

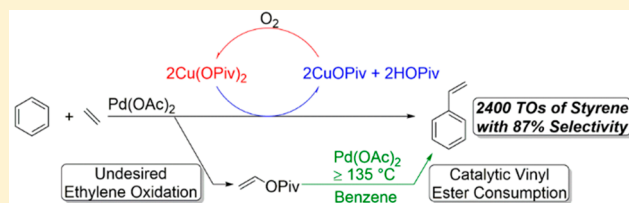
Styrene Production from Benzene and Ethylene Catalyzed by Palladium(II): Enhancement of Selectivity toward Styrene via Temperature-dependent Vinyl Ester Consumption

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Supporting Information

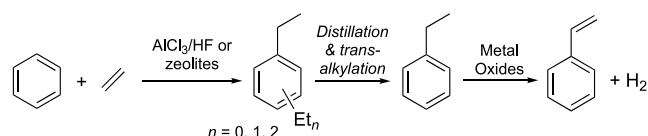
ABSTRACT: Oxidative ethylene hydrophenylation catalyzed by palladium(II) acetate with Cu(II) oxidants to produce styrene generally suffers from low selectivity and/or low yield. Commonly observed side products include vinyl carboxylates and stilbene. In this Article, the selectivity for styrene formation by Pd(OAc)₂ is studied as a function of reaction temperature, ethylene pressure, Brønsted acid additive, Cu(II) oxidant amount, and oxygen pressure. Under optimized conditions, at high temperatures (180 °C) and low olefin pressure (20 psig), nearly quantitative yield (>95%) of styrene is produced based on the limiting reagent copper(II) pivalate. We propose the selectivity for styrene versus vinyl pivalate at 180 °C is due to a palladium-catalyzed conversion of benzene and *in situ* formed vinyl pivalate to styrene.



INTRODUCTION

Alkenyl arenes are important precursors for fine chemical synthesis as well as for the preparation of plastics, elastomers, and surfactants.^{1,2} Currently, alkenyl arenes are produced on a large scale from benzene and olefins using acid-catalyzed arene alkylation with subsequent dehydrogenation of the alkyl arene.³ For many arene alkylation processes, polyalkylation is problematic. For example, in order to optimize the yield of ethylbenzene, energy consuming distillation and then trans-alkylation of benzene and polyethylbenzenes are required. Thus, current industrial routes to alkenyl arenes are often multistep and energy-intensive (Scheme 1).^{1,2,4} Olefin hydroarylation cata-

Scheme 1. Current Industrial Synthetic Routes for Ethylbenzene and Styrene Production



lyzed by transition metals involving aromatic C–H activation and olefin insertion provides an alternative strategy to synthesize alkyl or alkenyl arenes that can overcome some of the challenges of acid-catalyzed arene alkylation (Scheme 2).^{5–9} As shown in Scheme 2, metal-mediated olefin insertion provides an opportunity to control the regioselectivity of arene/olefin C–C bond formation, and the arene C–H activation step provides a strategy to influence the regioselectivity of the alkenylation when using substituted arenes. Furthermore, understanding the

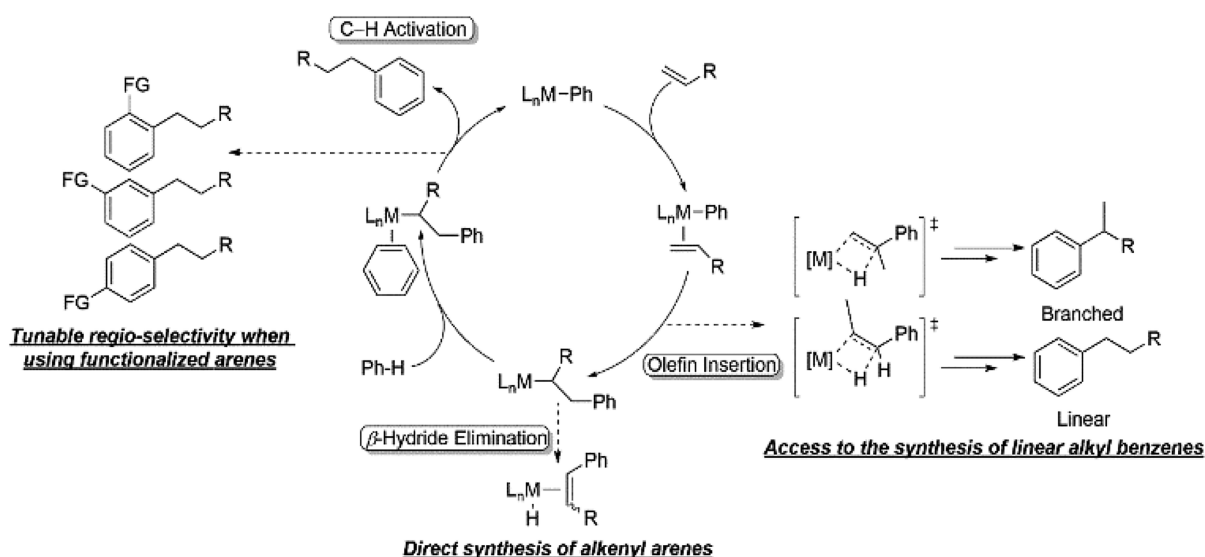
factors that influence β -hydride elimination can provide control over alkylation versus alkenylation.

Palladium-catalyzed oxidative alkenylation of arenes, also known as the Fujiwara–Moritani reaction, has traditionally been limited in substrate scope, as directing groups are often required.^{10–22} Direct arene alkenylation using unactivated arenes and olefins (e.g., benzene, toluene, ethylene, propylene, etc.) remains challenging with regard to selectivity, reaction rate, and catalyst longevity. Examples of transition metal-based catalysts for arene alkylation of simple hydrocarbon substrates include Pt,^{23–32} Ru,^{33–42} and Ir.^{43–45} In addition, catalytic oxidative arene alkenylation using Rh and Pd precursors has been reported.^{46–51}

We recently reported oxidative ethylene hydroarylation catalyzed by the rhodium precursor (^{Fl}DAB)Rh(TFA)(η^2 -C₂H₄) (^{Fl}DAB = *N,N'*-bis(pentafluorophenyl)-2,3-dimethyl-1,4-diaza-1,3-butadiene; TFA = trifluoroacetate) for the selective one-step production of styrene.⁵⁰ The complex converts benzene, ethylene, and Cu(II) carboxylate to styrene, Cu(I) carboxylate, and acetic acid with high selectivity and yields >95%. Turnover numbers >800 were demonstrated with catalyst stability up to 96 h. Aerobic catalysis, with and without *in situ* Cu(II) oxidant, was accomplished by coordination of the ligand 1,2-bis(*N*-7-azaindolyl)benzene (S-FP) to Rh.⁴⁸ Thus, the overall reaction is the conversion of benzene, olefin, and oxygen to alkenyl arene and water. Under optimized conditions, oxidative propylene hydrophenylation catalyzed by complex (S-FP)Rh(TFA)(η^2 -C₂H₄) gives >13,000 TOs of product.

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Scheme 2. General Catalytic Cycle for Transition-Metal-Catalyzed Olefin Hydroarylation Reaction through Aromatic C–H Activation and Olefin Insertion That Highlights Possible Advantages Compared to Traditional Acid-Catalyzed Processes (FG = Functional Group)



Palladium(II) has a similar electronic structure as Rh(I) and can also catalyze oxidative hydroarylation of olefins, but selectivity is often low, as undesired products can dominate. Fujiwara and co-workers reported styrene production using $\text{Pd}(\text{OAc})_2$ with AgOAc as the oxidant. This reaction produces a low yield (0.59 TOs) of styrene relative to the catalyst along with substantial amounts of stilbene and biphenyl.⁵² Periana and co-workers reported styrene production using $\text{Pd}(\text{OAc})_2$ with $\text{Cu}(\text{OAc})_2$ and O_2 as the terminal oxidant, but they observed significant vinyl acetate production (~ 2.5 times the amount of styrene produced).^{46,53} This observation is perhaps not surprising since Pd(II) is known to catalyze ethylene oxidation using CuCl_2 as oxidant in commercial processes.^{54–58} Sanford and co-workers reported that (3,5-dichloropyridyl) $\text{Pd}(\text{OAc})_2$ affords styrene from benzene and ethylene with 100% selectivity; however, the process suffers from low yields ($\sim 33\%$ relative to limiting reagent oxidant) and uses an expensive oxidant (PhCO_3^tBu) that cannot be regenerated aerobically.⁵⁹

In this work, we report an improved arene alkenylation process for the conversion of benzene and ethylene to styrene catalyzed by $\text{Pd}(\text{OAc})_2$ with the *in situ* air-recyclable oxidant $\text{Cu}(\text{OPiv})_2$ (OPiv = pivalate). The effects of olefin pressure, temperature, acid concentration, copper(II) loading, water, and ambient oxygen on the reactivity and selectivity have been investigated. Under optimized conditions, high selectivity for benzene vinylation with high efficiency for aerobic oxidant recycling have been achieved. We propose that the conversion of benzene and vinyl pivalate, formed from ethylene and $\text{Cu}(\text{OPiv})_2$, to styrene is central to the high selectivity for styrene formation. The Pd-catalyzed conversion of benzene and vinyl pivalate to styrene involves a metal-mediated C–O bond activation of the vinyl ester, and to our knowledge, it represents a new transformation.

RESULTS AND DISCUSSION

Oxidative Ethylene Hydrophenylation Catalyzed by Palladium(II) Acetate under Anaerobic Conditions. For all reported experiments, data are provided as the average of at

least three independent experiments with standard deviations given in parentheses. The use of $\text{Pd}(\text{OAc})_2$ as a catalyst precursor for oxidative ethylene hydrophenylation was investigated under various temperatures and ethylene pressures under anaerobic conditions (Figure 1). Under a nitrogen

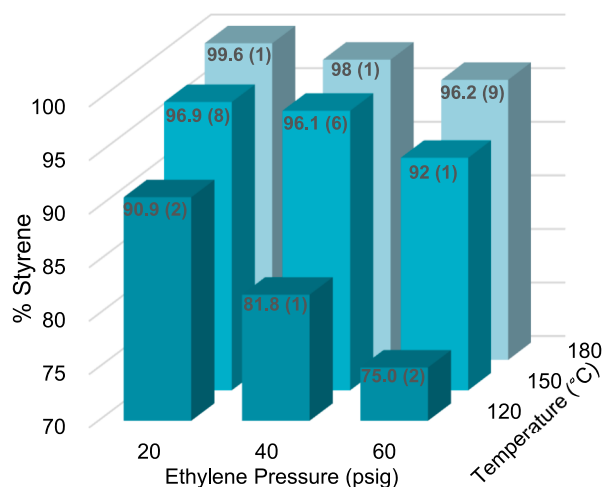
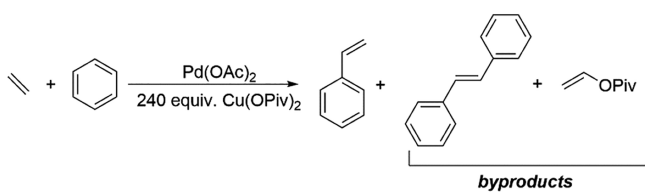


Figure 1. Selectivity for styrene production from oxidative ethylene hydrophenylation catalyzed by $\text{Pd}(\text{OAc})_2$ as a function of temperature and ethylene pressure. Conditions: 0.001 mol % of $\text{Pd}(\text{OAc})_2$ dissolved in 10 mL of benzene with HMB (hexamethylbenzene) as an internal standard, and 240 equiv (relative to Pd) of copper(II) pivalate are used. Percent styrene is the percentage of styrene versus vinyl pivalate production. The numbers in parentheses are standard deviations that are based on at least three independent experiments.

atmosphere, heating 10 mL of benzene solutions of $\text{Pd}(\text{OAc})_2$ (0.001 mol % relative to benzene) with 240 equiv of $\text{Cu}(\text{OPiv})_2$ at different temperatures (120–180 °C) and ethylene pressures (20–60 psig) affords styrene production. Two equivalents of $\text{Cu}(\text{OPiv})_2$ are required per equivalent of styrene, and thus, using 240 equiv of $\text{Cu}(\text{OPiv})_2$, the maximum theoretical turnover number for styrene production is 120 in the absence of *in situ* regeneration of $\text{Cu}(\text{OPiv})_2$. The catalytic reactions

Table 1. Ethylene Hydrophenylation under Anaerobic Conditions Using Pd(OAc)₂ as Catalyst Precursor and Cu(OPiv)₂ as the Oxidant


entry ^a	temperature (°C)	ethylene pressure (psig)	time ^b (hour)	styrene (TOs)	vinyl pivalate (TOs)	stilbene ^c (TOs)	selectivity (% styrene)
1	120	20	16	121(5)	14(1)	2(1)	88%
2	120	40	10	117(3)	25(3)	0.5(2)	82%
3	120	60	8	102.2(2)	34(1)	0.32(1)	77%
4	150	20	2	114(8)	3.6(5)	3.5(3)	94%
5	150	40	2	112(1)	4.5(5)	3.0(5)	94%
6	150	60	1	121(2)	10.9(6)	1.2(1)	91%
7	180	20	0.5	38(5)	0.2(1)	33(4)	51%
8	180	40	0.5	51(7)	1.0(3)	23(1)	67%
9	180	60	0.5	78(3)	2.5(2)	15(2)	84%

^aConditions: 0.001 mol % of Pd(OAc)₂ dissolved in 10 mL of benzene with HMB (hexamethylbenzene) as an internal standard, 240 equiv (relative to Pd) of copper(II) pivalate are used. ^bThe end point of reactions were determined by the color of the reaction mixture; the color change from blue to light brown indicates consumption of the Cu(II) oxidant (see Supporting Information). ^cStilbene indicates *trans*-stilbene. The numbers in parentheses are standard deviations that are based on at least three independent experiments.

produce substantial quantities of styrene, vinyl pivalate, and stilbene. Under optimized conditions at 150 °C, 94% selectivity for styrene is obtained (Table 1). Using higher reaction temperature and ethylene pressure requires less time for the reaction to reach completion, which is consistent with our observations for Rh-catalyzed processes.^{49,50,60} The selectivity for vinyl pivalate versus styrene varies with reaction conditions. As shown in Figure 1, the formation of styrene increases from 120 to 150 °C, but the production of styrene is reduced at 180 °C. There are two apparent issues at 180 °C: 1) the selectivity for stilbene is increased with ~10-fold more stilbene than observed at 150 °C, and 2) lower overall yields of all oxidation products are observed at 180 °C. At 150 °C and 20 psig of ethylene, a total of ~120 TOs are observed, while under the same condition at 180 °C (entry 7) ~70 TOs are observed. The amount of vinyl pivalate increases with increasing ethylene pressure. For example, entries 1, 2, and 3 are using the same reaction temperature (120 °C) and varying the pressure of ethylene in the reaction, and the reaction using the highest ethylene pressure (60 psig) produces 142% more vinyl pivalate than at 20 psig of ethylene. However, when higher temperature is applied to the reaction systems (e.g., entries 2, 5, and 8), the production of vinyl pivalate decreases by 96% with 25(3) TOs at 120 °C, 4.5(5) TOs at 150 °C, and only 1.0(3) at 180 °C.

The influence of olefin pressure on stilbene production was investigated at 180 °C where vinyl pivalate production is negligible. As shown in Figure 2, the production of stilbene is highly dependent on ethylene pressure. The ratio of styrene versus stilbene increases dramatically when temperature is increased from 120 to 180 °C. Since stilbene is likely produced by the oxidative hydroarylation of styrene formed *in situ*, the dissociation of styrene from the Pd catalyst might play a key role in determining the styrene/stilbene ratio. That is, as shown in Scheme 3, it is possible that dissociation of styrene via ligand exchange with ethylene is important to minimize stilbene formation since the ethylene/styrene exchange reaction likely depends on the concentration of ethylene. At higher temper-

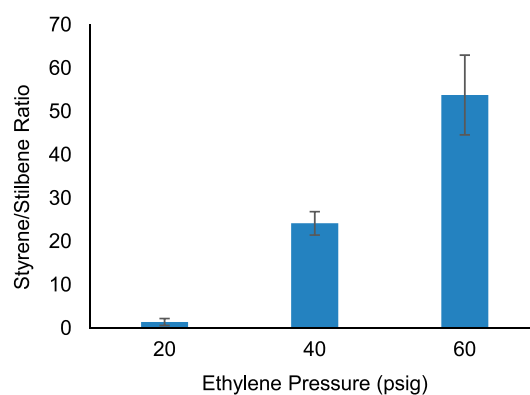
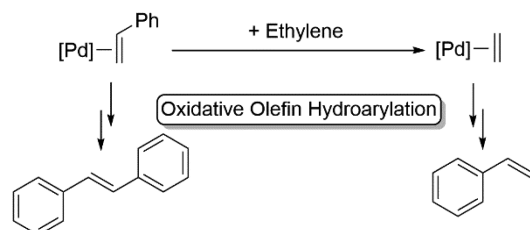


Figure 2. Ratio of styrene versus stilbene as a function of ethylene pressure at 180 °C. Conditions: 10 mL of benzene solution of 0.001 mol % Pd(OAc)₂, 240 equiv of Cu(OPiv)₂, 20, 40, or 60 psig at 180 °C for 30 min. Error bars represent standard deviations from at least three independent experiments.

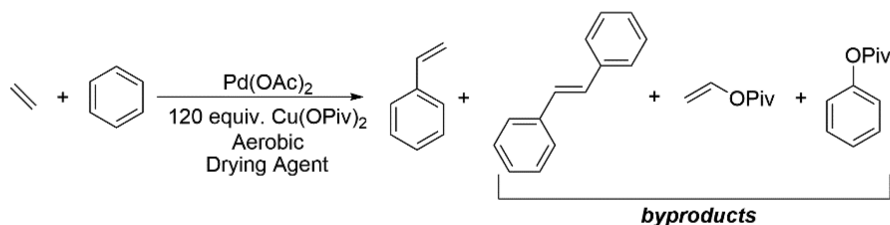
Scheme 3. Olefin Exchange Reaction between Ethylene and Styrene and Subsequent Olefin Hydroarylation Products^a



^aA higher ethylene concentration should facilitate styrene dissociation and reduce stilbene production.

ature and lower ethylene pressure, the concentration of ethylene decreases,⁶¹ which leads to more stilbene production.

Oxidative Ethylene Hydrophenylation Catalyzed by Palladium(II) Acetate under Aerobic Conditions. The conversion of CuX and HX to CuX₂ and water using air or

Table 2. Oxidative Ethylene Hydrophenylation under Aerobic Conditions Using Pd(OAc)₂ as Catalyst

entry	catalyst loading ^a (mol %)	oxygen source ^b	temperature (°C)	ethylene pressure (psig)	4 Å MS ^c (mg)	time (hour)	styrene (TOs)	vinyl pivalate (TOs)	stilbene (TOs)	phenyl pivalate (TOs)	selectivity (% styrene)
1	0.001	air	150	60	none	12	285(7)	32(1)	8.4(3)	4.3(1)	86%
2	0.001	oxygen	150	60	none	12	343(3)	37(3)	11.4(6)	5.4 ^d	86%
3	0.001	oxygen	150	60	300	12	567(27)	26.4(4)	112(5)	4(1)	80%
4	0.001	oxygen	120	60	300	48	282(18)	45(5)	7.0(3)	1.2(1)	84%
5	0.001	oxygen	180	40	300	12	52(8)	0	146(6)	74(4)	19%
6	0.0001	oxygen	150	60	300	24	2410(127)	98(6)	96(18)	156(15)	87%
7	0.0001	oxygen	180	60	300	12	356(16)	0	281(23)	815(79)	24%

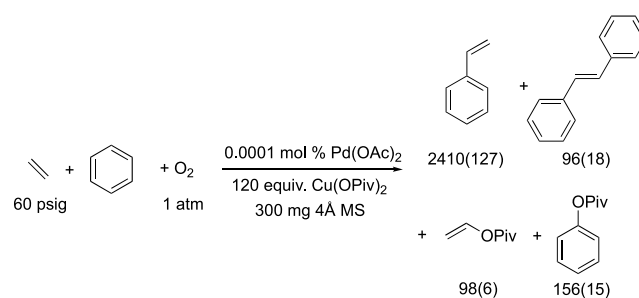
^aCatalyst loading is relative to benzene (10 mL). ^bThe reactions are purged by air or pure oxygen prior to the catalysis. ^c4 Å molecular sieves (powder) were dried at 200 °C under vacuum for 12 h prior to use. ^dThe standard deviation is lower than 0.1 TOs. The numbers in parentheses are standard deviations that are based on at least three independent experiments.

purified oxygen is efficient for many anions X (e.g., X = chloride, acetate, pivalate, etc.). This conversion forms the foundation of the commercial Hoechst–Wacker process for ethylene oxidation.^{55–58} As the Cu(II) oxidant can be efficiently recycled in air, the inclusion of air or pure dioxygen in the Pd-catalyzed conversion of benzene and ethylene to styrene with Cu(II) oxidant should enable higher product yields as the limiting reagent Cu(II) can be regenerated *in situ*.

Table 2 shows data for the oxidative ethylene hydrophenylation reaction under aerobic conditions. First, we compared the use of air and purified oxygen since the commercial ethylene oxidation process requires pure oxygen when used *in situ*.⁵⁸ More styrene production is observed when running catalysis under pure oxygen (Table 2, entries 1 and 2); however, catalyst deactivation still occurs after 48 h of reaction. One possible explanation of the catalyst deactivation is that water, which is generated from recycling the copper(II) oxidant, inhibits the formation of styrene (Figure S4). Molecular sieve is a commonly used additive in palladium mediated catalysis due to the ability to reduce water content as well as the possibility of limiting catalyst aggregation.^{62–65} To examine the hypothesis that water inhibits catalysis, we added molecular sieve (4 Å) and observed greater styrene production (entries 2 and 3). The catalysis was also performed at different temperatures, and the same selectivity trend is observed as with the anaerobic catalysis. At 120 °C, vinyl pivalate production is relatively high, while at 180 °C stilbene and phenyl pivalate are the major byproducts (entries 3, 4, and 5). The production of phenyl pivalate was observed as a minor byproduct for some conditions in our previously reported rhodium-catalyzed oxidative olefin hydroarylation.^{48–50} In our studies of Rh catalysis, we found that arene acetoxylation is likely mediated by CuX₂ (X = acetate, trimethyl acetate, 2-ethylhexanoate) and is a side reaction when temperature is ≥150 °C.

The effect of catalyst concentration on selectivity was also examined. When 0.0001 mol % catalyst (with respect to benzene) is used under optimized conditions, 2410 TOs of styrene are obtained with 87% selectivity after 24 h (Scheme 4). This lower catalyst loading of 0.0001 mol % results in reduced

Scheme 4. Oxidative Hydrophenylation of Ethylene under Optimized Aerobic Conditions after 24 h of Heating at 150 °C^a



^aTurnover numbers (TOs) are listed below products. Standard deviations, given in parentheses, are the result of at least three independent experiments.

stilbene production relative to styrene (Table 2, entry 6, styrene/stilbene = 24:1) compared to 0.001 mol % Pd loading (Table 2, entry 3, styrene/stilbene = 5:1), but the selectivity for vinyl pivalate is similar to approximately 20:1 ratio when using 0.001 mol % Pd vs approximately 26:1 for 0.0001 mol % loading. This observation consistent with our hypothesis (Scheme 3) that stilbene production is suppressed when the ethylene to styrene ratio is high.

The influence of catalyst loading on reaction rate was also examined. By heating 10 mL benzene solutions with different amounts of Pd(OAc)₂ with 60 psig of ethylene, 1 atm of pure oxygen, 300 mg of 4 Å molecular sieves, and 0.54 mM of Cu(OPiv)₂, we estimated the *k*_{obs} under six different catalyst loadings (0.001, 0.0025, 0.005, 0.01, 0.02, and 0.025 mol %) using the average TOF calculated from the 1 h of catalysis. Figure 3 shows a log–log plot of *k*_{obs} versus Pd concentration. A slope of 1.32(2) shows a reaction order between 1 and 1.5.

Thermal Decomposition of Palladium(II) Acetate under Catalytic Conditions. Samples of thermal decomposition of Pd(OAc)₂ with or without copper(II) oxidants are prepared accordingly. Heating 10 mL of a benzene solution of 0.05 mol % Pd(OAc)₂ under 40 psig of ethylene pressure with or

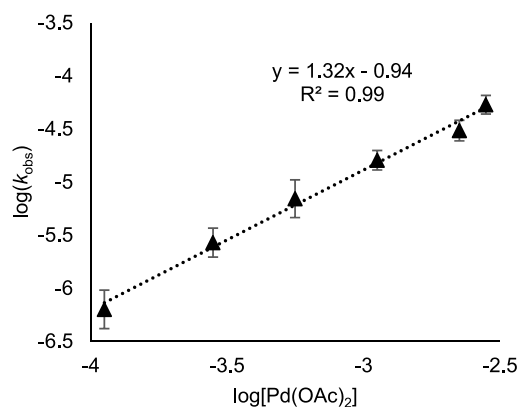
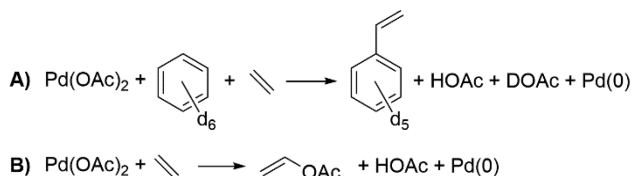


Figure 3. Log–log plot of the observed rate constant as a function of the concentration of Pd(OAc)₂ under aerobic conditions.

without 1 equiv of Cu(OPiv)₂, the reaction color changed from blue to colorless in 5 min for the catalysis with copper and from light yellow to gray for the reaction without copper. Under both conditions, a black precipitate formed. The reaction mixture was filtered, and the solid was washed with benzene several times. Scanning electron microscopy (SEM) analysis suggests that Pd(OAc)₂ is reduced to large spherical Pd particles with a size of ~300 μm (Figures S5 and S6). The identity of palladium is also confirmed by the energy-dispersive X-ray spectroscopy (EDS) (Figures S9 and S10).

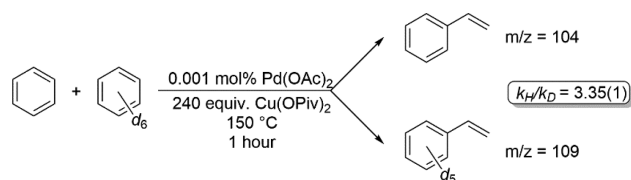
The decomposition of Pd(OAc)₂ was monitored by ¹H NMR spectroscopy. A thick-walled J-Young tube was charged with a benzene-*d*₆ solution of Pd(OAc)₂ and 40 psig of ethylene. Then the NMR tube was heated to 90 °C in oil bath. After 9 h, a palladium(0) mirror formed on the wall of the NMR tubes, and ¹H NMR spectroscopy revealed the formation of styrene-*d*₅, vinyl acetate, and free acetic acid (Figure S11). Scheme 5 outlines two overall processes that could lead to the decomposition of soluble Pd to Pd(s) that are consistent with our experimental observations.

Scheme 5. Two Proposed Pd(OAc)₂ Decomposition Processes That Produce Pd(0) and Acetic Acid: (A) Decomposition of Pd(OAc)₂ via Benzene C–H Activation; (B) Decomposition of Pd(OAc)₂ via Olefin C–H Activation



Kinetic Isotope Effect of the Palladium(II) Acetate-Catalyzed Oxidative Hydrophenylation of Ethylene. The kinetic isotope effect (KIE) of the palladium-catalyzed oxidative ethylene hydrophenylation reaction was measured for comparative rates in C₆H₆ and C₆D₆ using two methods (Scheme 6 and Figure 4). Catalysis was run at 150 °C using 1:1 molar ratio mixture of benzene and benzene-*d*₆ with a catalyst loading of 0.001 mol % of Pd(OAc)₂ and 240 equiv of Cu(OPiv)₂ under 40 psig of ethylene pressure (Scheme 6). After 1 h, the ratio of perprotio styrene [mass/charge ratio (*m/z*) = 104] to styrene-*d*₅ (*m/z* = 109) was determined by GC–MS and used to calculate KIE of 3.35(1).

Scheme 6. Kinetic Isotope Effect Measured Using 1:1 Ratio Mixture of Benzene and Benzene-*d*₆^a



^aAn observed KIE of 3.35(1) is obtained.

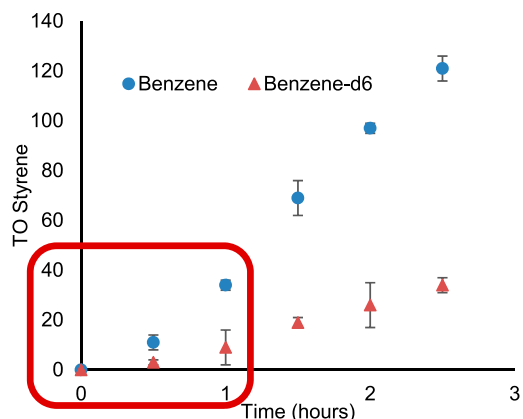


Figure 4. Plot of TOs of styrene and styrene-*d*₅ versus time for Pd(OAc)₂ catalyzed oxidative ethylene hydrophenylation reaction using benzene or benzene-*d*₆ as solvent. An induction period is observed for the first hour (in red). Conditions: 240 equiv of Cu(OPiv)₂ was added to a 10 mL benzene/benzene-*d*₆ solution of Pd(OAc)₂, the reactor was then pressurized by 40 psig of ethylene and heated to 150 °C.

Catalytic reactions were also performed separately in C₆H₆ or C₆D₆ at 150 °C with a catalyst loading of 0.001 mol % of Pd(OAc)₂ and 240 equiv of Cu(OPiv)₂ under 40 psig of ethylene pressure (Figure 4). The reaction solutions were analyzed by GC-FID to monitor TOs of styrene and styrene-*d*₅ every 30 min. Since we observed an apparent induction period during the first hour of the catalysis, the TOFs (TOFs = turnover frequencies) were determined from a linear fit of turnovers versus time for reactions between 1 and 3 h, during which time there is a linear fit (Figure 5). Using the slopes of TO vs time

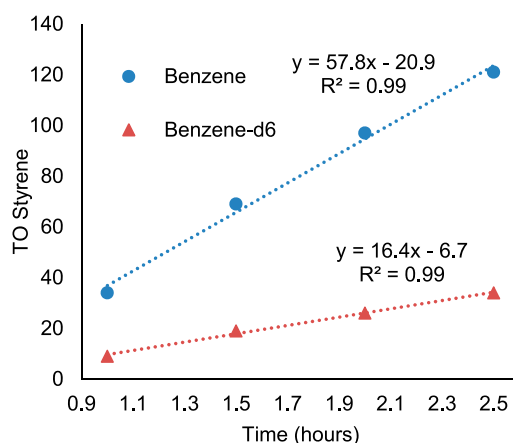
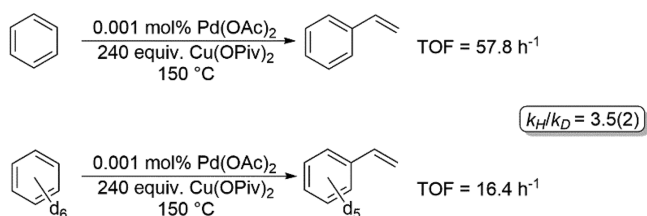


Figure 5. Linear fits of TOs of styrene and styrene-*d*₅ versus time for data between 1 and 3 h of reaction.

plots from reactions in C_6H_6 and C_6D_6 , a k_H/k_D of 3.5(2) was determined (Scheme 7). Thus, the KIEs calculated from the two

Scheme 7. Kinetic Isotope Effect Measured by Comparing the Rates of Catalysis in Benzene versus Benzene- d_6 after 2.5 h



independent methods, 3.35(1) and 3.5(2), are statistically identical. These KIEs are similar to reported KIEs from Crabtree and co-workers (4.1)⁶⁶ and Sanford and co-workers [4.5(4)]⁶⁷ in palladium catalyzed arene acetoxylation, and to those from Jones and co-workers (4.3 and 3.33)^{68,69} and our group [3.3(2)]⁶⁰ for similar d^8 Rh complex-catalyzed alkane isomerization and oxidative ethylene hydrophenylation. The observed primary KIE suggests that the palladium-catalyzed oxidative olefin hydroarylation undergoes a Pd-mediated C–H activation pathway and that the C–H activation step occurs after or during the rate limiting step.^{70,71}

Studies of Vinyl Ester Production and Consumption.

One major byproduct in palladium-acetate-catalyzed oxidative ethylene hydrophenylation using $Cu(OPiv)_2$ is the olefin oxidation product vinyl pivalate. We observed a significant decrease in the yield of vinyl pivalate when using higher reaction temperatures (≥ 150 °C) or lower ethylene pressures (≤ 40 psig, Figure 1). The influence of ethylene pressure could be explained by a likely first order dependence on ethylene concentration for the ethylene oxidation reaction to produce vinyl pivalate; however, the influence of reaction temperature was less clear.

We studied the ability of $Pd(OAc)_2$ to convert benzene and vinyl pivalate to styrene (Table 3). The conversion of vinyl pivalate and benzene to styrene is observed at ≥ 150 °C (Table 3, entries 1, 2, and 3). This process requires both the palladium catalyst and copper(II) oxidant (Table 3, entries 4, 5, and 6). This discovery helps to rationalize the higher styrene selectivity at higher reaction temperature (Figure 1, Table 2), as vinyl pivalate is rapidly converted to styrene.

In order to gain insight into this palladium-catalyzed ester consumption reaction, we studied other esters (Scheme 8). Only vinyl acetates are converted to the vinyl arene product. In

addition to the production of styrene and stilbene, the formation of vinyl pivalate is observed when vinyl acetate and copper(II) pivalate are present in reaction system. The ester exchange reaction is general, as indicated by the results shown in Table 4. For reactions of benzene using allyl acetate and methyl acrylate, only oxidative hydrophenylation of allyl acetate or methyl acrylate hydrophenylation are detected (see Figure S16). When the alkyl acetates ethyl acetate, *n*-propylacetate, and amyl acetate are used, no reaction was observed. These observations suggest that the conversion of ester and benzene to vinylbenzene requires a $C(sp^2)$ –O bond.

CONCLUSIONS

$Pd(OAc)_2$ -catalyzed oxidative ethylene hydrophenylation, which directly converts benzene, ethylene, and $Cu(II)$ oxidant to styrene, is shown to operate with high selectivity under optimized aerobic and anaerobic conditions. Our studies have revealed new insight into these reactions that led to conditions where >2400 TOs with $>85\%$ selectivity for styrene were achieved. Our conclusions include:

- (1) The identification of temperature-dependent vinyl ester conversion to alkenyl arene provides a strategy to reduce vinyl ester production. The conversion of vinyl ester and benzene to styrene occurs only at elevated temperatures and, to our knowledge, is a novel transformation.
- (2) Ethylene pressures and reaction temperatures play important roles for the ratio of vinyl pivalate to styrene. The production of vinyl pivalate increases with ethylene pressure. Importantly, the increased selectivity for styrene versus vinyl pivalate as a function of temperature is likely a result of a Pd-catalyzed conversion of vinyl pivalate and benzene to styrene.
- (3) The production of stilbene could not be avoided, but it can be limited by increasing the concentration of ethylene in the reaction mixture.
- (4) Catalysis under aerobic conditions gives higher catalytic TOs since $Cu(II)$ is regenerated *in situ*; however, the reaction rate is slower than catalysis under anaerobic conditions.

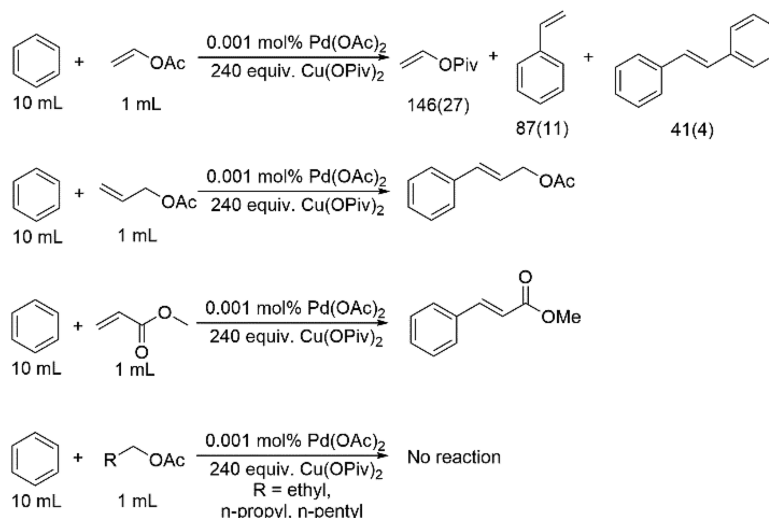
EXPERIMENTAL SECTION

General Considerations. Unless otherwise noted, all synthetic procedures were performed under anaerobic conditions in a nitrogen-filled glovebox or by using standard Schlenk techniques. Glovebox purity was maintained by periodic nitrogen purges and was monitored

Table 3. Conversion of Benzene and Vinyl Pivalate to Styrene Catalyzed by $Pd(OAc)_2$

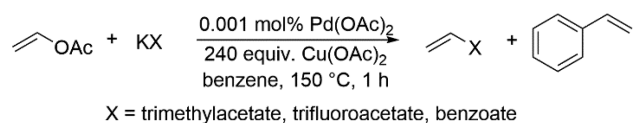
entry ^a	catalyst	oxidant	temperature (°C)	time (min)	consumption of vp ^b (TOs)	hydroarylation products ^c (TOs)
1	$Pd(OAc)_2$	$Cu(OPiv)_2$	120	300	0	0
2	$Pd(OAc)_2$	$Cu(OPiv)_2$	150	270	115(4)	120(7)
3	$Pd(OAc)_2$	$Cu(OPiv)_2$	180	30	126(7)	117(6)
4 ^d	$Pd(OAc)_2$	$Cu(OPiv)_2$	150	30	27(3)	19(6)
5	$Pd(OAc)_2$	NONE	150	300	0	0
6		$Cu(OPiv)_2$	150	300	0	0

^aConditions: 0.001 mol % of $Pd(OAc)_2$ dissolved in 10 mL of benzene with HMB (hexamethylbenzene) as an internal standard, 150 equiv of vinyl pivalate, 240 equiv of copper pivalate (if applicable). ^bvp = vinyl pivalate. ^cHydroarylation products include styrene, stilbene, and 1,1,2-triphenylethylene. ^d60 equiv of copper(II) pivalate is used in entry 4.

Scheme 8. Summary of Attempted Reactions with Various Acetates and Benzene^a

^aConditions: 0.001 mol % of Pd(OAc)₂, 240 equiv of Cu(OPiv)₂, 1 mL of corresponding ester, 150 °C, 1 h. Products were analyzed by GC/FID and GC/MS.

Table 4. Vinyl Ester Metathesis Using Potassium Salts as the Acetate Source



entry	X	production of vinyl-X (TOs)	styrene (TOs)
1	trimethyl acetate	18(1)	10(3)
2	trifluoroacetate	21(4)	11(1)
3	benzoate	9(1)	11(3)

by an oxygen analyzer ($O_2 < 15$ ppm for all reactions). Benzene was purified by passage through a column of activated alumina. ¹H NMR spectra were recorded on a Varian 600 spectrometer. ¹H NMR spectra are referenced against residual proton signals (¹H NMR) of the deuterated solvents. GC/MS was performed using a Shimadzu GCMS-QP2010 Plus system with a 30 m x 0.25 mm RTX-Qbond column with 8 μm thickness using electron impact ionization. GC/FID was performed using a Shimadzu GC-2014 system with a 30 m x 90.25 mm HP5 column with 0.25 μm film thickness. Styrene, vinyl pivalate, phenyl pivalate, biphenyl, and stilbene production was quantified using linear regression analysis of gas chromatograms of standard samples of authentic product. The slope, correlation coefficient, and response factor of the regression lines were 2.59, 0.99, and 2.54 for vinyl pivalate, 1.78, 0.99, and 1.72 for styrene, 1.53, 0.99, and 1.50 for phenyl pivalate, 1.07, 0.99, and 1.03 for biphenyl, and 0.83, 0.99, and 0.80 for stilbene, respectively. SEM images were taken from FEI Quanta 650 with energy dispersive X-ray spectroscopy (EDS). High tension for imaging was 10 kV, and spot size was 2.0–3.0. For EDS, the applied potential was still 10 kV, but the spot size was larger, 4.0. Copper(II) pivalate was synthesized according to a published procedure.⁷² All other reagents were used as received from commercial sources. Purity assessment of palladium acetate could be found in the [Supporting Information](#).

Catalytic Oxidative Ethylene Hydrophenylation under Anaerobic Conditions. A representative catalytic reaction under anaerobic condition is described. A stock solution containing Pd(OAc)₂ (0.063 g, 0.028 mmol), HMB (hexamethylbenzene) (0.091 g, 0.56 mmol), and benzene (250 mL) was prepared in a volumetric flask. Thick-walled Fisher–Porter reactors were charged with stock solution (10 mL) and Cu(OPiv)₂ (240 equiv relative to Pd(OAc)₂). The vessels were sealed, pressurized with ethylene, and

subsequently stirred and heated in oil baths. The reactions were sampled after all the copper was consumed, as indicated by a change in the color of the reaction from blue to colorless. Aliquots of the reaction mixture were analyzed by GC/FID using relative peak areas versus the internal standard.

Catalytic Oxidative Ethylene Hydrophenylation under Aerobic Conditions. A representative catalytic reaction under aerobic condition is described. A stock solution containing Pd(OAc)₂ (0.063 g, 0.028 mmol), HMB (hexamethylbenzene) (0.091 g, 0.56 mmol), and benzene (250 mL) was prepared in a volumetric flask. Thick-walled Fisher–Porter reactors were charged with stock solution (10 mL), Cu(OPiv)₂ (240 equiv relative to Pd(OAc)₂), and 300 mg of drying agent 4 Å molecular sieves (molecular sieves (powder) were dried at 200 °C under vacuum for at least 12 h prior to use). The vessels were sealed, purged by air/O₂ through a needle for 2 min and pressurized with different ethylene pressures, and subsequently stirred and heated different temperatures. The reactions were sampled after all the copper was consumed as indicated by a change in the color of the reaction from blue to brown. Aliquots of the reaction mixture were analyzed by GC/FID using relative peak areas versus the internal standard.

Scanning Electron Microscope (SEM) and Energy-dispersive X-ray Spectroscopy (EDS) Studies of Pd(OAc)₂ Decomposition under Catalytic Conditions: Sample Preparation. A stock solution containing 0.001 mol % Pd(OAc)₂ and benzene (100 mL) was prepared in a volumetric flask. Thick-walled Fisher–Porter reactors were charged with stock solution (10 mL) and Cu(OPiv)₂ (0 and 1 equiv relative to Pd(OAc)₂). The vessels were sealed and pressurized with 60 psig of ethylene. After heating in oil bath at 150 °C for 1 h, the reactor was cooled and sonicated for 5 min for SEM sample preparation. The well-dispersed ink was added dropwise onto an aluminum-foil-covered SEM sample stage.

¹H NMR Spectroscopy Studies of Thermal Deactivation of Pd(OAc)₂ under Catalytic Conditions. A 10 mL stock solution containing 0.57 mmol of Pd(OAc)₂ and 10 mL of C₆D₆ was prepared in volumetric flask. A thick-wall J-Young NMR tube was charged with 0.5 mL of the stock solution and sealed. Then, the tube was pressurized with 40 psig of ethylene.

Oxidative Hydrophenylation of Ethylene as a Function of Pd(OAc)₂. Six separate stock solutions were prepared in 10 mL volumetric flasks, each containing Pd(OAc)₂ (0.028, 0.022, 0.011, 0.0056, 0.0028, or 0.0011 mM), hexamethylbenzene (10 equiv relative to Pd(OAc)₂), and benzene (10 mL). Fisher–Porter reactors (three reactors per concentration level) were charged with stock solution (10 mL), copper(II) pivalate (0.54 mM), and 300 mg of 4 Å molecular sieves and purged with pure dioxygen for 2 min. The vessels were

sealed, pressurized with ethylene (60 psig), and stirred while heating in an oil bath at 150 °C. The reactions were sampled after 1 h. Aliquots of the reaction mixture were analyzed by GC/FID using relative peak area vs an internal standard (hexamethylbenzene).

Kinetic Isotope Effect (KIE) Experiment of Pd(II)-Catalyzed Oxidative Ethylene Hydrophenylation. *General Procedure for KIE Experiments (A):* Using a 1:1 Molar Mixture of C₆H₆ and C₆D₆. A stock solution containing Pd(OAc)₂ (0.112 mM) and a 1:1 molar mixture of C₆H₆ and C₆D₆ (100 mL) was prepared in a volumetric flask. Fisher–Porter reactors were charged with stock solution (10 mL) and Cu(OPiv)₂ (240 equiv relative to Pd(OAc)₂). The vessels were sealed, pressurized with ethylene (50 psig), and stirred while heated in an oil bath to 150 °C. The reactions were sampled at 1, 2, and 3 h. At each time point the reactors were cooled to room temperature, sampled, recharged with ethylene, and reheated. Aliquots of the reaction mixture were analyzed by GC/MS. KIEs were determined by examining the ratio of styrene (*m/z* = 104) to styrene-*d*₅ (*m/z* = 109) in the mass spectrum, accounting for the initial isotopic distribution and natural abundance. No change in the isotopic distribution for benzene was observed over the course of the reaction, and the observed isotopic distribution of product was consistent with the initial distribution. No *d*_{6–8} products were observed, except those predicted by the natural abundance of deuterium in ethylene.

General Procedure for KIE Experiments (B): Oxidative Hydrophenylation of Ethylene Using Pd(OAc)₂ in C₆D₆. A stock solution containing Pd(OAc)₂ (0.112 mM), hexamethylbenzene (20 equiv relative to Pd(OAc)₂), and C₆D₆ (50 mL) was prepared in a volumetric flask. Fisher–Porter reactors were charged with stock solution (20 mL) and copper(II) pivalate (26.9 mM). The vessels were sealed, pressurized with ethylene (50 psig), and stirred while heating in an oil bath to 150 °C. The reactions were sampled every 30 min for 3 h. At each time point the reactors were cooled to room temperature, sampled, recharged with ethylene, and reheated. Aliquots of the reaction mixture were analyzed by GC/FID using relative peak area vs an internal standard (hexamethylbenzene).

Conversion of Benzene and Vinyl Ester to Alkenyl Arene Catalyzed by Pd(OAc)₂. A representative catalytic reaction of vinyl ester consumption is described. A stock solution containing 0.001 mol % of Pd(OAc)₂, internal standard (HMB), and benzene (250 mL) was prepared in a volumetric flask. Thick-walled Fisher–Porter reactors were charged with stock solution (10 mL), Cu(OPiv)₂ (240 equiv relative to Pd(OAc)₂), and 1 mL of ester substrate. The vessels were sealed, pressurized with 70 psig of N₂, and subsequently stirred and heated in oil baths.

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.9b00349.

Detailed experimental procedures; representative gas chromatogram; scanning electron microscope; energy-dispersive X-ray spectroscopy (PDF)

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Notes

The authors declare no competing financial interest.

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