



Supporting Information

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Dynamic Kinetic Resolution During a Cascade Reaction on Substrates with Chiral All-Carbon Quaternary Centers **

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Experimental Section

General Procedures. All reactions were performed in oven-dried glassware under a positive pressure of argon. Flash Chromatography was performed as described by Still et al. (Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923) employing E. Merck silica gel 60 (230-400 mesh ASTM).

Materials. Tetrahydrofuran and diethyl ether were distilled under nitrogen from sodium-benzophenone ketyl. Methylene chloride, chloroform, toluene, and pyridine were distilled under nitrogen from calcium hydride. TLC analyses were performed on 250 μ m Silica Gel 60F₂₅₄ plates purchased from EM Science.

Instrumentation. Infrared spectra were recorded on a Perkin-Elmer 1600 series FT-IR spectrometer. ¹H and ¹³C NMR were recorded on either a Varian INOVA 500 or a Varian Mercury 400 spectrometer. ¹H-COSY and NOESY experiments were performed on a Varian INOVA 500 spectrometer. Chemical shifts for proton and carbon resonances are reported in ppm (δ) relative to chloroform. HPLC analyses were performed on Hewlett Packard 1100 series instrument.

(1*S*, 2*R*)-2-Hydroxy-1-(*E*)-oct-1-enyl-cyclopentanecarboxylic acid methyl ester: To a solution of 1-(*E*)-oct-1-enyl-2-oxo-cyclopentanecarboxylic acid methyl ester (0.57 g, 2.2 mmol, 1.0 equiv) and 0.2 M solution of (+)-Me-CBS catalyst in toluene (3.4 mL, 0.68 mmol, 0.3 equiv) in 9.5 mL of toluene at -78°C was slowly added a solution of catecholborane (0.51 mL, 4.77 mmol, 2.1 equiv) in 1.5 mL of toluene. After stirring at -78°C for 60 h, the reaction was quenched by addition of 7.8 mL of methanol and warmed to rt. The reaction was diluted with Et₂O and washed with pH=13 buffer, 3% aqueous HCl, sat. NaHCO₃ and brine. The organic layer was dried over MgSO₄, filtered and concentrated. Purification of the residue by flash chromatography (12% EtOAc in hexane) afforded (1*S*, 2*R*)-2-hydroxy-1-(*E*)-oct-1-enyl-cyclopentanecarboxylic acid methyl ester (0.20 g, 35% yield, 99% e.e. (HPLC Chiralcel OD, 1% isopropyl alcohol/hexane, 1 ml/min, 20°C, retention times: (1*R*, 2*S*)=9.74 min and (1*S*, 2*R*)=10.91 min)) as a colorless oil.

IR (neat) 3481, 2954, 1739, 1717, 1258 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ 0.87 (t, $J=7.0$ Hz, 3H), 1.22-1.38 (m, 8H), 1.60-1.69 (m, 2H), 1.78-1.96 (m, 3H), 1.98-2.04 (m, 2H), 2.17-2.25 (m, 1H), 2.97 (s, 1H), 3.70 (s, 3H), 4.16-4.18 (m, 1H), 5.39 (dt, $J=16.0$ Hz and 1.2 Hz, 1H), 5.61 (dt, $J=16.0$ Hz and 6.7 Hz, 1H);

¹³C NMR (100 MHz, CDCl₃) δ 14.4, 20.7, 22.9, 29.0, 29.3, 31.0, 31.4, 31.9, 32.9, 52.3, 60.9, 79.4, 129.5, 132.5, 175.8;

HRMS calcd for C₁₅H₂₆O₃ (M⁺) 254.1882; Found 254.1888.

The absolute stereochemistry was assigned using the model established by Corey et al.¹ The relative stereochemistry was assigned based on comparison of NMR data with those of corresponding cyclohexane β -ketoesters with known relative stereochemistry.²

(*S*)-1-(*E*)-Oct-1-enyl-2-oxo-cyclopentanecarboxylic acid methyl ester (5): To a solution (1*S*, 2*R*)-2-hydroxy-1-(*E*)-oct-1-enyl-cyclopentanecarboxylic acid methyl ester (0.20 g, 0.79 mmol, 1.0 equiv) in 5 mL of dichloromethane at rt was added Dess-Martin periodinane (0.37 g, 0.83 mmol, 1.1 equiv) followed by the slow addition of wet

dichloromethane until the reaction mixture became cloudy. The reaction was diluted with Et₂O and washed with 10% Na₂S₂O₃, sat. NaHCO₃ and brine. The organic layer was dried over MgSO₄, filtered and concentrated. Purification of the residue by flash chromatography (8% EtOAc in hexane) afforded (*S*)-1-(*E*)-oct-1-enyl-2-oxo-cyclopentanecarboxylic acid methyl ester (**5**) (0.19 g, 95% yield, 99% ee (HPLC Chiralcel OD, 0.3% isopropyl alcohol/hexane, 1 ml/min, 20°C, retention times: (*S*)-(**5**)=6.49 min and (*R*)-(**5**)=6.94 min)) as a colorless oil. ¹H-NMR and ¹³C-NMR data identical to those previously reported in the literature.³

9-[2-(*tert*-Butyl-diphenyl-silanyloxy)-ethyl]-8-hexyl-bicyclo[4.3.1]dec-6-ene-2,10-dione (6**):** To a solution of 1-(*E*)-oct-1-enyl-2-oxo-cyclopentanecarboxylic acid methyl ester (**5**) (29 mg, 0.10 mmol, 1 equiv) in 1.3 mL of toluene at –78°C was slowly added a 0.31 M solution of ((*E*)-4-bromomagnesium-but-3-enyloxy)-*tert*-butyl-diphenyl-silane (0.46 mL, 0.14 mmol, 1.3 equiv) in THF. The reaction was allowed to warm to 0°C and was then transferred via cannula to a mixture of 2.3 mL of THF and 6.9 mL of toluene. The resulting 0.01 M reaction mixture was stirred at rt for 12 h. The reaction was quenched by the addition of 2% aqueous acetic acid. The product was extracted with Et₂O and the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated. Purification of the residue by flash column chromatography (7% EtOAc in hexane) provided 10-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-9-hexyl-bicyclo[5.3.1]undec-7-ene-2,11-dione (**6**) (32 mg, 60% yield) as a colorless oil. ¹H-NMR and ¹³C-NMR data identical to those previously reported in the literature.³ The enantiomeric excess of the product was determined after desilylation (*vide infra*).

8-Hexyl-9-(2-hydroxy-ethyl)-bicyclo[4.3.1]dec-6-ene-2,10-dione: To a solution of 10-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-9-hexyl-bicyclo [5.3.1] undec-7-ene-2,11-dione (**15**) (17.0 mg, 0.032 mmol, 1.0 equiv) in 2 mL of dichloromethane was added HF•pyr (excess). After 30 min the reaction was quenched by the slow addition of sat. NaHCO₃. The product was extracted with Et₂O and the combined organic layers were

washed with sat. NaHCO₃ and brine, dried over MgSO₄, filtered and concentrated.

Purification of the residue by flash chromatography (40% EtOAc in hexane) afforded 8-hexyl-9-(2-hydroxy-ethyl)-bicyclo[4.3.1]dec-6-ene-2,10-dione (15.7 mg, 96% yield, 3% ee (HPLC Chiralcel OD, 1% isopropyl alcohol/hexane, 1 ml/min, 20°C, retention times: 23.28 min and 24.82 min)) as a colorless oil.

IR (neat) 3448, 2926, 1733, 1700, 1052 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ 0.89 (t, *J*=7.0 Hz, 3H), 1.26-1.34 (m, 8H), 1.44-1.54 (m, 2H), 1.60-1.75 (m, 3H), 1.87-1.90 (m, 1H), 2.07-2.14 (m, 2H), 2.36-2.43 (m, 3H), 2.56-2.63 (m, 2H), 3.11 (s, 1H), 3.73-3.76 (m, 2H), 5.84 (d, *J*=1.2 Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 14.5, 23.0, 27.7, 29.7, 31.9, 32.1, 33.9, 37.3, 38.7, 38.8, 43.5, 60.6, 67.5, 135.5, 145.4, 208.4, 208.9.

HRMS calcd for C₁₈H₂₈O₃ (M⁺) 292.2038; Found 292.2049.

(1*S*, 2*S*)-2-[(*E*)-4-(*tert*-Butyl-diphenyl-silanyloxy)-but-1-enyl]-2-hydroxy-1-(*E*)-oct-1-enyl-cyclopentanecarboxylic acid methyl ester (7**):** To a solution of (*S*)-1-(*E*)-oct-1-enyl-2-oxo-cyclopentanecarboxylic acid methyl ester (**5**) (15.4 mg, 0.06 mmol, 1.0 equiv) in 0.8 mL of toluene at -78°C was added a 0.25 M solution of ((*E*)-4-bromomagnesium-but-3-enyloxy)-*tert*-butyl-diphenyl-silane (0.36 mL, 0.09 mmol, 1.5 equiv). After 15 min the reaction was warmed up to 0°C for 10 min and quenched by addition of acetic acid. The product was extracted with ether and the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated. Purification of the residue by flash chromatography (7% EtOAc in hexane) afforded (1*S*, 2*S*) 2-[(*E*)-4-(*tert*-butyl-diphenyl-silanyloxy)-but-1-enyl]-2-hydroxy-1-(*E*)-oct-1-enyl-cyclopentanecarboxylic acid methyl ester (**7**) (27.7 mg, 81% yield, 99% ee (HPLC Chiralcel OD, 0.1% isopropyl alcohol/hexane, 1 ml/min, 20°C, retention times: (1*R*, 2*R*)-(**7**)=13.45 min and (1*S*, 2*S*)-(**7**)=14.56 min)) as a colorless oil.

IR (neat) 3435, 3056, 2929, 1726, 1241, 1111 cm⁻¹.

¹H NMR (500 MHz, CDCl₃) δ 0.87 (t, *J*=7.0 Hz, 3H), 1.04 (s, 9H), 1.25-1.30 (m, 6H), 1.34-1.37 (m, 2H), 1.76-1.84 (m, 3H), 1.89-1.91 (m, 1H), 2.05-2.15 (m, 5H), 2.28-2.33

(m, 2H), 3.57 (s, 3H), 3.66 (t, $J=6.7$ Hz, 2H), 5.58-5.64 (m, 2H), 5.70-5.80 (m, 2H), 7.36-7.43 (m, 6H), 7.65-7.68 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3) δ 14.4, 19.5, 19.6, 22.9, 27.2, 29.2, 29.6, 30.1, 31.9, 33.2, 36.1, 36.3, 51.9, 62.9, 64.0, 83.3, 126.7, 127.4, 127.8, 129.7, 133.8, 134.1, 134.4, 135.7, 174.6.

HRMS calcd for $\text{C}_{35}\text{H}_{50}\text{O}_4\text{Si}$ ($\text{M}+\text{Na}$) $^+$ 585.3376; Found 585.3403.

Standard procedure for the rearrangement reactions depicted in Scheme 5.

To a solution of vinyl tin (0.5 mmol, 2.5 equiv) in THF (2ml) at -78°C was slowly added $n\text{BuLi}$ (2.5M in Hexane, 0.2 ml, 0.5 mmol, 2.5 equiv). After stirring at -78°C for 30 min, a freshly prepared solution of MgBr_2 in ether-benzene (1M, 0.6 ml, 0.6 mmol, 3 equiv) was slowly added. The reaction was stirred for another 30 min at that temperature before a solution of keto-ester (0.2 mmol, 1 equiv) in toluene (3 ml) was added. After warming to 0°C , the reaction mixture was cannulated to pre-cooled toluene-THF mixture (toluene 15 ml, THF 3 ml) at 0°C . The reaction was allowed to warm to room temperature over 2 hrs and was stirred at room temperature for 18 hrs.

The reaction was quenched by 2% HOAc solution (5 ml). The aqueous phase was extracted by ether (10 mlx3). The combined organic phase was washed with NaHCO_3 aq (10 ml) and brine (10 ml) and was dried over anhydrous MgSO_4 . Solvent was removed at reduced pressure, and the crude product was purified by flash chromatography (5% EtOAc in hexane).

Using the standard procedure **10** was obtained in 75% yield as a colorless liquid.

^1H NMR (500MHz, CDCl_3) δ 0.01 (s, 3H), 0.03 (s, 3H), 0.87 (s, 9H), 0.97-1.03 (m, 1H), 1.20-1.30 (m, 2H), 1.32-1.56 (m, 3H), 1.63-1.80 (m, 3H), 1.80-1.90 (m, 1H), 1.90-1.98 (m, 2H), 2.05-2.19 (m, 2H), 2.20-2.30 (m, 2H), 2.30-2.52 (m, 4H), 3.18-3.22 (m, 1H)

^{13}C NMR (100 MHz, CDCl_3) δ 4.6, -3.6, 18.2, 21.0, 24.8, 26.0, 27.2, 28.9, 29.6, 31.8, 35.1, 35.4, 40.7, 43.5, 43.9, 65.9, 75.9, 137.4, 153.7, 209.0, 210.0

HRMS (CI) calcd. for $\text{C}_{23}\text{H}_{36}\text{O}_3\text{Si}$ ($\text{M}+\text{NH}_4$) $^+$ 406.2778; Found 406.2797

HPLC (OD, 0.3% IPA in Hexane, 1ml/min) RT: 5.897 (minor), 6.463 (major)

Using the standard procedure **13** was obtained in 75% yield as a colorless liquid.

¹H NMR (400MHz, CDCl₃) δ 0.00 (s, 5H), 0.86 (s, 9H), 1.34-1.47 (m, 4H), 1.52-1.70 (m, 4H), 1.83-1.91 (m, 1H), 1.91-2.12 (m, 4H), 2.30-2.50 (m, 5H), 2.58-2.70 (m, 2H), 3.57-3.65 (m, 1H)

¹³C NMR (100 MHz, CDCl₃) δ 4.6, -4.0, 18.1, 21.9, 22.6, 22.9, 25.4, 26.0, 29.0, 30.4, 33.7, 34.0, 36.8, 43.1, 56.5, 68.3, 79.1, 138.9, 145.7, 210.2, 210.3

HRMS (CI) calcd. for C₂₃H₃₆O₃Si (M+NH₄)⁺ 406.2770; Found 406.2770

Using the standard procedure **14** was obtained in 93% yield in 62% ds and as a colorless liquid.

¹H NMR (400MHz, CDCl₃) major: δ 0.08 (s, 6H), 0.86 (s, 9H), 1.18-1.28 (m, 1H), 1.30-1.42 (m, 1H), 1.45-1.55 (m, 1H), 1.56-1.91 (m, 5H), 1.92-2.15 (m, 2H), 2.20-2.66 (m, 7H), 2.68-2.71 (m, 1H), 3.60-3.68 (m, 1H); CDCl₃) minor: δ -0.03, (s, 3H), 0.02 (s, 3H), 0.80 (s, 9H), 1.18-1.28 (m, 1H), 1.30-1.42 (m, 1H), 1.45-1.55 (m, 1H), 1.56-1.91 (m, 5H), 1.92-2.15 (m, 2H), 2.20-2.66 (m, 7H), 2.71-2.78 (m, 1H), 4.11-4.17 (br, 1H)

¹³C NMR (100 MHz, CDCl₃) major: δ 4.6, -4.1, 18.1, 22.9, 25.8, 26.0, 29.1, 29.8, 31.3, 34.1, 35.0, 41.5, 42.7, 56.3, 69.2, 79.7, 136.2, 152.6, 208.8, 210.3; minor: δ 4.9, -4.3, 18.1, 24.4, 25.9, 26.1, 29.4, 29.9, 31.7, 33.5, 35.9, 37.0, 42.6, 57.1, 70.9, 73.7, 136.1, 153.4, 209.9, 212.0

HRMS (CI) calcd. for C₂₂H₃₄O₃Si (M+NH₄)⁺ 397.2175; Found 397.2181

Using the standard procedure **15** was obtained in 54% yield as a colorless liquid.

¹H NMR (500MHz, CDCl₃) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 1.03-1.15 (m, 1H), 1.15-1.38 (m, 3H), 1.40-1.50 (m, 1H), 1.60-1.80 (m, 4H), 1.80-1.95 (m, 3H), 1.98-2.18 (m, 3H), 2.18-3.33 (m, 3H), 2.41-2.56 (m, 2H), 2.60-2.76 (m, 2H), 3.30 (td, J= 11.3 Hz and 4.0 Hz)

¹³C NMR (100 MHz, CDCl₃) δ 4.7, -3.5, 18.2, 20.7, 25.2, 25.6, 26.0, 27.7, 28.9, 34.4, 35.8, 36.3, 37.5, 41.6, 50.5, 64.9, 74.1, 139.8, 146.0, 209.4, 210.8

HRMS (CI) calcd. for C₂₄H₃₈O₃Si (M=H)⁺ 403.2669; Found 403.2665

Compounds **9** and **12** have been prepared from the corresponding vinyl lithium compounds previously reported by Paquette *et al.*⁴

¹ Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551-5553

² Unpublished results .

³ Sheehan, S. M.; Lalic, G.; Chen, J. S.; Shair, M. D. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2714-2715.

⁴ Elmore, S. W.; Paquette, L. A. *J. Org. Chem.* **1995**, *60*, 889