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Iron-Catalyzed Regio- and Stereoselective Ring Opening of [2.2.1]
and [3.2.1] Oxabicyclic Alkenes with Grignard Reagent

Organic Letters

SUPPORTING INFORMATION

Experimental Section

General. All the reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under argon unless otherwise noted. Routine chromatographic purification was achieved with Kanto Silica gel 60 (spherical, neutral, 140-325 mesh). All ^1H NMR and ^{13}C NMR spectra were taken by using JEOL AL-400 NMR spectrometer. ^1H NMR spectra and ^{13}C NMR spectra are reported in ppm (δ) from internal standards, $(\text{CH}_3)_4\text{Si}$ (0 ppm) and CDCl_3 (77.0 ppm), respectively. IR spectra recorded on React IR 1000 Reaction Analysis System equipped with DuraSamplIR (ASI Applied Systems) are reported in cm^{-1} . Mass spectra are taken at Shimadzu GCMS-QP5000.

Solvent. Anhydrous tetrahydrofuran (THF) was purchased from Kanto Chemical Co and distilled from benzophenone ketyl under argon immediately before use. The water content of the solvent was confirmed with a Karl-Fischer moisture titrator (MKC-210, Kyoto Electronics Company) to be less than 20 ppm.

Materials. Unless otherwise noted, materials were purchased from Tokyo Kasei Co, Aldrich Inc., and other commercial suppliers and were used either distilled or

recrystallized before use. FeCl₃ purchased from Kanto Chemical Co., was activated by SOCl₂, dried thoroughly under reduced pressure, and stored under argon.

General procedure

To a solution of organomagnesium reagent (1.0 M in THF, 0.6 mL) and TMEDA (135.9 μ L, 0.90 mmol) in THF (0.75 mL), oxabicyclo alkene **1** (55.3 mg, 0.30 mmol) was added at 0 °C. To the reaction mixture, FeCl₃ (0.1 N in THF, 150 μ L, 0.015 mmol) was added at 0 °C. This solution was warmed to room temperature. After stirring for 3 hours, the reaction mixture was quenched with sat. NH₄Cl (0.2 mL). The reaction mixture was filtered through a pad of Florisil[®], and concentrated *in vacuo*. Purification with silica gel chromatography gave the corresponding compound.

(1*R,2*S**,5*S**,6*S**)-5,6-Bis(methoxymethyl)-2-phenylcyclohex-3-en-1-ol (2)**

IR (neat) 3369 (s), 3342 (s), 2896 (s), 2836 (w), 1493 (w), 1451 (m), 1393 (w), 1192 (m), 1092 (s), 1000 (m), 963 (w), 762 (s), 699 (s) cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.33-7.29 (m, 2H), 7.26-7.20 (m, 3H), 5.86 (ddd, *J* = 10.3, 3.5, 2.7 Hz, 1H), 5.82-5.79 (m, 1H), 3.90 (dq, *J* = 9.1, 1.9 Hz, 1H), 3.76 (d, *J* = 9.1 Hz, 1H), 3.57 (d, *J* = 7.6 Hz, 2H), 3.55-3.53 (m, 1H), 3.50 (d, *J* = 3.6 Hz, 2H), 3.39 (s, 3H), 3.36 (s, 3H), 2.65-2.61 (m, 1H), 2.52 (dq, *J* = 7.2, 2.0 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 142.4, 129.2, 128.9 (2C), 128.8, 128.0 (2C), 126.2, 72.9, 71.5, 67.5, 58.9, 58.8, 48.3, 41.5, 36.0.; Anal. Calcd for C₁₆H₂₂O₃: C, 73.25; H, 8.45. Found: C, 73.04; H, 8.18.

(1*R,2*S**,5*S**,6*S**)-5,6-Bis(methoxymethyl)-2-(*p*-methoxyphenyl)-cyclohex-3-en-1-ol (3)**

IR (neat) 3401 (br), 3401 (s), 2895, 2837, 1613 (m), 1584 (w), 1513 (s), 1463 (m), 1301 (m), 1247 (s), 1177 (s), 1096 (s), 1077 (s), 1034 (s), 961 (m), 818 (m), 799 (m) cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.09-7.07 (m, 2H), 6.76-6.74 (m, 2H), 5.77 (dd, *J* =

10.2, 3.4 Hz, 1H), 5.72-5.68 (m, 1H), 3.77-3.67 (m, 1H), 3.70 (s, 3H), 3.61 (d, $J = 9.0$ Hz, 1H), 3.50-3.48 (m, 2H), 3.45-3.38 (m, 3H), 3.31 (s, 3H), 3.29 (s, 3H), 2.60-2.54 (m, 1H), 2.45-2.35 (m, 1H), ^{13}C -NMR (100 MHz, CDCl_3) δ 158.1, 134.5, 129.8 (2C), 129.4, 129.0 (2C), 113.5, 72.9, 71.6, 67.5, 58.9, 58.8, 55.2, 47.5, 41.4, 36.0.; Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_4$: C, 69.84; H, 8.27. Found: C, 69.72; H, 8.54.

(1*R,2*S**,5*S**,6*S**)-5,6-Bis(methoxymethyl)-2-(*p*-methylphenyl)-cyclohex-3-en-1-ol**
(4)

IR (neat) 3408 (br), 2979 (s), 2896 (s), 1517, 1455, 1393, 1194, 1164, 1098 (s), 1077 (s), 963, 849, 793 (s) cm^{-1} ; ^1H -NMR (400 MHz, CDCl_3) δ 7.05 (s, 4H), 5.78 (dt, $J = 10.4$, 2.8 Hz, 1H), 5.72 (brd, $J = 10.4$ Hz, 1H), 3.85-3.83 (m, 1H), 3.61 (d, $J = 8.8$ Hz, 1H), 3.49 (d, $J = 8.0$ Hz, 1H), 3.42-3.41 (m, 3H), 3.31 (s, 3H), 3.29 (s, 3H), 3.23 (d, $J = 8.0$ Hz, 1H), 2.54 (m, 1H), 2.43 (dq, $J = 1.9$, 7.6 Hz, 1H), 2.24 (s, 3H); ^{13}C -NMR (100 MHz, CDCl_3) δ 139.2, 135.7, 129.0, 128.9 (2C), 128.7 (2C), 128.6, 72.9, 71.6, 67.6, 58.8, 58.8, 47.9, 41.4, 36.0, 21.0.

(1*R,2*S**,5*S**,6*S**)-5,6-Bis(methoxymethyl)-2-(*o*-methylphenyl)-cyclohex-3-en-1-ol**
(5)

IR (neat) 3413, 3400 (br), 2975 (s), 2894 (s), 2875 (s), 1490 (m), 1461, 1449, 1382, 1187, 1158, 1096 (s), 1077 (s), 965 (m), 834 (m), 753 (s), 729 (m) cm^{-1} ; ^1H -NMR (400 MHz, CDCl_3) δ 7.11-7.04 (m, 4H), 5.80 (dt, $J = 15.2$, 4.4 Hz, 1H), 5.67 (brd, $J = 15.2$ Hz, 1H), 3.90 (d, $J = 13.2$ Hz, 1H), 3.78 (brs, 1H), 3.67 (d, $J = 13.6$ Hz, 1H), 3.58 (d, $J = 10.8$ Hz, 2H), 3.51 (d, $J = 4.8$ Hz, 2H), 3.40 (s, 3H), 3.37 (s, 3H), 2.55 (m, 1H), 2.47-2.40 (m, 1H), 2.03 (s, 3H); ^{13}C -NMR (100 MHz, CDCl_3) δ 140.0, 135.4, 129.9, 129.8, 129.7, 129.0, 126.2, 125.5, 73.0, 71.6, 64.9, 58.9, 58.8, 44.2, 41.9, 35.9, 19.4.; Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C, 73.88; H, 8.75. Found: C, 73.60; H, 8.89.

(1R*,2R*,5S*,6S*)-5,6-Bis(methoxymethyl)-2-ethenylcyclohex-3-en-1-ol (6)

¹H-NMR (400 MHz, CDCl₃) δ 6.02 (ddd, *J* = 7.5, 10.8, 17.2 Hz, 1H), 5.70 (dt, *J* = 10.8, 3.2 Hz, 1H), 5.64-5.61 (m, 1H), 5.16-5.14 (m, 1H), 5.13 (brd, *J* = 8.8 Hz, 1H), 4.00 (d, *J* = 9.6 Hz, 1H), 3.85 (brd, *J* = 7.6 Hz, 1H), 3.36 (d, *J* = 7.6 Hz, 2H), 3.56 (d, *J* = 3.6 Hz, 2H), 3.37 (s, 3H), 3.36 (s, 3H), 2.89 (m, 1H), 2.56-2.55 (m, 1H), 2.40-2.35 (m, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 139.4, 128.5, 128.3, 115.4, 72.9, 71.4, 67.0, 58.9, 58.8, 46.3, 41.3, 36.2.

(1R*,2S*,5S*,6S*)-5,6-Bis(methoxymethyl)-2-(2-methyl-1-propenyl)-cyclohex-3-en-1-ol (7)

IR (neat) 2923, 2894, 2875, 1449, 1376, 1189, 1158, 1098, 1077, 961, 859, 782 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 5.64 (dt, *J* = 3.2, 10.0 Hz, 1H), 5.45 (d, *J* = 11.6 Hz, 1H), 5.36 (d, *J* = 11.6 Hz, 1H), 4.05 (d, *J* = 10.0 Hz, 1H), 3.72 (d, *J* = 10.0 Hz, 1H), 3.58-3.55 (m, 2H), 3.36 (d, *J* = 7.6 Hz, 2H), 3.39 (s, 3H), 3.37 (s, 3H), 3.03 (m, 1H), 2.57-2.54 (m, 1H), 2.39 (q, *J* = 8.0 Hz, 1H), 1.75 (s, 3H), 1.65 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 132.5, 130.4, 127.5, 124.9, 73.0, 71.4, 67.0, 58.9, 58.8, 41.3, 41.2, 35.9, 25.9, 18.0.; Anal. Calcd for C₁₄H₂₄O₃: C, 69.96; H, 10.07. Found: C, 70.05; H, 10.25.

(1R*,2S*,5S*,6S*)-5,6-Bis(methoxymethyl)-2-(1-dodecylethenyl)-cyclohex-3-en-1-ol (8)

IR (neat) 2956 (w), 2923 (s), 2853 (s), 1463 (s), 1378 (m), 1260 (m), 1202 (w), 1158 (w), 1100 (s), 1081 (w), 1025 (m), 973 (w), 892 (w), 847 (m), 803 (s), 720 (s) cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 5.72 (dt, *J* = 10.4, 3.2 Hz, 1H), 5.58 (brd, *J* = 10.4 Hz, 1H), 4.92 (d, *J* = 1.2 Hz, 1H), 4.78 (s, 1H), 3.84 (m, 1H), 3.57 (m, 2H), 3.45 (m, 3H), 3.39 (s, 3H), 3.35 (s, 3H), 2.88 (s, 1H), 2.55 (m, 1H), 2.33 (dd, *J* = 2.0, 5.6 Hz, 1H), 2.09 (m, 2H), 1.27 (m, 20H), 0.88 (t, *J* = 2.0, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 150.0, 128.6, 128.4, 111.2, 73.0, 71.9, 64.2, 58.9, 58.8, 47.4, 41.5, 36.1, 35.4, 31.9, 29.8, 29.7, 29.6 (2C), 29.5, 29.4, 29.3, 27.9, 22.7, 14.1.

(1*R,5*S**,6*S**)-5,6-Bis(methoxymethyl)cyclohex-3-en-1-ol (9)**

IR (neat) 3408 (s), 2980 (w), 2895 (s), 1451 (m), 1390, 1193 (m), 1100 (s), 1069 (m), 961 (w), 911 (w), 699 (w) cm^{-1} ; ^1H -NMR (400 MHz, CDCl_3) δ 5.64 (dt, $J = 3.2, 10$ Hz, 1 H), 5.48 (brd, $J = 10$ Hz, 1H), 4.18 (d, $J = 10$ Hz, 1H), 3.86-3.83 (m, 1H), 3.52 (dd, $J = 7.6, 9.6$ Hz, 1H), 3.47 (dd, $J = 7.6, 9.6$ Hz, 1H), 3.33-3.31 (m, 2H), 3.30 (s, 3H), 3.29 (s, 3H), 2.55 (m, 1H), 2.34 (ddd, $J = 2.8, 7.6, 10$ Hz, 1H), 2.30-2.23 (brd, $J = 18.0$ Hz, 1H), 2.30-2.23 (m, $J = 18.0$ Hz, 1H); ^{13}C -NMR (100 MHz, CDCl_3) δ 126.9, 125.8, 72.2, 72.1, 66.6, 59.0, 58.8, 39.9, 37.3, 33.6.; Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{O}_3$: C, 64.49; H, 9.74. Found: C, 64.53; H, 10.01.

(1*R,2*S**,5*R**,6*S**)-5,6-Bis(methoxymethyl)-4-methly-2-phenylcyclohex-3-en-1-ol (11)**

^1H -NMR (400 MHz, CDCl_3) δ 7.32-7.28 (m, 2H), 7.24-7.18 (m, 3H), 5.52 (s, 1H), 4.02 (d, $J = 10.4$ Hz, 1H), 3.83 (brd, $J = 10.4$ Hz, 1H), 3.70 (dd, $J = 10.4, 2.8$ Hz, 1H), 3.63-3.3.55 (m, 2H), 3.52 (d, $J = 2.8$ Hz, 1H), 3.42-3.40 (m, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 2.49 (brq, $J = 6.8$ Hz, 1H), 2.44 (brs, 1H), 1.83 (s, 3H); ^{13}C -NMR (100 MHz, CDCl_3) δ 142.9, 133.8, 128.9 (2C), 127.8 (2C), 126.0, 125.0, 72.9, 68.4, 67.2, 58.8, 58.7, 48.9, 42.4, 39.6, 21.9.; Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C, 73.88; H, 8.75. Found: C, 73.59; H, 8.59.

(1*R,2*S**,5*R**,6*R**,7*S**)-6-Methoxy-5,7-dimethyl-2-phenyl-cyclohept-3-en-1-ol (13)**

^1H -NMR (400 MHz, CDCl_3) δ 7.32-7.25 (m, 2H), 7.21-7.14 (m, 3H), 5.61 (brd, $J = 12$ Hz, 1H), 5.49 (brd, $J = 12$ Hz, 1H), 4.08-4.06 (m, 1H), 3.67 (s, 1H), 3.45 (s, 3H), 3.27 (t, $J = 2.4$ Hz, 1H), 2.67 (s, 1H), 2.01-1.99 (m, 1 H), 1.85 (s, 1H), 1.15 (d, $J = 7.2$ Hz, 3H), 1.05 (d, $J = 7.2$ Hz, 3H); ^{13}C -NMR (100 MHz, CDCl_3) δ 143.4, 134.4, 128.7 (2C), 128.5 (2C), 126.5, 126.4, 87.0, 78.6, 62.0, 47.6, 44.5, 39.5, 19.8, 17.3.

(1*R,2*S**)-1-Hydroxy-2-phenyldihydronaphtalene (15)**

¹H-NMR (400 MHz, CDCl₃) δ 7.08-7.30 (m, 9H), 6.62 (dd, *J* = 2.0, 6.0 Hz, 1H), 6.05 (dd, *J* = 9.8, 4.0 Hz, 1H), 4.85 (brs, 1H), 3.79 (ddd, *J* = 6.0, 4.0, 2.0 Hz, 1H), 1.43 (brs, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 137.7, 136.1, 132.6, 129.7, 129.2, 128.6, 128.5, 128.3, 128.2, 128.0, 127.4, 126.7, 126.5, 126.4, 71.3, 47.4.