Catalytic Enantioselective Diels-Alder Reactions of 1,4-Quinone Monoketals

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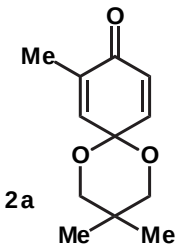
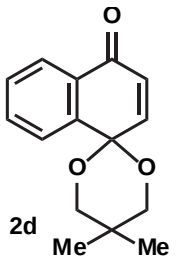
Supporting Information



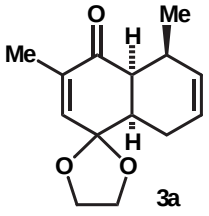
3,3,8-Trimethyl-1,5-dioxa-spiro[5.5]undeca-7,10-dien-9-one (2a): To a solution of 2,2-dimethyl-1,3-propanediol (1.04 g, 10.0 mmol) in CH_2Cl_2 (9 mL) were added *o*-cresol (104 µL, 108 mg, 1.00 mmol) and [bis(trifluoroacetoxy)iodo]benzene (946 mg, 2.20 mmol) at room temperature. The reaction mixture immediately turned black and then orange over a period of 30 min. Et_2O (50 mL) was added and the reaction mixture was extracted with a sat. $NaHCO_3$ solution (50 mL) and brine (50 mL). After drying over Na_2SO_4, the 1,4-quinone monoketal **2a** (125 mg, 648 µmol, 65%) was obtained by column chromatography [deactivated silica gel (5% NEt_3), hexane:Et_2O 100:0→5:1] as a colorless solid, mp 102°C; FTIR (film) 2965, 2891, 1678, 1648, 1621, 1363, 1079, 1018, 986, cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 7.15 (dd, 1H, *J* = 10.3, 3.1 Hz), 6.87 (m, 1H), 6.19 (d, 1H, *J* = 10.3 Hz), 3.71 (d, 2H, *J* = 11.4 Hz), 3.66 (d, 2H, *J* = 11.4 Hz), 1.89 (d, 3H, *J* = 1.8 Hz), 1.10 (s, 3H), 1.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 185.9, 140.6, 137.4, 135.6, 128.7, 89.3, 71.5, 30.2, 22.7, 22.6, 15.7; HRMS (EI) *m/z* calcd for $[C_{12}H_{16}O_3]^+$: 208.1100, found 208.1095.



5,5-Dimethyl-1'*H*-spiro[1,3-dioxane-2,1'-naphthalen-4'-one] (2d): To a solution of 2,2-dimethyl-1,3-propanediol (502 mg, 5.00 mmol) in DME (10 mL) was added 4,4-dimethoxy-4H-naphthalen-1-one (204 mg, 1.00 mmol) at room temperature. BF_3•OEt_2 (1.00 M in DME, 1.05 mL, 1.05 mmol) was added over a

period of 15 min. The reaction mixture was stirred for 20 min. Et_2O (25 mL) was added and the reaction mixture extracted with a sat. $NaHCO_3$ solution (25 mL) and brine (25 mL). After drying over Na_2SO_4, the naphthoquinone monoketal **2d** (174 mg, 711 μmol, 71%) was obtained by column chromatography [deactivated silica gel (5% NEt_3), hexane:Et_2O 5:1] as a colorless solid, mp 138-142°C (dec.); FTIR (film) 2959, 2876, 1673, 1601, 1471, 1330, 1304, 1072, 985 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.04 (dd, 1H, *J* = 7.7, 1.1 Hz), 7.98 (dd, 1H, *J* = 7.7, 0.7 Hz), 7.78 (d, 1H, *J* = 10.6 Hz), 7.68 (td, 1H, *J* = 7.7, 1.5 Hz), 7.50 (td, 1H, *J* = 7.7, 1.1 Hz), 6.45 (d, 1H, *J* = 10.6 Hz), 4.04 (d, 2H, *J* = 11.7 Hz), 3.63 (d, 2H, *J* = 12.1 Hz), 1.49 (s, 3H), 0.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 183.8, 142.1, 137.3, 133.7, 129.7, 129.34, 129.29, 126.9, 126.1, 90.5, 71.9, 30.2, 23.6, 22.5; HRMS (EI) *m/z* calcd for $[C_{15}H_{16}O_3]^+$: 244.1100, found 244.1100.

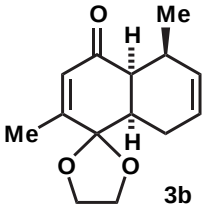
General Procedure for the Enantioselective Diels-Alder Reactions of 1,4-Quinone Monoketals: To 4Å molecular sieves (Aldrich, 5-6% H_2O, 2-3 μ particle size, 50 mg) was added a 0.02 M solution of *(S)*-2,2'-dihydroxy-1,1'-binaphthyl in CH_2Cl_2 (500 μL, 2.9 mg, 10 μmol) and a 0.30 M solution of $Cl_2Ti(OiPr)_2$ in toluene (33 μL, 10 μmol) at room temperature. The reddish brown reaction mixture was stirred for 1 h. A 0.50 M solution of the 1,4-quinone monoketal in CH_2Cl_2 (400 μL, 200 μmol) was added. After 10 min at room temperature, the diene (5 equiv) was added and the reaction was stirred until TLC [deactivated silica gel (NEt_3), hexane:Et_2O 1:2] showed complete conversion. Column chromatography [deactivated silica gel (5% NEt_3), hexane:Et_2O 5:1→1:2] gave the analytically pure Diels-Alder adducts.



3a

Diels-Alder Adduct 3a: (colorless oil, 99% yield, *endo/exo* >99:1, 98% ee): $[\alpha]^{20}_D$ –184 (*c* 1.6, $CHCl_3$); FTIR (film) 3021, 2925, 2877, 2848, 1690, 1371, 1112, 1103, 1023, 1001 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.11 (s, 1H), 5.62 (d, 1H, *J* = 9.9 Hz), 5.54 (m, 1H), 4.08 (m, 3H), 3.96 (m, 1H), 3.10 (t, 1H, *J* = 4.0 Hz), 2.50 (m, 1H), 2.45 (m, 1H), 2.23 (m, 1H), 1.97 (m, 1H), 1.78 (d, 3H, *J* = 1.5 Hz), 1.40 (d, 3H, *J* = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 200.7, 137.5, 136.4, 132.1, 123.7, 107.3, 65.3, 64.6, 49.1, 45.7, 33.4, 24.7, 18.5, 15.6; HRMS (EI) *m/z* calcd for $[C_{14}H_{18}O_3]^+$: 234.1256, found 234.1258.

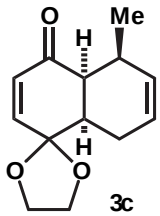
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 11.1 min, t_{major} = 12.0 min.



3b

Diels-Alder Adduct 3b: (colorless solid, 92% yield, *endo/exo* > 99:1, 96% ee): $[\alpha]^{20}_D$ –175 (*c* 1.29, $CHCl_3$); mp. 53–55°C; FTIR (film) 3021, 2956, 290 6, 2848, 1682, 1646, 1441, 1373, 1264, 1214, 1201, 1186, 1110, 1023, 998, 940 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.76 (d, 1H, *J* = 1.1 Hz), 5.58 (d, 1H, *J* = 9.9 Hz), 5.50 (m, 1H), 4.07 (m, 4H), 3.05 (t, 1H, *J* = 4.0 Hz), 2.41 (m, 2H), 2.16 (m, 1H), 1.94 (m, 1H), 1.83 (d, 3H, *J* = 1.1 Hz), 1.38 (d, 3H, *J* = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.7, 152.5, 132.2, 129.4, 123.8, 108.5, 66.3, 65.2, 48.7, 44.7, 33.5, 24.6, 18.6, 16.7; HRMS (EI) *m/z* calcd for $[C_{14}H_{18}O_3]^+$: 234.1256, found 234.1244.

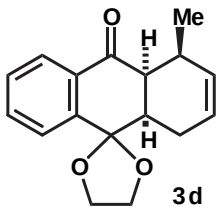
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 26.4 min, t_{major} = 30.0 min.



3c

Diels-Alder Adduct 3c: (colorless oil, 86% yield, *endo/exo* > 99:1, 84% ee): $[\alpha]^{20}_D$ –96.8 (*c* 0.76, $CHCl_3$); FTIR (film) 3022, 2927, 2851, 1695, 1122, 1111, 1019, 1004, 945 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.30 (dd, 1H, *J* = 10.3, 2.2 Hz), 5.88 (d, 1H, *J* = 10.3 Hz), 5.59 (m, 1H), 5.53 (m, 1H), 4.08 (m, 3H), 3.97 (m, 1H), 3.10 (t, 1H, *J* = 4.0 Hz), 2.45 (m, 2H), 2.23 (m, 1H), 1.97 (m, 1H), 1.37 (d, 3H, *J* = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.2, 141.0, 132.0, 130.7, 123.7, 106.9, 65.4, 64.7, 49.0, 45.4, 33.4, 24.6, 18.4; HRMS (EI) *m/z* calcd for $[C_{13}H_{16}O_3]^+$: 220.1100, found 220.1098.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99.5:0.5, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 21.3 min, t_{major} = 22.9 min.

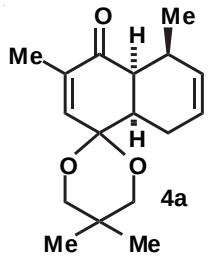


3d

Diels-Alder Adduct 3d: (colorless solid, 95% yield, *endo/exo* > 99:1, 92% ee): $[\alpha]^{20}_D$ –110 (*c* 0.88, $CHCl_3$); mp 89°C; FTIR (film) 3020, 2956, 2907, 2845, 1694, 1601, 1238, 1151, 1061 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.90

(dd, 1H, *J* = 7.7, 1.4 Hz), 7.59 (dd, 1H, *J* = 7.3, Hz), 7.54 (dd, 1H, *J* = 7.7, 1.5 Hz), 7.44 (dd, 1H, *J* = 7.5, 1.5 Hz), 5.66 (d, 1H, *J* = 10.3 Hz), 5.52 (m, 1H), 4.38 (m, 1H), 4.18 (m, 3H), 3.37 (t, 1H, *J* = 4.0 Hz), 2.67 (m, 1H), 2.55 (m, 1H), 2.25 (m, 1H), 1.81 (m, 1H), 1.50 (d, 3H, *J* = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.0, 139.6, 133.6, 132.5, 132.3, 129.3, 126.2, 126.0, 123.7, 108.2, 66.4, 64.6, 49.3, 45.4, 34.2, 25.0, 19.1; HRMS (EI) *m/z* calcd for $[C_{17}H_{18}O_3]^+$: 270.1256, found 270.1254.

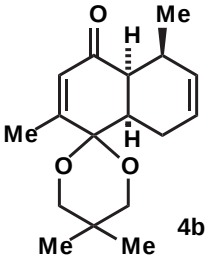
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 18.0 min, t_{major} = 20.2 min.



4a

Diels-Alder Adduct 4a: (colorless oil, 90% yield, *endo/exo* > 99:1, 99% ee): $[\alpha]^{20}_D$ –173.8 (*c* 0.86, $CHCl_3$); FTIR (film) 3022, 2955, 2927, 2871, 1689, 1464, 1396, 1371, 1103, 1019, 966 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.50 (s, 1H), 5.59 (d, 1H, *J* = 9.9 Hz), 5.51 (m, 1H), 3.60 (m, 3H), 3.51 (d, 1H, *J* = 11.7 Hz), 3.02 (m, 1H), 2.93 (m, 1H), 2.46 (m, 1H), 2.12 (m, 1H), 1.87 (m, 1H), 1.77 (s, 3H), 1.39 (d, 3H, *J* = 7.7 Hz), 1.04 (s, 3H), 0.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.8, 137.0, 135.1, 132.3, 123.9, 97.0, 71.6, 70.2, 47.8, 42.7, 33.9, 30.1, 24.2, 22.6, 22.5, 18.7, 15.8; HRMS (EI) *m/z* calcd for $[C_{17}H_{24}O_3]^+$: 276.1726, found 276.1722.

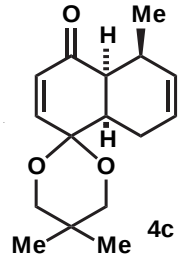
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99.5:0.5, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 7.5 min, t_{major} = 8.8 min.



4b

Diels-Alder Adduct 4b: (colorless solid, 94% yield, *endo/exo* > 99:1, 87% ee): $[\alpha]^{20}_D$ –128.1 (*c* 0.989, $CHCl_3$); mp 115°C; FTIR (film) 2954, 2926, 2877, 1673, 1120, 1112, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.71 (d, 1H, *J* = 1.5 Hz), 5.61 (br. d, 1H, *J* = 10.3 Hz), 5.52 (m, 1H), 3.83 (d, 1H, *J* = 11.4 Hz), 3.63 (d, 1H, *J* = 11.4 Hz), 3.51 (dd, 1H, *J* = 11.0, 2.5 Hz), 3.41 (dd, 1H, *J* = 11.4, 2.6 Hz), 3.29 (m, 1H), 2.90 (t, 1H, *J* = 3.9 Hz), 2.45 (m, 1H), 1.99 (d, 3H, *J* = 1.5 Hz), 1.94 (m, 2H), 1.41 (d, 1H, *J* = 7.7 Hz), 1.27 (s, 3H), 0.78 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.7, 153.9, 132.5, 128.3, 124.2, 98.5, 71.3, 69.6, 47.3, 35.7, 34.1, 29.8, 24.3, 23.3, 22.4, 18.8, 16.9; HRMS (EI) *m/z* calcd for $[C_{17}H_{24}O_3]^+$: 276.1726, found 276.1719.

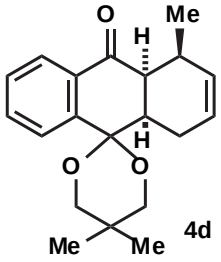
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 17.0 min, t_{major} = 20.5 min.



4c

Diels-Alder Adduct 4c: (colorless solid, 97% yield, *endo/exo* > 99:1, 93% ee): $[\alpha]^{20}_D$ –129.5 (*c* 1.00, $CHCl_3$); mp 77°C; FTIR (film) 3022, 2956, 2871, 1689, 1397, 1383, 1125, 1106, 1022 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.76 (dd, 1H, *J* = 10.3, 2.3 Hz), 5.88 (d, 1H, *J* = 10.3 Hz), 5.59 (br. d, 1H, *J* = 10.3 Hz), 5.52 (m, 1H), 3.67-3.48 (m, 4H), 3.06 (m, 1H), 2.88 (m, 1H), 2.45 (m, 1H), 2.15 (m, 1H), 1.90 (m, 1H), 1.39 (d, 3H, *J* = 7.7 Hz), 1.04 (s, 3H), 1.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.6, 139.3, 132.1, 130.5, 124.0, 96.8, 71.6, 70.4, 47.8, 43.4, 33.7, 30.2, 24.1, 22.7, 22.5, 18.6; HRMS (EI) *m/z* calcd for $[C_{16}H_{22}O_3]^+$: 262.1569, found 262.1572.

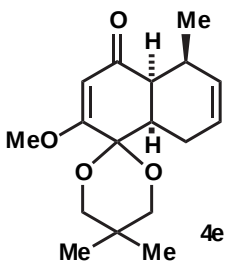
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 11.9 min, t_{major} = 12.7 min.



4d

Diels-Alder Adduct 4d: (colorless oil, 93% yield, *endo/exo* > 99:1, 95% ee): $[\alpha]^{20}_D$ –79.60 (*c* 1.09, $CHCl_3$); FTIR (film) 3021, 2955, 2929, 2870, 1697, 1245, 1125, 1087 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.92 (dd, 1H, *J* = 8.1, 0.9 Hz), 7.89 (dd, 1H, *J* = 7.7, 1.1 Hz), 7.64 (dt, 1H, *J* = 7.5, 1.5 Hz), 7.43 (dt, 1H, *J* = 7.7, 1.1 Hz), 5.69 (br. d, 1H, *J* = 9.9 Hz), 5.55 (m, 1H), 3.92 (d, 1H, *J* = 11.4 Hz), 3.82 (d, 1H, *J* = 11.4 Hz), 3.58 (d, 2H, *J* = 11.7 Hz), 3.50 (m, 1H), 3.21 (m, 1H), 2.60 (m, 1H), 2.19 (m, 1H), 1.79 (m, 1H), 1.53 (d, 3H, *J* = 7.7 Hz), 1.42 (s, 3H), 0.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.4, 140.9, 134.1, 132.6, 131.7, 129.3, 126.4, 126.0, 124.1, 98.2, 71.7, 70.2, 47.8, 36.2, 34.7, 30.0, 24.6, 23.5, 22.4, 19.1; HRMS (EI) *m/z* calcd for $[C_{20}H_{24}O_3]^+$: 312.17.26, found 312.1724.

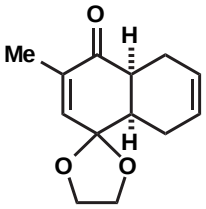
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 11.9 min, t_{major} = 13.1 min.



4e

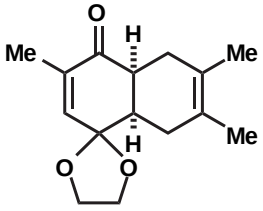
Diels-Alder Adduct 4e: (colorless oil, 91% yield, *endo/exo* > 99:1, 98% ee): $[\alpha]^{20}_{D}$ –142.6 (*c* 1.08 $CHCl_3$); FTIR (film) 2956, 2929, 2871, 1695, 1244, 1124, 1085, 1016 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.62 (br. d, 1H, *J* = 10.3 Hz), 5.57 (m, 1H), 5.18 (s, 1H), 3.74 (m, 2H), 3.72 (s, 3H), 3.63 (m, 2H), 3.08 (m, 1H), 2.96 (m, 1H), 2.48 (m, 1H), 2.14 (m, 2H), 1.44 (d, 3H, *J* = 7.8 Hz), 1.18 (s, 3H), 0.91 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.0, 169.0, 132.6, 124.2, 103.1, 97.6, 71.7, 71.1, 56.4, 46.7, 39.0, 33.9, 30.2, 24.1, 22.8, 22.5, 19.0; HRMS (EI) *m/z* calcd for $[C_{17}H_{24}O_4]^+$: 292.1675, found 292.1671.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 97:3, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 22.0 min, t_{major} = 24.8 min.



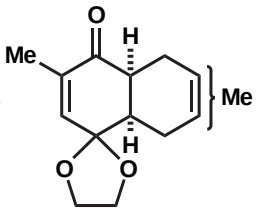
Diels-Alder Adduct of 1a and Butadiene: (colorless oil, 91% yield, 81% ee): $[\alpha]^{20}_{D}$ –152 (*c* 0.55, $CHCl_3$); FTIR (film) 3027, 2925, 2852, 1683, 1363, 1338, 1116, 1078, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.20 (m, 1H), 5.67 (m, 1H), 5.59 (m, 1H), 4.07 (m, 3H), 3.95 (m, 1H), 3.10 (m, 1H), 2.82 (dm, 1H, *J* = 17.9 Hz), 2.48 (m, 1H), 2.19 (m, 1H), 2.04 (m, 1H), 1.94 (m, 1H), 1.80 (d, 3H, *J* = 1.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.7, 138.4, 137.0, 125.5, 124.9, 107.0, 65.3, 64.6, 43.3, 42.4, 24.0, 23.8, 15.8; HRMS (EI) *m/z* calcd for $[C_{13}H_{16}O_3]^+$: 220.1100, found 220.1102.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 10.7 min, t_{major} = 12.3 min.



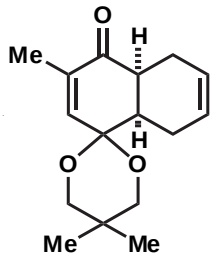
Diels-Alder Adduct of 1a and 2,3-Dimethylbutadiene: (colorless oil, 88% yield, 84% ee): $[\alpha]^{20}_{D}$ –205 (*c* 1.57, $CHCl_3$); FTIR (film) 2981, 2919, 2883, 1684, 1123, 1106, 1076 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.19 (m, 1H), 4.05 (m, 3H), 3.94 (m, 1H), 3.02 (m, 1H), 2.67 (d, 1H, *J* = 17.6 Hz) 2.43 (m, 1H), 2.00 (m, 2H), 1.89 (m, 1H), 1.77 (d, 3H, *J* = 1.5 Hz), 1.63 (s, 3H), 1.53 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.9, 138.3, 137.0, 124.2, 123.4, 107.0, 65.2, 64.5, 43.8, 43.0, 30.3, 30.0, 19.1, 18.9, 15.7; HRMS (EI) *m/z* calcd for $[C_{15}H_{20}O_3]^+$: 248.1413, found 248.1401.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 11.1 min, t_{major} = 22.0 min.



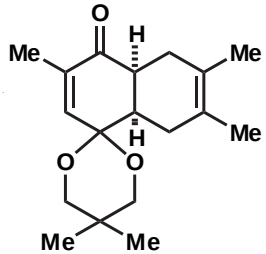
Diels-Alder Adduct of 1a and Isoprene: (colorless oil, 90% yield, 53:47 mixture of regioisomers, 84% ee and 72% ee): $[\alpha]^{20}_{D}$ –149.1 (*c* 1.08, $CHCl_3$); FTIR (film) 2960, 2925, 2854, 1685, 1447, 1369, 1114, 1080, 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.20 (m, 1H), 5.37 (m, 0.47H), 5.28 (m, 0.53H), 4.07 (m, 3H), 3.95 (m, 1H), 3.10 (m, 0.53H), 3.05 (m, 0.47H), 2.79 (dm, 0.47H, *J* = 8.2 Hz), 2.68 (d, 0.53H, *J* = 7.9 Hz), 2.47 (m, 0.47H), 2.39 (m, 0.57H), 2.20-1.82 (m, 4H), 1.79 (d, 1.41H, *J* = 1.5 Hz), 1.78 (d, 1.59H, *J* = 1.5 Hz), 1.68 (s, 1.59H), 1.59 (s, 1.41H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.8, 138.4, 138.3, 137.0, 132.7, 131.8, 119.4, 118.8, 107.2, 107.0, 65.2, 64.6, 43.9, 43.0, 42.9, 42.3, 28.8, 28.4, 24.3, 23.9, 23.7, 23.5, 15.8, 15.7; HRMS (EI) *m/z* calcd for $[C_{14}H_{18}O_3]^+$: 234.1256, found 234.1261.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99.5:0.5, flow 1.0 mL/min, detection at 254 nm, retention times: regioisomer 1: t_{minor} = 19.1 min, t_{major} = 27.5 min; regioisomer 2: t_{minor} = 16.9 min, t_{major} = 32.7 min.



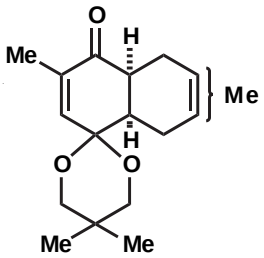
Diels-Alder Adduct of 2a and Butadiene: (colorless oil, 95% yield, 95% ee): $[\alpha]^{20}_{D}$ –233.4 (*c* 0.82, $CHCl_3$); FTIR (film) 3027, 2956, 2926, 2870, 1683, 1106, 1084, 1019, 923 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.60 (m, 1H), 5.67 (m, 1H), 5.59 (m, 1H), 3.59 (m, 4H), 3.05 (m, 1H), 2.96 (m , 1H), 2.85 (dm, 1H, *J* = 16.8 Hz), 2.08 (m, 2H), 1.87 (m, 1H), 1.81 (d, 3H, *J* = 1.5 Hz), 1.05 (s, 3H), 0.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.8, 137.4, 136.4, 125.6, 125.1, 96.7, 71.5, 70.2, 42.0, 39.1, 30.1, 23.9, 23.5, 22.60, 22.58, 15.9; HRMS (EI) *m/z* calcd for $[C_{16}H_{22}O_3]^+$: 262.1569, found 262.1568.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99.5:0.5, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 12.3 min, t_{major} = 17.1 min.



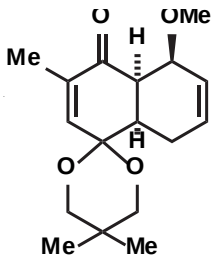
Diels-Alder Adduct of 2a and 2,3-Dimethylbutadiene: (colorless oil, 95% yield, 90% ee): $[\alpha]^{20}_D$ –225.3 (*c* 1.00, $CHCl_3$); FTIR (film) 2955, 2922, 2869, 1682, 1122, 1102, 1083, 1016, 992 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.59 (s, 1H), 3.58 (m, 4H), 2.96 (m, 1H), 2.91 (m, 1H), 2.70 (d, 1H, *J* = 17.2 Hz), 2.03 (m, 1H), 1.96-1.88 (m, 2H), 1.80 (d, 3H, *J* = 1.5 Hz), 1.63 (s, 3H), 1.53 (s, 3H), 1.04 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.0, 137.4, 136.6, 124.4, 123.5, 96.8, 71.5, 70.2, 42.6, 39.5, 30.3, 30.1, 29.8, 22.6, 19.2, 18.9, 15.9; HRMS (EI) *m/z* calcd for $[C_{18}H_{26}O_3]^+$: 290.1882, found 290.1886.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99:1, flow 1.0 mL/min, detection at 254 nm, retention times: t_{minor} = 8.0 min, t_{major} = 15.1 min.



Diels-Alder Adduct of 2a and Isoprene: (colorless oil, 91% yield, 56:44 mixture of regioisomers, 96% and 91% ee): $[\alpha]^{20}_D$ –226.4 (*c* 1.25, $CHCl_3$); FTIR (film) 2957, 2925, 2870, 1684, 1396, 1108, 1087, 1029, 995 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.62 (s, 0.56H), 6.57 (s, 0.44H), 5.37 (br. s, 0.56H), 5.28 (br. s, 0.44H), 3.70-3.50 (m, 4H), 3.04 (m, 0.44H), 2.99 (m, 0.56H), 2.96-2.66 (m, 2H), 2.10-1.75 (m, 3H), 1.81 (d, 1.32H, *J* = 1.6 Hz), 1.80 (d, 1.68H, *J* = 1.6 Hz), 1.68 (s, 1.32H), 1.58 (s, 1.68H), 1.05 (s, 1.32H), 1.04 (s, 1.68H), 1.00 (m, 1.68H), 0.98 (s, 1.32H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.9, 199.8, 137.5, 137.2, 136.5, 132.8, 132.0, 119.6, 119.0, 96.9, 96.7, 71.5, 70.2, 70.1, 42.5, 41.7, 39.7, 38.7, 30.15, 30.11, 28.6, 28.3, 24.1, 23.7, 23.5, 22.61, 22.59, 22.57, 16.0, 15.9; HRMS (EI) *m/z* calcd for $[C_{17}H_{24}O_3]^+$: 276.1726, found 276.1716.

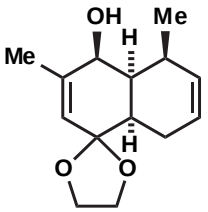
HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 99.5:0.5, flow 1.0 mL/min, detection at 254 nm, retention times: regioisomer 1: t_{minor} = 10.2 min, t_{major} = 20.0 min; regioisomer 2: t_{minor} = 12.0 min, t_{major} = 17.8 min.



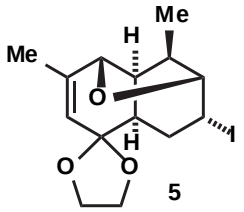
Diels-Alder Adduct of 2a and *E*-1-Methoxy-1,3-butadiene: (colorless oil which solidifies upon standing, 90% yield, *endo/exo* > 99:1, 99% ee): $[\alpha]^{20}_D$ –150.9 (*c* 1.30, $CHCl_3$); mp 91-93°C;FTIR (film) 2955, 2926, 2871, 1693, 1396, 1102, 1019 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.55 (m, 1H), 5.85 (dm, 1H, *J* =

10.3 Hz), 5.55 (m, 1H), 3.99 (m, 1H), 3.60 (m, 3H), 3.49 (m, 1H), 3.42 (s, 3H), 3.22 (m, 1H), 2.87 (m, 1H), 2.13 (dm, 1H, J = 19.0 Hz), 1.92 (m, 1H), 1.78 (d, 3H, J = 1.5 Hz), 1.01 (s, 3H), 1.00 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 197.6, 137.0, 134.7, 128.9, 125.4, 96.6, 78.1, 71.6, 70.3, 57.0, 45.3, 41.3, 30.2, 24.5, 22.7, 22.5, 15.7; HRMS (EI) *m/z* calcd for $[C_{17}H_{24}O_4]^+$: 292.1675, found 292.1661.

HPLC: column (*R,R*)-Whelk-O1, solvent: hexanes/*i*PrOH 95:5, flow 1.0 mL/min, detection at 254 nm, retention times: t_{major} = 24.5 min, t_{minor} = 28.8 min.



Luche-Reduction of 3a: To a solution of **3a** (98% ee, 150 mg, 640 μmol) in methanol (10 mL) was added $CeCl_3 \bullet 7H_2O$ (250 mg, 672 μmol) at 0°C. After 15 min, the solution was cooled to -78°C and $NaBH_4$ (25.4 mg, 672 μmol) was added. The reaction mixture was warmed up to 0°C over a period of 3 h. Et_2O (40 mL) was added and the solution was extracted with water (40 mL) and brine (40 mL), and dried over Na_2SO_4. Column chromatography [deactivated silica gel (5% NEt_3), hexane:Et_2O 2:1] gave a colorless oil (146 mg, 618 μmol, 97%), $[\alpha]^{20}_D$ –171.5 (*c* 1.00, $CHCl_3$); FTIR (film) 3562, 3015, 2957, 2881, 1374, 1155, 1099, 1070, 994, 967 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.78 (m, 2H), 5.31 (s, 1H), 4.00 (m, 4H), 3.85 (m, 1H), 2.62 (m, 1H), 2.22 (m, 3H), 2.06 (m, 2H), 1.84 (d, 3H, J = 1.5 Hz), 1.25 (d, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.2, 135.1, 126.6, 122.1, 108.2, 68.3, 64.9, 64.0, 39.6, 38.1, 33.1, 24.9, 20.7, 16.7; HRMS (CI) *m/z* calcd for $[C_{14}H_{20}O_3]^+$: 236.1413, found 236.1400.



Synthesis of the Iodo Ether 5: To a solution of the alcohol obtained above (98% ee, 47.0 mg, 199 μmol) in *t*BuOH (5 mL) were added pyridine (32.2 μL, 398 μmol) and iodine (106 mg, 41.8 μmol). The reaction was stirred for 12 h in the dark. Water (20 mL) and Et_2O (20 mL) were added to the yellowish solution. A few drops of sat. $Na_2S_2O_3$ solution were added until the aqueous layer decolorized. The organic layer was extracted with brine and dried over Na_2SO_4. Column chromatography [deactivated silica gel (5% NEt_3), hexane:Et_2O 8:1] gave a colorless oil (61.3 mg, 169

μmol, 85%). Colorless crystals of **5** were obtained from hexane, $[\alpha]^{20}_D$ –71.8 (*c* 1.01, $CHCl_3$); mp 81°C; FTIR (film) 2965, 2931, 2876, 1099, 1065, 981, 960 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.32 (t, 1H, *J* = 1.5 Hz), 4.36 (dd, 1H, *J* = 7.0, 4.2 Hz), 4.21 (d, 1H, *J* = 4.0 Hz), 4.04 (d, 1H, *J* = 4.4 Hz), 3.97 (m, 3H), 3.88 (m, 1H), 2.88 (q, 1H, *J* = 7.0 Hz), 2.30 (m, 2H), 2.03 (dd, 1H, *J* = 15.7, 6.6 Hz), 1.87 (d, 3H, *J* = 1.5 Hz), 1.08 (d, 3H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.0, 124.2, 109.0, 84.6, 76.8, 64.6, 64.5, 43.0, 39.6, 38.1, 32.1, 30.4, 21.1, 16.1; HRMS (EI) *m/z* calcd for $[C_{14}H_{19}O_3I]^+$: 362.0379, found 362.0366.

***Trans*-Decalin 6:** The Diels-Alder adduct **3a** (97% ee, 11.7 mg, 49.9 μmol) was dissolved in a 0.50 M solution of sodium methoxide in methanol (1 mL) and stirred for 2 d at 40°C. The reaction mixture was filtered through a small pad of silica gel (deactivated with 5% NEt_3), the solvent was removed in vacuo and the resulting yellowish oil was chromatographed [deactivated silica gel (5% NEt_3), hexane:Et_2O 2:1] to give **6** as a colorless oil (11.2 mg, 47.8 μmol, 96%). $[\alpha]^{20}_D$ +101.5 (*c* 0.64, $CHCl_3$); FTIR (film) 3022, 2956, 2926, 2886, 1681, 1153, 1125, 1051, 1035 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 6.40 (m, 1H), 5.64 (m, 1H), 5.47 (m, 1H), 4.08 (m, 3H), 3.90 (m, 1H), 2.56 (m, 1H), 2.36 (m, 2H), 2.15 (m, 2H), 1.79 (d, 3H, *J* = 1.5 Hz), 1.19 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.9, 140.6, 136.1, 132.5, 122.8, 105.9, 65.8, 65.3, 50.5, 43.7, 30.6, 22.9, 22.5, 15.9; HRMS (EI) *m/z* calcd for $[C_{14}H_{18}O_3]^+$: 234.1256, found 234.1262.

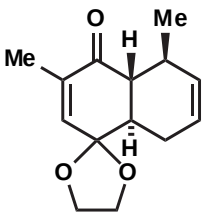


Table. Crystal data and structure refinement for **5**.

Empirical formula	$C_{14}H_{19}IO_3$	
Formula weight	362.19	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.8122 (7) Å	$\alpha = 90°$
	b = 9.8527 (8) Å	$\beta = 90°$
	c = 16.1513 (13) Å	$\gamma = 90°$
Volume	1402.3(2) $Å^3$	
Z	4	
Density (calculated)	1.716 Mg/m^3	
Absorption coefficient	2.282 mm^{-1}	
F(000)	720	
Crystal size	? x ? x ? mm^3	
θ range for data collection	2.42 to 27.78°.	
Index ranges	$-4 \le h \le 11$, $-11 \le k \le 12$, $-19 \le l \le 20$	
Reflections collected	8610	
Independent reflections	2999 [R_{int} = 0.0237]	
Completeness to θ = 27.78°	94.0 %	
Absorption correction	Empirical, SADABS	
Max. and min. transmission	0.960591 and 0.805996	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2999 / 0 / 163	
Goodness-of-fit on F^2	1.078	
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0349, wR2 = 0.0929	
R indices (all data)	R1 = 0.0382, wR2 = 0.0957	
Absolute structure parameter	-0.01(3)	
Largest diff. peak and hole	0.986 and -1.036 $e.Å^{-3}$	