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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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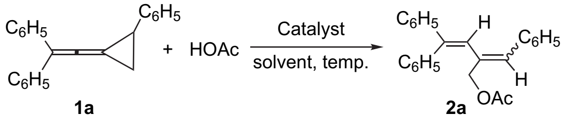
Table 1. Optimization of the reaction condition of **1a** with acetic acid



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 ^1H 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).

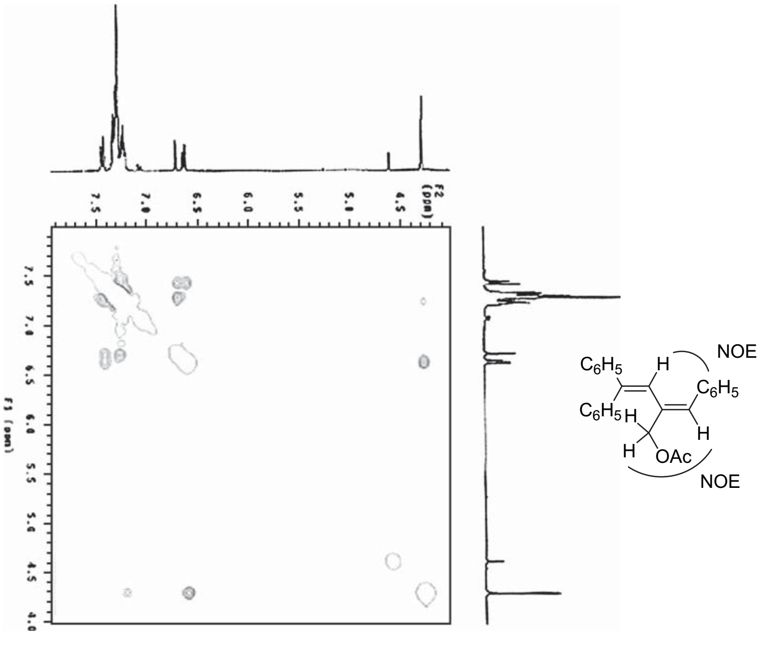


Figure 1.