Terminal Olefins to Linear α,β-Unsaturated Ketones: Pd(II)/Hypervalent Iodine Co-Catalyzed Wacker Oxidation-Dehydrogenation

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General Information: All commercially obtained reagents for the tandem Wacker/dehydrogenation reaction were used as received [1,4-benzoquinone, dimethyl sulfoxide, $PhI(OAc)_2$]. $Pd(CH_3CN)_4(BF_4)_2$ was prepared according to the published procedure[i] as a pale yellow powder and was stored in a glove box under an argon atmosphere. Alternatively, $Pd(CH_3CN)_4(BF_4)_2$ purchased from Strem Chemicals could be used successfully and was also stored in a glove box under an argon atmosphere. All Wacker-dehydrogenation reactions were run with no precautions to exclude O_2 or moisture. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized with UV and potassium permanganate stain. Flash chromatography was performed as described by Still using ZEOprep 60 ECO 43-60 micron silica gel (American International Chemical, Inc.). ^1H NMR spectra were recorded on a Varian Inova-500 (500 MHz) or Varian Unity-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sext. = sextet, sept. = septet, m = multiplet, b = broad, ap = apparent; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C NMR spectra were recorded on a Varian Unity-500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). IR spectra were recorded as thin films on NaCl plates on a Perkin-Elmer Spectrum BX and are reported in frequency of absorption (cm^{-1}). High-resolution mass spectra were obtained at the University of Illinois Mass Spectrometry Laboratory. Optical rotations were obtained using a JASCO DIP-360 digital polarimeter and a 3.5 x 50 mm cell and are reported as follows: $[\alpha]_\lambda^{ToC}$ (c = g/100 mL, solvent).

Preparation of $Pd(CH_3CN)_4(BF_4)_2$

While in the glove box under an atmosphere of argon, Pd sponge (250 mg, 2.35 mmol, 1.0 equiv.) was weighted into a flame-dried 100 mL 3-necked round-bottom flask. The flask was removed from the glove box, placed under a nitrogen atmosphere, and to it was added 29 mL CH_3CN. To the resulting fine gray suspension was quickly added solid $NOBF_4$ (590 mg, 5.50 mmol, 2.15 equiv.). Briefly, evacuated the reaction flask until the solvent began bubbling and then re-filled the flask with N_2; this evacuation/N_2 re-filling procedure was performed 3X. Stirred at room temperature under N_2 for 30 minutes and the previous evacuation/N_2 re-filling procedure was again performed 3X. Stirred an additional 30 minutes and performed the evacuation/N_2 re-filling procedure a final 3X. The resulting clear, yellow solution stirred overnight at room temperature and was filtered through a glass fritted funnel. The filtrate was concentrated under reduced pressure and the resulting crude product was redissolved in 10 mL CH_3CN. 200 mL anhydrous Et_2O was layered on top of the CH_3CN and the resulting mixture was cooled at -20 ^oC for 4h. The supernatant was decanted and the precipitate was triturated 2X with 10 mL Et_2O. The resulting hygroscopic, light yellow powder was placed under high vacuum for 4h and stored in the glove box under at atmosphere of argon at room temperature (956 mg, 91%).

General Procedure for the Pd(II) and Hypervalent Iodine-catalyzed Tandem Wacker/Dehydrogenation Reaction

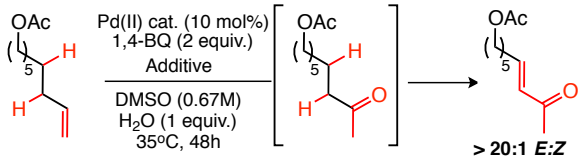
While in the glove box, $Pd(CH_3CN)_4(BF_4)_2$ (0.030 mmol, 0.10 equiv.) was weighed into a ½ dram borosilicate vial. Outside of the glove box, into a ½ dram borosilicate vial containing a Teflon stir bar was sequentially added terminal olefin starting material (0.30 mmol, 1.0 equiv.), 1,4-benzoquinone (0.60 mmol, 2.0 equiv.), and PhI(OAc) (0.075 mmol, 0.25 equiv.). Deionized H_2O (0.30 mmol, 1.0 equiv.) was next added *via* micropipetor. $Pd(CH_3CN)_4(BF_4)_2$ was carefully

transferred from the 1st ½ dram vial to the reaction vial using three aliquots of 0.15 mL DMSO (total solvent: 0.45 mL, 0.67 M with respect to terminal olefin). The vial was then sealed with a Teflon cap and placed in an aluminum block to stir at 35°C for 48 hours. The crude reaction mixture was purified directly using flash column chromatography (in general, gradient EtOAc/hexanes was used). For 0.50 mmol reactions, the reagents were scaled accordingly.

Table 1 Procedure

While in the glove box, $Pd(CH_3CN)_4(BF_4)_2$ (0.020 mmol, 0.10 equiv.) was weighed into a ½ dram borosilicate vial. Outside of the glove box, into a 2nd ½ dram borosilicate vial was sequentially added terminal olefin starting material (0.20 mmol, 1.0 equiv.), nitrobenzene (0.08 mmol, 0.40 equiv.) as internal standard, 1,4-benzoquinone (0.40 mmol, 2.0 equiv.), and hypervalent iodine reagent. Deionized H_2O (0.20 mmol, 1.0 equiv.) was next added *via* micropipetor, followed by 0.15 mL DMSO. The reaction vial mixture was stirred vigorously with a Teflon stirring bar and an aliquot was removed to measure the initial SM:nitrobenzene ratio. $Pd(CH_3CN)_4(BF_4)_2$ was transferred from the 1st ½ dram vial to the reaction vial using three aliquots of 0.050 mL DMSO (for a total reaction volume of 0.3 mL, [SM] = 0.67 M) and the reaction vial was then sealed with a Teflon cap and placed in an aluminum block to stir at 35°C for 48 hours. The crude reaction mixture was sampled for GC analysis and the yields of product(s) were quantified relative to a standard curve.

Table 1. Reaction Development



1 **2** **3**

entry	SM	catalyst	additive	yield 3[a]
1	**1**	$Pd(CH_3CN)_4(BF_4)_2$	--	13% (68% **2**)[b]
2	**1**	$Pd(CH_3CN)_4(BF_4)_2$	100% $PhI(OAc)_2$	56%
3	**1**	**$Pd(CH_3CN)_4(BF_4)_2$**	**25% $PhI(OAc)_2$**	**59% (55%[c])**
4	**1**	$Pd(CH_3CN)_4(BF_4)_2$	10% $PhI(OAc)_2$	38%
5	**1**	$Pd(CH_3CN)_4(BF_4)_2$	100% $PhI(OAc)_2$ 1 equiv. BQ	25%
6	**1**	$Pd(CH_3CN)_4(BF_4)_2$	25% IBX	58%
7	**2**	$Pd(CH_3CN)_4(BF_4)_2$	100% IBX No BQ	23%
8	**2**	--	100% IBX No BQ	8%
9	**1**	$Pd(OAc)_2$	25% $PhI(OAc)_2$	3%
10	**1**	$Pd(TFA)_2$	25% $PhI(OAc)_2$	36%
11	**1**	$Pd(TFA)_2$ 4,5-diazafluorenone	25% $PhI(OAc)_2$	35%
12	**1**	$Pd(OAc)_2$ 1,2-bis(benzylsulfinylethane)	25% $PhI(OAc)_2$	trace
13[d]	**1**	$Pd(TFA)_2$ DMSO	25% $PhI(OAc)_2$	--
14	**1**	No Pd(II)	25% $PhI(OAc)_2$	--

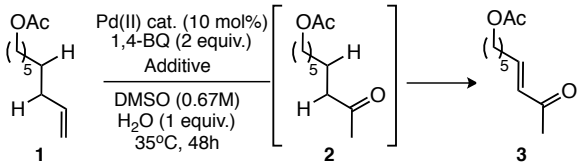
[a] Determined by GC, average of two runs at 0.1 mmol, relative to standard curve, external standard: nitrobenzene. [b] Yield of Wacker product **2** shown in parantheses. [c] Average isolated yield of **3** shown in parantheses (two runs at 0.3 mmol). [d] 0.67 M in AcOH.

Preparation of standard curve for Table 1: Stock solutions of nitrobenzene (197.0 mg, 1.60 mmol, 20.00 mL EtOAc) and authentic 8-oxononyl acetate (**2**) (100.1 mg,, 0.50 mmol, 5.00 mL EtOAc) and (*E*)-8-oxonon-6-en-1-yl acetate (**3**) (99.1 mg, 0.50 mmol, 5.00 mL EtOAc) were

prepared. To each of nine GC vials was added 500 μL nitrobenzene stock solution (4.9 mg, 0.040 mmol per vial), followed by an aliquot of the Wacker product **2** or dehydrogenated Wacker product **3** stock solutions, in increasing amounts (100 μL, 200 μL, …, 900 μL; 0.01 mmol, 0.02 mmol, …, 0.09 mmol). As such, the first GC vial represented a 10% yield of either Wacker product or dehydrogenated Wacker product for a 0.10 mmol reaction, while the ninth vial represented a 90% yield. These solutions were mixed thoroughly and analyzed by GC; a plot of % yield vs. measured product/nitrobenzene generated data points that could be readily fit to a linear equation of the form y = mx + b.

Entry 1: Followed the standard Table 1 procedure, omitting addition of $PhI(OAc)_2$. Run 1: 12% **3**; run 2: 13% **3**. Average = 13% **3**.
Entry 2: Followed the standard Table 1 procedure, including 1 equiv. (0.20 mmol) $PhI(OAc)_2$. Run 1: 54% **3**; run 2: 57% **3**. Average = 56% **3**.
Entry 3: Followed the standard Table 1 procedure, including 25 mol% (0.050 mmol) $PhI(OAc)_2$. Run 1: 59% **3**; run 2: 58% **3**. Average = 59% **3**.
Entry 4: Followed the standard Table 1 procedure, including 10 mol% (0.020 mmol) $PhI(OAc)_2$. Run 1: 40% **3**; run 2: 35% **3**. Average = 38% **3**.
Entry 5: Followed the standard Table 1 procedure, including 1 equiv. (0.20 mmol) $PhI(OAc)_2$ and only 1 equiv. (0.20 mmol) 1,4-BQ. Run 1: 22% **3**; run 2: 27% **3**. Average = 25% **3**.
Entry 6: Followed the standard Table 1 procedure, including 25 mol% (0.050 mmol) IBX. Run 1: 57% **3**; run 2: 58% **3**. Average = 58% **3**.
Entry 7: Beginning from methyl ketone **2** (0.20 mmol), included 1 equiv. (0.20 mmol) IBX and no 1,4-BQ. Run 1: 23% **3**; run 2: 22% **3**. Average = 23% **3**.
Entry 8: Beginning from methyl ketone **2** (0.20 mmol), included 1 equiv. (0.20 mmol) IBX and no 1,4-BQ and no Pd(II) catalyst. Run 1: 8% **3**; run 2: 8% **3**. Average = 8% **3**.
Entry 9: Followed the standard Table 1 procedure with 25 mol% $PhI(OAc)_2$ using $Pd(OAc)_2$ in place of $Pd(CH_3CN)_4(BF_4)_2$. Run 1: 4% **3**; run 2: 2% **3**. Average = 3% **3**.
Entry 10: Followed the standard Table 1 procedure with 25 mol% $PhI(OAc)_2$ using $Pd(TFA)_2$ in place of $Pd(CH_3CN)_4(BF_4)_2$. Run 1: 36% **3**; run 2: 36% **3**. Average = 36% **3**.
Entry 11: Followed the standard Table 1 procedure with 25 mol% $PhI(OAc)_2$ using $Pd(TFA)_2$ and 4,5-diazafluorenone (10 mol% of each) in place of $Pd(CH_3CN)_4(BF_4)_2$. Run 1: 35% **3**; run 2: 35% **3**. Average = 35% **3**.
Entry 12: Followed the standard Table 1 procedure with 25 mol% $PhI(OAc)_2$ using $Pd(OAc)_2$/1,2-bis(benzylsulfinylethane) in place of $Pd(CH_3CN)_4(BF_4)_2$. Run 1: trace **3**; run 2: trace **3**. Average = trace **3**.
Entry 13: Followed the standard Table 1 procedure with 25 mol% $PhI(OAc)_2$, using 10 mol% $Pd(TFA)_2$ and 20 mol% DMSO in place of $Pd(CH_3CN)_4(BF_4)_2$ and AcOH as solvent ([SM] = 0.67 M). Run 1: 0% **3**; run 2: 0% **3**. Average = 0% **3**.
Entry 14: Followed the standard Table 1 procedure with 25 mol% $PhI(OAc)_2$, omitting addition of $Pd(CH_3CN)_4(BF_4)_2$. Run 1: 0% **3**; run 2: 0% **3**. Average = 0% **3**.

Table SI 1. *Evaluation of role of hypervalent iodine reagent*



entry	SM	catalyst	additive	yield 3[a]
1	**2**	$Pd(CH_3CN)_4(BF_4)_2$	100% $PhI(OAc)_2$ No BQ	6%
2	**2**	$Pd(CH_3CN)_4(BF_4)_2$	25% PhI 100% AcOH	15%
3	**2**	$Pd(CH_3CN)_4(BF_4)_2$	100% IBX No BQ	23%
4	**2**	--	100% IBX No BQ	8%
5	**1**	$Pd(CH_3CN)_4(BF_4)_2$	25% $PhI(OPiv)_2$	57%
6	**1**	$Pd(CH_3CN)_4(BF_4)_2$	25% $PhI(TFA)_2$	45%
7	**1**	$Pd(CH_3CN)_4(BF_4)_2$	25% PhIO	51%
8	**1**	$Pd(CH_3CN)_4(BF_4)_2$	25% DMP	58%

[a] Determined by GC, average of two runs at 0.1 mmol, relative to standard curve, external standard: nitrobenzene.

Entry 1: Beginning from methyl ketone **2** (0.20 mmol), followed the standard Table 1 procedure, including 1 equiv. (0.20 mmol) $PhI(OAc)_2$. Run 1: 6% **3**; run 2: 6% **3**. Average = 6% **3**.
Entry 2: Beginning from methyl ketone **2** (0.20 mmol), included 25 mol% PhI and 100 mol% AcOH. Run 1: 14% **3**; run 2: 15% **3**. Average = 15% **3**.
Entry 3: Beginning from methyl ketone **2** (0.20 mmol), included 1 equiv. (0.20 mmol) IBX and no 1,4-BQ. Run 1: 23% **3**; run 2: 22% **3**. Average = 23% **3**.
Entry 4: Beginning from methyl ketone **2** (0.20 mmol), included 1 equiv. (0.20 mmol) IBX and no 1,4-BQ and no Pd(II) catalyst. Run 1: 8% **3**; run 2: 8% **3**. Average = 8% **3**.
Entry 5: Followed the standard Table 1 procedure, including 25 mol% (0.050 mmol) $PhI(OPiv)_2$. Run 1: 55% **3**; run 2: 58% **3**. Average = 57% **3**.
Entry 6: Followed the standard Table 1 procedure, including 25 mol% (0.050 mmol) $PhI(TFA)_2$. Run 1: 43% **3**; run 2: 47% **3**. Average = 45% **3**.
Entry 7: Followed the standard Table 1 procedure, including 25 mol% (0.050 mmol) PhIO. Run 1: 49% **3**; run 2: 53% **3**. Average = 51% **3**.
Entry 8: Followed the standard Table 1 procedure, including 25 mol% (0.050 mmol) DMP. Run 1: 57% **3**; run 2: 58% **3**. Average = 58% **3**.

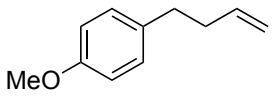
Table 2 Substrate Synthesis

4-phenyl-1-butene was purchased from Aldrich; 1-decene was purchased from Aldrich; 5-hexen-1-ol was purchased from Aldrich and protected as the known benzoate[ii] under standard conditions; methyl 2-methylhept-6-enoate[iii] was prepared according to the known procedure from methyl heptenoate.

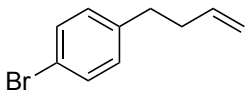
Representative Procedure for the Synthesis of Butenylated Arenes

To a flame-dried 100 mL round-bottom flask was added 4-trifluoromethylbenzyl bromide (1.0 g, 4.2 mmol, 1.0 equiv.) and 20 mL anhydrous THF. The reaction flask was cooled in an ice/water bath while under an atmosphere of nitrogen and allylmagnesium bromide was added dropwise (1.0 M in Et_2O, 8.4 mL, 8.4 mmol, 2.0 equiv.). The reaction was stirred for 2h near 0°C and then quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted 3X with CH_2Cl_2 and

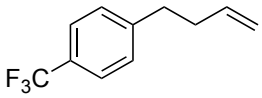
the combined organics were dried over $MgSO_4$, filtered through celite, and concentrated *in vacuo*. The crude product was purified by flash chromatography (1% → 3% EtOAc/hexanes), affording the desired product as a clear, colorless oil (0.76 g, 90%).



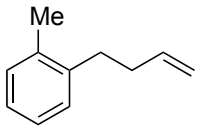
4-(4-methoxyphenyl)-1-butene: Prepared from 4-methoxybenzyl chloride according to the representative procedure as a colorless liquid (66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12-7.09 (m, 2H), 6.85-6.81 (m, 2H), 5.85 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 5.06-5.00 (m, 1H), 4.99-4.96 (m, 1H), 3.79 (s, 3H), 2.67-2.64 (m, 2H), 2.37-2.32 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 138.3, 134.1, 129.4, 115.0, 113.8, 55.4, 35.9, 34.6; IR (film, cm^{-1}): 3076, 3032, 2999, 2978, 2933, 2852, 2835, 1639, 1612, 1583, 1512, 1464, 1454, 1441, 1417, 1300, 1246, 1178, 1115, 1038, 997; HRMS (EI) *m/z* calc'd for $C_{11}H_{14}O$ $[M]^+$: 162.1045, found 162.1038.



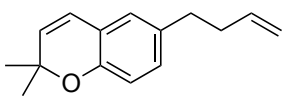
4-(4-bromophenyl)-1-butene: Prepared from 4-bromobenzyl bromide according to the representative procedure as a colorless liquid (77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 5.82 (ddt, *J* = 17.2, 10.4, 6.4 Hz, 1H), 5.06-4.96 (m, 2H), 2.68-2.64 (m, 2H), 2.34 (app q, *J* = 7.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.9, 137.7, 131.5, 130.4, 119.7, 115.4, 35.4, 34.9; IR (film, cm^{-1}): 3078, 3024, 2978, 2929, 2858, 1641, 1593, 1489, 1452, 1441, 1201, 1072, 1011; HRMS (EI) *m/z* calc'd for $C_{10}H_{11}Br$ $[M]^+$: 210.0044, found 210.0053.



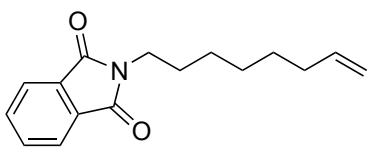
4-(4-trifluoromethylphenyl)-1-butene: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.84 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 5.05 (dd, *J* = 17.0, 1.5 Hz, 1H), 5.01 (d, *J* = 10.5 Hz, 1H), 2.79-2.76 (m, 2H), 2.40 (app q, *J* = 7.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.1, 137.5, 128.9, 128.4 (q, *J* = 32.3 Hz), 125.4 (q, *J* = 3.9 Hz), 124.5 (q, *J* = 271.5 Hz), 115.6, 35.3, 35.2; IR (film, cm^{-1}): 3080, 3047, 3008, 2983, 2933, 2860, 1643, 1620, 1443, 1417, 1327, 1165, 1124, 1068, 1020; HRMS (EI) *m/z* calc'd for $C_{11}H_{11}F_3$ $[M]^+$: 200.0813, found 200.0814.



4-(*o*-tolyl)-1-butene: Prepared from 2-methylbenzyl bromide according to the representative procedure as a colorless liquid (77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16-7.09 (m, 4H), 5.90 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 5.07 (app dq, *J* = 17.0, 1.5 Hz, 1H), 5.02-4.98 (m, 1H), 2.72-2.68 (m, 2H), 2.36-2.30 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 138.4, 136.0, 130.3, 128.9, 126.1, 126.0, 114.9, 34.4, 32.8, 19.4; IR (film, cm^{-1}): 3076, 3016, 2974, 2935, 2868, 1641, 1604, 1493, 1458, 1416, 1379, 995; HRMS (EI) *m/z* calc'd for $C_{11}H_{14}$ $[M]^+$: 146.1096, found 146.1090.

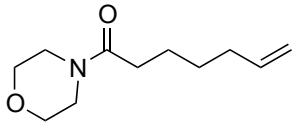


6-(but-3-en-1-yl)-2,2-dimethyl-2*H*-chromene: Prepared from 6-(bromomethyl)-2,2-dimethyl-2*H*-chromene according to the representative procedure as a colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.79 (d, *J* = 2.0 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.29 (d, *J* = 9.5 Hz, 1H), 5.85 (ddt, *J* = 16.5, 10.0, 6.5 Hz, 1H), 5.59 (d, *J* = 10.0 Hz, 1H), 5.04 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.97 (dd, *J* = 10.0, 1.0 Hz, 1H), 2.62-2.59 (m, 2H), 2.33 (app q, *J* = 7.5 Hz, 2H), 1.42 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 138.4, 134.2, 130.9, 129.0, 126.3, 122.5, 121.1, 116.2, 114.9, 76.1, 35.9, 34.7, 28.1; IR (film, cm^{-1}): 3076, 3039, 3012, 2976, 2927, 2854, 1639, 1614, 1491, 1464, 1439, 1383, 1371, 1362, 1261, 1211, 1169, 1153, 1128, 1107; HRMS (EI) *m/z* calc'd for $C_{15}H_{18}O$ $[M+]^+$: 214.1358, found 214.1361.

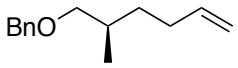


2-(oct-7-en-1-yl)isoindoline-1,3-dione: 8-bromo-1-octene (0.84 mL, 5.0 mmol, 1.0 equiv.), *N,N*-dimethylformamide (10 mL), and phthalimide potassium salt (1.02 g, 5.5 mmol, 1.1

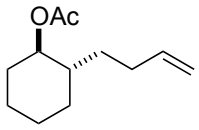
equiv.) were added sequentially to a 50 mL round-bottom flask and stirred at 60°C for 20 h. The crude reaction mixture was filtered through celite and the filtrate was partitioned between brine and Et_2O. The aqueous layer was extracted 2X with Et_2O and the combined organics were washed 2X with 1M aqueous NaOH and 3X with brine. The organics were filtered through a celite/silica plug (Et_2O) and concentrated under reduced pressure. Purification by flash chromatography (5% → 10% EtOAc/hexanes) afforded the title compound as a clear, colorless oil (1.21 g, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.5, 3.5 Hz, 2H), 7.70 (dd, *J* = 6.0, 3.5 Hz, 2H), 5.78 (ddt, *J* = 17.5, 10.5, 6.5 Hz, 1H), 4.97 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.91 (d, *J* = 10.0 Hz, 1H), 3.66 (app t, *J* = 7.3 Hz, 2H), 2.05-2.00 (m, 2H), 1.70-1.63 (m, 2H), 1.40-1.31 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 139.1, 134.0, 132.3, 123.3, 114.4, 38.2, 33.8, 28.8 (2 peaks), 28.7, 26.8; IR (film, cm^{-1}): 3074, 3032, 2976, 2931, 2856, 1772, 1714, 1639, 1616, 1466, 1437, 1396, 1369, 1338, 1188, 1053; HRMS (EI) *m/z* calc'd for $C_{16}H_{19}NO_2$ $[M]^+$: 257.1416, found 257.1413.



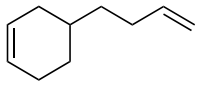
1-morpholinohept-6-en-1-one: Added 6-heptenoic acid (0.47 mL, 3.5 mmol, 1.0 equiv.), dichloromethane (15 mL), and carbonyl diimidazole (681 mg, 4.2 mmol, 1.2 equiv.) consecutively to a 40 mL borosilicate vial and stirred under an atmosphere of nitrogen at ambient temperature for 3h. Added morpholine (0.61 mL, 7.0 mmol, 2.0 equiv.) and stirred the resulting mixture overnight at ambient temperature. The crude reaction was concentrated under reduced pressure and purified directly by flash chromatography (50% → 70% EtOAc/hexanes), affording the title compound as a clear, colorless oil (331 mg, 48%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (ddt, *J* = 17.5, 10.5, 6.5 Hz, 1H), 5.01-4.97 (m, 1H), 4.93 (dd, *J* = 10.0, 1.5 Hz, 1H), 3.66-3.64 (m, 4H), 3.61-3.59 (m, 2H), 3.45-3.43 (m, 2H), 2.32-2.29 (m, 2H), 2.06 (app q, *J* = 7.0 Hz, 2H), 1.63 (app p, *J* = 7.5 Hz, 2H), 1.43 (app p, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 138.6, 114.8, 67.0, 66.8, 46.1, 42.0, 33.6, 33.0, 28.7, 24.8; IR (film, cm^{-1}): 3076, 2926, 2858, 1726, 1643, 1456, 1433, 1362, 1300, 1271, 1234, 1196, 1117, 1070, 1032, 995; HRMS (ESI) *m/z* calc'd for $C_{11}H_{19}NO_2$ $[M+H]^+$: 198.1494, found 198.1490.



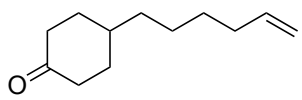
(*R*)-6-(benzyloxy)-5-methylhexene: While in the glove box, solid NaH (95%, 130 mg, 5.15 mmol, 2.5 equiv.) was added to a flame-dried 50 mL round-bottom flask. Outside of the glove box, the flask was placed under an atmosphere of nitrogen and to it was added 7 mL anhydrous THF. While being cooled in an ice/water bath, the reaction flask had neat (*R*)-2-methylhex-5-en-1-ol[iv] (235 mg, 2.06 mmol, 1.0 equiv.) added to it. Several crystals of imidazole were added and the cloudy mixture stirred at 0°C for 30 minutes. Benzyl bromide (0.24 mL, 2.06 mmol, 1.0 equiv.) and tetrabutylammonium iodide (78 mg, 0.21 mmol, 0.10 equiv.) were added successively and the reaction stirred 1.5 h at ambient temperature. The reaction was quenched with saturated aqueous NH_4Cl and the aqueous layer was extracted 3X with Et_2O. The combined organics were dried over $MgSO_4$, filtered through celite, concentrated *in vacuo*, and purified by flash chromatography (2% → 5% EtOAc/hexanes), affording the title compound as a colorless oil (190 mg, 45%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.32 (m, 4H), 7.31-7.26 (m, 1H), 5.81 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 5.00 (dd, *J* = 17.5, 2.0 Hz, 1H), 4.94 (dd, *J* = 10.0, 1.0 Hz, 1H), 4.53-4.48 (m, 2H), 3.33 (AB q, *J* = 9.0, 6.0 Hz, 1H), 3.26 (AB q, *J* = 9.0, 7.0 Hz, 1H), 2.16-2.07 (m, 1H), 2.06-1.98 (m, 1H), 1.84-1.75 (m, 1H), 1.59-1.52 (m, 1H), 1.26-1.18 (m, 1H), 0.94 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 138.9, 128.4, 127.6, 127.5, 114.4, 75.9, 73.1, 33.1, 33.0, 31.3, 17.1; IR (film, cm^{-1}): 3066, 3030, 2956, 2927, 2854, 2792, 1641, 1496, 1454, 1414, 1363, 1308, 1255, 1205, 1099, 1028, 995; HRMS (EI) *m/z* calc'd for $C_{14}H_{20}O$ $[M]^+$: 204.1514, found 204.1520. $[\alpha]_\lambda^{25}$ = -4.3 (c = 0.23, $CHCl_3$). Both the racemic and the chiral, non-racemic alcohol were converted to the Mosher esters for ^{1}H NMR analysis. The minor diastereomer was not detectable from the chiral, non-racemic alcohol, demonstrating that it had been prepared in >20:1 *dr*.



***trans*-2-(but-3-en-1-yl)cyclohexyl acetate:** The known racemic *trans*-alcohol[v] (275 mg, 1.78 mmol, 1.0 equiv.) was dissolved in 10 mL anhydrous CH_2Cl_2 and treated consecutively with 4-dimethylaminopyridine (44 mg, 0.36 mmol, 0.20 equiv.), triethylamine (0.74 mL, 5.34 mmol, 3.0 equiv.), and acetic anhydride (0.50 mL, 5.34 mmol, 3.0 equiv.). The reaction mixture stirred overnight at ambient temperature under an atmosphere of nitrogen; the crude reaction mixture was concentrated under reduced pressure and purified directly by flash chromatography (5% EtOAc/hexanes), affording the title compound as a clear, colorless oil (335 mg, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (ddt, *J* = 16.5, 10.0, 7.0 Hz, 1H), 5.00 (app dq, *J* = 17.5, 2.0 Hz, 1H), 4.95-4.92 (m, 1H), 4.49 (td, *J* = 10.0, 4.5 Hz, 1H), 2.17-2.09 (m, 1H), 2.04 (s, 3H), 2.00-1.92 (m, 2H), 1.92-1.86 (m, 1H), 1.75-1.70 (m, 1H), 1.67-1.62 (m, 1H), 1.62-1.55 (m, 1H), 1.50-1.42 (m, 1H), 1.37-1.24 (m, 2H), 1.23-1.11 (m, 2H), 0.99 (app qd, *J* = 13.0, 3.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 139.0, 114.4, 77.0, 41.4, 31.9, 31.4, 30.8, 30.1, 25.2, 24.6, 21.4; IR (film, cm^{-1}): 3078, 2995, 2976, 2935, 2860, 1738, 1641, 1450, 1371, 1242, 1032, 997; HRMS (ESI) *m/z* calc'd for $C_{12}H_{21}O_2$ $[M+H]^+$: 197.1542, found 197.1552.

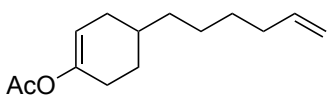


4-(but-3-en-1-yl)cyclohex-1-ene: To a solution of 3-cyclohexene-1-methanol (1.0 mL, 8.6 mmol, 1.0 equiv.) in anhydrous pyridine (10 mL) in an ice/water bath was added solid *p*TsCl (1.89 g, 9.9 mmol, 1.15 equiv.). The resulting clear, yellow solution warmed to ambient temperature and stirred overnight under an atmosphere of nitrogen. The crude mixture was then diluted with CH_2Cl_2 (50 mL) and the organic layer was washed with 1M aqueous HCl, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over Na_2SO_4, filtered through celite, concentrated under reduced pressure and the crude tosylate was used without further purification. To a flame-dried 100 mL round-bottom flask was added CuCl (171 mg, 1.7 mmol, 0.20 equiv.) and 21 mL anhydrous Et_2O. The reaction was cooled in an ice/water bath and allylmagnesium chloride (1.0 M, 17 mmol, 2.0 equiv.) was added in a dropwsie fashion. Stirred at 0°C for 10 minutes and to the resulting gray mixture was added a solution of crude tosylate in 7 mL Et_2O over several minutes. The reaction was allowed to warm to ambient temperature and stir overnight. The reaction was then carefully quenched with saturated aqueous NH_4Cl and the layers were separated and extracted 3X with Et_2O. The combined organics were dried over $MgSO_4$, filtered through celite, concentrated under reduced pressure, and purified by filtration through a silica plug (hexanes). The title compound was isolated as a pale yellow liquid (0.92 g, 79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (ddt, *J* = 17.0, 10.0, 6.5, 1H), 5.68-5.63 (m, 2H), 5.01 (app dq, *J* = 17.0, 2.0 Hz, 1H), 4.95-4.92 (m, 1H), 2.14-2.06 (m, 3H), 2.06-2.01 (2H), 1.78-1.71 (m, 1H), 1.69-1.61 (m, 1H), 1.60-1.52 (m, 1H), 1.42-1.30 (m, 2H), 1.26-1.18 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.4, 127.2, 126.7, 114.3, 36.0, 33.1, 31.9, 31.3, 29.0, 25.4; IR (film, cm^{-1}): 3078, 3022, 2976, 2914, 2848, 1641, 1454, 1435, 993; HRMS (EI) *m/z* calc'd for $C_{10}H_{16}$ $[M+H]^+$: 136.1252, found 136.1256.

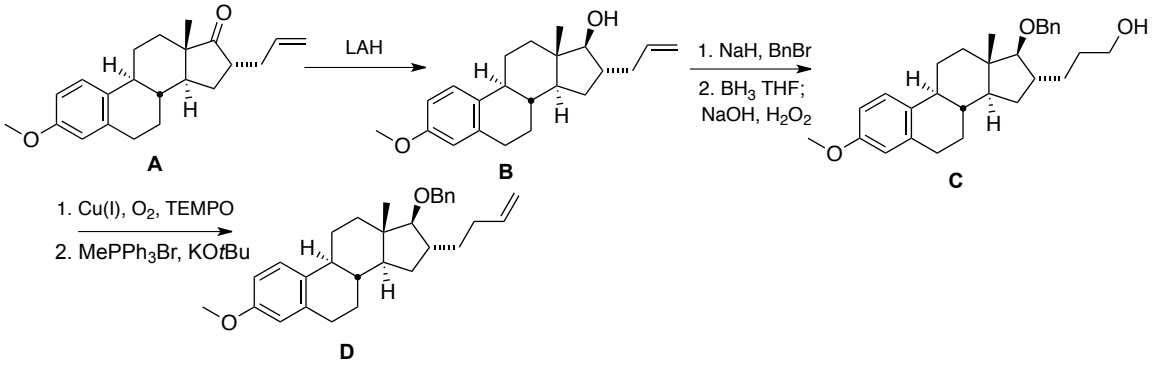


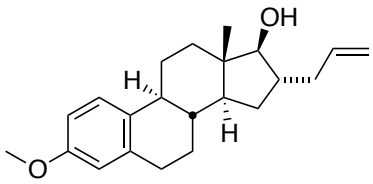
4-(hex-5-en-1-yl)cyclohexan-1-one: Solid $LiAlH_4$ (95%, 117 mg, 2.93 mmol, 0.5 equiv.) was added to a solution of 3-ethoxy-6-(hex-5-en-1-yl)cyclohexen-2-enone (1.3 g, 5.8 mmol, 1.0 equiv.) in anhydrous Et_2O (12 mL) while being cooled in an ice/water bath. The resulting mixture stirred for 5 min at 0°C and then warmed to room temperature for 30 min. The reaction was judged to be complete by ^{1}H NMR and was thereafter cooled in an ice/water bath and quenched by careful addition of 8 mL 25% H_2SO_4. After 30 min stirring the crude reaction mixture was partitioned between H_2O and Et_2O. The aqueous layer was extracted 2X with Et_2O and the combined organics were washed successively with saturated aqueous Na_2CO_3 and brine. The organics were collected, dried over $MgSO_4$, filtered through celite, and concentrated under reduced pressure. The title compound was used without further purification (0.98 g, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 4.99 (dd, *J* = 17.5, 2.0 Hz, 1H), 4.92 (d, *J* = 15.5 Hz, 1H), 2.40-2.26 (m, 4H), 2.10-1.98 (m, 4H), 1.74-1.62 (m, 1H), 1.46-1.24 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.6, 139.0, 114.5, 41.0, 36.1, 35.5, 33.8, 32.9, 29.1, 26.9; IR (film,

cm^{-1}): 3076, 2926, 2856, 1718, 1641, 1462, 1448, 1433, 1333, 1246, 1169, 1128, 993; HRMS (EI) *m/z* calc'd for $C_{12}H_{20}O$ [M+H]$^+$: 180.1514, found 180.1521.

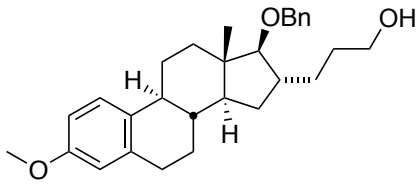


4-(hex-5-en-1-yl)cyclohex-1-en-1-yl acetate: 4-(hex-5-en-1-yl)cyclohexan-1-one (0.45 g, 2.5 mmol, 1.0 equiv) was dissolved in 25 mL isopropenyl acetate and treated with *p*TsOH (30 mg, 0.16 mmol, 0.065 equiv.). The reaction was heated to reflux for 24h, concentrated under reduce pressure, and purified by flash chromatography (hexanes → 2% EtOAc/hexanes → 5% EtOAc/hexanes), affording the title compound as a clear, colorless oil (498 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (ddt, *J* = 17.0, 10.5, 7.0 Hz, 1H), 5.33-5.32 (m, 1H), 4.99 (dd, *J* = 17.0, 2.0 Hz, 1H), 4.95-4.92 (m, 1H), 2.29-2.14 (m, 2H), 2.11 (s, 3H), 2.10-2.01 (m, 3H), 1.84-1.70 (m, 2H), 1.60-1.52 (m, 1H), 1.42-1.24 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 148.4, 139.2, 114.4, 113.6, 35.8, 33.9, 32.9, 30.2, 29.2, 28.9, 26.8, 26.7, 21.2; IR (film, cm^{-1}): 3076, 2927, 2854, 1757, 1693, 1641, 1454, 1439, 1367, 1294, 1219, 1122, 1039, 995; HRMS (ESI) *m/z* calc'd for $C_{14}H_{22}O_2Na$ [M+Na]$^+$: 245.1517, found 245.1524.



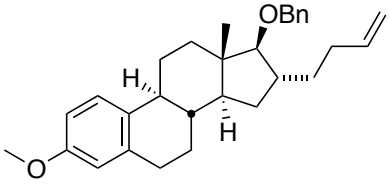


Allyl estradiol derivative B: To a solution of the known allyl estrone derivative **A**[vi] (2.70 g, 8.3 mmol) in anhydrous THF (50 mL) at -78°C was quickly added solid $LiAlH_4$ (95%, 535 mg, 13.4 mmol, 1.6 equiv.) and the reaction stirred at this temperature for 30 min. The reaction was carefully quenched by adding 0.54 mL H_2O slowly, followed by 0.54 mL 1M aqueous NaOH, and 3X 0.54 mL H_2O. The reaction was allowed to warm to ambient temperature, filtered through celite, and concentrated under reduced pressure. The resulting white foam was used without further purification in the next step (2.34 g, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 9.0 Hz, 1H), 6.71 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.63 (d, *J* = 3.0 Hz, 1H), 5.88 (ddt, *J* = 17.0, 10.5, 7.0 Hz, 1H), 5.09 (dd, *J* = 16.5, 2.0 Hz, 1H), 5.04-5.02 (m, 1H), 3.78 (s, 3H), 3.33 (d, *J* = 7.5 Hz, 1H), 2.90-2.80 (m, 2H), 2.36-2.26 (m, 2H), 2.23-2.12 (m, 2H), 1.95-1.82 (m, 3H), 1.64-1.52 (m, 2H), 1.52-1.38 (m, 3H), 1.38-1.18 (m, 3H), 0.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 138.0, 137.9, 132.7, 126.3, 115.8, 113.8, 111.5, 87.4, 55.2, 48.4, 44.1, 44.0, 43.2, 39.6, 38.6, 36.8, 29.8, 29.7, 27.3, 26.3, 12.0; IR (film, cm^{-1}): 3394 (br), 3070, 3037, 2974, 2931, 2868, 1699, 1639, 1610, 1576, 1500, 1454, 1439, 1381, 1338, 1313, 1281, 1255, 1236, 1180, 1146, 1122, 1101, 1038; HRMS (ESI) *m/z* calc'd for $C_{22}H_{31}O_2$ [M+H]$^+$: 327.2324, found 327.2316. $[\alpha]_\lambda^{25}$ = +36.5 (c = 1.14, $CHCl_3$).



Benzyloxy estradiol derivative C: To a solution of the 2° alcohol **B** (2.30 g, 7.0 mmol, 1.0 equiv.) in anhydrous THF (25 mL) in a flame-dried 100 mL round-bottom flask at 0°C was added NaH (60% in mineral oil, 840 mg, 21.0 mmol, 3.0 equiv.). The reaction stirred 30 min at 0°C and neat

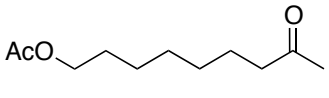
benzyl bromide (2.08 mL, 17.5 mmol, 2.5 equiv.) and solid tetrabutylammonium iodide (259 mg, 0.70 mmol, 0.10 equiv.) were added. The reaction stirred overnight at room temperature, and was then heated to reflux for 18h due to incomplete conversion of starting material. After reflux, the reaction cooled to room temperature and was partitioned between EtOAc and H_2O and the organic layer was washed 3X with H_2O. The organic layer was collected, dried over $MgSO_4$, filtered through celite, and concentrated *in vacuo*. The crude product was purified by flash chromatography (hexanes → 2% EtOAc/hexanes → 5% EtOAc/hexanes), but was only isolated in ~80% purity and used directly in the next step. To a solution of the benzyloxy allyl derivative (1.87 g, 4.5 mmol, 1.0 equiv.) in anhydrous THF (40 mL) at 0°C was added 1.0M BH_3-THF (4.5 mL, 4.5 mmol, 1.0 equiv.) dropwise. The resulting mixture stirred at this temperature under an atmosphere of argon for 1.5h and was carefully quenched with 1.5 mL 3M aqueous NaOH, followed by 0.60 mL 30% aqueous H_2O_2. The quenched reaction stirred at ambient temperature for 1.5h and was partitioned between H_2O and EtOAc. The aqueous layer was extracted 3X with EtOAc and the combined organics were dried over $MgSO_4$, filtered through celite, concentrated *in vacuo*, and purified by flash chromatography (20% → 40% EtOAc/hexanes). The primary alcohol was isolated as a white solid (1.10 g, 56%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.32 (m, 4H), 7.10-7.26 (m, 1H), 7.20 (d, *J* = 9.0 Hz, 1H), 6.72 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.63 (d, *J* = 3.0 Hz, 1H), 4.74 (d, *J* = 11.5 Hz, 1H), 4.51 (d, *J* = 11.5 Hz, 1H), 3.78 (s, 3H), 3.68-3.59 (m, 2H), 3.17 (d, *J* = 7.5 Hz, 1H), 2.91-2.90 (m, 2H), 2.33-2.25 (m, 1H), 2.23-2.14 (m, 1H), 2.13-2.08 (m, 1H), 2.02-1.94 (m, 1H), 1.88-1.82 (m, 1H), 1.66-1.50 (m, 6H), 1.50-1.38 (m, 2H), 1.38-1.24 (m, 4H), 0.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 139.1, 138.1, 132.7, 128.5, 127.9, 127.6, 126.4, 113.9, 111.6, 95.4, 73.1, 63.3, 55.3, 48.9, 44.8, 43.9, 41.6, 39.0, 38.6, 32.3, 31.5, 30.0 (2 peaks), 27.3, 26.6, 12.7; IR (film, cm^{-1}): 3417 (br), 2931, 2864, 1610, 1576, 1498, 1452, 1381, 1352, 1313, 1281, 1255, 1238, 1142, 1093, 1074, 1039; HRMS (ESI) *m/z* calc'd7 for $C_{29}H_{39}O_3$ $[M+H]^+$: 435.2899, found 435.2897. $[\alpha]_\lambda^{25}$ = -21.5 (c = 0.26, $CHCl_3$).



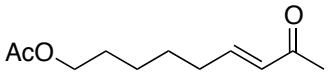
Benzyloxy estradiol butene derivative D: The primary alcohol was oxidized according to the procedure of Hoover and Stahl.[vii] The primary alcohol (1.1 g, 2.5 mmol, 1.0 equiv.), *N*-methyl imidazole (19.9 μL, 0.25 mmol, 0.10 equiv.), bipyridine (19.5 mg, 0.125 mmol, 0.05 equiv.), $[Cu(CH_3CN)_4]PF_6$ (46.6 mg, 0.125 mmol, 0.05 equiv.), and TEMPO (19.5 mg, 0.125 mmol, 0.05 equiv.) were each dissolved in 3 mL CH_3CN and added successively to a 100 mL round-bottom flask. The mixture was stirred at ambient temperature under an atmosphere of O_2 for 8h, at which point TLC analysis indicated complete consumption of starting material. The crude reaction was filtered through a pad of silica (1:1 Et_2O:hexanes) and the filtrate was concentrated under reduce pressure. The resulting aldehyde was used immediately in the next step (1.0 g, 93%). To a flame-dried 3-necked 100 mL round-bottom flask was added $MePPh_3Br$ (3.29 g, 9.2 mmol, 4.0 equiv.) and 8 mL anhydrous THF. The flask was cooled in an ice/water bath while under an atmosphere of N_2 and solid K*o*tBu (95%, 980 mg, 9.3 mmol, 3.6 equiv.) was added quickly; the resulting yellow mixture stirred at 0°C for 1h and the estrone-derived aldehyde was added as a solution in 6 mL anhydrous THF. After stirring 1h at 0°C, the reaction was quenched with saturated aqueous NH_4Cl and allowed to warm to ambient temperature. The reaction was partitioned between water and CH_2Cl_2 and extracted 3X with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered through celite, concentrated *in vacuo*, and purified by flash chromatography (2% EtOAc/hexanes → 5% EtOAc/hexanes). The title compound was isolated as a white solid (0.90 g, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.33 (m, 4H), 7.30-7.25 (m, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 6.71 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.63 (d, *J* = 2.5 Hz, 1H), 5.83 (ddt, *J* = 17.0, 10.5, 6.5 Hz, 1H), 5.00 (dd, *J* = 17.5, 2.0 Hz, 1H), 4.95-4.92 (m, 1H), 4.73 (d, *J* = 11.5 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 3.16 (d, *J* = 7.0 Hz, 1H), 2.91-2.80 (m, 2H), 2.32-2.26 (m, 1H), 2.23-2.16 (m, 1H), 2.15-2.06 (m, 2H), 2.06-2.00 (m, 1H), 2.00-1.92 (m, 1H), 1.90-1.83 (m, 1H), 1.73-1.65 (m, 1H), 1.62-1.48 (m, 3H), 1.48-1.38 (m, 1H),

1.38-1.22 (m, 4H), 0.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 139.3, 138.1, 132.8, 128.4, 127.8, 127.6, 126.4, 114.3, 113.9 (2 peaks), 111.6, 95.4, 73.1, 55.4, 48.9, 44.7, 44.0, 41.7, 39.0, 38.7, 35.4, 32.8, 30.0, 29.8, 27.3, 26.6, 12.7; IR (film, cm^{-1}): 3068, 3030, 2974, 2929, 2866, 2846, 1639, 1610, 1576, 1498, 1452, 1381, 1352, 1313, 1281, 1255, 1238, 1207, 1180, 1138, 1124, 1099, 1039, 995; HRMS (EI) *m/z* calc'd for $C_{30}H_{38}O_2$ $[M]^+$: 430.2872, found 430.2876. $[\alpha]_\lambda^{25}$ = -8.8 (c = 0.75, $CHCl_3$).

Table 1 Products

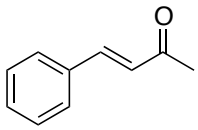


8-oxononyl acetate: non-8-en-1-yl acetate was reacted according to a modified version of the general procedure, excluding $PhI(Oac)_2$ and only stirring at 35°C for 18 h. Purification by flash chromatography (10% → 20% EtOAc/hexanes) afforded the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.04 (t, *J* = 7.0 Hz, 2H), 2.42 (t, *J* = 7.5 Hz, 2H), 2.13 (s, 3H), 2.04 (s, 3H), 1.64-1.53 (m, 4H), 1.38-1.24 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 171.3, 64.6, 43.7, 30.0, 29.1, 28.6, 25.8, 23.7, 21.1; IR (film, cm^{-1}): 2935, 2858, 1738, 1716, 1464, 1433, 1412, 1387, 1365, 1242, 1163, 1038; HRMS (ESI) *m/z* calc'd for $C_{11}H_{21}O_3$ $[M+H]^+$: 201.1491, found 201.1492.

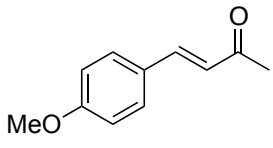


(*E*)-8-oxonon-6-en-1-yl acetate: non-8-en-1-yl acetate (55.3 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (10% → 20% EtOAc/hexanes) afforded the title compound as a colorless oil. Run 1 (32.5 mg, 0.164 mmol, 55% yield); run 2 (32.6 mg, 0.164 mmol, 55% yield). **Average yield: 55%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (dt, *J* = 16.0, 6.5 Hz, 1H), 6.07 (d, *J* = 16.0 Hz, 1H), 4.05 (t, *J* = 6.5 Hz, 2H), 2.24 (s, 3H), 2.26-2.21 (m, 2H), 2.04 (s, 3H), 1.64 (p, *J* = 7.0 Hz, 2H), 1.51 (p, *J* = 7.0 Hz, 2H), 1.39 (p, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 171.3, 148.1, 131.5, 64.3, 32.3, 28.4, 27.8, 27.0, 25.6, 21.1; IR (film, cm^{-1}): 2937, 2862, 1739, 1697, 1676, 1628, 1462, 1433, 1387, 1365, 1250, 1045, 982; HRMS (ESI) *m/z* calc'd for $C_{11}H_{19}O_3$ $[M+H]^+$: 199.1334, found 199.1338.

Table 2 Products

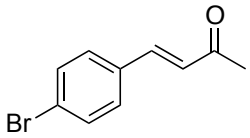


(*E*)-4-phenylbut-3-en-2-one: 4-phenyl-1-butene (66.1 mg, 0.50 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 10% EtOAc/hexanes) afforded the title compound as a pale yellow oil. Run 1 (49.0 mg, 0.335 mmol, 67% yield); run 2 (49.6 mg, 0.339 mmol, 68% yield). **Average yield: 68%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.52 (d, *J* = 16.0 Hz, 1H), 7.41-7.39 (m, 3H), 6.72 (d, *J* = 16.5 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 143.5, 134.5, 130.6, 129.0, 128.3, 127.2, 27.6; IR (film, cm^{-1}): 3082, 3062, 3043, 3028, 1691, 1668, 1624, 1610, 1576, 1495, 1450, 1423, 1358, 1329, 1294, 1257, 1205, 1182, 976; HRMS (ESI) *m/z* calc'd for $C_{10}H_{11}O$ $[M+H]^+$: 147.0810, found 147.0813.

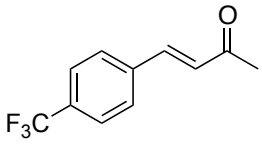


(*E*)-4-(4-methoxyphenyl)but-3-en-2-one: 4-(4-methoxyphenyl)-1-butene (81.1 mg, 0.50 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 15% → 25% EtOAc/hexanes) afforded the title compound as an off-white solid. Run 1 (59.9 mg, 0.340 mmol, 68% yield); run 2 (61.2 mg, 0.347 mmol, 69% yield). **Average yield: 69%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.46 (m, 3H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.61 (d, *J* = 16.0 Hz, 1H), 3.85 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.6, 161.7, 143.4, 130.1, 127.2, 125.2, 114.6, 55.6, 27.6; IR (film, cm^{-1}): 3045, 3005, 2958, 2941,

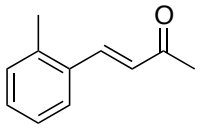
2914, 2846, 1682, 1601, 1574, 1512, 1464, 1423, 1360, 1302, 1250, 1174, 1109, 1022, 989; HRMS (ESI) *m/z* calc'd for $C_{11}H_{13}O_2$ $[M+H]^+$: 177.0916, found 177.0919.



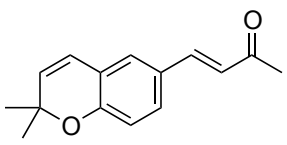
(*E*)-4-(4-bromophenyl)but-3-en-2-one: 4-(4-bromophenyl)-1-butene (63.3 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 15% → 25% EtOAc/hexanes) afforded the title compound as an off-white solid. Run 1 (43.1 mg, 0.191 mmol, 64% yield); run 2 (41.7 mg, 0.185 mmol, 62% yield). **Average yield: 63%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 16.5 Hz, 1H), 7.40 (d, *J* = 14.0 Hz, 2H), 6.70 (d, *J* = 16.0 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.2, 124.1, 133.5, 132.4, 129.8, 127.7, 124.9, 27.9; IR (film, cm^{-1}): 3055, 3020, 2970, 2927, 2856, 1658, 1637, 1608, 1585, 1486, 1417, 1402, 1361, 1261, 1074, 1009, 978; HRMS (ESI) *m/z* calc'd for $C_{10}H_{10}OBr$ $[M+H]^+$: 224.9915, found 224.9917.



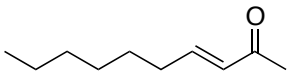
(*E*)-4-(4-(trifluoromethyl)phenyl)but-3-en-2-one: 4-(4-(trifluoromethyl) phenyl)-1-butene (60.1 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (10% → 20% EtOAc/hexanes) afforded the title compound as a white solid. Run 1 (38.7 mg, 0.181 mmol, 60% yield); run 2 (40.1 mg, 0.187 mmol, 62% yield). **Average yield: 61%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.63 (m, 3H), 7.52 (d, *J* = 16.5 Hz, 1H), 6.77 (d, *J* = 16.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 141.4, 138.0, 132.1 (q, *J* = 33.3 Hz), 129.2, 128.5, 126.0 (q, *J* = 3.9 Hz), 123.9 (q, *J* = 272.5 Hz), 27.9; IR (film, cm^{-1}): 3051, 3022, 2964, 2926, 1689, 1668, 1616, 1577, 1416, 1362, 1327, 1259, 1207, 1171, 1130, 1113, 1068, 1018, 982; HRMS (ESI) *m/z* calc'd for $C_{11}H_{10}OF_3$ $[M+H]^+$: 215.0684, found 215.0688.



(*E*)-4-(*o*-tolyl)but-3-en-2-one: 4-(*o*-tolyl)-1-butene (73.1 mg, 0.50 mmol) was reacted according to the general procedure. Purification by flash chromatography (2% → 5% EtOAc/hexanes) afforded the title compound as a yellow oil. Run 1 (49.1 mg, 0.306 mmol, 61% yield); run 2 (51.0 mg, 0.318 mmol, 64% yield). **Average yield: 63%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 16.5 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 2H), 6.65 (d, *J* = 16.0 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.4, 140.9, 137.9, 133.4, 130.9, 130.3, 128.2, 126.5 (2 peaks), 27.9, 19.8; IR (film, cm^{-1}): 3055, 3026, 2972, 2956, 2926, 2870, 1691, 1670, 1645, 1612, 1599, 1485, 1462, 1425, 1360, 1315, 1296, 1257, 1221, 1178, 976; HRMS (ESI) *m/z* calc'd for $C_{11}H_{13}O$ $[M+H]^+$: 161.0966, found 161.0964.

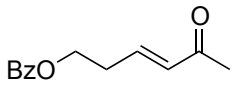


(*E*)-4-(2,2-dimethyl-2*H*-chromen-6-yl)but-3-en-2-one: 6-(but-3-en-1-yl)-2,2-dimethyl-2*H*-chromene (64.3 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 10% EtOAc/hexanes) afforded the title compound as a pale yellow oil. Run 1 (44.6 mg, 0.195 mmol, 65% yield); run 2 (44.6 mg, 0.195 mmol, 65% yield). **Average yield: 65%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 16.5 Hz, 1H), 7.31 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.18 (d, *J* = 2.0 Hz, 1H), 6.78 (d, *J* = 8.5 Hz, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 6.32 (d, *J* = 10.0 Hz, 1H), 5.66 (d, *J* = 10.0 Hz, 1H), 2.35 (s, 3H), 1.45 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 155.5, 143.5, 131.6, 129.9, 127.2, 126.4, 124.9, 121.8, 121.5, 117.0, 77.3, 28.4, 27.6; IR (film, cm^{-1}): 3039, 3024, 2974, 2929, 1687, 1664, 1641, 1616, 1601, 1572, 1491, 1429, 1362, 1325, 1273, 1254, 1213, 1155, 1128, 1107, 978; HRMS (ESI) *m/z* calc'd for $C_{15}H_{17}O_2$ $[M+H]^+$: 229.1229, found 229.1234.

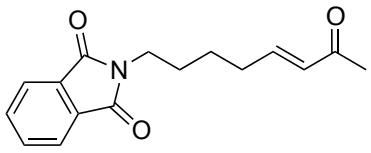


(*E*)-dec-3-en-2-one: 1-decene (70.1 mg, 0.50 mmol) was reacted according to the general procedure. Purification by flash chromatography (1% → 3% → 5% EtOAc/petroleum ether) afforded

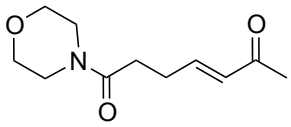
the title compound as a pale yellow oil. Run 1 (46.8 mg, 0.303 mmol, 61% yield); run 2 (45.9 mg, 0.298 mmol, 60% yield). **Average yield: 61%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (dt, *J* = 16.5, 6.5 Hz, 1H), 6.07 (d, *J* = 16.0 Hz, 1H), 2.24 (s, 3H), 2.24-2.20 (m, 2H), 1.50-1.42 (m, 2H), 1.35-1.25 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.9, 148.8, 131.4, 32.6, 31.7, 29.0, 28.2, 26.9, 22.6, 14.2; IR (film, cm^{-1}): 2956, 2929, 1699, 1678, 1628, 1466, 1431, 1362, 1254, 1282, 1254, 1176, 978; HRMS (ESI) *m/z* calc'd for $C_{10}H_{19}O$ $[M+H]^+$: 155.1436, found 155.1435. A 1.0 mmol reaction (140.2 mg 1-decene) performed according to the standard conditions led to a comparable yield of α,β-unsaturated ketone product (89.0 mg, 0.578 mmol, 58% yield).



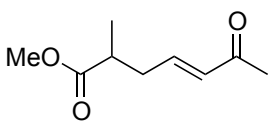
(*E*)-5-oxohex-3-en-1-yl benzoate: hex-5-en-1-yl benzoate (61.3 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 15% → 25% EtOAc/petroleum ether) afforded the title compound as a pale yellow oil. Run 1 (36.0 mg, 0.165 mmol, 55% yield); run 2 (34.4 mg, 0.158 mmol, 53% yield). **Average yield: 54%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 6.84 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.21 (d, *J* = 16.0 Hz, 1H), 4.46 (t, *J* = 6.0 Hz, 2H), 2.71 (qd, *J* = 6.0, 1.0 Hz, 2H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 166.5, 143.1, 133.3, 133.2, 130.0, 129.6, 128.5, 62.8, 31.9, 27.1; IR (film, cm^{-1}): 3062, 3033, 3006, 2960, 2904, 1720, 1699, 1678, 1630, 1603, 1452, 1427, 1362, 1315, 1275, 1176, 1117, 1070, 1026, 976; HRMS (ESI) *m/z* calc'd for $C_{13}H_{14}O_3Na$ $[M+Na]^+$: 241.0841, found 241.0846.



(*E*)-2-(7-oxooct-5-en-1-yl)isoindoline-1,3-dione: 2-(oct-7-en-1-yl)isoindoline-1,3-dione (77.2, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (15% → 25% → 35% EtOAc/petroleum ether) afforded the title compound as a white solid. Run 1 (46.0 mg, 0.170 mmol, 57% yield); run 2 (46.5 mg, 0.171 mmol, 57% yield). **Average yield: 57%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87-7.83 (m, 2H), 7.74-7.70 (m, 2H), 6.76 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.07 (d, *J* = 16.0 Hz, 1H), 3.71 (t, *J* = 7.0 Hz, 2H), 2.28 (q, *J* = 7.0 Hz, 2H), 2.23 (s, 3H), 1.73 (p, *J* = 7.0 Hz, 2H), 1.56-1.50 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 168.5, 147.5, 134.1, 132.2, 131.8, 123.4, 37.7, 32.0, 28.3, 27.0, 25.4; IR (film, cm^{-1}): 3055, 3026, 2972, 2937, 2883, 2864, 1772, 1711, 1670, 1628, 1466, 1437, 1398, 1363, 1335, 1255, 1232, 1219, 1188, 1173, 1039, 984; HRMS (ESI) *m/z* calc'd for $C_{16}H_{18}NO_3$ $[M+H]^+$: 272.1287, found 272.1290.

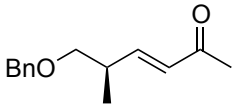


(*E*)-1-morpholinohept-4-ene-1,6-dione: 1-morpholinohept-6-en-1-one (59.2 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (20% → 40% acetone/hexanes) afforded the title compound and the corresponding Wacker product as an inseparable mixture. Further chromatography provided a nearly pure sample of the title compound for characterization as a colorless oil. Run 1 (34.7 mg, 0.164 mmol, 55% yield); run 2 (32.5 mg, 0.154 mmol, 51% yield). **Average yield: 53%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (dt, *J* = 16.0, 6.5 Hz, 1H), 6.10 (d, *J* = 16.5 Hz, 1H), 3.69-3.67 (m, 4H), 3.64-3,62 (m, 2H), 3.47-3.45 (m, 2H), 2.59 (q, *J* = 6.5 Hz, 2H), 2.48 (t, *J* = 7.5 Hz, 2H). 2.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 170.0, 146.8, 131.9, 67.0, 66.6, 45.9, 42.1, 31.3, 27.6, 27.1; IR (film, cm^{-1}): 2960, 2924, 2912, 2856, 1695, 1672, 1647, 1460, 1439, 1362, 1300, 1271, 1255, 1236, 1194, 1117, 1070, 1028; HRMS (ESI) *m/z* calc'd for $C_{11}H_{18}NO_3$ $[M+H]^+$: 212.1287, found 212.1289.

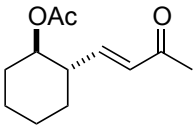


(±)-(*E*)-methyl 2-methyl-6-oxohept-4-enoate: methyl 2-methylhept-6-enoate (78.1 mg, 0.50 mmol) was reacted according to the general procedure. Purification by flash chromatography (10% → 20%

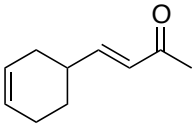
EtOAc/hexanes) afforded the title compound as a colorless oil. Run 1 (47.4 mg, 0.279 mmol, 56% yield); run 2 (47.4 mg, 0.279 mmol, 56% yield). **Average yield: 56%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.72 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.09 (d, *J* = 15.5 Hz, 1H), 3.69 (s, 3H), 2.67-2.60 (m, 1H), 2.60-2.55 (m, 1H), 2.38-2.32 (m, 1H), 2.24 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.4, 175.8, 144.6, 133.0, 51.9, 38.6, 36.2, 27.1, 17.0; IR (film, cm^{-1}): 2978, 2954, 2881, 2846, 1738, 1699, 1676, 1630, 1460, 1435, 1362, 1255, 1211, 1196, 1171, 1126, 1092, 1063, 1022, 984; HRMS (ESI) *m/z* calc'd for $C_9H_{15}O_3$ $[M+H]^+$: 171.1021, found 171.1027.



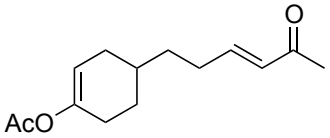
(*R*,*E*)-6-(benzyloxy)-5-methylhex-3-en-2-one: (*R*)-6-(benzyloxy)-5-methylhexene (61.3 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 10% → 20% EtOAc/hexanes) afforded the title compound as a colorless oil. Run 1 (40.1 mg, 0.184 mmol, 61%); run 2 (40.1 mg, 0.184 mmol, 61%. **Average yield: 61%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 6.79 (dd, *J* = 16.0, 7.0 Hz, 1H), 6.11 (dd, *J* = 16.0 Hz, 1.0 Hz, 1H), 4.52 (s, 2H), 3.42 (d, *J* = 6.0 Hz, 2H), 2.68 (septet, *J* = 7.0 Hz, 1H), 2.25 (s, 3H), 1.10 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.0, 150.5, 138.2, 130.7, 128.5, 127.8, 127.7, 74.0, 73.2, 37.1, 27.0, 16.2; IR (film, cm^{-1}): 3064, 3030, 3005, 2966, 2933, 2860, 2796, 1697, 1676, 1628, 1496, 1454, 1425, 1360, 1309, 1255, 1205, 1184, 1155, 1097, 1028, 984; HRMS (ESI) *m/z* calc'd for $C_{14}H_{19}O_2$ $[M+H]^+$: 219.1385, found 219.1388. $[\alpha]_\lambda^{25}$ = +1.5 (c = 0.13, $CHCl_3$). The product was analyzed by chiral GC (Astec CHIRALDEX GT-A, 120°C isothermal); major enantiomer t_R = 109.9 min, minor enantiomer t_R = 107.8 min. *er* = 98.4:1.6. Racemic sample: t_R = 108.0, t_R = 110.1.



(±)-*trans*-2-((*E*)-3-oxobut-1-en-1-yl)cyclohexyl acetate: *trans*-2-(but-3-en-1-yl)cyclohexyl acetate (58.9 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 15% → 25% EtOAc/hexanes) afforded the title compound as a colorless oil. Run 1 (40.9 mg, 0.195 mmol, 65%); run 2 (41.4 mg, 0.197 mmol, 66%. **Average yield: 66%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.03 (d, *J* = 16.0 Hz, 1H), 4.66 (td, *J* = 10.0, 4.5 Hz, 1H), 2.32-2.25 (m, 1H), 2.22 (s, 3H), 2.04-1.99 (m, 1H), 1.97 (s, 3H), 1.84-1.78 (m, 2H), 1.75-1.69 (m, 1H), 1.40-1.22 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.9, 170.6, 149.0, 131.8, 74.8, 46.7, 31.5, 30.8, 26.8, 24.6, 24.4, 21.3; IR (film, cm^{-1}): 2935, 2860, 1736, 1699, 1678, 1628, 1450, 1435, 1373, 1238, 1032, 982; HRMS (ESI) *m/z* calc'd for $C_{12}H_{18}O_3Na$ $[M+Na]^+$: 233.1154, found 233.1162.

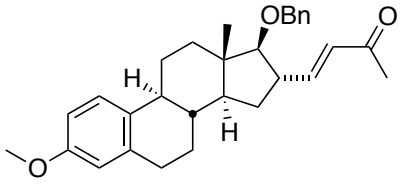


(±)-(*E*)-4-(cyclohex-3-en-1-yl)but-3-en-2-one: 4-(but-3-en-1-yl)cyclohex-1-ene (68.1 mg, 0.50 mmol) was reacted according to the general procedure. Purification by flash chromatography (1% → 3% → 5% EtOAc/hexanes) afforded the title compound as a colorless oil. Run 1 (45.2 mg, 0.301 mmol, 60%); run 2 (43.8 mg, 0.292 mmol, 58%). **Average yield: 59%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.79 (dd, *J* = 16.0, 7.0 Hz, 1H), 6.08 (dd, *J* = 16.5 Hz, 1.0 Hz, 1H), 5.74-5.65 (m, 2H), 2.50-2.42 (m, 1H), 2.25 (s, 3H), 2.20-2.14 (m, 1H), 2.13-2.07 (m, 2H), 1.97-1.89 (m, 1H), 1.87-1.81 (m, 1H), 1.52-1.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.1, 152.4, 129.5, 127.1, 125.3, 36.7, 30.3, 27.7, 27.0, 24.5; IR (film, cm^{-1}): 3024, 2916, 2856, 2839, 1697, 1676, 1626, 1452, 1437, 1363, 1317, 1254, 1205, 1176, 1140, 982; HRMS (ESI) *m/z* calc'd for $C_{10}H_{15}O$ $[M+H]^+$: 151.1123, found 151.1131.

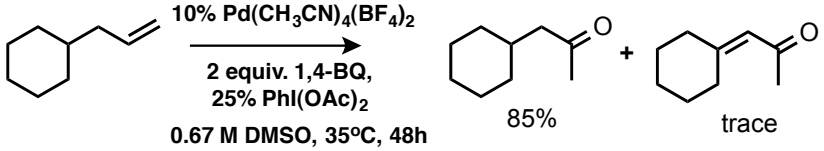


(±)-(*E*)-4-(5-oxohex-3-en-1-yl)cyclohex-1-en-1-yl acetate: 4-(hex-5-en-1-yl)cyclohex-1-en-1-yl acetate (66.7 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 15% EtOAc/hexanes) afforded the title compound as a colorless oil. Run 1 (36.6 mg, 0.155 mmol, 52%); run 2 (35.0 mg, 0.148 mmol, 49%). **Average yield: 51%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80

(dt, *J* = 16.0, 6.5 Hz, 1H), 6.08 (d, *J* = 16.0 Hz, 1H), 5.33-5.32 (m, 1H), 2.30-2.18 (m, 4H), 2.24 (s, 3H), 2.11 (s, 3H), 2.09-2.05 (m, 1H), 1.86-1.74 (m, 2H), 1.66-1.58 (m, 1H), 1.52-1.37 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 169.6, 148.4, 148.2, 131.5, 113.2, 34.1, 32.5, 30.2, 30.0, 28.7, 27.0, 26.5, 21.2; IR (film, cm^{-1}): 3005, 2918, 2852, 1755, 1695, 1674, 1626, 1454, 1435, 1365, 1254, 1223, 1159, 1149, 1122, 1041, 982; HRMS (ESI) *m/z* calc'd for $C_{14}H_{20}O_3Na$ $[M+Na]^+$: 259.1310, found 259.1320.

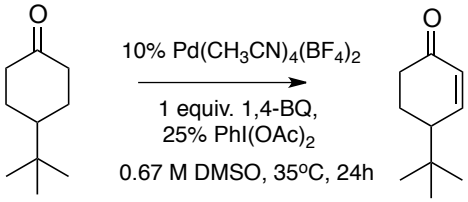


α,β-unsaturated ketone 19: estradiol derivative **D** (86.1 mg, 0.20 mmol) was reacted according to the general procedure. Purification by flash chromatography (5% → 10% acetone/hexanes) afforded Wacker product and the title compound as colorless residues. Wacker product (run 1: 26.0 mg, 0.060 mmol; run 2: 34.5 mg, 0.080 mmol) was re-exposed to the standard reaction conditions (reagents scaled accordingly) and the combined yield of the title compound was reported in Table 2: Run 1 (51.5 mg, 0.116 mmol, 58%); run 2 (48.8 mg, 0.110 mmol, 55%). **Average yield: 57%.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 7.20 (d, *J* = 8.5 Hz, 1H), 6.79 (dd, *J* = 16.0, 8.5 Hz, 1H), 6.72 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.63 (d, *J* = 2.5 Hz, 1H), 6.09 (d, *J* = 16.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 3.36 (d, *J* = 7.5 Hz, 1H), 2.92-2.77 (m, 3H), 2.34-2.29 (m, 1H), 2.24-2.18 (m, 1H), 2.22 (s, 3H), 2.12-2.08 (m, 1H), 1.86-1.75 (m, 2H), 1.62-1.57 (m, 1H), 1.55-1.50 (m, 1H), 1.50-1.40 (m, 2H), 1.38-1.29 (m, 2H), 0.94 (s, 3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 157.7, 152.0, 138.7, 138.0, 132.4, 129.9, 128.5, 127.9, 127.8, 126.4, 114.0, 111.7, 93.3, 72.9, 55.4, 55.3, 49.2, 45.5, 44.8, 44.0, 38.6, 38.3, 30.5, 29.9, 27.2, 26.5, 12.7; IR (film, cm^{-1}): 2945, 2904, 2873, 2846, 1695, 1672, 1620, 1576, 1498, 1454, 1433, 1358, 1313, 1282, 1254, 1240, 1207, 1178, 1142, 1122, 1099, 1043, 1032, 980; HRMS (ESI) *m/z* calc'd for $C_{30}H_{37}O_3$ $[M+H]^+$: 445.2743, found 445.2737. $[\alpha]_\lambda^{25}$ = + 22.1 (c = 0.19, $CHCl_3$).



Allylcyclohexane (12.4 mg, 0.10 mmol) was reacted according to the general procedure including 40 mol% nitrobenzene as internal standard and the reaction was analyzed by GC. GC analysis revealed complete conversion to the Wacker product (85% uncorrected GC yield), with only trace quantities of the α,β-unsaturated ketone **20** detectable (this product was synthesized from cyclohexanone using a Horner-Wadsworth Emmons reagent[viii]).

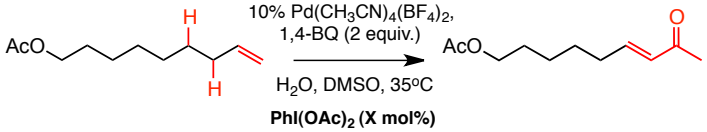
Equation 1



4-*tert*-butylcyclohexanone (46.2 mg, 0.30 mmol) was reacted according to a modification of the general procedure, including a single equivalent of 1,4-benzoquinone, stirring the reaction at 35°C for 24h, instead of 48h, and excluding H_2O. Purification by flash chromatography (10% EtOAc/hexanes) afforded a mixture of the product and 4-*tert*-butylphenol as a colorless oil. Run 1 (7.5:1 product: 4-*tert*-butylphenol, 38.3 mg product, 84%); run 2 (8.7:1 product: 4-*tert*-butylphenol, 34.1 mg product, 75%). **Average yield: 80%.**

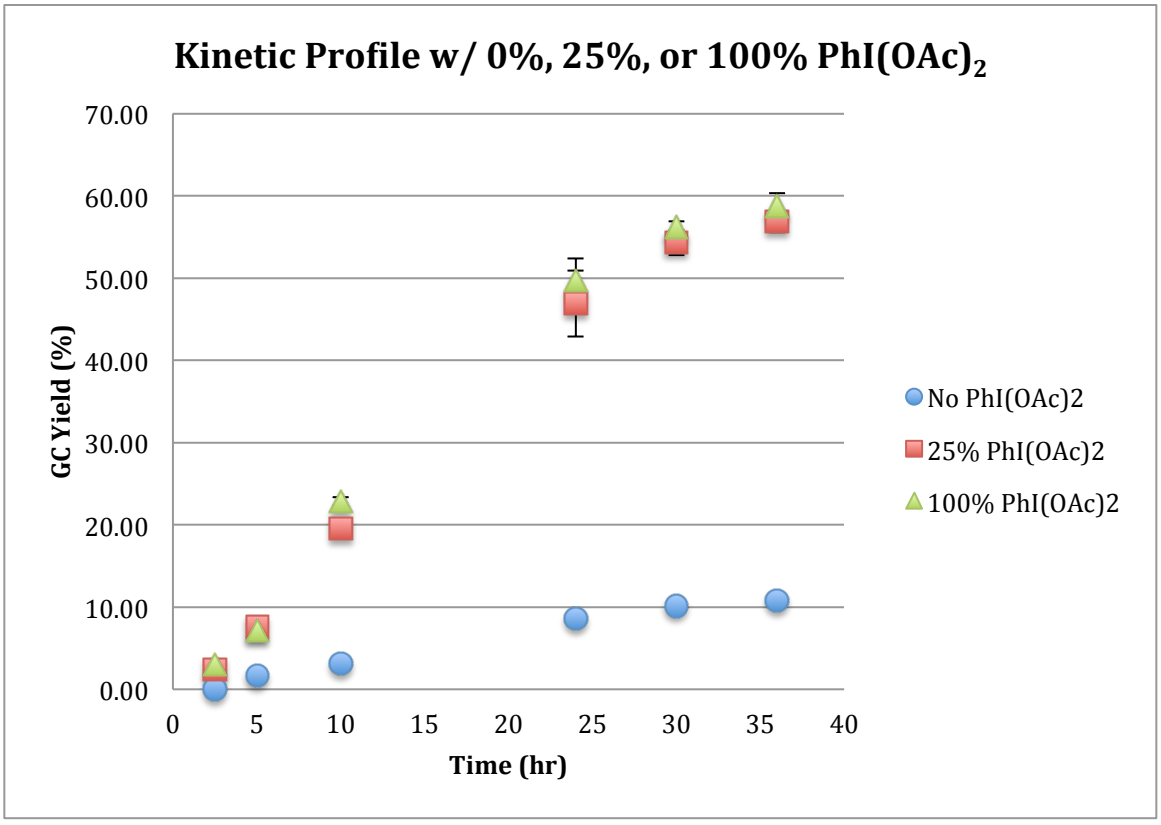
Figure SI 1: Kinetic Profile

Figure 2. Overall kinetic profile



General procedure was followed for terminal olefin **1**, including either 0 mol%, 25 mol%, or 100 mol% $PhI(OAc)_2$. The reaction was monitored by GC analysis, with measurements taken at 2.5 h, 5h, 10h, 24h, 30h, and 36h. Results are reported as the average of three runs, with yields calculated with respect to a standard curve, including error bars for the calculated standard deviation. At 2.5h timepoint, terminal olefin had been completely consumed in each case, leading to ~90% yield of the Wacker product **2**.

Time (hr)	**2.5**	**5**	**10**	**24**	**30**	**36**
No PhI(OAc)2						
Run 1 GC Yield	0.00	1.80	3.30	8.70	10.80	10.50
Run 2 GC Yield	0.00	1.50	3.00	8.40	9.60	11.10
Run 3 GC Yield	0.00	1.70	3.20	8.60	10.00	10.80
Average GC Yield	0.00	1.67	3.17	8.57	10.13	10.80
std dev	0.00	0.15	0.15	0.15	0.61	0.30
25% PhI(OAc)2						
Run 1 GC Yield	2.70	7.20	18.40	46.40	52.70	55.40
Run 2 GC Yield	2.40	7.80	20.80	51.20	55.70	57.50
Run 3 GC Yield	2.30	7.80	19.40	43.20	54.60	57.80
Average GC Yield	2.47	7.60	19.53	46.93	54.33	56.90
std dev	0.21	0.35	1.21	4.03	1.52	1.31
100% PhI(OAc)2						
Run 1 GC Yield	3.30	7.50	22.90	52.70	56.90	60.20
Run 2 GC Yield	3.00	7.20	22.30	49.10	56.30	57.20
Run 3 GC Yield	2.70	6.90	23.30	47.40	55.40	59.00
Average GC Yield	3.00	7.20	22.83	49.73	56.20	58.80
std dev	0.30	0.30	0.50	2.71	0.75	1.51



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