Broad Spectrum Enantioselective Diels-Alder Catalysis by Chiral, Cationic Oxazaborolidines

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Supplementary Materials

Materials and Methods. Unless stated otherwise, reactions were performed in flame-dried glassware under a positive pressure of nitrogen using freshly distilled solvents. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F₂₅₄ precoated plates (0.25 mm). Flash chromatography was performed using Baker silica gel (40 μ m particle size). ¹H and ¹³C NMR chemical shifts are reported as δ using residual solvent signal as an internal standard. High-resolution mass spectral analyses were performed at the Harvard University Mass Spectrometry Center. Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane and trifluoromethanesulfonic (triflic) acid¹ were distilled from phosphorus pentoxide. Toluene was distilled from sodium. Acrolein, diethyl fumarate, ethyl acrylate, ethyl crotonate and 2(5*H*)-furanone were distilled from calcium hydride. Acrylic acid and crotonyl chloride were distilled from anhydrous calcium chloride. 2-Cyclohepten-1-one, 2-cyclohexen-1-one, 2-cyclopenten-1-one and ethyl vinyl ketone were distilled from anhydrous magnesium sulfate. 1,3-Cyclopentadiene was cracked at 170 °C and re-distilled (stored over 4A molecular sieves). Purified cyclopentadiene and triflic acid were stored

¹ Triflic acid reacts with P₂O₅ to form triflic anhydride. Therefore, only a small amount of P₂O₅ was used and the forerun containing triflic anhydride was discarded.

in a $-80\text{ }^{\circ}\text{C}$ freezer. Boroxines,² chiral α,α -diaryl-2-pyrrolidinemethanol ligands,³ and 1,4-quinone monoketals⁴ were prepared according to literature procedures.

General Procedure for the Preparation and Use of Chiral Diels-Alder Catalysts. A 100-mL, two-necked, round-bottomed flask equipped with a stir bar, a glass stopper and a 50-mL pressure-equalizing addition funnel (containing a cotton plug and ca. 10 g of 4A molecular sieves,⁵ and functioning as a Soxhlet extractor) fitted on top with a reflux condenser and a nitrogen inlet adaptor was charged with (*S*)-(-)- α,α -bis(3,5-dimethylphenyl)-2-pyrrolidinemethanol (93.9 mg, 0.303 mmol), tri-*o*-tolylboroxine (35.8 mg, 0.101 mmol) and 35 mL of toluene. The resulting solution was heated to reflux (bath temperature $\sim 145\text{ }^{\circ}\text{C}$). After 4 h, the reaction mixture was cooled to ca. $60\text{ }^{\circ}\text{C}$ and the addition funnel and condenser were quickly replaced with a short-path distillation head. The mixture was concentrated by distillation (air-cooling) to a volume of ca. 5 mL. This distillation protocol was repeated three times by re-charging with 3 x 5 mL of toluene. The solution was then allowed to cool to room temperature and the distillation head was quickly replaced with a nitrogen inlet adaptor. Concentration *in vacuo* (ca. 0.1 mmHg, 1 h) afforded the corresponding oxazaborolidine as a clear oil which can then be dissolved in CH_2Cl_2 and used in Diels-Alder experiments.

To an aliquot of the oxazaborolidine precursor (0.160 mmol, theoretical) in 2 mL of CH_2Cl_2 at $-78\text{ }^{\circ}\text{C}$ was added triflic acid (0.200 M solution in CH_2Cl_2 , freshly prepared, 667 μL , 0.133 mmol) dropwise. During the addition, the catalyst solution turned orange in color but cleared up instantaneously. Near the end, a small amount of orange precipitate was observed.

² Corey, E. J.; Shibata, T.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 3808.

³ (a) Mathre, D. J.; Jones, T. K.; Xavier, L. C.; Blacklock, T. J.; Reamer, R. A.; Mohan, J. J.; Jones, E. T. T.; Hoogsteen, K.; Baum, M. W.; Grabowski, E. J. J. *J. Org. Chem.* **1991**, *56*, 751. (b) Xavier, L. C.; Mohan, J. J.; Mathre, D. J.; Thompson, A. S.; Carroll, J. D.; Corley, E. G.; Desmond, R. In *Organic Syntheses*; Wiley: New York, 1996; Vol. 74, pp. 50-71.

⁴ (a) Breuning, M.; Corey, E. J. *Org. Lett.* **2001**, *3*, 1559. (b) Rose, P. A.; Lei, B.; Shaw, A. C.; Walker-Simmons, M. K.; Napper, S.; Quail, J. W.; Abrams, S. R. *Can. J. Chem.* **1996**, *74*, 1836.

⁵ Molecular sieves (pellets) were dried *in vacuo* at ca. $200\text{ }^{\circ}\text{C}$ with a heat gun for 10 min prior to use.

After 10 to 15 min at $-78\text{ }^{\circ}\text{C}$, the orange precipitate disappeared and a colorless homogeneous solution was obtained. As an example, 2-cyclohexen-1-one (64.6 μL , 64.1 mg, 0.667 mmol) and cyclopentadiene (1:1 (v/v) solution in CH_2Cl_2 , 550 μL , 3.33 mmol, added dropwise along side of the flask via syringe) were added successively. The reaction mixture was stirred for 15 h at $-20\text{ }^{\circ}\text{C}$ and then quenched by addition of 200 μL of Et_3N . After the mixture was warmed to room temperature, the solvent was removed by rotary evaporation and the residue was purified by silica gel chromatography (gradient elution with 4-5% Et_2O -pentane) to afford 106 mg (98%) of the Diels-Alder adduct (*vide infra*).⁶

Physical Data of the Diels-Alder Products:⁷

1-[(1*R*, 2*R*, 4*R*)-Bicyclo[2.2.1]hept-5-en-2-yl]-propan-1-one.⁸ Purification by column chromatography (gradient elution with 1-3% Et_2O -pentane) afforded 99.0 mg (99%) of product as a colorless oil: ^1H NMR (400 MHz, CDCl_3) δ 6.12 (dd, 1H, $J = 2.9, 5.7$ Hz), 5.80 (dd, 1H, $J = 2.9, 5.7$ Hz), 3.20 (bs, 1H), 2.99 (app. dt, 1H, $J = 4.4, 8.4$ Hz), 2.87 (bs, 1H), 2.45 (dq, 1H, $J = 7.3, 17.6$ Hz), 2.39 (dq, 1H, $J = 7.3, 17.6$ Hz), 1.73 (ddd, 1H, $J = 3.7, 8.8, 11.7$ Hz), 1.48 (ddd, 1H, $J = 2.6, 4.4, 11.7$ Hz), 1.42 (ddd, 1H, $J = 1.8, 4.0, 8.4$ Hz), 1.30 (d, 1H, $J = 8.8$ Hz), 1.00 (app. t, 3H, $J = 7.3$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 211.5, 137.6, 131.3, 51.2, 49.9, 45.9,

⁶ After elution of the Diels-Alder adduct, the ligand-containing fractions were eluted with 10% $\text{MeOH}-\text{CH}_2\text{Cl}_2$ and concentrated in vacuo. This material was dissolved in CH_2Cl_2 and hydrolyzed by stirring with aqueous 2N NaOH solution for 2 h. The organic phase was collected, concentrated and purified by column chromatography (elution with EtOAc) to afford pure ligand (95-99% recovery).

⁷ The physical and spectral data of several Diels-Alder adducts are known. For (*1S*, *2S*, *4S*)-Bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde and (*1S*, *2S*, *3R*, *4S*)-3-Methylbicyclo[2.2.1]hept-5-ene-2-carboxaldehyde, see (a) Ishihara, K.; Kurihara, H.; Matsumoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1998**, *120*, 6920. (b) Hashimoto, S.-I.; Komeshima, N.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 437. For 1-[(1*R*, 2*R*, 3*S*, 4*R*)-3-methylbicyclo[2.2.1]hept-5-en-2-yl]-propan-1-one, see (c) Northrup, A. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 2458.

⁸ Kumareswaran, R.; Vankar, P. S.; Reddy, M. V. R.; Pitre, S. V.; Roy, R.; Vankar, Y. D. *Tetrahedron* **1999**, *55*, 1099.

42.6, 34.8, 27.4, 7.8; FTIR (neat) 3061, 2974, 2940, 2905, 2874, 1711; HRMS (EI) calcd for $[C_{10}H_{14}O]$ ($[M]^+$): 150.1045; found 150.1048; R_f 0.43 (Hex-EtOAc 9:1); $[\alpha]_D^{23} +111$ (c 0.76, $CHCl_3$, 97 % ee, pure *endo*). The minor *exo* isomer was separated: 1H NMR (400 MHz, $CDCl_3$) δ 6.15 (dd, 1H, $J = 2.9, 5.7$ Hz), 6.12 (dd, 1H, $J = 2.9, 5.3$ Hz), 2.94 (bs, 1H), 2.90 (bs, 1H), 2.57 (dq, 1H, $J = 7.3, 17.6$ Hz), 2.48 (dq, 1H, $J = 7.3, 17.6$ Hz), 2.37 (ddd, 1H, $J = 1.3, 4.6, 8.8$ Hz), 1.86 (ddd, 1H, $J = 3.7, 4.6, 11.4$ Hz), 1.40 (d, 1H, $J = 8.4$ Hz), 1.31 (m, 1H), 1.25 (ddd, 1H, $J = 2.6, 8.8, 11.4$ Hz), 1.07 (app. t, 3H, $J = 7.3$ Hz). Diastereoselectivity (*endo-exo* ratio) and enantioselectivity were determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 100 °C, 25 psi); retention times: 23.2 min (*endo*, major), 24.6 min (*endo*, minor), 18.5 min (*exo*, major), 18.2 min (*exo*, minor). The absolute configuration was assigned by comparison with an authentic sample prepared from (–)-(1*S*, 2*S*, 4*S*)-bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (*vide supra*; EtMgBr addition followed by Dess-Martin oxidation) and GC analysis.

(1*R*, 2*R*, 4*R*)-Bicyclo[2.2.1]hept-5-ene-2-carboxylic Acid.⁹ Purification by column chromatography (40% EtOAc-hexanes) afforded 91 mg (99%) of product as a colorless oil. The physical and spectral data were identical to those previously reported for this compound: 1H NMR (500 MHz, $CDCl_3$) δ 11.76 (brs, 1H), 6.21 (dd, 1H, $J = 3.0, 5.0$ Hz), 6.01 (dd, 1H, $J = 3.0, 5.0$ Hz), 3.24 (s, 1H), 2.98 (dt, 1H, $J = 9.5, 4.0$ Hz), 2.92 (s, 1H), 1.90-1.95 (m, 1H), 1.44-1.47 (m, 1H), 1.39-1.43 (m, 1H), 1.29 (d, 1H, $J = 8.0$ Hz). Diastereoselectivity (*endo-exo* ratio) and enantioselectivity were determined by transformation¹⁰ with oxalyl chloride to the acid chloride, conversion to the corresponding ethyl ester and GC analysis. The absolute configuration was determined by optical rotation: $[\alpha]_D^{23} +137$ (c 3.0, 95% EtOH, 98 % ee).^{9b}

⁹ (a) Sarakinos, G.; Corey, E. J. *Org. Lett.* **1999**, *1*, 1741. (b) Poll, T.; Sobczak, A.; Hartmann, H.; Helmchen, G. *Tetrahedron . Lett.* **1985**, *26*, 3095.

¹⁰ Stille, J. R.; Santarsiero, B. D.; Grubbs, R. H. *J. Org. Chem.* **1990**, *55*, 843.

Ethyl (1R, 2R, 4R)-Bicyclo[2.2.1]hept-5-ene-2-carboxylate.¹¹ Purification by column chromatography (10% Et₂O-pentane) afforded 106 mg (96%) of product as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 6.17 (dd, 1H, *J* = 3.5, 7.0 Hz), 5.91 (dd, 1H, *J* = 3.5, 7.5 Hz), 4.02-4.10 (m, 2H), 3.18-3.19 (m, 1H), 2.92 (dt, 1H, *J* = 11.5, 5.0 Hz), 2.88 (brs, 1H), 1.85-1.91 (m, 1H), 1.38-1.43 (m, 2H), 1.24-1.27 (m, 1H), 1.21 (t, 3H, *J* = 8.5 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 174.7, 137.6, 132.3, 60.0, 49.5, 45.6, 43.3, 42.5, 29.1, 14.2; FTIR (KBr) 2985, 2977, 2945, 1737, 1336, 1191 ; [α]_D²³ +138 (*c* 1.0, CHCl₃, >99 % ee). Diastereoselectivity (*endo-exo* ratio) and enantioselectivity were determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 100 °C, 25 psi); retention times: 13.8 min (*exo*), 16.1 min (*endo*, major), 17.4 min (*endo*, minor). The absolute configuration was assigned by reduction¹¹ with LiAlH₄ to the corresponding alcohol, conversion to the (*R*)-MTPA ester derivative and comparison with ¹H NMR spectra of the known (*R*)-MTPA ester prepared from (*1S*, *2S*, *4S*)-bicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (*vide supra*).

Ethyl (1R, 2R, 3S, 4R)-3-Methylbicyclo[2.2.1]hept-5-ene-2-carboxylate. Purification by column chromatography (10% Et₂O-pentane) afforded 55 mg (46%) of product as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 6.24 (dd, 1H, *J* = 4.0, 7.0 Hz), 5.97 (dd, 1H, *J* = 3.5, 7.0 Hz), 4.01-4.10 (m, 2H), 3.09 (s, 1H), 2.44 (m, 1H), 2.92 (dd, 1H, *J* = 4.5, 5.5 Hz), 1.77-1.83 (m, 1H), 1.51-1.53 (m, 1H), 1.41 (dq, 1H, *J* = 2.5, 10.5 Hz), 1.21 (t, 3H, *J* = 8.5 Hz), 1.16 (d, 3H, *J* = 9.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 174.7, 138.6, 133.2, 60.0, 52.5, 48.8, 45.9(2C), 37.7, 20.9,

¹¹ Jung, M. E.; Vaccaro, W. D.; Buszek, K. R. *Tetrahedron. Lett.* **1989**, 30, 1893.

14.2; FTIR (KBr) 2962, 2927, 1733, 1183. Diastereoselectivity (*endo-exo* ratio) was determined by ^1H NMR analysis of the crude mixture: δ 6.24 (dd, 1H, $J = 4.0, 7.0$ Hz, *endo*, major), 6.19 (dd, 1H, $J = 4.0, 7.0$ Hz, *exo*, minor). Enantioselectivity was determined by reduction with NaBH_4 to the corresponding alcohol, conversion to the (*R*)-MTPA ester derivative and ^1H NMR integration (500 MHz, CDCl_3): δ 4.11 (dd, 1H, $J = 11.0, 7.0$ Hz, minor), 4.05 (dd, 1H, $J = 11.0, 7.0$ Hz, major). The absolute configuration was determined by reduction with LiAlH_4 to the corresponding alcohol and measurement of optical rotation: $[\alpha]_{\text{D}}^{23} +67.7$ (c 0.89, EtOH, >98% ee).¹²

2,2,2-Trifluoroethyl (1*R*, 2*R*, 3*S*, 4*R*)-3-Methylbicyclo[2.2.1]hept-5-ene-2-carboxylate.

2,2,2-Trifluoroethyl crotonate: To a stirred solution of freshly distilled crotonyl chloride (5.6 mL, 52 mmol) in 2,2,2-trifluoroethanol (38 mL, 0.52 mol) was added pyridine (6.3 mL, 78 mmol) at 0°C and the reaction mixture was stirred at room temperature for 48 h. The mixture was extracted with pentane (50 mL X 7) and the combined extract was concentrated to about 150 mL in volume. The pentane solution was washed with saturated citric acid solution (20 mL X 3), dried over sodium sulfate, filtered and concentrated to give a colorless oil product (2.3 g, 26 %). ^1H NMR (400 MHz, CDCl_3) δ 7.11 (dq, 1H, $J = 7.2, 15.6$ Hz), 5.91 (dq, 1H, $J = 13.6, 2.0$ Hz), 4.51 (q, 1H, $J = 8.4$ Hz), 1.93 (dd, 1H, $J = 7.2, 1.6$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 164.6, 147.7, 120.8, 60.64, 60.27, 59.9, 59.5, 18.2; FTIR (KBr) 2977, 1744, 1660, 1279, 1164.

The titled Diels-Alder adduct was purified by column chromatography (10% Et_2O -pentane) to afford 145 mg (93%) of product as a colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 6.28 (dd, 1H, $J = 3.3, 5.8$ Hz), 5.98 (dd, 1H, $J = 2.8, 5.8$ Hz), 4.43-4.50 (m, 1H), 4.32-4.40 (m, 1H), 3.15 (brs, 1H), 2.49 (m, 1H), 2.46 (t, 1H, $J = 3.8$ Hz), 1.82-1.88 (m, 1H), 1.56 (d, 1H, $J = 8.5$

¹² (a) Vandewalle, M.; Eycken, J. V.; Oppolzer, W.; Vullioud, C. *Tetrahedron*. **1986**, 42, 4035. (b) Fujioka, H.; Nagatomi, Y.; Kotoku, N.; Kitagawa, H.; Kita, Y. *Tetrahedron*. **2000**, 56, 10141.

Hz), 1.45-1.49 (m, 1H), 1.53 (d, 3H, $J = 7.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 173.0, 139.1, 132.9, 60.4, 60.1, 59.8, 59.5, 52.0, 48.7, 46.0, 45.9, 38.0, 20.7; FTIR (KBr) 2967, 2876, 1756, 1410, 1321, 1281, 1181; $[\alpha]_{\text{D}}^{23} +95.4$ (c 1.0, CHCl_3 , >98 % ee). Diastereoselectivity (*endo-exo* ratio) was determined by ^1H NMR analysis of the crude mixture: δ 6.33 (dd, 1H, $J = 3.0, 6.0$ Hz, *exo*, minor), 6.28 (dd, 1H, $J = 3.3, 5.8$ Hz, *endo*, major). Enantioselectivity and absolute configuration were determined by reduction with NaBH_4 to the corresponding alcohol, conversion to the (*R*)-MTPA ester derivative and ^1H NMR integration (500 MHz, CDCl_3): δ 4.11 (dd, 1H, $J = 11.0, 7.0$ Hz, minor), 4.05 (dd, 1H, $J = 11.0, 7.0$ Hz, major).

(1*R*, 2*S*, 6*R*, 7*S*)-Tricyclo[5.2.1.0^{2,6}]dec-8-ene-2-carboxaldehyde.^{7a} Cyclopentene-1-carboxaldehyde.¹³ (Cyclopenten-1-yl)methanol¹⁴ (164 mg, 1.67 mmol) was oxidized in dichloromethane (5 mL) at -55 °C with oxalyl chloride (0.167 mL, 1.83 mmol), DMSO (0.260 mL, 3.66 mmol) and triethylamine (1.16 mL, 8.35 mmol) via the procedure described by Swern.¹⁵ The reaction mixture was allowed to warm to room temperature and quenched with water. The aqueous layer was extracted with dichloromethane (5 mL X 4). The combined extract was dried over anhydrous magnesium sulfate and concentrated to give the crude aldehyde as a pale yellow oil. This crude product was purified by silica gel chromatography to furnish 102 mg (64%) of product as a colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 9.80 (s, 1H), 6.86-6.88 (m, 1H), 2.59-2.63 (m, 2H), 2.51-2.55 (m, 2H), 2.01 (app. t, 1H, $J = 7.5$ Hz), 1.98 (app. t, 1H, $J = 7.5$ Hz).

The titled Diels-Alder adduct was purified by column chromatography (gradient elution with 5-20% Et_2O -pentane) afforded 103 mg (95%) of product as a colorless oil. The physical

¹³ Kozikowski, A. P.; Tuckmantel, W. *J. Org. Chem.* **1991**, 56, 2826.

¹⁴ Salomon, R. G.; Ghosh, S.; Zagorski, M. G.; Reitz, M. *J. Org. Chem.* **1982**, 47, 829.

¹⁵ Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, 43, 2480.

and spectral data were identical to those previously reported for this compound: ^1H NMR (500 MHz, CDCl_3) δ 9.70 (s, 1H), 6.27 (dd, 1H, $J = 3.0, 5.5$ Hz), 6.17 (dd, 1H, $J = 3.3, 5.3$ Hz), 2.92 (brs, 1H), 2.81-2.84 (m, 1H), 2.81 (brs, 1H), 1.77-1.82 (m, 1H), 1.63-1.72 (m, 2H), 1.61 (d, 1H, $J = 8.5$ Hz), 1.57 (d, 1H, $J = 8.5$ Hz), 1.45-1.54 (m, 1H), 1.19-1.25 (m, 1H), 1.06-1.13 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 204.9, 138.8, 135.9, 68.4, 51.6, 50.7, 47.1, 46.3, 29.8, 29.7, 29.3; FTIR (KBr) 2961, 2954, 2948, 2869, 1716, 1693; $[\alpha]_{\text{D}}^{23} -20.1$ (c 1.0, CHCl_3 , 94 % ee). Diastereoselectivity (*exo-endo* ratio) was determined by ^1H NMR analysis of the crude mixture: δ 9.70 (s, 1H, *exo*, major), 9.42 (s, 1H, *endo*, minor). Enantioselectivity was determined by reduction with NaBH_4 to the corresponding alcohol, conversion to the (*R*)-MTPA ester derivative and ^1H NMR integration (500 MHz, CDCl_3): δ 2.68 (brs, 1H, major), 2.63 (brs, 1H, minor). The absolute configuration was assigned by analogy.²

Diethyl (1*R*, 2*S*, 3*S*, 4*S*)-Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate.¹⁶ Purification by column chromatography (10% Et_2O -pentane) afforded 157 mg (99%) of product as a colorless oil. The physical and spectral data were identical to those previously reported for this compound: ^1H NMR (500 MHz, CDCl_3) δ 6.27 (dd, 1H, $J = 3.3, 5.8$ Hz), 6.06 (dd, 1H, $J = 2.8, 5.3$ Hz), 4.16 (q, 2H, $J = 7.5$ Hz), 4.06-4.12 (m, 2H), 3.37 (app. t, 1H, $J = 4.0$ Hz), 3.25 (m, 1H), 3.11 (m, 1H), 2.67 (dd, 1H, $J = 1.5, 4.5$ Hz), 1.61 (d, 1H, $J = 8.5$ Hz), 1.43-1.45 (m, 1H), 1.27 (t, 3H, $J = 7.5$ Hz), 1.23 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 174.5, 173.3, 137.6, 135.0, 60.8, 60.5, 47.8 (2C), 47.2 (2C), 45.7, 14.2 (2C). Enantioselectivity was determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 110 °C, 25 psi); retention times: 68.3 min (*endo*, minor), 69.9 min (*endo*, major). The absolute configuration was determined by optical rotation: $[\alpha]_{\text{D}}^{23} +103$ (c 1.0, CHCl_3 , 98 % ee).¹⁶

¹⁶ Ito, Y. N.; Ariza, X.; Beck, A. K.; Bohac, A.; Ganter, C.; Gawley, R. E.; Kuhnle, F. N. M.; Tuleja, J.; Wang, Y. M.; Seebach, D. *Helv. Chim. Acta* **1994**, 77, 2071.

(1*R*, 2*S*, 3*R*, 4*S*)-3-Hydroxymethyl-bicyclo[2.2.1]hept-5-ene-2-carboxylic Acid Lactone.¹⁷

Purification by column chromatography (gradient elution with 20-50% EtOAc-hexanes) afforded 94 mg (94%) of product as a pale yellow solid. The physical and spectral data were identical to those previously reported for this compound: ¹H NMR (500 MHz, CDCl₃) δ 6.26-6.27 (m, 2H), 4.26 (app. t, 1H, *J* = 4.0 Hz), 3.77 (dd, 1H, *J* = 3.0, 10.0 Hz), 3.31 (brs, 1H), 3.23 (dd, 1H, *J* = 4.5, 9.5 Hz), 3.07-3.11 (m, 2H), 1.62 (d, 1H, *J* = 8.0 Hz), 1.44 (d, 1H, *J* = 9.0 Hz). The *exo* isomer was separated: ¹H NMR (500 MHz, CDCl₃) δ 6.24 (dd, 1H, *J* = 3.0, 5.5 Hz), 6.18 (dd, 1H, *J* = 3.0, 5.5 Hz), 4.48 (app. t, 1H, *J* = 4.0 Hz), 4.00 (dd, 1H, *J* = 4.0, 9.5 Hz), 3.27 (brs, 1H), 2.90 (brs, 1H), 2.65 (d, 1H, *J* = 8.5 Hz), 2.54-2.58 (m, 1H), 1.55 (dt, 1H, *J* = 10.0, 1.5 Hz), 1.48 (d, 1H, *J* = 9.5 Hz). Diastereoselectivity (*endo-exo* ratio) was determined by ¹H NMR analysis of the crude mixture: δ 6.31 (dd, 1H, *J* = 3.0, 6.0 Hz, *endo*, major), 6.24 (dd, 1H, *J* = 3.0, 5.5 Hz, 1H, *exo*, minor). Enantioselectivity was determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 130 °C, 25 psi); retention times: 12.2 min (*endo*, minor), 13.3 min (*endo*, major). The absolute configuration was determined by optical rotation: [α]_D²³ +129.7 (*c* 0.52, CHCl₃, 98 % ee, pure *endo*).¹⁷

¹⁷ Takano, S.; Kurotaki, A.; Ogasawara, K. *Synthesis* **1987**, 1075.

(1R, 2R, 6R, 7S)-Tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one.¹⁸ Purification by column chromatography (5% Et₂O-pentane) afforded 98.2 mg (99%) of product as a colorless solid. The physical and spectral data were identical to those previously reported for this compound: ¹H NMR (400 MHz, CDCl₃) δ 6.18 (dd, 1H, *J* = 2.9, 5.9 Hz), 6.07 (dd, 1H, *J* = 2.9, 5.5 Hz), 3.15 (bs, 1H), 2.96 (bs, 1H), 2.92 (m, 1H), 2.81 (ddd, 1H, *J* = 1.1, 4.4, 9.2 Hz), 2.10 (m, 1H), 1.95 (m, 2H), 1.48 (m, 2H), 1.38 (d, 1H, *J* = 8.8 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 222.3, 136.1, 134.7, 54.2, 52.2, 47.4, 46.9, 41.1, 40.5, 22.6; FTIR (KBr) 3057, 2969, 2941, 2868, 1732; mp 94-96 °C (subl.); *R*_f 0.40 (Hex-EtOAc 4:1); [*α*]_D²³ +254 (*c* 0.51, CHCl₃, 92 % ee, pure *endo*). The *exo* isomer was separated: ¹H NMR (400 MHz, CDCl₃) δ 6.19 (dd, 1H, *J* = 2.9, 5.5 Hz), 6.15 (dd, 1H, *J* = 2.9, 5.9 Hz), 3.09 (bs, 1H), 2.75 (bs, 1H), 2.53 (m, 2H), 2.42 (m, 1H), 2.26 (m, 2H), 1.52 (m, 1H), 1.42 (app. dt, 1H, *J* = 1.5, 9.5 Hz), 1.27 (d, 1H, *J* = 9.5 Hz). Diastereoselectivity (*exo-endo* ratio) and enantioselectivity were determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 130 °C, 25 psi); retention times: 18.7 min (*endo*, major), 16.6 min (*endo*, minor), 14.1 min (*exo*). The absolute configuration was assigned by optical rotation.^{18a}

(1R, 2R, 7R, 8S)-Tricyclo[6.2.1.0^{2,7}]undec-9-en-3-one.¹⁸ Purification by column chromatography (gradient elution with 4-5% Et₂O-pentane) afforded 106 mg (98%) of product as a colorless oil. The physical and spectral data were identical to those previously reported for this compound: ¹H NMR (400 MHz, CDCl₃) δ 6.18 (dd, 1H, *J* = 2.9, 5.9 Hz), 6.01 (dd, 1H, *J* = 2.9, 5.9 Hz), 3.27 (bs, 1H), 2.88 (bs, 1H), 2.72 (dd, 1H, *J* = 3.7, 10.3 Hz), 2.67 (m, 1H), 2.32 (m, 1H),

¹⁸ (a) Takano, S.; Kamikubo, T.; Moriya, M.; Ogasawara, K. *Synthesis* **1994**, 601. (b) Ref. 7c.

1.94 (m, 2H), 1.74 (m, 2H), 1.45 (app. dt, 1H, $J = 1.8, 8.4$ Hz), 1.31 (d, 1H, $J = 8.4$ Hz), 0.77 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 215.3, 137.5, 134.8, 51.5, 48.2, 46.4, 45.1, 41.3, 39.3, 27.9, 21.7; FTIR (neat) 3064, 2962, 2942, 2866, 1706; R_f 0.21 (Hex-EtOAc 9:1); $[\alpha]_D^{23} +233$ (c 0.99, CHCl_3 , 95 % ee, pure *endo*). The *exo* isomer was: ^1H NMR (400 MHz, CDCl_3) δ 6.17 (dd, 1H, $J = 3.1, 5.7$ Hz), 6.09 (dd, 1H, $J = 3.1, 5.7$ Hz), 3.32 (bs, 1H), 2.61 (bs, 1H), 2.46 (m, 1H), 2.21 (ddd, 1H, $J = 7.7, 11.0, 18.3$ Hz), 1.99 (m, 4H), 1.75 (m, 1H), 1.29 (app. dt, 1H, $J = 1.8, 9.2$ Hz), 1.17 (d, 1H, $J = 9.2$ Hz), 0.93 (m, 1H). Diastereoselectivity (*exo-endo* ratio) and enantioselectivity were determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 130 °C, 25 psi); retention times: 20.0 min (*endo*, major), 19.4 min (*endo*, minor), 16.1 min (*exo*, major), 17.4 min (*exo*, minor). The absolute configuration was assigned by optical rotation.^{18a}

(1*R*, 2*R*, 8*R*, 9*S*)-Tricyclo[7.2.1.0^{2,8}]dodec-10-en-3-one.^{18b} Purification by column chromatography (5% Et_2O -pentane) afforded 111 mg (94%) of product as a colorless oil. The physical and spectral data were identical to those previously reported for this compound: ^1H NMR (400 MHz, CDCl_3) δ 6.35 (dd, 1H, $J = 2.9, 5.5$ Hz), 5.87 (dd, 1H, $J = 2.9, 5.9$ Hz), 3.14 (dd, 1H, $J = 3.3, 10.3$ Hz; CHCHCO , positive nOe with δ 2.41 (CHCHCO) and 1.28 (one of CHCH_2CH)), 2.95 (bs, 1H), 2.66 (bs, 1H), 2.41 (m, 2H), 2.17 (ddd, 1H, $J = 2.6, 10.6, 15.7$ Hz), 1.87 (m, 1H), 1.71 (m, 1H), 1.53 (m, 3H), 1.39 (app. dt, 1H, $J = 1.8, 8.4$ Hz), 1.28 (d, 1H, $J = 8.4$ Hz; one of CHCH_2CH , positive nOe with δ 3.14 (CHCHCO) and 2.41 (CHCHCO)), 0.71 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 213.5, 137.4, 132.2, 58.1, 48.4, 47.7, 44.7, 42.5, 41.4, 30.3, 27.1, 22.8; FTIR (neat) 2959, 2931, 2866, 1701; R_f 0.30 (Hex-EtOAc 9:1); $[\alpha]_D^{23} +10.7$ (c 0.96, CHCl_3 , 93 % ee, pure *endo*). The *exo* isomer was separated. Diastereoselectivity (*exo-endo* ratio) and enantioselectivity were determined by GC analysis using a J & W Scientific Cyclosil-

B column (30 m x 0.25 mm, 130 °C, 25 psi); retention times: 31.1 min (*endo*, major), 28.6 min (*endo*, minor), 24.2 min (*exo*, major), 24.8 min (*exo*, minor). The *endo* geometry assigned is consistent with nOe data (*vide supra*). The absolute configuration was assigned by analogy with (*1R, 2R, 6R, 7S*)-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one and (*1R, 2R, 7R, 8S*)-tricyclo[6.2.1.0^{2,7}]undec-9-en-3-one and optical rotation.^{18b}

(*1'R, 4'S, 4a'R, 8a'S*)-1',4',4a',8a'-Tetrahydro-7'-methylspiro{1,3-dioxolane-2,5'(8'*H*)-[1',4']methanonaphthalen-8'-one}. Purification by column chromatography (4:1:95 Et₂O-Et₃N-pentane) afforded 98.2 mg (80%) of product as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 6.07 (m, 1H), 6.03 (dd, 1H, *J* = 2.9, 5.6 Hz), 5.79 (dd, 1H, *J* = 2.9, 5.4 Hz), 4.08 (m, 1H), 3.98 (m, 3H), 3.28 (bs, 1H), 3.15 (bs, 1H), 3.03 (dd, 1H, *J* = 4.4, 8.8 Hz; CHCHCO, positive nOe with δ 1.30 (one of CHCH₂CH)), 2.80 (ddd, 1H, *J* = 1.2, 3.7, 8.8 Hz; CHCHCO, positive nOe with δ 1.30 (one of CHCH₂CH)), 1.68 (d, 3H, *J* = 1.5 Hz), 1.39 (app. dt, 1H, *J* = 1.7, 8.8 Hz), 1.30 (d, 1H, *J* = 8.8 Hz; one of CHCH₂CH, positive nOe with δ 3.03 (CHCHCO) and 2.80 (CHCHCO)); ¹³C NMR (125 MHz, CDCl₃) δ 200.4, 140.7, 139.7, 135.7, 133.1, 104.4, 65.4, 64.1, 50.3, 48.8, 47.5, 46.6, 46.2, 15.7; FTIR (neat) 3061, 2986, 2883, 1668; HRMS (EI) calcd for [C₁₄H₁₆O₃] ([M]⁺): 232.1100; found 232.1105; R_f 0.30 (Hex-EtOAc 9:1); [α]_D²³ +53.2 (*c* 0.77, CHCl₃, 92 % ee). Enantioselectivity were determined by GC analysis using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm, 160 °C, 25 psi); retention times: 31.5 min (*endo*, major), 30.4 min (*endo*, minor). The *endo* geometry assigned is consistent with nOe data (*vide supra*). The absolute configuration was assigned by analogy with (*1R, 2R, 6R, 7S*)-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one and (*1R, 2R, 7R, 8S*)-tricyclo[6.2.1.0^{2,7}]undec-9-en-3-one.

(1'R, 4'S, 4a'R, 8a'S)-1',4',4a',8a'-Tetrahydro-5,5,7'-trimethylspiro{1,3-dioxane-2,5'(8'H)-[1',4']methanonaphthalen-8'-one}. Purification by column chromatography (1:1:98 EtOAc-Et₃N-hexanes) afforded 140 mg (98%) of product as a colorless solid. ¹H NMR (400 MHz, CDCl₃) δ 6.54 (m, 1H), 5.90 (dd, 1H, *J* = 2.9, 5.5 Hz), 5.71 (dd, 1H, *J* = 2.9, 5.7 Hz), 3.67 (d, 1H, *J* = 11.4 Hz), 3.54 (dd, 1H, *J* = 1.1, 11.4 Hz), 3.50 (d, 1H, *J* = 11.4 Hz), 3.43 (dd, 1H, *J* = 1.1, 11.4 Hz), 3.22 (bs, 1H), 3.14 (bs, 1H), 3.06 (dd, 1H, *J* = 4.0, 8.4 Hz), 3.02 (ddd, 1H, *J* = 1.3, 3.1, 8.4 Hz), 1.70 (d, 3H, *J* = 1.1 Hz), 1.39 (app. dt, 1H, *J* = 1.7, 8.4 Hz), 1.34 (d, 1H, *J* = 8.4 Hz), 1.07 (s, 3H), 0.90 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 201.5, 139.8, 138.1, 135.7, 132.5, 95.0, 70.9, 70.2, 50.7, 49.1, 47.7, 45.6, 44.8, 29.9, 22.8, 22.3, 18.9; FTIR (neat) 3063, 2958, 2939, 2865, 1674; HRMS (EI) calcd for [C₁₇H₂₂O₃] ([M]⁺): 274.1569; found 274.1563; mp 103-104 °C; R_f 0.25 (Benzene-EtOAc 19:1); [α]_D²³ +35.2 (*c* 0.91, CHCl₃, 92 % ee). Enantioselectivity were determined by HPLC analysis using a Regis (*S,S*)-Whelk-O1 column (1% *i*-PrOH in hexanes for elution; 1 mL/min; λ 254 nm); retention times: 22.9 min (*endo*, major), 27.5 min (*endo*, minor). The *endo* geometry and absolute stereochemistry were assigned by analogy with (*1'R, 4'S, 4a'R, 8a'S*)-1',4',4a',8a'-tetrahydro-7'-methylspiro{1,3-dioxolane-2,5'(8'*H*)-[1',4']methanonaphthalen-8'-one}.

General Procedure for the Preparation of Crystalline BF₃ Complexes 5, 6 and 7: A 10-mL glass tube equipped with a stir bar was charged with methyl cinnamate (250 mg), and 1 mL of dichloromethane under an atmosphere of nitrogen. The clear solution was cooled to -20 °C and

boron trifluoride gas (Matheson) was introduced by bubbling using a needle. The corresponding BF_3 complex precipitated as a white solid. Upon warming to room temperature, the solid dissolved to afford a pale yellow solution. Dried hexanes (1 mL) was added slowly along the side of the glass tube via syringe and the resulting dichloromethane-hexanes bilayer was allowed to stand under an atmosphere of nitrogen for 16 h. The supernatant was removed and the crystals were carefully washed with dichloromethane (1 mL x 2) and dried *in vacuo* for 1 h to afford clear, colorless crystals suitable for X-ray structure determination.