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, Phl(OAc)₂]. Pd(CH₃CN)₄(BF₄)₂ was prepared according to the published procedure as a pale yellow powder and was stored in a glove box under an argon atmosphere. Alternatively, Pd(CH₃CN)₄(BF₄)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 O₂ 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.). \(^1\)H 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 (CDCl₃ 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 (CDCl₃ 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: [α]D, °C (c = g/100 mL, solvent).

Preparation of Pd(CH₃CN)₄(BF₄)₂

While in the glove box under an atmosphere of argon, Pd sponge (250 mg, 2.35 mmol, 1.0 equiv.) was weighed 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 CH₃CN. To the resulting fine gray suspension was quickly added solid NOBF₄ (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 N₂; this evacuation/N₂ re-filling procedure was performed 3X. Stirred at room temperature under N₂ for 30 minutes and the previous evacuation/N₂ re-filling procedure was again performed 3X. Stirred an additional 30 minutes and performed the evacuation/N₂ 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 CH₃CN. 200 mL anhydrous Et₂O was layered on top of the CH₃CN and the resulting mixture was cooled at -20 °C for 4h. The supernatant was decanted and the precipitate was triturated 2X with 10 mL Et₂O. 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(CH₃CN)₄(BF₄)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 Phl(OAc) (0.075 mmol, 0.25 equiv.). Deionized H₂O (0.30 mmol, 1.0 equiv.) was next added via micropipetor. Pd(CH₃CN)₄(BF₄)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(CH₂CN)₆(BF₄)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 H₂O (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(CH₂CN)₆(BF₄)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](image)

**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-oxononyl-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$_3$CN)$_4$(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$_3$CN)$_4$(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$_3$CN)$_4$(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$_3$CN)$_4$(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$_3$CN)$_4$(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$_3$CN)$_4$(BF$_4$)$_2$. Run 1: 0% 3; run 2: 0% 3. Average = 0% 3.
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 under standard conditions; methyl 2-methylhept-6-enoate 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 Et₂O, 8.4 mL, 8.4 mmol, 2.0 equiv.). The reaction was stirred for 2h near 0°C and then quenched with saturated aqueous NH₄Cl. The aqueous layer was extracted 3X with CH₂Cl₂ and...
the combined organics were dried over MgSO₄, 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%). ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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’t for C₁₁H₁₄O [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%). ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₀H₁₁Br [M⁺]: 210.0044, found 210.0053.

**4-(4-trifluoromethylphenyl)-1-butene:** ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 146.1, 137.5, 128.9, 128.4 (q, J = 32.3 Hz), 124.5 (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, 2926, 2860, 1643, 1620, 1443, 1417, 1327, 1165, 1124, 1068, 1020; HRMS (EI) m/z calc’d for C₁₁H₁₁F₃ [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%). ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₁H₁₄ [M⁺]: 146.1096, found 146.1090.

**6-(but-3-en-1-yl)-2,2-dimethyl-2H-chromene:** Prepared from 6-(bromomethyl)-2,2-dimethyl-2H-chromene according to the representative procedure as a colorless liquid. ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₅H₁₆O [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
racemic alcohol, demonstrating that it had been prepared in >20:1 

dι1H), 1.69 (d, J = 7.6 Hz, 2H), 5.78 (ddt, J = 17.5, 10.5, 6.5 Hz, 1H), 4.97 (dd, J = 17.0, 1.5 Hz, 1H), 4.31 (d, J = 10.0 Hz, 1H), 1.366 (app t, J = 7.9 Hz, 2H), 2.05-2.00 (m, 2H), 1.70-1.63 (m, 2H), 1.40-1.31 (m, 6H); 13C NMR (125 MHz, CDCl3) δ 168.0, 139.5, 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 (ESI) m/z calc'd for C16H18NO2 [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%). 1H NMR (500 MHz, CDCl3) δ 7.51 (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), 3.26 (AB q, J = 7.9 Hz, 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); 13C NMR (125 MHz, CDCl3) 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 C11H15NO2 [M]+: 198.1494, found 198.1490.

(R)-6-(benzoxymethyl)hept-6-en-1-one: 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-oliv (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 NH4Cl and the aqueous layer was extracted 3X with Et2O. The combined organics were dried over MgSO4, 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%). 1H NMR (500 MHz, CDCl3) 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); 13C NMR (125 MHz, CDCl3) δ 139.2, 138.9, 128.4, 127.8, 127.6, 114.5, 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 (ESI) m/z calc’d for C13H16O [M]+: 204.1514, found 204.1520. [α]D25 = −4.3 (c = 0.23, CHCl3). Both the racemic and the chiral, non-racemic alcohol were converted to the Mosher esters for 1H 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 (275 mg, 1.78 mmol, 1.0 equiv.) was dissolved in 10 mL anhydrous CH₂Cl₂ 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 mixture was concentrated under reduced pressure and purified directly by flash chromatography (5% EtOAc/hexanes), affording the title compound as a clear, colorless oil (0.92 g, 79%).

**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 pTsCl (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 CH₂Cl₂ (50 mL) and the organic layer was washed with 1M aqueous HCl, saturated aqueous sodium bicarbonate, and brine. The organic layer was then dried over Na₂SO₄, 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 Et₂O. The reaction was cooled in an ice/water bath and allylmagnesium chloride (1.0 M, 17 mmol, 2.0 equiv.) was added in a dropwise fashion. Stirred at 0°C for 10 minutes and to the resulting gray mixture was added a solution of crude tosylate in 7 mL Et₂O over several minutes. The reaction was allowed to warm to ambient temperature and stir overnight. The reaction was then carefully quenched with saturated aqueous NH₄Cl and the layers were separated and extracted 3X with Et₂O. The combined organics were dried over MgSO₄, filtered through celite, concentrated under reduced pressure, and purified by filtration through a silica plug (hexanes).

**4-(hex-5-en-1-yl)cyclohexan-1-one:** Solid LiAlH₄ (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-ene (1.3 g, 5.8 mmol, 1.0 equiv.) in anhydrous Et₂O (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 'H NMR and was thereafter cooled in an ice/water bath and quenched by careful addition of 8 mL 25% H₂SO₄. After 30 min stirring the crude reaction mixture was partitioned between H₂O and Et₂O. The aqueous layer was then extracted 2X with Et₂O and the combined organics were washed successively with saturated aqueous Na₂CO₃ and brine. The organics were collected, dried over MgSO₄, filtered through celite, and concentrated under reduced pressure. The title compound was used without further purification (0.98 g, 95%).

- **IR (film, cm⁻¹):** 3078, 2995, 2976, 2860, 1738, 1641, 1454, 1371, 1242, 1032, 997; HRMS (ESI) m/z calc'd for C₁₁H₁₂O₂ [M+H⁺]: 197.1542, found 197.1552.
- **IR (film, cm⁻¹):** 3078, 2995, 2976, 2860, 1738, 1641, 1450, 1371, 1242, 1032, 997; HRMS (ESI) m/z calc'd for C₁₀H₁₆ [M+H⁺]: 136.1252, found 136.1258.
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 pTsOH (30 mg, 0.16 mmol, 0.065 equiv.). The reaction was heated to reflux for 24 h, concentrated under reduced pressure, and purified by flash chromatography (hexanes → 5% EtOAc/hexanes → 10% EtOAc/hexanes), affording the title compound as a clear, colorless oil (498 mg, 90%).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_2$Na [M+Na]$^+$: 245.1517, found 245.1524.

Allyl estradiol derivative B: To a solution of the known allyl estrone derivative A (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$_2$O slowly, followed by 0.54 mL 1M aqueous NaOH, and 3X 0.54 mL H$_2$O. 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$_3$) $\delta$ 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$_3$) $\delta$ 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, 1399, 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. $[\alpha]_D^{25} = +36.5$ (c = 1.14, CHCl$_3$).

Benzylx 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 H₂O and the organic layer was washed 3X with H₂O. The organic layer was collected, dried over MgSO₄, 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 benzylxy allyl derivative (1.87 g, 4.5 mmol, 1.0 equiv.) in anhydrous THF (40 mL) at 0°C was added 1.0M BH₃·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 H₂O₂. The quenched reaction stirred at ambient temperature for 1.5h and was partitioned between H₂O and EtOAc. The aqueous layer was extracted 3X with EtOAc and the combined organics were dried over MgSO₄, 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%). ¹H NMR (500 MHz, CDCl₃) δ 7.38-7.32 (m, 4H), 7.20-7.26 (m, 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₂₃H₃₅O₃ [M+H]+: 435.2899, found 435.2897; [α]D²⁰ = -21.5 (c = 0.26, CHCl₃).

**Benzyloxy estradiol butene derivative D:** The primary alcohol was oxidized according to the procedure of Hoover and Stahl.¹⁰ 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(CH₃CN)₂]PF₆ (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 CH₂CN and added successively to a 100 mL round-bottom flask. The mixture was stirred at ambient temperature under an atmosphere of O₂ 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 Et₂O: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 Me₃PBr (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 N₂ and solid K₂[Fe(CN)₆] (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 NH₄Cl and allowed to warm to ambient temperature. The reaction was partitioned between water and CH₂Cl₂ and extracted 3X with CH₂Cl₂. The combined organics were dried over MgSO₄, 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%). ¹H NMR (500 MHz, CDCl₃) 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),
Table 1 Products

**8-oxonononyl acetate**: non-8-en-1-yl acetate was reacted according to a modified version of the general procedure, excluding Ph(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. H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 calcd for C₁₁H₂₁O₃ [M⁺]: 201.1491, found 201.1492.

**Table 2 Products**

**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%. H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 198.7, 171.3, 148.1, 134.1, 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 calcd for C₁₁H₁₀O₃ [M⁺]: 199.1334, found 199.1338.

**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%. H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 calcd for C₁₉H₁₇O [M⁺]: 271.1081, found 271.1080.

**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%. H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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,
(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$_3$) $\delta$ 7.54 (d, $J$ = 6.5 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$_3$) $\delta$ 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$_{11}$H$_{13}$O$_2$ [M+H]$^+$: 177.0916, found 177.0919.

(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$_3$) $\delta$ 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$_3$) $\delta$ 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$_{10}$OBr [M+H]$^+$: 224.9915, found 224.9917.

(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$_3$) $\delta$ 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$_3$) $\delta$ 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-2H-chromen-6-yl)but-3-en-2-one: 6-(but-3-en-1-yl)-2,2-dimethyl-2H-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$_3$) $\delta$ 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$_3$) $\delta$ 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$^{-1}$): 3029, 3024, 2974, 2929, 1687, 1664, 1641, 1616, 1501, 1572, 1491, 1429, 1382, 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\(_3\)) \(\delta 6.80\) (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\(_3\)) \(\delta 198.9, 148.8, 131.4, 32.6, 31.7, 29.0, 28.2, 26.9, 22.6, 14.2\); IR (film, cm\(^{-1}\)): 2956, 2929, 1699, 1678, 1628, 1466, 1431, 1362, 1254, 1282, 1254, 1176, 978; HRMS (ESI) \(m/z\) calc'd for \(\text{C}_{10}\text{H}_{19}\text{O} [\text{M+H}]^+:\) 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 \(\alpha,\beta\)-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% \(\rightarrow\) 15% \(\rightarrow\) 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\(_3\)) \(\delta 8.02\) (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\(_3\)) \(\delta 198.3, 166.5, 143.1, 133.3, 133.2, 130.0, 129.6, 128.5, 62.8, 31.9, 27.1\); 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 \(\text{C}_{13}\text{H}_{14}\text{O}_3\text{Na} [\text{M+Na}]^+:\) 241.0841, found 241.0846.

(E)-2-(7-octooct-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% \(\rightarrow\) 25% \(\rightarrow\) 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\(_3\)) \(\delta 7.87-7.83\) (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\(_3\)) \(\delta 198.7, 168.5, 147.5, 134.1, 132.2, 131.8, 123.4, 37.7, 32.0, 28.3, 27.0, 25.4\); 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 \(\text{C}_{16}\text{H}_{18}\text{NO}_3 [\text{M+H}]^+:\) 272.1287, found 272.1290.

(E)-1-morpholinohept-4-ene-1,6-dione: 1-morpholinohept-6-ene-1-one (59.2 mg, 0.30 mmol) was reacted according to the general procedure. Purification by flash chromatography (20% \(\rightarrow\) 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\(_3\)) \(\delta 6.86\) (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\(_3\)) \(\delta 198.7, 170.0, 146.8, 131.9, 67.0, 66.6, 45.9, 42.1, 31.3, 27.6, 27.1\); 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 \(\text{C}_{18}\text{H}_{18}\text{NO}_3 [\text{M+H}]^+:\) 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% \(\rightarrow\) 20%
(R,E)-6-(benzoxyl)-5-methylhex-3-en-2-one:  (R)-6-(benzoxyl)-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), 6.03 (dd, \(J = 16.0, 1.0\) 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 199.0, 157.0, 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, 994; HRMS (ESI) \(m/z\) calc'd for C\(_{15}\)H\(_{19}\)O\(_3\)Na [M+Na]\(^+\): 233.1154, found 233.1162.

(z)-trans-2-((E)-3-oxobut-1-enyl)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, \(J = 16.0, 1.0\) 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\(_{19}\)O\(_3\)Na [M+Na]\(^+\): 233.1154, found 233.1162.

(z)-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, \(J = 16.5, 1.0\) 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.

(z)-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$_3$) $\delta$ 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$_3$Na [M+Na]$^+$: 259.1310, found 259.1320.

**a,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% $\rightarrow$ 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$_3$) $\delta$ 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$_3$) $\delta$ 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. [α]$_D^{26}$ = + 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 a,β-unsaturated ketone 20 detectable (this product was synthesized from cyclohexanone using a Horner-Wadsworth Emmons reagent\textsuperscript{19}).

**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$_2$O. 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%**.
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.

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Kinetic Profile w/ 0%, 25%, or 100% PhI(OAc)$_2$

- No PhI(OAc)$_2$
- 25% PhI(OAc)$_2$
- 100% PhI(OAc)$_2$

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