

Palladium-Catalyzed Intramolecular Oxidative Alkylation of Unactivated Olefins

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Supporting Information

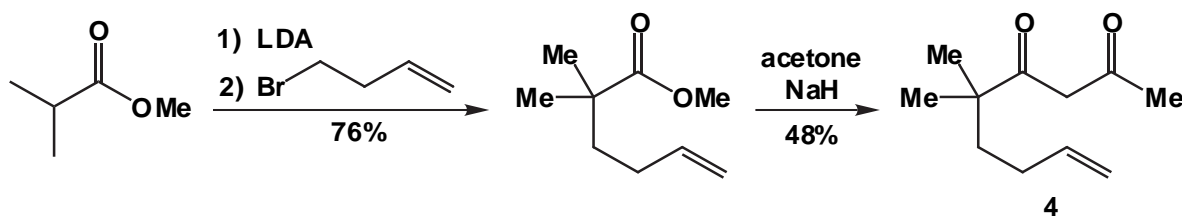
Experimental procedures, analytical and spectroscopic data for new compounds and cyclohexanones (14 pages).

Experimental

General Methods. Reactions were performed under an atmosphere of nitrogen employing standard Schlenk techniques unless otherwise stated. NMR were obtained on a Varian spectrometer operating at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR in CDCl_3 unless otherwise noted. IR spectra were obtained on a Bomem MB-100 FT IR spectrometer. Gas chromatography was performed on a HP 5890 gas chromatography equipped with a 25 m polydimethylsiloxane capillary column. Flash column chromatography was performed employing 200-400 mesh silica gel (EM); all compounds were isolated as colorless oils unless otherwise noted. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). For compounds that exist as mixtures of enol and keto tautomers, the enol:keto ratio for each compound was determined by ^1H NMR spectroscopy in CDCl_3 ; only the resonances corresponding to the predominant tautomer are given. Thin layer chromatography (TLC) was performed on SiO_2 plates eluting with a 5:1 mixture of hexanes–EtOAc unless noted otherwise. 1,4-Dioxane (Aldrich anhydrous) and $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (Strem) were used as received. 1,2-Dichloroethane (DCE) was distilled from CaH_2 under nitrogen. 8-Nonene-2,4-dione (Table 1, entry 6)¹ and 1-phenyl-7-octene-1,3-dione (Table 1, entry 8)² were prepared according to published procedures. All other reagents were purchased from major chemical suppliers and were used as received.

ζ -Alkenyl β -diketones

5,5-Dimethyl-8-nonene-2,4-dione (4). Dione **4** was synthesized in two steps in 36% overall yield from methyl isobutyrate as outlined in Scheme S1.



Scheme S1

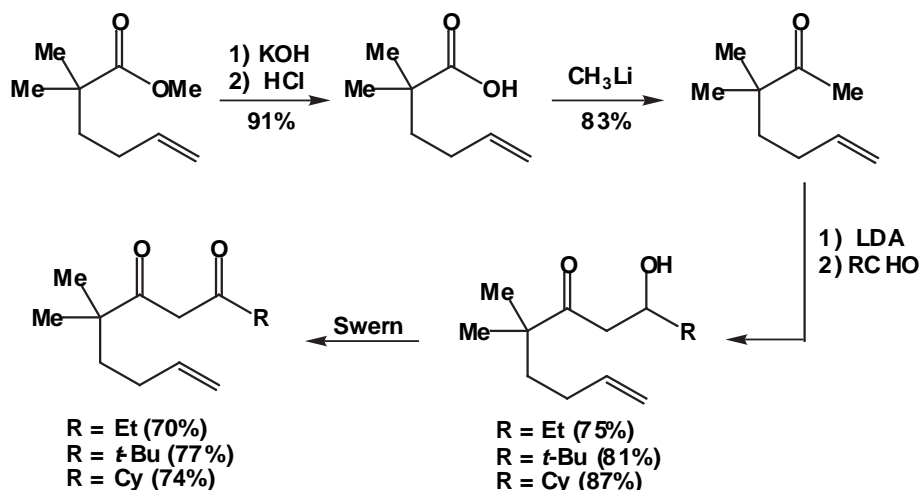
A solution of methyl isobutyrate (5.0 g, 49 mmol) in THF (15 mL) was added slowly to a solution of LDA [generated from *n*-BuLi (21 mL in hexanes, 2.5 M, 52 mmol) and diisopropylamine (5.5 g, 54 mmol) in THF (65 mL)] at $-78\text{ }^{\circ}\text{C}$ and stirred for 20 min. The resulting solution was treated with a solution of 4-bromo-1-butene (7.4 g, 55 mmol) in HMPA (10 mL) and stirred at $-78\text{ }^{\circ}\text{C}$ for 12 h. Aqueous HCl (1 N, 30 mL) was added and the resulting mixture was extracted with ether ($3 \times 50\text{ mL}$). The combined organic fractions were washed with water ($4 \times 20\text{ mL}$) and saturated NaHCO_3 ($2 \times 20\text{ mL}$), dried, and concentrated. The oily residue was distilled under vacuum ($64\text{ }^{\circ}\text{C}$, 50 mm Hg) to give methyl 2,2-dimethyl-5-hexenoate (5.8 g, 76%).

A suspension of methyl 2,2-dimethyl-5-hexenoate (3.1 g, 20 mmol) and NaH (2.0 g, 83.3 mmol) in ether (50 mL) and DMF (30 mL) was heated at $70\text{ }^{\circ}\text{C}$ for 1 h. The resulting mixture was cooled to $0\text{ }^{\circ}\text{C}$ and water (30 mL) and aqueous HCl (2 N, 20 mL) were added. The mixture was extracted with ether, and the combined ether extracts were dried and concentrated. The resulting oily residue was chromatographed (SiO_2 ; hexanes–ether = 50:1 \rightarrow 30:1) to give **2** (1.75g, 48%).

For methyl 2,2-dimethyl-5-hexenoate:³ ^1H NMR: δ 5.76 (tdd, $J = 6.4, 10.4, 16.8\text{ Hz}$, 1 H), 4.89-5.01 (m, 2 H), 3.64 (s, 3 H), 1.93-2.00 (m, 2 H), 1.58-1.62 (m, 2 H), 1.17 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 178.4, 138.6, 114.6, 51.8, 42.2, 40.0, 29.5, 25.3.

For 5,5-dimethyl-8-nonene-2,4-dione (4). Enol:keto = 20:1. ^1H NMR: δ 15.8 (br s, 1 H), 5.75 (tdd, $J = 6.4, 10.0, 16.8\text{ Hz}$, 1 H), 5.57 (s, 1 H), 4.88-5.00 (m, 2 H), 2.05 (s, 3 H), 1.89-1.96 (m, 2 H), 1.55-1.60 (m, 2 H), 1.12 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 199.4, 192.5, 138.8, 114.5, 96.9, 42.4, 40.0, 29.2, 25.6, 25.3. IR (neat, cm^{-1}): 2973, 2940, 1650, 1600, 1473. TLC: $R_f = 0.72$. Anal. calcd (found) for $\text{C}_{11}\text{H}_{18}\text{O}_2$: H, 9.95 (9.95); C, 72.49 (72.44).

6,6-Dimethyl-9-decene-3,5-dione (Table 1, entry 1). 6,6-Dimethyl-9-decene-3,5-dione was synthesized in four steps from methyl 2,2-dimethyl-5-hexenoate in 40% overall yield employing the route shown in Scheme S2. The aldol addition and Swern oxidation were performed according to a published procedure.⁴



Scheme S2

A solution of methyl 2,2-dimethyl-5-hexenoate (5.8 g, 37 mmol) and KOH (8.0 g, 143 mmol), in a water (25 mL)/THF (30 mL)/methanol (80 mL) was stirred at 25 °C for 1 h and at 40 °C for 1 h and then treated with ice (40 g). The resulting mixture was acidified (pH = 1) by slow addition of concentrated hydrochloric acid (25 mL) and extracted with ether (4 × 100 mL). The combined organic fractions were washed with brine (40 mL), dried (MgSO₄), concentrated, and distilled under vacuum (65 °C, 200 mTorr) to give 2,2-dimethyl-5-hexenoic acid (4.8 g, 91%).

A THF solution of methyl lithium (97 mL, 1.4 M, 136 mmol) was added to a solution of 2,2-dimethyl-5-hexenoic acid in THF (100 mL) at 0 °C, stirred for 3 h, and quenched by sequential addition of SiMe₃Cl (50 mL, 37 mmol), aqueous HCl (3 N, 20 mL), and ice (100 g). The resulting mixture was extracted with ether (3 × 100 mL) and the combined organic fractions were washed with brine (50 mL), dried (MgSO₄), concentrated, and distilled under vacuum (60-65 °C, 50 mm Hg) to give 3,3-dimethyl-6-hepten-2-one (3.6 g, 83%).

3,3-Dimethyl-6-hepten-2-one (2.0 g, 11 mmol) was added slowly to a solution of LDA [generated from *n*-BuLi (3.8 mL, 2.5 M, 9.5 mmol) and diisopropylamine (1.0 g, 9.5 mmol) in THF (20 mL)] at -78 °C and stirred for 15 min. Propionaldehyde (0.55 g, 9.5 mmol) was added dropwise to the resulting white suspension, stirred for 1 h, and quenched with saturated aqueous ammonium chloride (6 mL) at -78 °C. The resulting suspension was warmed to room temperature and extracted with ether (200 mL). The ether

extract was washed with brine and the combined aqueous fractions were extracted with ether (2×30 mL). The combined organic fractions were dried (MgSO_4), concentrated, and chromatographed (SiO_2 ; hexanes–ether = 10:1 \rightarrow 1:2) to give 3-hydroxy-6,6-dimethyl-9-decene-5-one (1.2 g, 75%).

Solutions of DMSO (0.83 mL, 12 mmol) in CH_2Cl_2 (2 mL) and 3-hydroxy-6,6-dimethyl-9-decene-5-one (1.1 g, 5.4 mmol) in CH_2Cl_2 (3 mL) were added sequentially to a solution of oxalyl chloride (0.51 mL, 5.8 mmol) in CH_2Cl_2 (10 mL) at -78 °C and stirred for 1.5 h and then treated with triethylamine (5 g, 50 mmol). The resulting solution was stirred for 10 min, warmed to room temperature, and treated with water (10 mL). Ether (50 mL) was added, the layers were separated, and the aqueous layer was extracted with ether (2×25 mL). The combined organic fractions were washed with aqueous HCl (1 N, 2×10 mL) and saturated aqueous NaHCO_3 (2×10 mL), dried (MgSO_4), concentrated, and chromatographed (SiO_2 ; hexanes–ether = 50:1 \rightarrow 25:1) to give 6,6-dimethyl-7-decene-3,5-dione (0.73 g, 70%).

For 2,2-dimethyl-5-hexenoic acid:⁵ ^1H NMR: δ 5.78 (tdd, $J = 6.3, 10.2, 16.5$ Hz, 1 H), 4.91-5.04 (m, 2 H), 2.00-2.07 (m, 2 H), 1.60-1.66 (m, 2 H), 1.20 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 184.2, 137.6, 113.9, 41.3, 38.8, 28.5, 24.2. Anal. calcd (found) for $\text{C}_8\text{H}_{14}\text{O}_2$: H, 9.92 (9.81); C, 67.57 (67.42).

For 3,3-dimethyl-6-hepten-2-one:⁶ ^1H NMR (300 MHz): δ 5.73 (tdd, $J = 6.3, 9.9, 16.8$ Hz, 1 H), 4.88-4.99 (m, 2 H), 2.07 (s, 3 H), 1.84-1.96 (m, 2 H), 1.53-1.59 (m, 2 H), 1.08 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz): δ 213.0, 137.6, 113.9, 46.9, 38.3, 28.4, 24.4, 23.6. Anal. calcd (found) for $\text{C}_9\text{H}_{16}\text{O}$: H, 11.50 (11.39); C, 77.09 (76.97).

For 3-hydroxy-6,6-dimethyl-9-decene-5-one. ^1H NMR (300 MHz): δ 5.66-5.80 (m, 1 H), 4.89-5.00 (m, 2 H), 3.85-3.95 (m, 1 H), 3.28 (d, $J = 2.7$ Hz, 1 H), 2.60-2.27 (m, 1 H), 2.46 (m, 1 H), 1.85-1.93 (m, 2 H), 1.36-1.63 (m, 4 H), 1.10 (s, 6 H), 0.92 (t, $J = 7.5$ Hz, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz): δ 216.7, 137.5, 114.0, 68.4, 46.9, 42.9, 42.3, 38.3, 28.6, 28.3, 23.5, 9.3. IR (neat, cm^{-1}): 3445, 2969, 2933, 1696. TLC: $R_f = 0.24$. Anal. calcd (found) for $\text{C}_{12}\text{H}_{22}\text{O}_2$: H, 11.18 (10.92); C, 72.68 (72.51).

For 6,6-dimethyl-9-decene-3,5-dione: Enol:keto = 12:1. ^1H NMR: δ 15.8 (s, 1 H), 5.77 (tdd, $J = 6.4, 10.0, 16.8$ Hz, 1 H), 5.57 (s, 1 H), 4.90-5.01 (m, 2 H), 3.34 (q, $J = 7.6$ Hz, 2 H), 1.91-1.97 (m, 2 H), 1.57-1.62 (m, 2 H), 1.14 (s, 6 H), 1.13 (t, $J = 7.6$ Hz, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 198.9, 196.9, 138.8,

114.5, 95.6, 42.3, 40.0, 32.2, 29.3, 25.4, 9.9. IR (neat, cm^{-1}): 2974, 2939, 1600, 1460. TLC: $R_f = 0.74$. Anal. calcd (found) for $\text{C}_{12}\text{H}_{20}\text{O}_2$: H, 10.27 (10.13); C, 73.43 (73.21).

2,6,6-Trimethyl-9-decene-3,5-dione (Table 1, entry 2). 2,6-Dimethylheptane-3,5-dione, a solution of *n*-BuLi in hexanes (2.5 M, 5.1 mL, 12.8 mmol), and 4-bromo-1-butene (3.2 g, 24 mmol) were added sequentially to a suspension of NaH in THF at 0 °C and stirred overnight. Saturated aqueous NH_4Cl and aqueous HCl (2 N, 10 mL) were added and the resulting mixture was extracted with ether (3 \times 30 mL). The combined ether extracts were dried (MgSO_4) and distilled under vacuum (50 °C, 300 mm Hg) to give 2,6,6-trimethyl-9-decene-3,5-dione (1.34 g, 50%). Enol:keto = 10:1. ^1H NMR: δ 15.9 (br s, 1 H), 5.77 (tdd, $J = 6.4, 10.0, 16.8$ Hz, 1H), 5.59 (s, 1 H), 4.90-5.01(m, 2 H), 2.48 (septet, $J = 6.8$ Hz, 1 H), 1.92-1.98 (m, 2 H), 1.57-1.62 (m, 2 H), 1.14 (d, $J = 6.8$ Hz, 6 H), 1.4 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 200.0, 199.8, 138.8, 114.5, 94.2, 42.5, 40.1, 37.3, 25.4, 19.6. IR (neat, cm^{-1}): 2968, 2872, 1594, 1466. TLC: $R_f = 0.75$. Anal. calcd (found) for $\text{C}_{13}\text{H}_{22}\text{O}_2$: H, 10.54 (10.46); C, 74.24 (74.21).

2,2,6,6-Tetramethyl-9-decene-3,5-dione (Table 1, entry 3). 2,2,6,6-Tetramethyl-9-decene-3,5-dione was synthesized in two steps from 3,3-dimethyl-6-hepten-2-one in 62% overall yield employing a procedure similar to that described above for the synthesis of 6,6-dimethyl-9-decene-3,5-dione depicted in Scheme S2.

For 3-hydroxy-2,2,6,6-tetramethyl-9-decene-5-one: ^1H NMR: δ 5.79 (tdd, $J = 6.8, 10.0, 16.8$ Hz, 1 H), 4.91-5.02 (m, 2 H), 3.64 (dd, $J = 1.2, 10.0$ Hz, 1 H), 3.16 (br s, 1 H), 2.69 (dd, $J = 1.6, 17.2$ Hz, 1 H), 3.38 (dd, $J = 2.0, 17.2$ Hz, 1 H), 1.84-2.00 (m, 2 H), 1.58-1.62 (m, 2 H), 1.13 (s, 3 H), 1.12 (s, 3 H), 0.90 (s, 9 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 218.1, 138.4, 114.9, 75.2, 48.1, 39.3, 38.5, 34.4, 29.2, 25.9, 24.4. IR (neat, cm^{-1}): 3545, 2960, 2871, 1697, 1472. TLC: $R_f = 0.45$. Anal. calcd (found) for $\text{C}_{14}\text{H}_{26}\text{O}_2$: H, 11.58 (11.49); C, 74.29 (74.37).

For 2,2,6,6-tetramethyl-9-decene-3,5-dione: Enol:keto $\geq 30:1$. ^1H NMR: δ 16.2 (s, 1 H), 5.77 (tdd, $J = 6.4, 10.0, 17.2$ Hz, 1 H), 5.71 (s, 1 H), 4.8-5.08 (m, 2 H), 1.92-1.99 (m, 2 H), 1.58-1.62 (m, 2 H), 1.17 (s, 9 H), 1.15 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 201.6, 200.5, 138.9, 114.5, 91.9, 42.8, 40.1, 39.6, 29.3, 27.6, 25.5. IR (neat, cm^{-1}): 2970, 2942, 1601, 1470. TLC: $R_f = 0.87$. Anal. calcd (found) for $\text{C}_{14}\text{H}_{24}\text{O}_2$: H, 10.78 (10.69); C, 74.95 (75.01).

1-Cyclohexyl-4,4-dimethyl-7-octene-1,3-dione (Table 1, entry 4). 1-Cyclohexyl-4,4-dimethyl-7-octene-1,3-dione was synthesized in two steps from 3,3-dimethyl-6-hepten-2-one in 64% overall yield employing a procedure similar to that described above for the synthesis of 6,6-dimethyl-9-decene-3,5-dione depicted in Scheme S2.

For 1-Cyclohexyl-1-hydroxy-4,4-dimethyl-7-octene-3-one: ^1H NMR (300 MHz): δ 5.71 (tdd, $J = 6.3, 10.2, 16.2$ Hz, 1 H), 4.87-4.98 (m, 2 H), 3.71 (br s, 1 H), 2.40-2.49 (m, 1 H), 2.60-2.66 (m, 1 H), 1.83-1.90 (m, 2 H), 1.69-1.75 (m, 2 H), 1.53-1.63 (m, 4 H), 0.94-1.30 (m, 7 H), 1.08 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 217.0, 137.5, 114.0, 71.0, 47.0, 42.2, 39.8, 38.3, 28.3, 27.6, 25.8, 25.5, 25.4, 23.5. IR (neat, cm^{-1}): 3507, 2925, 2852, 1696, 1641. TLC: $R_f = 0.31$. Anal. calcd (found) for $\text{C}_{11}\text{H}_{16}\text{O}_2$: H, 11.18 (11.12); C, 76.14 (76.07).

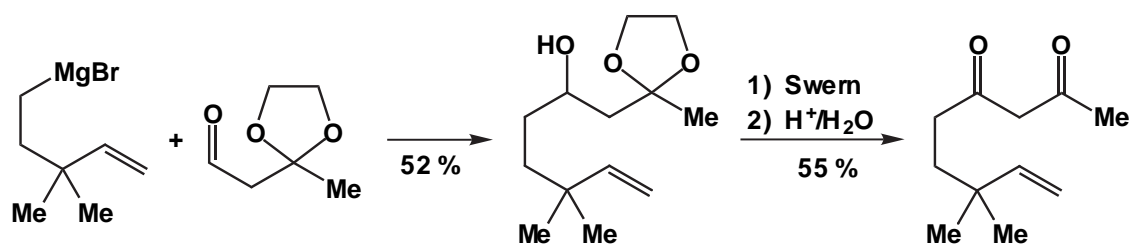
For 1-Cyclohexyl-4,4-dimethyl-7-octene-1,3-dione: Enol:keto = 20:1. ^1H NMR: δ 16.0 (s, 1 H), 5.77 (tdd, $J = 6.4, 10.0, 15.2$ Hz, 1 H), 5.58 (s, 1 H), 4.98 (qd, $J = 1.6, 17.2$ Hz, 1 H), 4.91 (tdd, $J = 1.2, 2.0, 10.4$ Hz, 1 H), 2.19 (tt, $J = 3.2, 11.6$ Hz, 1 H), 1.91-1.98 (m, 2 H), 1.78-1.87 (m, 4 H), 1.66-1.70 (m, 1 H), 1.57-1.60 (m, 2 H), 1.18-1.43 (m, 5 H), 1.14 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 200.4, 198.6, 138.9, 114.5, 94.5, 47.2, 42.6, 40.1, 29.8, 29.3, 26.0, 25.4. IR (neat, cm^{-1}): 2930, 2855, 1620, 1597, 1450. TLC: $R_f = 0.50$. Anal. calcd (found) for $\text{C}_{16}\text{H}_{26}\text{O}_2$: H, 10.47 (10.58); C, 76.75 (76.59).

6-Methyl-9-decene-3,5-dione (Table 1, entry 5). 6-Methyl-9-decene-3,5-dione was synthesized from 3,5-heptadione and 4-bromo-1-butene in 33 % yield after vacuum distillation (70 °C, 50 mmHg) employing a procedure similar to that used to synthesize 2,6,6-trimethyl-9-decene-3,5-dione. Enol:keto = 5:1. ^1H NMR: δ 15.5 (br s, 1 H), 5.72-5.82 (m, 1 H), 5.47 (s, 1 H), 4.94-5.03 (m, 2 H), 2.32 (q, $J = 7.6$ Hz, 2 H), 2.04 (q, $J = 7.6$ Hz, 2 H), 1.69-1.78 (m, 1 H), 1.41-1.51 (m, 1 H), 1.05-1.15 (m, 7 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 197.3, 196.5, 138.3, 115.1, 97.7, 41.7, 33.3, 31.9, 31.6, 17.7, 9.8. IR (neat, cm^{-1}): 2975, 2935, 1603, 1454, 911. TLC: $R_f = 0.78$. Anal. calcd (found) for $\text{C}_{11}\text{H}_{18}\text{O}_2$: H, 9.95 (10.03); C, 72.49 (72.38).

2,2-Dimethyl-9-decene-3,5-dione (Table 1, entry 7). Enol:keto = 19:1. 2,2-Dimethyl-9-decene-3,5-dione was synthesized from 5,5-dimethyl-hexane-2,4-dione and 4-bromo-1-butene in 27% yield following vacuum distillation (58 °C, 250 mTorr) employing a procedure similar to that used to synthesize 6-methyl-9-decene-3,5-dione. ^1H NMR: δ 15.9 (br s, 1 H), 5.78 (tdd, $J = 6.8, 10.2, 16.8$ Hz, 1H), 5.58 (s,

1 H), 4.97-5.05 (m, 2 H), 2.31 (t, $J = 7.6$ Hz, 2 H), 2.09 (q, $J = 7.6$ Hz, 2 H), 1.71 (quintet, $J = 7.6$ Hz, 2 H), 1.16 (s, 9 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 200.5, 195.4, 138.1, 115.5, 95.4, 39.2, 38.2, 33.3, 27.5, 25.0. IR (neat, cm^{-1}): 2976, 2935, 1604, 1455. TLC: $R_f = 0.83$. Anal. calcd (found) for $\text{C}_{12}\text{H}_{20}\text{O}_2$: H, 10.27 (10.16); C, 73.43 (73.28).

7,7-Dimethyl-8-nonene-2,4-dione (Table 1, entry 9). 7,7-Dimethyl-8-nonene-2,4-dione was synthesized from (2-methyl-[1,3]dioxolan-2-yl)acetaldehyde in 29% overall yield employing the procedure shown in Scheme S3.



Scheme S3

5-Bromo-3,3-dimethyl-1-pentene (0.73 g, 4.5 mmol) was added dropwise to a suspension of Mg (0.24 g, 10.0 mmol) in ether (25 mL) and the mixture was refluxed for 20 min and cooled to room temperature. (2-Methyl-[1,3]dioxolan-2-yl)acetaldehyde (0.52 g, 4.0 mmol) was added dropwise and the resulting suspension was stirred at room temperature for 5 h, quenched with saturated aqueous NH_4Cl , and extracted with ether. The combined organic fractions were washed with brine, dried (MgSO_4), and concentrated under vacuum. The resulting oily residue was chromatographed (SiO_2 ; hexanes-ether = 25:1 \rightarrow 5:1) to give 5,5-dimethyl-1-(2-methyl-[1,3]dioxolan-2-yl)-hept-6-en-2-ol (0.47 g, 52%).

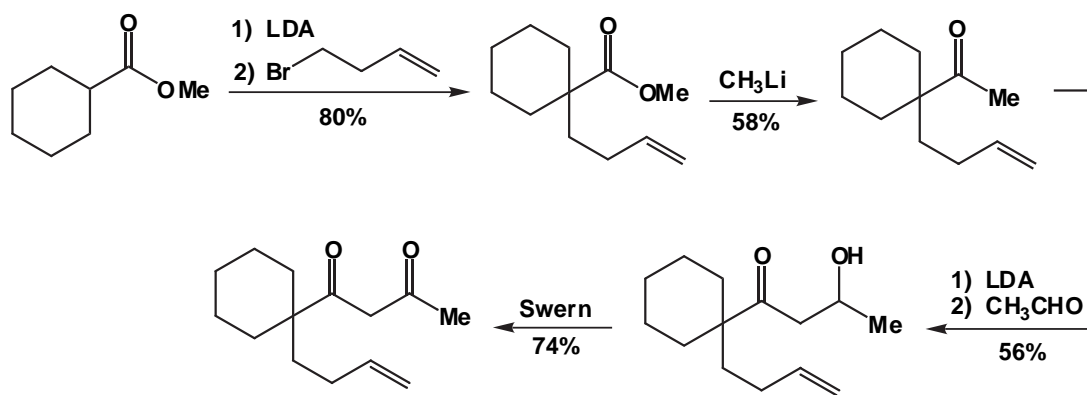
5,5-Dimethyl-1-(2-methyl-[1,3]dioxolan-2-yl)-hept-6-en-2-ol (1.26 g, 5.50 mmol) was oxidized employing a procedure analogous to that used to synthesize 6,6-dimethyl-9-decene-3,5-dione and was purified by chromatography (SiO_2 ; hexanes-ether = 25:1) to give 7,7-dimethyl-8-nonene-2,4-dione (0.55 g, 55%) as a yellow oil.

For 5,5-Dimethyl-1-(2-methyl-[1,3]dioxolan-2-yl)-6-hepten-2-ol: ^1H NMR: δ 5.78-5.71 (m, 1 H), 4.91 (s, 1 H), 4.87 (dd, $J = 1.6, 6.8$ Hz, 1 H), 3.98 (m, 4 H), 3.84-3.78 (m, 1 H), 3.59 (s, 1 H),

1.82 (dd, $J = 1.6, 14.8$ Hz, 1 H), 1.74 (dd, $J = 9.6, 14.8$ Hz, 1 H), 1.50-1.37 (m, 2 H), 1.35 (s, 3 H), 1.34-1.22 (m, 2 H), 0.98 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 148.6, 110.8, 68.9, 65.0, 64.6, 45.2, 38.5, 36.6, 32.7, 27.1, 26.9, 24.5. IR (neat, cm^{-1}): 3526, 3079, 2955, 2884, 1645, 1557, 1540, 1472, 1456, 1416, 1376, 1302, 1105, 1039. TLC: $R_f = 0.19$. Anal. calcd (found) for $\text{C}_{13}\text{H}_{24}\text{O}_3$: H, 10.59 (10.47); C, 68.38 (68.19).

For 7,7-Dimethyl-8-nonene-2,4-dione: Enol:keto = 10:1. ^1H NMR: δ 15.46 (s, 1 H), 5.72 (dd, $J = 10.8, 17.4$ Hz, 1 H), 5.47 (s, 1 H), 4.96 (dd, $J = 1.6, 10.8$ Hz, 1 H), 4.92 (dd, $J = 1.6, 17.4$ Hz, 1 H), 2.22-2.16 (m, 2 H), 2.03 (s, 3 H), 1.61-1.57 (m, 2 H), 1.00 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 195.7, 191.0, 147.6, 111.7, 100.0, 38.2, 36.7, 34.5, 26.9, 25.1. IR (neat, cm^{-1}): 3082, 2997, 2961, 2928, 2869, 1728, 1711, 1620, 1454, 1416, 1362, 1285, 1239, 1160, 1127, 1001. TLC: $R_f = 0.48$. Anal. calcd (found) for $\text{C}_{11}\text{H}_{18}\text{O}_2$: H, 9.95 (10.02); C, 72.49 (72.36).

1-(1-But-3-enylcyclohexyl)butane-1,3-dione (Table 1, entry 10). 1-(1-But-3-enylcyclohexyl)butane-1,3-dione was synthesized in five steps in 19% overall yield from methyl cyclohexanecarboxylate employing the route shown in Scheme S4.



Scheme S4

Methyl cyclohexanecarboxylate (8.0 g, 56.3 mmol) was added to a solution of LDA [generated from $n\text{-BuLi}$ (2.5 N in hexanes, 22.5 mL, 56.3 mmol) and diisopropylamine (7.0 g, 69 mmol) in THF (60 mL) at 0°C] over 1 h at -78°C and the resulting solution was stirred for 30 min. A solution of 4-bromo-1-butene (8.0 g, 60 mmol) in HMPA (10 mL) was added dropwise over 30 min at -78°C and stirred for 40 min, warmed to room temperature, and stirred for 2 h. Ice (20 g) and aqueous HCl (3 N, 30 mL) were

added and the resulting mixture was extracted with ether (4 × 50 mL). The combined organic fractions were washed with water (3 × 10 mL), dried (MgSO₄), concentrated, and distilled under vacuum (64-66 °C, 350 mTorr) to give 1-(3-butenyl)-1-carbomethoxycyclohexane (8.8 g, 80%).

A solution of methyl lithium (50 mL, 1.4 N in THF, 70 mmol) was added to a solution of 1-(3-butenyl)-1-carbomethoxycyclohexane (6.0 g, 30 mmol) in THF (40 mL) at 0 °C and stirred for 1 h. Ice (20 g) and aqueous HCl (3 N, 20 mL) were added and the mixture was extracted with ether (3 × 50 mL). The combined organic fractions were dried (MgSO₄), concentrated, and chromatographed (SiO₂; hexanes–EtOAc = 50:1) to give 1-acetyl-1-(3-butenyl)cyclohexane (3.2 g, 58%).

1-Acetyl-1-(3-butenyl)cyclohexane (2.0 g, 11 mmol) was added slowly to a solution of LDA [generated from *n*-BuLi (5.5 mL, 2.5 M, 14 mmol) and diisopropylamine (1.4 g, 14 mmol) in THF (20 mL)] at –78 °C and stirred for 15 min. Acetaldehyde (0.54 g, 12 mmol) was added dropwise to the resulting white suspension and stirred for 1 h. Aqueous ammonium chloride (6 mL) was added at –78 °C and the resulting mixture was extracted with ether (200 mL). The ether extract was washed with brine and the combined aqueous fractions were extracted with ether (2 × 30 mL). The combined organic fractions were dried (MgSO₄), concentrated, and chromatographed (SiO₂; hexanes–ether = 33:1 → 1:2) to give 1-(1-but-3-enylcyclohexyl)-3-hydroxybutan-1-one (1.4 g, 56%).

(1-But-3-enylcyclohexyl)-3-hydroxybutan-1-one was oxidized employing the procedure used to synthesize 6,6-dimethyl-9-decene-3,5-dione and was purified by chromatography (SiO₂; hexanes–ether = 50:1 → 25:1) to give 1-(1-but-3-enyl-cyclohexyl)-butane-1,3-dione in 74% yield.

For 1-(3-butenyl)-1-carbomethoxycyclohexane. ¹H NMR (300 MHz): δ 5.83 (tdd, *J* = 6.3, 10.5, 16.8 Hz, 1 H), 4.99-5.10 (m, 2 H), 3.76 (s, 3 H), 2.17 (m, 2 H), 1.99-2.06 (m, 2 H), 1.62-1.78 (m, 4 H), 1.25-1.47 (m, 6 H). ¹³C{¹H} NMR: δ 176.4, 137.8, 117.7, 50.7, 46.1, 39.0, 33.5, 27.8, 25.2, 22.5. TLC: *R_f* = 0.66. Anal. calcd (found) for C₁₂H₂₀O₂: H, 10.27 (10.27); C, 73.43 (73.33).

For 1-Acetyl-1-(3-butenyl)cyclohexane: ¹H NMR (300 MHz): δ 5.83 (tdd, *J* = 6.6, 10.2, 16.8 Hz, 1 H), 5.00-5.10 (m, 2 H), 2.19 (s, 3 H), 2.06-2.12 (m, 2 H), 1.90-1.98 (m, 2 H), 1.61-1.68 (m, 6 H), 1.36-1.39 (m, 4 H). ¹³C{¹H} NMR (75 MHz): δ 212.8, 137.6, 113.9, 51.2, 37.4, 32.6, 27.4, 25.4, 24.6, 22.2. TLC: *R_f* = 0.55. Anal. calcd (found) for C₁₂H₂₀O: H, 11.18 (11.27); C, 79.94 (79.71).

For 1-(1-But-3-enylcyclohexyl)-3-hydroxy-1-butanone: ^1H NMR (300 MHz): δ 5.71 (tdd, J = 6.3, 10.2, 16.8 Hz, 1 H), 4.89-4.99 (m, 2 H), 4.12-4.20 (m, 1 H), 3.43 (br s, 1 H), 2.64 (dd, J = 2.7, 18.0 Hz, 1 H), 2.43 (dd, J = 9.0, 18.0 Hz, 1 H), 1.94-1.99 (m, 2 H), 1.77-1.86 (m, 2 H), 1.50-1.57 (m, 5 H), 1.23 (br s, 6 H), 1.17 (d, J = 6.3 Hz, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz): δ 216.5, 137.4, 114.1, 63.3, 51.2, 44.2, 37.3, 32.3, 27.4, 25.2, 22.1, 21.7. IR (neat, cm^{-1}): 3439, 2931, 2860, 1693. TLC: R_f = 0.17. Anal. calcd (found) for $\text{C}_{14}\text{H}_{24}\text{O}_2$: H, 10.78 (10.78); C, 74.95 (74.91).

For 1-(1-But-3-enyl-cyclohexyl)-1,3-butanedione: Enol:keto = 10:1. ^1H NMR: δ 16.0 (br s, 1 H), 5.73 (tdd, J = 6.4, 10.0, 16.8 Hz, 1 H), 5.62 (s, 1 H), 4.87-4.98 (m, 2 H), 2.07 (s, 3 H), 1.86-1.97 (m, 4 H), 1.47-1.61 (m, 5 H), 1.26-1.42 (m, 5 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 200.0, 191.1, 138.9, 114.5, 98.1, 46.8, 39.8, 33.8, 28.3, 26.3, 25.3, 22.9. IR (neat, cm^{-1}): 2933, 2855, 2359, 2340, 1601, 1455. TLC: R_f = 0.69. Anal. calcd (found) for $\text{C}_{14}\text{H}_{24}\text{O}_2$: H, 9.97 (9.81); C, 75.63 (75.46).

Cyclohexenones

2-Acetyl-3,6,6-trimethyl-2-cyclohexenone (5) (Catalytic in 2). Alkenyl dione **4** (91 mg, 0.50 mmol) was added via syringe pump over 3 h into a well-stirred suspension of CuCl_2 (200 mg, 1.48 mmol) and **2** (7 mg, 0.027 mmol) in 1,2-dichloroethane (DCE, 10 mL). The resulting mixture was filtered through a plug of silica gel and eluted with ether (30 mL). The resulting solution was dried (MgSO_4) and concentrated to give an oil that was chromatographed (SiO_2 , hexane–ether = 5:1 \rightarrow 1:2) to give **5** (86 mg, 96%).

5 (Catalytic in 2 and CuCl_2). Alkenyl dione **4** (91 mg, 0.50 mmol) was added slowly over 2 h to a suspension of **2** (7 mg, 0.027 mmol), CuCl_2 (8 mg, 0.06 mmol), and HCl (2 N in Et_2O , 40 μl , 0.08 mmol) in DCE (10 mL) under O_2 (1 atm). Work-up and chromatography gave **5** (64 mg, 71%).

For 5: ^1H NMR: δ 2.34-2.37 (m, 2 H), 2.25 (s, 3 H), 1.87 (s, 3 H), 1.78 (t, J = 6.4 Hz, 2 H), 1.08 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 205.0, 202.1, 157.7, 138.2, 40.5, 35.5, 31.6, 29.5, 24.1, 21.6. IR (neat, cm^{-1}): 2965, 2924, 2701, 1662, 1626. TLC: R_f = 0.22. Anal. calcd (found) for $\text{C}_{11}\text{H}_{16}\text{O}_2$: H, 8.95 (9.01); C, 73.30 (73.16).

The remaining cyclohexenones were synthesized employing a procedure analogous to that used to synthesize **5** employing a catalytic amount of **2** and a stoichiometric amount of CuCl₂.

3,6,6-Trimethyl-2-propionyl-2-cyclohexenone (Table 1, entry 1). ¹H NMR: δ 2.51 (q, *J* = 7.2 Hz, 2 H), 2.34 (t, *J* = 6.0 Hz, 2 H), 1.82 (s, 3 H), 1.77 (t, *J* = 6.0 Hz, 2 H), 1.07 (s, 6 H), 1.03 (t, *J* = 7.6 Hz, 3 H). ¹³C{¹H} NMR: δ 208.2, 202.2, 157.0, 138.1, 40.5, 37.2, 35.4, 29.3, 24.1, 21.5, 7.9. IR (neat, cm⁻¹): 2975, 2926, 1704, 1661. TLC: *R_f* = 0.22. Anal. calcd (found) for C₁₂H₁₈O₂: H, 9.34 (9.36); C, 74.19 (73.99).

2-Isobutyryl-3,6,6-trimethyl-2-cyclohexenone (Table 1, entry 2). ¹H NMR : δ 2.79 (septet, *J* = 6.8 Hz, 1 H), 2.33-2.36 (m, 2 H), 1.81 (s, 3 H), 1.77 (t, *J* = 6.0 Hz, 2 H), 1.07 (s, 6 H), 1.03 (d, *J* = 7.2 Hz, 6 H). ¹³C{¹H} NMR: δ 211.2, 202.4, 157.7, 137.6, 41.1, 40.5, 35.4, 29.3, 24.1, 21.8, 17.9. IR (neat, cm⁻¹): 2970, 2930, 1697, 1660. TLC: *R_f* = 0.36. Anal. calcd (found) for C₁₃H₂₀O₂: H, 9.68 (9.61); C, 74.96 (74.97).

2-(2,2-Dimethyl-propionyl)-3,6,6-trimethyl-2-cyclohexenone (Table 1, entry 3). White needles, mp 55-56 °C. ¹H NMR: δ 2.32 (t, *J* = 6.0 Hz, 2 H), 1.78 (t, *J* = 6.0 Hz, 2 H), 1.77 (s, 3 H), 1.10 (s, 9 H), 1.07 (s, 6 H). ¹³C{¹H} NMR: δ 215.5, 202.3, 154.9, 138.6, 44.7, 40.6, 35.7, 29.0, 27.3, 24.2, 22.2. IR (neat, cm⁻¹): 3011, 2970, 1740, 1439, 1369, 1215. TLC: *R_f* = 0.27. Anal. calcd (found) for C₁₁H₁₆O₂: H, 9.97 (9.89); C, 75.63 (75.71).

2-Cyclohexanecarbonyl-3,6,6-trimethyl-2-cyclohexenone (Table 1, entry 4). White powder, mp 60-61 °C. ¹H NMR: δ 2.50-2.52 (m, 1 H), 2.36 (t, *J* = 6.0 Hz, 2 H), 1.82-1.86 (m, 2 H), 1.83 (s, 3 H), 1.79 (t, *J* = 6.0 Hz, 2 H), 1.72 (br d, *J* = 6.8 Hz, 2 H), 1.62 (br d, *J* = 7.2 Hz, 1 H), 1.05-1.31 (m, 5 H), 1.10 (s, 6 H). ¹³C{¹H} NMR: δ 210.7, 202.5, 157.6, 137.8, 50.9, 40.6, 35.5, 29.4, 28.2, 24.2, 21.9. IR (neat, cm⁻¹): 3024, 2971, 1729, 1375. TLC: *R_f* = 0.27. Anal. calcd (found) for C₁₆H₂₄O₂: H, 9.74 (9.89); C, 77.38 (77.26).

6-Ethyl-3-methyl-2-propionyl-2-cyclohexenone (Table 1, entry 5). ¹H NMR: δ 2.55 (q, *J* = 7.2 Hz, 2 H), 2.24-2.46 (m, 3 H), 1.98 (qd, *J* = 4.4, 13.2 Hz, 1 H), 1.80 (s, 3 H), 1.80-1.86 (m, 1 H), 1.05 (d, *J* = 6.8 Hz, 3 H), 1.00 (t, *J* = 7.6 Hz, 3 H). ¹³C{¹H} NMR: δ 208.0, 199.7, 158.3, 139.3, 40.9, 37.4,

31.7, 30.0, 21.6, 15.1, 7.8. IR (neat, cm^{-1}): 2974, 2934, 1700, 1661, 1376. TLC: $R_f = 0.24$. Anal. calcd (found) for $\text{C}_{11}\text{H}_{16}\text{O}_2$: H, 8.95 (9.00); C, 73.30 (73.15).

2-Acetyl-3-methyl-2-cyclohexenone (Table 1, entry 6). ^1H NMR: δ 2.33-2.38 (m, 4 H), 2.27 (s, 3 H), 1.94 (quintet, $J = 6.4$ Hz, 2 H), 1.89 (s, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 204.6, 197.1, 160.1, 139.9, 37.6, 32.4, 31.9, 21.9. IR (neat, cm^{-1}): 2950, 1701, 1662, 1425. TLC: $R_f = 0.16$. Anal. calcd (found) for $\text{C}_9\text{H}_{12}\text{O}_2$: H, 7.95 (7.83); C, 71.03 (70.90).

2-(2,2-Dimethylpropionyl)-3-methyl-2-cyclohexenone (Table 1, entry 7). ^1H NMR: δ 2.37 (t, $J = 6.0$ Hz, 2 H), 2.33 (t, $J = 6.0$ Hz, 2 H), 1.98 (quintet, $J = 6.0$ Hz, 2 H), 1.81 (s, 3 H), 1.13 (s, 9 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 215.2, 197.2, 156.9, 14.01, 44.7, 37.3, 31.8, 27.2, 22.5, 22.0. IR (neat, cm^{-1}): 2970, 2925, 1699, 1661, 1423. TLC: $R_f = 0.13$. Anal. calcd (found) for $\text{C}_{12}\text{H}_{18}\text{O}_2$: H, 9.34 (9.37); C, 74.19 (74.26).

2-Benzoyl-3-methyl-2-cyclohexenone (Table 1, entry 8). ^1H NMR: δ 7.85-7.83 (m, 2 H), 7.58-7.54 (m, 1 H), 7.46-7.43 (m, 2 H), 2.51 (t, $J = 6.8$ Hz, 2 H), 2.50 (t, $J = 6.4$ Hz, 2 H), 2.13 (m, 2 H), 1.87 (s, 3 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 197.5, 192.7, 160.1, 138.1, 137.1, 134.0, 129.4, 129.0, 37.6, 32.3, 22.4, 22.2. TLC: $R_f = 0.08$. ^1H NMR data was consistent with the published data.⁷

2-Acetyl-3,4,4-trimethyl-2-cyclohexenone (Table 1, entry 9). Tan solid, mp 51-53 $^\circ\text{C}$. ^1H NMR: δ 2.48 (d, $J = 6.8$ Hz, 1 H), 2.46 (d, $J = 6.8$ Hz, 1 H), 2.29 (s, 3 H), 1.86 (d, $J = 6.8$ Hz, 2 H), 1.83 (s, 3 H), 1.19 (s, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 205.8, 196.9, 164.7, 139.5, 37.0, 36.0, 34.7, 32.1, 26.5, 16.8. IR (neat, cm^{-1}): 2964, 2920, 2869, 1709, 1666, 1607, 1547, 1468, 1422, 1376, 1354, 1333, 1308, 1280, 1211, 1162. TLC: $R_f = 0.22$. Anal. calcd (found) for $\text{C}_{11}\text{H}_{16}\text{O}_2$: H, 8.95 (8.98); C, 73.30 (73.26).

2-Acetyl-3-methyl-spiro[5.5]undec-2-en-1-one (Table 1, entry 10). ^1H NMR: δ 2.35 (t, $J = 6.0$ Hz, 2 H), 2.28 (s, 3 H), 1.89 (s, 3 H), 1.87 (t, $J = 6.0$ Hz, 2 H), 1.76-1.69 (m, 2 H), 1.66-1.59 (m, 2 H), 1.55-1.32 (m, 6 H). $^{13}\text{C}\{^1\text{H}\}$ NMR: δ 205.0, 156.7, 43.5, 31.7, 31.6, 30.1, 29.0, 26.1, 21.8, 21.4. IR (neat, cm^{-1}): 2925, 2861, 1698, 1659, 1447. TLC: $R_f = 0.24$. Anal. calcd (found) for $\text{C}_{14}\text{H}_{20}\text{O}_2$: H, 9.15 (9.28); C, 76.33 (76.49).

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