Supporting Information for

On the Stereochemistry of the Dihydropyrone Diels-Alder Reaction

Punit P. Seth and Nancy I. Totah*

Department of Chemistry, University of Iowa, Iowa City, IA 52242

General Methods:

All air sensitive reactions were performed in base washed, flame dried glassware under an atmosphere of argon. Reaction solvents were dried over CaH_2 (benzene, dichloromethane) or sodium/benzophenone ketyl (toluene, tetrahydrofuran) and were distilled just prior to use. Analytical thin layer chromatography was performed on EM silica gel 60F glass plates (0.25mm). Flash column chromatography was performed using EM silica gel 60 (230-400 mesh). ^1H NMR spectra were recorded on Bruker AC-300 or WM-360 spectrometers. Chemical shifts are reported in ppm, downfield from tetramethylsilane using residual $CHCl_3$ as the internal standard (δ 7.27 ppm). ^{13}C NMR spectra were recorded on a Bruker WM-360 (90 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm, downfield from tetramethylsilane using residual $CHCl_3$ as the internal standard (δ 77.0 ppm). IR spectra were obtained with a Mattson Cygnus 25 instrument. Elemental Analyses were performed by Atlantic Microlab, Inc.; Norcross, GA.

Experimental Procedures:

General Procedure for Diels-Alder Reactions:

Thermal Conditions: A solution of diene (0.6 mmol) and dihydropyrone (0.2 mmol) in toluene (1 mL) was warmed to reflux and stirred for 24 h. After this time, the reaction mixture was cooled to room temperature and concentrated, and the residue purified by flash chromatography (SiO_2; 3-7% EtOAc (gradient) in hexanes containing 1% Et_3N) to provide a mixture of endo and exo diastereomers.

Lewis Acid Catalyzed Conditions: To a solution of the dihydropyrone (0.2 mmol) and diene (0.8 mmol) in THF (1.5mL) was added $ZnCl_2$ (0.2mL of a 1M solution in THF), and the resulting mixture stirred at the temperature indicated in Table 1. After 2 h, the reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash chromatography (SiO_2; 3-7% EtOAc (gradient) in hexanes containing 1% Et_3N) to provide a mixture of endo and exo diastereomers.

Cycloadduct 10a: endo ^1H NMR ($CDCl_3$, 360 MHz): δ 5.17 (1H, dt, J = 5.2, 1.4), 4.74 (1H, m), 4.49 (1H, dd, J = 5.1, 1.0), 4.16 (2H, m), 3.24 (3H, s), 2.71 (1H, d, J = 16.2), 2.39 (1H, d, J = 16.2), 2.29 (2H, m), 1.31 (3H, s), 1.30 (3H, s), 1.23 (3H, t, J = 7.2), 0.88 (9H, s), 0.14 (3H, s), 0.09 (3H, s). ^{13}C NMR ($CDCl_3$): δ 205.5, 168.7, 150.7, 100.6, 76.0, 73.5, 68.2, 62.1, 61.5, 57.2, 51.3, 33.5, 30.6, 26.2, 25.4 (3C), 17.9, 14.0, -4.2, -4.8. exo ^1H NMR ($CDCl_3$, 360 MHz): δ 5.08 (1H, d, J = 1.8), 4.68 (1H, d, J = 6.0), 4.64 (1H, d, J = 2.0), 4.23 (2H, q, J = 7.1), 3.38 (3H, s), 2.67 (1H, d, J = 14.3), 2.56 (1H, m), 2.39 (1H, d, J = 14.3), 2.16 (1H, d, J = 18.4, 1.3), 1.38 (3H, s), 1.30 (3H, s), 1.28 (3H, t, J = 7.1), 0.90 (9H, s), 0.16 (3H, s), 0.13 (3H, s). ^{13}C NMR ($CDCl_3$): δ 204.2, 167.9, 148.7, 103.2, 77.0, 75.8, 70.9, 66.6, 61.1, 58.1, 49.7, 34.6, 30.9, 25.6 (3C), 25.0, 17.9, 14.1, -4.3, -4.8. Anal. Calcd for $C_{21}H_{36}O_6Si$ (mixture): C, 61.13%; H, 8.79%. Found: C, 61.25%; H, 8.73%.

Cycloadduct 10b: endo ^1H NMR ($CDCl_3$, 360 MHz): δ 5.15 (1H, m), 4.43 (1H, d, J = 6.1), 4.20 (1H, d, J = 4.9), 3.28 (3H, s), 2.82 (1H, d, J = 15.9), 2.69 (1H, m), 2.48 (1H, d, J = 15.9), 2.41 (1H, d, J = 18.7), 1.34 (3H, s), 1.30 (3H, s), 0.94 (9H, s), 0.21 (3H, s), 0.19 (3H, s). ^{13}C NMR ($CDCl_3$): δ 199.9, 152.0, 116.9, 98.7, 77.1, 74.4, 68.2, 57.2, 52.1, 51.6, 33.4, 30.6, 25.5 (3C), 25.2, 17.9, -4.3, -4. 7. exo ^1H NMR ($CDCl_3$, 360 MHz): δ 5.04 (1H, d, J = 1.1), 4.59 (1H, d, J = 1.2), 4.33 (1H, d, J = 5.1), 3.39 (3H, s), 2.78 (1H, d, J = 14.4), 2.74 (1H, m), 2.47 (1H, d, J = 14.4), 2.26 (1H, dd, J = 18.8, 1.3), 1.42 (3H, s), 1.27 (3H, s), 0.94 (9H, s), 0.22 (3H, s), 0.21 (3H, s). ^{13}C NMR ($CDCl_3$): δ 199.3, 149.4, 115.0, 100.9, 76.7, 76.6, 71.1, 58.8, 57.3, 49.0, 33.7, 30.9, 25.5 (3C), 23.9, 17.9, -4.3, -4.8. Anal. Calcd for $C_{19}H_{31}NO_4Si$ (mixture): C, 62.43%; H, 8.55%; N, 3.83%. Found: C, 62.52%; H, 8.64%; N, 3.84%.

Cycloadduct 10c: ^1H NMR ($CDCl_3$, 360 MHz): (mixture of diastereomers) endo δ 7.85 (2H, m), 7.70 (1H, m), 7.58 (2H, m), 5.10 (1H, d, J = 7.4), 5.05 (1H, dt, J = 5.6, 1.4), 4.03 (1H, d, J = 5.6), 3.06 (3H, s), 2.97 (1H, dd, J = 18.6, 7.1), 2.79 (1H, d, J =

15.6), 2.46 (1H, d, J = 15.6), 2.39 (1H, d, J = 18.6), 1.32 (3H, s), 1.22 (3H, s), 0.95 (9H, s), 0.25 (3H, s), 0.24 (3H, s). ^{13}C NMR ($CDCl_3$): δ 201.6, 154.1, 136.6, 134.3, 130.8 (2C), 128.7 (2C), 97.4, 75.9, 75.5, 73.8, 66.3, 57.4, 51.2, 35.2, 29.7, 27.1, 25.5 (3C), 17.9, -4.2, -4.4. Anal. Calcd for $C_{24}H_{36}O_6SSi$: C, 59.97%; H, 7.55%. Found: C, 60.08%; H, 7.58%.

Cycloadduct 10d: ^{1}H NMR ($CDCl_3$, 360 MHz): (mixture of diastereomers) endo δ 5.18 (1H, dd, J = 4.1, 1.1), 4.84 (1H, m), 4.49 (1H, d, J = 5.5), 3.27 (3H, s), 2.66 (1H, d, J = 15.7), 2.44 (1H, d, J = 15.7), 2.31 (2H, m), 2.24 (3H, s), 1.33 (3H, s), 1.30 (3H, s), 0.89 (9H, s), 0.15 (3H, s), 0.11 (3H, s). exo δ 5.02 (1H, d, J = 1.5), 4.73 (1H, d, J = 1.9), 4.62 (1H, d, J = 6.1), 3.41 (3H, s), 2.72 (1H, d, J = 14.0), 2.51 (1H, m), 2.31 (3H, s), 2.43 (1H, d, J = 14.0), 2.08 (1H, d, J = 18.8), 1.38 (3H, s), 1.22 (3H, s), 0.88 (9H, s), 0.12 (3H, s), 0.09 (3H, s). Anal. Calcd for $C_{20}H_{34}O_5Si$: C, 62.79%; H, 8.96%. Found: C, 63.00%; H, 9.12%.

Amino Alcohol Obtained by Reduction of Cycloadduct 11: endo ^{1}H NMR ($CDCl_3$, 360 MHz): δ 4.89 (1H, dd, J = 4.6, 2.0), 4.13 (1H, dd, J = 11.6, 6.6), 3.63 (1H, d, J = 5.6), 3.53 (3H, m), 3.42 (1H, d, J = 9.8), 2.42 (3H, s), 2.35 (3H, s), 2.29 (1H, m), 2.04 (1H, d, J = 18.5), 1.88 (1H, t, J = 13.1), 1.77 (1H, dd, J = 13.1, 6.7), 1.24 (6H, s), 0.93 (9H, s), 0.17 (3H, s), 0.15 (3H, s). ^{13}C NMR ($CDCl_3$): δ 149.6, 97.4, 72.5, 72.0, 69.9, 66.7, 61.9, 46.3, 43.6, 42.6, 41.5, 33.4, 31.2, 25.6 (3C), 23.3, 18.0, -4.3, -4.4. Anal. Calcd for $C_{20}H_{39}NO_4Si$: C, 62.29%; H, 10.19%; N, 3.63%. Found: C, 62.46%; H, 10.33%; N, 3.60%.

Cycloadduct 12a: endo ^{1}H NMR ($CDCl_3$, 360 MHz): δ 4.78 (1H, m), 4.38 (1H, s), 4.18 (2H, q, J = 7.2), 3.33 (3H, s), 2.66 (1H, d, J = 15.9), 2.46 (1H, d, J = 15.9), 2.37 (2H, m), 1.76 (3H, t, J = 1.6), 1.34 (3H, s), 1.33 (3H, s), 1.25 (3H, t, J = 7.2), 0.93 (9H, s), 0.11 (3H, s), 0.10 (3H, s). ^{13}C NMR ($CDCl_3$): δ 205.6, 168.8, 143.2, 110.8, 81.9, 73.6, 68.5, 62.9, 61.6, 60.0, 51.4, 33.9, 30.6, 26.1, 25.7 (3C), 18.2, 15.0, 14.0, -3.7, -3.8. exo ^{1}H NMR ($CDCl_3$, 360 MHz): δ 4.83 (1H, dd, J = 6.0, 1.4), 4.49 (1H, s), 4.21 (2H, m), 3.38 (3H, s), 2.64 (1H, m), 2.57 (1H, d, J = 14.2), 2.43 (1H, d, J = 14.2), 2.14 (1H, dd, J = 17.6, 1.4), 1.75 (3H, s), 1.33 (6H, s), 1.25 (3H, t, J = 7.2), 0.93 (9H, s), 0.11 (3H, s), 0.10 (3H, s). ^{13}C NMR ($CDCl_3$): δ 203.3, 168.1, 142.5, 112.7, 80.1, 75.5, 71.1, 67.2, 61.2, 59.9, 49.9, 34.8, 30.9, 25.9, 25.7 (3C), 18.1, 14.1, 12.5, -3.9 (2C). Anal. Calcd for $C_{22}H_{38}O_6Si$ (mixture): C, 61.94%; H, 8.98%. Found: C, 61.89%; H, 9.04%.

Cycloadduct 12b: endo ^{1}H NMR ($CDCl_3$): δ 4.42 (1H, d, J = 5.3), 4.05 (1H, s), 3.32 (3H, s), 2.72 (1H, d, J = 15.9), 2.68 (1H, m), 2.52 (1H, d, J = 15.9), 2.43 (1H, dt, J = 18.1, 1.5), 1.75 (3H, s), 1.34 (3H, s), 1.30 (3H, s), 0.95 (9H, s), 0.17 (6H, s). ^{13}C NMR ($CDCl_3$): δ 200.1, 144.3, 117.1, 108.8, 82.7, 74.3, 68.2, 59.8, 52.6, 51.5, 33.6, 30.6, 25.7 (3C), 25.2, 18.2, 14.6, -3.6, -3.8. Anal. Calcd for $C_{20}H_{33}O_4NSi$: C, 63.23%; H, 8.75%; N, 3.69%. Found: C, 63.26%; H, 8.81%; N, 3.60%.

Cycloadduct 13: endo ^{1}H NMR ($CDCl_3$, 360 MHz): δ 5.12 (1H, dd, J = 5.0, 2.0), 4.48 (2H, t, J = 5.2), 4.18 (2H, q, J = 7.2), 3.25 (3H, s), 2.65 (1H, d, J = 16.8), 2.44 (1H, d, J = 16.5), 2.24 (1H, m), 1.31 (6H, s), 1.24 (3H, t, J = 7.2), 1.16 (3H, d, J = 7.3), 0.91 (9H, s), 0.17 (3H, s), 0.10 (3H, s). ^{13}C NMR ($CDCl_3$): δ 205.7, 168.9, 153.2, 100.2, 76.4, 73.1, 71.8, 63.1, 61.5, 57.6, 51.0, 34.9, 30.5, 26.6, 25.6 (3C), 18.1, 14.0, 12.8, -4.1, -5.1. exo ^{1}H NMR ($CDCl_3$, 360 MHz): δ 5.04 (1H, m), 4.54 (1H, d, J = 3.6), 4.50 (1H, m), 4.22 (2H, m), 3.32 (3H, s), 2.56 (1H, d, J = 14.9), 2.43 (1H, d, J = 14.9), 2.33 (1H, m), 1.35 (3H, s), 1.31 (3H, s), 1.27 (3H, t, J = 7.0), 1.16 (3H, d, J = 7.6), 0.92 (9H, s), 0.19 (3H, s), 0.17 (3H, s). ^{13}C NMR ($CDCl_3$): δ 203.1, 167.5, 152.8, 101.0, 77.8, 76.3, 75.4, 65.4, 61.0, 57.7, 49.8, 39.8, 30.8, 27.4, 25.6 (3C), 18.0, 17.1, 14.0, -4.3, -4.7. Anal. Calcd for $C_{22}H_{38}O_6Si$ (mixture): C, 61.94%; H, 8.98%. Found: C, 61.88%; H, 8.83%.

Cycloadduct 14: endo ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.52 (1H, dd, J = 5.4, 1.4), 4.32 (1H, s), 4.18 (2H, m), 3.35 (3H, s), 2.56 (2H, m), 2.29 (1H, m), 1.72 (3H, d, J = 2.1), 1.34 (6H, s), 1.26 (3H, t, J = 7.2), 1.17 (3H, d, J = 7.2), 0.95 (9H, s), 0.05 (6H, s). ^{13}C NMR ($CDCl_3$): δ 202.0, 168.0, 147.9, 111.4, 80.0, 78.2, 75.3, 65.9, 61.3, 59.0, 49.9, 40.4, 30.9, 28.7, 25.8 (3C), 18.3, 17.9, 14.4, 14.0, -3.7, -4.1. IR (film): 2934, 2859, 1739, 1708, 1249 cm^{-1} exo ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.70 (1H, d, J = 4.0), 4.44 (1H, s), 4.24 (2H, m), 3.32 (3H, s), 2.46 (2H, m), 2.32 (1H, m), 1.76 (3H, d, J = 1.3), 1.32 (3H, s), 1.30 (3H, s), 1.28 (3H, t, J = 7.0), 1.22 (3H, d, J = 7.2), 0.95 (9H, s), 0.12 (6H, s). ^{13}C NMR ($CDCl_3$): δ 206.0, 168.8, 145.9, 111.9, 81.9, 73.2, 71.8, 63.0, 61.5, 61.0, 50.7, 35.0, 30.5, 26.7, 25.8 (3C), 18.3, 15.0, 14.1, 13.5, -3.6, -4.5. IR (film): 2934, 2860, 1725, 1682, 1195 cm^{-1}

1-Oxadecalone 16: ^{1}H NMR ($CDCl_3$, 360 MHz): ketone **16**: δ 5.18 (1H, m), 4.48 (1H, d, J = 1.8), 4.29 (2H, q, J = 7.2), 4.02 (1H, s), 3.43 (3H, s), 2.95 (1H, dd, J = 15.1, 4.8), 2.70 (1H, dd, J = 15.1, 2.5), 2.54 (2H, m), 1.36-1.24 (9H, m), 1.24 (3H, s). hemiacetal **16a**: δ 4.76 (1H, s), 4.69 (1H, t, J = 5.8), 4.30 (2H, m), 3.78 (1H, s), 3.58 (3H, s), 2.78 (2H, d, J = 5.7), 2.29 (1H, d, J = 14.2), 1.98 (1H, d, J = 14.2), 1.49 (3H, s), 1.37-1.24

(6H, m), 1.24 (3H, s). ^{13}C NMR ($CDCl_3$): ketone **16**: δ 208.7, 201.7, 167.6, 90.5, 78.6, 74.4, 72.6, 64.0, 62.7, 62.6, 50.2, 40.5, 29.8, 26.5, 24.1, 13.9. hemiacetal **16a**: δ 201.3, 169.2, 102.9, 86.2, 85.4, 73.1, 69.4, 61.8, 61.4, 59.8, 42.4, 40.1, 33.4, 27.7, 14.1, 13.2.

1-Oxadecalone 17: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.09 (1H, m), 4.43 (1H, d, J = 1.8), 4.25 (2H, q, J = 7.1), 3.41 (3H, s), 3.19 (1H, dd, J = 14.9, 5.6), 2.96 (1H, s), 2.62 (1H, dd, J = 14.9, 3.1), 2.58 (1H, d, J = 15.0), 2.49 (1H, d, J = 15.0), 1.47 (3H, s), 1.33 (3H, s), 1.30 (3H, t, J = 7.1), 1.27 (3H, s).