Supporting Information

Hydrogen-Mediated Aldol Reductive Coupling of Vinyl Ketones Catalyzed by Rhodium: High syn-Selectivity through the Effect of Tri-2-furylphosphine

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Please Note: Crystallographic data for **6a** and **10a** have been submitted separately as CIF files. Compound **6a** was recrystallized from a DCM-hexane mixture and the dinitrobenzoate of **10a** was crystallized from an ether-hexane mixture. In both instances, clear needles were obtained (**6a**, MP = 140-141 °C; **10a**, MP = 105-106 °C).

I. Experimental Procedure

General: Dichloromethane (DCM) was distilled from calcium hydride. Chemical reagents were purchased from Aldrich and Strem Chemicals, Inc. Commercially available aldehydes and enones were purified immediately prior to use. Deuterated solvents were used as received from Cambridge Isotope Laboratories. Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates (DC-Fertigplatten Kieselgel 60 F₂₅₄). Flash chromatography was performed on silica gel 60 (200-400 mesh). NMR spectra were recorded on a Varian Mercury 400, or Unity+ 300 spectrometer. ¹H NMR spectra were obtained at 400 MHz or 300 MHz, as indicated. ¹³C NMR spectra were obtained at either 100MHz or 75 MHz, as indicated. High resolution mass spectra were obtained on a Micromass ZAB-E spectrometer. FT-IR spectra were obtained using a Nicolet Impact 410 spectrometer. Melting points were obtained on a Thomas-Hoover Unimelt apparatus and are uncorrected.

General Procedure for the Coupling of Enones and Aldehydes: To a 13 mm × 100 mm test-tube were added Li₂CO₃ (10 mol%), Fur₃P (12 mol%), Rh(COD)₂OTf (5 mol%), aldehyde (100 mol%) and dichloromethane (1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) followed by H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and enone (300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir until consumption of aldehyde was observed, as revealed by TLC analysis. The reaction mixture was evaporated onto silica and the aldol products were separated by flash chromatography (SiO₂: EtOAc/Hexane).

Transformations providing the following aldol products were conducted under slightly different conditions. For aldols **1a** and **1b**, the reaction was conducted at 0.3 M concentration using 150 mol% of enone. For compounds **4a** and **4b**, the reaction was conducted using 4 mol% Li₂CO₃, 4.8 mol% Fur₃P, 2 mol% Rh(COD)₂OTf, and 500 mol% enone. Finally, for entry **8a** and **8b**, the reaction was conducted using 20 mol% Li₂CO₃, 24 mol% Fur₃P and 10 mol% Rh(COD)₂OTf. All reactions were conducted at ambient temperature and pressure.

Preparation of 3,5-dinitrobenzoate of **10a**: A solution of alcohol **10a** (67 mg, 0.23 mmol, 100 mol%) in THF (1.0 mL) was placed in 0 °C bath and placed under Ar atmosphere. To the reaction mixture was added pyridine (20 μL, 0.25 mmol, 110 mol%) and 3,5-dinitrobenzoyl chloride (57 mg, 0.25 mmol, 110 mol%). The reaction mixture was allowed to stir for 18 hours, at which point the reaction mixture was diluted with ether and the ethereal layer was washed with water. The organic phase was collected, dried (MgSO₄), filtered and evaporated. Chromatographic purification of the residue provides the title compound as a viscous oil (76 mg, 0.15 mmol) in 68 % yield. Crystallization from an ether-hexane mixture provides **10a** as clear needles (MP = 105-106 °C).

II. Spectroscopic Data for Aldol Products

¹H NMR (400 MHz, CDCl₃): δ 1.06 (d, *J* = 7.2 Hz, 3H), 2.24 (s, 3H), 2.86 (dq, *J* = 3.0, 7.3 Hz, 1H), 3.57 (d, *J* = 2.4 Hz, 1H), 5.28-5.29 (m, 1H), 7.51-7.55 (m, 2H), 8.18-8.22 (m, 2H).

¹³C NMR (75 MHz, CDCl₃): δ 9.4, 29.1, 52.3, 71.6, 123.5, 126.7, 147.1, 149.1, 213.4.

HRMS: Calcd [M+1] for C₁₁H₁₃NO₄ : 224.0923; Found: 224.0925.

FTIR (film): 3447, 3057, 2985, 1701, 1604, 1522, 1348, 1264, 1176, 1109, 853, 737 cm⁻¹.

¹H NMR (300 MHz, CDCl₃): δ 1.04 (d, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.3 Hz, 3H), 2.46 (dq, *J* = 18.2, 7.2 Hz, 1H), 2.62 (dq, *J* = 18.2, 7.3 Hz, 1H), 2.85 (dq, *J* = 3.2, 7.3 Hz, 1H), 3.63 (d, *J* = 2.3 Hz, 1H), 5.22-5.24 (m, 1H), 7.50-7.54 (m, 2H), 8.18-8.22 (m, 2H).

¹³C NMR (75 MHz, CDCl₃): δ 7.5, 9.9, 35.1, 51.4, 72.0, 123.4, 126.7, 147.1, 149.1, 216.1.

HRMS: Calcd [M+1] for C₁₂H₁₅NO₄ : 238.1079; Found: 238.1080.

FTIR (film): 3945, 3686, 3500, 3054, 2984, 2877, 2686, 2306, 1699, 1606, 1522, 1422, 1349, 1265, 1111, 979, 896, 852, 738 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.14 (d, $J = 7.2$ Hz, 3H), 2.16 (s, 3H), 2.61-2.77 (dq, $J = 5.1, 7.2$ Hz, 1H), 2.90 (d, $J = 2.7$ Hz, 1H), 3.41-3.53 (m, 2H), 4.09-4.10 (m, 1H), 4.51 (s, 2H), 7.26-7.36 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): 11.0, 29.2, 48.6, 70.2, 71.6, 73.3, 127.6, 127.7, 128.3, 137.7, 212.2.

HRMS Calcd [M+1] for C₁₃H₁₈O₃ : 223.1334; Found: 223.1330.

FTIR (film): 3439, 3031, 2920, 2867, 1704, 1455, 1360, 1252, 1207, 1181, 1094, 1028, 957, 916, 739, 699 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.00 (t, $J = 7.4$, 3H), 1.12 (d, $J = 7.2$ Hz, 3H), 2.40-2.57 (m, 2H), 2.73-2.80 (dq, $J = 5.1$, 7.2 Hz, 1H), 2.93 (s, 1H), 3.40-3.47 (m, 2H), 4.05 (q, $J = 5.4$, 1H), 4.50 (s, 2H), 7.26-7.36 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): 7.4, 11.5, 35.2, 47.6, 70.5, 71.6, 73.3, 127.7, 128.3, 137.7, 214.9.

HRMS Calcd [M+1] for C₁₄H₂₀O₃ : 237.1491; Found: 237.1488.

FTIR (film): 3502, 3064, 3031, 2977, 2938, 1705, 1497, 1455, 1410, 1376, 1250, 1208, 1099, 1028, 976, 915, 738, 699 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.23 (d, *J* = 7.2 Hz, 3H), 2.16 (s, 3H), 2.56 (dq, *J* = 3.4, 7.2 Hz, 1H), 2.67-2.68 (br, 1H), 2.69 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.79 (dd, *J* = 13.7, 7.9 Hz, 1H), 4.18-4.22 (m, 1H), 7.20-7.26 (m, 3H), 7.28-7.33 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 9.9, 29.1, 40.3, 49.9, 72.0, 126.5, 128.5, 129.2, 138.1, 213.4.

HRMS: Calcd [M+1] for C₁₂H₁₆O₂: 193.1229; Found: 193.1227.

FTIR (film): 3501, 3054, 2985, 2685, 2306, 1701, 1603, 1496, 1455, 1358, 1266, 1171, 1031, 909, 896, 734 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.03 (t, *J* = 7.4 Hz, 3H), 1.22 (d, *J* = 7.2 Hz, 3H), 2.43 (dq, *J* = 18.1, 7.3 Hz, 1H), 2.52 (dq, *J* = 18.1, 7.3 Hz, 1H), 2.59 (dq, *J* = 3.4, 7.2 Hz, 1H), 2.68 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.72-2.72 (m, 1H), 2.79 (dd, *J* = 13.7, 8.2 Hz, 1H), 4.14-4.19 (m, 1H), 7.20-7.33 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): δ 7.5, 10.3, 35.0, 40.3, 48.8, 72.2, 126.4, 128.4, 129.1, 138.2, 216.1.

HRMS: Calcd [M+1] for C₁₃H₁₈O₂: 207.1385; Found: 207.1385.

FTIR (film): 3943, 3512, 3054, 2984, 2941, 2685, 2305, 1698, 1604, 1496, 1455, 1421, 1379, 1265, 1110, 1030, 976, 896, 737 cm⁻¹.

4a

¹H NMR (400 MHz, CDCl₃): 1.37 (d, $J = 7.2$ Hz, 3H), 2.25 (s, 3H), 2.83-2.89 (dq, $J = 4.4, 7.2$ Hz, 1H), 3.21 (s, 1H), 4.90 (d, $J = 4.4$ Hz, 1H), 7.27-7.32 (m, 3H), 7.41-7.43 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 11.6, 29.0, 52.0, 63.5, 85.6, 87.6, 122.2, 128.2, 128.5, 131.6, 211.6.

HRMS Calcd [M+1] for C₁₃H₁₄O₂: 203.1072; Found: 203.1075.

FTIR (film): 3436, 3057, 2984, 2937, 1705, 1599, 1491, 1457, 1443, 1420, 1359, 1266, 1028, 967, 759, 737 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.07 (t, *J* = 7.2 Hz, 3H), 1.36 (d, *J* = 7.2 Hz, 3 H), 2.52-2.64 (m, 2H), 2.85-2.91 (dq, *J* = 4.6, 7.2 Hz, 1H), 3.26 (s, 1H), 4.87 (d, *J* = 4.4 Hz, 1H), 7.26-7.33 (m, 3H), 7.39-7.43 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): 7.4, 11.9, 35.0, 51.2, 63.6, 85.5, 87.8, 122.3, 128.2, 128.4, 131.6, 214.3.

HRMS Calcd [M+1] for C₁₄H₁₆O₂: 217.1229; Found: 217.1230.

FTIR (film): 3426, 2978, 2938, 1707, 1643, 1599, 1490, 1459, 1443, 1407, 1378, 1266, 1029, 978, 758, 737 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.14 (d, *J* = 7.2 Hz, 3H), 1.61-1.68 (m, 1H), 1.73-1.82 (m, 1H), 2.18 (s, 3H), 2.57-2.66 (m, 1H), 3.28 (d, *J* = 2.1, 1 H), 3.60-3.71 (m, 2H), 4.10-4.13 (m, 1H), 4.51 (s, 2H), 7.26-7.36 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): 10.6, 29.3, 33.6, 51.5, 68.5, 70.5, 73.2, 127.5, 127.6, 128.3, 137.8, 212.8.

HRMS Calcd [M+1] for C₁₄H₂₀O₃: 237.1491; Found: 237.1496.

FTIR (film): 3433, 3031, 2924, 2868, 1701, 1455, 1362, 1207, 1181, 1098, 1028, 737, 699 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.03 (t, $J = 7.4$ Hz, 3H), 1.13 (d, $J = 7.2$ Hz, 3H), 1.60-1.67 (m, 1H), 1.80-1.71 (m, 1H), 2.45-2.56 (dq, $J = 2.7, 7.2$ Hz, 2H), 2.58-2.65 (dq, $J = 4.4, 8.2$ Hz, 1H), 3.35 (s, 1H), 3.60-3.70 (m, 2H), 4.06-4.09 (m, 1H), 4.5 (s, 2H), 7.25-7.36 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): 7.5, 11.0, 33.6, 35.3, 50.4, 68.5, 70.6, 73.2, 127.5, 127.6, 128.3, 137.8, 215.5.

HRMS Calcd [M+1] for C₁₅H₂₂O₃: 251.1647; Found: 251.1648.

FTIR (film): 3501, 2975, 2938, 2876, 1707, 1455, 1411, 1364, 1099, 1028, 975, 739, 699 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.29 (d, *J* = 7.5 Hz, 3H), 2.23 (s, 3H), 2.68 (dq, *J* = 4.2, 7.2 Hz, 1H), 2.93-2.95 (m, 1H), 3.75 (dd, *J* = 14.4, 4.4 Hz, 1H), 3.85 (dd, *J* = 14.2, 7.4 Hz, 1H), 4.25-4.30 (m, 1H), 7.72-7.74 (m, 2H), 7.84-7.88 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 10.9, 29.2, 41.7, 49.4, 69.9, 123.7, 132.1, 134.4, 169.0, 212.4.

HRMS: Calcd [M] for C₁₄H₁₅NO₄: 261.1001; Found: 261.1004.

FTIR (film): 3435, 3053, 2978, 2935, 2872, 2306, 1640, 1446, 1383, 1351, 1266, 1114, 1076, 896, 743 cm⁻¹.

Mp = 140-141 °C.

¹H NMR (400 MHz, CDCl₃): δ 1.05 (t, J = 7.2 Hz, 3H), 1.27 (d, J = 7.2 Hz, 3H), 2.51 (dq, J = 18.1, 7.2 Hz, 1H), 2.60 (dq, J = 18.1, 7.2 Hz, 1H), 2.69 (dq, J = 4.3, 7.2 Hz, 1H), 3.10 (d, J = 3.8 Hz, 1H), 3.73 (dd, J = 14.2, 4.6 Hz, 1H), 3.85 (dd, J = 14.0, 7.5 Hz, 1H), 4.23-4.28 (m, 1H), 7.71-7.76 (m, 2H), 7.83-7.88 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 7.4, 10.9, 34.7, 41.3, 48.2, 69.6, 123.3, 131.8, 134.0, 168.6, 214.8.

HRMS: Calcd [M] for C₁₅H₁₇NO₄: 275.1158; Found: 275.1158.

FTIR (film): 3454, 3054, 2986, 2305, 2254, 1773, 1714, 1642, 1422, 1397, 1265, 909, 748 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.22 (d, J = 7.5 Hz, 3H), 2.26 (s, 3H), 2.80-2.86 (dq, J = 3.8, 7.3 Hz, 1H), 3.29 (s, 1H), 4.70 (t, J = 4.8 Hz, 1H), 6.14-6.20 (dd, J = 15.7, 5.8 Hz, 1H), 7.04-7.10 (dd, J = 15.7, 1.4 Hz, 1H), 7.36-7.43 (m, 1H), 7.53-7.58 (m, 2H), 7.91 (d, J = 8.2, 1H).

¹³C NMR (100 MHz, CDCl₃): 10.7, 29.3, 51.3, 71.9, 124.3, 126.4, 128.1, 128.7, 132.4, 133.0, 134.6, 147.6, 212.8.

HRMS Calcd [M+1] for C₁₃H₁₅NO₄: 249.1001; Found: 249.1003.

FTIR (film): 3426, 2981, 2937, 2878, 1704, 1607, 1571, 1522, 1477, 1443, 1422, 1346, 1267, 1180, 1144, 1127, 1064, 1022, 968, 861, 786, 738, 702 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): 1.06 (t, $J = 7.4$ Hz, 3H), 1.21 (d, $J = 7.2$ Hz, 3H), 2.51-2.67 (m, 2H), 2.81-2.88 (dq, $J = 3.9, 7.4$ Hz, 1H), 3.31 (d, $J = 2.7$ Hz, 1H), 4.66 (bs, 1H), 6.14-6.20 (dd, $J = 15.7, 5.8$ Hz, 1H), 7.05-7.09 (dd, $J = 15.9, 1.2$ Hz, 1H), 7.37-7.42 (m, 1H), 7.53-7.58 (m, 2H), 7.9 (d, $J = 8.2$ Hz, 1H).

¹³C NMR (100 MHz, CDCl₃): 7.4, 11.0, 35.3, 50.2, 72.1, 124.3, 126.3, 128.0, 128.7, 132.4, 133.0, 134.6, 147.6, 215.5.

HRMS Calcd [M+1] for C₁₄H₁₇NO₄: 264.1236; Found: 264.1230.

FTIR (film): 3425, 2980, 2939, 2880, 1704, 1648, 1607, 1572, 1525, 1460, 1408, 1347, 1305, 1266, 1112, 1020, 969, 861, 785, 739, 703 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 7.5 Hz, 3H), 1.26-1.36 (m, 2H), 1.43-1.52 (m, 8H), 2.21 (s, 3H), 2.57 (dq, *J* = 3.0, 7.3 Hz, 1H), 3.92-3.96 (m, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 9.6, 14.0, 22.5, 26.0, 29.1, 29.2, 31.7, 34.0, 50.8, 71.0, 214.0.

HRMS: Calcd [M+1] for C₁₁H₂₂O₂: 187.1698; Found: 187.1699.

FTIR (film): 3942, 3512, 3054, 2931, 2858, 2685, 2306, 1701, 1422, 1359, 1265, 1175, 896, 738 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J = 6.8 Hz, 3H), 1.06 (t, J = 7.2 Hz, 3H), 1.13 (d, J = 7.2 Hz, 3H), 1.25-1.35 (m, 8H), 1.43-1.52 (m, 2H), 2.48 (dq, J = 17.9, 7.3 Hz, 1H), 2.57 (dq, J = 18.0, 7.3 Hz, 1H), 2.58 (dq, J = 3.0, 7.2 Hz, 1H), 2.73 (br, 1H), 3.87-3.93 (m, 1H).

¹³C NMR (100 MHz, CDCl₃): δ 7.6, 9.9, 14.0, 22.6, 26.0, 29.2, 31.8, 34.0, 35.1, 50.0, 71.1, 216.8.

HRMS: Calcd [M] for C₁₂H₂₄O₂: 200.1776; Found: 200.1778.

FTIR (film): 3447, 3053, 2985, 2932, 2858, 2305, 2253, 1698, 1461, 1422, 1379, 1265, 912, 743 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.17 (d, *J* = 7.2 Hz, 3H), 1.67-1.85 (m, 2H), 2.19 (s, 3H), 2.61 (dq, *J* = 3.8, 7.2 Hz, 1H), 3.20 (d, *J* = 3.8 Hz, 1H), 3.77-3.93 (m, 3H), 7.71-7.75 (m, 2H), 7.83-7.87 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 10.5, 29.3, 33.0, 34.8, 51.1, 68.4, 123.2, 131.9, 134.0, 168.6, 212.8.

HRMS: Calcd [M] for C₁₅H₁₇NO₄: 275.1158; Found: 275.1156.

FTIR (film): 3469, 3054, 2986, 2305, 2254, 1771, 1710, 1468, 1397, 1372, 1265, 1177, 951, 910, 741 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.03 (t, J = 7.2 Hz, 3H), 1.15 (d, J = 7.2 Hz, 3H), 1.67-1.84 (m, 2H), 2.49 (dq, J = 18.1, 7.2 Hz, 1H), 2.57 (dq, J = 18.1, 7.3 Hz, 1H), 2.64 (dq, J = 4.4, 7.2 Hz, 1H), 3.34 (d, J = 4.1 Hz, 1H), 3.77-3.91 (m, 3H), 7.71-7.75 (m, 2H), 7.81-7.87 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 7.4, 11.0, 33.0, 34.8, 35.3, 50.1, 68.6, 123.2, 131.9, 133.9, 168.6, 215.5.

HRMS: Calcd [M] for C₁₆H₁₉NO₄: 289.1314; Found: 289.1316.

FTIR (film): 3466, 3054, 2985, 2305, 2254, 1771, 1710, 1468, 1397, 1265, 952, 911, 741 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 1.14 (d, J = 7.2 Hz, 3H), 2.03 (s, 3H), 2.31 (dq, J = 4.3, 7.1 Hz, 1H), 2.81-2.82 (m, 1H), 4.17-4.23 (m, 1H), 4.26 (d, J = 11.3 Hz, 1H), 4.32 (d, J = 7.2 Hz, 1H), 4.46 (d, J = 11.3 Hz, 1H), 7.27-7.43 (m, 10H).

¹³C NMR (100 MHz, CDCl₃): δ 10.1, 28.3, 48.2, 70.7, 75.0, 82.6, 127.6, 127.8, 128.0, 128.4, 128.5, 128.8, 137.6, 137.9, 210.5.

HRMS: Calcd [M+1] for C₁₉H₂₂O₃: 299.1647; Found: 299.1647.

FTIR (film): 3943, 3568, 3055, 2986, 2878, 2306, 1710, 1604, 1494, 1454, 1357, 1265, 1178, 1066, 1028, 988, 910, 738 cm⁻¹.

Mp = 105-106 °C.