Supporting Information

**Asymmetric Induction in Hydrogen-Mediated Reductive Aldol Additions
to α -Amino Aldehydes Catalyzed by Rhodium: Selective Formation of
syn-Stereotriads Directed by Intramolecular Hydrogen-Bonding**

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Table of Contents

I. General Procedure	S2
II. Procedures and Characterizations	S3
III. Determination of Relative Stereochemistry	S33

I. General Procedure

General: Dichloromethane (DCM) was distilled from calcium hydride. Chemical reagents were purchased from Aldrich and Strem Chemicals, Inc and used without further purification. Commercially available enones were purified prior to usage. 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 on a Nicolet Impact 410 spectrometer. Melting points were obtained on a Thomas-Hoover Unimelt apparatus and are uncorrected. Optical rotations were obtained on an Atago POLAX-2L polarimeter. HPLC analyses were performed on a Varian ProStar system with Daicel Chiralpak, Chiralcel columns in hexanes/isopropanol solvent mixtures.

Literature Preparations of Aldehydes: *N*-Boc-L-phenylglycinal (3a)¹, *N*-Boc-L-alaninal (4a)², *N*-Boc-L-leucinal (5a)¹, *N*-Me-*N*-Boc-L-leucinal (*N*-Me-5a)³, *N*-Boc-L-phenylalaninal (6a)^{1, 4}, *N*-Boc-L-valinal (7a)¹, *N*-Boc-*O*-TBDPS-L-serinal (8a)¹ were prepared by literature methods.

General Procedure for the Coupling of Enones and Aldehydes: To a 13 mm × 100 mm test-tube were added Li₂CO₃ (10 mol%), (2-furyl)₃P (12 mol%), Rh(COD)₂OTf (5 mol%), aldehyde (100 mol%) and dichloromethane (1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and 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 at 25 °C for 16 hours. The reaction mixture was evaporated onto silica and the aldol products were separated by flash chromatography (SiO₂: EtOAc/Hexane).

¹ Dondoni, A.; Perrone, D.; Merino, P. *J. Org. Chem.* **1995**, *60*, 8074-8080.

² Vescovi, A.; Knoll, A.; Koert, U. *Organic & Biomolecular Chem.* **2003**, *1*, 2983-2997.

³ Greenberger, L. M.; Loganzo, F. Jr.; Discafani-Marro, C. M.; Zask, A.; Ayral-Kaloustian, S. *PCT Int. Appl.* **2004**, 442 pp.

⁴ The *N*-Boc-L-phenylalaninal with high optical purity was prepared by reduction of phenylalanine, Boc-protection, and oxidation. (a) McKennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarn, M. *J. Org. Chem.* **1993**, *58*, 3568-3571. (b) Sharma, G. V. M.; Reddy, J. J.; Lakshmi, P. S.; Krishna, P. R. *Tetrahedron Lett.* **2004**, *45*, 6963-6965. (c) Ocejó, M.; Vicario, J. L.; Badía, D.; Carrillo, L.; Reyes, E. *Synlett* **2005**, 2110-2112.

II. Procedures and Characterizations

(1*S*,2*S*,3*S*)-(2-Hydroxy-3-methyl-4-oxo-1-phenyl-pentyl)-carbamic acid *tert*-butyl ester (**3b**).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (2.8 mg, 10 mol%), (2-furyl)₃P (10.7 mg, 12 mol%), Rh(COD)₂OTf (9.0 mg, 5 mol%), *N*-Boc-L-phenylglycinal (90 mg, 100 mol%) and dichloromethane (0.38 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (94 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 95 mg as viscous yellowish oil (81 % yield).

TLC: R_f 0.5 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 7.26-7.37 (m, 5H), 5.42 (d, *J* = 7.9 Hz, 1H), 4.65 (br, 1H), 4.11 (br, 1H), 2.67 (br, 1H), 2.56-2.63 (m, 1H), 2.17 (s, 3H), 1.42 (br, 9H), 1.23 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 212.3, 156.0, 140.4, 128.7, 127.6, 126.6, 79.7, 74.9, 56.9, 48.6, 29.2, 28.3, 11.8.

HRMS: Calcd [M+1] for C₁₇H₂₅NO₄: 308.1862; Found: 308.1862.

FTIR (film): 3440, 3155, 2981, 2253, 1794, 1705, 1494, 1369, 1251, 1167, 1094, 904 cm⁻¹.

[α]_D = + 30.0 (c = 0.50, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-(2-Hydroxy-3-methyl-4-oxo-1-phenyl-hexyl)-carbamic acid *tert*-butyl ester (3c).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (2.4 mg, 10 mol%), (2-furyl)₃P (9.0 mg, 12 mol%), Rh(COD)₂OTf (7.5 mg, 5 mol%), *N*-Boc-L-phenylglycinal (77 mg, 100 mol%) and dichloromethane (0.32 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and ethyl vinyl ketone (100 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 84 mg as a white solid (80 % yield).

TLC : R_f 0.6 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 7.23-7.35 (m, 5H), 5.46 (d, *J* = 8.2 Hz, 1H), 4.62 (br, 1H), 4.08 (br, 1H), 2.76 (br, 1H), 2.66 (quintet, *J* = 6.9 Hz, 1H), 2.54 (dq, A of ABX, *J*_{AB} = 18.1 Hz, *J*_{AX} = 7.2 Hz, 1H), 2.42 (dq, B of ABX, *J*_{AB} = 18.1 Hz, *J*_{BX} = 7.2 Hz, 1H), 1.41 (br, 9H), 1.20 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 215.0, 155.8, 140.6, 128.6, 127.4, 126.5, 79.7, 75.1, 56.7, 47.8, 35.2, 28.2, 12.4, 7.5.

HRMS: Calcd [M+1] for C₁₈H₂₇NO₄: 322.2018; Found: 322.2020.

FTIR (film): 3155, 2982, 2384, 2254, 1794, 1708, 1602, 1550, 1468, 1381, 1166, 1095, 911 cm⁻¹.

MP: 88 – 89 °C.

[α]_D = + 21.7 (c = 0.69, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-(2-Hydroxy-1,3-dimethyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (4b).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.2 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-L-alaninal (88 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (125 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 98 mg as colorless oil (79 % yield).

TLC : R_f 0.45 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 4.84 (d, *J* = 8.5 Hz, 1H), 3.73-3.76 (m, 1H), 3.68 (br, 1H), 3.15 (br, 1H), 2.70 (quintet, *J* = 7.0 Hz, 1H), 2.21 (s, 3H), 1.44 (s, 9H), 1.20 (d, *J* = 7.2 Hz, 3H), 1.18 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 212.7, 156.1, 79.4, 74.8, 49.4, 48.5, 29.2, 28.3, 18.6, 12.1.

HRMS: Calcd [M+1] for C₁₂H₂₃NO₄: 246.1705; Found: 246.1707.

FTIR (film): 3435, 3055, 2981, 2935, 2305, 1703, 1506, 1454, 1393, 1367, 1266, 1167, 1079, 1024, 992, 896 cm⁻¹.

[α]_D = - 24.3 (c = 2.47, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-(2-Hydroxy-1,3-dimethyl-4-oxo-hexyl)-carbamic acid *tert*-butyl ester (4c).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.2 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-L-alaninal (88 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and ethyl vinyl ketone (152 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 121 mg as colorless oil (92 % yield).

TLC : R_f 0.6 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 4.71 (br, 1H), 3.73-3.77 (m, 1H), 3.65 (br, 1H), 2.85 (br, 1H), 2.67-2.74 (m, 1H), 1.44 (s, 9H), 1.18 (d, *J* = 7.2 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 215.4, 156.0, 79.4, 75.0, 48.5, 35.0, 28.5, 28.3, 18.8, 12.3, 7.5.

HRMS: Calcd [M+1] for C₁₃H₂₅NO₄: 260.1862; Found: 260.1860.

FTIR (film): 3435, 3055, 2980, 2937, 1703, 1506, 1456, 1367, 1266, 1166, 1102, 1025, 976, 896 cm⁻¹.

[α]_D = - 24.0 (c = 2.08, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-(2-Hydroxy-1-isobutyl-3-methyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (5b).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.2 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-L-leucinal (111 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (125 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 101 mg as colorless oil (68 % yield).

TLC : R_f 0.35 (Hexane/EtOAc, 3/1).

¹H NMR (400 MHz, CDCl₃): δ 4.70 (d, *J* = 9.2 Hz, 1H), 3.76-3.80 (m, 1H), 3.60-3.66 (m, 1H), 2.90 (d, *J* = 5.8 Hz, 1H), 2.72 (quintet, *J* = 7.2 Hz, 1H), 2.21 (s, 3H), 1.60-1.68 (m, 1H), 1.44-1.50 (m, 1H), 1.44 (s, 9H), 1.26-1.34 (m, 1H), 1.20 (d, *J* = 7.2 Hz, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 212.9, 156.2, 79.3, 74.0, 50.9, 49.5, 41.9, 29.4, 28.3, 24.8, 23.0, 22.1, 12.9.

HRMS: Calcd [M+1] for C₁₅H₂₉NO₄: 288.2175; Found: 288.2178.

FTIR (film): 3374, 2960, 2871, 1711, 1564, 1502, 1453, 1367, 1251, 1166, 1042, 955, 868 cm⁻¹.

[α]_D = - 42.5 (c = 2.24, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*R*,3*R*)-(2-Hydroxy-1-isobutyl-3-methyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (*iso*-5b).

The title minor product was separated as a white solid. Crystallization from an ether-hexane mixture provided ***iso*-5b** as thin needles.

TLC : R_f 0.30 (Hexane/EtOAc, 3/1).

¹H NMR (400 MHz, CDCl₃): δ 4.33 (d, J = 9.0 Hz, 1H), 3.71-3.76 (m, 1H), 3.58-3.64 (m, 1H), 3.12 (br, 1H), 2.73-2.77 (m, 1H), 2.21 (s, 3H), 1.60-1.70 (m, 1H), 1.44 (s, 9H), 1.24 (d, J = 7.0 Hz, 3H), 1.19-1.24 (m, 1H), 0.93 (d, J = 6.5 Hz, 3H), 0.91-0.94 (m, 1H), 0.91 (d, J = 6.1 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 213.8, 155.9, 79.5, 74.4, 51.2, 48.7, 40.6, 28.8, 28.3, 24.7, 23.8, 21.4, 11.0.

HRMS: Calcd [M+1] for C₁₅H₂₉NO₄: 288.2175; Found: 288.2182.

FTIR (film): 3350, 2967, 2875, 2100, 1686, 1525, 1459, 1378, 1311, 1272, 1237, 1176, 1124, 1078, 1035, 1004, 965, 908, 876 cm⁻¹.

MP: 102 – 103 °C.

[α]_D = - 11.8 (c = 0.85, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*R*,3*R*)-(2-Hydroxy-1-isobutyl-3-methyl-4-oxo-pentyl)-methyl-carbamic acid *tert*-butyl ester (*N*-Me-iso-5b).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (8.1 mg, 10 mol%), (2-furyl)₃P (30.4 mg, 12 mol%), Rh(COD)₂OTf (25.5 mg, 5 mol%), *N*-Me-*N*-Boc-*L*-leucinal (244 mg, 100 mol%) and dichloromethane (1.1 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (268 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 60 mg as colorless oil (18 % yield).

TLC : R_f 0.4 (Hexane/EtOAc, 3/1).

¹H NMR (400 MHz, DMSO, complex mixture of rotomers): δ 4.80-5.01 (m, 1H), 3.86-4.08 (m, 1H), 3.74-3.86 (m, 1H), 3.52-3.74 (m, 1H), 2.54-2.68 (m, 3H), 2.32-2.40 (m, 1H), 2.07-2.10 (m, 3H), 1.42-1.49 (m, 1H), 1.25-1.40 (m, 10H), 0.93-1.00 (m, 3H), 0.81-0.91 (d, 6H).

¹³C NMR (100 MHz, DMSO, complex mixture of rotomers): δ 200.1, 155.4, 155.0, 78.7, 78.5, 55.1, 50.1, 49.5, 49.1, 36.9, 29.4, 28.0, 27.5, 24.5, 24.3, 23.9, 21.4, 21.3, 9.4, 9.0.

HRMS: Calcd [M+1] for C₁₆H₃₁NO₄: 302.2331; Found: 302.2337.

FTIR (film): 3945, 3673, 3446, 3055, 2984, 2686, 2306, 1684, 1456, 1422, 1394, 1367, 1326, 1266, 1152, 1109, 1048, 984, 897 cm⁻¹.

[α]_D = - 31.6 (c = 0.79, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1S,2S,3S)-(2-Hydroxy-1-isobutyl-3-methyl-4-oxo-hexyl)-carbamic acid *tert*-butyl ester (5c).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.7 mg, 10 mol%), (2-furyl)₃P (14.1 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-L-leucinal (110 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and ethyl vinyl ketone (125 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 120 mg as colorless oil (78 % yield).

TLC : R_f 0.45 (Hexane/EtOAc, 3/1).

¹H NMR (400 MHz, CDCl₃): δ 4.67 (d, *J* = 9.6 Hz, 1H), 3.78-3.81 (m, 1H), 3.56-3.62 (m, 1H), 2.80 (br, 1H), 2.73 (quintet, *J* = 7.2 Hz, 1H), 2.48-2.63 (m, 2H), 1.58-1.68 (m, 1H), 1.44 (s, 9H), 1.40-1.50 (m, 1H), 1.26-1.35 (m, 1H), 1.19 (d, *J* = 7.2 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 215.5, 156.1, 79.1, 73.9, 50.8, 48.7, 42.1, 35.1, 28.3, 24.7, 22.9, 22.2, 13.2, 7.4.

HRMS: Calcd [M+1] for C₁₆H₃₁NO₄: 302.2331; Found: 301.2334.

FTIR (film): 3440, 2961, 1711, 1564, 1502, 1453, 1367, 1250, 1170, 1109, 1021, 975, 867 cm⁻¹.

[α]_D = - 26.2 (c = 1.72, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-(1-Benzyl-2-hydroxy-3-methyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (6b).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.2 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-L-phenylalaninal (123 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (125 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 133 mg of colorless oil (84 % yield).

TLC : R_f 0.4 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 7.30-7.32 (m, 2H), 7.19-7.21 (m, 3H), 4.80 (d, *J* = 8.5 Hz, 1H), 3.75-3.83 (m, 2H), 3.03 (br, 1H), 2.80-2.94 (m, 2H), 2.70 (quintet, *J* = 7.1 Hz, 1H), 2.15 (s, 3H), 1.39 (s, 9H), 1.19 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 213.1, 156.1, 138.1, 129.2, 128.4, 126.5, 79.5, 72.3, 54.1, 49.8, 38.8, 29.3, 28.3, 12.8.

HRMS: Calcd [M+1] for C₁₈H₂₇NO₄: 322.2018; Found: 322.2015.

FTIR (film): 3451, 2977, 2933, 2865, 2805, 2606, 1961, 1714, 1494, 1445, 1383, 1351, 1296, 1248, 1153, 1121, 1076, 1043, 934, 845 cm⁻¹.

[α]_D = - 29.0 (c = 2.07, CHCl₃, 94 % ee).

¹H NMR Spectrum

¹³C NMR Spectrum

HPLC

6a-racemic: $t_1 = 9.7$ min, $t_2 = 11.0$ min (Chiralpak AD-H column - 4.6×250 mm, *i*PrOH/Hexane = 5/95, 1 mL/min, 254 nm).

6a-chiral: $t_{\text{major}} = 11.0$ min, $t_{\text{minor}} = 9.8$ min, ee = 94 %.

6b-racemic: $t_{\text{major-1}} = 6.5$ min, $t_{\text{major-2}} = 7.8$ min, $t_{\text{minor-1}} = 5.5$ min, $t_{\text{minor-2}} = 6.0$ min, dr = 20:1 (Chiralcel OJ-H column - 4.6×250 mm, *i*PrOH/Hexane = 5/95, 1 mL/min, 254 nm).

6b-chiral: $t_{\text{major}} = 6.6$ min, $t_{\text{minor}} = 8.1$ min, ee = 94 %.

(1*S*,2*S*,3*S*)-(1-Benzyl-2-hydroxy-3-methyl-4-oxo-hexyl)-carbamic acid *tert*-butyl ester (6c).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.2 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-L-phenylalaninal (123 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and ethyl vinyl ketone (152 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 154 mg of colorless oil (93 % yield).

TLC : R_f 0.55 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 7.26-7.30 (m, 2H), 7.18-7.23 (m, 3H), 4.79 (d, *J* = 9.2 Hz, 1H), 3.79-3.83 (m, 1H), 3.72-3.78 (m, 1H), 3.07 (br, 1H), 2.95-2.83 (m, 2H), 2.83 (br, 1H), 2.71 (quintet, *J* = 7.2 Hz, 1H), 2.38-2.61 (m, 2H), 1.38 (s, 9H), 1.17 (d, *J* = 7.2 Hz, 3H), 1.01 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 215.7, 156.0, 138.2, 129.2, 128.4, 126.3, 79.5, 72.5, 65.8, 54.0, 48.9, 39.0, 35.1, 28.3, 15.2, 13.2, 7.5.

HRMS: Calcd [M+1] for C₁₉H₂₉NO₄: 336.2175; Found: 336.2175.

FTIR (film): 3432, 3055, 2980, 2937, 1704, 1499, 1456, 1392, 1367, 1266, 1169, 1080, 1023, 976, 895 cm⁻¹.

[α]_D = - 30.9 (c = 1.78, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-(2-Hydroxy-1-isopropyl-3-methyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (7b**).**

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (4.1 mg, 10 mol%), (2-furyl)₃P (15.4 mg, 12 mol%), Rh(COD)₂OTf (12.9 mg, 5 mol%), *N*-Boc-L-valinal (111 mg, 100 mol%) and dichloromethane (0.55 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (125 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 87 mg of white solid (58 % yield). Crystallization from an ether-hexane mixture provides **7b** as clear needles.

TLC : R_f 0.6 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 4.78 (d, *J* = 9.2 Hz, 1H), 3.99-4.03 (m, 1H), 3.17-3.22 (m, 1H), 2.66-2.73 (m, 2H), 2.20 (s, 3H), 1.81-1.89 (m, 1H), 1.45 (s, 9H), 1.20 (d, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 213.2, 156.5, 79.2, 71.3, 58.2, 57.3, 49.9, 38.4, 30.3, 29.5, 28.3, 19.7, 19.0, 12.8.

HRMS: Calcd [M+1] for C₁₄H₂₇NO₄: 274.2018; Found: 274.2019.

FTIR (film): 3436, 3054, 2985, 2685, 2410, 2305, 1707, 1606, 1549, 1501, 1422, 1367, 1265, 1170, 896 cm⁻¹.

MP: 120 – 121 °C.

[α]_D = - 16.4 (c = 1.22, CHCl₃).

(1*S*,2*S*,3*S*)-(2-Hydroxy-1-isopropyl-3-methyl-4-oxo-hexyl)-carbamic acid *tert*-butyl ester (7c).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.3 mg, 12 mol%), Rh(COD)₂OTf (12.0 mg, 5 mol%), *N*-Boc-L-valinal (104 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and ethyl vinyl ketone (153 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 82 mg of white solid (56 % yield).

TLC : R_f 0.65 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 4.80 (d, *J* = 9.2 Hz, 1H), 4.00-4.03 (m, 1H), 3.13-3.18 (m, 1H), 2.76 (br, 1H), 2.71 (quintet, *J* = 7.2 Hz, 1H), 2.44-2.61 (m, 2H), 1.80-1.89 (m, 1H), 1.44 (s, 9H), 1.18 (d, *J* = 7.2 Hz, 3H), 1.04 (t, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 215.8, 156.5, 79.2, 71.5, 58.2, 49.1, 35.2, 30.6, 28.3, 19.7, 19.0, 13.0, 7.5.

HRMS: Calcd [M+1] for C₁₅H₂₉NO₄: 288.2175; Found: 288.2173.

FTIR (film): 3436, 3055, 2978, 2877, 2409, 2348, 1703, 1502, 1461, 1391, 1367, 1266, 1171, 1021, 975, 895 cm⁻¹.

MP: 96 – 98 °C.

[α]_D = - 10.8 (c = 1.39, CHCl₃).

¹H NMR Spectrum

¹³C NMR Spectrum

(1*S*,2*S*,3*S*)-[1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxy-3-methyl-4-oxo-pentyl]-carbamic acid *tert*-butyl ester (8b).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.3 mg, 10 mol%), (2-furyl)₃P (12.3 mg, 12 mol%), Rh(COD)₂OTf (10.3 mg, 5 mol%), *N*-Boc-*O*-TBDPS- L-serinal (188 mg, 100 mol%) and dichloromethane (0.44 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (108 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 181 mg of colorless oil (83 % yield).

TLC : R_f 0.5 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 7.63-7.68 (m, 4H), 7.37-7.47 (m, 6H), 5.11 (d, *J* = 9.2 Hz, 1H), 4.14-4.17 (m, 1H), 3.84 (dd, A of ABX, *J*_{AB} = 10.6 Hz, *J*_{AX} = 3.8 Hz, 1H), 3.78 (dd, B of ABX, *J*_{AB} = 10.6 Hz, *J*_{BX} = 4.1 Hz, 1H), 3.65-3.67 (m, 1H), 3.26 (d, *J* = 2.7 Hz, 1H), 2.72 (quintet, *J* = 7.2 Hz, 1H), 2.18 (s, 3H), 1.44 (s, 9H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.07 (s, 9H).

¹³C NMR (100 MHz, CDCl₃): δ 211.9, 155.9, 135.5, 135.5, 132.4, 130.0, 127.9, 79.4, 2.9, 66.7, 52.4, 49.2, 29.5, 28.3, 26.8, 19.1, 12.9.

HRMS: Calcd [M+1] for C₂₈H₄₁NO₅Si: 500.2832; Found: 500.2834.

FTIR (film): 3441, 3053, 2965, 2933, 2860, 2306, 1963, 1709, 1589, 1501, 1473, 1428, 1392, 1367, 1266, 1170, 1113, 913, 872, 823 cm⁻¹.

[α]_D = + 11.8 (c = 2.96, CHCl₃).

(1*S*,2*S*,3*S*)-[1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxy-3-methyl-4-oxo-pentyl]-carbamic acid *tert*-butyl ester (8b) – alternate reaction conditions involving *tert*-amyl alcohol as an additive.

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (1.3 mg, 10 mol%), (2-furyl)₃P (4.9 mg, 12 mol%), Rh(COD)₂OTf (4.1 mg, 5 mol%), *N*-Boc-*O*-TBDPS-L-serinal (75.5 mg, 100 mol%), dichloromethane (0.18 mL, 1.0 M) and 2-methyl-2-butanol (0.19 mL, 1000 mol%). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and methyl vinyl ketone (108 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 74.1 mg of colorless oil (85 % yield, dr 7:1).

¹H NMR Spectrum

(1*S*,2*S*,3*S*)-[1-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxy-3-methyl-4-oxo-hexyl]-carbamic acid *tert*-butyl ester (8c).

To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.8 mg, 10 mol%), (2-furyl)₃P (14.2 mg, 12 mol%), Rh(COD)₂OTf (11.9 mg, 5 mol%), *N*-Boc-*O*-TBDPS- L-serinal (219 mg, 100 mol%) and dichloromethane (0.51 mL, 1.0 M). Then the test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and ethyl vinyl ketone (152 μL, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at 25 °C for 16 hours. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 231 mg of yellowish solid (88 % yield).

TLC : R_f 0.6 (Hexane/EtOAc, 2/1).

¹H NMR (400 MHz, CDCl₃): δ 7.63-7.69 (m, 4H), 7.38-7.46 (m, 6H), 5.17 (d, *J* = 9.2 Hz, 1H), 4.15-4.18 (m, 1H), 3.82 (dd, A of ABX, *J*_{AB} = 10.6 Hz, *J*_{AX} = 3.8 Hz, 1H), 3.78 (dd, B of ABX, *J*_{AB} = 10.6 Hz, *J*_{BX} = 4.3 Hz, 1H), 3.59-3.61 (m, 1H), 3.30 (d, *J* = 2.7 Hz, 1H), 2.75 (quintet, *J* = 7.3 Hz, 1H), 2.41-2.60 (m, 2H), 1.44 (s, 9H), 1.18 (d, *J* = 6.5 Hz, 3H), 1.07 (s, 9H), 1.03 (d, *J* = 7.4 Hz, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 214.6 155.7, 135.5, 135.5, 132.4, 129.9, 127.8, 79.3, 73.1, 66.7, 52.4, 48.4, 35.4, 28.3, 26.8, 13.3, 7.5.

HRMS: Calcd [M] for C₂₉H₄₃NO₅Si: 514.2989; Found: 514.2991.

FTIR (film): 3443, 3072, 3052, 2977, 2934, 2860, 1962, 1900, 1822, 1705, 1590, 1502, 1462, 1428, 1392, 1367, 1263, 1170, 1112, 1043, 1025, 975, 857, 824 cm⁻¹.

MP: 102 – 103 °C.

[α]_D = + 9.8 (c = 2.05, CHCl₃).

III. Determination of Relative Stereochemistry

The aldol product **5b** and *N*-Me-**5b** were converted to the corresponding 3,5-dinitrobenzoate to give single crystals for X-ray determination.

3,5-Dinitro-benzoic acid (1*S*,2*S*)-2-*tert*-butoxycarbonylamino-4-methyl-1-[(1*S*)-1-methyl-2-oxo-propyl]-pentyl ester (3,5-dinitrobenzoate of **5b).**

A solution of alcohol **5b** (79 mg, 100 mol%) in DCM (1.4 mL, 0.2 M) was placed in 0 °C bath and placed under Ar atmosphere. To the reaction mixture was added triethylamine (115 μ L, 300 mol%) and 3,5-dinitrobenzoyl chloride (70 mg, 110 mol%). The reaction mixture was allowed to stir for 5 hours at ambient temperature. The reaction mixture was diluted with DCM and organic layer was washed with water, dried (MgSO_4), filtered and evaporated. The title compound was purified by flash chromatography (SiO_2 : EtOAc/Hexane) to afford 27 mg as a white solid and 61 mg of alcohol **5b** was recovered (21 % yield, 92 % conversion yield).

TLC : R_f 0.65 (Hexane/EtOAc, 3/1).

^1H NMR (400 MHz, CDCl_3): δ 9.26 (t, J = 2.2 Hz, 1H), 9.16 (d, J = 2.2 Hz, 2H), 5.63 (dd, J = 3.2, 8.5 Hz, 1H), 4.44 (d, J = 9.8 Hz, 1H), 4.01-4.08(m, 1H), 3.10 (quintet, J = 7.5 Hz, 1H), 2.27 (s, 3H), 1.64-1.73 (m, 1H), 1.42 (s, 9H), 1.23-1.30 (m, 2H), 1.17 (d, J = 7.2 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 209.0, 162.1, 155.7, 148.7, 129.5, 122.6, 79.9, 79.1, 49.8, 47.3, 41.5, 29.0, 28.2, 24.8, 23.0, 21.8, 13.1.

HRMS: Calcd [M] for $\text{C}_{22}\text{H}_{31}\text{N}_3\text{O}_9$: 481.2060; Found: 481.2057.

FTIR (film): 3412, 3104, 2960, 2256, 1733, 1702, 1628, 1548, 1508, 1460, 1392, 1366, 1345, 1270, 1163, 1120, 1076, 1016, 912 cm^{-1} .

MP: 104 – 106 °C.

¹H NMR Spectrum

¹³C NMR Spectrum

Unit cell packing diagram: The view is approximately down the **b**-axis. Dashed lines are indicative of H-bonding interactions.

(1*S*,2*R*,3*R*)-(2-Hydroxy-1-isobutyl-3-methyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (*iso*-5b).

Unit cell packing diagram: The view is approximately down the **a** axis. Molecules 2 are shown in wireframe form, while molecules 1 are in ball-and-stick format. The molecules H-bond in columns parallel to the **a** axis.

3,5-Dinitro-benzoic acid (1*R*,2*S*)-2-(*tert*-butoxycarbonyl-methyl-amino)-4-methyl-1-[(1*R*)-1-methyl-2-oxo-propyl]-pentyl ester (3,5-dinitrobenzoate of *N*-Me-5b).

A solution of alcohol ***N*-Me-5b** (30 mg, 100 mol%) in DCM (0.5 mL, 0.2 M) was placed in 0 °C bath and placed under Ar atmosphere. To the reaction mixture was added triethylamine (42 µL, 300 mol%) and 3,5-dinitrobenzoyl chloride (25 mg, 110 mol%). The reaction mixture was allowed to stir for 20 hours at ambient temperature. The reaction mixture was diluted with DCM and organic layer was washed with water, dried (MgSO₄), filtered and evaporated. The title compound was purified by flash chromatography (SiO₂: EtOAc/Hexane) to afford 20 mg as a white solid and 17 mg of alcohol ***N*-Me-5b** was recovered (40 % yield, 70 % conversion yield).

TLC: R_f 0.7 (Hexane/EtOAc, 3/1).

HRMS: Calcd [M] for C₂₃H₃₂N₃O₉: 495.2217; Found: 495.2216.

FTIR (film): 3444, 2961, 2254, 1737, 1685, 1629, 1549, 1461, 1392, 1368, 1345, 1274, 1162, 1077, 908 cm⁻¹.

MP: 99 – 101 °C.

Unit cell packing diagram: The view is approximately down the **b** axis.

(1*S*,2*S*,3*S*)-2-Hydroxy-1-isopropyl-3-methyl-4-oxo-pentyl)-carbamic acid *tert*-butyl ester (7b).

Unit cell packing diagram: The view is approximately down the **a** axis. Molecules 1 are shown in ball-and-stick form while molecules 2 are in wireframe display format.