Lewis Acid Catalyzed Tandem Diels-Alder Reaction/Ring Expansion as an Equivalent of a [4+3] Cycloaddition

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Supporting Information

General Information
All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring. Low temperature (-78 °C) was maintained using dry ice/acetone. Hexanes and THF were distilled over sodium and benzophenone, or purified by passage through a bed of activated alumina. Dichloromethane was distilled over calcium hydride or purified by passage through a bed of activated alumina. Purification of reaction products was carried out by flash chromatography using Merck silica gel 60 (230-400 mesh). ¹H NMR spectra were measured on Varian Gemini-300 (300 MHz), 400 (400 MHz) or VXR 500 (500 MHz) spectrometers and are reported in ppm using TMS as an internal standard (TMS at 0.00 ppm). Data reported as (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, b=broad; integration; coupling constant(s) in Hz). ¹³C NMR spectra were recorded on Varian Gemini-300 (75 MHz) or VXR 500 (125 MHz) spectrometer and reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Infrared (IR) spectra were recorded on a Nicolet Impact series 420 IR. High resolution mass spectra were obtained at the University at Buffalo Mass Spectrometry Laboratory.

Experimental Procedures and Physical Data:

(1S, 3S, 5R) (1R, 3R, 5S)-3-Methyl-bicyclo[3.2.1]oct-6-en-2-one (3a). Aluminum chloride powder (380 mg, 0.5 equiv.) was added in one portion to a stirred solution of methacrolein (2a) (400 mg, 5.70 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 30 min. Freshly distilled cyclopentadiene (944 mg, 14.28 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred for an additional 50 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm for 10 min and then placed in an ice water bath. Aluminum chloride powder (457 mg, 0.6 equiv.) was then added in one portion and the reaction mixture was stirred for a further 1 h. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 3a as colorless oil: 698 mg (90% yield); Rf 0.26 (7% ether in pentane); ¹H NMR (500 MHz, CDCl₃) δ 6.24 (dd, J = 5.0, 4.0 Hz, 1H), 5.81 (dd, J = 5.0, 4.0 Hz, 1H), 3.06 (t, J = 3.5 Hz, 1H), 2.77 (m, 1H), 2.57-2.62 (m, 1H), 2.15-2.29 (m, 3H), 1.17-1.21 (m, 3H), 1.13 (d, J = 7.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 209.3, 140.9, 129.9, 54.3, 40.5, 37.7, 37.1, 33.1, 20.7; IR (neat) 3049, 2940, 2868, 1712 (C=O), 1586, 1464 cm⁻¹; HRMS (El) calcd for C₉H₁₂O [M⁺], required m/z: 136.0883, found m/z: 136.0886.
(1S, 3S, 5R) (1R, 3R, 5S)-3-Ethyl-bicyclo[3.2.1]oct-6-en-2-one (3b). Aluminum chloride powder (270 mg, 0.5 equiv.) was added in one portion to a stirred solution of ethylacrolein (2b) (340 mg, 4.04 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 15 min. Freshly distilled cyclopentadiene (668 mg, 10.10 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred for an additional 50 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm for 10 min and then placed in an ice water bath. Aluminum chloride powder (324 mg, 0.6 equiv.) was then added in one portion and the reaction mixture was stirred for a further 1 h. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 3b as colorless oil: 485 mg (80% yield); Rf 0.35 (7% ether in pentane).¹H NMR (500 MHz, CDCl₃) δ 6.25 (dd, J = 6.5, 4.0 Hz, 1H), 5.79 (dd, J = 6.5, 4.0 Hz, 1H), 3.05 (t, J = 4.5 Hz, 1H), 2.79 (m, 1H), 2.41-2.48 (m, 1H), 2.12-2.24 (m, 1H), 1.71-1.80 (m, 1H), 1.40-1.48 (m, 1H), 1.27-1.33 (m, 1H), 0.86-0.91 (m, 1H), 0.82 (t, J = 9.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 208.4, 140.6, 129.6, 54.5, 46.6, 37.6, 37.2, 29.7, 27.2, 10.8; IR (neat) 3060, 2959, 2943, 2871, 1707 (C=O), 1459 cm⁻¹; HRMS (EI) calcd for C₁₀H₁₄O [M]+, required m/z: 150.1039, found m/z: 150.1043.

(1S, 3S, 4S, 5R) (1R, 3R, 4R, 5S)-3,4-Dimethyl-bicyclo[3.2.1]oct-6-en-2-one (3c). Dimethylaluminum chloride (2.26 mL, 1.0M in hexanes) was added in one portion to a stirred solution of trans-2-methyl-2-butenal (2c) (364 mg, 4.33 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 15 min. Freshly distilled cyclopentadiene (747 mg, 11.29 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred for an additional 30 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm gradually for 30 min and then placed in an ice water bath. Aluminum chloride powder (663 mg, 11.29 mmol, 1.1 equiv.) was then added in one portion and the reaction mixture was stirred for a further 1 h. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 3c as colorless oil: 261 mg (40% yield); Rf 0.32 (7% ether in pentane).¹H NMR (500 MHz, CDCl₃) δ 6.28 (dd, J = 5.5, 3.0 Hz, 1H), 5.96 (dd, J = 5.5, 3.0 Hz, 1H), 3.03 (t, J = 4.0 Hz, 1H), 2.66-2.74 (m, 2H), 2.42-2.47 (m, 1H), 2.28-2.33 (m, 1H), 2.13 (d, J = 11.5 Hz, 1H), 1.09 (d, J = 7.5 Hz, 3H), 0.89 (d, J = 7.5Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 210.9, 138.5, 132.4, 54.5, 46.6, 37.6, 37.2, 29.7, 27.2, 10.8; IR (neat) 3065, 2929, 2869, 1705 (C=O), 1455 cm⁻¹; HRMS (EI) calcd for C₁₀H₁₄O [M]+, required m/z: 150.1039, found m/z: 150.1039.
Aluminum chloride powder (137 mg, 0.5 equiv.) was added in one portion to a stirred solution of cyclopent-1-enecarbaldehyde (2d) (180 mg, 1.87 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 15 min. Freshly distilled cyclopentadiene (309 mg, 4.68 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred for an additional 50 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm for 10 min and then placed in an ice water bath. Aluminum chloride powder (165 mg, 0.6 equiv.) was then added in one portion and the reaction mixture was stirred for a further 1 h. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2 ×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using hexanes-ethyl acetate (90:10) as eluent to give 3d as colorless oil: 260 mg (86% yield); R f 0.25 (7% ether in pentane).

The relative configuration of 3d was confirmed by X-ray analysis of its 2,4-dinitropheylhydrozone derivative. The X-ray crystallographic data has been submitted to the Cambridge Structural Database [Gerlits, O. O.; Coppens, P. Private Communication (1078) 2003, CCDC 219152].

The 2,4-dinitropheylhydrozone derivative of 3d was synthesized according to reference 3: To a stirred solution of 3d (66 mg, 0.40 mmol) in ethanol (5 mL) was added 2,4-dinitropheylhydrazine (89 mg, 0.45 mmol). The resulted orange suspension was kept stirring overnight at room temperature. The crude reaction mixture was poured into water (10 mL) and the aqueous phase was extracted with ether (45 mL). The organic solution was washed with brine, dried over magnesium sulfate and concentrated. The crude product was purified by flash chromatography on silica gel using hexanes-ethyl acetate (8:1) as eluent to give the derivative of 3d: 95 mg (69% yield).

(4aS, 5R, 8S, 9aS) (4aR, 5S, 8R, 9aR)-1,2,3,4,4a,5,8,9a-Octahydro-5,8-methano-benzocyclohepten-9-one (3e).

Dimethylaluminum chloride (0.82 mL, 1.0 M in hexanes) was added in one portion to a stirred solution of cyclohexenecarboxaldehyde (2e) (180 mg, 1.63 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 15 min. Freshly distilled cyclopentadiene (540 mg, 8.17 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred between -40 °C to -50 °C for an additional 80 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm for 10 min and then placed in an ice water bath. Aluminum chloride powder (130 mg, 0.6 equiv.) was then added in one portion and the reaction mixture was stirred for a further 15 min. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2 ×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (98:2 to 97:3) as eluent to give 3e as...
colorless oil: 60 mg (21% yield); Rf 0.40 (3% ether in pentane). 1H NMR (500 MHz, CDCl3) δ 6.27 (dd, J = 5.5, 3.0 Hz, 1H), 5.98 (dd, J = 5.5, 3.0 Hz, 1H), 3.02 (t, J = 3.5 Hz, 1H), 2.68-2.74 (m, 2H), 2.34-2.40 (m, 1H), 2.27-2.31 (m, 1H), 2.19 (d, J = 11.0 Hz, 1H), 1.84-1.92 (m, 1H), 1.36-1.58 (m, 6H), 1.25-1.32 (m, 1H); 13C NMR (75 MHz, CDCl3) δ 209.9, 139.9, 132.1, 54.6, 46.7, 43.7, 39.7, 37.4, 27.1, 26.5, 23.0, 22.7; IR (neat) 3063, 2937, 2857, 1709 (C=O), 1446 cm−1; HRMS (EI) calcd for C12H16O [M]+, required m/z: 176.1196, found m/z: 176.1202.

(3R, 4R)-4-Methyl-3-phenyl-cyclopent-1-enecarbaldehyde (4). A solution of substrate 151 (310.0 mg, 1.26 mmol) in THF (30 mL) was degassed for 20 min and charged with argon. The solution was cooled to -78 °C with dry ice acetone bath followed by adding dropwise LiAlH4 (1.26 mL, 1.0 M in THF). The resulting mixture was kept in acetone-dry ice bath for 30 min and then the acetone-dry ice bath was removed. After 30 min, the reaction was quenched with 10 mL distilled water followed by addition of diethyl ether (100 mL). The organic layer was separated and washed with distilled water (25 mL × 2), brine (25 mL × 2) and dried over MgSO4, filtered, and concentrated. The residue was dissolved in dry dichloromethane (5 mL) followed by adding PCC (500 mg, 2.32 mmol). The resulting mixture was kept stirring at room temperature for 1.5 h. Then diethyl ether (10 mL) was added, filtered through Florisil, washed with ether (40 mL) and concentrated. The crude product was purified by column chromatography on silica gel using hexanes-ethyl acetate (7:1) as eluent to give 4 as colorless oil: 84 mg (36% yield for two steps); 1H NMR (400 MHz, CDCl3) δ 9.88 (s, CHO, 1H), 7.24-7.35 (m, 3H), 7.05-7.07 (m, 2H), 6.91 (m, 1H), 6.13-6.15 (m, 1H), 2.74-2.82 (m, 2H), 2.25-2.28 (m, 2H), 0.63 (d, J = 7.2 Hz); 13C NMR (75MHz, CDCl 3) δ 190.1, 153.9, 147.8, 138.7, 128.5, 128.3, 126.9, 55.4, 37.3, 36.0, 16.8; IR (neat) 1678 (C=O) cm−1; HRMS (EI) calcd for C13H14O [M]+, required m/z: 186.1039, found m/z: 186.1042.

(1R, 2R, 3aR, 4R, 7S, 7aS)-2-Methyl-1-phenyl-1,2,3,4,7,7a-hexahydro-4,7-methano-indene-3a-carbaldehyde (5a). To a stirred solution of 4 (40 mg, 0.21 mmol) in dry dichloromethane (10 mL) was added dropwise a solution of 0.96 mL Et2AlCl (1.0 M in hexane) at -78 °C. The resulting yellow solution was stirred for 10 min followed by adding freshly distilled cyclopentadiene (71 mg, 1.07 mmol) via syringe. The resulting mixture was kept stirring at -78 °C for 3 h. The reaction was quenched by addition of 6 mL saturated NaHCO3 solution with syringe while the yellow color of the solution disappeared. After 10 min, the acetone-dry ice bath was removed and the reaction mixture was allowed to warm to room temperature, extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO4, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using hexanes-ethyl acetate (90:10) as eluent to give 5a and 5b (5:1 ratio) as colorless oil: 22 mg (40% yield); 1H NMR (500 MHz, CDCl3) exo 5a: δ 9.90 (s, 1H, CHO), 7.18-7.31 (m, 5H), 6.40 (dd, 1H, J = 5.5, 3.0 Hz), 6.33 (dd, 1H, J = 5.5, 3.0 Hz), 3.43 (dd, 1H, J = 8.0, 4.0 Hz), 2.95 (d, 2H, J = 11.0 Hz), 2.76 (t, 1H, J = 7.5 Hz), 2.46 (m, 1H), 1.89 (dd, 1H, J =13.5, 2.5 Hz), 1.77 (d, 1H, J = 9.0 Hz), 1.62 (m, 2H), 0.48 (d, 2H, J = 7.0 Hz). 

13C NMR (75MHz, CDCl3) δ 205.4, 142.0, 139.8, 135.7, 128.2, 128.1, 125.9, 68.0, 52.3, 42.8, 37.7, 17.0; IR (neat) 1678 (C=O) cm−1; HRMS (EI) calcd for C18H20O [M]+, required m/z: 252.1514, found m/z: 252.1526. Endo 5b: 1H NMR (500 MHz, CDCl3) 9.62 (s, CHO).
(2R, 3R, 3aS, 4S, 7R, 8aR)-2-Methyl-3-phenyl-2,3,3a,4,7,8a-hexahydro-1H-4,7-methano-azulen-8-one (6).

The procedure was the same as that used for the formation of 5a except the reaction was quenched at 0 °C, the yield is 45%. 1H NMR (500 MHz, CDCl₃) δ 7.31-7.34 (t, J = 7.5 Hz, 2H), 7.20-7.24 (m, 3H), 6.21 (dd, J = 5.5, 2.8 Hz, 1H), 5.93 (dd, J = 5.5, 2.8 Hz, 1H), 3.01-3.12 (m, 4H), 2.87 (dd, J = 7.5, 4.5 Hz, 1H), 2.32-2.36 (m, 1H), 2.24-2.27 (m, 1H), 2.20 (dd, J = 11.0 Hz, 1H), 2.05 (dd, J = 13.0, 9.0 Hz, 1H), 1.81-1.87 (m, 1H), 0.60 (d, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 209.9, 141.3, 140.0, 132.4, 128.8, 128.7, 126.8, 54.6, 52.5, 48.2, 42.5, 40.6, 39.8, 39.6, 39.2, 15.5; IR (neat) 2951, 2930, 2871, 1705 (C=O) cm⁻¹; HRMS (EI) calcd for C₁₈H₂₀O [M]+, required m/z: 252.1514, found m/z: 252.1525.

3-Methyl-bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (7). Aluminum chloride powder (380 mg, 0.5 equiv.) was added in one portion to a stirred solution of methacrolein (2f) (400 mg, 5.70 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 30 min. Freshly distilled cyclopentadiene (944 mg, 14.28 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred for an additional 50 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm for 10 min and then placed in an ice water bath. Aluminum chloride powder (457 mg, 0.6 equiv.) was then added in one portion and the reaction mixture was stirred for a further 1 h. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 7 as colorless oil (endo/exo = 2/1): 550 mg (71% yield); The physical and spectral data were identical to those previously reported for this compound: 5 1H NMR (500 MHz, CDCl₃) endo: δ 9.37 (d, J = 3.0 Hz, CHO), 6.29 (dd, J = 5.5, 3.0 Hz, 1H), 6.05 (dd, J = 5.5, 3.0 Hz, 1H), 3.13 (br, 1H), 2.56 (br, 1H), 2.33 (dd, J = 7.5, 3.5 Hz, 1H), 1.82 (m, 1H), 1.57 (m, 1H), 1.48 (m, 1H), 1.17 (d, J = 7.0 Hz, 3H).

2-Methyl-bicyclo[2.2.2]oct-5-ene-2-carbaldehyde (16). Aluminum chloride powder (228 mg, 0.5 equiv.) was added in one portion to a stirred solution of methacrolein (2a) (240 mg, 3.42 mmol) in dry CH₂Cl₂ (5 mL) in a 25 mL round bottom flask at -78 °C and the reaction mixture was then stirred for 30 min. 1,3-cyclohexadiene (685 mg, 8.55 mmol), precooled to -78 °C for at least 30 min, was then added dropwise by syringe to the reaction mixture and the mixture was stirred for an additional 50 min. The dry ice-acetone bath was then removed and the reaction flask was allowed to warm for 10 min and then placed in an ice water bath. Aluminum chloride powder (273 mg, 0.6 equiv.) was then added in one portion and the reaction mixture was stirred for a further 1 h. The reaction was then quenched with saturated sodium bicarbonate solution (10 mL) and extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 16 as colorless oil (endo/exo = 5/1): 390 mg (76% yield); The physical and spectral data were identical to those previously reported for this compound: 6 1H NMR (500 MHz, CDCl₃) endo: δ 9.33 (s, CHO), 7.13 (s, CHO), 6.25 (m, 2H), 2.60 (m, 1H), 2.48 (m, 1H), 2.01 (s, CHO), 6.90 (s, CHO), 1.90 (d, J = 13.0, 3.5, 3.0 Hz, 1H), 1.90 (d, J = 12.5, 9.5, 3.0, 2.5 Hz, 1H), 1.53 (m, 1H), 1.32-1.10 (m, 3H), 1.16 (s, 3H).
(1S, 3R, 5R) (1R, 3S, 5S)-3-Methyl-bicyclo[3.2.1]oct-6-en-2-one (8a). Hydrochloric acid (1.0 mL, 1.0 M in ether) was added in one portion to a stirred solution of substrate 3a (136 mg, 1.0 mmol) in dry CH₂Cl₂ (1 mL) in a 10 mL round bottom flask at room temperature and the reaction mixture was then stirred for 30 min. The reaction was quenched with saturated sodium bicarbonate solution (5 mL) and extracted with ether (80 mL), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 8a as colorless oil: 112 mg (83% yield); Rf 0.39 (7% ether in pentane). ¹H NMR (500 MHz, CDCl₃) δ 6.23 (dd, J = 5.5, 3.0 Hz, 1H), 6.07 (dd, J = 5.5, 3.0 Hz, 1H), 3.03 (dd, J = 5.0, 3.0 Hz, 1H), 2.78-2.84 (m, 2H), 2.41-2.46 (m, 1H), 1.96-2.02 (m, 1H), 1.85 (d, J = 11.0 Hz, 1H), 1.44-1.50 (ddd, J = 13.0, 10.0, 3.0 Hz, 1H), 1.03 (d, J = 6.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 213.2, 138.0, 132.8, 56.0, 44.3, 39.5, 38.1, 35.4, 15.0; IR (neat) 3067, 2934, 2862, 1712 (C=O), 1460, 1189, 785, 743 cm⁻¹; HRMS (EI) calcd for C₉H₁₂O [M]+, required m/z: 136.0883, found 136.0881.

(1S, 3R, 5R) (1R, 3S, 5S)-3-Ethyl-bicyclo[3.2.1]oct-6-en-2-one (8b). Hydrochloric acid (0.33 mL, 1.0 M in ether) was added in one portion to a stirred solution of substrate 3b (50 mg, 0.33 mmol) in dry CH₂Cl₂ (1 mL) in a 10 mL round bottom flask at room temperature and the reaction mixture was then stirred for 30 min. The reaction was quenched with saturated sodium bicarbonate solution (3 mL) and extracted with ether (50 mL), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 8b as colorless oil: 40 mg (80% yield); Rf 0.35 (7% ether in pentane). ¹H NMR (500 MHz, CDCl₃) δ 6.22 (dd, J = 5.5, 2.5 Hz, 1H), 5.79 (dd, J = 5.5, 3.0 Hz, 1H), 3.01 (dd, J = 5.0, 3.0 Hz, 1H), 2.84-2.87 (m, 1H), 2.56-2.65 (m, 1H), 2.38-2.44 (m, 1H), 1.93-1.99 (m, 1H), 1.83 (d, J = 11.0 Hz, 1H), 1.75-1.82 (m, 1H), 1.48 (ddd, J = 13.0, 10.0, 3.0 Hz, 1H), 1.29-1.37 (m, 1H), 0.86 (t, J = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 212.6, 138.1, 132.6, 56.2, 44.3, 43.7, 39.3, 32.2, 22.6, 11.1; IR (neat) 3055, 2934, 2862, 1712(C=O), 1460, 1189, 779, 737 cm⁻¹; HRMS (EI) calcd for C₁₀H₁₄O [M]+, required m/z: 150.1039, found 150.1037.

(1S, 3R, 4S, 5R) (1R, 3S, 4R, 5S)-3,4-Dimethyl-bicyclo[3.2.1]oct-6-en-2-one (8c). Hydrochloric acid (0.64 mL, 1.0 M in ether) was added in one portion to a stirred solution of substrate 3c (87 mg, 0.64 mmol) in dry CH₂Cl₂ (1.5 mL) in a 10 mL round bottom flask at room temperature and the reaction mixture was then stirred for 30 min. The reaction was quenched with saturated sodium bicarbonate solution (5 mL) and extracted with ether (50 mL), and the combined extracts were washed with water and brine, dried over MgSO₄, and carefully
concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (93:7) as eluent to give 8c as colorless oil: 80 mg (92% yield); Rf 0.41 (7% ether in pentane).

1H NMR (500 MHz, CDCl₃) δ 6.29 (dd, J = 6.0, 3.0 Hz, 1H), 6.11 (dd, J = 6.0, 3.0 Hz, 1H), 3.02 (dd, J = 5.0, 3.0 Hz, 1H), 3.0 (dt, J = 11.0, 5.5 Hz, 1H), 2.25-2.31 (m, 1H), 1.95-1.99 (m, 1H), 1.87 (d, J = 11.5 Hz, 1H), 1.63-1.69 (m, 1H), 1.06 (d, J = 7.0 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 212.6, 136.5, 133.9, 55.7, 45.8, 45.7, 43.5, 41.2, 18.6, 12.9; IR (neat) 3065, 2961, 2929, 2869, 1711 cm⁻¹; HRMS (EI) calcd for C₁₀H₁₄O [M⁺]: 150.1039, found 150.1033.

CHO

(3aS, 4S, 7R, 7aR)-(3aR, 4R, 7S, 7aS)-1,2,3,4,7,7a-Hexahydro-4,7-methano-indene-3a-carbaldehyde (9b).

1H NMR (500 MHz, CDCl₃) δ 9.46 (s, 1H, CHO), 6.23 (dd, J = 5.5, 3.0 Hz, 1H), 6.1 (dd, J = 5.5, 3.0 Hz, 1H), 2.75 (br, 1H), 2.64 (br, 1H), 2.30 (dt, J = 8.0 Hz, 1H), 2.16 (dd, J = 13.0, 7.0 Hz, 1H), 1.88-1.99 (m, 2H), 1.77 (d, J = 9.0 Hz, 1H), 1.55-1.66 (m, 1H), 1.17-1.33 (m, 3H); 13C NMR (125 MHz, CDCl₃) δ 205.9, 138.8, 135.6, 69.1, 50.2, 48.0, 46.9, 44.8, 31.70, 31.69, 29.6.

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(1S, 2S, 4S)-(1R, 2R, 4R)-2-Triisopropylsilanyloxy-bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (12). A mixture of 2-(triisopropylsilyloxy) acrolein (400 mg, 1.75 mmol) and cyclopentadiene (1 mL, 14.91 mmol) was heated under microwave condition (105 °C, 90 W) for 1 h. The 1HNMR of the crude mixture showed 89% conversion. The mixture was separated by silica-gel chromatography (hexanes as eluent) to give 12 as colorless oil: 96 mg pure exo and 143 mg a mixture of exo and endo (47% yield overall); exo isomer: 1H NMR (500 MHz, CDCl₃) δ 9.83 (s, CHO, 1H), 6.41 (dd, J = 5.5, 3.5 Hz, 1H), 6.11 (dd, J = 5.5, 3.5 Hz, 1H), 2.93 (m, 2H), 2.36 (dd, J = 12.0, 3.5 Hz, 1H), 1.45 (d, J = 9.0 Hz, 1H), 1.30-1.33 (m, 1H), 0.98-1.09 (m, 2H); 13C NMR (125 MHz, CDCl₃) δ 203.2, 139.7, 133.2, 88.6, 50.9, 45.4, 43.1, 38.4, 18.1, 18.0, 13.1; IR (neat) 2950, 2847, 1732 (C=O), 1471, 1178, 1145, 1096, 998, 884, cm⁻¹; HRMS (ESI) calcd for C₁₇H₃₀O₂Si [M + H⁺]: 295.2088, found m/z: 295.2086.

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(1S, 2R, 5S)-(1R, 2S, 5R)-2-Triisopropylsilanyloxy-bicyclo[3.2.1]oct-6-en-3-one (11a). Sc(OTf)₃ (8.5 mg, 0.017 mmol) was added in one portion to a stirred solution of Diels-Alder adduct 12 (50 mg, 0.17 mmol) in dry CH₂Cl₂ (1 mL) in a 10 mL round bottom flask at 0 °C and the reaction mixture was then stirred for 2 h as it slowly warmed to room temperature. Then the reaction mixture was diluted with 5 mL H₂O and extracted with diethyl ether (2×). The combined extracts were washed with water and brine, dried over MgSO₄, and then concentrated. The crude product which was purified over silica gel by flash chromatography using hexane-ether (25 :1) to give 11a as colorless oil: 36 mg (72% yield). The physical and spectral data were identical to those previously reported for this compound: 1H NMR (500 MHz, CDCl₃) δ 6.08 (m, 2H), 4.34 (d, J = 3.5 Hz, 1H), 3.02 (m, 1H), 2.87 (m, 1H), 2.33-2.43 (m, 2H), 2.10-2.15 (m, 1H), 1.81 (d, J = 11.0 Hz, 1H), 1.04-1.15 (m, 21H); 13C NMR (125 MHz, CDCl₃) δ 207.8, 136.7, 133.6, 81.6, 48.2, 45.5, 41.3, 39.3, 18.0, 17.9, 12.4.
The 2-(S)-exo Diels-Alder adduct 13 (85% ee) was synthesized by using Faller’s Ruthenium catalyst [CyRuCl(S)-BINAPO]SbF$_6$ (4% loading). The enantioselectivity was determined by $^1$HNMR using shift reagent Eu(hfc)$_3$ and the diastereoselectivity was determined by $^1$H NMR of crude mixture.

\[ \text{Faller’s Ru Catalyst} \]

(1R, 3R, 5S)-3-Methyl-bicyclo[3.2.1]oct-6-en-2-one (14). Aluminum chloride (54 mg, 0.41 mmol) was added in one portion to a stirred solution of substrate 13 (50 mg, 0.36 mmol) in dry CH$_2$Cl$_2$ (2 mL) in a 10 mL round bottom flask at 0 °C and the reaction mixture was then stirred for 2h. The reaction was then quenched with saturated sodium bicarbonate solution (5 mL) and extracted with ether (2×), and the combined extracts were washed with water and brine, dried over MgSO$_4$, and carefully concentrated due to the volatility of the product. The crude product was purified by column chromatography on silica gel using pentane-diethyl ether (97:3) as eluent to give 14 as colorless oil: 37 mg (74% yield); R$_f$ 0.26 (7% ether in pentane). $[\alpha]_{25}^D = 422.3\,^o\,(c = 2.3, \text{CHCl}_3)$. The enantiomeric excess was determined by GC using a Chiraldex B-DM column [flow 1 ml/min, 105 °C/30 min, 30 m × 0.25 mm, 1 mg/ml; t$_r$ = 23.80 and 24.86 min; 85% ee].

GC analysis of the enantiomeric excess for the compound 14.
References