JOC The Journal of Organic Chemistry

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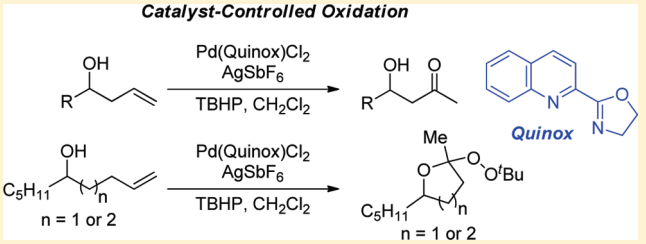
Catalyst-Controlled Wacker-Type Oxidation of Homoallylic Alcohols in the Absence of Protecting Groups

Jessica R. McCombs, Brian W. Michel, and Matthew S. Sigman*

University of Utah, Department of Chemistry, 315 S. 1400 E, Salt Lake City, Utah 84112, United States

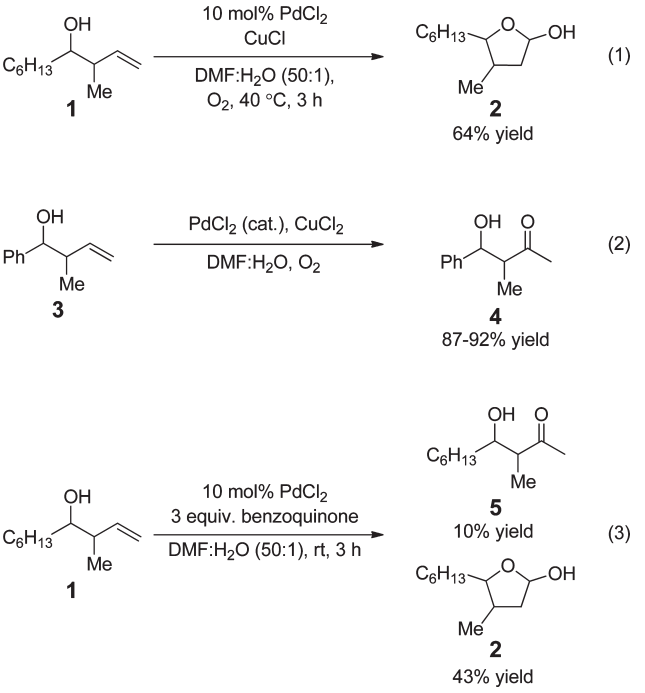
Supporting Information

ABSTRACT: Homoallylic alcohols are oxidized to β-hydroxy ketones using a TBHP-mediated Pd-catalyzed Wacker-type oxidation. The use of a bidentate ligand, quinoline-2-oxazoline (Quinox), and $TBHP_{(aq)}$ as the terminal oxidant provides good yields of the desired products with reaction times significantly reduced as compared to the Tsuji–Wacker oxidation. Additionally, *bis*- and *tris*-homoallylic alcohols are oxidized to provide cyclic peroxyketals, presumably via nucleophilic attack of the methyl ketone product.



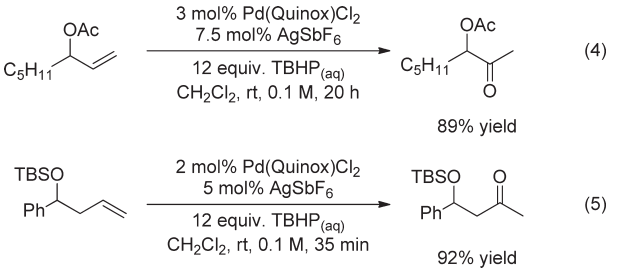
In the Tsuji–Wacker oxidation, the oxidation of terminal olefins to methyl ketones is catalyzed by palladium salts in the presence of a mixed DMF/H_2O solvent system, which has found widespread application in synthesis.[1−4] While simple alkenes are generally compatible with Tsuji–Wacker oxidation, the introduction of a proximal heteroatom can lead to unpredictable distributions of aldehyde and ketone products.[5] For example, homoallylic alcohols are a substrate class that offers a unique set of challenges, as they can undergo intramolecular *anti*-Markovnikov cyclization in competition with Markovnikov attack from water or hydroxide (*vida infra*). Despite this, homoallylic alcohols are attractive substrates for the Wacker oxidation, because they can be easily prepared in enantiomerically enriched form and, upon Wacker oxidation, yield an aldol product equivalent. The strategy of aldehyde allylation and subsequent Wacker oxidation has been commonly employed in synthesis; however, protecting groups are usually required.[6,7]

The selectivity in the Tsuji–Wacker oxidation of homoallylic alcohols appears to be dependent on numerous factors, including substitution on the substrate and the precise conditions used. Highlighting this disparity, Tsuji and co-workers have reported that homoallylic alcohol substrates such as **1** yield lactol product **2** in the presence of CuCl (eq 1),[8] while Yamamoto and co-workers observed the methyl ketone product **4** from a similar substrate **3** in the presence of $CuCl_2$ (eq 2). Additionally, the selectivity of these reactions can be affected by the choice of oxidant. For example, the use of the organic oxidant benzoquinone favors the formation of lactols, such as **2** (eq 3).[8] Furthermore, Santelli and co-workers have reported that subtle distal electronic variations in 11-vinyl-13β-hydroxy steroids affect the selectivity between aldehyde and ketone products.[9−11] Due to these limitations, we sought to develop general reaction conditions, which predictably provide the ketone product from a Wacker-type oxidation, and herein we report success in these efforts.



In our pursuit of ligand-modulated alkene functionalization reactions, we recently reported a copper-free catalyst system for Wacker-type oxidations that utilizes a bidentate ligand (Quinox) on palladium along with *tert*-butylhydroperoxide (TBHP) as the oxidant.[12] This system successfully oxidizes substrates bearing protected allylic and homoallylic alcohols with high selectivity for the Markovnikov (i.e., methyl ketone) product (eqs 4 and 5). The TBHP-mediated Wacker-type oxidation is proposed to

Received: March 2, 2011
Published: March 29, 2011



proceed through a well-defined *syn*-oxypalladation that favors Markovnikov attack due to the coordinatively saturated nature of palladium (Figure 1a). While protected homoallylic alcohols, such as **6**, are excellent substrates for the Pd(Quinox)−TBHP system (Figure 1b), unprotected substrates were not previously evaluated.

While the general optimization of the Pd(Quinox)−TBHP system has been reported,[12] 4-hydroxynon-1-ene (**8**) was used as a model substrate to determine the optimal conditions for unprotected homoallylic alcohols (Table 1). It was found that starting the reaction at 0 °C, as compared to room temperature, led to higher yields of the methyl ketone product (Table 1, entries 1−2). This is in contrast to our previous reports, where the reaction outcome using various substrates appeared insensitive to temperature. A minimum of 3 mol % catalyst was also found to be necessary for complete conversion of the starting material (Table 1, entry 3). It should be noted that the methyl ketone was the only observed product, and no lactol or aldehyde products were detected.

The scope of this transformation was evaluated, and it was found that, for secondary alcohols, 3 mol % catalyst was sufficient to achieve good yields in 5 h (Table 2, entry 1). Tertiary alcohols tended to react slower, where incomplete conversion was observed using 3 mol % catalyst. However, increasing the catalyst loading to 5 mol % led to efficient reactions (Table 2, entries 2 and 4−5). Santelli and co-workers observed tertiary alcohol substrates to yield the aldehyde product via *anti*-Markovnikov hydroxypalladation using modified Tsuji−Wacker conditions, which is in contrast to our observations using Pd(Quinox)−TBHP.[9−11] For comparison, these tertiary alcohol substrates were subjected to Tsuji−Wacker conditions, which resulted in inferior yields (Table 2 entries 3 and 6). A mixture of internal olefin isomers was also recovered from the reaction mixture, as determined by ^{1}H NMR. For substrates with a secondary benzylic alcohol, the reaction yielded a complex mixture of products with 62% recovered starting material (Table 2, entry 7). However, a tertiary benzylic alcohol was compatible, giving 50% conversion at 5 mol % catalyst, while a catalyst loading of 10 mol % lead to 100% conversion and 79% isolated yield (Table 2, entries 8−9). When a homoallylic alcohol derived from aldehyde crotylation was evaluated, the use of 5 mol % catalyst led to a 57% yield, and an average of 32% starting material was recovered (Table 2, entry 10).[13] This result is particularly interesting when compared with previous examples, where analogous substrates favor the lactol or ketone product in a condition-dependent manner (eqs 1 and 2). With the exception of a secondary benzylic alcohol, the Pd(Quinox)−TBHP catalyst system demonstrates high selectivity for the desired methyl ketone, regardless of substitution on the substrates evaluated.

To investigate the effect of the position of the alcohol relative to the olefin, *bis*- and *tris*-homoallylic alcohols (**10** and **12**) were also evaluated (eqs 6 and 7). When these substrates were

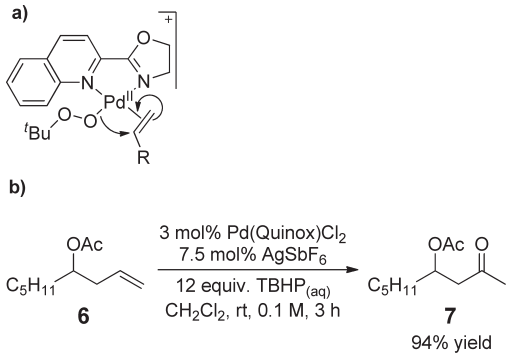
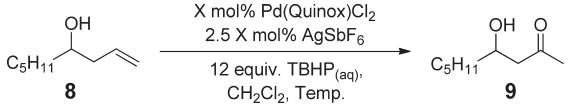


Figure 1. (a) Proposed *syn*-oxypalladation. (b) Acetate-protected homoallylic alcohol **6** is converted exclusively to methyl ketone **7** in high yield.

Table 1. Optimization of Conditions



Entry	mol % Catalyst (X)	Temp	Time (h)	% Conversion	% Yield[a]
1	3	rt	19	97	65
2	3	0 °C	5	99	75
3	2	rt	4	64	42

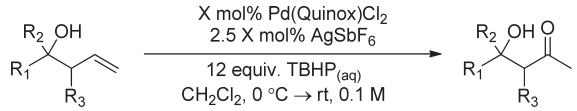
[a] Yields determined by GC based on $C_{12}H_{26}$ (∼10 wt %) internal standard.

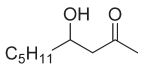
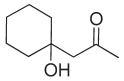
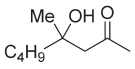
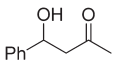
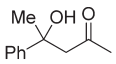
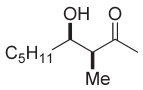
subjected to the standard conditions, Wacker cyclization products were not observed; instead, the products isolated were identified as cyclic peroxyketals **11** and **13**. It is hypothesized that the methyl ketone is initially formed by TBHP-mediated Wacker oxidation (Scheme 1). These types of compounds, however, are known to exist as mixtures of the ketone and cyclic hemiketal, due to the favorable formation of a five- or six-membered ring.[14] The hemiketal is then susceptible to oxygen-assisted nucleophilic substitution by the excess TBHP in solution, which yields the peroxyketal products. These interesting and uncommon products may have applications in targeted synthesis.

In conclusion, after modest optimization, it has been demonstrated that the Pd(Quinox)Cl_2−TBHP catalyst system can selectively oxidize olefin substrates bearing homoallylic alcohols to their corresponding methyl ketone products. This is proposed to be due to the catalyst-controlled nature of this oxidation system, which is in contrast to the substrate control often observed in the Tsuji−Wacker oxidation. Furthermore, *bis*- and *tris*-homoallylic alcohols are oxidized to interesting cyclic peroxyketal products. It is proposed that selective Markovnikov oxidation does occur, but that favorable ring sizes along with the excess TBHP present in the reaction mixture lead to the formation of these products. The short reaction times and predictability afforded by the Pd(Quinox)−TBHP system should allow for this method to be a useful tool for synthetic chemists in the preparation of β-hydroxyketones.

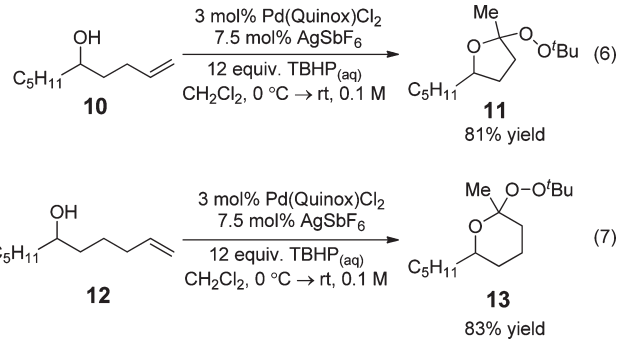
dx.doi.org/10.1021/jo200462a |*J. Org. Chem.* 2011, 76, 3609–3613

Table 2. Scope of TBHP-Mediated Wacker-Type Oxidation



Entry	Product	Catalyst Loading X	Time	% yield[a]
1		3	5 h	81
2		5	6.5 h	71
3		10 (Tsuji)[b]	30 h	34
4		5	5 h	84
5		5	5 h	83[c]
6		10 (Tsuji)[b]	30 h	26
7		3	24 h	--
8		5	8 h	44[d]
9		10	8 h	79[e]
10		5	24 h	57[f,g]

[a] All yields represent an average of two experiments on at least a 1 mmol scale unless noted otherwise. [b] Experiments conducted using Tsuji–Wacker conditions (10 mol % $PdCI_2$, 1 equiv of CuCI, (7:1) DMF/H_2O, rt, O_2 balloon). [c] Experiment conducted on a 7 mmol scale. [d] An average of 50% starting material was recovered. [e] Single experiment. [f] An average of 35% starting material was recovered. [g] This reaction was perfromed at room temperature.

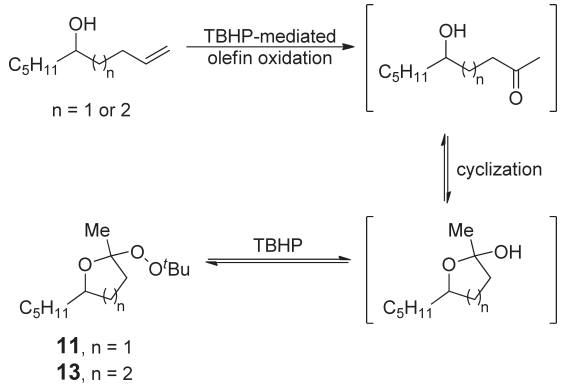


EXPERIMENTAL SECTION

A procedure for a one-pot synthesis of Quinox is outlined in a recent publication.[15] ALTHOUGH NO PROBLEMS OCCURRED DURING THESE STUDIES, HIGHLY CONCENTRATED SOLUTIONS OF TBHP IN THE PRESENCE OF TRANSITION METALS CAN BE EXPLOSIVE.

General Procedure for Optimization Reactions. In the dark, $AgSbF_6$ and Pd(Quinox)Cl_2 were added to a small vial. CH_2Cl_2 was added to the vial followed by the desired quantity of TBHP. The mixtures were allowed to stir for 10 min, and the desired temperature was established. The substrate was added as a standard solution in CH_2Cl_2. Aliquots (~100 μL) were taken periodically and passed through a silica pipet, eluting with ethyl acetate. These samples were then analyzed by gas chromatography, and the amount of product was measured relative to an internal standard of dodecane (~10 wt % as compared to substrate). Peak integrations were corrected with a response factor calculated from samples of known molar ratio.

Scheme 1. Proposed Formation of Peroxyketals 11 and 13



General Procedure for the Pd(Quinox)Cl_2–TBHP Oxidation. In the dark, $AgSbF_6$ (25.8 mg, 0.075 mmol, 0.075 equiv) and Pd(quinox)Cl_2 (11.3 mg, 0.03 mmol, 0.03 equiv) were added to a 25-mL round bottomed flask with a stir bar. CH_2Cl_2 (1.7 mL) was charged to the flask and the mixture was stirred for 10 min, after which time TBHP (1.7 mL, 12 mmol, 12 equiv) was added along with the remaining CH_2Cl_2 (6.6 mL), turning the mixture from pale yellow to orange. The flask was placed in an ice bath, and after 10 min the substrate (1.0 mmol, 1 equiv) was added. The reaction mixture was allowed to slowly warm to room temperature. Once TLC analysis indicated complete consumption of the starting material, the reaction was cooled to 0 °C and quenched with a saturated solution of Na_2SO_3 (15 mL) to consume excess TBHP. The mixture was transferred to a separatory funnel and diluted with hexanes (25 mL). The aqueous layer was extracted with hexanes (3 × 25 mL). The combined organic phases were washed with H_2O (3 × 10 mL) and brine (25 mL) and then dried over $MgSO_4$. After filtration and concentration under reduced pressure, the crude material was purified by flash chromatography and the product containing fractions were combined and concentrated under reduced pressure.

*Non-1-ene-4-ol (**8**).* This compound was prepared according to the literature procedure.[16] Analytical data are consistent with the literature.[17]

*Non-1-en-4-yl acetate (**6**).* To a 10 mL round bottomed flask equipped with a stir bar were charged triethylamine (626 μL, 4.5 mmol, 3 equiv), 4-*N*,*N*-dimethylaminopyridine (DMAP) (18.5 mg, 0.15 mmol, 0.1 equiv), and non-1-ene-4-ol **8** (226 mg, 1.5 mmol, 1 equiv). The mixture was cooled to 0 °C in an ice bath, and acetic anhydride (425 μL, 4.5 mmol, 3 equiv) was added in a dropwise fashion. After 1.5 h, TLC analysis showed complete consumption of the starting material. The reaction was quenched with H_2O, diluted with Et_2O (10 mL), and transferred to a separatory funnel. The aqueous phase was extracted with Et_2O (3 × 10 mL). The combined organics were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography eluting with 3% Et_2O in hexanes to yield non-1-en-4-yl acetate **6** (264 mg, 1.43 mmol) as a colorless oil in 90% yield. R_f = 0.21 (3:97 Et_2O/Hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 5.70–5.80 (m, 1H), 5.03–5.12 (m, 2H), 4.88–4.95 (m, 1H), 2.24–2.37 (m, 2H), 2.00 (s, 3H), 1.49–1.57 (m, 2H), 1.20–1.39 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 21.4, 22.7, 25.2, 31.8, 33.8, 38.9, 73.6, 117.7, 134.1, 171.0. IR (neat): 3079 (w), 2931 (m), 2860 (m), 1737 (s), 1643 (w) cm^{-1}. HRMS: *m*/*z* (ESI/TOF MS E+) Calculated $[C_{11}H_{22}O_2^+]$ 185.1542, observed 185.1554.

1-Allylcyclohexanol. This compound was prepared according to the literature procedure.[16] Analytical data match the literature.[18]

dx.doi.org/10.1021/jo200462a |*J. Org. Chem.* 2011, 76, 3609–3613

4-Methyloct-1-en-4-ol. This compound was prepared according to the literature procedure.[16] Analytical data match the literature.[19]

1-Phenylbut-3-en-1-ol. This compound was prepared according to the literature procedure.[16]Analytical data match the literature.[20]

2-Phenylpent-4-en-2-ol. This compound was prepared according to the literature procedure.[16] Analytical data match the literature.[21]

3-Methylnon-1-en-4-ol. This compound was prepared according to the literature procedure.[22]Analytical data match the literature.[23]

*Dec-1-en-5-ol (**10**).* Dec-1-en-5-ol was prepared according to the literature procedure, and analytical data match.[24]

*Undec-1-en-6-ol (**12**).* To an oven-dried three-necked 100 mL round bottomed flask containing a stir bar was weighed freshly ground magnesium turnings (395 mg, 16 mmol, 4 equiv). A nitrogen atmosphere was established, and Et_2O (8 mL) was cannulated into the flask. The bromide, 5-bromo-1-pentene (190 μL, 1.6 mmol, 0.4 equiv), was charged to the flask by syringe addition. The remaining 5-bromo-1-pentene (760 μL, 6.4 mmol, 1.6 equiv) was dissolved in dry Et_2O (40 mL) and was slowly cannulated to the flask containing the magnesium turnings. The mixture was heated to 45 °C in an oil bath and refluxed for 1 h, at which point it was cooled to room temperature. In an oven-dried 250 mL round bottomed flask with a stir bar were charged 1-hexanal (480 μL, 4 mmol, 1 equiv) and Et_2O (18 mL). This flask was cooled in a dry ice/isopropanol bath, and the Grignard solution was cannulated to this flask in a dropwise fashion. The reaction mixture was subsequently allowed to warm to room temperature. TLC analysis confirmed the consumption of the aldehyde after 5 h which was quenched at 0 °C with 1 M HCl solution. The aqueous portion was extracted with Et_2O (3 × 35 mL). The combined organics were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography with 20% Et_2O in hexanes to provide undec-1-en-6-ol **12** (504 mg, 2.96 mmol) as a colorless oil in 74% yield. R_f = 0.20 (5:25:70 Acetone/Et_2O/Hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.75−5.86 (m 1H), 4.94 (dd, J = 16 Hz, 1H), 3.52−3.63 (m, 1H), 1.95−2.15 (m, 2H), 1.57−1.07 (m, 12H), 0.86 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.8, 25.1, 25.5, 32.1, 34.0, 37.1, 37.7, 72.0, 114.7, 139.0. IR (neat): 3335 (br m), 3077 (w), 2927 (s), 2858 (m), 1641 (w) cm^{-1}. HRMS: m/z (ESI/TOF MS E+) Calculated [$C_{11}H_{23}O^+$] 171.1749, observed 171.1749.

*2-Oxononan-4-yl Acetate (**7**).* The general procedure for the TBHP-mediated Wacker oxidation was followed using non-1-en-4-yl acetate **6** (197 mg, 1.07 mmol) and purified by flash chromatography eluting with 15% ethyl acetate in hexanes to afford 2-oxononan-4-yl acetate **7** in a 94% yield (202 mg, 1.01 mmol). R_f = 0.26 (15:85 Ethyl Acetate/Hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.19−5.28 (m, 1H), 2.47 (dd, 1H J = 16.1, 7.42 Hz), 2.60 (dd, 1H J = 16.2, 5.36 Hz), 2.17 (s, 3H), 2.03 (s, 3H), 1.51−1.62 (m, 2H), 1.20−1.40 (m, 6H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 21.3, 22.6, 25.0, 30.6, 31.7, 34.2, 40.1, 70.4, 170.6, 206.0. IR (neat): 2931 (m), 2861 (m), 1735 (s), 1717 (s) cm^{-1}. HRMS: m/z (ESI/TOF MS E+) Calculated [$C_{11}H_{20}O_3Na^+$] 223.1310, observed 223.1313.

4-Hydroxynonan-2-one (Table 2, entry 1, 9). The general procedure for the TBHP-mediated Wacker oxidation was followed using non-1-en-4-ol **8** (142 mg, 1.00 mmol and 152 mg, 1.07 mmol respectively). The crude mixtures were purified by flash chromatography eluting with 33% ethyl acetate in hexanes to afford 4-hydroxynonan-2-one **9** (132 mg, 0.83 mmol and 123 mg, 0.78 mmol respectively) as a colorless oil in an 81% average yield. The spectral data were in accordance with the previous report.[25]

1-(1-Hydroxycyclohexyl)propan-2-one (Table 2, entry 2). The general procedure for the TBHP-mediated Wacker oxidation was followed with the exception that 0.05 equiv of Pd(Quinox)Cl_2 and 0.125 equiv of $AgSbF_6$ were found to be necessary for the oxidation of 1-allylcyclohexanol (145 mg, 1.03 mmol and 158 mg, 1.13 mmol respectively). The crude mixtures were purified by flash chromatography eluting with 30% Et_2O and 5% acetone in hexanes to afford 1-(1-hydroxycyclohexyl)propan-2-one (111 mg, 0.71 mmol and 129 mg, 0.83 mmol respectively) as a colorless oil in a 71% average yield. R_f = 0.21 (65:30:5 Hexanes/Ethyl Acetate/Acetone). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.16 (s, 1H), 2.61 (s, 2H), 2.18 (s, 3H), 1.76−1.20 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 26.0, 32.3, 37.8, 53.13, 70.8, 221.2. IR (neat): 3481 (br m), 2929 (s), 2857 (m), 1697 (s) cm^{-1}. HRMS: m/z (ESI/TOF MS E+) Calculated [$C_9H_{16}O_2Na^+$] 179.1048, observed 179.1057.

1-(1-Hydroxycyclohexyl)propan-2-one (Table 2, entry 3, Tsuji−Wacker). In a 10 mL side arm flask, a stir bar, $PdCl_2$ (18 mg, 0.1 mmol, 0.1 equiv), CuCl (100 mg, 1.0 mmol, 1.0 equiv), and 7:1 DMF/H_2O (1.5 mL) were added. The flask was equipped with an O_2 balloon and allowed to stir vigorously for 1 h, during which time the mixture turned from black to green. Substrate (142 mg, 1.0 mmol, 1.0 equiv) was then charged to the flask, and the reaction mixture was allowed to stir for 30 h before being quenched with 25% HCl (15 mL). The mixture was transferred to a separatory funnel with Et_2O and separated. The aqueous portion was extracted with ether (3 × 15 mL), and the combined organic portions were washed with $NaHCO_3$ (20 mL) and brine (20 mL) before being dried over $MgSO_4$. The organic phase was filtered and concentrated under reduced pressure. The crude material was purified by silica gel flash chromatography eluting with 15% ethyl acetate in hexanes to yield 1-(1-hydroxycyclohexyl)propan-2-one in a 34% yield (53 mg, 0.34 mmol) and 11% recovered isomerized starting material (16 mg).

4-Hydroxy-4-methyloctan-2-one (Table 2, entry 4). The general procedure for the TBHP-mediated Wacker oxidation was used for 4-methyloct-1-en-4-ol with the modifications that 0.05 equiv of Pd(Quinox)Cl_2 and 0.125 equiv of $AgSbF_6$ were found to be necessary for full consumption of the substrate. The reactions were performed with 142 mg (1.00 mmol) and 143 mg (1.01 mmol) of 4-methyloct-1-en-4-ol respectively. The crude mixture was purified by flash chromatography eluting with 50% Et_2O in hexanes to afford 4-hydroxy-4-methyloctan-2-one as a colorless oil in 84% average yield (130 mg, 0.82 mmol and 136 mg, 0.86 mmol). R_f = 0.21 (30:5:65 Et_2O/Acetone/Hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 1H), 2.67 (d, 1H J = 17.3 Hz), 2.60 (d, J = 17.0 Hz, 1H), 2.19 (s, 3H), 1.52−1.48 (m, 6H), 1.34−1.29 (m, 3H), 1.21 (s, 3H), 0.91 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 23.0, 26.0, 26.6, 31.8, 41.5, 52.1, 71.5, 211.0. IR (neat): 3463 (br w), 2957 (m), 2933 (m), 2863 (m), 1699 (s) cm^{-1}. HRMS: m/z (ESI/TOF MS E+) Calculated [$C_9H_{18}O_2Na^+$] 181.1204, observed 181.1214.

4-Hydroxy-4-methyloctan-2-one (Table 2, entry 5). The general procedure for the TBHP-mediated Wacker oxidation was used for 4-methyloct-1-en-4-ol with the modifications that 0.05 equiv of Pd(Quinox)Cl_2 and 0.125 equiv of $AgSbF_6$ were found to be necessary for full consumption of the substrate. The reactions were performed with 981 mg (6.9 mmol) of 4-methyloct-1-en-4-ol. The crude mixture was purified by flash chromatography eluting with 50% Et_2O in hexanes to afford 4-hydroxy-4-methyloctan-2-one as a colorless oil in 83% yield (908 mg, 5.74 mmol).

4-Hydroxy-4-methyloctan-2-one (Table 2, entry 6, Tsuji−Wacker). In a 10 mL side arm flask, a stir bar, $PdCl_2$ (18 mg, 0.1 mmol, 0.1 equiv), CuCl (99 mg, 1.0 mmol, 1.0 equiv), and 7:1 DMF/H_2O (1.5 mL) were added. The flask was equipped with an O_2 balloon and allowed to stir vigorously for 1 h during which the mixture turned from black to green. Substrate (140 mg, 0.98 mmol, 1.0 equiv) was then charged to the flask, and the reaction mixture was allowed to stir for 30 h before being quenched with 25% HCl (15 mL). The mixture was transferred to a separatory funnel with Et_2O and separated. The aqueous portion was extracted with ether (3 × 15 mL), and the combined organic portions were washed with $NaHCO_3$ (20 mL) and brine (20 mL) before being dried over $MgSO_4$. The organic phase was filtered and concentrated under reduced pressure. The crude material was purified by silica gel flash chromatography eluting with 25:5:70 Et_2O/Acetone/Hexanes

to yield 4-hydroxy-4-methyloctan-2-one in a 26% yield (40 mg, 0.25 mmol) and 15% recovered isomerized starting material (22 mg).

4-Hydroxy-4-phenylpentan-2-one (Table 2, entry 8). The general procedure for the TBHP-mediated Wacker oxidation was used with the modification that 0.05 equiv of Pd(Quinox)Cl_2 and 0.125 equiv of $AgSbF_6$ were used. The reactions were performed with 163 mg (1.00 mmol) and 161 mg (0.99 mmol) of 2-phenylpent-4-en-2-ol respectively. The crude mixture was purified by flash chromatography eluting with 25% Et_2O and 5% acetone in hexanes to afford 4-hydroxy-4-phenylpentan-2-one as a colorless oil in 44% average yield (80 mg, 0.45 mmol and 78 mg, 0.44 mmol). The spectral data were in accordance with the previous reports.[26]

4-Hydroxy-4-phenylpentan-2-one (Table 2, entry 9). The general procedure for the TBHP-mediated Wacker oxidation was used with the modification that 0.10 equiv of Pd(Quinox)Cl_2 and 0.25 equiv of $AgSbF_6$ were used. The reaction was performed with 162 mg (1.00 mmol) of 2-phenylpent-4-en-2-ol. The crude mixture was purified by flash chromatography eluting with 25% Et_2O and 5% acetone in hexanes to afford 4-hydroxy-4-phenylpentan-2-one as a colorless oil in 79% yield (140.8 mg, 0.79 mmol). The spectral data were in accordance with the previous reports.[26]

4-Hydroxy-3-methylnonan-2-one (Table 2, entry 10). The general procedure for the TBHP-mediated Wacker oxidation was used with the modification that 0.05 equiv of Pd(Quinox)Cl_2 and 0.125 equiv of $AgSbF_6$ were used. The reactions were performed with 159 mg (1.02 mmol) and 155 mg (0.99 mmol) of 3-methylnon-1-en-4-ol respectively. Purified by flash chromatography eluting with 50% Et_2O in hexanes to afford the title compound as a colorless oil in 57% average yield (93.9 mg, 0.55 mmol and 103 mg, 0.60 mmol). The spectral data were in accordance with the previous report.[27]

2-(*tert*-Butylperoxy)-2-methyl-5-pentyltetrahydrofuran (11). The general procedure for the TBHP-mediated Wacker oxidation was followed using dec-1-en-5-ol **10**. The reactions were performed with 155.0 mg (0.99 mmol) and 155.9 mg (1.00 mmol) of **10** respectively. The crude product was purified by flash chromatography eluting with 20% Et_2O in hexanes to afford 2-(*tert*-butylperoxy)-2-methyl-5-pentyltetrahydrofuran **11** as a colorless oil in 83% average yield (200 mg, 0.82 mmol and 206 mg, 0.84 mmol). R_f = 0.67 (20:80 Et_2O/Hexanes). ^1H NMR (500 MHz, $CDCl_3$) δ 4.11−4.17 (m, 1H), 2.00−2.10 (m, 2H), 1.80−1.87 (m, 2H), 1.58−1.66 (m, 2H), 1.48 (s, 3H), 1.16−1.51 (m, 6H), 1.22 (s, 9H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.4, 23.0, 23.8, 25.8, 27.0, 31.2, 32.3, 35.6, 35.8, 79.5, 80.2, 111.5. IR (neat): 2976 (m), 2957 (m), 2930 (s), 2861 (w), 1460 (m) cm^{-1}. HRMS: m/z (ESI/TOF MS E+) Calculated [$C_{14}H_{28}O_3Na^+$] 267.1936, observed 267.1945

2-(*tert*-Butylperoxy)-2-methyl-6-pentyltetrahydro-2*H*-pyran (13). The general procedure for the TBHP-mediated Wacker oxidation was used for undec-1-ene-6-ol **12**. The reactions were performed with 158 mg (0.93 mmol) and 169 mg (0.99 mmol) of **12** respectively. The crude mixture was purified by flash chromatography eluting with 25% Et_2O in hexanes to afford 2-(*tert*-butylperoxy)-2-methyl-6-pentyltetrahydro-2*H*-pyran **13** as a colorless oil in 81% average yield (196 mg, 0.76 mmol and 204 mg, 0.79 mmol). R_f = 0.70 (20:80 Et_2O/Hexanes). ^1H NMR (500 MHz, $CDCl_3$, ppm) δ 3.81−3.88 (m, 1H), 1.79−1.65 (m, 4H), 1.61−1.39 (m, 2H), 1.38 (s, 3H), 1.36−1.25 (m, 4H), 1.23 (s, 9H), 0.87 (t, J = 7.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 14.4 (CH_3), 19.9 (CH_2), 23.0 (CH_2), 25.3 (CH_2), 27.0 (CH_2), 27.2 (CH_3), 30.7 (CH_2), 32.1 (CH_2), 33.6 (CH_2), 36.3 (CH_2), 70.3 (CH), 78.8 (C), 101.5 (C). IR (neat): 2977 (m), 2934 (s), 2871 (m), 1457 (m) cm^{-1}. HRMS: m/z (ESI/TOF MS E+) Calculated [$C_{15}H_{30}O_3Na^+$] 281.2093, observed 281.2101.

■ ASSOCIATED CONTENT

Supporting Information. Copies of NMR Spectra. This information is available free of charge via the Internet at http://pubs.acs.org

■ AUTHOR INFORMATION

Corresponding Author
*Email: sigman@chem.utah.edu.

■ ACKNOWLEDGMENT

This work was supported by the National Institutes of Health (NIGMS RO1 GM63540).

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