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FULL PAPER

Palladium-catalyzed Aerobic Synthesis of Terminal Acetals from Vinylarenes Assisted by π-Acceptor Ligands

Satoko Matsumura,[a] Ruriko Sato,[a] Sonoe Nakaoka,[a] Wakana Yokotani,[a] Yuka Murakami,[a] Yasutaka Kataoka,[a] and Yasuyuki Ura*[a]

Abstract: Terminal acetals were synthesized from various vinylarenes and 1,2- or 1,3-diols using a simple $PdCl_2(MeCN)_2$/methoxy-*p*-benzoquinone (MeOBQ)/CuCl catalyst system and 1 atm of O_2 under mild reaction conditions, via anti-Markovnikov nucleophilic attack of an oxygen nucleophile to the coordinated vinylarenes. Cyclic α,β-unsaturated carbonyl compounds such as MeOBQ and *N*-phenylmaleimide were especially effective as additives to afford the higher yields of desired terminal acetals. Kinetic experiments indicated that the added MeOBQ operates as a π-acceptor ligand for palladium to accelerate the reaction, and that dissociation of a chloride ion from palladium precedes the rate determining step.

Introduction

Direct synthesis of acetals from alkenes and alcohols is a useful method which formally involves two steps, i.e. oxidation of alkenes to aldehydes or ketones and their protection.[1] Although Markovnikov selectivity is mainly observed in the Pd-catalyzed intramolecular acetalization and hemiacetalization of alkenols,[2-12] intermolecular acetalization of alkenes having an electron-withdrawing group[13-15] or a directing group[16, 17] proceeds selectively in an anti-Markovnikov manner to give terminal acetals. As for vinylarenes, internal acetals are formed by using a $PdCl_2$(sparteine)/$CuCl_2$ catalyst system under O_2,[18] while terminal acetals are obtained by other Pd[13, 19, 20], Fe[21], and iodine[22] catalyst systems (Scheme 1). However, a drawback of most of the latter reactions is that they require stoichiometric amount of oxidants other than O_2 such as CuCl (combined with O_2),[13] *p*-benzoquinone (BQ),[19] $PhI(OAc)_2$,[21] and oxone.[22] Although an aerobic anti-Markovnikov acetalization of styrene using a $PdCl_2(MeCN)_2$/CuCl catalyst system has also been reported, only one example (with 1,3-propanediol) was shown in the literature.[20] Considering that the formation of arylacetaldehydes from vinylarenes (such as anti-Markovnikov Wacker-type oxidation[23-29] and Fe[30, 31] or Ru[32, 33]-catalyzed epoxidation-isomerization) is still rare, the accessible aerobic synthesis of the corresponding terminal acetals can be an attractive alternative.[34]

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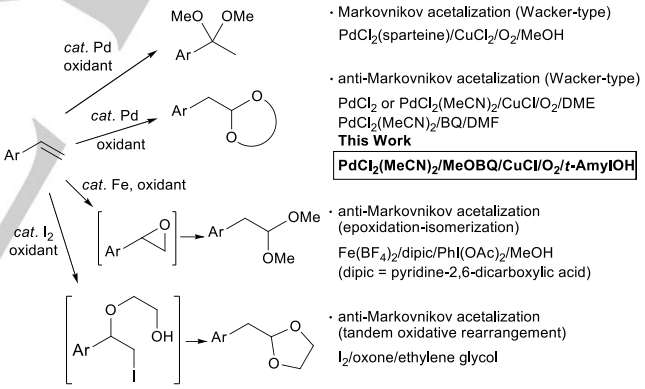
Recently, we have developed a maleimide-assisted aerobic anti-Markovnikov Wacker-type oxidation of vinylarenes to arylacetaldehydes.[29] In this reaction, a bulky alcohol, i.e. *t*-AmylOH used as a solvent is responsible for the regioselectivity, and electron-deficient alkenes such as maleimide used as an additive would operate as a π-acceptor ligand to enhance the catalytic activity and stabilize Pd(0) intermediates. We expected that this approach can also be applicable to the related reaction, i.e. acetalization, and thus developed a Pd-catalyzed aerobic synthesis of terminal acetals from various vinylarenes and diols, under milder reaction conditions than those for previously reported Pd/Cu-catalyzed acetalization (Scheme 1).[20] Kinetic experiments indicated that an electron-deficient alkene (methoxy-*p*-benzoquinone, MeOBQ) operates as a ligand to accelerate the reaction efficiently.

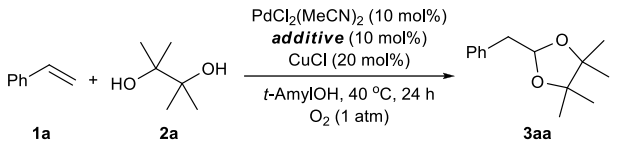


Scheme 1. Catalytic Markovnikov and anti-Markovnikov acetalization of vinylarenes.

Results and Discussion

Styrene (**1a**) and pinacol (**2a**) were used as initial substrates By using $PdCl_2(MeCN)_2$ (10 mol%) and CuCl (20 mol%) as catalysts and *t*-AmylOH as a solvent, the reaction proceeded at 40 °C under 1 atm of O_2 to form the desired terminal acetal **3aa** in 42% yield (Table 1, entry 1). Effects of a catalytic amount (10 mol%) of additives were then examined. As mentioned above, electron-deficient, π-acidic compounds were mainly tested. BQ afforded a higher yield of the product (entry 2). Among other substituted *p*-quinones, mono-substituted *p*-quinones, i.e. MeBQ and MeOBQ gave better yields of **3aa** (65% and 69% yields, respectively, entries 3 and 9). On the other hand, relatively bulky,

Table 1. Effects of additives on the synthesis of terminal acetals from vinylarenes using O_2.[a]



1a 2a 3aa

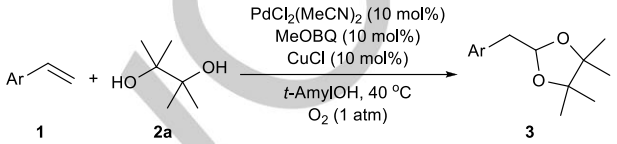
Entry	Additive	Conv. of **1a** (%)[b]	Yield of **3aa** (%)[b]
1	none	95	42
2	BQ[c]	98	54
3	MeBQ	92	65
4	2,5-Me_2BQ	97	57
5	2,6-Me_2BQ	90	41
6	Me_4BQ	82	39
7	^{t}BuBQ	94	45
8	2,6-$^t Bu_2$BQ	87	39
9	MeOBQ	100	69
10[d]	MeOBQ	97	84
11[e]	MeOBQ	92	78
12	2,5-$(MeO)_2$BQ	97	31
13	2,5-Ph_2BQ	95	33
14	maleic anhydride	100	55
15	maleimide	100	57
16	*N*-methylmaleimide	100	63
17	*N*-phenylmaleimide	98	69
18	methyl acrylate	93	48
19	methyl vinyl ketone	99	48
20	dimethyl maleate	97	35
21	$P(OPh)_3$	19	10
22	PPh_3	0	0
23	NEt_3	0	0
24	pyridine	92	35

[a] Reaction conditions: **1a** (0.50 mmol), **2a** (1.50 mmol), $PdCl_2(MeCN)_2$ (0.050 mmol), additive (0.050 mmol), CuCl (0.10 mmol), *t*-AmylOH (2.0 mL), 40 °C, O_2 (1 atm), 24 h. [b] Determined by ^{1}H NMR. [c] BQ = *p*-benzoquinone. [d] 10 mol% of CuCl (0.050 mmol) was used. [e] 5 mol% of CuCl (0.025 mmol) was used.

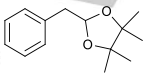
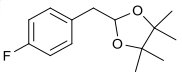
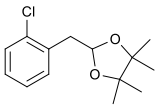
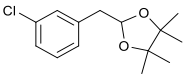
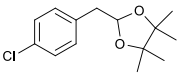
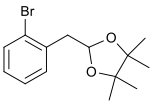
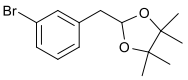
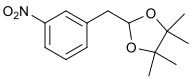
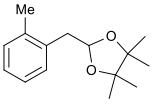
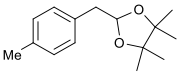
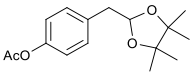
di- and tetra-substituted *p*-quinones were ineffective (entries 5–8) or decreased the yield (entries 12 and 13) except for 2,5-Me_2BQ (entry 4). Maleic anhydride and maleimides, which were most effective for the aerobic anti-Markovnikov Wacker-type oxidation of vinylarenes to arylacetaldehydes,[29] were also appropriate for the present acetalization (entries 14–17). Among them, *N*-phenylmaleimide gave a result comparable to MeOBQ (entry 17). Other α,β-unsaturated carbonyl compounds were inefficient (entries 18–20). Although phosphorus and nitrogen ligands were also examined, the results were poor in all cases (entries 21–24). The effect of the amount of CuCl was also examined using MeOBQ as an additive (entries 9–11), and 10 mol% was found to be the best (84% yield, entry 10). In these reactions shown in Table 1, small amounts of three other byproducts were also observed, i.e. benzaldehyde acetal (**4aa**), phenylacetaldehyde (**5a**), and benzaldehyde (**6a**), in 10–20% total yield in general.[35] The formation of **5a** can occur via the hydrolysis of **3aa** or alkenyl ether intermediates (vide infra) by in-situ generated H_2O. Further aerobic oxidation of **5a** would afford **6a**,[29] which reacts with **2a** to give **4aa**.

The optimized reaction conditions were then applied to various vinylarenes (Table 2). In some cases, prior to isolation, the reaction mixture was treated with aqueous HCl to

Table 2. Scope of vinylarenes for the synthesis of terminal acetals from vinylarenes using O_2.[a]



1 2a 3

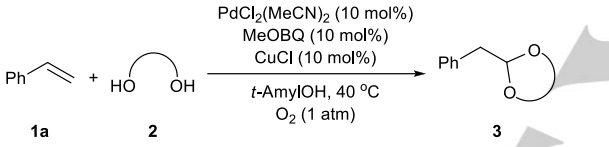
Entry	Product		Time (h)	Yield of **3** (%)[b]
1		**3aa**	24	84 (72)
2		**3ba**	24	62 (55)
3		**3ca**	30	67 (59)
4		**3da**	30	70 (56)
5		**3ea**	24	62 (61)
6		**3fa**	33	67 (31)
7		**3ga**	27	72 (57)
8		**3ha**	27	65 (54)
9		**3ia**	32	80 (61)
10		**3ja**	24	63 (51)
11		**3ka**	24	67 (40)

[a] Reaction conditions: **1** (1.0 mmol), **2a** (3.0 mmol), $PdCl_2(MeCN)_2$ (0.10 mmol), MeOBQ (0.10 mmol), CuCl (0.10 mmol), *t*-AmylOH (4.0 mL), 40 °C, O_2 (1 atm), 24–36 h. [b] Determined by ^{1}H NMR. Isolated yields are shown in parentheses.

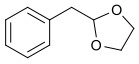
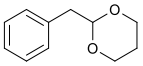
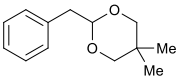
preferentially deprotect small amounts of the byproducts, i.e. benzaldehyde acetals **4**, for better separation by column chromatography.[35] Most styrenes with an electron-withdrawing or donating group afforded good yields of corresponding terminal acetals **3**. Somewhat longer reaction times were required for 2-substituted styrenes (entries 3, 6, and 9). Although 2- and 4-methoxystyrenes were also examined, less than 5% yields of corresponding terminal acetals were observed along with the formation of 2- or 4-methoxyphenylacetaldehyde (13%, 10%) and 2- or 4-methoxybenzaldehyde (16%, 11%), in spite of relatively high conversions of the substrates (76% after 96 h for 2-methoxystyrene and 74% after 32 h for 4-methoxystyrene). In the case of 2-vinylnaphthalene, although 79% of the substrate was converted after 24 h, only 10% of the desired acetal was obtained, with 16% of 2-naphthalenecarboxaldehyde.

The scope of diols was also examined (Table 3).[35] Ethylene glycol regioselectively afforded a low yield of **3ab** (entry 1). This regioselectivity contrasts to the reaction of styrene with ethylene glycol using a $PdCl_2(MeCN)_2$/BQ/DMF system that afforded a mixture of terminal and internal acetals in an almost 1:1 ratio.[19] 1,3-Propanediol gave a better yield of **3ac** (entry 2). 2,2-Dimethyl-1,3-propanediol was also applicable (entry 3).

Table 3. Scope of diols for the synthesis of terminal acetals from vinylarenes using O_2.[a]



1a 2 3

Entry	Product		Time (h)	Yield of **3** (%)[b]
1		**3ab**	28	48 (24)
2		**3ac**	80	86 (49)
3		**3ad**	72	73 (42)

[a] Reaction conditions: **1a** (1.0 mmol), **2** (3.0 mmol), $PdCl_2(MeCN)_2$ (0.10 mmol), MeOBQ (0.10 mmol), CuCl (0.10 mmol), *t*-AmylOH (4.0 mL), 40 °C, O_2 (1 atm), 28–80 h. [b] Determined by ^{1}H NMR. Isolated yields are shown in parentheses.

To shed light on the reaction mechanism, kinetic experiments were performed. Initial rates (v_0) for the formation of **3aa** were measured by ^{1}H NMR under various initial concentrations of **1a**, **2a**, $PdCl_2(MeCN)_2$, *n*-Bu_4NCl (used as a Cl^- source), and MeOBQ (Figure 1a–e). The changes in $[\mathbf{1a}]_0$ appeared to slightly affect v_0 at higher concentrations (52–320 mM) than $[PdCl_2(MeCN)_2]_0$ (26 mM) (Figure 1a), and the changes in $[\mathbf{2a}]_0$ hardly influenced v_0 (Figure 1b). On the other hand, the changes in $[PdCl_2(MeCN)_2]_0$ and $[n\text{-}Bu_4NCl]_0$ influenced the rates distinctly (Figure 1c and 1d), and the reaction orders were estimated to be 1 and -1, respectively. In the case of MeOBQ, v_0 increased in proportion to $[MeOBQ]_0$ when $[MeOBQ]_0$ was below $[PdCl_2(MeCN)_2]_0$ (26 mM), and became almost constant when

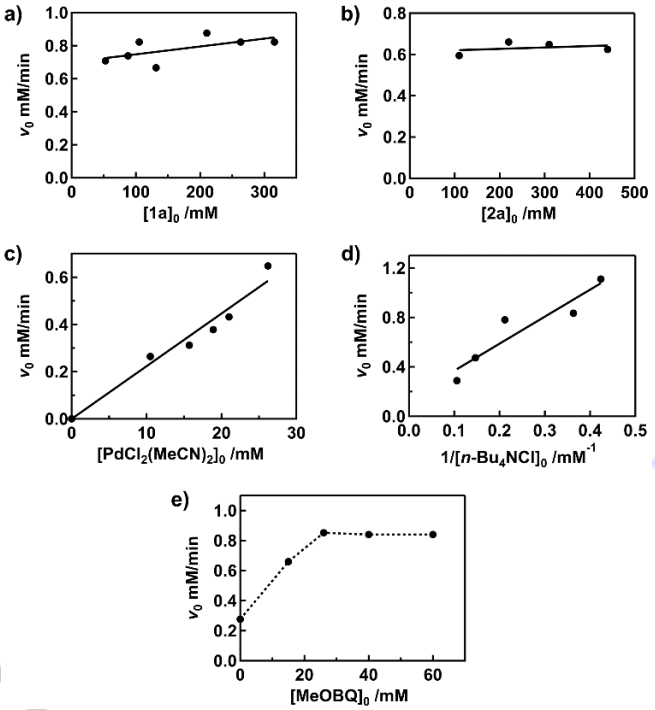
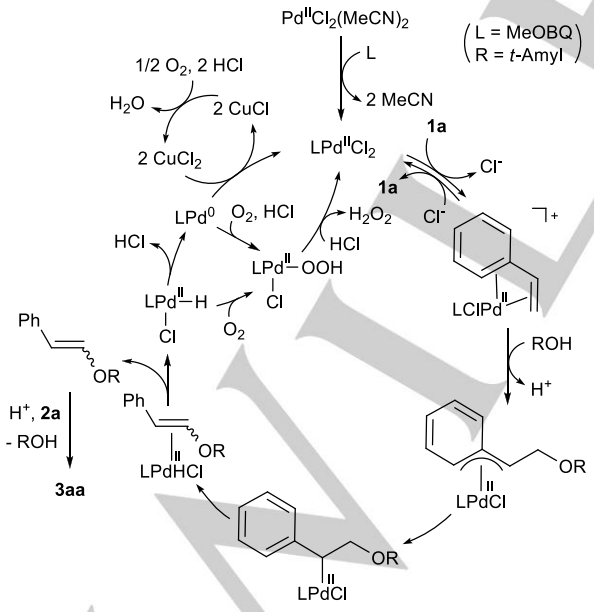


Figure 1. The effects of initial concentrations of (a) **1a**, (b) **2a**, (c) $PdCl_2(MeCN)_2$, (d) *n*-Bu_4NCl, and (e) MeOBQ, on the initial rates (v_0) for the formation of **3aa**. Reaction conditions: **1a** (52–320 mM for a; 100 mM for b–e), **2a** (310 mM for a, c–e; 110–460 mM for b), $PdCl_2(MeCN)_2$ (26 mM for a–b, d–e; 10–26 mM for c), MeOBQ (21 mM for a–d; 0–60 mM for e), CuCl (21 mM for a–c, e), *n*-Bu_4NCl (2.4–9.4 mM for d), *t*-AmylOH (0.15 mL for a, d–e; 0.35 mL for b–c), $CDCl_3$ (0.95 mL for a, d–e; 0.75 mL for b–c), 40 °C, O_2 (1 atm).

$[MeOBQ]_0$ was equal to or higher than $[PdCl_2(MeCN)_2]_0$ (Figure 1e). This result indicates that one molecule of MeOBQ would operate as a ligand for Pd to accelerate the reaction, and that an excess amount of MeOBQ does not interfere.

Based on the results of kinetic experiments, a possible mechanism is proposed in Scheme 2. The $LPdCl_2$ species (L = MeOBQ) is formed from $PdCl_2(MeCN)_2$ by ligand exchange. Dissociation of Cl^- and coordination of **1a** afford $[LPdCl(\eta^4\text{-}\mathbf{1a})]^+$. The coordination of **1a** to $[LPdCl]^+$ would be in pre-equilibrium, which can explain the result shown in Figure 1a.[36] Anti-Markovnikov nucleophilic attack of *t*-AmylOH to the coordinated **1a** and deprotonation forms a π-benzyl intermediate. If diols **2** attack the coordinated **1a** instead of *t*-AmylOH, the formation of internal acetals would also be expected when primary diols such as ethylene glycol, 1,3-propanediol, and 2,2-dimethyl-1,3-propanediol are used, due to less steric hindrance between the phenyl group in **1a** and the diols, according to our previous study.[19] However, even these cases, only the terminal acetals were observed and no internal acetals were detected as shown in Table 3. These results can be rationalized by the regioselective nucleophilic attack of the bulky *t*-AmylOH onto the terminal carbon of the coordinated **1a** rather than the attack of the diols. After isomerization from the π-benzyl intermediate to a σ-benzyl intermediate, β-hydrogen elimination results in alkenyl ethers and a LPdHCl species. The alkenyl ethers are converted to **3aa** in the

presence of H^+ and **2a**. HCl dissociates from LPdHCl to give LPd(0), which is reoxidized by $CuCl_2$ to reproduce $LPdCl_2$. Alternatively, insertion of O_2 into the Pd-H bond of LPdHCl or reaction of LPd(0) with O_2 and HCl may proceed to afford a PdOOH species,[37-42] and subsequent protonolysis by HCl also gives $LPdCl_2$. These pathways do not require the aid of a Cu salt. When the reaction of **1a** with **2a** was performed in the absence of CuCl (the reaction conditions shown in Table 2 without CuCl), 98% of **1a** was converted and 47% of **3aa** was formed after 24 h, indicating that the pathways involving the PdOOH species are also likely to reproduce $LPdCl_2$. The key roles of the π-acceptor ligands such as MeOBQ, would be acceleration of the steps for the nucleophilic attack of *t*-AmylOH to the coordinated **1a** and for the reduction from Pd(II) to Pd(0), as well as stabilization of the in-situ generated electron-rich Pd(0) species to suppress the decomposition to Pd black, similar to those in the maleimide-assisted aerobic anti-Markovnikov Wacker-type oxidation of vinylarenes.[29] The Eyring plot for the reaction of **1a** with **2a** afforded the activation parameters, $\Delta H^{\ddagger} = 8.7 \pm 0.8$ kcal mol^{-1} and $\Delta S^{\ddagger} = -49 \pm 3$ cal mol^{-1} K^{-1}, respectively.[43] The large negative $\Delta S^{\ddagger}$ value indicates that the rate determining step would be the nucleophilic attack of *t*-AmylOH to the coordinated **1a**, rather than the other steps such as the reduction from Pd(II) to Pd(0). Although the coordination of a π-acceptor ligand to Pd(II) species is not as efficient as to Pd(0) species because of the weak π-back donation, there are still several reported examples such as Pd(II)-maleic anhydride complexes characterized by X-ray analysis.[44, 45] Evidence of the coordination of BQ to Pd(II) in solution has been provided by an NMR study.[46] Moreover, *p*-quinones have been known to promote various steps in Pd-catalyzed reactions such as coordination of alkenes, nucleophilic addition, and reductive elimination, by coordinating to Pd(II).[47]



Scheme 2. A proposed mechanism.

Conclusions

Palladium-catalyzed synthesis of terminal acetals from various vinylarenes and 1,2- or 1,3-diols under 1 atm of O_2 and mild reaction conditions has been developed. Cyclic α,β-unsaturated carbonyl compounds such as *p*-quinones, maleic anhydride, and maleimides were effective as additives to afford the higher yields of desired terminal acetals. Among them, MeOBQ and *N*-phenylmaleimide were the best. Kinetic experiments indicated that the added MeOBQ operates as a π-acceptor ligand for palladium to accelerate the reaction, and that dissociation of a chloride ion from palladium precedes the rate determining step. The key roles of the π-acceptor ligands would be acceleration of the steps for the nucleophilic attack of *t*-AmylOH to the coordinated vinylarenes and for the reduction from Pd(II) to Pd(0), as well as stabilization of the in-situ generated electron-rich Pd(0) species to suppress the decomposition to Pd black. We believe that this catalyst system using cyclic α,β-unsaturated carbonyl compounds as ligands can also be applied to other reactions related to Wacker-type oxidation to enhance the catalytic activity.

Experimental Section

General Information

Unless otherwise indicated, all reactions were performed under an oxygen atmosphere (1 atm). $PdCl_2(MeCN)_2$[48] was prepared as described in the literature. *t*-AmylOH was purchased from Wako Pure Chemical Industries and Tokyo Chemical Industry Co. Ltd. and was degassed by carrying out three freeze-pump-thaw cycles. Other chemicals were also commercially available and were used without further purification. Flash column chromatography was performed using silica gel SILICYCLE SiliaFlash F60 (40–63 μm, 230–400 mesh). NMR spectra were recorded on a Bruker AV-300N (300 MHz (^{1}H), 75 MHz (^{13}C), 282 MHz (^{19}F)) spectrometer. Chemical shift values (δ) were expressed relative to $SiMe_4$ for ^{1}H and ^{13}C NMR. CF_3CO_2H was used as an external standard for ^{19}F NMR. High-resolution mass spectra were recorded on a JEOL JMS-T100LC spectrometer (ESI-TOF MS) with positive ionization mode.

Synthesis of Terminal Acetals 3

2-(Phenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3aa): To a reaction vessel, CuCl (10.0 mg, 0.10 mmol), $PdCl_2(MeCN)_2$ (25.9 mg, 0.10 mmol), MeOBQ (13.8 mg, 0.10 mmol), and pinacol (355 mg, 3.0 mmol) were added, and O_2 was purged. To the mixture, *t*-AmylOH (4 mL) and styrene (115 μL, 1.0 mmol) were added and the reaction mixture was stirred at 40 °C for 24 h. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 2.4 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 4 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3aa** as a colorless oil (159 mg, 0.72 mmol, 72% yield). The spectral data for **3aa** were in accordance with those reported in the literature.[19]

2-(*p*-Fluorophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ba): The reaction was performed in a similar manner as **3aa**. After cooling to

room temperature, the solvent and volatile materials were evaporated. To the residue, 3 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 4 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3ba** as a colorless oil (130 mg, 0.55 mmol, 55% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23–7.18 (m, 2H), 7.00–6.90 (m, 2H), 5.19 (t, J = 4.8 Hz, 1H), 2.87 (d, J = 4.8 Hz, 2H), 1.18 (s, 6H), 1.15 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9 ($^1J_{CF}$ = 244 Hz), 132.3 ($^4J_{CF}$ = 3.0 Hz), 131.5 ($^2J_{CF}$ = 8.3 Hz), 115.1 ($^3J_{CF}$ = 21 Hz), 101.0, 82.1, 42.2, 24.2, 22.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ -117.8. HRMS (ESI): *m*/*z* calcd for $C_{14}H_{19}FO_2Na$ $[M+Na]^+$ 261.1267, found 261.1284.

2-(*o*-Chlorophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ca): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3ca** as a colorless oil (151 mg, 0.59 mmol, 59% yield). The spectral data for **3ca** were in accordance with those reported in the literature.[19]

2-(*m*-Chlorophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3da): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 5 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 5 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1 with 1% triethylamine) to afford **3da** as a colorless oil (142 mg, 0.56 mmol, 56% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25–7.13 (m, 4H), 5.20 (t, J = 4.8 Hz, 1H), 2.87 (d, J = 4.8 Hz, 2H), 1.18 (s, 6H), 1.15 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 133.9, 130.1, 129.5, 128.3, 126.7, 100.7, 82.1, 42.7, 24.2, 22.1. HRMS (ESI): *m*/*z* calcd for $C_{14}H_{19}ClO_2Na$ $[M+Na]^+$ 277.0971, found 277.0986.

2-(*p*-Chlorophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ea): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3ea** as a colorless oil (78 mg, 0.31 mmol, 61% yield). The spectral data for **3ea** were in accordance with those reported in the literature.[19]

2-(*o*-Bromophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3fa): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1 with 1% triethylamine) to afford **3fa** as a colorless oil (94 mg, 0.31 mmol, 31% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (dd, J = 1.2, 7.8 Hz, 1H), 7.33 (dd, J = 1.8, 7.5 Hz, 1H), 7.25 (dd, J = 1.1, 7.5 Hz, 1H), 7.08 (dt, J = 1.5, 7.7 Hz, 1H), 5.30 (t, J = 5.1 Hz, 1H), 3.10 (d, J = 5.1 Hz, 2H), 1.22 (s, 6H), 1.19 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.3, 132.7, 132.3, 128.3, 127.4, 125.2, 122.3, 99.9, 82.2, 43.0, 24.2, 22.2. HRMS (ESI): *m*/*z* calcd for $C_{14}H_{19}BrO_2Na$ $[M+Na]^+$ 321.0466, found 321.0470.

2-(*m*-Bromophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ga): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3ga** as a colorless oil (170 mg, 0.57 mmol, 57% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.37–7.33 (m, 1H), 7.21–7.13 (m, 2H), 5.21 (t, J = 4.8 Hz, 1H), 2.86 (d, J = 4.8 Hz, 2H), 1.18 (s, 6H), 1.15 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 133.0, 129.8, 129.6, 128.7, 122.3, 100.6, 82.1, 42.6, 24.1, 22.1. HRMS (ESI): *m*/*z* calcd for $C_{14}H_{19}BrO_2Na$ $[M+Na]^+$ 321.0466, found 321.0454.

2-(*m*-Nitrophenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ha): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1 with 1% triethylamine) to afford **3ha** as a colorless oil (144 mg, 0.54 mmol, 54% yield). The spectral data for **3ha** were in accordance with those reported in the literature.[19]

2-(*o*-Methylphenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ia): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 3 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 3 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3ia** as a colorless oil (144 mg, 0.61 mmol, 61% yield). The spectral data for **3ia** were in accordance with those reported in the literature.[19]

2-(*p*-Methylphenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ja): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 3 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 4 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20/1 with 1% triethylamine) to afford **3ja** as a colorless oil (119 mg, 0.51 mmol, 51% yield). The spectral data for **3ja** were in accordance with those reported in the literature.[19]

2-(*p*-Acetoxyphenylmethyl)-4,4,5,5-tetramethyl-1,3-dioxolane (3ka): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 1 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 7 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1 with 1% triethylamine) to afford **3ka** as a colorless oil (111 mg, 0.40 mmol, 40% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28–7.25 (m, 2H), 7.01–6.98 (m, 2H), 5.21 (t, J = 4.8 Hz, 1H), 2.89 (d, J = 5.1 Hz, 2H), 2.29 (s, 3H), 1.18 (s, 6H), 1.16 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.64, 149.35, 134.3, 131.0, 121.3, 100.9, 82.1, 42.5, 24.2, 22.2 21.2. HRMS (ESI): *m*/*z* calcd for $C_{16}H_{22}O_4Na$ $[M+Na]^+$ 301.1416, found 301.1425.

2-(Phenylmethyl)-1,3-dioxolane (3ab): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1 with 1% triethylamine) to afford **3ab** as a colorless oil (40 mg, 0.24 mmol, 24% yield). The spectral data for **3ab** were in accordance with those reported in the literature.[19]

2-(Phenylmethyl)-1,3-dioxane (3ac): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 3 M HCl aq. (1.25 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 1 h. The mixture was then neutralized with $NaHCO_3$ aq., and

Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1 with 1% triethylamine) to afford **3ac** as a colorless oil (87 mg, 0.49 mmol, 49% yield). The spectral data for **3ac** were in accordance with those reported in the literature.[22]

2-(Phenylmethyl)-5,5-dimethyl-1,3-dioxane (3ad): The reaction was performed in a similar manner as **3aa**. After cooling to room temperature, the solvent and volatile materials were evaporated. To the residue, 3 M HCl aq. (1.5 mL) and THF (2.5 mL) were added, and the reaction mixture was stirred at 40 °C for 2 h. The mixture was then neutralized with $NaHCO_3$ aq., and Et_2O was added to extract. The organic layer was dried over $MgSO_4$, and was filtrated. The filtrate was evaporated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 7/1 with 1% triethylamine) to afford **3ad** as a colorless oil (86 mg, 0.42 mmol, 42% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31–7.19 (m, 5H), 4.60 (t, J = 5.1 Hz, 1H), 3.59 (d, J = 10.8 Hz, 2H), 3.38 (d, J = 10.8 Hz, 2H), 2.94 (d, J = 5.1 Hz, 2H), 1.19 (s, 3H), 0.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ136.7, 129.6, 128.2, 126.4, 102.6, 77.3, 41.6, 30.1, 23.0, 21.8. HRMS (ESI): *m/z* calcd for $C_{13}H_{18}O_2Na$ $[M+Na]^+$ 229.1205, found 229.1213.

Kinetic Experiments

All the reactions were performed in sealed J. young NMR tubes (528-LPV-8). $PdCl_2(MeCN)_2$, MeOBQ, CuCl (or *n*-Bu_4NCl), and pinacol were placed in the NMR tube under argon. The tube was cooled in an ice bath. *t*-AmylOH, methyl benzoate (as an internal standard, 15 μL, 0.12 mmol), styrene, and $CDCl_3$ were added to the above mixture at 0 °C, and O_2 (10 mL) was passed through the reaction mixture via syringe. The sample was then introduced into a NMR probe at 25 ˚C, and was warmed to 40 °C immediately. The increase of the integration of C*H* signal (5.23 ppm) for **3aa** was followed by ^{1}H NMR spectroscopy. The moment at which the probe temperature reached to 40 °C was regarded as a starting time. The initial rates were calculated from the maximum slopes on the graphs plotted the concentration of **3aa** vs. reaction time.

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Keywords: acetals • electron-deficient compounds • palladium • synthetic methods • vinylarenes

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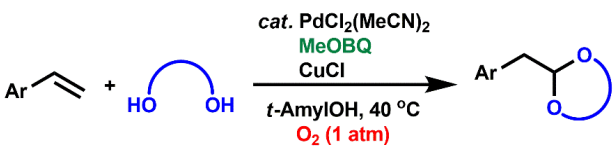

Terminal acetals were synthesized from various vinylarenes and diols using a $PdCl_2(MeCN)_2$/methoxy-*p*-benzoquinone (MeOBQ)/CuCl catalyst system and 1 atm of O_2 under mild reaction conditions, via anti-Markovnikov nucleophilic attack of an oxygen nucleophile to the coordinated vinylarenes. MeOBQ operated as a ligand for palladium to accelerate the reaction.

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Palladium-catalyzed Aerobic Synthesis of Terminal Acetals from Vinylarenes Assisted by π-Acceptor Ligands