Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

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Mass Spectrometric Screening of Enantioselective Diels-Alder Reactions

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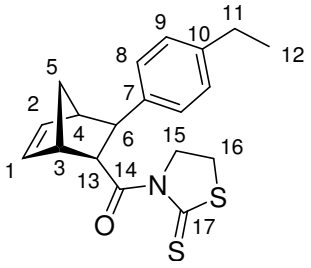
Supporting Information

General

All reactions were performed in flame-dried glassware under argon using Schlenk techniques or under purified N_2 in a glovebox (Mbraun Labmaster 130).

Air- or moisture-sensitive reagents were transferred using oven-dried gas-tight syringes or canulas and were introduced into the apparatus through septa. Solvents were distilled from calcium hydride (dichloromethane) or sodium (diethyl ether) and stored under nitrogen. Solvents were degassed by using the "freeze-pump-thaw" technique (three cycles). Reagents were purchased from Acros, Aldrich, Fluka, Strem or Lancaster and used without further purification. Column chromatography: Merck silica gel 60 (Darmstadt, 40-63 nm). For TLC analyses precoated Macherey-Nagel Polygram SIL G/UV_{254} plates were used and the compounds visualized with the help of UV light. All NMR experiments were performed on Bruker Avance 400 or 500 spectrometers. ^{1}H and ^{13}C NMR spectra are referenced relative to tetramethylsilane using the solvent residual peaks and the solvent signals, respectively, as internal standards.[1] MS spectra: VG70-250 or Finnigan MAT 95Q (EI) and MAR 312 (FAB) with 3-nitrobenzyl alcohol (NBA) as matrix. Elemental analyses were performed by the Micro Analytical Laboratory of the University of Basel. IR spectra: Perkin Elmer 1600 FTIR spectrometer. Melting points were determined on a Büchi 535 apparatus and are uncorrected. Optical rotations were measured on a Perkin Elmer polarimeter 341 equipped with a Na lamp. ESI-MS spectra were recorded on a Varian 1200L Quadrupol MS/MS spectrometer using mild desolvation conditions (copper(II)-catalyzed Dield-Alder reactions: 40 psi nebulizing gas, 4.9 kV spray voltage, 17 psi drying gas at 100 °C, 38 V capillary voltage, 1300-1800 V detector voltage; Organocatalyzed Diels-Alder reactions: 40 psi nebulizing gas, 4.9 kV spray voltage, 18 psi drying gas at 200 °C, 38 V capillary voltage, 1300-1800 V detector voltage). Every spectrum consisted of at least 25 averaged scans. Samples were diluted prior to their analysis and measured using direct injection.

***endo* 3-{[(1*S*,2*R*,3*R*,4*R*)-(4-Ethylphenyl)-bicyclo[2.2.1]hept-5-en-2-yl]carbonyl}-2-thiazolidinethione (2*R*)-1a**



(2*R*)-**1a**

According to a procedure by EVANS,[2] Cu(II)$(OTf)_2$ (72.0 mg, 0.20 mmol) and (*S,S*)-*t*Bu-box ligand **5c** (65.0 mg, 0.22 mmol) were mixed together in a glove box. After connecting the flask to a Schlenk line, dichloromethane (2 mL) was added and the green reaction mixture was stirred for 2.5 hours at r.t.. The reaction mixture was cooled to -78 °C and compound **4a** (277 mg, 1.00 mmol) in dichloromethane (2 mL) was added, immediately followed by cyclopentadiene (0.83 mL, 10.0 mmol). After 72 hours at -35 °C, ethyl acetate/Et_2O (1:1, 3 mL) was added and the mixture was directly applied to a short column (SiO_2, 1.5 × 4 cm) and eluted with Et_2O (3 × 20 mL). After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, 3 × 25 cm, ethyl acetate/hexanes 1:5) and recrystallisation (Et_2O/pentane) to give compound (2*R*)-**1a** (299 mg, 87%, *endo* ee >99%, *endo:exo* 97:3, >99% conversion) as yellow needles.

$C_{19}H_{21}NOS_2$ (343.51):

m.p. 73-74 °C (Et_2O/pentane).

$\mathbf{R_f}$ = 0.63 (ethyl acetate/hexanes 1:1).

^{1}H NMR (400.1 MHz, CD_2Cl_2): δ = 1.20 (t, ^3J = 7.8 Hz, 3 H, CH_3), 1.49 (ob. dq, ^2J = 8.6 Hz, J = 1.8 Hz, 1 H, CHC*H*HCH), 1.80 (d, ^2J = 8.6 Hz, 1 H, CHCH*H*CH), 2.59 (q, ^3J = 7.6 Hz, 2 H, CH_2CH$_3$), 2.94 (d, J = 1.5 Hz, 1 H, C*H*(4)), 3.16-3.35 (m, 3 H, PhC*H*, SCH_2), 3.53 (s, 1H, C*H*(3)), 4.46-4.50 (m, 2 H, NCH_2), 5.13 (dd, ^3J = 4.6 Hz, J = 3.3 Hz, 1H, C*H*C=O), 5.93 (dd, ^3J = 5.6 Hz, J = 2.8 Hz, 1H, C*H*(1)=CH), 6.50 (dd, ^3J = 5.8 Hz, J = 3.3 Hz, 1H, C*H*(2)=CH), 7.12 (d, ^3J = 8.3 Hz, 2 H, H_{ar}), 7.18 (d, ^3J = 8.3 Hz, 2 H, H_{ar}).

^{13}C{^{1}H} NMR (100.6 MHz, CD_2Cl_2): δ = 15.5 (CH_3, 12), 28.3 (CH_2, 11), 28.4 (CH_2, 16), 47.5 (CH_2, 5), 47.5 (CH, 3), 47.8 (CH, 6), 50.2 (CH, 4), 51.5 (CH, 13), 57.1 (CH_2, 15), 127.6 C_{ar}H), 128.0 (C_{ar}H), 132.2 (CH, 1), 140.2 (CH, 2), 141.0 (C, 10), 142.2 (C, 7), 175.6 (C, 14), 202.0 (C, 17).

IR (KBr): $\tilde{\nu}$ = 2967s, 2872m, 1699s, 1512m, 1458m, 1367s, 1328m, 1277s, 1220m, 1160s, 1049s, 826m, 761m, 702m.

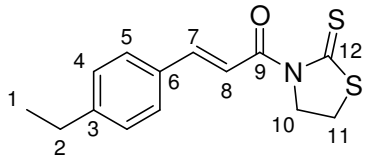
MS (FAB, NBA (subtr)), *m/z* (%): 344 ([M+H]$^+$, 20), 277 (20), 225 (10), 159 (100).

$[\alpha]_D^{20}$ = −157.3 (c = 0.50, dichloromethane).

EA calcd (%) for $C_{19}H_{21}NOS_2$: C, 66.44; H, 6.16; N, 4.08. Found: C, 66.25; H, 6.23; N, 3.89.

HPLC: Chiralcel OD-H, i-propanol/heptane (5:95), 0.5 mL/min, 20 °C, 210 nm, t_R = 21.8 min (major), t_R = 48.2 min (minor).

3-[(*E*)-3-(4-Ethylphenyl)-2-propenoyl]-2-thiazolidinethione 4a



4a

According to a procedure by EVANS,[2] oxalyl chloride (0.28 mL, 3.30 mmol) and *N,N*-dimethylformamide (0.02 mL, 0.25 mmol) were added dropwise to compound **11** (see below) (290 mg, 1.65 mmol) in dichloromethane (7 mL) at 0 °C. After stirring for 3 hours at ambient temperature, the solvent and excess oxalyl chloride were removed under reduced pressure. The remaining off-white solid was dissolved in dichloromethane (4 mL) and cooled to -78 °C. 2-Thiazolidinethione (197 mg, 1.65 mmol) was added, followed by dropwise addition of triethylamine (0.25 mL, 1.82 mmol). The reaction mixture became bright yellow and a suspension formed. After stirring for 30 min at -78 °C and 30 min at 0 °C the transparent yellow solution was diluted with Et_2O (10 mL), washed with saturated aqueous $NaHCO_3$ (10 mL) and water (10 mL). Drying (Na_2SO_4) and removal of the solvent under reduced pressure gave a yellow oil. The crude product was purified by column chromatography (SiO_2, 2 × 12 cm, ethyl acetate/hexanes 1:4) followed by recrystallization (dichloromethane/pentane) to give compound **4a** (309 mg, 68%) as a yellow amorphous solid.

$C_{14}H_{15}NOS_2$ (277.41):

m.p. 65-66 °C (ethyl acetate/hexanes).

R_f = 0.27 (ethyl acetate/hexanes 1:4).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.6 Hz, 3 H, CH_3), 2.66 (q, ^3J = 7.6 Hz, 2 H, CH_2CH$_3$), 3.37 (t, ^3J = 7.6 Hz, 2 H, SCH_2), 4.59 (t, ^3J = 7.3 Hz, 2 H, NCH_2), 7.22 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.48 (d, ^3J = 7.8 Hz, 2 H, H_{ar}), 7.68 (d, $^3J_{trans}$ = 15.6 Hz, 1 H, CHC=O), 7.84 (d, $^3J_{trans}$ = 15.4 Hz, 1 H, C_6H_4CH).

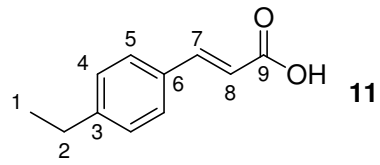
^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 15.3 (CH_3, 1), 28.8 (CH_2, 2), 29.1 (CH_2, 11), 56.0 (CH_2, 10), 118.9 (CH, 8), 128.5 (C_{ar}H), 128.7 (C_{ar}H), 132.2 (C, 6), 144.3 (CH, 7), 147.4 (C, 3), 167.4 (C, 9), 201.7 (C, 12).

IR (KBr): $\tilde{\nu}$ = 2922m, 1681s, 1611s, 1374m, 1325s, 1283m, 1163s, 1049m, 819m, 676m.

MS (EI, 70 eV, 100 °C), *m*/*z* (%): 277 ([M]$^+$, 39), 159 (100), 131 (22), 115 (14), 91([C_7H_7]$^+$, 10).

EA calcd (%) for $C_{14}H_{15}NOS_2$: C, 60.62; H, 5.45; N, 5.05; O, 5.77. Found: C, 60.67; H, 5.47; N, 5.05; O, 5.90.

(*E*)-3-(4-Ethylphenyl)-acrylic acid 11



11

Ethyl ester **12** (1.00 mg, 4.90 mmol) (see below) was dissolved in 1 M aqueous NaOH (19.6 mL, 19.6 mmol) and ethanol (40 mL) and the reaction mixture was heated at reflux for 4 hours. After cooling, the solvent was removed under reduced pressure and the remaining white slurry was completely dissolved in water. The pH-value of the solution was reduced to 1 with conc. HCl and the aqueous phase was extracted with Et_2O (5 × 80 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and the solvent was removed under reduced pressure to give compound **11** (0.860 g, 99%) as an amorphous colorless solid.

$C_{11}H_{12}O_2$ (176.21):

m.p. 155.5-156.5 °C (Et_2O).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.25 (t, ^3J = 7.6 Hz, 3 H, CH_2CH_3), 2.68 (q, ^3J = 7.6 Hz, 2 H, CH_2CH_3), 6.42 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, CHC=O), 7.24 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.48 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.77 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C_6H_4CH).

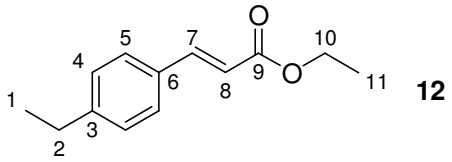
^{13}C{^{1}H}NMR (100.6 MHz, $CDCl_3$): δ = 15.3 (CH_3, 1), 28.8 (CH_2, 2), 116.1 (CH, 8), 128.5 ($C_{ar}H$, 4), 128.5 ($C_{ar}H$, 5), 131.5 (C, 6), 147.2 (CH, 7), 147.6 (C, 3), 172.2 (C, 9).

IR (KBr): $\tilde{\nu}$ = 2958s, 1675s, 1628s, 1513m, 1426s, 1320s, 1291s, 1226s, 1180s, 942s, 822s, 687s, 546s.

MS (EI, 70 eV, r.t.), *m*/*z* (%): 176 ([M]$^+$, 97), 161 ([M$^-$$CH_3$]$^+$, 100), 147 ([M$^-$$C_2H_5$]$^+$, 17), 131 ([M]$^+$, 16), 115 (33), 91 ([$C_7H_7$]$^+$, 10).

EA calcd (%) for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86; O, 18.16. Found: C, 74.81; H, 6.86; O, 18.21.

(*E*)-Ethyl 3-(4-ethylphenyl)-acrylate 12



12

According to a procedure by SCHULTZ,[3] $Pd(PPh_3)_4$ (32.2 mg, 28.0 µmol) in *N,N*-dimethylacetamide (10 mL) was added to a solution of 1-ethyl-4-iodobenzene (6.00 g, 26.0 mmol), ethyl acrylate (3.15 mL, 29.0 mmol) and sodium acetate (2.87 g, 35.0 mmol) in *N,N*-dimethylacetamide (80 mL) at 140 °C. After 24 hours at this temperature, the reaction mixture was cooled to r.t. and diluted with hexanes (250 ml). The solution was washed with water (3 × 150 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, 8 × 20 cm, ethyl acetate/hexanes 1:10) to give compound **12** (3.24 g, 61%) as a colorless oil.

$C_{13}H_{16}O_2$ (204.26):

R_f = 0.45 (ethyl acetate/pentane 1:10).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.32 (t, ^3J = 7.1 Hz, 3 H, CH_3), 2.66 (q, ^3J = 7.6 Hz, 2 H, CH_2CH$_3$), 4.26 (q, ^3J = 7.1 Hz, 2 H, OCH_2CH$_3$), 6.39 (d, $^3J_{trans}$ = 16.2 Hz, 1 H, C*H*C=O), 7.21 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.45 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.67 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C_6H_4C*H*).

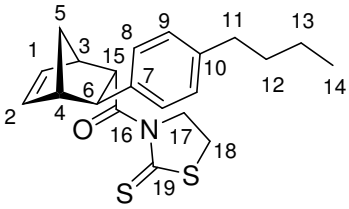
^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 14.3 (CH_3, 1), 15.3 (CH_3, 11), 28.8 (CH_2, 2), 60.4 (CH_2, 10), 117.2 (CH, 8), 128.1 (C_{ar}H, 4), 128.4 (C_{ar}H, 5), 131.9 (C, 6), 144.6 (CH, 7), 146.9 (C, 3), 167.2 (C, 9).

MS (EI, 70 eV, r.t.), *m*/*z* (%): 204 ($[M]^+$, 75), 189 ($[M^-CH_3]^+$, 11), 176 ($[M]^+$, 22), 159 ($[M^-C_2H_5O]^+$, 100), 131 ($[M^-C_3H_3O_2]^+$, 45), 115 (31), 91 ($[C_7H_7]^+$, 16).

IR (NaCl): $\tilde{\nu}$ = 2967s, 1724s, 1633s, 1568m, 1513s, 1456m, 1418m, 1366s, 1318s, 1262s, 1037s, 984s, 828s.

EA calcd (%) for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89; O, 15.66. Found: C, 76.16; H, 7.90; O, 15.89.

***endo* 3-{[(1*R*,2*S*,3*S*,4*S*)-(4-*n*-Butylphenyl)-bicyclo[2.2.1]hept-5-en-2-yl]carbonyl}-2-thiazolidinethione (2*S*)-1b**



(2*S*)-**1b**

According to a procedure by EVANS,[2] Cu(II)(OTf)$_2$ (72.0 mg, 0.20 mmol) and (*R,R*)-*t*Bu-box ligand **5c** (65.0 mg, 0.22 mmol) were mixed together in a glove box. After connecting the flask to a Schlenk line, dichloromethane (2 mL) was added and the green reaction mixture was stirred for 2.5 hours at r.t.. The reaction mixture was cooled to -78 °C and compound **4b** (305 mg, 1.00 mmol) in dichloromethane (2 mL) was added, immediately followed by cyclopentadiene (0.83 mL, 10.0 mmol). After 72 hours at -35 °C, ethyl acetate/Et$_2$O (1:1, 3 mL) was added and the mixture was directly applied to a short column (SiO$_2$, 1.5 × 4 cm) and eluted with Et$_2$O (3 × 20 mL). After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography (SiO$_2$, 3 × 25 cm, ethyl acetate/hexanes 1:5) and recrystallisation (Et$_2$O/pentane) to give compound (2*S*)-**1b** (245 mg, 66%, *endo* ee >99%, *endo:exo* 97:3, 100% conversion) as yellow needles.

$C_{21}H_{25}NOS_2$ (371.56):

m.p. 66-67 °C (Et$_2$O/pentane).

R$_f$ = 0.69 (ethyl acetate/hexanes 1:1).

^{1}H NMR (400.1 MHz, CD_2Cl_2): δ = 0.92 (t, ^3J = 7.3 Hz, 3 H, C*H*$_3$), 1.34 (sext, ^3J = 7.3 Hz, C*H*$_2$CH$_3$), 1.48 (ob. dq, ^2J = 8.8 Hz, J = 1.8 Hz, 1 H, CHCH*H*CH), 1.54-1.60 (m, 2 H, C*H*$_2$CH$_2$CH$_3$), 1.80 (d, ^2J = 8.8 Hz, 1 H, CHC*H*HCH), 2.56 (t, ^3J = 7.8 Hz, 2 H, C*H*$_2$CH$_2$ CH$_2$CH$_3$), 2.94 (m, 1 H, C*H*(4)), 3.16-3.33 (m, 2 H, SC*H*$_2$), 3.27 (dd, ^3J = 5.5 Hz, J = 1.5 Hz, 1 H, PhC*H*), 3.53 (m, 1 H, C*H*(3)), 4.46-4.50 (m, 2 H, NC*H*$_2$), 5.13 (dd, ^3J = 5.3 Hz, J = 3.6 Hz, 1H, C*HC*=O), 5.92 (dd, ^3J = 5.6 Hz, J = 2.8 Hz, 1H, C*H*(1)=CH), 6.50 (dd, ^3J = 5.6 Hz, J = 3.0 Hz, 1H, C*H*(2)=CH), 7.10 (d, ^3J = 8.4 Hz, 2 H, H_{ar}), 7.17 (d, ^3J = 7.8 Hz, 2 H, H_{ar}).

^{13}C{^{1}H} NMR (100.6 MHz, CD_2Cl_2): δ = 13.8 (CH_3, 14), 22.5 (CH_2, 13), 28.3 (CH_2, 18), 33.8 (CH_2, 12), 35.1 (CH_2, 11), 47.5 (CH, 3), 47.5 (CH_2, 5), 47.8 (CH, 6), 50.3 (CH, 4), 51.4 (CH, 15), 57.1 (CH_2, 17), 127.5 ($C_{ar}H$), 128.5 ($C_{ar}H$), 132.2 (CH, 1), 140.2 (CH, 2), 140.9 (C, 10), 140.9 (C, 7), 175.6 (C, 16), 202.0 (C, 19).

IR (KBr): $\tilde{\nu}$ = 2924m, 1686s, 1511m, 1458m, 1368s, 1264s, 1170s, 1037s, 820m, 764m, 701s.

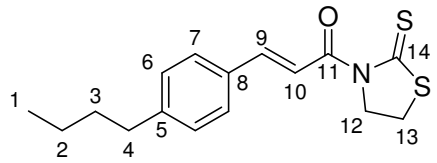
MS (EI, 70eV, ca. 150 °C), *m*/*z* (%): 337 ([M-H_2S]$^+$, 6), 305 (46), 187 (100), 131 (19), 115 (16), 66 (5), 57 ([C_4H_9]$^+$, 5).

$[\alpha]_D^{20}$ = +176.6 (c = 0.51, dichloromethane).

EA calcd (%) for $C_{21}H_{25}NOS_2$: C, 67.89; H, 6.78; N, 3.77. Found: C, 67.87; H, 6.70; N, 3.86.

HPLC: Chiralcel OD-H, i-propanol/heptane (5:95), 0.5 mL/min, 20 °C, 210 nm, t_R = 19.3 min (major), t_R = 43.8 min (minor).

3-[(*E*)-3-(4-*n*-Butylphenyl)-2-propenoyl]-2-thiazolidinethione 4b



4b

According to a procedure by EVANS,[2] oxalyl chloride (1.27 mL, 15.0 mmol) and *N,N*-dimethylformamide (0.02 mL, 0.25 mmol) were added dropwise to compound **13** (see below) (1.22 g, 6.00 mmol) in dichloromethane (24 mL) at 0 °C. After stirring for 3 hours at ambient temperature, the solvent and excess oxalyl chloride were removed under reduced pressure. The remaining off-white solid was dissolved in dichloromethane (15 mL) and cooled to -78 °C. 2-Thiazolidinethione (715 mg, 6.00 mmol) was added, followed by dropwise addition of triethylamine (0.90 mL, 6.60 mmol). The reaction mixture became bright yellow and a suspension formed. After stirring for 30 min at -78 °C and 30 min at 0 °C the transparent yellow solution was diluted with Et_2O (20 mL), washed with saturated aqueous $NaHCO_3$ (20 mL) and water (20 mL). Drying (Na_2SO_4) and removal of the solvent under reduced pressure gave a yellow oil. The crude product was purified by column chromatography (SiO_2, 5 × 12 cm, ethyl acetate/hexanes 1:4) followed by recrystallization (dichloromethane/pentane) to give compound **4b** (1.28 g, 70%) as yellow prisms.

$C_{16}H_{19}NOS_2$ (305.46):

m.p. 59.0-60.5 °C (dichloromethane/pentane).

R_f =0.70 (ethyl acetate/hexanes 1:1).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.35 (sext, ^3J = 7.6 Hz, 2 H, CH_2CH$_3$), 1.56-1.64 (m, 2 H, CH_2CH$_2$CH$_3$), 2.63 (t, ^3J = 7.6 Hz, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 3.37 (t, ^3J = 7.3 Hz, 2 H, SCH_2), 4.59 (t, ^3J = 7.3Hz, 2 H, NCH_2), 7.20 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.47 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.68 (d, $^3J_{trans}$ = 15.6 Hz, 1 H, CHC=O), 7.83 (d, $^3J_{trans}$ = 15.4 Hz, 1 H, C_6H_4CH).

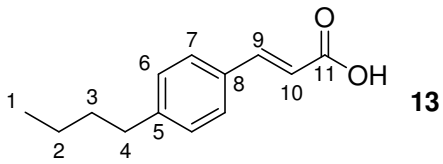
$^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ = 13.9 (CH_3, 1), 22.3 (CH_2, 2), 29.1 (CH_2, 3), 33.3 (CH_2, 4), 35.6 (CH_2, 13), 56.0 (CH_2, 12), 118.8 (CH, 10), 128.6 ($C_{ar}H$), 129.0 ($C_{ar}H$), 132.2 (C, 8), 144.4 (CH, 9), 146.1 (C, 5), 167.5 (C, 11), 201.7 (C, 14).

IR (KBr): $\tilde{\nu}$ = 2943s, 1674s, 1597s, 1510m, 1461m, 1326s, 1262s, 1220s, 1151s, 1056s, 823s, 718s.

MS (EI, 70 eV, 150 °C), *m/z* (%): 305 ($[M]^+$, 39), 187 (100), 131 (25), 115 (19), 57 ($[C_4H_9]^+$, 6).

EA calcd (%) for $C_{16}H_{19}NOS_2$: C, 62.92; H, 6.27; N, 4.59. Found: C, 62.82; H, 6.27; N, 4.57.

(*E*)-3-(4-*n*-Butylphenyl)-acrylic acid 13



13

Butyl ester **14** (5.60 g, 21.5 mmol) was dissolved in 1 M aqueous NaOH (86.2 mL, 86.2 mmol) and ethanol (180 mL) and the reaction mixture was heated at reflux for 4 hours. After cooling, the solvent was removed under reduced pressure and the remaining white slurry was completely dissolved in water. The pH-value of the solution was reduced to 1 with conc. HCl and the aqueous phase was extracted with Et_2O (5 × 100 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and the solvent was removed under reduced pressure to give compound **13** (4.29 g, 97%) as a colorless crystalline solid.

$C_{13}H_{16}O_2$ (204.26):

m.p. 137-138 °C (ethanol).

R_f = 0.20 (ethyl acetate/hexanes 1:3).

^1H NMR (400.1 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.35 (sext, ^3J = 7.8 Hz, 2 H, CH_2CH$_3$), 1.57-1.65 (m, 2 H, CH_2CH$_2$CH$_3$), 2.64 (t, ^3J = 7.6 Hz, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 6.41 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C*H*C=O), 7.21 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.47 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.77 (d, $^3J_{trans}$= 15.9 Hz, 1 H, C_6H_4C*H*).

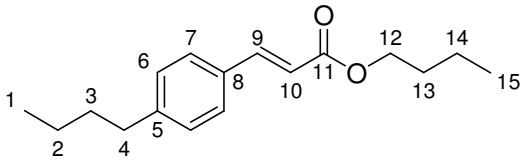
$^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ = 13.9 (CH_3, 1), 22.3 (CH_2, 2), 33.3 (CH_2, 3), 35.6 (CH_2, 4), 116.0 (CH, 10), 128.4 ($C_{ar}H$), 129.1 ($C_{ar}H$), 131.5 (C, 8), 146.3 (C, 5), 147.1 (CH, 9), 171.9 (C, 11).

IR (KBr): $\tilde{\nu}$ = 3448s, 2926s, 2586m, 1685s, 1623s, 1511m, 1422s, 1314s, 1281m, 1222m, 939s, 810m.

MS (EI, 70 eV, ca. 100 °C), *m/z* (%): 204 ($[M]^+$, 43), 161 ($[M^-C_3H_7]^+$, 100), 115 (17).

EA calcd (%) for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89. Found: C, 76.32; H, 7.88.

(*E*)-*n*-Butyl 3-(4-*n*-butylphenyl)-acrylate 14



14

According to a procedure by SCHULTZ,[3] $Pd(PPh_3)_4$ (41.0 mg, 35.0 µmol) in *N,N*-dimethylacetamide (10 mL) was added to a solution of 1-butyl-4-iodobenzene (6.22 g, 35.0 mmol), *n*-butyl acrylate (6.00 mL, 42.0 mmol) and sodium acetate (4.02 g, 49.0 mmol) in *N,N*-dimethylacetamide (110 mL) at 140 °C. After 24 hours at this temperature, the reaction mixture was cooled to room temperature and diluted with hexanes (250 ml). The solution was washed with water (3 × 150 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, 5 × 20 cm, ethyl acetate/hexanes 1:10) to give compound **14** (5.60 g, 62%) as a colorless transparent oil.

$C_{17}H_{24}O_2$ (260.37):

R_f = 0.77 (ethyl acetate/hexanes 1:3).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, CH_3), 0.97 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.31-1.49 (m, 4 H, CH_2CH$_3$), 1.56-1.72 (m, 4 H, CH_2CH$_2$CH$_3$), 2.62 (t, ^3J = 7.6 Hz, 2 H, C_6H_4CH_2), 4.20 (t, ^3J = 6.8 Hz, 2 H, OCH_2), 6.39 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C*H*C=O), 7.19 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.44 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.66 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C_6H_4C*H*).

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 13.7 (CH_3), 13.9 (CH_3),19.2 (CH_2, 14), 22.3 (CH_2, 2), 30.8 (CH_2, 13), 33.4 (CH_2, 3), 35.5 (CH_2, 4), 64.3 (CH_2, 12), 117.2 (CH, 10), 128 (C_{ar}H,), 128.9 (C_{ar}H,), 131.9 (C, 8), 144.6 (CH, 9), 145.6 (C, 5), 167.3 (C, 11).

IR (NaCl): $\tilde{\nu}$ = 2958s, 1713s, 1637s, 1462m, 1315s, 1269m, 1169s, 984s, 827m.

MS (EI, 70 eV, ca. 50 °C), *m/z* (%): 260 ($[M]^+$, 34), 217 ($[M^-C_3H_7]^+$, 19), 204 ($[M^-C_4H_8]^+$, 100), 187 (46), 161 (57), 131 (18), 115 (27), 91 (4), 41 (8).

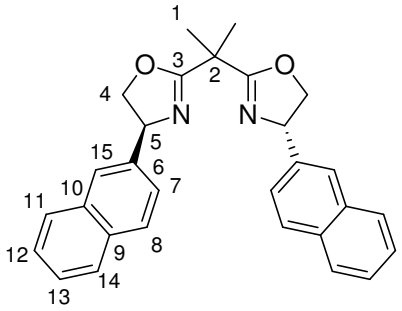
EA calcd (%) for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.41; H, 9.33.

The spectroscopic data are in agreement with that previously reported in the literature.[4]

Box ligand synthesis

The box ligands were prepared according to a procedure by EVANS.[5]

2,2-Bis{2-[4(*S*)-(2'-naphthyl)-1,3-oxazolinyl]}propane 5a



5a

Ligand **5a** was obtained as a colorless amorphous solid in 58% yield.

$C_{29}H_{26}N_2O_2$ (434.53):

m.p. 170-172 °C (Et_2O) [lit.,[6] 173-174 °C].

R_f = 0.30 (ethyl acetate/hexanes 1:1).

^{1}H NMR (400.1 MHz, CD_2Cl_2): δ = 1.70 (s, 6 H, CH_3), 4.24 (dd, ^3J = 8.4 Hz, ^3J = 7.6 Hz, 2 H, C*H*), 4.75 (dd, ^2J = 10.1 Hz, ^3J = 8.6 Hz, 2 H, C*H*H), 5.39 (dd, ^2J = 10.1 Hz, ^3J = 7.6 Hz, 2 H, C*H*H), 7.38-7.48 (m, 6 H, H_{ar}), 7.73-7.83 (m, 8 H, H_{ar}).

^{13}C{^{1}H} NMR (100.6 MHz, CD_2Cl_2): δ = 24.3 (CH_3, 1), 39.1 (C, 2), 69.8 (CH, 5), 75.3 (CH_2, 4), 124.8 ($C_{ar}H$), 125.5 ($C_{ar}H$), 125.9 ($C_{ar}H$), 126.2 ($C_{ar}H$), 127.6 ($C_{ar}H$), 127.9 ($C_{ar}H$), 128.6 ($C_{ar}H$), 132.9 (C_{ar}), 133.4 (C_{ar}), 140.2 (C_{ar}), 170.4 (C, 3).

IR (KBr): $\tilde{\nu}$ = 3352 bs, 2933s, 1714m, 1425s, 1347s, 1056s.

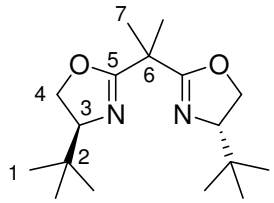
MS (EI, 70 eV, ca. 250 °C), *m*/*z* (%): 434 ([M]$^+$, 53), 307 (8), 265 (20), 239 (100), 154 (100), 69 (13), 41 (7).

[α]$_D^{20}$ = −240.0 (c = 0.22, CH_2Cl_2, >99% ee) [lit.,[6] −232.5 (c = 0.55, $CHCl_3$)].

HPLC: Chiralcel AD, i-propanol/heptane (20:80), 1.00 mL/min, 20 °C, 220 nm, t_R = 7.7 min (major).

The spectroscopic data are in agreement with that previously reported in the literature.[6]

2,2-Bis{2-[4(*S*)-*t*-butyl-1,3-oxazolinyl]}propane 5c[5]



5c

Ligand **5c** was obtained as colorless plates in 73% yield.

$C_{17}H_{30}N_2O_2$ (294.43):

m.p. 86-87 °C (pentane) [lit.,[5] 88.9-89.8 °C].

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.86 (s, 18 H, CH_3), 1.50 (s, 6 H, CH_3), 3.84 (dd, ^3J = 10.0 Hz, ^3J = 7.0 Hz, 2 H, C*H*), 4.05-4.16 (m, 4 H, CH_2).

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 24.4 (CH_3, 7), 25.6 (CH_3, 1), 33.9 (C, 2), 38.6 (C, 6), 69.0 (CH_2, 4), 75.3 (CH, 5), 168.6 (C, 5).

IR (KBr): $\tilde{\nu}$ = 2956s, 2870m, 1660s, 1478s, 1360s, 1259s, 1146s, 1123s, 978s, 925s.

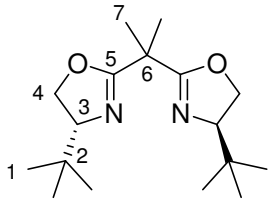
MS (FAB, NBA (subtr)), *m*/*z* (%): 295 ([M+H]$^+$, 100), 237 (11), 195 (11), 169 (13), 57 (31), 41 (22).

$[\alpha]_D^{20}$ = −128.20 (c = 0.61, MeOH) [lit.,[5] +113.2 (c = 1.22, dichloromethane)].

EA calcd (%) for $C_{17}H_{30}N_2O_2$: C, 69.35; H, 10.27; N, 9.51; O, 10.87. Found: C, 69.32; H, 10.13; N, 9.43; O, 10.97.

The spectroscopic data are in agreement with that previously reported in the literature.[5]

2,2-Bis{2-[4(*R*)-*t*-butyl-1,3-oxazolinyl]}propane (*R*)-5c

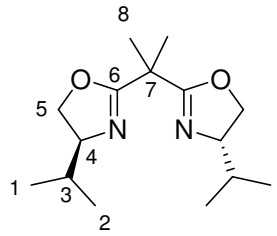


(*R*)-**5c**

Ligand (*R*)-**5c** was obtained as colorless plates in 91% yield.

$[\alpha]_D^{20}$ = +100.0 (c = 0.25, dichloromethane).

2,2-Bis{2-[4(*S*)-i-propyll-1,3-oxazolinyl]}propane 5d



5d

Ligand **5d** was obtained as a colorless transparent oil in 93% yield.

$C_{15}H_{26}N_2O_2$ (266.38):

^{1}H NMR (400.1 MHz, CD_2Cl_2): δ = 0.83 (d, ^3J = 6.8 Hz, 6 H, CHCH_3), 0.90 (d, ^3J = 6.8 Hz, 6 H, CHCH_3), 1.44 (s, 6 H, CH_3), 1.66-1.77 (m, 2 H, CHCH$_3$), 3.85-3.97 (m, 4 H, CH_2), 4.16-4.21 (m, 2 H, NCH).

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 17.6 (CH_3, 1/2), 18.3 (CH_3, 1/2), 24.3 (CH_3, 8), 32.5 (CH, 3), 38.6 (C, 7), 70.2 (CH_2, 5), 71.8 (CH, 4), 168.5 (C, 6).

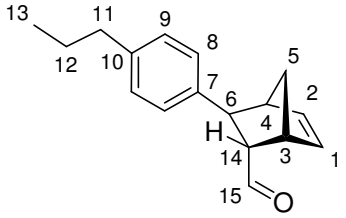
IR (NaCl): $\tilde{\nu}$ = 2960s, 1662s, 1467s, 1353m, 1248m, 1144s, 1112s, 980s, 925m.

MS (FAB, NBA (subtr)), *m/z* (%): 267 ([M+H]$^+$, 100), 181 (15), 155 (13), 69 (21), 41 (22).

$[\alpha]_D^{20}$ = −125.6 (c = 1.09, CH_2Cl_2).

The spectroscopic data are in agreement with that previously reported in the literature.[7]

***endo* 3-[(1*R*,2*S*,3*S*,4*S*)-(4-*n*-Propylphenyl)-bicyclo[2.2.1]hept-5-ene]-2-carbaldehyde (2*S*)-7a**



(2*S*)-**7a**

According to a procedure by IZAWA and MUKAIYAMA,[8, 9] compound (2*S*)-**15** (28.0 mg, 78.7 µmol) (see below) was added in one portion to a solution of diisobutylaluminium hydride (1.7 M in toluene, 0.06 mL, 94.0 µmol) in toluene (0.4 mL) at -78 °C. An extra 0.3 mL of toluene were added to dissolve all solid. After stirring for 20 minutes at -78 °C and 3 hours at -20 °C the reaction mixture was quenched with 1 M H_2SO_4 (0.2 mL), diluted with dichloromethane (10 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a colorless oil. The crude product was purified by flash column chromatography (SiO_2, 1 × 10 cm, ethyl acetate/hexanes 1:4) to give compound (2*S*)-**7a** (16 mg, 85%) as a colorless oil.

$C_{17}H_{20}O$ (240.34):

R_f = 0.81 (ethyl acetate/hexanes 1:4).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.94 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.60 (m, 3 H, CH_2CH$_3$, CHCH*H*CH), 1.81 (d, ^3J = 8.8 Hz, 1 H, CHC*H*HCH), 2.56 (t, ^3J = 7.3 Hz, 2 H, CH_2CH$_2$CH$_3$), 2.97-2.99 (m, 1 H, C*H*C(=O)H), 3.05 (d, ^3J = 4.0 Hz, 1 H, PhC*H*), 3.09-3.10 (m, 1 H, C*H*(4)), 3.32 (s, 1 H, C*H*(3)), 6.16 (dd, ^3J = 5.8 Hz, J = 2.8 Hz, 1H, C*H*(1)=CH), 6.41 (dd, ^3J = 5.8 Hz, J = 3.3 Hz, 1H, C*H*(2)=CH), 7.12 (d, ^3J = 8.3 Hz, 2 H, H_{ar}), 7.17 (d, ^3J = 7.8 Hz, 2 H, H_{ar}), 9.59 (d, ^3J = 2.3 Hz, 1 H, C*H*=O).

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 13.9 (CH_3, 13), 24.5 (CH_2, 12), 37.5 (CH_2, 11), 45.1 (CH, 3), 45.4 (CH, 6), 47.1 (CH_2, 5), 48.5 (CH, 4), 60.8 (CH, 14), 127.2 ($C_{ar}H$), 128.6 ($C_{ar}H$), 133.7 (CH, 1), 139.2 (CH, 2), 140.6 (C, 7), 140.7 (C, 10), 203.7 (C, 15).

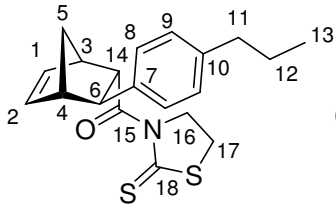
IR (NaCl): $\tilde{\nu}$ = 2962s, 2711m, 1718s, 1513s, 1332m.

MS (EI, 70eV, r.t.), *m/z* (%): 175 ([M-C_5H_5]$^+$, 44), 131 ([M-C_9H_{14}]$^+$, 100), 117 (8), 66 (17).

$[\alpha]_D^{20}$ = +103.0 (c = 0.20, dichloromethane).

EA calcd (%) for $C_{17}H_{20}O$: C, 84.96; H, 8.39. Found: C, 84.95; H, 8.57.

***endo* 3-{[(1*R*,2*S*,3*S*,4*S*)-(4-*n*-Propylphenyl)-bicyclo[2.2.1]hept-5-en-2-yl]carbonyl}-2-thiazolidinethione (2*S*)-15**



(2*S*)-**15**

According to a procedure by EVANS,[2] Cu(II)$(OTf)_2$ (36.0 mg, 0.10 mmol) and (*R,R*)-*t*Bu-box ligand **5c** (32.0 mg, 0.11 mmol) were mixed together in a glove box. After connecting the flask to a Schlenk line, dichloromethane (1 mL) was added and the green reaction mixture was stirred for 2.5 hours at r.t.. The reaction mixture was cooled to -78 °C and compound **16** (146 mg, 0.50 mmol) (see below) in dichloromethane (1 mL) was added, immediately followed by cyclopentadiene (0.42 mL, 5.0 mmol). After 72 hours at -35 °C, ethyl acetate/Et_2O (1:1, 3 mL) was added and the mixture was directly applied to a short column (SiO_2, 1 × 4 cm) and eluated with Et_2O (3 × 20 mL). After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography (SiO_2, 2 × 20 cm, ethyl acetate/hexanes 1:5) and recrystallisation (Et_2O/pentane) to give compound (2*S*)-**15** (127 mg, 71%, *endo* ee >99%, *endo:exo* 97:3, 100% conversion) as yellow needles.

$C_{20}H_{23}NOS_2$ (357.53):

m.p. 95-96 °C (Et_2O/pentane).

$\mathbf{R_f}$ = 0.69 (ethyl acetate/hexanes 1:1).

^{1}H NMR (400.1 MHz, CD_2Cl_2): δ = 0.93 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.49 (ob. dq, ^2J = 8.8 Hz, ^3J = 3.5 Hz, ^3J = 1.8 Hz, 1 H, CHCH*H*CH), 1.69 (sext, ^3J = 7.6 Hz, CH_2CH$_3$), 1.80 (d, ^2J = 8.6 Hz, 1 H, CHC*H*HCH), 2.54 (t, ^3J = 7.6 Hz, 2 H, CH_2CH$_2$CH$_3$), 2.94 (d, ^3J = 1.5 Hz, 1 H, C*H*(4)), 3.16-3.35 (m, 2 H, SCH_2), 3.27 (dd, ^3J = 4.8 Hz, J = 1.3 Hz,, 1 H, PhC*H*), 3.54 (s, 1 H, C*H*(3)), 4.46-4.50 (m, 2 H, NCH_2), 5.13 (dd, ^3J = 5.1 Hz, J = 3.6 Hz, 1H, C*H*C=O), 5.92 (dd, ^3J = 5.5 Hz, J = 2.8 Hz, 1H, C*H*(1)=CH), 6.51 (dd, ^3J = 5.6 Hz, J = 3.0 Hz, 1H, C*H*(2)=CH), 7.19 (d, ^3J = 8.3 Hz, 2 H, H_{ar}), 7.17 (d, ^3J = 8.1 Hz, 2 H, H_{ar}).

^{13}C{^{1}H} NMR (100.6 MHz, CD_2Cl_2): δ = 13.7 (CH_3, 13), 24.7 (CH_2, 12), 28.3 (CH_2, 17), 37.5 (CH_2, 11), 47.5 (CH, 3), 47.5 (CH_2, 5), 47.8 (CH, 6), 50.3 (CH, 4), 51.4 (CH, 14), 57.1 (CH_2, 16), 127.5 ($C_{ar}H$), 128.5 ($C_{ar}H$), 132.2 (CH, 1), 140.2 (CH, 2), 140. 7 (C, 10), 141.0 (C, 7), 175.6 (C, 15), 202.0 (C, 18).

IR (KBr): $\tilde{\nu}$ = 2950s, 1712s, 1511m, 1459m, 1432m, 1364s, 1327s, 1278s, 1215s, 1154s, 1027s, 803s, 755s, 707s.

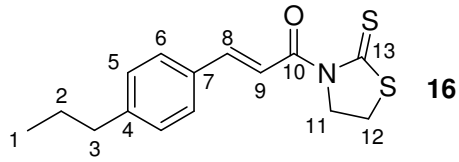
MS (FAB, NBA (subtr)), *m/z* (%): 358 ([M+H]$^+$, 40), 291 ([M-C_5H_6]$^+$, 26), 239 (24), 173 ([291-C_9H_{10}]$^+$, 100), 91 (9), 43 ([C_3H_7]$^+$, 11).

$[\alpha]_D^{20}$ = +188.9 (c = 0.49, dichloromethane).

EA calcd (%) for $C_{20}H_{23}NOS_2$: C, 67.19; H, 6.48; N, 3.93. Found: C, 67.00; H, 6.57; N, 3.93.

HPLC: Chiralcel OD-H, i-propanol/heptane (5:95), 0.5 mL/min, 20 °C, 210 nm, t_R = 19.0 min (minor), t_R = 39.7 min (major).

3-[(*E*)-3-(4-*n*-Propylphenyl)-2-propenoyl]-2-thiazolidinethione 16



16

According to a procedure by EVANS,[2] oxalyl chloride (1.39 mL, 16.4 mmol) and *N,N*-dimethylformamide (0.02 mL, 0.25 mmol) were added dropwise to compound **17** (1.56 g, 8.21 mmol) (see below) in dichloromethane (27 mL) at 0 °C. After stirring for 3 hours at ambient temperature, the solvent and excess oxalyl chloride were removed under reduced pressure. The remaining off-white solid was dissolved in dichloromethane (20 mL) and cooled to -78 °C. 2-Thiazolidinethione (979 mg, 8.21 mmol) was added, followed by dropwise addition of triethylamine (1.26 mL, 9.03 mmol). The reaction mixture became

bright yellow and a suspension formed. After stirring for 30 min at -78 °C and 30 min at 0 °C the transparent yellow solution was diluted with Et_2O (20 mL), washed with saturated aqueous $NaHCO_3$ (20 mL) and water (20 mL). Drying (Na_2SO_4) and removal of the solvent under reduced pressure gave a yellow oil. The crude product was purified by column chromatography (SiO_2, 5 × 12 cm, ethyl acetate/hexanes 1:4) followed by recrystallization (dichloromethane/pentane) to give compound **16** (1.21 g, 51%) as yellow prisms.

$C_{15}H_{17}NOS_2$ (291.43):

m.p. 77.5-78.5 °C (dichloromethane/pentane).

$\mathbf{R_f}$ = 0.52 (ethyl acetate/hexanes 1:1).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.94 (t, ^3J = 7.3 Hz, 3 H, CH_2CH_3), 1.64 (sext, ^3J = 7.3 Hz, 2 H, CH_2CH_3), 2.60 (t, ^3J = 7.3 Hz, 2 H, $CH_2CH_2CH_3$), 3.37 (t, ^3J = 7.6 Hz, 2 H, SCH_2), 4.59 (t, ^3J = 7.6Hz, 2 H, NCH_2), 7.20 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.48 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.69 (d, $^3J_{trans}$ = 15.4 Hz, 1 H, CHC=O), 7.84 (d, $^3J_{trans}$ = 15.4 Hz, 1 H, C_6H_4CH).

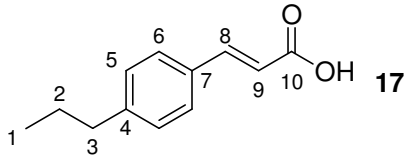
^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 13.8 (CH_3, 1), 24.3 (CH_2, 2), 29.1 (CH_2, 3), 38.0 (CH_2, 12), 56.0 (CH_2, 11), 118.8 (CH, 9), 128.6 ($C_{ar}H$), 129.1 ($C_{ar}H$), 132.3 (C, 7), 144.4 (CH, 8), 145.9 (C, 4), 167.5 (C, 10), 201.7 (C, 13).

IR (KBr): $\tilde{\nu}$ = 2920s, 1682s, 1607s, 1461w, 1378s, 1326s, 1280s, 1219s, 1171s, 1056s, 682s.

MS (EI, 70 eV, 150 °C), *m*/*z* (%): 291 ($[M]^+$, 42), 173 (100), 131 (27), 115 (23), 43 ($[C_3H_7]^+$, 9).

EA calcd (%) for $C_{15}H_{17}NOS_2$: C, 61.82; H, 5.88; N, 4.81. Found: C, 61.65; H, 5.63; N, 4.82.

(*E*)-3-(4-*n*-Propylphenyl)-acrylic acid 17



17

Butyl ester **18** (2.50 g, 10.1 mmol) (see below) was dissolved in 1 M aqueous NaOH (40.4 mL, 40.4 mmol) and ethanol (80 mL) and the reaction mixture was heated at reflux for 4 hours. After cooling, the solvent was removed under reduced pressure and the remaining white slurry was completely dissolved in water. The pH-value of the solution was reduced to 1 with conc. HCl and the aqueous phase was extracted with Et_2O (5 × 80 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and the solvent was removed under reduced pressure to give compound **17** (1.84 g, 96%) as colorless prisms.

$C_{12}H_{14}O_2$ (190.24):

m.p. 168.5-169.5 °C (ethanol).

$\mathbf{R_f}$ = 0.32 (ethyl acetate/hexanes 1 : 3).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.65 (sext, ^3J = 7.3 Hz, 2 H, CH_2CH$_3$), 2.62 (t, ^3J = 7.3 Hz, 2 H, CH_2CH$_2$CH$_3$), 6.42 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C*H*C=O), 7.21 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.47 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.78 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C_6H_4C*H*), 9.94 (br s, 1 H, OH).

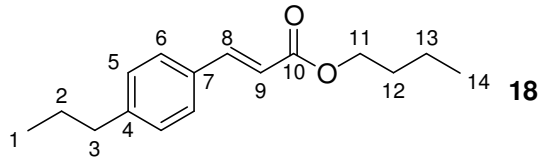
^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 13.8 (CH_3, 1), 24.3 (CH_2, 2), 37.9 (CH_2, 3), 116.1 (CH, 9), 128.4 (C_{ar}H), 129.1 (C_{ar}H), 131.6 (C, 7), 146.0 (C, 4), 147.1 (CH, 8), 172.4 (C, 10).

IR (KBr): $\tilde{\nu}$ = 2960s, 2584s, 1680s, 1619s, 1511m, 1418s, 1310s, 1280s, 1215s, 941s, 810s, 686s.

MS (EI, 70 eV, ca. 50 °C), *m/z* (%): 190 ([M]$^+$, 42), 161 ([M–C_2H_5]$^+$, 100), 115 (28), 91 ([C_7H_7]$^+$, 6).

EA calcd (%) for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.83; H, 7.50.

***(E)*-*n*-Butyl 3-(4-*n*-propylphenyl)-acrylate 18**



18

According to a procedure by SCHULTZ,[3] $Pd(PPh_3)_4$ (26.0 mg, 23.0 µmol) in *N,N*-dimethylacetamide (10 mL) was added to a solution of 1-propyl-4-iodobenzene (3.52 g, 22.6 mmol), n-butyl acrylate (3.87 mL, 27.1 mmol) and sodium acetate (2.60 g, 31.6 mmol) in *N,N*-dimethylacetamide (65 mL) at 140 °C. After 24 hours at this temperature, the reaction mixture was cooled to room temperature and diluted with hexanes (250 ml). The solution was washed with water (3 × 150 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, 5 × 18 cm, ethyl acetate/hexanes 1:10) to give compound **18** (2.74 g, 49%) as a yellow transparent oil.

$C_{16}H_{22}O_2$ (246.34):

$\mathbf{R_f}$ = 0.55 (ethyl acetate/hexanes 1:3).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 0.95 (t, ^3J = 7.8 Hz, 3 H, CH_3), 0.97 (t, ^3J = 7.8 Hz, 3 H, CH_3), 1.39-1.49 (m, 2 H, CH_2CH$_3$), 1.60-1.73 (m, 4 H, CH$_2$CH_2CH$_2$, CH_2CH$_3$), 2.60 (t, ^3J = 7.6 Hz, 2 H, CH_2(3)CH2CH3), 4.20 (t, ^3J = 6.6 Hz, 2 H, OCH_2), 6.40 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C*H*C=O), 7.19 (d, ^3J = 7.6 Hz, 2 H, H_{ar}), 7.44 (d, ^3J = 7.6 Hz, 2 H, H_{ar}), 7.66 (d, $^3J_{trans}$ = 15.9 Hz, 1 H, C_6H_4C*H*).

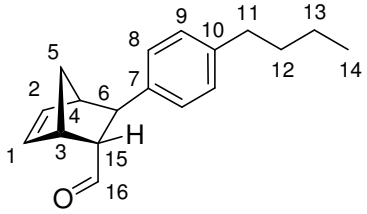
$^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ = 13.7 (CH_3), 13.8 (CH_3), 19.2 (CH_2, 13), 24.3 (CH_2, 2), 30.8 (CH_2, 12), 37.9 (CH_2, 3), 64.3 (CH_2, 11), 117.2 (CH, 9), 128.0 ($C_{ar}H$), 129.0 ($C_{ar}H$), 132.0 (C, 7), 144.6 (CH, 8), 145.4 (C, 4), 167.3 (C, 10).

MS (EI, 70 eV, r.t.), *m*/*z* (%): 246 ($[M]^+$, 35), 217 ($[M-C_2H_5]^+$, 15), 190 ($[M-C_4H_8]^+$, 100), 173 (57), 161 (67), 131 ($[M-C_9H_7O]^+$, 22), 115 (33), 91 (5), 43 (9).

IR (NaCl): $\tilde{\nu}$ = 2960s, 2871s, 1713s, 1637s, 1461m, 1315m, 1272m, 1170s, 984m, 828m.

EA calcd (%) for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.00; H, 9.14.

***endo* 3-[(1*S*,2*R*,3*R*,4*R*)-(4-*n*-Butylphenyl)-bicyclo[2.2.1]hept-5-ene]-2-carbaldehyde (2*R*)-7b**



(2*R*)-**7b**

According to a procedure by IZAWA and MUKAIYAMA,[8, 9] compound (2*R*)-**1b** (42.0 mg, 112 µmol) was added in one portion to a solution of diisobutylaluminium hydride (1.7 M in toluene, 0.09 mL, 134 µmol) in toluene (0.4 mL) at -78 °C. An extra 0.3 mL of toluene were added to dissolve all solid. After stirring for 20 minutes at -78 °C and 3 hours at -20 °C the reaction mixture was quenched with 1 M H_2SO_4 (0.2 mL), diluted with dichloromethane (10 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a colorless oil. The crude product was purified by flash column chromatography (SiO_2, 1 × 12 cm, ethyl acetate/hexanes 1:4) to give compound (2*R*)-**7b** (21 mg, 74%) as a colorless oil.

$C_{18}H_{22}O$ (254.37):

R_f = 0.95 (ethyl acetate/hexanes 1:1).

^1H NMR (400.1 MHz, $CDCl_3$): δ = 0.92 (t, ^3J = 7.3 Hz, 3 H, C*H*$_3$), 1.35 (sext, ^3J = 7.6 Hz, C*H*$_2$CH$_3$), 1.54-1.62 (m, 3 H, C*H*$_2$CH$_2$CH$_3$, CHCH*H*CH), 1.80 (d, ^3J = 8.8 Hz, 1 H, CHC*H*HCH), 2.58 (t, ^3J = 7.8 Hz, 2 H, C*H*$_2$CH$_2$CH$_2$CH$_3$), 2.97-2.95 (m, 1 H, C*H*C(=O)H), 3.04-3.05 (m, 1 H, PhC*H*), 3.09-3.10 (m, 1 H, C*H*(4)), 3.32 (s, 1 H, C*H*(3)), 6.16 (dd, ^3J = 5.8 Hz, J = 2.8 Hz, 1H, C*H*(1)=CH), 6.41 (dd, ^3J = 5.6 Hz, J = 3.3 Hz, 1H, C*H*(2)=CH), 7.11 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 7.17 (d, ^3J = 8.1 Hz, 2 H, H_{ar}), 9.58 (d, ^3J = 2.2 Hz, 1 H, *H*C=O).

^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): δ = 13.9 (CH_3, 14), 22.4 (CH_2, 13), 33.6 (CH_2, 12), 35.1 (CH_2, 11), 45.1 (CH, 3), 45.4 (CH, 6), 47.1 (CH_2, 5), 48.5 (CH, 4), 60.8 (CH, 15), 127.2 ($C_{ar}H$), 128.6 ($C_{ar}H$), 133.7 (CH, 1), 139.2 (CH, 2), 140.6 (C, 7), 140.8 (C, 10), 203.7 (C, 16).

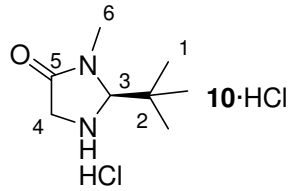
IR (NaCl): $\tilde{\nu}$ = 2959s, 2865s, 2713m, 1719s, 1513m, 1458m, 1333m, 1069m, 721s.

MS (EI, 70eV, r.t.), *m*/*z* (%): 189 ([M-C_5H_5]$^+$, 5), 131 ([M-C_9H_{14}]$^+$, 100), 117 (8), 66 (12).

$[\alpha]_D^{20}$ = −67.2 (c = 0.50, dichloromethane).

EA calcd (%) for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.89; H, 8.73.

(*S*)-2-(*t*-Butyl)-3-methyl-4-imidazolidinone 10·HCl



According to a procedure by MACMILLAN,[10] (*S*)-2-(*t*-butyl)-3-methyl-4-imidazolidinone **10**·TFA[11] was dissolved in saturated aqueous $NaHCO_3$. The aqueous phase was extracted three times with dichloromethane. The organic extracts were dried (Na_2SO_4) and the solvent was removed under reduced pressure to give a colorless oil, which was dissolved in Et_2O. Upon addition of HCl solution (2 M in Et_2O) compound **10**·HCl precipitated as a colorless amorphous solid.

$C_8H_{17}ClN_2O$ (192.69):

m.p. 172-173 °C (Et_2O).

^{1}H NMR (400.1 MHz, CD_2Cl_2): δ = 1.19 (s, 9 H, CH_3), 2.99 (s, 3 H, NCH_3), 3.75 (d, ^3J = 15.9 Hz, 1H, CH_2), 3.94 (d, ^3J = 15.9 Hz, 1H, CH_2), 4.61 (s, 1 H, C*H*).

^{13}C{^{1}H} NMR (100.6 MHz, CD_2Cl_2): δ = 24.9 (CH_3, 1), 31.4 (CH3, 6), 36.6 (C, 2), 53.4 (CH_2, 4), 82.1 (C, 3), 190.1 (C, 5).

IR (KBr): $\tilde{\nu}$ = 2985s, 2928s, 2567s, 2463s, 2376s, 1710s, 1580s, 1776s, 1417s, 1327s, 1256s, 1123m, 1032m, 677m, 627m, 571m.

MS (FAB, NBA (subtr)), *m*/*z* (%): 310 (10), 157 ([(M+H)-HCl]$^+$, 100), 100 (19).

$[\alpha]_D^{20}$ = +55.8 (c = 1.00, MeOH).

EA calcd (%) for $C_8H_{17}ClN_2O$: C, 49.87; H, 8.89; N, 14.54; O, 8.30. Found: C, 49.93; H, 8.75; N, 14.53.

General procedure for ESI-MS screening of the copper(II)-box-catalyzed retro-Diels-Alder reaction

In a typical reaction copper(II)box-catalyst (5.0 µmol, 8 mM in dichloromethane) prepared from 1 eq. $Cu(OTf)_2$ and 1.1 eq. of the box ligand, was mixed with a solution of the quasienantiomers (2 × 12.5 µmol, 20 mM in dichloromethane). After stirring the reaction mixture for 1 hour at 100 °C, it was cooled in an ice bath, an aliquot was diluted to 10^{-5} M (3 mL dichloromethane) and analyzed by ESI-MS. The selectivity of the catalyst was determined by integration of the peaks of the major isotopes for both dienophile complexes. Generally, the spectra were recorded both in the centroid and profile mode.

HPLC samples were prepared by filtrating the reaction mixture through a small plug of silica gel (ethyl acetate/Et_2O 1:1, eluation with Et_2O) followed by removal of the solvent under reduced pressure. The enantiomeric excess was determined by HPLC analysis: Chiralcel OD-H, i-propanol/heptane (5:95), 0.5 mL/min, 20 °C, 210 nm/259nm, t_R = 34.6 min (Bu-dienophile **4b**), t_R = 40.0 min (Et-dienophile **4a**).

Typical procedure for the preparative, forward Diels-Alder reaction using copper(II)-box catalysts

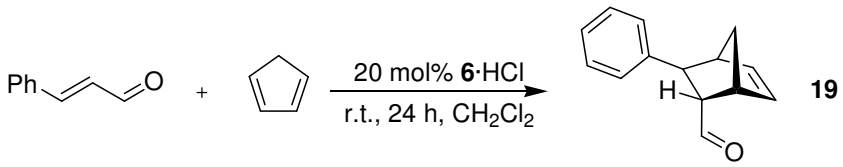
The preparative Diels-Alder reaction was carried out according to a procedure by EVANS.[2] In a Young tube $Cu(OTf)_2$ (20 mol%) and the *t*-butyl-box ligand **5c** (22 mol%) in dichloromethane (0.3 mL) were stirred for 2.5 hours at r.t.. The mixture was cooled to -78 °C and compound **4b** (1 eq.) in dichloromethane (100 mM) was added, immediately followed by cyclopentadiene (10 eq.). After stirring the mixture for 1 hour at 100 °C, it was filtered through a plug of silica gel (ethyl acetate/Et_2O 1:1) and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, 1 × 8 cm, ethyl acetate/hexanes 1:5) to give compound (2*R*)-**1b** as a yellow oil (31% yield, *endo:exo* 86:14, 28% endo *ee*). The enantiomeric excess was determined by HPLC analysis (Diacel Chiralcel OD-H, i-propanol/heptane (5:95), 0.5 mL/min, 20 °C, 210 nm, t_R = 19.3 min (*R*), t_R = 43.8 min (*S*).

General procedure for the organocatalyzed retro-Diels-Alder reaction

In a typical reaction the organocatalyst (1.25 µmol) was added to a solution of quasienantiomers (2 × 3.12 µmol, 20 mM in dichloromethane) and the mixture was stirred for 24 hours at r.t.. When screening multi-catalyst mixtures, the organocatalysts (3 × 1.25 µmol) were added to a solution of quasienantiomers (2 × 3.12 µmol, 20 mM in dichloromethane) and the mixture was stirred for 1 hour at 50 °C.

An aliquot of the reaction mixture was diluted to 10^{-4} M (2 mL acetonitrile) and analyzed by ESI MS. Catalyst-mixtures were diluted to 10^{-3} M (1 mL acetonitrile). The selectivity of the catalyst was determined by integration of the peaks of the major isotopes for both dienophile adducts. Generally, the spectra were recorded both in the centroid and profile mode.

General procedure for the preparative, forward Diels-Alder reaction using organocatalysts



The preparative Diels-Alder reaction was carried out according to a procedure by MACMILLAN.[12] Cinnamaldehyde (1 eq.) was added to a solution of (5*S*)-2,2,3-trimethyl-5-benzyl-4-imidazolidinone **6**·HCl (20 mol%) in dichloromethane (20 mM). The mixture was stirred for 2 minutes before addition of cyclopentadiene (3 eq.). After stirring for 24 hours at r.t., the mixture was washed with water (50 mL) and then with brine (20 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product. It was purified by flash column chromatography (SiO_2, 1 × 12 cm, ethyl acetate/hexanes 1:10) to give product **19** as a colorless transparent oil. The enantiomeric excess and diastereomeric ratio were determined by chiral GC (ß-CD DetTButSil (SE54) column 60 °C → 180 °C (10 min), 1.5 °C/min, t_R = 58.2 min (*exo* (2*S*)), t_R = 58.5 (*endo* (2*S*)), t_R = 59.0 min (*exo* (2*R*)), t_R = 59.6 (*endo* (2*R*)).

The spectroscopic data were in agreement with that previously reported for the *endo* compound.[13]

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