

Triflimide Activation of a Chiral Oxazaborolidine Leads to a More General Catalytic System for Enantioselective Diels-Alder Addition

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Supporting Information

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). NMR spectra were recorded on Varian Innova-500, or Mercury-400 instruments and calibrated using residual undeuterated solvent as an internal reference. IR spectra were recorded on a Nicolet 5ZDX series or Avatar 360 FT-IR spectrometer. Low-resolution mass (CI) spectra were obtained by using a Platform II mass spectrometer. High-resolution mass spectral analyses were performed at the Harvard University Mass Spectrometry Center. Gas chromatography (GC) analyses were performed on Hewlett-Packard 6850 Series GC System equipped with flame ionization detector using a J & W Scientific Cyclosil-B column (30 m x 0.25 mm). Commercial grade reagents and solvents were used without further purification except as indicated below. Dichloromethane was distilled from phosphorus pentoxide. Toluene was distilled from sodium. Diethyl fumarate, 1,3-cyclohexadiene, 2,3-dimethyl-1,3-butadiene and isoprene were distilled from calcium hydride. 1,3-Cyclopentadiene was cracked at 170 °C and re-distilled (stored over 4A molecular sieves). 2,2,2-Trifluoroethyl cinnamate,¹ 2-trimethylsilylmethyl-1,3-butadiene,² 2-(triisopropylsilyloxy)-1,3-butadiene,³ 2,3-Dimethyl-[1,4]benzoquinone⁴ and 3-iodo-2,5-

¹ Fife, T. H.; Przystas, T. J.; Pujari, M. P. *J. Am. Chem. Soc.* **1988**, *110*, 8157.

² Sakurai, H.; Hosomi, A.; Saito, M.; Sasaki, K.; Iguchi, H.; Sasaki, J.-I.; Araki, Y. *Tetrahedron* **1983**, *39*, 883.

³ Corey, E. J.; Guzman-Perez, A.; Loh, T.-P. *J. Am. Chem. Soc.* **1994**, *116*, 3611.

⁴ Fischt, S.; Mulbaier, M.; Giannis, A. *Tetrahedron* **2001**, *57*, 4863.

dimethyl-[1,4]benzoquinone⁵ were prepared according to literature procedures. The dienes (stored over 4A molecular sieves) were stored at $-80\text{ }^{\circ}\text{C}$.

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,⁶ and functioning as a Soxhlet extractor) fitted on top with a reflux condenser and a nitrogen inlet adaptor was charged with (*S*)-(-)- α,α -diphenyl-2-pyrrolidinemethanol (82.0 mg, 0.324 mmol, from Acros), tri-*o*-tolylboroxine⁷ (38.0 mg, 0.107 mmol) and 25 mL of toluene. The resulting solution was heated to reflux (bath temperature $\sim 145\text{ }^{\circ}\text{C}$). After 3 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 or toluene and used in two Diels-Alder experiments.

To an aliquot of the oxazaborolidine precursor (0.160 mmol, theoretical) in 0 ~ 2.0 mL of CH_2Cl_2 or toluene at $-25\text{ }^{\circ}\text{C}$ was added trifluoromethanesulfonimide (0.20 M solution in CH_2Cl_2 or toluene, freshly prepared, 667 μL , 0.133 mmol) dropwise. After 10 min at $-25\text{ }^{\circ}\text{C}$, a colorless homogeneous catalyst solution was ready for use in the Diels-Alder reactions. As an example, a solution of 3-iodo-2,5-dimethyl-[1,4]benzoquinone (174 mg, 0.665 mmol) in CH_2Cl_2 (0.7 mL) and 2-(triisopropylsilyl)oxy-1,3-butadiene (194 μL , 166 mg, 0.733 mmol) were added successively at $-93\text{ }^{\circ}\text{C}$. The reaction mixture was stirred for 16 h at $-78\text{ }^{\circ}\text{C}$ and then quenched

⁵ Cressman, H. W. J.; Thirtle, J. R. *J. Org. Chem.* **1966**, *31*, 1279.

⁶ Molecular sieves (pellets) were dried *in vacuo* at ca. $200\text{ }^{\circ}\text{C}$ with a gas burner for 10 min prior to use.

⁷ Corey, E. J.; Shibata, T.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 3803.

by addition of 20 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 2-5% EtOAc-hexanes) to afford 322 mg (99%) of the Diels-Alder adduct (*vide infra*).⁸

The corresponding racemic products for the determination of enantioselectivity were prepared by using ethylaluminum dichloride (20 mol%) as a Lewis acid catalyst.

Determination of Diastereoselectivity, Enantioselectivity and Absolute Configuration of the Diels-Alder Adducts Reported in Tables 1-8

Table 1, entries 1 and 2 : 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) ; Vandewalle, M.; Eycken, J. V.; Oppolzer, W.; Vullioud, C. *Tetrahedron*. **1986**, *42*, 4035. Fujioka, H.; Nagatomi, Y.; Kotoku, N.; Kitagawa, H.; Kita, Y. *Tetrahedron*. **2000**, *56*, 10141.

Table 1, entries 3 and 4: Diastereoselectivity (*endo, exo* ratio) and enantioselectivity were determined by GC analysis (110 $^\circ\text{C}$, 25 psi); retention times: 99.0 min (*exo*, minor), 114.6 min (*exo*, major), 116.3 min (*endo*, major), 120.9 (*endo*, minor). The absolute configuration was determined by analogy with (+)-(*1R, 2R, 3S, 4R*)-3-methyl-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester.

⁸ After elution of the Diels-Alder adduct, the ligand-containing fractions were eluted with 20% MeOH- CH_2Cl_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).

Table 2, entry 1 : Enantioselectivity was determined by GC analysis (110 °C, 25 psi); retention times: 68.3 min (*endo*, minor), 69.9 min (*endo*, major). The absolute configuration was determined by optical rotation: $[\alpha]_{\text{D}}^{23} +106$ (*c* 1.0, CHCl₃, >99 % ee) ; 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.

Table 2, entry 2 : Enantioselectivity was determined by reduction with LiAlH₄ to the corresponding diol, conversion to the (*R*)-MTPA ester derivative and ¹H NMR integration (500 MHz, CDCl₃): δ 4.36 (dd, 2H, *J* = 11.0, 5.0 Hz, minor), 4.25 (d, 4H, *J* = 4.5 Hz, major), 4.20 (dd, 2H, *J* = 11.0, 6.5 Hz, minor). The absolute configuration was determined by reduction with LiAlH₄ to the corresponding diol and measurement of optical rotation: $[\alpha]_{\text{D}}^{23} +69.4$ (*c* 0.5, CHCl₃, 93% ee) ; Heathcock, C. H.; Davis, B. R.; Hadley, C. R. *J. Med. Chem.* **1989**, 32, 197.

Table 2, entry 3 : Enantioselectivity was determined by GC analysis (120 °C, 25 psi); retention times: 68.0 min (minor), 69.3 min (major). The absolute configuration was determined by reduction with LiAlH₄ to the corresponding diol and measurement of optical rotation: $[\alpha]_{\text{D}}^{23} -92.5$ (*c* 0.89, CHCl₃, 98% ee); 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.

Table 2, entry 4 : Enantioselectivity was determined by GC analysis (120 °C, 25 psi); retention times: 76.6 min (minor), 77.9 min (major). The absolute configuration was determined by analogy with (+)-(*1S*, *2S*)-Cyclohex-4-ene-1,2-dicarboxylic acid diethyl ester.

Table 3, entry 1 : Diastereoselectivity (*endo-exo* ratio) and enantioselectivity were determined by GC analysis (100 °C, 25 psi); retention times: 5.5 min (*exo*) 6.4 (*endo*, major), 7.1 min (*endo*, minor). The absolute configuration was determined by reduction with LiAlH₄ to the corresponding alcohol and measurement of optical rotation: $[\alpha]_{\text{D}}^{23} +80.9$ (*c* 1.0, 95% EtOH, >99% ee); Kitagawa, O.; Izawa, H.; Sato, K.; Dobashi, A.; Taguchi, T. *J. Org. Chem.* **1998**, 63, 2634.

Table 3, entry 2 : Enantioselectivity was determined by GC analysis (90 °C, 25 psi); retention times: 25.0 (major), 26.0 min (minor). The absolute configuration was determined by reduction

with LiAlH_4 to the corresponding alcohol and measurement of optical rotation: $[\alpha]_{\text{D}}^{23} +10.7$ (c 1.0, 95% EtOH, 98% ee); Kitagawa, O.; Izawa, H.; Sato, K.; Dobashi, A.; Taguchi, T. *J. Org. Chem.* **1998**, *63*, 2634.

Table 3, entry 3: Enantioselectivity was determined by GC analysis (90 °C, 25 psi); retention times: 20.8 min (major), 21.9 min (minor). The absolute configuration was determined by analogy with (+)-(1*R*)-4-Methyl-cyclohex-3-enecarboxylic acid 2,2,2-trifluoro-ethyl ester.

Table 3, entry 4: Enantioselectivity was determined by GC analysis (75 °C, 25 psi); retention times: 25.7 min (minor), 26.4 min (major). The absolute configuration was determined by conversion to (R)-(+)-terpineol and measurement of optical rotation: $[\alpha]_{\text{D}}^{23} +102.6$ (c 1.0, EtOH, 98 % ee) ; Fuller, A. T.; Kenyon, J. *J. Chem. Soc. Chem. Comm.* **1924**, *125*, 2311. Evans, D. A.; Chapman, K.T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238.

Table 3, entry 5: Enantioselectivity was determined by GC analysis (65 °C, 25 psi); retention times: 22.7 min (minor), 23.4 min (major). The absolute configuration was determined by analogy (+)-(1*R*)-4-Methyl-cyclohex-3-enecarboxylic acid 2,2,2-trifluoro-ethyl ester.

Table 4, entry 1: Enantioselectivity was determined by GC analysis (140 °C, 25 psi); retention times: 15.1 min (minor), 15.7 min (major). The absolute configuration was determined by analogy with (+)-(1*R*, 2*R*, 7*R*, 8*S*)-tricyclo[6.2.1.0^{2,7}]undec-9-en-3-one; Ryu, D. H.; Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 9992.

Table 4, entry 2: Enantioselectivity was determined by GC analysis (140 °C, 25 psi); retention times: 9.64 min (minor), 10.17 min (major). The absolute configuration was determined by analogy with (+)-(1*R*, 2*R*, 6*R*, 7*S*)-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one; Ryu, D. H.; Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 9992.

Table 4, entry 3: Enantioselectivity was determined by GC analysis (150 °C, 25 psi); retention times: 14.78 min (minor), 15.18 min (major). The absolute configuration was determined by analogy with (+)-(1*R*, 2*R*, 8*R*, 9*S*)-tricyclo[7.2.1.0^{2,8}]dodec-10-en-3-one; Ryu, D. H.; Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 9992.

Table 4, entry 4: Enantioselectivity was determined by reduction with LiAlH_4 to the corresponding alcohol (~1:1 diastereomer mixture), conversion to the (*R*)-MTPA ester derivative and ^1H NMR integration (500 MHz, CDCl_3): δ 0.81 (t, 3H, $J = 7.5$ Hz, minor), 0.78 (t, 3H, $J = 7.5$ Hz major). The absolute configuration was determined by analogy with (+)-1-[(*1R*, 2*R*, 4*R*)-bicyclo[2.2.1]hept-5-en-2-yl]-propan-1-one; Ryu, D. H.; Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 9992.

Table 5, entry 1: Enantioselectivity was determined by HPLC analysis using a Regis (*S*, *S*)-Whelk-O1 column (1% *i*-PrOH in hexanes for elution; 0.6 mL/min; λ 254 nm); retention times: 29.7 min (major), 34.9 min (minor). The absolute configuration was determined by analogy with (+)-(*1S*, 2*R*, 7*S*, 8*R*)-2,5-dimethyl-tricyclo[6.2.2.0^{2,7}]dodeca-4,9-diene-3,6-dione.

Table 5, entry 2: Enantioselectivity was determined by GC analysis (140 °C, 25 psi); retention times: 23.2 (major), 23.7 min (minor). The absolute configuration was determined by analogy with (+)-(*1S*, 2*R*, 7*S*, 8*R*)-2,5-dimethyl-tricyclo[6.2.2.0^{2,7}]dodeca-4,9-diene-3,6-dione.

Table 5, entry 3: Enantioselectivity was determined by GC analysis (140 °C, 25 psi); retention times: 29.3 (major), 30.1 min (minor). The absolute configuration was assigned by comparison with an authentic sample prepared from (+)-(*1S*, 2*R*, 7*S*, 8*S*)-4-iodo-2,5-dimethyl-tricyclo[6.2.2.0^{2,7}]dodeca-4,9-diene-3,6-dione (*vide infra*; $n\text{Bu}_3\text{SnH}$ reduction) and GC analysis.

Table 5, entry 4: Enantioselectivity was determined by GC analysis (135 °C, 25 psi); retention times: 17.3 (major), 17.9 min (minor). The absolute configuration was determined by analogy with (+)-(*1S*, 2*R*, 7*S*, 8*R*)-2,5-dimethyl-tricyclo[6.2.2.0^{2,7}]dodeca-4,9-diene-3,6-dione.

Table 6, entry 1: Enantioselectivity was determined by GC analysis (130 °C, 25 psi); retention times: 51.4 (major), 52.8 min (minor). The absolute configuration was assigned by selective Luche reduction^{9,10}, NBS bromination¹⁰ and X-ray crystallographic analysis of (*4S*, 4*aS*, 6*S*, 7*S*, 8*aR*)-6-bromo-4,7-dihydroxy-2,3,7-trimethyl-4*a*,5,6,7,8,8*a*-hexahydro-4*H*-naphthalen-1-one (*vide infra*).

⁹ Breuning, M.; Corey, E. J. *Org. Lett.* **2001**, *3*, 1559.

¹⁰ White, J. D.; Choi, Y. *Org. Lett.* **2000**, *2*, 2373.

Table 6, entry 2: Enantioselectivity was determined by S_E2' protonation-desilylation with $BF_3 \cdot CH_3COOH$ ¹¹ to the corresponding methylene cyclohexane derivative and GC analysis (130 °C, 25 psi); retention times: 45.0 (major), 45.7 min (minor). The absolute configuration was determined by analogy with (+)-(4*aR*, 8*aS*)-2,3,6-trimethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone.

Table 6, entry 3: Enantioselectivity was determined by desilylation (*vide infra*) with 10% HF to the corresponding ketone and GC analysis (155 °C, 25 psi); retention times: 58.4 (major), 59.7 min (minor). The absolute configuration was determined by analogy with (+)-(4*aR*, 8*aS*)-2,3,6-trimethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone.

Table 7, entry 1: Enantioselectivity was determined by GC analysis (110 °C, 25 psi); retention times: 65.9 (major, 6-methyl isomer), 67.0 min (minor, 6-methyl isomer), 72.1 (major, 7-methyl isomer), 76.3 min (minor, 7-methyl isomer). The absolute configuration of 6-isomer was assigned by comparison with an authentic sample prepared from (-)-(4*aR*, 8*aS*)-3-iodo-2,4*a*,6-trimethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone (*vide infra*; *n*Bu₃SnH reduction) and GC analysis. The absolute configuration of 7-isomer was determined by analogy with the 6-isomer.

Table 7, entry 2: Enantioselectivity was determined by GC analysis (135 °C, 25 psi); retention times: 77.1 (minor, 7-isomer), 79.3 min (major, 7-isomer), 82.9 (major, 6-isomer), 83.6 min (minor, 6-isomer). The absolute configurations of each isomers were determined by analogy with (4*aR*, 8*aS*)-2,4*a*,6-trimethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone and (4*aR*, 8*aS*)-2,4*a*,7-trimethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone.

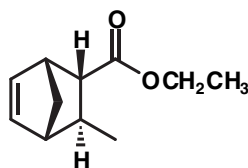
Table 8, entry 1: Diastereoselectivity (6-methyl, 7-methyl ratio) and enantioselectivity were determined by reduction with *n*Bu₃SnH to the corresponding quinone adduct (*vide supra*) and GC analysis. The absolute configuration was determined by analogy with (-)-(4*aR*, 8*aS*)-3-iodo-2,4*a*-dimethyl-6-(triisopropyl-silyloxy)-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone.

¹¹ Corey, E. J.; Letavic, M. A. *J. Am. Chem. Soc.* **1995**, *117*, 9616.

Table 8, entry 2: Enantioselectivity was determined by subsequent desilylation with 10% HF, reduction with $n\text{Bu}_3\text{SnH}$ to the ketone compound and GC analysis (120 °C, 25 psi); retention times: 169.4 (major), 172.5 min (minor). The absolute configuration was assigned by X-ray crystallographic analysis of (*4aR*, *8aS*) -3 -Iodo -2, 4a -dimethyl -4a, 7, 8, 8a -tetrahydro- 5*H* -naphthalene -1, 4, 6-trione.

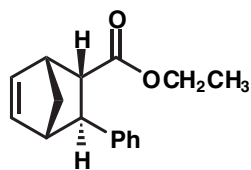
Table 8, entry 3: Enantioselectivity was determined by reduction with $n\text{Bu}_3\text{SnH}$ to the corresponding quinone adduct (*vide supra*) and GC analysis. The absolute configuration was assigned by X-ray crystallographic analysis.

Experimental Procedures and Physical Data of the Diels-Alder Products:¹²

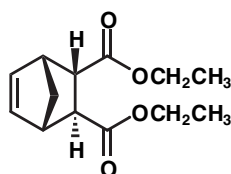


(*1R*, *2R*, *3S*, *4R*)-3-methyl-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester^{12a} (Table 1, entries 1 and 2). Purification by column chromatography (gradient elution with 2-20% Et₂O-pentane) afforded 170 mg (94%) of product as a colorless oil. The physical and spectral data were identical to those previously reported for this compound.

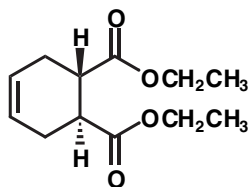
¹² The physical and spectral data of Diels-Alder adducts and several racemic adducts are known. For (*1R*, *2R*, *3S*, *4R*)-3-methyl-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid ethyl ester and (*1R*, *2S*, *3S*, *4S*)-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid diethyl ester, see (a) Ryu, D. H.; Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 9992. For cyclohex-4-ene-1,2-dicarboxylic acid diethyl ester, see (b) Mundy, B. P.; Theodore, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 2005. For 6,7-dimethyl-3,4,4a,5,8,8a-hexahydro-2*H*-naphthalen-1-one, see (c) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1993**, *58*, 7216. For 2,5-dimethyl-tricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione, see (d) Mehta, G.; Srikrishna, A.; Reddy, A. V.; Nair, M. S. *Tetrahedron* **1981**, *37*, 4543. For 2,4a,6,7-tetramethyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone, see (e) Liu, C.; Burnell, D. J. *J. Org. Chem.* **1997**, *62*, 3683. For 2,3,6-trimethyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone, see (f) Rodriguez, J.-G.; Pablo, A. D.; Smith-Verdier, P. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3957.



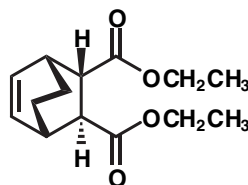
(1R, 2S, 3S, 4S)-3-Phenyl-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid 2,2,2-trifluoro-ethyl ester (Table 1, entries 3 and 4). After the reaction mixture was treated with 20 mL of acetone, cyclopentadiene polymer was removed by filtration through filter paper. The filtrate was concentrated *in vacuo* and the residue was purified by silica gel chromatography (gradient elution with 1-3% Et₂O-pentane) to afford 156 mg (79%) of the product as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.32 (m, 5H), 6.46 (dd, 1H, *J* = 5.6, 2.8 Hz), 6.11 (dd, 1H, *J* = 6.0, 2.8 Hz), 4.55 (dq, 1H, *J* = 12.8, 8.4 Hz), 4.39 (dq, 1H, *J* = 12.8, 8.4 Hz), 3.35 (s, 1H), 3.13 (dd, 1H, *J* = 5.2, 2.0 Hz), 3.08-3.10 (m, 2H), 1.83 (d, 1H, *J* = 9.2 Hz), 1.63 (ddd, 1H, *J* = 8.8, 3.6, 2.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 172.7, 143.6, 139.6, 134.1, 128.5, 127.4, 126.2, 123.0 (q, 1C, *J* = 276 Hz), 60.2 (q, 1C, *J* = 36.4 Hz), 51.8, 48.3, 47.5, 47.3, 46.4; ¹⁹F NMR (282MHz, CDCl₃) δ -74.2 (t, *J* = 8.3 Hz); FTIR (neat) 2975, 1751, 1281, 1149; LRMS (CI) calcd for [C₁₆H₁₆F₃O₂] ([MH]⁺): 297; found 297.



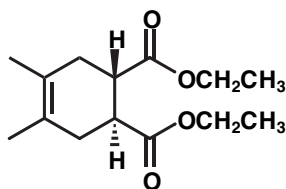
(1R, 2S, 3S, 4S)-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid diethyl ester^{12a} (Table 2, entry 1). Purification by column chromatography (gradient elution with 4-15% Et₂O-pentane) afforded 157 mg (99%) of product as a colorless oil. The physical and spectral data were identical to those previously reported for this compound.



(1S, 2S)-Cyclohex-4-ene-1,2-dicarboxylic acid diethyl ester^{12b} (Table 2, entry 2). Purification by column chromatography (gradient elution with 2-15% Et₂O-pentane) afforded 138 mg (92%) of product as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 5.66-5.67 (m, 2H), 4.13 (q, 2H, *J* = 7.2 Hz), 4.12 (q, 2H, *J* = 7.2 Hz), 2.78-2.86 (m, 2H), 2.36-2.45 (m, 2H), 2.11-2.20 (m, 2H), 1.23 (t, 6H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 174.8 (x2), 124.9 (x2), 60.5 (x2), 41.2 (x2), 27.9 (x2), 14.1(x2); FTIR (neat) 2980, 2936, 1731, 1179, 1150; LRMS (CI) calcd for [C₁₂H₁₉O₄] ([MH]⁺): 227; found 227; [α]_D²³ +113.0 (*c* 1.0, CHCl₃, 93 % ee).

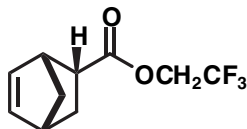


(1R, 2S, 3S, 4S)-Bicyclo[2.2.2]oct-5-ene-2,3-dicarboxylic acid diethyl ester (Table 2, entry 3). Purification by column chromatography (gradient elution with 2-15% Et₂O-pentane) afforded 151mg (90%) of product as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 6.33 (dd, 1H, *J* = 7.5, 7.5 Hz), 6.15 (dd, 1H, *J* = 7.5, 7.5 Hz), 4.11-4.17 (m, 2H), 4.06 (q, 2H, *J* = 8.0 Hz), 3.11 (dd, 1H, *J* = 6.0, 2.5 Hz), 2.98-3.01 (m, 1H), 2.90-2.93 (m, 1H), 2.84-2.86 (m, 1H), 1.58-1.64 (m, 1H), 1.43-1.49 (m, 1H), 1.25-1.30 (m, 1H), 1.24 (t, 3H, *J* = 7.0 Hz), 1.19 (t, 3H, *J* = 7.0 Hz), 1.06-1.13 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 174.1, 173.8, 134.5, 132.3, 60.7, 60.5, 45.8, 45.1, 32.5, 32.4, 24.4, 20.2, 14.2, 14.1; FTIR (neat) 2978, 2953, 1724, 1183, 1037; HRMS (CI) calcd for [C₁₂H₂₄NO₄] ([MNH₄]⁺): 270.1706; found 270.1714; [α]_D²³ +51.6 (*c* 1.0, CHCl₃, 98 % ee).



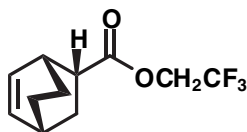
(1S, 2S)-4,5-Dimethyl-cyclohex-4-ene-1,2-dicarboxylic acid diethyl ester (Table 2, entry 4).

Purification by column chromatography (gradient elution with 2-10% Et₂O-pentane) afforded 169 mg (99%) of product as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 4.08-4.17 (m, 4H), 2.76-2.82 (m, 2H), 2.25 (d, 2H, *J* = 16.5 Hz), 2.09-2.15 (m, 2H), 1.61 (s, 6H), 1.24 (t, 6H, *J* = 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 174.9 (x2), 123.9 (x2), 60.4 (x2), 42.1 (x2), 34.2 (x2), 18.6 (x2), 14.1 (x2); FTIR (neat) 2981, 2913, 1730, 1180, 1153; LRMS (CI) calcd for [C₁₄H₂₃O₄] ([MH]⁺): 255; found 225; [α]_D²³ +137.5 (*c* 1.0, CHCl₃, 98 % ee).



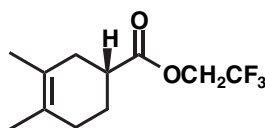
(1R, 2R, 4R)-Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid 2,2,2-trifluoro-ethyl ester (Table 3,

entry 1). Purification by column chromatography (gradient elution with 2-5% Et₂O-pentane) afforded 142 mg (97%) of product as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 6.22 (dd, 1H, *J* = 5.6, 3.2 Hz), 5.92 (dd, 1H, *J* = 5.6, 2.8 Hz), 4.49 (dq, 1H, *J* = 12.8, 8.4 Hz), 4.35 (dq, 1H, *J* = 12.8, 8.4 Hz), 3.26 (s, 1H), 3.04 (dt, 1H, *J* = 4.0, 9.2 Hz), 2.94 (s, 1H), 1.95 (ddd, 1H, *J* = 11.6, 9.2, 3.6 Hz), 1.42-1.48 (m, 2H), 1.30 (d, 1H, *J* = 8.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 138.1, 132.0, 123.0 (q, 1C, *J* = 276 Hz), 60.0 (q, 1C, *J* = 36.4 Hz), 49.6, 45.8, 42.9, 42.5, 29.2; ¹⁹F NMR (282MHz, CDCl₃) δ -74.3 (t, *J* = 8.5 Hz); FTIR (neat) 2977, 1755, 1281, 1148; LRMS (CI) calcd for [C₁₀H₁₁F₃O₂] ([M]⁺): 220; found 220; [α]_D²³ +90.3 (*c* 1.0, CHCl₃, >99 % ee).¹³

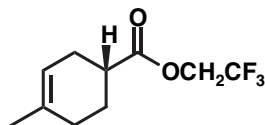


¹³ The Diels-Alder adduct contains 2% of *exo* isomer.

(1*R*, 2*R*, 4*R*)-Bicyclo[2.2.2]oct-5-ene-2-carboxylic acid 2,2,2-trifluoro-ethyl ester (Table 3, entry 2). Purification by column chromatography (gradient elution with 2-5% Et₂O-pentane) afforded 126 mg (81%) of product as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 6.33 (dd, 1H, *J* = 7.6, 7.6 Hz), 6.13 (dd, 1H, *J* = 7.6, 7.6 Hz), 4.80 (dq, 1H, *J* = 12.8, 8.4 Hz), 4.37 (dq, 1H, *J* = 12.8, 8.4 Hz), 2.94-2.98 (m, 1H), 2.73 (ddd, 1H, *J* = 9.8, 5.2, 2.4 Hz), 2.61-2.64 (m, 1H), 1.78 (ddd, 1H, *J* = 12.2, 6.0, 2.4 Hz), 1.68 (ddt, 1H, *J* = 13.2, 5.2, 3.2 Hz), 1.56-1.63 (m, 1H), 1.49 (tt, 1H, *J* = 10.8, 2.4 Hz), 1.32 (tt, 1H, *J* = 11.8, 3.6 Hz), 1.20-1.28 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 174.1, 135.8, 131.1, 123.3 (q, 1C, *J* = 276 Hz), 60.4 (q, 1C, *J* = 36.4 Hz), 42.7, 32.6, 29.7, 29.4, 25.4, 24.5; ¹⁹F NMR (282MHz, CDCl₃) δ -74.3 (t, *J* = 8.3 Hz); FTIR (neat) 2946, 2869, 1755, 1279, 1148; LRMS (CI) calcd for [C₁₁H₁₄F₃O₂] ([MH]⁺): 235; found 235; [α]_D²³ +32.0 (c 1.0, CHCl₃, 98 % ee).

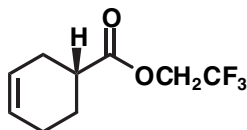


(1*R*)-3,4- Dimethyl-cyclohex-3-enecarboxylic acid 2,2,2-trifluoro-ethyl ester (Table 3, entry 3). Purification by column chromatography (gradient elution with 2-4% Et₂O-pentane) afforded 154 mg (98%) of product as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 4.43-4.52 (m, 2H), 2.60-2.68 (m, 1H), 2.19-2.27 (m, 1H), 2.08-2.17 (m, 1H), 1.95-2.06 (m, 3H), 1.65-1.73 (m, 1H), 1.62 (s, 3H) 1.60 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 174.3, 125.4, 123.5, 123.0 (q, 1C, *J* = 276 Hz), 60.1 (q, 1C, *J* = 36.1 Hz), 39.8, 33.3, 30.6, 25.6, 18.9, 18.8; ¹⁹F NMR (282MHz, CDCl₃) δ -74.3 (t, *J* = 8.3 Hz); FTIR (neat) 2930, 1756, 1284, 1167; LRMS (CI) calcd for [C₁₁H₁₆F₃O₂] ([MH]⁺): 237; found 237; [α]_D²³ +67.1 (c 1.0, CHCl₃, 98 % ee).



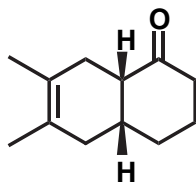
(1R)-4-Methyl-cyclohex-3-enecarboxylic acid 2,2,2-trifluoro-ethyl ester (Table 3, entry 4).

Purification by column chromatography (gradient elution with 2-4% Et₂O-pentane) afforded 146 mg (99%) of product as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 5.37-5.38 (m, 1H), 4.43-4.52 (m, 2H), 2.58-2.64 (m, 1H), 2.23-2.29 (m, 2H), 1.98-2.07 (m, 3H), 1.70-1.79 (m, 1H), 1.65 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 174.3, 133.8, 123.1 (q, 1C, *J* = 276 Hz), 118.7, 60.1 (q, 1C, *J* = 36.1 Hz), 38.8, 29.0, 27.4, 25.2, 23.4; ¹⁹F NMR (282MHz, CDCl₃) δ -74.3 (t, *J* = 8.5 Hz); FTIR (neat) 2933, 1760, 1280, 1168; LRMS (CI) calcd for [C₁₀H₁₅F₃O₃] ([MH₂O]⁺): 240; found 240; [α]_D²³ +67.9 (c 1.0, CHCl₃, 98 % ee).



(1R)-Cyclohex-3-enecarboxylic acid 2,2,2-trifluoro-ethyl ester (Table 3, entry 5).

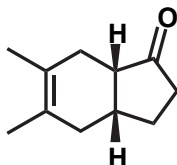
Purification by column chromatography (gradient elution with 1-3% Et₂O-pentane) afforded 133 mg (96%) of product as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 5.65-5.71 (m, 2H), 4.42-4.54 (m, 2H), 2.65-2.71 (m, 1H), 2.27-2.30 (m, 2H), 2.07-2.12 (m, 1H), 2.02-2.05 (m, 1H), 1.68-1.76 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 174.1, 126.7, 124.7, 123.0 (q, 1C, *J* = 276 Hz), 60.1 (q, 1C, *J* = 36.6 Hz), 38.8, 27.1, 24.8, 24.1; ¹⁹F NMR (282MHz, CDCl₃) δ -74.4 (t, *J* = 8.5 Hz); FTIR (neat) 2927, 1753, 1277, 1147; LRMS (CI) calcd for [C₉H₁₂F₃O₂] ([MH]⁺): 209; found 209; [α]_D²³ +53.3 (c 1.0, CHCl₃, 95 % ee).



(4aR, 8aS)-6,7-Dimethyl-3,4,4a,5,8,8a-hexahydro-2H-naphthalen-1-one^{12c} (Table 4, entry 1).

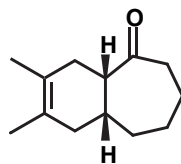
Purification by column chromatography (gradient elution with 2-10% Et₂O-pentane) afforded

114 mg (96%) 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 2.66 (dd, 1H, J = 11.0, 6.0 Hz), 2.39 (dt, 1H, J = 14.0, 6.5 Hz), 2.22-2.36 (m, 3H), 1.94-2.02 (m, 1H), 1.68-1.91 (m, 6H), 1.61 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 213.0, 123.4, 122.7, 49.1, 39.7, 36.4, 33.8, 30.0, 28.2, 24.0, 19.1, 18.7.



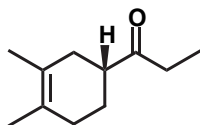
(3aR, 7aS)-5,6-Dimethyl-2,3,3a,4,7,7a-hexahydro-inden-1-one (Table 4, entry 2).

Purification by column chromatography (gradient elution with 2-10% Et_2O -pentane) afforded 102.0 mg (94%) of product as a colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 2.41-2.47 (m, 1H), 2.28-2.31 (m, 1H), 2.22-2.24 (m, 1H), 2.14-2.22 (m, 2H), 2.01-2.08 (m, 1H), 1.92-1.99 (m, 2H), 1.05 (ddd, 1H, J = 16.8, 8.5, 4.5 Hz), 1.58-1.69 (m, 1H), 1.58 (s, 3H), 1.55 (d, 3H, J = 1.0 Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 219.8, 123.9, 123.3, 47.6, 34.1, 32.8, 32.6, 27.7, 26.2, 19.3, 18.7; FTIR (neat) 2912, 2878, 2831, 1738, 1128; LRMS (CI) calcd for $[\text{C}_{11}\text{H}_{17}\text{O}]$ ($[\text{MH}]^+$): 165; found 165.

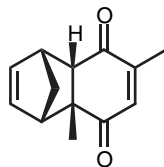


(4aS, 9aR)-2,3-Dimethyl-1,4,4a,6,7,8,9,9a-octahydro-benzocyclohepten-5-one (Table 4,

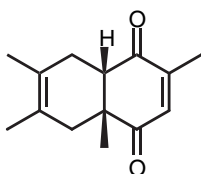
entry 3). Purification by column chromatography (gradient elution with 2-10% Et_2O -pentane) afforded 86.0 mg (67%) of product as a colorless oil: ^1H NMR (500 MHz, CDCl_3) δ 2.61-2.67 (m, 2H), 2.41 (ddd, 1H, J = 14.3, 8.0, 3.0 Hz), 2.20-2.26 (m, 1H), 2.12-2.17 (m, 3H), 1.65-1.82 (m, 4H), 1.60 (s, 3H), 1.55-1.60 (m, 3H), 1.57 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 215.8, 123.7 (x2), 50.4, 43.7, 38.9, 34.4, 32.8, 31.8, 28.0, 24.3, 19.1, 18.6; FTIR (neat) 2917, 2857, 1695, 1447; LRMS (CI) calcd for $[\text{C}_{13}\text{H}_{21}\text{O}]$ ($[\text{MH}]^+$): 193; found 193.



1-((1*R*)-3,4-Dimethyl-cyclohex-3-enyl)-propan-1-one (Table 4, entry 4). Purification by column chromatography (gradient elution with 2-10% Et₂O-pentane) afforded 95.0 mg (87%) of product as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 2.52-2.60 (m, 1H), 2.48 (dq, 2H, *J* = 7.2, 7.2 Hz), 2.08-2.16 (m, 1H), 1.93-2.01 (m, 3H), 1.84-1.91 (m, 1H), 1.61 (s, 3H), 1.59 (s, 3H), 1.46-1.57 (m, 1H), 1.04 (t, 3H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 214.5, 125.3, 124.1, 47.3, 33.8, 33.3, 31.3, 25.5, 19.0, 18.8, 7.8; FTIR (neat) 2976, 2906, 2833, 1708, 1452, 1115; LRMS (CI) calcd for [C₁₁H₁₉O] ([MH]⁺): 167; found 167.

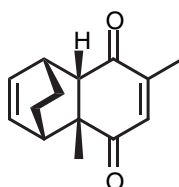


(1*R*, 2*R*, 7*S*, 8*R*)-2,5-Dimethyl-tricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione^{12d} (Table 5, entry 1). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes) afforded 133 mg (99%) of product as a pale yellow solid: ¹H NMR (500 MHz, CDCl₃) δ 6.37 (d, 1H, *J* = 1.5 Hz), 6.03 (dd, 1H, *J* = 5.5, 3.0 Hz), 5.88 (dd, 1H, *J* = 5.5, 3.0 Hz), 3.33 (s, 1H), 2.98 (s, 1H), 2.75 (d, 1H, *J* = 4.0 Hz), 1.85 (d, 3H, *J* = 1.5 Hz), 1.60 (d, 1H, *J* = 9.5 Hz), 1.44 (d, 1H, *J* = 9.0 Hz), 1.37 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 202.6, 200.0, 150.8, 139.1, 138.0, 134.2, 56.8, 53.4, 53.0, 49.1, 46.2, 26.2, 16.0; FTIR (neat) 2981, 1663, 1247; LRMS (CI) calcd for [C₁₃H₁₅O₂] ([MH]⁺): 203; found 203; [α]_D²³ +11.1 (*c* 1.0, CHCl₃, >99% ee).

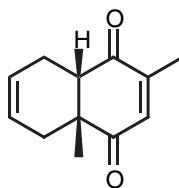


(4*aR*, 8*aS*)- 2,4*a*,6,7-Tetramethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone^{12e} (Table 5, entry 2). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes)

afforded 144 mg (99%) of product as a pale yellow solid, which was crystallized from pentane: mp 32-33 °C; ¹H NMR (500 MHz, CDCl₃) δ 6.39-6.40 (m, 1H), 2.77 (t, 1H, *J* = 6.0 Hz), 2.42-2.47 (m, 1H), 2.33 (d, 1H, *J* = 17.0 Hz), 1.99-2.04 (m, 1H), 1.92 (d, 3H, *J* = 1.0 Hz), 1.61 (d, 1H, *J* = 18.0 Hz), 1.57 (s, 3H), 1.51 (s, 3H), 1.20 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 202.5, 200.3, 148.1, 134.8 (x2), 122.5, 52.6, 48.4, 38.7, 29.3, 22.6, 18.8, 18.5, 16.0; FTIR (neat) 2915, 1674, 1374, 1218; HRMS (EI) calcd for [C₁₄H₁₈O₂] ([M]⁺): 218.1307; found 218.1308; [α]_D²³ -110.4 (*c* 1.0, CHCl₃, >99% ee).

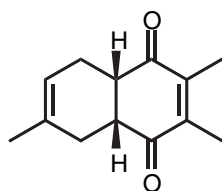


(1*S*, 2*R*, 7*S*, 8*R*)-2,5-Dimethyl-tricyclo[6.2.2.0^{2,7}]dodeca-4,9-diene-3,6-dione (Table 5, entry 3). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes) afforded 142 mg (99%) of product as a pale yellow solid, which was crystallized from hexanes: mp 71-72 °C; ¹H NMR (500 MHz, CDCl₃) δ 6.42 (d, 1H, *J* = 1.0 Hz), 6.19 (dd, 1H, *J* = 7.0, 7.0 Hz), 6.01 (dd, 1H, *J* = 7.0, 7.0 Hz), 2.92-2.93 (m, 1H), 2.80-2.82 (m, 1H), 2.42 (d, 1H, *J* = 1.5 Hz), 1.85 (d, 3H, *J* = 1.5 Hz), 1.75-1.81 (m, 1H), 1.62-1.68 (m, 1H), 1.26 (tt, 1H, *J* = 12.0, 3.5 Hz), 1.24 (s, 3H), 1.11 (tt, 1H, *J* = 13.0, 3.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 202.5, 200.1, 150.0, 138.9, 136.2, 131.7, 58.0, 50.8, 38.9, 36.9, 26.1, 25.8, 18.6, 16.1; FTIR (neat) 2953, 2869, 1660, 1215; HRMS (EI) calcd for [C₁₄H₁₆O₂] ([M]⁺): 216.1150; found 216.1148; [α]_D²³ +15.1 (*c* 1.0, CHCl₃, >99% ee).



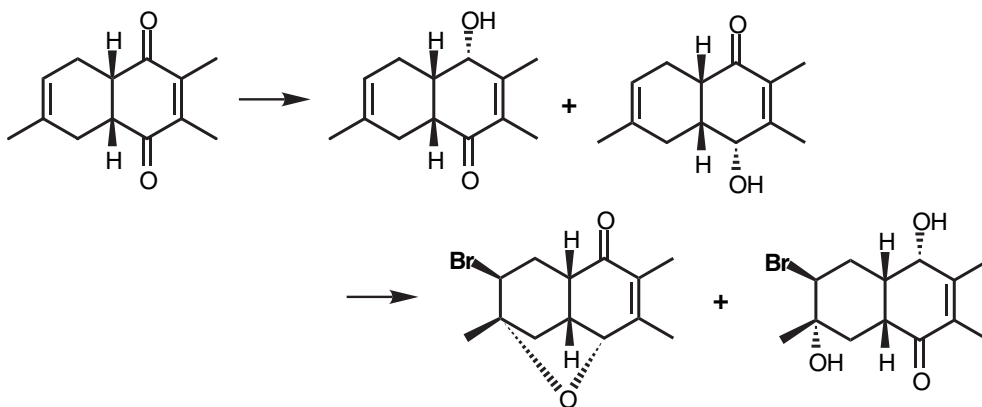
(4*aR*, 8*aS*)- 2,4*a*-Dimethyl-4*a*,5,8,8*a*-tetrahydro-[1,4]naphthoquinone (Table 5, entry 4). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes) afforded

123 mg (97%) of product as a pale yellow oil: ^1H NMR (500 MHz, CDCl_3) δ 6.40 (q, 1H, $J = 1.5$ Hz), 5.62 (dddd, 1H, $J = 10.0, 7.0, 2.5, 2.5$ Hz), 5.51-5.56 (m, 1H), 2.77 (t, 1H, $J = 5.0$ Hz), 2.59 (dddd, 1H, $J = 16.0, 8.0, 4.0, 2.0$ Hz), 2.37 (dddd, 1H, $J = 18.5, 5.0, 2.5, 2.5$ Hz), 2.09 (dddd, 1H, $J = 18.0, 9.0, 6.0, 3.0$ Hz), 1.92 (d, 3H, $J = 2.0$ Hz), 1.70-1.75 (m, 1H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.3, 200.0, 148.3, 134.7, 124.0, 123.6, 51.6, 47.7, 32.4, 22.6, 22.1, 16.0; FTIR (neat) 2921, 1678, 1428, 1231; LRMS (CI) calcd for $[\text{C}_{12}\text{H}_{15}\text{O}_2]$ ($[\text{MH}]^+$): 191; found 191; $[\alpha]_D^{23}$ -140.3 (c 1.0, CHCl_3 , 91% ee).



(4aR, 8aS)-2,3,6-Trimethyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone^{12f} (Table 6, entry 1).

Purification by column chromatography (gradient elution with 2-7% EtOAc-hexanes) afforded 151 mg (99%) of product as a pale yellow solid, which was crystallized from pentane: mp 42-43 °C; ^1H NMR (500 MHz, CDCl_3) δ 5.32-5.33 (m, 1H), 3.17 (q, 1H, $J = 6.0$ Hz), 3.09 (q, 1H, $J = 6.5$ Hz), 2.28-2.37 (m, 2H), 2.07-2.13 (m, 1H), 1.97-2.02 (m, 1H), 1.94 (s, 6H), 1.62 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 200.1, 199.8, 143.8, 143.7, 131.6, 118.3, 46.5, 45.7, 28.9, 24.9, 23.3, 12.8 (x2); FTIR (neat) 2919, 1672, 1241, 1377; LRMS (CI) calcd for $[\text{C}_{13}\text{H}_{17}\text{O}_2]$ ($[\text{MH}]^+$): 205; found 205; $[\alpha]_D^{23}$ +19.0 (c 1.0, CHCl_3 , 90% ee).

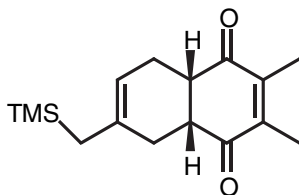


(1*S*,2*S*,4*S*,8*R*,9*R*)-2-Bromo-1,6,7-trimethyl-11-oxa-tricyclo[6.2.1.0^{4,9}]undec-6-en-5-one and (4*S*,4*aS*,6*S*,7*S*,8*aR*)-6-Bromo-4,7-dihydroxy-2,3,7-trimethyl-4*a*,5,6,7,8,8*a*-hexahydro-4*H*-naphthalen-1-one. To a solution of 2,3-dimethyl quinone adduct (90% ee, 122 mg, 0.60 mmol) in methanol (10 mL) was added CeCl₃·7H₂O (238 mg, 0.64 mmol) at 0°C. After 15 min, the solution was cooled to -78°C and NaBH₄ (23.8 mg, 0.64 mmol) was added. The reaction mixture was warmed up to -20°C over a period of 2 h. Et₂O (40 mL) was added and the solution was extracted with water (40 mL) and brine (40 mL), and dried over Na₂SO₄. Column chromatography (gradient elution with 5-40 % EtOAc-hexanes) gave an inseparable mixture of the hydroxy ketones (1: 1.4) as a white solid (122 mg, 99%). This mixture of the hydroxy ketones (61.3mg, 0.30 mmol) was dissolved in THF (3 mL). The solution was cooled down to -78 °C and N-bromosuccinimide (63mg, 0.099mmol) was added at -78 °C. The reaction mixture was warmed up to room temperature over a period of 3 h and passed through a short silica gel pad with EtOAc-Hexanes (1:1) as eluent. The concentrated eluent was purified by column chromatography (gradient elution with 5-40% EtOAc-hexanes) to afford 34 mg (40%) of bromoether as a colorless oil and 22 mg (24%) of diol as a white solid.

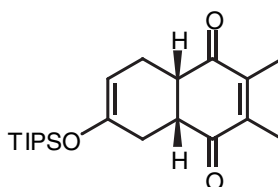
Bromoether; ¹H NMR (500 MHz, CDCl₃) δ 4.33 (s, 1H), 4.06 (d, 1H, *J* = 6.0 Hz), 2.79-2.83 (m, 1H), 2.65 (d, 1H, *J* = 12.0 Hz), 2.61-2.62 (m, 1H), 2.53 (ddd, 1H, *J* = 16.0, 10.5, 6.0 Hz), 2.17 (dd, 1H, *J* = 15.5, 8.0 Hz), 2.01 (s, 3H), 1.75 (s, 3H), 1.73 (dd, 1H, *J* = 13.0, 4.5 Hz), 1.50 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 202.0, 145.9, 129.8, 84.4, 79.7, 54.5, 41.6, 40.4, 36.9, 34.8, 24.3, 19.2, 11.1; DEPT ¹³C NMR (125 MHz, CDCl₃) Up: 79.7, 54.5, 41.6, 40.4, 24.3, 19.2, 11.1 Down: 36.9, 34.8; FTIR (neat) 2931, 2868, 1678, 924; LRMS (CI) calcd for [C₁₃H₁₈BrO₂] ([MH]⁺): 285, 287; found 285, 287; [α]_D²³ +103.6 (*c* 1.0, CHCl₃, >90% ee).

Diol; Recrystallization from dichloromethane provided colorless crystals suitable for X-ray structure determination: mp 123-124 °C; ¹H NMR (400 MHz, CDCl₃, 50 °C) δ 4.66 (brs, 1H), 4.27 (brs, 1H), 2.91-2.95 (m, 1H), 2.52 (s, 1H), 2.50-2.55 (m, 1H), 2.24 (ddd, 1H, *J* = 14.4, 11.6, 3.2 Hz), 2.01-2.08 (m, 1H), 2.01 (t, 3H, *J* = 1.2 Hz), 1.81 (dd, 3H, *J* = 2.0, 1.2 Hz), 1.76 (d, 1H, *J* = 6.0 Hz), 1.42 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 200.3, 130.7 (X2), 92.9, 71.8, 71.0, 43.5

(X3), 37.1 (X2), 11.4 (X2); FTIR (neat) 3476, 3349, 2926, 2852, 1637, 1072; LRMS (CI) calcd for $[C_{13}H_{18}BrO_2]$ ($[MH-H_2O]^+$): 285, 287; found 285, 287; $[\alpha]_D^{23}$ -43.6 (*c* 0.39, $CHCl_3$, >90% ee).

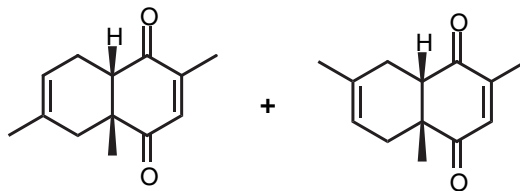


(4aR, 8aS)- 2,3 – Dimethyl – 6 - (trimethyl - silanylmethyl) - 4a,5,8,8a – tetrahydro - [1,4] naphthoquinone (Table 6, entry 2). Purification by column chromatography (gradient elution with 2-7% EtOAc-hexanes) afforded 176 mg (96%) of product as a pale yellow oil: 1H NMR (500 MHz, $CDCl_3$) δ 5.16 (brs, 1H), 3.17 (q, 1H, *J* = 5.5 Hz), 3.09 (q, 1H, *J* = 6.0 Hz), 2.33-2.37 (m, 2H), 2.11-2.16 (m, 1H), 1.96-2.03 (m, 1H), 1.97 (s, 3H), 1.96 (d, 3H, *J* = 1.0 Hz), 1.41 (dd, 2H, *J* = 20.0, 14.0 Hz), 0.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 199.8, 143.9, 143.6, 133.3, 115.9, 46.8, 46.0, 29.7, 27.6, 25.3, 13.0, 12.9, -1.28 (x3); FTIR (neat) 2951, 1674, 1244, 839; LRMS (CI) calcd for $[C_{16}H_{25}O_2Si]$ ($[MH]^+$): 277; found 277; $[\alpha]_D^{23}$ +59.5 (*c* 1.0, $CHCl_3$, >99% ee).

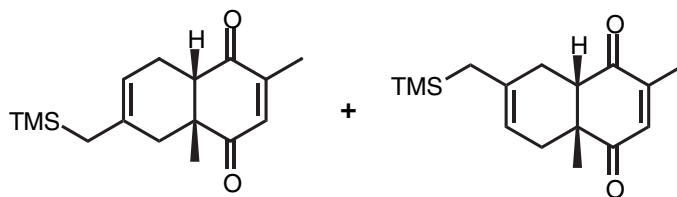


(4aR, 8aS)- 2, 3 – Dimethyl – 6 - (triisopropyl - silanyloxy) - 4a, 5, 8, 8a – tetrahydro - [1,4] naphthoquinone (Table 6, entry 3). Purification by column chromatography (gradient elution with 2-7% EtOAc-hexanes) afforded 237 mg (98%) of product as a pale yellow oil: 1H NMR (500 MHz, $CDCl_3$) δ 4.80-4.81 (m, 1H), 3.26 (q, 1H, *J* = 5.5 Hz), 3.08 (q, 1H, *J* = 6.0 Hz), 2.50-2.55 (m, 1H), 2.35-2.41 (m, 1H), 2.15-2.19 (m, 2H), 1.98 (d, 3H, *J* = 1.0 Hz), 1.96 (d, 3H, *J* = 1.0 Hz), 1.07-1.16 (m, 3H), 1.05 (d, 18H, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 199.0, 148.1, 144.0, 143.7, 100.2, 46.9, 45.9, 28.4, 24.3, 17.9 (x6), 13.0, 12.9, 12.5 (x3); FTIR

(neat) 2942, 2865, 1674, 1191; LRMS (CI) calcd for $[C_{21}H_{35}O_3Si]$ ($[MH]^+$): 363; found 363; $[\alpha]_D^{23} +38.2$ (c 1.0, $CHCl_3$, >99% ee).

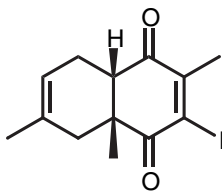


(4aR, 8aS)-2,4a,6-Trimethyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone and (4aR, 8aS)-2,4a,7-trimethyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone (Table 7, entry 1). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes) afforded 134 mg (99%) of product (6-methyl isomer: 7-methyl isomer = 62: 38) as a pale yellow oil: 1H NMR (500 MHz, $CDCl_3$) δ 6.45-6.46 (m, 1H), 5.36-5.38 (m, 0.62H), 5.28-5.30 (m, 0.38H), 2.87 (t, 0.38H, $J = 5.5$ Hz), 2.80 (t, 0.62H, $J = 5.5$ Hz), 2.59 (dddd, 0.62H, $J = 18.0, 8.5, 4.5, 2.0$ Hz), 2.51-2.55 (m, 0.38H), 2.39-2.44 (m, 0.38H), 2.36 (d, 0.62H, $J = 17.5$ Hz), 2.11-2.17 (m, 0.62H), 2.03-2.07 (m, 0.38H), 1.98 (d, 3H, $J = 1.5$ Hz), 1.76 (d, 0.38H, $J = 18.5$ Hz), 1.69 (s, 1.14H), 1.65 (d, 0.62H, $J = 17.5$ Hz), 1.62 (d, 1.86H, $J = 1.5$ Hz), 1.28 (s 1.86H), 1.28 (s 1.14H); ^{13}C NMR (125 MHz, $CDCl_3$, 6-methyl isomer) δ 202.5, 200.4, 148.4, 134.9, 131.0, 117.9, 51.8, 48.5, 37.2, 23.5 (x2), 22.7, 16.2 ; ^{13}C NMR (125 MHz, $CDCl_3$, 7-methyl isomer) δ 202.9, 200.2, 148.4, 135.0, 131.2, 117.8, 52.5, 47.7, 33.0, 27.5, 23.2, 22.2, 16.1; FTIR (neat) 2967, 2916, 1674, 1215; LRMS (EI) calcd for $[C_{13}H_{17}O_2]$ ($[MH]^+$): 205; found 205.

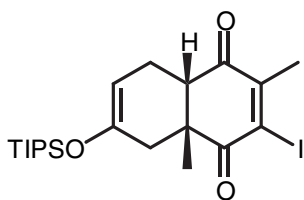


(4aR, 8aS)-2,4a-Dimethyl-6-(trimethylsilylmethyl)-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone and (4aR, 8aS)-2,4a-dimethyl-7-(trimethylsilylmethyl)-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone (Table 7, entry 2). Purification by column chromatography (gradient elution with 2-7% EtOAc-hexanes) afforded 180 mg (98%) of product (6-silylmethyl

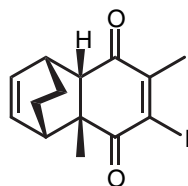
isomer: 7-silanylmethyl isomer = 48: 52) as a pale yellow oil: ^1H NMR (500 MHz, CDCl_3) δ 6.44-6.45 (m, 1H), 5.17-5.18 (m, 0.48H), 5.09-5.10 (m, 0.52H), 2.84 (dd, 0.52H, $J = 6.0, 4.0$ Hz), 2.77 (t, 0.48H, $J = 5.0$ Hz), 2.59-2.64 (m, 0.48H), 2.52-2.56 (m, 0.52H), 2.40 (dd, 0.52H, $J = 17.5, 2.0$ Hz), 2.33 (dd, 0.48H, $J = 17.5, 2.0$ Hz), 2.12-2.17 (m, 0.48H), 1.99-2.05 (m, 0.52H), 1.98 (d, 3H, $J = 1.5$ Hz), 1.75-1.79 (m, 0.52H), 1.63 (d, 0.48H, $J = 17.5$ Hz), 1.45 (s, 0.96H), 1.37 (s, 1.04H), 1.28 (s 1.44H), 1.28 (s 1.56H), 0.03 (s, 4.68H), -0.03 (s, 4.32H); ^{13}C NMR (125 MHz, CDCl_3 , 6-isomer) δ 203.0, 200.3, 148.5, 134.9, 132.5, 115.2, 52.6, 48.7, 38.0, 27.9, 23.4, 21.8, 16.2, -1.2; ^{13}C NMR (125 MHz, CDCl_3 , 7-isomer) δ 202.6, 199.9, 148.4, 134.8, 132.9, 115.5, 51.7, 47.6, 33.2, 27.6, 27.5, 22.6, 16.2, -1.2; FTIR (neat) 2952, 1676, 1247, 842; LRMS (EI) calcd for $[\text{C}_{16}\text{H}_{25}\text{O}_2\text{Si}]$ ($[\text{MH}]^+$): 277; found 277.



(4aR, 8aS)- 3-Iodo-2,4a,6-trimethyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone (Table 8, entry 1). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes) afforded 217 mg (99%) of product as a pale yellow oil: ^1H NMR (500 MHz, CDCl_3) δ 5.34-5.35 (m, 1H), 2.80 (t, 1H, $J = 6.0$ Hz), 2.50-2.57 (m, 1H), 2.34 (d, 1H, $J = 17.5$ Hz), 2.26 (s, 3H), 2.12-2.17 (m, 1H), 1.70 (d, 1H, $J = 17.5$ Hz), 1.61 (d, 3H, $J = 1.0$ Hz), 1.32 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 195.5, 194.8, 154.9, 130.9, 125.5, 117.7, 51.2, 46.9, 37.6, 23.7, 23.5 (x2), 23.3; FTIR (neat) 2969, 2929, 1682, 1208; HRMS (EI) calcd for $[\text{C}_{13}\text{H}_{15}\text{IO}_2]$ ($[\text{M}]^+$): 330.0117; found 330.0110; $[\alpha]_{\text{D}}^{23}$ -87.9 (c 1.0, CHCl_3 , >99% ee, 6-methyl isomer). The minor 7-methyl isomer was separated by recrystallization from pentane at -20 °C.

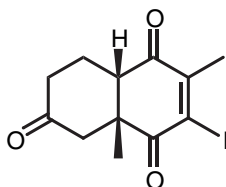


(4aR, 8aS)-3-Iodo-2,4a-dimethyl-6-(triisopropylsilyloxy)-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone (Table 8, entry 2). Purification by column chromatography (gradient elution with 2-5% EtOAc-hexanes) afforded 322 mg (99%) of product as a pale yellow oil: ^1H NMR (500 MHz, CDCl_3) δ 4.76 (t, 1H, $J = 4.0$ Hz), 2.74 (t, 1H, $J = 5.3$ Hz), 2.55-2.61 (m, 1H), 2.45 (dd, 1H, $J = 17.5, 2.0$ Hz), 2.23 (s, 3H), 2.13-2.20 (m, 1H), 1.82 (d, 1H, $J = 17.5$ Hz), 1.34 (s, 3H), 1.01-1.12 (m, 3H), 1.00 (dd, 18H, $J = 7.5, 2.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 194.6, 194.1, 154.9, 147.1, 125.2, 99.1, 51.1, 47.4, 37.0, 23.6 (x2), 22.3, 17.8 (x6), 12.4 (x3); FTIR (neat) 2942, 2865, 1685, 1204; LRMS (CI) calcd for $[\text{C}_{21}\text{H}_{34}\text{IO}_3\text{Si}]$ ($[\text{MH}]^+$): 489; found 489; $[\alpha]_{\text{D}}^{23}$ -58.8 (c 1.0, CHCl_3 , >99% ee).

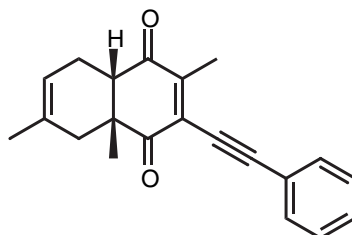


(1S,2R,7S,8S)-4-Iodo-2,5-dimethyl-tricyclo[6.2.2.0^{2,7}]dodeca-4,9-diene-3,6-dione (Table 8, entry 3). Purification by column chromatography (gradient elution with 2-10% EtOAc-hexanes) afforded 226 mg (99%) of product as a pale yellow solid. Recrystallization from hexanes provided pale yellow crystals suitable for X-ray structure determination: mp 98-99 °C; ^1H NMR (500 MHz, CDCl_3) δ 6.21 (dd, 1H, $J = 7.0, 7.0$ Hz), 6.04 (dd, 1H, $J = 7.0, 7.0$ Hz), 2.97-2.98 (m, 1H), 2.91-2.92 (m, 1H), 2.47 (d, 1H, $J = 1.5$ Hz), 2.19 (s, 3H), 1.80-1.86 (m, 1H), 1.64-1.70 (m, 1H), 1.31 (s, 3H), 1.27-1.33 (m, 1H), 1.12-1.21 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 195.4, 194.6, 157.0, 136.1, 132.1, 130.3, 57.4, 50.0, 39.8, 36.3, 26.4, 25.9, 24.0, 18.7; FTIR (neat)

2954, 1668, 1587; LRMS (CI) calcd for $[C_{14}H_{14}IO_2]$ ($[M-H]^-$): 341; found 341; $[\alpha]_D^{23} +73.3$ (c 1.0, $CHCl_3$, >99% ee).



(4aR, 8aS) -3 -Iodo -2, 4a -dimethyl -4a, 7, 8, 8a -tetrahydro- 5H -naphthalene -1, 4, 6-trione. To a stirred solution of the iodo (triisopropylsilyl)oxy quinone adduct (110 mg, 0.23 mmol) in CH_3CN (1 mL) was added a diluted HF solution (48% aqueous HF : $CH_3CN=1:4$) (0.5 mL) and the reaction mixture was stirred for 3hrs at room temperature. Water (15 mL) and CH_2Cl_2 (4 mL) were added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (4 mLx3). The combined extract was dried over sodium sulfate and concentrated *in vacuo* to give pale yellow oily residue. The residue was purified by column chromatography (gradient elution with 10-30% EtOAc-hexanes) to afford 67 mg (90%) of product as a pale yellow solid. Recrystallization from a mixture solvent (EtOAc: Hexanes=1:3) provided pale yellow crystals suitable for X-ray structure determination: mp 129-130 °C; 1H NMR (400 MHz, $CDCl_3$) δ 2.98 (dd, 1H, $J = 7.2, 4.8$ Hz), 2.78 (dd, 1H, $J = 14.4, 1.2$ Hz), 2.41-2.49 (m, 1H), 2.37 (ddd, 1H, $J = 7.6, 6.0, 1.6$ Hz), 2.32 (s, 3H), 2.25 (ddd, 1H, $J = 21.2, 7.6, 6.0$ Hz), 2.15 (d, 1H, $J = 14.8$ Hz), 2.04-2.12 (m, 1H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.6, 193.9, 193.2, 155.4, 125.3, 53.3, 50.9, 48.4, 38.1, 24.9, 24.7, 23.6; FTIR (neat) 2963, 1716, 1678, 1205, 733; LRMS (CI) calcd for $[C_{12}H_{13}IO_3]$ ($[M]^+$): 332; found 332; $[\alpha]_D^{23} -14.4$ (c 1.0, $CHCl_3$, >99% ee).



(4aR, 8aS)-2,4a,6-Trimethyl-3-phenylethynyl-4a,5,8,8a-tetrahydro-[1,4]naphthoquinone.

To a stirred solution of the iodo trimethyl quinone adduct (22 mg, 0.067 mmol) in CH₃CN (0.5 mL) were added pyridine (8 μL, 0.099 mmol) and a catalytic amount of tetrakis(triphenylphosphine)palladium followed by copper phenylacetylide (18.6 mg, 0.12 mmol) at room temperature. After 1 hour the reaction mixture was filtered through a cotton plug. Water (5 mL) and CH₂Cl₂ (2 mL) were added to the filtrate and the layers were separated. The aqueous layer was extracted with CH₂Cl₂ (4 mL x3). The combined extract was dried over sodium sulfate and concentrated *in vacuo* to give pale yellow oily residue. The residue was purified by column chromatography (gradient elution with 2-4% EtOAc-hexanes) to afford 20 mg (99%) of product as a pale yellow oil: ¹H NMR (400 MHz, CDCl₃) δ 7.55-7.58 (m, 2H), 7.34-7.40 (m, 3H), 5.37-5.39 (m, 1H), 2.86 (t, 1H, *J* = 6.2 Hz), 2.54-2.63 (m, 1H), 2.47 (d, 1H, *J* = 18.0 Hz), 2.25 (s, 3H), 2.14-2.23 (m, 1H), 1.72 (d, 1H, *J* = 17.6 Hz), 1.65 (d, 3H, *J* = 1.2 Hz), 1.35 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 199.1, 198.4, 148.7, 132.0, 131.2, 130.3, 129.6, 128.4, 122.1, 117.8, 106.3, 83.1, 51.6, 48.5, 37.1, 24.1, 23.4, 23.2, 15.4; FTIR (neat) 2913, 2360, 2200, 1679, 1375; LRMS (CI) calcd for [C₂₁H₂₁O₂] ([MH]⁺): 305; found 305.