 10H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 55.1, 66.9, 113.6, 125.2, 127.5, 127.8, 127.9, 128.07, 128.13, 129.4, 129.7, 130.6, 131.5, 132.5, 140.1, 142.5, 144.3, 159.0, 170.4. IR (CH_2Cl_2) ν 3056, 3026, 2932, 2836, 1738, 1605, 1509, 1444, 1374, 1252, 1176, 1032, 756, 700 cm^{-1}. MS (%) *m*/*z* 384 (M^+, 7), 43 (100), 49 (79), 57 (58), 324 (57), 51 (45), 84 (44), 105 (39), 207 (30). HRMS (MALDI) calcd for $C_{26}H_{24}O_3Na$: 407.1618, found: 407.1626 (M+Na^+).

4.2.5. Compound 2e. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.99 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 4.29 (s, 2H, CH_2), 6.60 (s, 1H), 6.65 (s, 1H), 7.08–7.30 (m, 11H, Ar), 7.44 (d, J=7.5 Hz, 2H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.98 (s, 3H, CH_3), 2.35 (s, 6H, $2CH_3$), 4.60 (s, 2H, CH_2), 6.60 (s, 1H), 6.65 (s, 1H), 7.08–7.30 (m, 13H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 21.1, 21.3, 66.8, 123.9, 127.4, 127.9, 128.2, 128.8, 128.9, 129.3, 129.7, 132.1, 133.9, 136.8, 137.2, 137.5, 137.7, 139.9, 144.8, 170.5. IR (CH_2Cl_2) ν 3023, 2920, 2853, 1740, 1067, 1509, 1493, 1445, 1369, 1228, 1023, 822, 752, 700 cm^{-1}. MS (%) *m*/*z* 382 (M^+, 3), 43 (100), 322 (82), 307 (73), 215 (36), 105 (35), 91 (30), 323 (28), 229 (28). HRMS (MALDI) calcd for $C_{27}H_{26}O_2Na$: 405.1825, found: 405.1845 (M+Na^+).

4.2.6. Compound 2f. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.02 (s, 3H, CH_3), 4.36 (s, 2H, CH_2), 6.59 (s, 1H), 6.60 (s, 1H), 6.95–7.38 (m, 13H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.02 (s, 3H, CH_3), 4.65 (s, 2H, CH_2), 6.55 (s, 1H), 6.59 (s, 1H), 6.95–7.38 (m, 13H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 66.8, 115.0 (d, J=11.0 Hz), 115.3 (d, J=11.8 Hz), 125.0, 127.5, 128.2, 129.1, 129.5 (d, J=8.0 Hz), 131.3 (d, J=8.1 Hz), 132.7, 133.1, 135.7 (d, J=3.9 Hz), 136.5, 138.5 (d, J=3.9 Hz), 142.9, 162.4 (d, J=246.4 Hz), 162.6 (d, J=246.8 Hz), 170.4. IR (CH_2Cl_2) ν 3050, 3019, 2919, 2850, 1740, 1600, 1508, 1446, 1371, 1275, 1226, 1158, 1095, 1029, 838, 764, 751, 698 cm^{-1}. MS (%) *m*/*z* 390 (M^+, 0.31), 49 (100), 84 (54), 51 (29), 86 (28), 43 (27), 47 (13), 127 (11), 330 (10). HRMS (MALDI) calcd for $C_{25}H_{20}O_2F_2Na$: 413.1324, found: 413.1333 (M+Na^+).

4.2.7. Compound 2g. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.00 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.32 (s, 2H, CH_2), 6.56 (s, 1H), 6.58 (s, 1H), 6.81–6.88 (m, 4H, Ar), 7.13–7.30 (m, 7H, Ar), 7.44 (d, J=7.2 Hz, 2H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.99 (s, 3H, CH_3), 3.80 (s, 6H, $2OCH_3$), 4.62 (s, 2H, CH_2), 6.50 (s, 1H), 6.64 (s, 1H), 6.81–6.88 (m, 4H, Ar), 7.07–7.30 (m, 9H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 55.13, 55.19, 66.8, 113.4, 113.5, 122.8, 127.3, 128.2, 129.16, 129.19, 130.9, 131.7, 132.5, 134.0, 135.4, 136.9, 144.1, 159.30, 159.32, 170.5. IR (CH_2Cl_2) ν 3028, 3001, 2954, 2934, 2836, 1739, 1605, 1573, 1511, 1463, 1443, 1369, 1287, 1247, 1175, 1110, 1033, 974, 919, 834, 754, 738, 699 cm^{-1}. MS (%) *m*/*z* 414 (M^+, 18), 354 (100), 135 (70), 353 (42), 242 (34), 323 (29), 355 (27), 341 (27), 84 (25). HRMS (MALDI) calcd for $C_{27}H_{26}O_4Na$: 437.1723, found: 437.1724 (M+Na^+).

4.2.8. Compound 2h. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.02 (s, 3H, CH_3), 4.37 (s, 2H, CH_2), 6.63 (s, 2H), 7.07–7.36 (m, 13H, Ar). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.02 (s, 3H, CH_3), 4.65 (s, 2H, CH_2), 6.59 (s, 2H), 7.07–7.36 (m, 13H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.9, 66.8, 125.9, 127.7, 128.3, 128.4, 128.6, 128.9, 129.1, 131.0, 132.9, 133.3, 133.9, 134.0, 136.5, 138.0, 140.6, 142.6, 170.4. IR (CH_2Cl_2) ν 3019, 2920, 2846, 1740, 1590, 1491, 1368, 1275, 1260, 1227, 1091, 1014, 831, 764, 750, 697 cm^{-1}. MS (%) *m*/*z* 422 (M^+, 9), 327 (100), 277 (73), 362 (62), 278 (47), 292 (46), 364 (41), 215 (40), 43 (37). HRMS (MALDI) calcd for $C_{25}H_{20}O_2Cl_2Na$: 445.0733, found: 445.0745 (M+Na^+).

4.2.9. Compound 2i. A yellow oil, (*E*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 0.77 (t, J=6.6 Hz, 3H, CH_3), 0.92 (t, J=6.9 Hz, 3H, CH_3), 1.12–1.15 (m, 4H, $2CH_2$), 1.26–1.41 (m, 4H, $2CH_2$), 1.85 (t, J=7.5 Hz, 2H, CH_2), 2.07 (t, J=6.3 Hz, 2H, CH_2), 2.09 (s, 3H, CH_3), 4.65 (s, 2H), 5.74 (s, 1H), 6.48 (s, 1H), 7.15–7.34 (m, 3H, Ar), 7.41 (d, J=7.8 Hz, 2H). (*Z*-isomer): ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 0.88–0.95 (m, 6H, $2CH_3$), 1.26–1.41 (m, 8H, $4CH_2$), 2.07–2.13 (m, 2H, CH_2), 2.09 (s, 3H, CH_3), 2.27 (t, J=7.8 Hz, 2H, CH_2), 4.74 (s, 2H, CH_2), 5.77 (s, 1H), 6.58 (s, 1H), 7.15–7.34 (m, 5H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.9, 14.0, 21.0, 22.5, 22.8, 29.5, 29.9, 30.8, 35.8, 68.7, 120.3, 126.9, 127.9, 128.5, 128.9, 133.9, 137.1, 145.2, 170.7. (*Z*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.9, 14.0, 20.9, 22.4, 22.8, 30.3, 30.4, 30.8, 36.7, 63.6, 124.8, 127.0, 128.1, 128.3, 128.7, 132.1, 136.7, 145.2, 170.7. IR (CH_2Cl_2)

ν 3059, 3025, 2956, 2930, 2871, 1743, 1599, 1494, 1456, 1376, 1228, 1027, 966, 915, 803, 751, 696 cm^{-1}. MS (%) *m/z* 314 (M^+, 1), 91 (100), 43 (74), 155 (40), 197 (37), 41 (36), 141 (28), 115 (27), 211 (26). HRMS (EI) calcd for $C_{21}H_{30}O_2$: 314.2246, found: 314.2252.

4.2.10. Compound 2j. A yellow oil, (*E*-isomer): ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.44 (d, J=0.6 Hz, 3H, CH_3), 1.78 (d, J=1.2 Hz, 3H, CH_3), 2.10 (s, 3H, CH_3), 4.66 (s, 2H), 5.76 (s, 1H), 6.48 (s, 1H), 7.15–7.41 (m, 5H, Ar). (*Z*-isomer): ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.86 (s, 3H, CH_3), 1.87 (d, J=1.2 Hz, 3H, CH_3), 2.07 (s, 3H, CH_3), 4.74 (s, 2H, CH_2), 5.79 (d, J=1.2 Hz, 1H), 6.59 (s, 1H), 7.15–7.41 (m, 5H, Ar). (*E*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 19.6, 21.0, 25.7, 68.5, 120.7, 126.8, 128.0, 128.7, 128.8, 133.6, 137.1, 137.5, 170.8. (*Z*-isomer): ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 19.6, 21.0, 26.8, 63.6, 125.2, 127.1, 128.3, 128.7, 133.1, 133.6, 136.5, 136.8, 171.0. IR (CH_2Cl_2) ν 3059, 3019, 2968, 2920, 1741, 1488, 1446, 1374, 1228, 1029, 965, 920, 751, 696 cm^{-1}. MS (%) *m/z* 230 (M^+, 4), 43 (100), 155 (81), 91 (51), 170 (32), 115 (29), 129 (19), 128 (18), 77 (17). HRMS (EI) calcd for $C_{15}H_{18}O_2$: 230.1307, found: 230.1304.

4.3. General procedure for palladium-catalyzed reaction of vinylidenecyclopropane 1c with deuterated acetic acid

Under an argon atmosphere, vinylidenecyclopropane **1c** (0.3 mmol), $Pd(PPh_3)_4$ (10 mol %), DPEphos (20 mol %), toluene (2.0 mL) and deuterated acetic acid (1.5 mmol) were added into a Schlenk tube. The mixture was stirred at 80 °C for 46 h. Then the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography.

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Supplementary data

^1H and ^{13}C NMR spectroscopic data and analytic data for compounds **2a–2j**. This material is available free of charge via the Internet. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.07.052.

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