

A Mild, Catalytic and Highly Selective Method for the Oxidation of α,β -Enones to 1,4-Enediones

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Supplementary Material

General

¹H NMR and ¹³C NMR Spectra were recorded on Bruker DPX 400 or 500 spectrometer in deuterium chloroform. High resolution mass spectral (HRMS) analyses were measured on a Kratos 890 spectrometer by means of EI techniques. All anhydrous solvents were dried by standard techniques and freshly distilled before use or purchased in anhydrous form from Fluka. All flash chromatography was carried out using dry-packed Merck 9385 Kieselgel 60 silica gel. Reactions were monitored by thin layer chromatography (TLC), carried out on Kieselgel 60 PF₂₅₄ (Merck) 0.2 mM plates. All reactions were carried out under air unless stated otherwise.

3-Acetyl-2-cyclopentenone. A 25 mL round-bottom flask equipped with a stir bar was charged under air with Pd(OH)₂-C (20%) (8.5 mg, 0.016 mmol), K₂CO₃ (11.0 mg, 0.08 mmol), CH₂Cl₂ (1 mL) and 1-acetyl-1-cyclopentene (37 μ L, 0.32 mmol). The mixture was cooled to 4 °C with ice bath, and *t*-butylhydroperoxide (TBHP) (160 μ L, 1.6 mmol) was added with vigorous stirring. The flask was sealed (without removal of air) with a rubber septum and allowed to warm up to 24 °C. The reaction mixture was stirred at 24 °C for 48 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH₂Cl₂. After removal of the solvent by rota evaporation at 24 °C, the crude product was purified by flash column chromatography (hexane/ether, 50:50) to provide 32 mg (81%) of 3-acetyl-2-cyclopentenone as a clear oil. ¹H NMR (400 MHz, CDCl₃): δ 6.62 (t, *J* = 1.8 Hz, 1 H), 2.76 (m, 2 H), 2.50 (m, 2 H), 2.48 (s, 3 H). ¹³C NMR (400 Hz, CDCl₃): δ 210.2, 197.2, 137.0, 135.5, 35.4, 27.8, 26.3 ; IR (film): 1715, 1681 cm⁻¹; HRMS (EI) *m/z*, calcd 124.0524, found, 124.0527.

3-Acetyl-2-cyclohexenone. Into a 25 mL round-bottom flask equipped with a stir bar was placed Pd(OH)₂-C (20%) (8.5 mg, 0.016 mmol), K₂CO₃ (11.0 mg, 0.08 mmol), CH₂Cl₂ (1 mL) and 1-acetyl-cyclohexene (41 μ L, 0.32 mmol) under air. The mixture was cooled to 4 °C with ice bath, and TBHP (160 μ L, 1.6 mmol) was added. The flask was sealed with a septum and the resulting mixture was stirred at 4 °C for 36 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH₂Cl₂. After removal of the solvent by rota evaporation at 24 °C, the crude product was purified by flash column chromatography (hexane-ether, 60:40) to provide 38 mg (86%) of 3-acetyl-2-cyclohexenone as a yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 6.58 (bs, 1 H), 2.51 (m, 2 H), 2.49 (m, 2 H), 2.41 (s, 3 H), 2.01 (m, 2 H). ¹³C NMR (400 Hz, CDCl₃): δ 204.1, 202.7, 157.2,

135.0, 40.4, 29.0, 26.0, 24.4. IR (film): 1676 (br) cm^{-1} . HRMS (EI) m/z , calcd, 138.0681, found, 138.0677.

4-Cyclopentene-1,3-dione Monoethylene Ketal. A 25-mL round-bottom flask equipped with a stir bar is charged with 20% $\text{Pd}(\text{OH})_2\text{-C}$ (17 mg, 0.032 mmol Pd), K_2CO_3 (11 mg, 0.08 mmol), 1 mL of CH_2Cl_2 , 2-cyclopenten-1-one ethylene ketal (76 μL , 0.64 mmol). The mixture was cooled to 4 $^\circ\text{C}$ with ice bath and TBHP (160 μL , 1.6 mmol) was added with vigorous stirring. The flask was sealed (without removal of air) with a rubber septum and allowed to warm up to 24 $^\circ\text{C}$ and the content was stirred for 24 h at which time an additional 8.5 mg of 20% $\text{Pd}(\text{OH})_2\text{-C}$ (0.016 mmol), 5.5 mg of K_2CO_3 (0.04 mmol) and 80 μL of *t*-BuOOH (0.8 mmol) were added. The reaction was stirred at 24 $^\circ\text{C}$ for another 24 h and a third batch of 8.5 mg of 20% $\text{Pd}(\text{OH})_2\text{-C}$ (0.016 mmol), 5.5 mg of K_2CO_3 (0.04 mmol) and 80 μL of *t*-BuOOH (0.8 mmol) were added. After an additional 24 h at 24 $^\circ\text{C}$ thin layer chromatographic analysis indicated that the reaction was complete. The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane–ether, 40 : 60) to provide 72 mg (80%) of 4-cyclopentene-1,3-dione mono-ethylene ketal as a clear oil. ^1H NMR (400 MHz, CDCl_3): δ 7.21 (d, J = 6.2 Hz, 1 H), 6.20 (d, J = 6.2 Hz, 1 H), 4.06 (m, 4 H), 2.61 (s, 2 H); ^{13}C NMR (400 Hz, CDCl_3): δ 203.9, 156.2, 135.3, 111.6, 65.1, 45.2; IR (film): 1723 cm^{-1} ; HRMS (EI) m/z , calcd 140.0473, found, 140.0469.

2-Cyclohexene-1,4-dione Monoethylene Ketal. A 10 mL round-bottom flask equipped with a stir bar was charged under air with $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (17 mg, 0.032 mmol), K_2CO_3 (11 mg, 0.08 mmol) and CH_2Cl_2 (0.5 mL) and 2-cyclohexen-1-one ethylene ketal (45 μL , 0.32 mmol). (For preparation see *Tetrahedron Lett.* **1980**, 21, 1357). The mixture was cooled to 4 $^\circ\text{C}$ with ice bath and TBHP (40 μL , 0.4 mmol) was added. The flask was sealed with a septum and the reaction was stirred at 4 $^\circ\text{C}$ for 4 h and the second batch of TBHP (160 μL , 1.6 mmol) was added. The reaction was stirred at 4 $^\circ\text{C}$ for another 60 h and shown to be complete by TLC analysis. The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane–ether, 50 : 50) to provide 39 mg (79%) of 2-cyclohexene-1,4-dione monoethylene ketal as a clear oil. ^1H NMR (400 MHz, CDCl_3): δ 6.63 (d, J = 11.0 Hz, 1 H), 6.02 (d, J = 11.0 Hz, 1 H), 4.05 (m, 4 H), 2.62 (t, J = 5.6 Hz, 2 H), 2.20 (t, J = 5.6 Hz, 2 H); ^{13}C NMR (400 Hz, CDCl_3): δ 200.6, 148.3, 132.5, 67.0, 37.2, 34.8; IR (film): 1678 cm^{-1} ; HRMS (EI) m/z , calcd 154.0630, found, 154.0635.

2-Cyclohepten-1,4-dione. A 10 mL round-bottom flask equipped with a stir bar was charged under air with $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (8.5 mg, 0.016 mmol), K_2CO_3 (5.5 mg, 0.08 mmol), CH_2Cl_2 (1 mL), 2-cyclohepten-1-one (80%) (45 μL , 0.32 mmol). The mixture was cooled to 4 $^\circ\text{C}$ with ice bath and TBHP (80 μL , 0.8 mmol) was added with vigorous stirring. The flask was sealed (without removal of air) with a rubber septum and allowed to warm up to 24 $^\circ\text{C}$ and the contents were stirred for 24 h at which time an additional 8.5 mg of 20% $\text{Pd}(\text{OH})_2\text{-C}$ (0.016 mmol), 5.5 mg of K_2CO_3 (0.04 mmol) and 80 μL of *t*-BuOOH (0.8 mmol) were added. The reaction mixture was stirred at 24 $^\circ\text{C}$ for an additional 36 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash

column chromatography (hexane–ether, 50:50) to provide 33 mg (82%) of 2-cyclohepten-1,4-dione as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 6.45 (s, 2 H), 2.80 (m, 4 H), 2.06 (m, 2 H). ^{13}C NMR (400 Hz, CDCl_3): δ 201.8, 138.0, 44.2, 18.9; IR (film): 1671 cm^{-1} ; HRMS (EI) m/z , calcd 124.0524, found, 124.0530.

(E)-1-Phenyl-2-penten-1,4-dione. Into 25 mL round-bottom flask equipped with a stir bar was placed $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (8.5 mg, 0.016 mmol), K_2CO_3 (11.0 mg, 0.08 mmol) and CH_2Cl_2 (1 mL) under air. The mixture was cooled to 4 $^\circ\text{C}$, and (E)-1-phenyl-2-penten-1-one (54 μL , 0.32 mmol), and TBHP (160 μL 1.6 mmol) was added. The flask was sealed with a septum and the contents stirred at 4 $^\circ\text{C}$ for 36 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane–ether, 80 : 20) to provide 50 mg (90%) of (E)-1-phenyl-2-penten-1,4-dione as a yellow solid. ^1H NMR (400 MHz, CDCl_3): δ 7.99 (m, 2 H), 7.70 (d, J = 15.8 Hz, 1 H), 7.64 (m, 1 H), 7.52 (m, 2 H), 7.09 (d, J = 15.8 Hz, 1 H), 2.42 (s, 3 H); ^{13}C NMR (400 Hz, CDCl_3): δ 197.8, 190.5, 138.6, 136.6, 134.0, 133.8, 128.9, 128.7, 29.1; IR (film): 1660 cm^{-1} ; HRMS (EI) m/z , calcd 174.0681, found, 174.0678.

(E)-3-Nonen-2,5-dione (1). A 10 mL round-bottom flask equipped with a stir bar was charged under air with $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (8.5 mg, 0.016 mmol), K_2CO_3 (5.5 mg, 0.04 mmol), CH_2Cl_2 (1 mL), and (E)-3-nonen-2-one (54 μL , 0.32 mmol). The mixture was cooled to 4 $^\circ\text{C}$ with ice bath and TBHP (80 μL , 0.8 mmol) was added with vigorous stirring. The flask was sealed (without removal of air) with a rubber septum and allowed to warm up to 24 $^\circ\text{C}$ and the contents were stirred for 24 h at which time an additional 8.5 mg of 20% $\text{Pd}(\text{OH})_2\text{-C}$ (0.016 mmol), 5.5 mg of K_2CO_3 (0.04 mmol) and 80 μL of *t*-BuOOH (0.8 mmol) were added. The reaction mixture was stirred at 24 $^\circ\text{C}$ for an additional 48 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane–ether, 50 : 50) to provide 40 mg (81%) of (E)-3-nonen-2,5-dione as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ 6.91 (d, J = 14.8 Hz, 1 H), 6.82 (d, J = 14.8 Hz, 1 H), 2.70 (t, J = 6.9 Hz, 2 H), 2.35 (s, 3 H), 1.59 (m, 2 H), 1.40 (m, 2 H), 0.91 (t, J = 6.1 Hz, 3 H). ^{13}C NMR (400 Hz, CDCl_3): δ 201.6, 199.3, 137.6, 137.3, 41.5, 28.5, 26.4, 22.6; IR (film): 1704, 1683 cm^{-1} ; HRMS (EI) m/z , calcd 154.0994, found, 154.0987.

4-*t*-Butylperoxy-4-isopropyl-2-cyclohexenone (6) and 4-Hydroxy-4-isopropyl-2-cyclohexenone (7a). Into a 25 mL round-bottom flask equipped with a stir bar was placed $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (8.5 mg, 0.016 mmol), K_2CO_3 (5.5 mg, 0.04 mmol), CH_2Cl_2 (1 mL) and 4-isopropyl-2-cyclohexenone (45 μL , 0.32 mmol) under air. The mixture was cooled to 4 $^\circ\text{C}$ with ice bath and TBHP (80 μL , 0.8 mmol) was added. The flask was sealed with a rubber septum and degassed and refilled with argon through a balloon. The mixture was allowed to warm up to 24 $^\circ\text{C}$ with vigorous stirring. After a period of 24 h an additional 8.5 mg of 20% $\text{Pd}(\text{OH})_2\text{-C}$ (0.016 mmol), 5.5 mg of K_2CO_3 (0.04 mmol) and 80 μL of *t*-BuOOH (0.8 mmol) were added. The reaction mixture was stirred at 24 $^\circ\text{C}$ for an additional 36 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane–ether, 50 : 50) to provide 44 mg (61%) 4-*t*-

butylperoxy-4-isopropyl-2-cyclohexenone (**6**) and 11 mg (22%) 4-hydroxy-4-isopropyl-2-cyclohexenone (**7a**) as yellow liquids.

For **6**: ^1H NMR (400 MHz, CDCl_3): δ 6.85 (d, J = 10.0 Hz, 1 H), 6.08 (d, J = 10.0 Hz, 1 H), 2.72 (m, 1 H), 2.38 (m, 1 H), 2.26 (m, 1 H), 2.18 (m, 1 H), 2.06 (m, 1 H), 1.19 (s, 9 H), 0.98 (d, J = 7.0 Hz, 3 H), 0.96 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (400 Hz, CDCl_3): δ 200.2, 152.5, 131.0, 80.9, 79.9, 35.0, 33.1, 34.2, 26.8, 17.8, 17.0; IR (film): 1690 cm^{-1} ; HRMS (EI) m/z , calcd, 226.1569, found, 226.1565.

For **7a**: ^1H NMR (400 MHz, CDCl_3): δ 6.79 (d, J = 10.0 Hz, 1 H), 5.88 (d, J = 10.0 Hz, 1 H), 2.65 (m, 1 H), 2.40 (m, 1 H), 2.13 (m, 1 H), 1.96 (m, 1 H), 1.02 (d, J = 7.0 Hz, 3 H), 0.99 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (500 Hz, CDCl_3): δ 197.7, 152.1, 127.7, 77.9, 35.0, 32.2, 29.2, 15.6, 14.8; IR (film): 3468, 1668 cm^{-1} ; HRMS (CI) m/z , calcd, 154.0994, found, 154.0990.

For **7b**: Into a 25 mL round-bottom flask equipped with a stir bar was placed $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (8.5 mg, 0.016 mmol), K_2CO_3 (11.0 mg, 0.08 mmol), CH_2Cl_2 (1 mL) and 4-isopropyl-2-cyclohexenone (45 μL , 0.32 mmol) under air. The mixture was cooled to 4 $^\circ\text{C}$, and TBHP (40 μL , 0.4 mmol) was added. The flask was sealed with a septum and the reaction mixture was stirred at 4 $^\circ\text{C}$ for 4 h and the second batch of TBHP (80 μL , 0.8 mmol) was added. The reaction mixture was stirred at 4 $^\circ\text{C}$ for 12 h and a new compound was shown to be formed in addition to 4-hydroxy-4-isopropyl-2-cyclohexenone and 4-*t*-butylperoxy-4-isopropyl-2-cyclohexenone by TLC analysis. The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane–ether, 50 : 50) to provide 11 mg (15%) 4-*t*-butylperoxy-4-isopropyl-2-cyclohexenone, 6 mg (12%) 4-hydroxy-4-isopropyl-2-cyclohexenone and 2 mg (4%) 1-oxo-2-cyclohexen-4-yl hydroperoxide (**7b**) as liquids. Found for **7b**: ^1H NMR (500 MHz, CDCl_3): δ 7.40 (s, 1 H), 6.82 (d, J = 10.0 Hz, 1 H), 6.16 (d, J = 10.0 Hz, 1 H), 2.76 (m, 1 H), 2.45 (m, 1 H), 2.28 (m, 2 H), 2.12 (m, 1 H), 1.05 (d, J = 7.0 Hz, 3 H), 1.01 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (500 Hz, CDCl_3): δ 199.1, 149.2, 132.2, 82.7, 34.1, 33.1, 25.8, 17.4, 16.5; IR (film): 2356, 1670 cm^{-1} ; HRMS (EI) m/z , calcd, 170.0943, found, 170.0945.

5-Methyl-5-*t*-butylperoxy-3-hexen-2-one. Into a 25 mL round-bottom flask equipped with a stir bar was placed $\text{Pd}(\text{OH})_2\text{-C}$ (20%) (8.5 mg, 0.016 mmol), K_2CO_3 (11.0 mg, 0.08 mmol), CH_2Cl_2 (1 mL) and 5-methyl-3-hexen-2-one (43 μL , 0.32 mmol) under air. The mixture was cooled to 4 $^\circ\text{C}$ with ice bath and TBHP (160 μL , 1.6 mmol) was added. The flask was sealed with a septum and degassed and refilled with argon through a balloon. The reaction mixture was stirred at 4 $^\circ\text{C}$ for 48 h (reaction complete by TLC analysis). The reaction mixture was then filtered through a short pad of silica gel and washed with CH_2Cl_2 . After removal of the solvent by rota evaporation at 24 $^\circ\text{C}$, the crude product was purified by flash column chromatography (hexane/ether, 95 : 5) to provide 52 mg (81%) of 5-methyl-5-*t*-butylperoxy-3-hexen-2-one as a clear oil. ^1H NMR (400 MHz, CDCl_3): δ 6.88 (d, J = 16.5 Hz, 1 H), 6.10 (d, J = 16.5 Hz, 1 H), 2.28 (s, 3 H), 1.32 (s, 6 H), 1.21 (s, 9 H); ^{13}C NMR (400 Hz, CDCl_3): δ 201.5, 151.9, 128.9, 79.7, 79.4, 27.1, 26.7, 24.8; IR (film): 1680 cm^{-1} ; HRMS (EI) m/z , calcd, 200.1412, found, 200.1418.

Coproduction of *t*-Butyl Alcohol

Into 25 mL round-bottom flask equipped with a stir bar was placed Pd(OH)₂-C (20%) (8.5 mg, 0.016 mmol), K₂CO₃ (11.0 mg, 0.08 mmol) and CH₂Cl₂ (1 mL) under air. The mixture was cooled to 4 °C, and (E)-1-phenyl-2-penten-1-one (54 μL, 0.32 mmol), and TBHP (160 μL, 1.6 mmol) was added. The flask was sealed with a septum and the reaction mixture was stirred at 4 °C and monitored by GC analysis. During the first two hours, *t*-butyl alcohol was formed as the main product (30% with regards to TBHP) and the conversion of the starting material is only 10%.