Supplementary Material:

INTRAMOLECULAR DIELS-ALDER REACTIONS OF DECATRIENOATES: REMOTE STEREOCONTROL AND CONFORMATIONAL ACTIVATION

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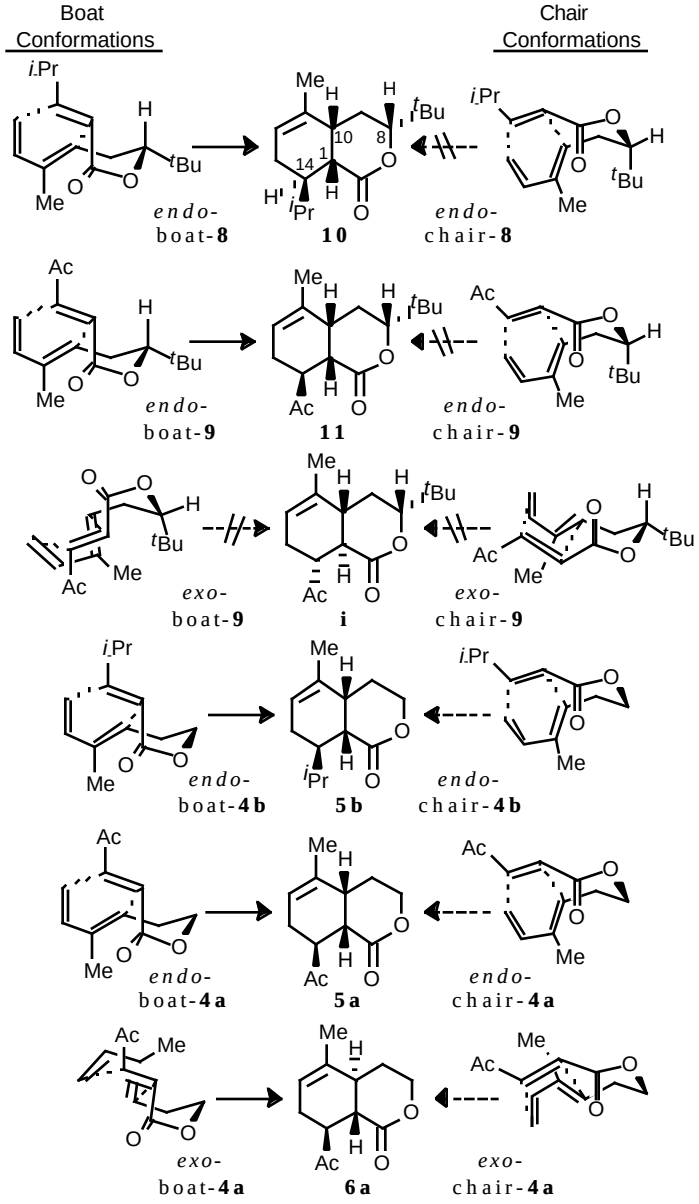
Controlling Bridgehead Stereochemistry



Experimental

Preparation of 2. A 1.5 M DIBAL-H in toluene (13.7 mL, 20.5 mmol) was diluted in toluene (5 mL). Ethyl (E)-4-methyl-3,5-hexadienoate (**1**, 1.54 g, 10 mmol) was dissolved in toluene (10 mL) and added dropwise to the prepared DIBAL-H solution at 0 °C. The reaction mixture was stirred for 2 h at 0 °C, quenched with 20 mL of cosolvent (toluene:methanol = 1:1). 1M HCl (aq) solution was added to make acidic solution. The reaction mixture was filtered and extracted with ether and dried with anhydrous $MgSO_4$. The solvent was evaporated under vacuum. Column chromatography (20 % EtOAc/Hex) afforded the title compound as a yellow oil. (1.0 g, 9.1 mmol, 91 %): FTIR (KBr) 3346, 2930, 2882, 1683, 1660 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.73 (s, 3H), 2.37 (q, J = 6.9 Hz, 2H), 2.73 (s, br, 1H), 3.60 (t, J = 6.7 Hz, 2H), 4.93 (d, J = 10.7 Hz, 1H), 5.08 (d, J = 17.4 Hz, 1H), 5.45 (t, J = 7.3 Hz, 1H), 6.34 (dd, J = 17.4, 10.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7, 31.7, 62.0, 111.1, 128.2, 136.3, 141.1.

Preparation of 4a. A solution of (E)-4-oxo-2-pentenoic acid (**3a**, 0.68 g, 5.9 mmol), DCC (1.34 g, 6.5 mmol), (E)-4-methyl-3,5-hexadien-1-ol (**2**, 0.73 g, 6.5 mmol) and DMAP (0.072 g, 0.59 mmol) in dichloromethane (30 mL) was stirred for 12 h at rt. The N,N-dicyclohexylurea was filtered and the filtrate was washed with water and dried ($MgSO_4$) and the solvent was evaporated under vacuum. Column chromatography (20 % EtOAc/Hex) afforded the title compound as a colorless oil (0.98 g, 4.7 mmol, 80 %): FTIR (KBr) 1722, 1702, 1686, 1255 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.76 (s,

3H), 2.35 (s, 3H), 2.54 (q, J = 7.0 Hz, 2H), 4.23 (t, J = 6.9 Hz, 2H), 4.98 (d, J = 10.7 Hz, 1H), 5.14 (d, J = 17.4 Hz, 1H), 5.46 (t, J = 7.2 Hz, 1H), 6.36 (dd, J = 17.4, 10.7 Hz, 1H), 6.63 (d, J = 16.1 Hz, 1H), 7.00 (d, J = 16. 1Hz, 1H), ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.4, 27.3, 27.6, 64.2, 111.4, 126.5, 130.9, 136.4, 139.7, 140.6, 165.0, 197.0.

Preparation of 5a and 6a. A solution of (E)-4-Methyl-3,5-hexadienyl (E)-4-oxo-2-pentenoate (**4a**, 0.21 g, 1.0 mmol) in toluene (5 mL) was stirred for 5 h at 125 ℃ in a sealed tube. The solvent was evaporated under vacuum. Column chromatography (20 % EtOAc/Hex) afforded the title compound a colorless oil (**5a**, 66 mg) and a colorless solid (**6a**, 44 mg) (total yield: 0.11 g, 0.52 mmol, 52 %). **5a.** Yield: 31%; FTIR (KBr) 2915, 1702, 1162 cm^{-1}; ^{1}H NMR (300 MHz,$CDCl_3$) δ 1.62 (s, 3H), 1.76 (m, 1H), 2.18 (s, 3H), 2.14-2.20 (m, 1H), 2.44 (s, br, 2H), 2.83 (m, 1H), 3.33 (m, 2H), 4.24 (m, 2H), 5.53 (s, br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 23.8, 27.0, 27.2, 32.9, 40.2, 47.0, 66.1, 121.7, 134.3, 173.1, 208.8. **6a**. Yield: 21%; mp 134.1-134.3 ℃; FTIR (KBr) 1729, 1707, 1176 cm-1; 1H NMR (300 MHz, CDCl3) d 1.65-1.80 (m, 1H), 1.69 (s, 3H), 2.01 (m, 1H), 2.27-2.37 (m, 3H), 2.34 (s, 3H), 2.89 (m, 2H), 4.38 (m, 2H), 5.45 (s, br, 1H), ; ^{13}C NMR (75 MHz,$CDCl_3$) δ 20.0, 25.9, 28.2, 30.1, 36.2, 44.0, 45.7, 65.6, 120.6, 133.7, 174.1, 211.5. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.36; H, 7.93.

Preparation of 4b. Yield: 73 %; FTIR (KBr) 2961, 1715, 1163 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, J = 6.8 Hz, 6H), 1. 74 (s, 3H), 2.44 (m, 1H), 2.49 (q, J = 7.1 Hz, 2H), 4.12 (t, J = 7.0 Hz, 2H), 4.95 (d, J

= 10.7 Hz, 1H), 5.10 (d, J = 17.4 Hz, 1H), 5.45 (t, J = 7.3 Hz, 1H), 5.74 (dd, J = 15.7, 1.5 Hz, 1H), 6.35 (dd, J = 17.4, 10.7 Hz, 1H), 6.91 (dd, J = 15.7, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.4, 20.9, 27.5, 30.6, 63.0, 111.1, 118.2, 127.0, 136.1, 140.7, 155.1, 166.4. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.10; H, 9.74.

Preparation of 5b. A solution of (E)-4-Methyl-3,5-hexadienyl (E)-4-methyl-2-pentenoate (**4b**, 120 mg, 0.58 mmol) in toluene (5 mL) was stirred for 20 h at 220 ℃ in a sealed tube. The solvent was evaporated under vacuum. Column chromatography (20 % EtOAc/Hex) afforded the title compound as a colorless oil (52 mg, 0.25 mmol, 43 %): FTIR (KBr) 2960, 2870, 1732, 1728 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 6.6 Hz, 6H), 1.44-1.71(m, 1H), 1.65 (s, 3H), 1.83-2.27 (m, 5H), 2.54 (s, br, 1H), 2.79 (m, 1H), 4.22 (m, 2H), 5.50 (s, br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.4, 20.5, 20.9, 24.3, 26.1, 26.8, 32.8, 39.4, 43.0, 66.2, 124.2, 132.1, 173.9. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.81; H, 9.76.

Preparation of 7. 3-Methyl-1,4-pentadiene (0.98 mL, 8.2 mmol) was diluted in THF (16 mL) at -78 ℃. To this solution 1.6 M n-BuLi (6.1mL, 9.8 mmol) in hexane was added dropwise at -78 ℃. The reaction mixture was stirred for 20 min. at -78 ℃ and for 1.5 h at rt. The reaction mixture was cooled down to -78 ℃ again. To this solution trimethylacetaldehyde (0.9 mL, 8.2 mmol) in THF (33 mL) was added dropwise at -78 ℃. The deep red reaction mixture was changed to a slight yellow solution. The reaction mixture was stirred for 15 min. at 0 ℃. After decolorization to quench the reaction a

saturated NH_4Cl (aq) was added at 0 °C. The reaction mixture was warmed to rt. Ether (10 mL) was added then ether layer was collected. Water layer was extracted with EtOAc (3x). The combined organic layer was washed with a saturated $NaHCO_3$ (aq) and water, dried with anhydrous $MgSO_4$, and filtered. The solvent was evaporated under vacuum. Column chromatography (20% EtOAc/Hex) afforded the title compound as a yellow oil (1.2 g, 7.4 mmol, 90%): FTIR (KBr) 3434, 2954, 2868 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (s, 9H), 1.55 (s, br, 1H), 1.77 (s, 3H), 2.12-2.41 (m, 2H), 3.28 (d, br, J = 10.1 Hz, 1H), 4.96 (d, J = 10.7 Hz, 1H), 5.12 (d, J = 17.4 Hz, 1H), 5.59 (t, J = 7.4 Hz, 1H), 6.40 (dd, J = 17.4, 10.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 25.7, 30.8, 34.8, 79.4, 111.1, 130.2, 136.4, 141.3.

Preparation of 8. Yield: 87 %**;** FTIR (KBr) 2961, 2871, 1715, 1163 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (s, 9H), 1.05 (d, J = 6.8 Hz, 6H), 1.70 (s, 3H), 2.29-2.49 (m, 3H), 4.82-4.90 (m, 2H), 5.03 (d, J = 17.6 Hz, 1H), 5.41 (t, J = 7.2 Hz, 1H), 5.72 (dd, J = 15.7, 1.4 Hz, 1H), 6.31 (dd, J = 17.3, 10.7 Hz, 1H), 6.88 (dd, J = 15.7, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.6, 21.2, 26.0, 29.0, 30.8, 34.7, 79.7, 110.5, 118.7, 128.8, 135.4, 141.3, 154.9, 166.5. Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.05; H, 10.59.

Preparation of 10. A solution of (E)-2,2,6-trimethyl-5,7-octadien-3-yl (E)-4-methyl-2-pentenoate (**8**, 130 mg, 0.50 mmol) in toluene (5 mL) was stirred for 12 h at 200 °C in a sealed tube. The solvent was evaporated under vacuum. Column chromatography (20 %

EtOAc/Hex) afforded the title compound as a colorless solid (72 mg, 0.27 mmol, 55 %): mp 101.9-102.1 ºC; FTIR (KBr) 2956, 2922, 2854, 1726 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (d, J = 6.5 Hz, 6H), 0.97 (s, 9H), 1.31 (m, 1H), 1.56-2.30 (m, 5H), 1.65 (s, 3H), 2.52 (m, 1H), 2.74 (t, J = 6.7 Hz, 1H), 3.89 (d, J = 11.9 Hz, 1H), 5.39 (s, br, 1H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 19.1, 21.1, 21.2, 23.8, 25.5, 27.4, 27.8, 34.0, 34.1, 37.4, 40.9, 85.1, 121.3, 133.9, 174.6. Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found:: C, 77.40; H, 10.80.

Preparation of 11. A solution of (E)-4-oxo-2-pentenoic acid (**3a**, 0.75 g, 6.6 mmol), DCC (1.4 g, 6.6 mmol), (E)-2,2,6-trimethyl-5,7-octadien-3-ol (**7**, 1.0 g, 6.0 mmol) and DMAP (0.080 g, 0.66 mmol) in dichloromethane (30 mL) was stirred for 12 h at rt. The N,N-dicyclohexylurea was filtered and the filtrate was washed with water and dried ($MgSO_4$) and the solvent was evaporated under vacuum. Column chromatography (20 % EtOAc/Hex) afforded the title compound as a colorless solid (1.43 g, 5.4 mmol, 91 %): mp 92.1-92.4 ºC; FTIR (KBr) 2960, 1720, 1702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (s, 9H), 1.10 (dd, J = 11.7, 1.9 Hz, 1H), 1.59 (s, 3H), 2.16 (s, 3H), 2.25 (ddd, 13.8, 8.2, 1.1 Hz, 1H), 2.33-2.44 (m, 1H), 2.48-2.60 (m, 1H), 2.72-2.86 (m, 1H), 3.17 (m, 1H), 3.35 (ddd, J = 9.8, 3.1, 1.1 Hz, 1H), 3.94 (dd, J = 9.8, 3.1 Hz, 1H), 5.40 (s, br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.1, 23.8, 25.5, 27.3, 29.0, 32.8, 33.6, 38.1, 46.2, 84.2, 119.0, 135.8, 174.3, 209.4. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.88; H, 9.26.