Mechanistic investigations of bipyrimidine-promoted palladium-catalyzed allylic acetoxylation of olefins[1]

Bo-Lin Lin, Jay A. Labinger, and John E. Bercaw

Abstract: Several pyridine-like ligands were found to improve $Pd(OAc)_2$-catalyzed allylic oxidation of allylbenzene to cinnamyl acetate by *p*-benzoquinone in acetic acid. The best ligand examined, bipyrimidine, was used to identify the catalyst precursor for this system, (bipyrimidine)$Pd(OAc)_2$, which was fully characterized. Mechanistic studies suggest the reaction takes place through disproportionation of (bipyrimidine)$Pd(OAc)_2$ to form a bipyrimidine-bridged dimer, which reacts with olefin to form a Pd^{II}-olefin adduct, followed by allylic C–H activation to produce (η^3-allyl)Pd^{II} species. The (η^3-allyl)Pd^{II} intermediate undergoes a reversible acetate attack to generate a Pd^0-(allyl acetate) adduct, which subsequently reacts with *p*-benzoquinone to release allyl acetate and regenerate (bipyrimidine)$Pd(OAc)_2$. No KIE is observed for the competition experiment between allylbenzene-d_0 and allylbenzene-d_5 (CD_2=$CDCD_2C_6H_5$), suggesting that allylic C–H activation is not rate-determining. Catalytic allylic acetoxylations of other terminal olefins as well as cyclohexene were also effected by (bipyrimidine)$Pd(OAc)_2$.

Key words: olefin, palladium catalysis, allylic C–H oxidation, *p*-benzoquinone, bipyrimidine.

Résumé : On a observé que plusieurs ligands apparentés à la pyridine améliorent l'oxydation allylique de l'allylbenzène en acétate de cinnamyle par la *p*-benzoquinone dans l'acide acétique et catalysée par le $Pd(OAc)_2$. On a utilisé le meilleur ligand étudié, la bipyrimidine, pour identifier le précurseur du catalyseur pour ce système, le (bipyrimidine)$Pd(OAc)_2$, qui a été complètement caractérisé. Des études mécanistiques suggèrent que la réaction se produit par le biais d'une réaction de dismutation du (bipyrimidine)$Pd(OAc)_2$ qui conduit à la formation d'un dimère à pont bipyrimidine qui réagit avec l'oléfine pour conduire à un adduit Pd(II)-oléfine, le tout suivi de l'activation du C–H allylique conduisant à la formation de l'espèce (η^3-allyl)Pd(II). L'intermédiaire (η^3-allyl)Pd(II) subit une attaque réversible par l'ion acétate qui génère un adduit Pd°-(acétate d'allyle) qui réagit subséquemment avec la *p*-benzoquinone pour libérer l'acétate d'allyle et régénérer le (bipyrimidine)$Pd(OAc)_2$. On n'observe aucun effet isotopique cinétique pour l'expérience de compétition entre l'allylbenzène-d_0 et l'allylbenzène-d_5 (CD_2=$CDCD_2C_6H_5$); ce résultat suggère que l'activation allylique n'est pas l'étape cinétiquement déterminante. Les acétoxylations allyliques catalytiques du cyclohexène et d'autres oléfines terminales sont aussi affectées par le (bipyrimidine)$Pd(OAc)_2$.

Mots-clés : oléfine, catalyseur de palladium, oxydation de C–H allylique, *p*-benzoquinone, bipyrimidine.

[Traduit par la Rédaction]

Introduction

The selective oxidation of allylic C–H bonds offers a valuable approach to the construction of complex molecules (1). While earlier catalysts based on copper or selenium suffer from problems, such as limited substrate scope, low yields, and poor selectivities (2), extensive work on systems based on Pd(II) has led to some remarkably selective allylic C–H activations and oxidations (3, 4). The solvent often plays a key role in achieving selective oxidation to allyl acetates: in neat acetic acid, only symmetrical cyclic olefins are selectively oxidized with $Pd(OAc)_2$ (5), whereas terminal olefins can be selectively oxidized in DMSO/acetic acid (6), and yields can be further improved in dimethylacetamide (DMA) (7). The combination of Pd(II) with sulfoxide ligands also selectively oxidizes terminal olefins (8); this reaction has been successfully applied for catalytic allylic aminations (9) and macrolactonizations (10).

To date, no catalytic system has been reported to selectively oxidize both terminal and internal olefins to allyl acetates. Furthermore, in no case has the active catalytic species been characterized, which complicates the study and understanding of reaction mechanisms and impedes further development of new catalysts. Herein, we disclose a well-defined new catalyst precursor, (bipyrimidine)$Pd(OAc)_2$, that effects selective allylic acetoxylations of terminal olefins and

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This paper is dedicated to Professor Richard Puddephatt for his great contributions in Organometallic Chemistry.

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cyclohexene in acetic acid, and offer evidence for its mechanism of operation.

Experimental

All starting materials are commercially available and used as received without any further purification. $[(\eta^3\text{-}1\text{-phenylallyl})PdCl]_2$ (11) and $[(\eta^3\text{-}1\text{-phenylallyl})Pd(OAc)]_2$ (12) were synthesized according to literature procedures. Allylbenzene-d_5 ($C_6H_5CD_2CD{=}CD_2$) was synthesized by a modified literature procedure (13) where allyl bromide-d_5 was used instead of allyl bromide-d_0. Unless otherwise noted, all manipulations were carried out in air. ^{1}H and ^{13}C NMR spectra were recorded at room temperature on Varian Mercury 300 (^{1}H, 299.8 MHz; ^{13}C, 125.9 MHz) spectrometers. NMR spectra were referenced to residual solvent peak ($CDCl_3$: ^{1}H, 7.26 ppm; ^{13}C, 77.23 ppm; CD_3COOD: ^{1}H, 2.04 ppm) and reported in parts per million (ppm). Multiplicities were reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m), and broad resonance (br). GC measurements were taken on an Agilent 6890 series GC instrument with an Agilent HP-5 column. The X-ray structure was obtained at Caltech X-ray Crystallography Laboratory. High-resolution mass spectra were obtained at Caltech Mass Spectrometry Laboratory. Reaction yields are corrected for the purities of the starting materials.

(Bipyrimidine)Pd(OAc)$_2$ (1)

A solution of 25 mg $Pd(OAc)_2$ and 17.8 mg bipyrimidine (BPM) in 4.5 mL glacial acetic acid was stirred for 30 min, resulting in a clear yellow solution. After removing the solvent under vacuum, $(BPM)Pd(OAc)_2$ (**1**) was obtained as a yellow powder, pure enough for NMR analyses. A yellow crystal of $[(BPM)Pd(OAc)_2{\cdot}H_2O]$ was obtained by slow evaporation of a chloroform solution of a 1:1:1 mixture of BPM, $Pd(OAc)_2$, and acetic acid under air. ^{1}H NMR ($CDCl_3$) δ: 9.20 (dd, 2H, $^3J_{HH}$ = 4.8 Hz, $^4J_{HH}$ = 2.2 Hz), 8.68 (dd, 2H, $^3J_{HH}$ = 5.7 Hz, $^4J_{HH}$ = 2.2 Hz), 7.73 (dd, 2H, $^3J_{HH}$ = 5.7 Hz, 4.8 Hz), 2.13 (s, 6H). ^{13}C NMR ($CDCl_3$) δ: 178.9, 160.5, 157.6, 124.2, 23.3. HR-MS (FAB+) *m/z* calcd. for $C_{10}H_9N_4O_2Pd^+$: $(M - OAc)^+$ 322.9796; found: 322.9774.[3]

General procedure for allylic oxidation (Table 2, entries 1, 2, 3, 5, and 6)

A solution of 25 mg $Pd(OAc)_2$ and 17.6 mg BPM in 4.5 mL glacial acetic acid was stirred for ~30 min, followed by sequential additions of 10 equiv. of olefin and 20 equiv. of benzoquinone. The mixture was heated at 70 °C with stirring, in a 20 mL glass vial sealed with a Teflon-lined cap and PTFE tape. After the reported time, the reaction mixture was cooled to room temperature in a water bath and neutralized with 50 mL of an aqueous solution of 6.2 g NaOH. The resultant mixture was extracted with 3 × 100 mL CH_2Cl_2. Organic portions were combined and dried over $MgSO_4$. Volatiles were removed under vacuum. The resultant oil was further purified by flash silica-gel column chromatography.

trans-*Cinnamyl acetate (Table 2, entry 1)*

Allylbenzene: 98% pure. Reaction time: 34 h. Eluent: 1:10 (*v*/*v*) EtOAc/hexanes. The product was isolated as a mixture of cis and trans isomers. Mass: 146 mg; overall yield: 76%; NMR yield of the trans isomer: 72%. ^{1}H NMR ($CDCl_3$) δ: 7.20–7.45 (m, 5H), 6.60–6.71 (d, 1H, $^3J_{HH}$ = 15.9 Hz), 6.24–6.35 (dt, 1H, $^3J_{HH}$ = 15.9 Hz, 6.6 Hz), 4.71–4.76 (dd, 2H, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 1.3 Hz), 2.11 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 171.1, 136.4, 134.4, 128.9, 128.3, 126.9, 123.4, 65.3, 21.3. HR-MS (FAB+) *m/z* calcd. for $C_{11}H_{12}O_2$: 176.0837; found: 176.0832.

trans-p-*Methylcinnamyl acetate (Table 2, entry 2)*

p-Allyltoluene: 99% pure. Reaction time: 32 h 46 min. Eluent: 1:10 (*v*/*v*) EtOAc/hexanes. The product was isolated as a mixture of cis and trans isomers. Mass: 165 mg; overall yield: 78%; NMR yield of the trans isomer: 75%. ^{1}H NMR ($CDCl_3$) δ: 7.26–7.32 (d, 2H, $^3J_{HH}$ = 8.1 Hz), 7.10–7.17 (d, 2H, $^3J_{HH}$ = 8.1 Hz), 6.58–6.68 (d, 1H, $^3J_{HH}$ = 15.9 Hz), 6.18–6.30 (dt, 1H, $^3J_{HH}$ = 15.9 Hz, 6.6 Hz), 4.68–4.76 (dd, 2H, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 1.3 Hz), 2.35 (s, 3H), 2.10 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 171.1, 138.2, 134.5, 133.6, 129.6, 126.8, 122.3, 65.5, 21.5, 21.3. HR-MS (FAB+) *m/z* calcd. for $C_{12}H_{14}O_2$: 190.0994; found: 190.0995.

trans-p-*Methoxycinnamyl acetate (Table 2, entry 3)*

p-Methoxyallylbenzene: 98% pure. Reaction time: 16 h. Eluent: 1.5:10 (*v*/*v*) EtOAc/hexanes. The product was isolated as a mixture of cis and trans isomers. Mass: 118 mg; overall yield: 53%; NMR yield of the trans isomer: 50%. ^{1}H NMR ($CDCl_3$) δ: 7.30–7.36 (d, 2H, $^3J_{HH}$ = 8.4 Hz), 6.82–6.89 (d, 2H, $^3J_{HH}$ = 8.4 Hz), 6.55–6.64 (d, 1H, $^3J_{HH}$ = 15.3 Hz), 6.10–6.21 (dt, 1H, $^3J_{HH}$ = 15.3 Hz, 6.6 Hz), 4.66–4.74 (dd, 2H, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 1.3 Hz), 3.80 (s, 3H), 2.09 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 171.2, 159.8, 134.3, 129.2, 128.1, 121.0, 114.2, 65.6, 55.5, 21.3. HR-MS (FAB+) *m/z* calcd. for $C_{12}H_{14}O_3$: 206.0943; found: 206.0952.

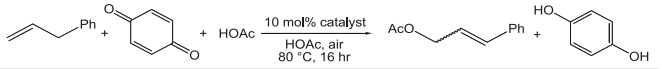
1-Acetoxy-trans-*2-decene (Table 2, entry 5)*

Reaction time: 20 h. Eluent: 1:10 (*v*/*v*) EtOAc/hexanes. The product was isolated as a mixture of allylic acetates along with (1-acetoxy-)3-, 4-, and 5-decenes. Both ^{1}H NMR and GC gave the estimated ratio of allylic acetates (sum of *trans*-primary allylic acetate, *cis*-primary allylic acetate, and secondary allylic acetate) to other isomers to be ~3.8. Only 1-acetoxy-*trans*-2-decene was fully characterized. Mass: 171 mg; overall yield: 78%; NMR yield of 1-acetoxy-*trans*-2-decene: 54%. ^{1}H NMR ($CDCl_3$) δ: 5.70–5.83 (m, 1H), 5.49–5.62 (m, 1H), 4.47–4.53 (dd, 2H, $^3J_{HH}$ = 6.6 Hz, $^4J_{HH}$ = 1 Hz), 2.06 (s, 3H), 1.92–2.08 (m, 2H), 1.27 (br s, 10H), 0.87 (t, 3H, $^3J_{HH}$ = 6.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 171.1, 137.0, 123.9, 65.6, 32.5, 32.0, 29.6, 29.3, 29.1, 22.9, 21.3, 14.3. HR-MS (FAB+) *m/z* calcd. for $C_{12}H_{14}O_2$: 198.1620; found: 198.1625.

1-Acetoxy-3-cyclohexyl-trans-*2-propene (Table 2, entry 6)*

Allylcyclohexane: 96% pure. Reaction time: 20 h. Eluent: 1:10 (*v*/*v*) EtOAc/hexanes. The product was isolated as a mixture of allylic acetates, 3-cyclohexylidenepropyl acetate, and 3-cyclohexenylpropyl acetates. The ratio of allylic acetates (sum of *trans*-primary allylic acetate, *cis*-primary allylic acetate, and secondary allylic acetate) to other isomers was estimated to be ~6.2 by ^{1}H NMR and GC. Only 1-acetoxy-3-cyclohexyl-*trans*-2-propene was fully characterized. Mass: 150 mg; overall yield: 77%; NMR yield of 1-acetoxy-3-cyclohexyl-*trans*-2-propene: 65%. ^{1}H NMR

Table 1. Nitrogen ligand effects on $Pd(OAc)_2$-catalyzed allylic acetoxylation of allylbenzene.



Entry	Catalyst	Yield[a,b]
1	10 mol% $Pd(OAc)_2$	13%
2	10 mol% $Pd(OAc)_2$ + 10 mol% 2,2′-bipyrimidine	76%
3	10 mol% $Pd(OAc)_2$ + 20 mol% pyridine	35%
4	10 mol% $Pd(OAc)_2$ + 10 mol% 1,10-phenanthroline	47%
5	10 mol% $Pd(OAc)_2$ + 10 mol% 2,2′-bipyridine	—[c]

Note: General experimental procedure: A mixture of catalyst, 0.7 mL glacial acetic acid, allylbenzene, 1 equiv. BQ, and 20 µL nitrobenzene (internal standard for GC) is stirred and heated in a sealed vial at 80 °C for 16 h.

[a]Sum of *cis* and *trans* isomers; GC yields.

[b]Conversions of allylbenzene: entry 1–3, 100%; entry 4, 87%; entry 5, 3%.

[c]No product detected.

($CDCl_3$) δ: 5.66–5.75 (dd, 1H, $^3J_{HH} \approx 15.6$ Hz, 6.3 Hz), 5.44–5.55 (dtd, 1H, $^3J_{HH} = 15.6$ Hz, 6.6 Hz, $^4J_{HH} = 1.1$ Hz), 4.46–4.52 (d, 2H, $^3J_{HH} = 6.6$ Hz), 2.05 (s, 3H), 1.84–2.05 (m, 1H), 0.94–1.79 (m, 10H). ^{13}C NMR ($CDCl_3$) δ: 171.1, 142.4, 121.5, 65.8, 40.6, 32.7, 26.3, 26.2, 21.3. HR-MS (FAB+) *m/z* calcd. for $C_{11}H_{18}O_2$: 182.1307; found: 182.1313.

Allyl acetate (Table 2, entry 4)

A 5 mL round-bottom flask was charged with 27.1 mg (BPM)$Pd(OAc)_2$ (10 mol%), 153 mg BQ (2 equiv.), 20 µL nitrobenzene, and 2.2 mL glacial acetic acid. Propylene (15.7 mL, 1 atm) was then condensed into the flask by liquid nitrogen after degassing (1 atm = 101.325 kPa). The mixture was stirred and heated at 70 °C for 24 h. An aliquot of the reaction mixture was taken and filtered through a short pipette of silica gel with Et_2O as the eluent for GC analysis. The GC-peak area of allyl acetate relative to nitrobenzene was used to calculate the yield. Allyl acetate was the only allylic oxidation product observed by ^1H NMR. GC Yield: 45%.

Cyclohexenyl acetates (Table 2, entry 7)

The general procedure above was followed, except for the use of 20 equiv. of cyclohexene and 24 equiv. of benzoquinone, and heating at 80 °C. After 24 h, the mixture was cooled to room temperature by water bath and neutralized by 6.2 g NaOH in 50 mL H_2O. The resultant mixture was extracted by 3 × 100 mL CH_2Cl_2. Organic portions were combined and dried over $MgSO_4$. Volatiles were removed under vacuum. The resultant oil was further purified by reduced-pressure distillation. A ~2.8:1 mixture of cyclohex-2-enyl acetate and cyclohex-3-enyl acetate was obtained. Mass: 160 mg; overall yield: 51.3%.

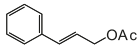
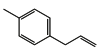
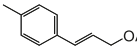
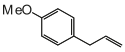
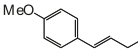
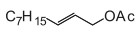
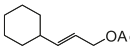
Cyclohex-2-enyl acetate

^1H NMR ($CDCl_3$) δ: 5.87–5.98 (m, 1H), 5.63–5.73 (m, 1H), 5.18–5.27 (m, 1H), 2.03 (s, 3H), 1.53–2.45 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 171.0, 132.9, 125.9, 68.3, 28.5, 25.1, 21.6, 19.1. HR-MS (FAB+) *m/z* calcd. for $C_8H_{12}O_2$: 140.0837; found: 140.0841.

Cyclohex-3-enyl acetate

^1H NMR ($CDCl_3$) δ: 5.62–5.67 (m, 1H), 5.51–5.60 (m, 1H), 4.93–5.03 (m, 1H), 2.03 (s, 3H), 1.53–2.45 (m, 6H).

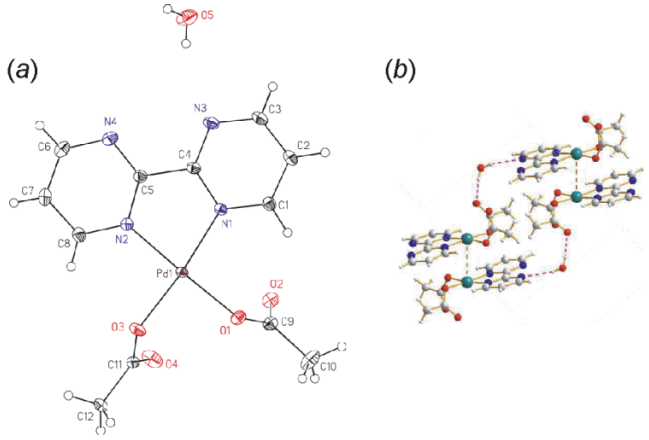
Table 2. (Bipyrimidine)$Pd(OAc)_2$-catalyzed allylic acetoxylation of olefins.

Entry	Olefin	Temp. (°C)	Time (h)	Major product (NMR yield)	Overall yield[a]
1		70	34	 (72%)	76%
2		70	33	 (75%)	78%
3		70	16	 (50%)	53%
4		70	24		45%
5		70	20	 (54%)	77%
6		70	20	 (65%)	77%
7		80	24	 (33%)	51%

Note: Entry 1–6: 10 mol% catalyst loading and 2 equiv. BQ; Entry 7: 5 mol% catalyst loading and 1.2 equiv. BQ; All reactions except 4 and 7 are near completion.

[a]Product isolated as a mixture of isomers: Entries 1–3: *cis*- + *trans*-1° allyl acetates; Entries 5–7: C=C bond migration results in minor products such as homoallyl acetates; Entries 5 and 6: small amounts of 2° allyl acetates observed.

Fig. 1. X-ray crystallographic structure and the crystal packing of [(bipyrimidine)$Pd(OAc)_2 \cdot H_2O$] (see Supplementary data).[3]



Scheme 1.

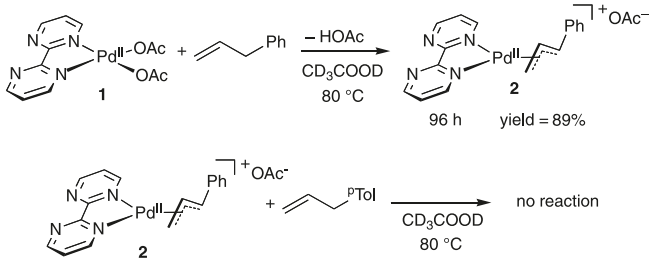


Table 3. Crystal data and structure refinement for [(BPM)Pd(OAc)$_2$·H$_2$O]

Empirical formula	$C_{12}H_{12}N_4O_4Pd·H_2O$
Formula mass	400.67
Crystallization solvent	Dichloromethane
Crystal habit	Block
Crystal size (mm)	0.36 × 0.31 × 0.27
Crystal colour	Yellow
λ Mo Kα (Å)	0.710 73
Temperature (K)	100(2)
a (Å)	9.6974(3)
b (Å)	14.9781(4)
c (Å)	10.0106(3)
β (°)	98.7400(10)
V (Å^3)	1437.14(7)
Z	4
Crystal system	Monoclinic
Space group	$P2_1/n$
$D_{calcd.}$ (Mg/m^3)	1.852
F(000)	800
θ range for data collection	2.47° to 44.89°
Completeness to θ = 44.89°	77.7%
Index ranges	$-18 \le h \le 17$, $-29 \le k \le 29$, $-17 \le l \le 17$
Reflections collected	28 065
Independent refl.	9164 [R_{int} = 0.0588]
Absorption coefficient (mm^{-1})	1.321
Absorption correction	None
Max. and min. transmission	0.7168 and 0.6477
Hydrogen placement	Difference Fourier map
Data, restraints, parameters	9164, 0, 255
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.485
Final *R* indices [$I > 2\sigma(I)$, 7498 refl.]	R_1 = 0.0305, wR_2 = 0.0664
R indices (all data)	R_1 = 0.0393, wR_2 = 0.0678
Max shift/error	0.004
Average shift/error	0.000
Largest diff. peak and hole (e Å^{-3})	1.503 and –1.576

^{13}C NMR ($CDCl_3$) δ: 171.0, 127.0, 123.9, 70.0, 30.9, 27.5, 23.5, 21.6.

[(Bipyrimidine)Pd(η^3-1-phenylallyl)]$^+$(OAc)$^-$ (2)

Route 1

A mixture of 8.6 mg (BPM)Pd(OAc)$_2$ and 29.5 μL allylbenzene in 0.7 mL CD_3COOD was heated in a J–Young NMR tube under nitrogen at 80 °C for 96 h. The yield of compound **2** based on Pd was 89%, as estimated by ^{1}H NMR.

Route 2

A 2:1 ratio of AgOAc (3.8 mg) and [(η^3-1-phenylallyl)PdCl]$_2$ (5.5 mg) was stirred in 1 mL of acetone at room temperature for 30 min. After filtering off the precipitate, solvent was pumped away under vacuum. To the resultant yellow solid was added 3.6 mg BPM and 0.7 mL CD_3COOD. ^{1}H NMR shows that [(BPM)Pd(η^3-1-phenylallyl)]$^+$(OAc)$^-$ was formed quantitatively. Unfortunately, compound **2** is not isolable owing to rapid decomposition to Pd metal in the absence of acetic acid. ^{1}H NMR (CD_3COOD) δ: 9.24 (br s 4H), 7.78 (br s 2H), 7.46–7.82 (m, 5H), 6.59 (app dt, 1H, $^3J_{HH}$ = 12.3 Hz, 7.2 Hz), 5.06 (d, 1H, $^3J_{HH}$ = 12.3 Hz), 4.68 (d, 1H, $^3J_{HH}$ = 7.2 Hz), 3.87(d, 1H, $^3J_{HH}$ = 12.3 Hz). HR-MS (FAB+) *m*/*z* calcd. for $C_{17}H_{15}N_4Pd^+$: (M – OAc)$^+$ 381.0332; found: 381.0343.

(Bipyrimidine)[Pd(OAc)$_2$]$_2$ (3)

3.6 mg BPM and 10 mg Pd(OAc)$_2$ (2 equiv.) were mixed with 0.7 mL CD_3COOD. A clear yellow solution was obtained after stirring for 2 h. The solution contained an equilibrated mixture of Pd(OAc)$_2$, (BPM)Pd(OAc)$_2$ (**1**), and (BPM)[Pd(OAc)$_2$]$_2$ (**3**). The equilibrium constant was estimated to be ~25 mol^{-1} L by ^{1}H NMR. NMR yield of compound **3** based on BPM: 35%. ^{1}H NMR (CD_3COOD) δ: 8.75 (d, 4H, $^3J_{HH}$ = 5.7 Hz), 7.78 (t, 2H, $^3J_{HH}$ = 5.7 Hz). MS (MALDI) *m*/*z* calcd. for $C_{16}H_{18}N_4Pd_2^+$: (M$^+$) 605.919; found: 605.7228.

[(Bipyrimidine)Pd(η^3-2-propenyl)]$^+$(OAc)$^-$

To a solution of compound **1** in 0.7 mL CD_3COOD was added 2.4 μL allyl acetate (1 equiv.). After degassing, the solution was heated at 80 °C for 15 h. According to the ^{1}H NMR spectrum, ~50% of the starting material was converted to [(BPM)Pd(η^3-2-propenyl)]$^+$. ^{1}H NMR (CD_3COOD) δ: 9.32 (br s 4H), 7.99 (br s 2H), 6.03–6.19 (tt, 1H, $^3J_{HH}$ = 6.6 Hz, 12.6 Hz), 4.72–4.76 (dd, 2H, $^2J_{HH}$ = 1.3 Hz, $^3J_{HH}$ = 6.6 Hz), 3.60–3.72 (d, 2H, $^3J_{HH}$ = 12.6 Hz). HR-MS (FAB+) *m*/*z* calcd. for $C_{11}H_{11}N_4Pd^+$: (M – OAc)$^+$ 305.0019; found: 305.0044.

Exchange between *trans*-cinnamyl acetate and CD_3COOD

A mixture of compound **2** and 10 μL *trans*-cinnamyl acetate (3 equiv.) in 0.7 mL CD_3COOD was heated in a J–Young NMR tube under nitrogen at 80 °C. After 16 h 5 min, 20% of the starting $PhCH{=}CHCO_2CH_3$ was converted to $PhCH{=}CHCO_2CD_3$. No change of compound **2** was detected. Control experiments were carried out under similar conditions except that compound **2** was absent or replaced by an equimolar amount of NaOAc. In neither case was acetate scrambling detected by ^{1}H NMR.

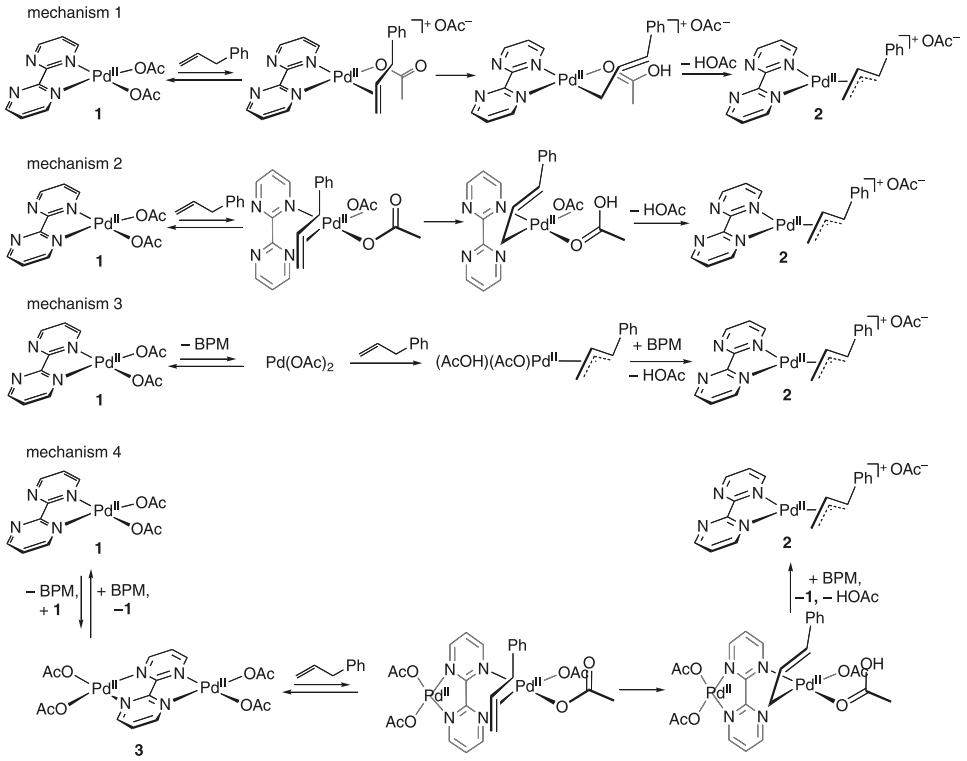
Competition between allylbenzene-d_0 and allylbenzene-d_5

A mixture of 4.3 mg (BPM)Pd(OAc)$_2$ (~5 mol%), 10 μL nitrobenzene (internal standard), 15 μL allylbenzene-d_0, 15 μL allylbenzene-d_5, 25 mg BQ, and 0.35 mL CH_3COOH was heated in a sealed vial with stirring at 80 °C. Aliquots (~5 μL) were taken at certain times by microsyringe for GC analysis. The GC signals of allylbenzene-d_0 and allylbenzene-d_5 are fully separated, but those of the two isotopologs of *trans*-cinnamyl acetate are not.

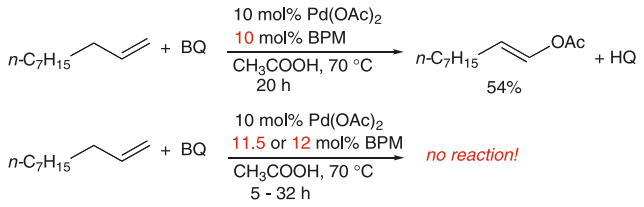
Results and discussion

The oxidation of allylbenzene by *p*-benzoquinone (BQ) in acetic acid at 80 °C, with Pd(OAc)$_2$ as the catalyst, leads to only a 13% yield of cinnamyl acetate (100% consumption of allylbenzene). Several other unidentified products, probably

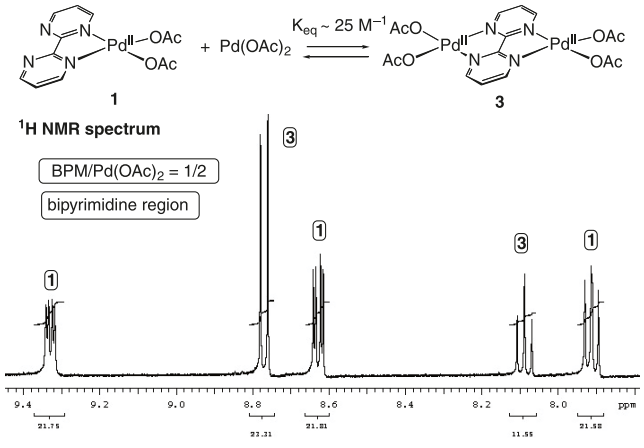
Scheme 2.



Scheme 3.



Scheme 4.



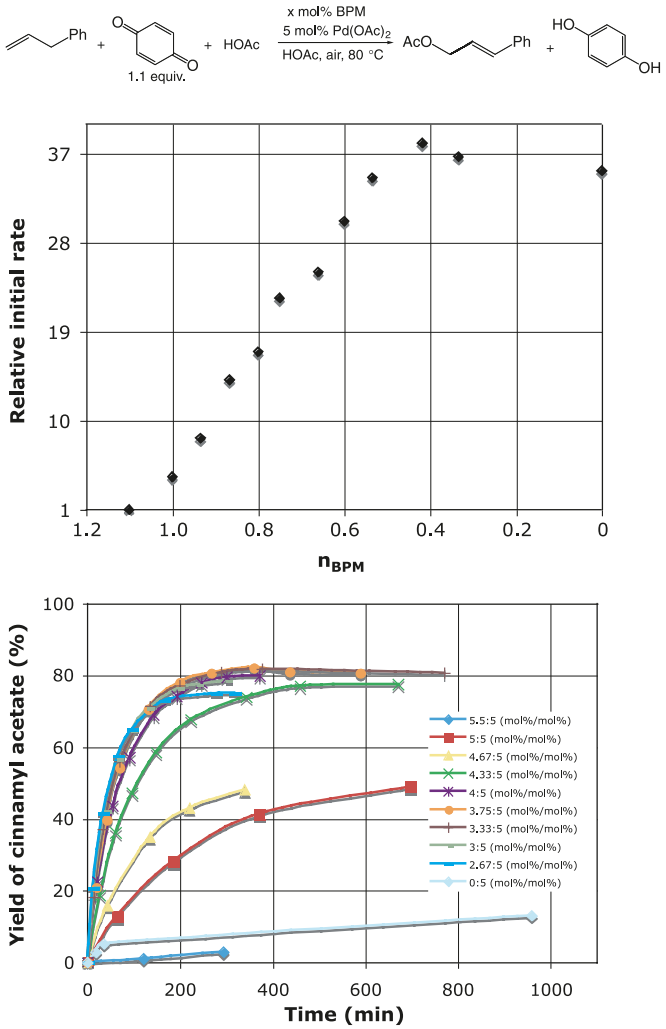
including the same Wacker-type products previously reported from reaction at 40 °C (6b), are observed. The selectivity for cinnamyl acetate is significantly improved by the addition of pyridine-like nitrogen ligands (with the exception of 2,2′-bipyridine, which shuts down the reaction) (Table 1). Among the ligands tested, bipyrimidine (BPM) is the best, leading to a 76% yield of cinnamyl acetate in 16 h at 80 °C.

Studies of substrate scope (Table 2) indicate that both benzylic C–H and methoxy groups are compatible with the acetoxylation (Table 2, entries 2 and 3). Unfortunately, the yield for olefins with alkyl groups at the allylic position (Table 2, entries 5 and 6) suffers from olefin isomerization, giving byproducts such as homoallylic acetates. Cyclohexene is also an active substrate for the reaction, producing a mixture of cyclohex-2-enyl acetate and cyclohex-3-enyl acetate (~ 2.8:1) (Table 2, entry 7). Interestingly, cyclohex-2-enyl acetate becomes the only allylic oxidation product if (1,10-phenanthroline)$Pd(OAc)_2$ or *bis*(oxazoline)$Pd(OAc)_2$ (14) is used as the catalyst.

The reaction of bipyrimidine with $Pd(OAc)_2$ in CD_3COOD forms (BPM)$Pd(OAc)_2$ (**1**) in quantitative yield after 30 min at room temperature, as monitored by ^1H NMR. A crystal structure for (BPM)$Pd(OAc)_2$·H_2O was obtained (Fig. 1; Table 3).[3] Heating (BPM)$Pd(OAc)_2$ with allylbenzene (10 equiv.) in CD_3COOD at 80 °C for ~4 day affords [(BPM)Pd(η^3-1-phenylallyl)]$^+$$(OAc)^-$ (**2**), the product

[3] Supplementary data for this article are available on the journal Web site (canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 3834. For more information on obtaining material refer to cisti-icist.nrc-cnrc.gc.ca/cms/unpub_e.shtml. CCDC 634014 contains the crystallographic data for this manuscript. These data can be obtained, free of charge, via www.ccdc.cam.ac.uk/conts/retrieving.html (Or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax +44 1223 336033; or deposit@ccdc.cam.ac.uk).

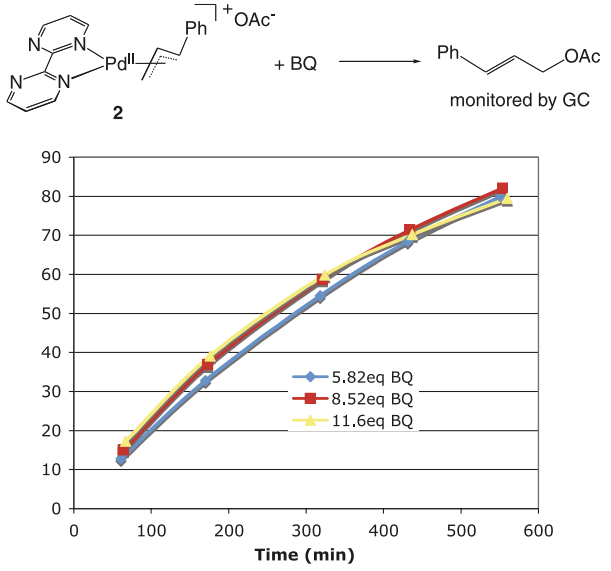
Fig. 2. Effect of BPM to $Pd(OAc)_2$ ratio on allylic oxidation of allylbenzene by benzoquinone, $Pd(OAc)_2$ fixed to be 5 mol%. Upper graph: initial rates of the disappearance of allylbenzene relative to that of n(BPM)/n(Pd) = 1.1; lower graph: appearance of cinnamyl acetate.



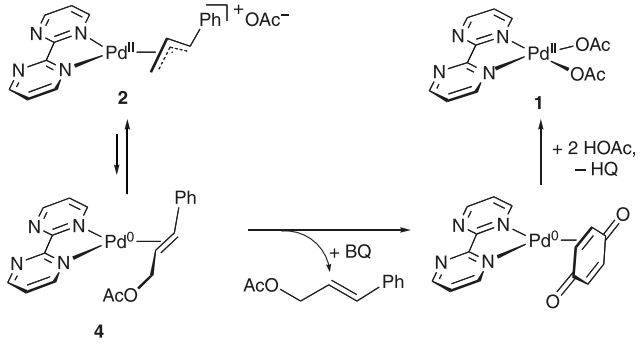
of allylic C–H activation, in ~89% yield (Scheme 1). Furthermore, the allylic C–H activation is irreversible, because neither olefin exchange nor deuterium incorporation into the allyl fragment is observed after heating **2** with *p*-allyltoluene in CD_3COOD at 80 °C for 15 h (Scheme 1). Similar irreversibility was also proposed for the sulfoxide–$Pd(OAc)_2$ system (8).

The reaction between allylbenzene and $(BPM)Pd(OAc)_2$ could occur via the displacement by the olefin of either an acetate or a coordinated BPM nitrogen to form a Pd(II)–olefin adduct, followed by allylic C–H activation to form **2** (Scheme 2, mechanisms 1 and 2). For either mechanism, addition of excess BPM should not have a significant effect on the reaction rate (a mixture of $Pd(OAc)_2$ and 1.15 equiv. BPM in CD_3COOD affords 1 equiv. $(BPM)Pd(OAc)_2$ and 0.15 equiv. free BPM (NMR)). However, no reaction is seen for allylbenzene or 1-decene when a slight excess (≤20 mol% relative to $Pd(OAc)_2$) of BPM is added (Scheme 3), clearly ruling out either mechanism for the acetoxylation.

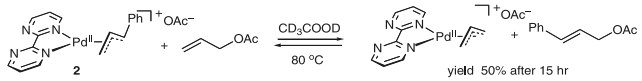
Fig. 3. Oxidation of $(\eta^3$-allyl)Pd^{II} by benzoquinone is independent of the concentration of benzoquinone.



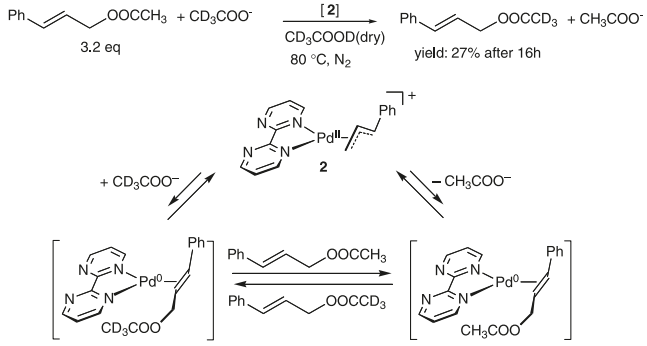
Scheme 5.



Scheme 6.

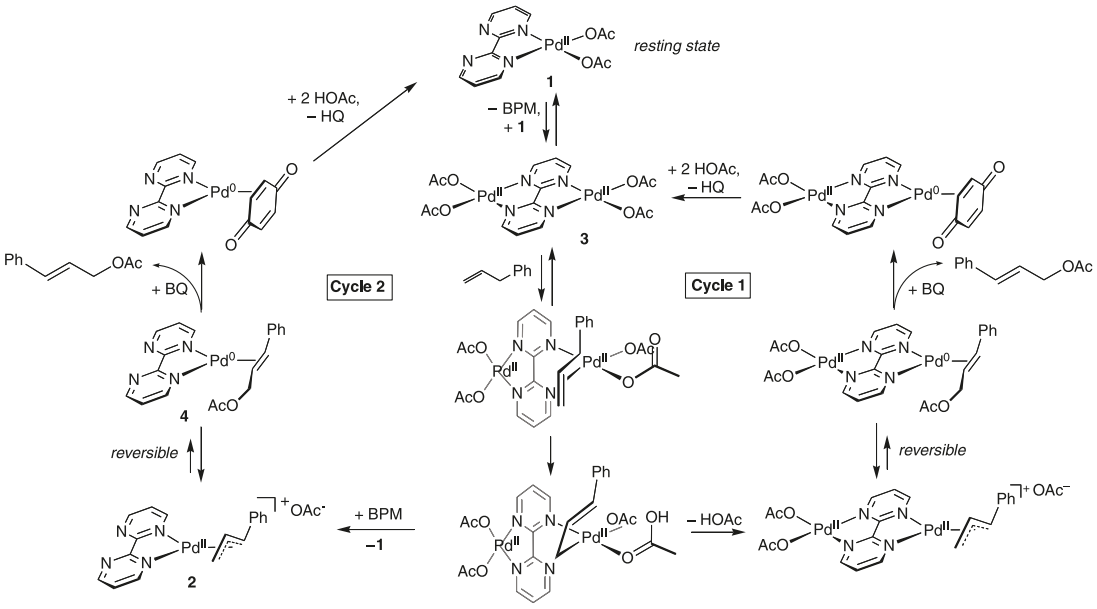


Scheme 7.



Full dissociation of BPM from $(BPM)Pd(OAc)_2$, forming $Pd(OAc)_2$, which then catalyzes the reaction, would be consistent with the inhibitory effect of excess BPM (Scheme 2,

Scheme 8.

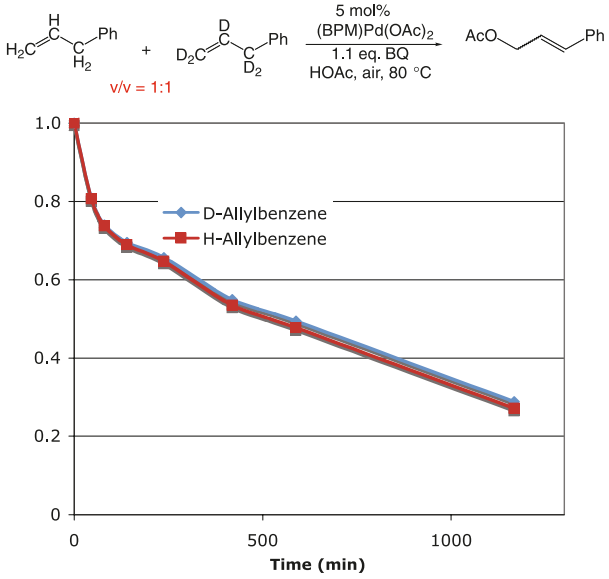


mechanism 3), but this is also unlikely to be the mechanism because $Pd(OAc)_2$ does not lead to selective allylic oxidation under current catalytic conditions (Table 1, entry 1). The nonselective oxidation catalyzed by $Pd(OAc)_2$ must originate in the allylic C–H activation of allylbenzene by $Pd(OAc)_2$ rather than a subsequent step, because the solvolysis of $[(\eta^3\text{-1-phenylallyl})Pd(OAc)]_2$ in wet acetic acid at 75 °C quantitatively forms allylic oxidation products (allylic acetates and cinnamaldehyde; the latter results from water as the nucleophile) (15).

In a further experiment, a mixture of $(BPM)Pd(OAc)_2$ and $Pd(OAc)_2$ in CD_3COOD (generated in situ by combining $Pd(OAc)_2$ and BPM in a 2:1 ratio) reacts to form a new species, characterized by ^{1}H NMR and MALDI as the BPM-bridged $Pd(OAc)_2$ dimer **3** (Scheme 4). The reaction does not reach 100% conversion, but equilibrates with K_{eq} ~ 25 mol^{-1} L, as estimated by ^{1}H NMR. The resultant mixture reacts with allylbenzene under air *at room temperature* to form an η^3-allyl species, cinnamyl acetate, and palladium black.

We propose that dimer **3** is the active species for the reaction with allylbenzene, because the $Pd(OAc)_2$-only system results in less selective oxidation of allylbenzene, while heating is required for the reaction between $(BPM)Pd(OAc)_2$ and allylbenzene. According to our proposal, in the latter reaction, small amounts of dimer and free BPM are formed via disproportionation of $(BPM)Pd(OAc)_2$, explaining the inhibition by excess BPM. The coordination of a second equivalent of $Pd(OAc)_2$ to BPM would be expected to weaken a Pd–N bond and thus facilitate the coordination of olefin; the Pd–olefin adduct subsequently undergoes allylic C–H activation to form **2** (Scheme 2, mechanism 4). This mechanism is further supported by the observation that the initial consumption rate of allylbenzene increases as the ratio of BPM to $Pd(OAc)_2$ decreases; the best overall yields (~82%) were obtained by combining 3–4 mol% BPM with 5 mol% $Pd(OAc)_2$ (Fig. 2).

Fig. 4. No significant KIE is observed for competition reaction between allylbenzene-d_0 and allylbenzene-d_5.



Although **2** is stable in CD_3COOD at 80 °C, the addition of benzoquinone (BQ) releases cinnamyl acetate (16) and generates $(BPM)Pd(OAc)_2$ and hydroquinone (HQ). It has been proposed that coordination of benzoquinone to Pd^{II} induces acetate attack (8, 17), but we find that the rate of the reaction between **2** and benzoquinone in acetic acid is independent of the benzoquinone concentration when at least 5.8 equiv. are used (Fig. 3), which argues against this mechanism.

Instead, we believe that reversible attack of acetate at the η^3-allyl moiety (18) occurs in the absence of benzoquinone to form the (unobservable) Pd^0(allyl acetate) species **4** (Scheme 5). Such a route is suggested by the reaction between allyl acetate and **2** in CD_3COOD, which generates

cinnamyl acetate and [(BPM)Pd(η^3-propenyl)]$^+$(OAc)$^-$ (Scheme 6), and by the fact that **2** catalyzes exchange of labeled and unlabeled acetate between *trans*-cinnamyl acetate and CD_3COOD (Scheme 7). (BPM)Pd^0(cinnamyl acetate) complex **4** then reacts with BQ to release cinnamyl acetate and form (BPM)Pd^0(BQ) (19), followed by a redox reaction with acetic acid to generate (BPM)$Pd(OAc)_2$ and hydroquinone (HQ) to complete the catalytic cycle (Scheme 5).

Scheme 8 shows a mechanism consistent with all current observations. Allylic C–H activation of allybenzene by dimer **3** leads to a dimeric (η^3-allyl)Pd^{II} complex, which can react either with benzoquinone to release cinnamyl acetate and regenerate the active dimer **3** (Scheme 8, cycle 1), or with free BPM (generated from the disproportionation) to form the monomeric (η^3-allyl)Pd^{II} **2**, followed by reaction with benzoquinone to release cinnamyl acetate and regenerate (BPM)$Pd(OAc)_2$ (Scheme 8, cycle 2). We assume that the mechanistic inferences from the stoichiometric reactions described above, which would be rigorously applicable only to the monomeric intermediates in cycle 2, most probably would be valid for the analogous dimeric intermediates of cycle 1 as well.

If cycle 2 is the dominant pathway, the rate-determining step for the whole catalytic cycle must occur before the formation of (η^3-allyl)Pd^{II} because the only Pd species observed by ^{1}H NMR during the reaction is (BPM)$Pd(OAc)_2$. In addition, the BPM inhibitory effect suggests a pre-equilibrium between (BPM)$Pd(OAc)_2$ and **3**. Therefore, either the olefin coordination or allylic C–H activation would be rate-determining. A competition experiment using a 1:1 (*v*/*v*) ratio of allylbenzene-d_0 and allylbenzene-d_5 (CD_2=$CDCD_2C_6H_5$) shows no kinetic isotope effect for the consumption rate of allylbenzene (Fig. 4), suggesting olefin coordination rather than C–H activation is rate-determining.

However, if cycle 1 is the dominant pathway, we cannot rule out the possibility that acetate attack on the dimeric (η^3-allyl)Pd^{II} complex is rate-determining. In that case, the dimeric (η^3-allyl)Pd^{II} complex would be the major species *within* the actual catalytic cycle, but it could still be unobservable if the equilibrium between **1** and **3** strongly favours the former. Since at present we do not know which cycle is dominant, we cannot conclusively identify the rate-determining step.

In summary, we have reported (BPM)$Pd(OAc)_2$ as a well-defined new catalyst for allylic C–H oxidation of olefins. Mechanistic studies have provided insight to understand the catalysis and led to further improvement of the reaction yield for the oxidation of allylbenzene. More studies are underway to explore the potential of the dimeric species and its derivatives in catalytic allylic C–H oxidations.

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