

Supporting Information

Palladium(0)-Catalyzed Ring Cleavage of Cyclobutanone Oximes Leading to Nitriles via β -Carbon Elimination

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General Methods. NMR spectra were recorded on JEOL EX-400 (^1H NMR, 400 MHz; ^{13}C NMR, 100 MHz) instruments for solutions in CDCl_3 with Me_4Si as an internal standard: the following abbreviations are used; s: singlet, d: doublet, t: triplet, q: quartet, quintet, m: multiplet. FT-IR spectra (thin film for liquids, KBr disk for solids) were recorded on a Nicolet Impact 400 spectrometer. Melting points are uncorrected. Column chromatography on SiO_2 was performed with Merck silica gel 60. Recycling preparative high performance liquid chromatography (HPLC) was performed on a JAI LC-908-G30 instrument (600 mm \times 20 mm \times 2, JAIGEL-1H and JAIGEL-2H dual styrene polymer columns) equipped with ultraviolet (UV) and refractive-index (RI) detector and CHCl_3 as an eluent. Elemental analysis was done at the Microanalytical Center of Kyoto University.

Commercially available organic and inorganic compounds were used without further purification except for the solvent, which was distilled by the known method before use. $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (dba=dibenzylideneacetone) and $\text{Pd}(\text{PPh}_3)_4$ were synthesized by the literature methods.

Typical Procedure for Preparation of 3-Phenylcyclobutanone *O*-Acetyloxime (1a). To a mixture of hydroxylamine hydrochloride (12 mmol), sodium acetate (15 mmol), ethanol (7 mL) and water (3 mL) in a 30-mL two-necked flask was added 3-

phenylcyclobutanone (10 mmol) and the mixture was stirred at 100 °C for 12 h. The reaction mixture was cooled to room temperature and then ethanol was removed under reduced pressure and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over MgSO₄. The solvent was removed under vacuum and the residue was subjected to column chromatography on SiO₂ with EtOAc–hexane (2/8) as an eluent to give 3-phenylcyclobutanone oxime (100%). To a mixture of 3-phenylcyclobutanone oxime (5 mmol), triethylamine (10 mmol) and CH₂Cl₂ (10 mL) in a 30-mL two-necked flask was added acetic anhydride (7 mmol) at 0 °C. After 6 h, water was added to the above solution, and the mixture was diluted with diethyl ether. The organic layer was washed with water and dried over MgSO₄. The solvent was removed under vacuum and the residue was subjected to column chromatography on SiO₂ with EtOAc–hexane (1/9) as an eluent to give **1a** (4.3 mmol, 86%) as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 2.16 (s, 3H), 3.05–3.22 (m, 2H), 3.44–3.54 (m, 2H), 3.65 (qui, *J* = 8.3 Hz, 1H), 7.23–7.28 (m, 3H), 7.33–7.38 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 19.5, 32.5, 39.4, 39.5, 126.4, 126.9, 128.8, 143.1, 165.0, 168.6. Anal. Calcd for C₁₂H₁₃NO₂: C, 70.92; H, 6.45; N, 6.89. Found: C, 71.01; H, 6.32; N, 6.83. The *O*-acyloximes described below were obtained in 65–80% yields in two steps from the corresponding cyclobutanones.

3-Phenylcyclobutanone *O*-trimethylacetyloxime (1b). This compound was prepared by the same method described above using trimethylacetyl chloride instead of acetic anhydride. Colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 1.28 (s, 9H), 3.06–3.24 (m, 2H), 3.44–3.56 (m, 2H), 3.66 (qui, *J* = 8.3 Hz, 1H), 7.23–7.28 (m, 3H), 7.33–7.38 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 27.3, 32.5, 38.8, 39.3, 39.5, 126.3, 126.9, 128.7, 143.1, 165.5, 175.3. Anal. Calcd for C₁₅H₁₉NO₂: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.63; H, 7.92; N, 5.70.

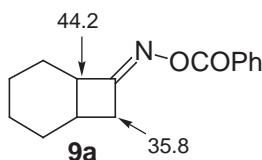
3-Phenylcyclobutanone *O*-benzoyloxime (1c). This compound was prepared by the same method described above using benzoyl chloride. Colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 3.20–3.32 (m, 2H), 3.54–3.77 (m, 3H), 7.24–7.30 (m, 3H), 7.34–7.42 (m, 2H), 7.47 (t, *J* = 7.3 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 8.05–8.09 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 32.5, 39.4, 39.5, 126.3, 126.9, 128.5, 128.7, 128.9, 129.6, 133.2, 143.0,

163.9, 166.0. Anal. Calcd for C₁₇H₁₅NO₂: C, 76.96; H, 5.70; N, 5.71. Found: C, 77.17; H, 5.67; N, 5.70.

3-Hexylcyclobutanone O-benzoyloxime (4): Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.29 (br s, 8H), 1.50–1.60 (m, 2H), 2.35–2.46 (m, 1H), 2.60–2.75 (m, 2H), 3.18–3.30 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.55–7.60 (m, 1H), 8.02–8.08 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 14.1, 22.6, 27.3, 28.4, 29.1, 31.8, 36.2, 37.5, 37.5, 128.5, 129.2, 129.6, 133.2, 164.1, 167.7. Anal. Calcd for C₁₇H₂₃NO₂: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.69; H, 8.58; N, 5.06.

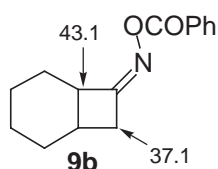
3-tert-Butylcyclobutanone O-benzoyloxime (6): Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 0.92 (s, 9H), 2.34 (qui, *J* = 8.4 Hz, 1H), 2.80–2.91 (m, 2H), 2.95–3.10 (m, 2H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 8.05 (d, *J* = 7.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 25.9, 31.4, 32.8, 32.9, 39.0, 128.5, 129.2, 129.6, 133.2, 164.0, 166.7. Anal. Calcd for C₁₅H₁₉NO₂: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.44; H, 7.76; N, 5.59.

(E)-Bicyclo[4.2.0]octan-7-one O-benzoyloxime (9a). Generally, it is possible to distinguish syn and anti oximes by ¹³C NMR since the chemical shift of α-carbon syn to OH appears upfield than that of the carbon anti to OH at the same position.¹² Thus, we estimated the configurations of **9a** and **9b** according to this trend. Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 1.30–2.00 (m, 8H), 2.40–2.52 (m, 1H), 2.73 (ddd, *J* = 16.1, 5.1, 2.4 Hz, 1H), 3.02 (ddd, *J* = 16.1, 8.6, 1.7 Hz, 1H), 3.40–3.50 (m, 1H), 7.43–7.48 (m, 2H), 7.55–7.61 (m, 1H), 8.01–8.05 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 21.0, 21.6, 23.7, 25.8, 26.7, 35.8, 44.2, 128.4, 129.1, 129.4, 133.0, 164.2, 170.5. Anal. Calcd for C₁₅H₁₇NO₂: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.84; H, 7.27; N, 5.75.



(Z)-Bicyclo[4.2.0]octan-7-one O-benzoyloxime (9b): White solid; mp 73.0–73.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 1.25–1.75 (m, 6H), 1.80–2.05 (m, 2H),

2.42–2.52 (m, 1H), 2.79 (ddd, $J = 16.1, 4.4, 2.4$ Hz, 1H), 3.05 (dd, $J = 16.1, 8.3$ Hz, 1H), 3.37–3.44 (m, 1H), 7.46 (t, $J = 7.3$ Hz, 2H), 7.58 (t, $J = 7.3$ Hz, 1H), 8.05 (d, $J = 7.3$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.4, 21.6, 23.4, 26.8, 27.8, 37.1, 43.1, 128.4, 129.4, 129.6, 133.1, 164.2, 171.0. Anal. Calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.11; H, 7.09; N, 5.73.



***exo*-Tricyclo[4.2.1.0^{2,5}]nonan-3-one *O*-benzoyloxime (12, *E/Z* mixture):** White solid; ^1H NMR (400 MHz, CDCl_3) δ 1.10–1.30 (m), 1.50–1.80 (m), 2.24–2.36 (m), 2.50–2.66 (m), 3.00–3.15 (m), 3.17–3.27 (m), 7.39–7.60 (m), 7.98–8.08 (m). Anal. Calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.23; H, 6.69; N, 5.48.

4,4-Dibutylcyclobutanone *O*-benzoyloxime (14): Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 0.93 (t, $J = 7.3$ Hz, 6H), 1.17–1.39 (m, 8H), 1.50–1.56 (m, 4H), 2.76 (d, $J = 3.9$ Hz, 2H), 2.78 (d, $J = 3.9$ Hz, 2H), 7.45 (t, $J = 7.8$ Hz, 2H), 7.58 (t, $J = 7.8$ Hz, 1H), 8.05 (d, $J = 7.8$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.1, 23.1, 26.5, 36.7, 37.3, 42.2, 42.2, 128.5, 129.2, 129.6, 133.2, 164.1, 167.0. Anal. Calcd for $\text{C}_{19}\text{H}_{27}\text{NO}_2$: C, 75.71; H, 9.03; N, 4.65. Found: C, 75.71; H, 8.82; N, 4.56.

Spiro[3.5]nonan-2-one *O*-benzoyloxime (16): Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 1.38–1.62 (m, 10H), 2.77 (d, $J = 3.9$ Hz, 2H), 2.79 (d, $J = 3.9$ Hz, 2H), 7.43–7.48 (m, 2H), 7.55–7.61 (m, 1H), 8.03–8.08 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 23.2, 25.4, 34.9, 37.3, 42.6, 42.7, 128.5, 129.2, 129.6, 133.2, 164.1, 166.8. Anal. Calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.85; H, 7.51; N, 5.34.

Typical Procedure for the Reaction of Cyclobutanone *O*-Acyloximes. To a mixture of $\text{Pd}_2(\text{dba})_3\text{-CHCl}_3$ (0.0125 mmol), (*R*)-(+)-BINAP (0.0375 mmol) and THF (2 mL) in a 10-mL two-necked flask were added K_2CO_3 (0.50 mmol), cyclobutanone *O*-acyloxime (0.50 mmol) and THF (3 mL) under N_2 and the mixture was stirred at 90 °C (bath

temp.) until the reaction had reached completion by monitoring with TLC analysis. The reaction mixture was cooled to room temperature and then filtered through a pad of Florisil. The filtrate was concentrated under vacuum to give a yellow oil, which was subjected to column chromatography on SiO₂ with diethyl ether-hexane (4/96) as an eluent. All major products were isolated and identified by ¹H and ¹³C NMR, IR and C, H, N combustion analysis. The yields of the products **2**, **3**, **10**, **11** were determined by GLC using pentamethylbenzene as an internal standard. Compounds **5**, **7**, and **8** were isolated as a mixture of isomers. Isolation of **13**, **15** and **17** was carried out using preparative HPLC after column chromatography, because a small amount of unidentified products could not be separated from the major products.

(E)-3-Phenyl-2-butenenitrile (3): Colorless oil; IR (neat) 3063, 2214 (C≡N), 1608, 1575, 1496, 1446, 1381, 1261, 827, 757, 692 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.47 (s, 3H), 5.62 (s, 1H), 7.38–7.48 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 20.2 (q), 95.6 (d), 117.6 (s), 125.9 (d), 128.8 (d), 130.3 (d), 138.3 (s), 159.8 (s). Anal. Calcd for C₁₀H₉N: C, 83.88; H, 6.34; N, 9.78. Found: C, 84.10; H, 6.52; N, 9.75.

3-Methyl-2-nonenitrile (5, E and Z mixture): Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 0.89 (t, *J* = 6.8 Hz, 3H, *E*-isomer), 0.89 (t, *J* = 6.8 Hz, 3H, *Z*-isomer), 1.25–1.55 (m), 1.90 (d, *J* = 1.5 Hz, 3H, *Z*-isomer), 2.04 (d, *J* = 1.0 Hz, 3H, *E*-isomer), 2.17 (t, *J* = 7.3 Hz, 2H, *E*-isomer), 2.40 (t, *J* = 7.3 Hz, 2H, *Z*-isomer), 5.10 (q, *J* = 1.0 Hz, 1H, *E*- and *Z*-isomer). Anal. Calcd for C₁₀H₁₇N: C, 79.41; H, 11.33; N, 9.26. Found: C, 79.31; H, 11.43; N, 9.05.

4,4-Dimethyl-3-methylenepentanenitrile (7) and (E)-3,4,4-trimethyl-2-pentenitrile (8): Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 1.10 (s, 9H, **7**), 1.11 (s, 9H, **8**), 2.08 (s, 3H, **8**), 3.13 (s, 2H, **7**), 5.13 (s, 1H, **7**), 5.18 (s, 1H, **8**), 5.23 (s, 1H, **7**). Anal. Calcd for C₈H₁₃N: C, 77.99; H, 10.64; N, 11.37. Found: C, 77.70; H, 10.80; N, 11.09.

2-Methylene-1-cyclohexanecarbonitrile (10): Colorless oil; IR (neat) 2941, 2862, 2245 (C≡N), 1652, 1447, 901 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.47–2.14 (m,

7H), 2.43 (ddd, $J = 13.9, 5.7, 3.9$ Hz, 1H), 3.25 (dd, $J = 9.3, 4.4$ Hz, 1H), 4.93 (s, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 24.2 (t), 27.1 (t), 32.0 (t), 33.5 (t), 35.8 (d), 110.6 (t), 120.1 (s), 142.2 (s). Anal. Calcd for $\text{C}_8\text{H}_{11}\text{N}$: C, 79.29; H, 9.15; N, 11.56. Found: C, 79.50; H, 9.07; N, 11.42.

2-Cyclohexen-1-ylacetonitrile (11): Colorless oil; IR (neat) 3022, 2927, 2862, 2246 ($\text{C}\equiv\text{N}$), 1449, 1425, 724, 676 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.27–1.38 (m, 1H), 1.45–1.57 (m, 1H), 1.65–1.74 (m, 1H), 1.83–1.98 (m, 3H), 2.25 (dd, $J = 19.0, 16.6$ Hz, 1H), 2.27 (dd, $J = 17.8, 16.6$ Hz, 1H), 2.37–2.47 (m, 1H), 5.50 (dd, $J = 10.3, 2.4$ Hz, 1H), 5.78 (ddd, $J = 10.3, 5.9, 3.4$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 20.7 (t), 23.8 (t), 24.8 (t), 28.5 (t), 32.4 (d), 118.8 (s), 127.7 (d), 130.2 (d). Anal. Calcd for $\text{C}_8\text{H}_{11}\text{N}$: C, 79.29; H, 9.15; N, 11.56. Found: C, 79.21; H, 9.37; N, 11.27.

3-Methylene-2-norbornanecarbonitrile (13): Colorless oil; IR (neat) 2970, 2877, 2237 ($\text{C}\equiv\text{N}$), 1665, 899, 862 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 1.26–1.40 (m, 2H), 1.46 (dd, $J = 10.3, 1.5$ Hz, 1H), 1.65–1.75 (m, 2H), 1.80 (d, $J = 10.3$ Hz, 1H), 2.71 (s, 1H), 2.85 (s, 1H), 2.97 (d, $J = 1.5$ Hz, 1H), 5.02 (s, 1H), 5.13 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 27.7 (t), 28.6 (t), 37.9 (t), 38.0 (d), 42.2 (d), 44.5 (d), 108.0 (t), 120.8 (s), 149.8 (s). Anal. Calcd for $\text{C}_9\text{H}_{11}\text{N}$: C, 81.16; H, 8.32; N, 10.52. Found: C, 81.21; H, 8.57; N, 10.42.

2,2-Dibutylcyclopropanecarbonitrile (15): Colorless oil; IR (neat) 2958, 2932, 2862, 2234 ($\text{C}\equiv\text{N}$), 1467 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.87–0.97 (m, 8H), 1.15 (dd, $J = 8.3, 5.4$ Hz, 1H), 1.22–1.60 (m, 12H); ^{13}C NMR (100 MHz, CDCl_3) δ 9.3 (d), 14.0 (q), 14.0 (q), 21.0 (t), 22.7 (t), 22.8 (t), 28.3 (t), 28.3 (s), 32.4 (t), 34.8 (t), 121.0 (s). Anal. Calcd for $\text{C}_{12}\text{H}_{21}\text{N}$: C, 80.38; H, 11.81; N, 7.81. Found: C, 80.47; H, 11.64; N, 7.60.

Spiro[2.5]octane-1-carbonitrile (17): Colorless oil; IR (neat) 2931, 2855, 2233 ($\text{C}\equiv\text{N}$), 1779, 1446, 973, 881, 843, 791 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.92 (dd, $J = 5.4, 4.9$ Hz, 1H), 0.95 (dd, $J = 8.3, 4.9$ Hz, 1H), 1.15 (dd, $J = 8.3, 5.4$ Hz, 1H), 1.18–1.30 (m, 1H), 1.35–1.68 (m, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 9.1 (d), 20.9 (t), 24.9 (t), 25.3 (t), 25.4 (t), 27.7 (s), 32.2 (t), 35.2 (t), 120.8 (s). Anal. Calcd for $\text{C}_9\text{H}_{13}\text{N}$: C, 79.95; H, 9.69; N, 10.36. Found: C, 80.10; H, 9.69; N, 10.06.