Journal Name

ARTICLE

# Novel Binaphthyl and Biphenyl α- and β-Amino Acids and Esters: Organocatalysis of Asymmetric Diels Alder Reactions. A Combined Synthetic and Computational Study.

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## Experimental Detail

Melting points were recorded using a Büchi B-545 Melting Point apparatus. Optical rotations were obtained using a Bellingham and Stanley Ltd ADP440 polarimeter and the solvents used for these measurements were of HPLC-grade quality. IR spectra were recorded on a Perkin-Elmer 100 FT-IR spectrophotometer; samples were used as thin films on KBr plates. NMR spectra were recorded on a Bruker 500 MHz Spectrometer. Chemical shifts were recorded in parts per million (ppm), *J* values are given in Hertz (Hz) and are referenced against tetramethylsilane or the residual deuteriated solvents peak. High-resolution mass spectra were obtained from the EPSRC Mass Spectrometry Unit at the University of Swansea. Enantiomeric excesses were determined by chiral high performance liquid chromatography using a Hitachi Elite LaChrom HPLC system using an L-2200 autosampler, L-2130 pump and L-2400 UV detector. All HPLC samples were run against racemic mixture as a standard and using a hexane-isopropanol mixture; conditions varied and are provided in detail below. Unless otherwise stated, all starting materials were sourced from commercial suppliers and were used without any purification. THF and $Et_2O$ were distilled from the sodium-benzophenone ketyl radical. Toluene, $CH_2Cl_2$ and $CH_3CN$ were distilled over $CaH_2$; DMF was distilled over $MgSO_4$. Needles and glassware were oven-dried and allowed to cool under a positive pressure of nitrogen gas prior to use. Light petroleum ether was distilled at 40-60 °C to remove impurities. Dicyclopentadiene was cracked on the day of use to produce cyclopentadiene.

**_(S)_-(+)-[1,1']-Binaphthalene-2,2'-diol _bis_-trifluoromethane sulfonate [21]**

_(S)_-[1,1]-2-2'-Binaphthalene diol (10.00 g, 35 mmol) and 4-dimethylaminopyridine (1.71 g, 14 mmol, 0.4 equiv.) were dissolved in anhydrous dichloromethane (300 mL). The solution was cooled to –78 °C. 2,6-Lutidine (12.2 mL, 104 mmol, 3.0 equiv.) and trifluoromethanesulfonic anhydride (18.0 mL, 104 mmol, 3.0 equiv.)

were added to the mixture. The solution turned from yellow to pink and was allowed to reach room temperature overnight. Over this time period the reaction mixture turned from pale pink to dark brown. Silica gel (~10 g) was added and the solvent was removed under reduced pressure. The residue was placed on a sintered funnel and washed repeatedly with petroleum ether (~2 L). The petroleum ether fractions were combined and the solvents removed under reduced pressure to yield the title compound as a colourless solid (19.2 g, 100%), which was employed in the next step without further purification.

m.p. 86-88 °C (Lit[21] 83-85 °C); $[\alpha]_D^{23}$ +144 ° (*c*=1.00, $CHCl_3$) [Lit[21] $[\alpha]_D^{21}$: +148 º, (*c* 1.00, $CHCl_3$)]; $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3060, 1592, 1509, 1423, 1219, 1140, 1066, 963, 941, 739, 704, 634; $^1$H NMR (500 MHz; $CDCl_3$) 8.14 (2H, d, J= 9.0 Hz), 8.01 (2H, d, J= 8.2 Hz), 7.62 (2H, d, J= 9.0 Hz), 7.59 (2H, ddd, J= 8.1, 6.8, 1.1 Hz), 7.41 (2H, ddd, J= 8.1, 6.8, 1.1 Hz), 7.27-7.23 (2H, m); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.5, 133.2, 132.4, 132.1, 128.4, 128.0, 127.4, 126.8, 123.5, 119.4, 116.9.

**(*S*)-(+)-2,2'-Dimethyl-[1,1']-binaphthalene** [41]

*(S)*-[1,1']-Binaphthalene-2,2'-diol-bis-trifluoromethanesulfonate (15.50 g, 28 mmol) and 1,3-bis(diphenylphosphino)propane nickel (II) chloride (1.07 g, 1.97 mmol, 0.07 equiv.) were dissolved in anhydrous $Et_2O$ (300 mL). The mixture was cooled to –78 °C. A solution of methyl magnesium bromide (3M in $Et_2O$, 38 mL, 113 mmol, 4.0 equiv.) was added slowly and the reaction mixture was allowed to reach room temperature overnight. The excess Grignard reagent was quenched at 0 °C with $H_2O$ (50 mL), and the mixture was diluted with $Et_2O$ (100 mL). The solution was stirred for 30 min. The solids were filtered through a plug of celite and washed with $Et_2O$ (~50 mL). The filtrate was transferred to a separating funnel and a few drops of aqueous HCl (37%) were added. The organic layer was washed with $H_2O$ (5 x 50 mL) and saturated brine (2 x 30 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure. The residue was recrystallized (hot methanol) to yield the title compound as a colourless crystalline solid (7.5 g, 95%).

m.p. 75–77 °C (Lit[41] 77–79 °C); $[\alpha]_D^{23}$ +36.5 ° (*c* 1.00, $CHCl_3$) [Lit[41] $[\alpha]_D^{21}$ +37.7 °, (*c* 1.00, $CHCl_3$)]; $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3049, 3007, 2858, 1506, 1443, 1421, 1351, 1219; $^1$H NMR (500 MHz, $CDCl_3$) 7.88 (4H, t, *J*= 8.0 Hz) 7.50 (2H, d, *J*= 8.5 Hz), 7.38 (2H, ddd, *J*= 8.0, 6.8, 1.1 Hz), 7.20 (2H, ddd, *J*= 8.0, 6.8, 1.1 Hz), 7.04 (2H, d, *J*= 8.1 Hz), 2.03 (6H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 135.1, 134.3, 132.8, 132.2, 128.7, 127.9, 127.4, 126.1, 125.6, 124.9, 20.0.

**(*S*)-(–)-2,2'-Bis-bromomethyl-[1,1']-binaphthalene (–)-7** [21]

*(S)*-2,2'-Dimethyl-[1,1']-binaphthalene (4.00 g, 14.2 mmol), *N*-bromosuccinimide (6.30 g, 35.4 mmol, 2.5 equiv.) and azobisisobutyronitrile (0.23 g, 1.4 mmol, 0.1 equiv.) were dissolved in cyclohexane (28 mL, 14 % *w/v* solution). The mixture was heated at reflux for 4 h until completion was observed using TLC. The reaction mixture was cooled to 0 °C, and EtOAc (9 mL) and distilled water (56 mL) were added. The mixture was stirred for 1 h to allow for precipitation, and filtration yielded the title compound as a beige solid (4.76 g, 77%).

m.p. 188-190 °C (Lit[21] 180-183 °C) $[\alpha]_D^{23}$ –174.4 ° (*c* 1.00, $CHCl_3$) [Lit[21] for (*R*)-2,2'-*Bis*-bromomethyl-[1,1']binaphthalene $[\alpha]_D^{20}$ +186.4 °, (*c* 1.00, benzene)]; $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3054, 2986, 2305, 1723, 1421, 1265, 896, 740, 705; $^1$H NMR (500 MHz, $CDCl_3$) 8.02 (2H, d, *J*= 8.6 Hz), 7.92 (2H, d, *J*= 8.2 Hz), 7.75 (2H, d, *J*= 8.6 Hz), 7.49 (2H, ddd, *J*= 8.0, 6.8, 1.0 Hz), 7.27 (2H, ddd, *J*= 8.0, 6.8, 1.1 Hz), 7.08-7.07 (2H, d, *J*= 8.5 Hz), 4.25 (4H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 134.2, 134.1, 133.3, 132.5, 129.4, 128.0, 127.8, 126.9, 126.8, 126.8, 32.7.

**(*S*)-(+)-3,5-Dihydrodinaphtho-[2,1-c:1',2'-e]-oxepine (+)-9** [21]

*(S)*-2,2'-Bis(bromomethyl)-[1-1']-binaphthalene (3.20 g, 7.3 mmol) was suspended in a mixture of saturated aqueous sodium carbonate and 1,4-dioxane (1:1, 100 mL), and the mixture heated at reflux for 12 h. The mixture was allowed to cool to room temperature and extracted with $Et_2O$ (3 x 30 mL). The combined organic layers were washed with $H_2O$ (20 mL) and saturated brine (2 x 40 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the resulting yellow oil was purified using column chromatography on silica gel (100:0-90:10 light petroleum ether/EtOAc) to give a colourless solid. Recrystallization of the solid ($CHCl_3$ in hexane) yielded the title compound as a colourless solid (1.88 g, 87%).

m.p. 170-173 °C (Lit[21] 180-183 °C); $[\alpha]_D^{20}$ +527.0 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3054, 2986, 2304, 1420, 1265, 1055, 896, 820; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.03 (4H, dd, *J*= 16.3, 8.3 Hz), 7.67 (2H, d, *J*= 8.3 Hz), 7.58 (2H, dd, *J*= 8.6, 0.6 Hz), 7.54 (2H, ddd, *J*= 8.1, 6.8, 1.2 Hz), 7.34 (2H, ddd, *J*= 8.3, 6.8, 1.3 Hz) 4.69 (2H, d, *J*= 11.4 Hz), 4.24 (2H, d, *J*= 11.4 Hz); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 135.5, 134.0, 133.6, 131.2, 129.2, 128.4, 127.7, 127.4, 126.0, 126.0, 67.5.

**(*S*)-(–)-2'-Bromomethyl-[1,1']-binaphthalene-2-carboxaldehyde (–)-10** [21]

(*S*)-2,7-Dihydrodinaphtho-[2,1-c;1',2'-e]-oxepine (4.80 g, 16.2 mmol) was dissolved in cyclohexane (80 mL), and the solution cooled in an ice bath. Bromine (0.9 mL, 18.2 mmol, 1.125 equiv.) was added slowly. The ice bath was removed and the reaction mixture heated at reflux for 1 h, which caused the dark red reaction mixture to turn yellow. The solvent was removed under reduced pressure and the residue redissolved in $Et_2O$ (70 mL). The solution was washed with saturated aqueous sodium hydrogen carbonate (2 x 50 mL) and saturated brine (2 x 60 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified using column chromatography on silica gel (9:1 light petroleum/EtOAc) to yield the title compound as a colourless solid (3.04 g, 50%).

m.p. 147-149 °C (Lit[21] 151-153 °C); $[\alpha]_D^{23}$ –142.0 ° (*c* 1.00, $CHCl_3$) [Lit[2] for (*R*)-2'-Bromomethyl-[1,1']binaphthalene-2-carboxaldehyde $[\alpha]_D^{20}$ +144.7 ° (*c* 1.02, $CHCl_3$)]; $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3054, 2986, 2305, 1689, 1422, 1265, 896, 740, 705, 600; $^1$H NMR (500 MHz, $CDCl_3$) δ 9.56 (1H, d, *J*= 1.0 Hz), 8.21 (1H, d, *J*= 8.5 Hz), 8.09 (1H, d, *J*= 8.5 Hz), 8.05 (1H, d, *J*= 8.5 Hz), 8.00 (1H, d, *J*= 8.5 Hz), 7.94 (1H, d, *J*= 8.0 Hz), 7.72 (1H, d, *J*= 8.5 Hz), 7.62 (1H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.50 (1H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.35 (1H, ddd, *J*= 8.5, 7.0, 1.5 Hz, 1H), 7.29 (1H, ddd, *J*= 8.5, 7.0, 1.5 Hz), 7.24 (1H, dd, *J*= 8.0, 0.5 Hz), 7.02 (1H, dd, *J*= 8.5, 0.5 Hz), 4.33 (1H, d, *J*= 10.0 Hz), 4.08 (1H, d, *J*= 10.0 Hz); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 191.8, 141.6, 136.3, 134.7, 133.6, 133.0, 132.5, 132.4, 130.2, 129.9, 129.4, 129.2, 128.5, 128.2, 127.41, 127.40, 127.0, 126.6, 122.4, 31.9.

**_(S)_-(+)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (+)-6** [19a]

_(S)_-2,2'-Bis-(bromomethyl)-[1-1']-binaphthalene (2.50 g, 5.7 mmol) and allylamine (0.5 mL, 6.25 mmol, 1.1 equiv.) were dissolved in acetonitrile (25 mL). Anhydrous potassium carbonate (2.36 g, 17.1 mmol, 3.0 equiv.) was added and the reaction mixture heated at reflux overnight or until completion was observed using TLC. The reaction mixture was cooled to room temperature, diluted with dichloromethane (40 mL) and filtered to remove potassium carbonate. The filtrate was washed with $H_2O$ (3 x 10 mL) and saturated brine (2 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure yielding an orange solid. Recrystallization (hot acetone) yielded the title compound as a pale yellow solid (1.60 g, 84%).

m.p. 167-169 °C (Lit [19a] 148-149 °C); $[\alpha]_D^{23}$ +396.2 ° (_c_ 1.80, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3944, 3054, 2987, 2829, 2685, 2410, 2305, 1508, 1421, 1263, 1156, 896, 820; $^1$H NMR (500 MHz, $CDCl_3$) 7.96 (4H, d, _J_= 8.3 Hz), 7.56 (2H, d, _J_= 8.2 Hz), 7.49-7.45 (4H, m), 7.31 (2H, ddd, _J_= 8.3, 6.8, 1.1 Hz), 6.07-5.95 (1H, m), 5.29 (1H, dd, _J_= 17.1, 1.3 Hz), 5.24 (1H, d, _J_= 10.0 Hz), 3.76 (2H, d, _J_= 12.5 Hz), 3.17 (2H, d, _J_= 12.5 Hz), 3.16-3.12 (2H, m); $^{13}$C NMR (126 MHz, $CDCl_3$) 136.3, 135.1, 133.4, 133.2, 131.4, 128.4, 128.3, 127.8, 127.5, 125.8, 125.5, 118.1, 58.5, 54.8.

**_(S)_-(+)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (+)-8**

Method A: (_S_)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (1.00 g, 3.0 mmol) was dissolved in dichloromethane (50 mL). The solution was cooled to 0 °C, and _N_-bromosuccimide (0.56 g, 3.13 mmol, 1.05 equiv.) added. The mixture was stirred for 1 h or until completion was observed using TLC. The solvent was removed under reduced pressure to yield the crude bromide salt as an orange foamy solid (3.83 g crude mass, not routinely isolated). The crude _(S)_-4-allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium bromide was dissolved in a minimum volume of ethanol, and a solution of sodium tetraphenylborate (1.13 g, 3.3 mmol, 1.1 equiv.) in the minimum volume of acetonitrile added. The solution was stirred for 10 min. The bright yellow precipitate was collected by filtration and washed with cold ethanol to yield the title compound as a yellow solid, which was dried at 70 °C overnight (1.55 g, 80%).

Method B: (_S_)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (2.12 g, 6.3 mmol) was dissolved in anhydrous dichloromethane (100 mL). Dried crushed 4Å molecular sieve and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2.87 g, 12.6 mmol, 2 equiv.) were added. The mixture was stirred at ambient temperature for 2 h or until completion was observed using TLC. A solution of sodium tetraphenylborate (2.37 g, 6.93 mmol, 1.1 equiv.), in the minimum volume of acetonitrile was added, and the reaction stirred for a further 10 min. The solvent was removed under reduced pressure and the orange residue triturated in hot EtOH to yield the title compound as a bright yellow solid (1.9 g, 46%).

Method C: (_S_)-2'-Bromomethyl-[1,1']-binaphthalene-2-carboxaldehyde (1.41 g, 3.76 mmol) was dissolved in EtOH (15 mL), and a solution of allylamine (0.3 mL, 3.76 mmol, 1 equiv.) in ethanol (0.5 mL) added dropwise. The mixture was warmed to 35 °C and stirred for 4 h or until consumption of starting material was observed by TLC. The mixture was allowed to reach room temperature, and a solution of sodium tetraphenylborate (1.42 g, 4.14 mmol, 1.10 equiv.) in the minimum volume of acetonitrile added. The solution was stirred for 10 min, the solvents were removed under reduced pressure, and the crude residue triturated in hot EtOH to yield the title compound as a bright yellow solid (1.59 g, 65%).

m.p.* 160 °C (*_decomp._); $[\alpha]_D^{23}$ +410.5 ° (_c_ 1.00, MeCN); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3054, 2987, 2685, 2410, 2305, 1521, 1263, 1156, 896; $^1$H NMR (500 MHz, d6-DMSO) δ 9.55 (1H, s), 8.38 (1H, d, _J_= 8.6 Hz), 8.25 (2H, t, _J_= 8.8 Hz), 8.08 (2H, dd, _J_= 14.3, 8.3 Hz), 7.85 (1H, d, _J_= 8.5 Hz), 7.79 (1H, t, _J_= 7.4 Hz), 7.55 (1H, t, _J_= 7.5 Hz), 7.49 (1H, t, _J_= 7.6 Hz), 7.44 (1H, d, _J_= 8.5 Hz), 7.29 (1H, t, _J_= 7.7 Hz), 7.18 (8H, s), 6.99 (1H, d, _J_= 8.7 Hz), 6.92 (8H, t, _J_= 7.3 Hz), 6.78 (4H, t, _J_= 7.1 Hz), 6.03–5.89 (1H, m), 5.65 (1H, d, _J_= 17.5 Hz), 5.53 (1H, d, _J_= 10.1 Hz), 5.14 (1H, d, _J_= 13.5 Hz), 4.84 (2H, d, _J_= 5.5 Hz), 4.69 (1H, d, _J_= 13.6 Hz); $^{13}$C NMR (126 MHz, d6-DMSO) δ 169.6, 164.4, 141.0, 136.6, 136.0, 135.2, 133.8, 131.31, 131.24, 130.5, 129.8, 129.6, 129.5, 129.2, 128.1, 127.51, 127.46, 127.2, 126.8, 126.7, 125.80, 125.78, 125.76, 125.74, 124.3, 122.0, 64.1, 62.0 56.3; HRMS (NSI-FTMS) _m/z_: $[M\text{-}BPh_4]^+$ Calcd for $[C_{25}H_{20}N]^+$ 334.1596; Found 334.1595.

**(3S,11cS)-(+)-4-Allyl-3-methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine**

(_S_)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (843 mg, 1.29 mmol) was dissolved in anhydrous THF (20 mL). The solution was cooled to –78 °C, and a solution of methyl magnesium bromide (3M in $Et_2O$, 2.2 mL, 6.45 mmol, 5 equiv.) was added slowly. The mixture was allowed to reach room temperature overnight. The excess Grignard reagent was quenched with $H_2O$ (5 mL), and the reaction mixture diluted with $Et_2O$ (30 mL). The organic layer was washed with $H_2O$ (20 mL) and saturated brine (10 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified using column chromatography on silica gel (7:3 light petroleum/EtOAc 3% TEA) to yield the title compound as a colourless oil (388 mg, 86%).

$[\alpha]_D^{25}$ +317 ° (_c_ 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3048, 3005, 2959, 2928, 2904, 2805, 2866, 1506, 1366, 1264, 1112, 819, 750, 738;$^1$H NMR (500 MHz, $CDCl_3$) δ 7.95-7.87 (4H, m), 7.65 (1H, d, _J_= 8.3 Hz), 7.48 (1H, dd, _J_= 8.6, 0.7 Hz), 7.44–7.38 (3H, m), 7.33 (1H, d, _J_= 8.3 Hz), 7.21 (2H, dddd, _J_= 8.1, 7.0, 5.7, 1.3 Hz), 6.00 (1H, dddd, _J_= 17.6, 10.1, 7.6, 5.5 Hz), 5.25 (1H, dd, _J_= 17.0, 1.5 Hz), 5.19 (1H, dd, _J_= 11.0, 1.0 Hz), 4.04 (1H, q, _J_= 7.3 Hz), 3.72 (1H, d, _J_= 11.0 Hz), 3.26 (1H, ddt, _J_= 13.6, 5.4, 1.4 Hz), 3.15 (1H, dd, _J_= 13.7, 7.6 Hz), 3.10 (1H, d, _J_= 11.0 Hz), 0.54 (3H, d, _J_= 7.4 Hz); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 137.4, 136.6, 135.8, 135.1, 133.3, 133.2, 132.9, 132.1, 132.0, 129.2, 128.8, 128.4, 128.1, 128.0, 127.42, 127.40, 125.9, 125.7, 125.5, 117.9, 61.9, 61.0, 56.8, 22.2; HRMS (NSI-FTMS) _m/z_: $[M+H]^+$ Calcd for $[C_{26}H_{24}N]^+$ 350.1909; Found 350.1902.

**(3_S_,11cS)-(+)-3-Methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine**

(3_S_,11cS)-4-Allyl-3-methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine (700 mg, 2.00 mmol) was dissolved in anhydrous dichloromethane (20 mL). $Pd(PPh_3)_4$ (92 mg, 0.08 mmol, 0.04 equiv.) and 1,3-dimethylbarbituric acid (937 mg, 6.00 mmol, 3 equiv.) were added, and the reaction mixture was heated at reflux overnight or until TLC showed complete consumption of the starting material. The reaction was allowed to cool to room temperature, and washed with

1 M NaOH (2 x 15 mL), $H_2O$ (2 x 10 mL), and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified using column chromatography on silica gel (10% MeOH in $CH_2Cl_2$) to yield the title compound as a yellow foam (341 mg, 55%).

m.p. 110-112 °C, $[\alpha]_D^{23}$ +498.0 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3049, 2951, 2923, 2864, 1673, 1594, 1075, 819, 750; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.99–7.89 (4H, m), 7.61 (1H, d, *J*= 8.3 Hz), 7.50–7.45 (3H, m), 7.41 (1H, d, *J*= 8.2 Hz), 7.37 (1H, d, *J*= 8.3 Hz) 7.29–7.21 (2H, m), 4.41 (1H, q, *J*= 7.3 Hz), 3.86 (1H, d, *J*= 12.4 Hz), 3.78 (1H, d, *J*= 12.3 Hz), 2.31 (1H, s), 0.72 (3H, d, *J*= 7.2 Hz); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 138.5, 135.4, 133.5, 133.3, 133.2, 132.20, 132.17, 129.2, 129.1, 128.4, 128.2, 127.3, 127.2, 127.0, 126.1, 125.8, 125.7, 125.7, 57.3, 48.4, 22.5; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{23}H_{20}N]^+$ 310.1596; Found 310.1589.

**(+)-*tert*-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl) acetate (+)-28**

A mixture of zinc dust (1.90 g, 29.1 mmol, 10 equiv.), anhydrous THF (40 mL) and TMSCl (0.37 mL, 2.9 mmol, 1 equiv.) was heated at reflux for 30 min. tert-Butyl bromoacetate (0.43 mL, 2.9 mmol) was added, and the mixture heated at reflux for a further 30 min. The mixture was cooled to –78 °C. (*S*)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (1.90 g, 2.9 mmol) was dissolved in anhydrous THF (40 mL), and the solution transferred into the zinc slurry at –78 °C using a cannula. The mixture was stirred at –78 °C for 1 h, and t-butyl bromoacetate (4.3 mL, 29.1 mmol, 10 equiv.) added in small portions over 20 min, while maintaining the temperature. The mixture was allowed to reach room temperature and reaction progress monitored by TLC. Saturated aqueous ammonium chloride (5 mL) was added. $Et_2O$ (50 mL) was added, and the mixture filtered through a pad of celite. The filtrate was washed with $H_2O$ (3 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a yellow oil. The product was purified using column chromatography on silica gel (9:1 light petroleum ether/ EtOAc) to yield the title compound as a colourless oil (932 mg, 71%).

$[\alpha]_D^{22}$ +158 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3052, 2978, 1724, 1507, 1367, 1264, 1150, 820;$^1$H NMR (500 MHz, $CDCl_3$) δ 7.98-7.90 (4H, m), 7.62 (1H, d, *J*= 8.3 Hz), 7.48-7.41 (4H, m), 7.36 (1H, d, *J*= 8.1 Hz), 7.27-7.19 (2H, m), 5.97 (1H, m), 5.25 (1H, dd, *J*= 17.1, 1.5 Hz) 5.19 (1H, *appt* d, *J*= 10.2 Hz) 4.41 (1H, t, *J*= 7.8 Hz), 3.71 (1H, d, *J*= 10.9 Hz), 3.35–3.20 (2H, m), 3.08 (1H, d, *J*= 10.9 Hz), 1.73 (1H, dd, *J*= 15.1, 7.0 Hz), 1.51 (1H, dd, *J*= 15.1, 8.4 Hz), 1.15 (9H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 171.3, 136.1, 135.5, 135.2, 135.0, 133.5, 133.3, 133.0, 131.9, 131.8, 129.9, 129.0, 128.4, 128.3, 128.1, 128.0, 127.6, 127.4, 125.9, 125.7, 125.6, 125.6, 118.0, 79.9, 64.1, 61.4, 56.1, 42.6, 27.9; HRMS ($Cl^+$) *m/z*: $[M+H]^+$ Calcd for $[C_{31}H_{32}NO_2]^+$ 450.2433; Found for: 450.2424.

**(+)-*tert*-Butyl 2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (+)-30**

*tert*-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-acetate (1.20 g, 2.67 mmol) was dissolved in anhydrous dichloromethane (60 mL). 1,3-Dimethylbarbituric acid (1.25 g, 8.00 mmol, 3 equiv.) and $Pd(PPh_3)_4$ (0.06 g, 0.05 mmol, 0.02 equiv.) were added, and the mixture heated at reflux overnight or until full consumption of the starting material was observed by TLC. The mixture was allowed to reach room temperature, and the solvent removed under reduced pressure. The residue was redissolved in $Et_2O$ (50 mL) and the solution washed with 1 M NaOH solution (2 x 10 mL), $H_2O$ (2 x 10 mL), and saturated brine (10 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified using column chromatography on silica gel (6:4 light petroleum ether/EtOAc) to yield the title compound as a fluffy pale yellow foam (0.92 g, 84%).

m.p. 78-79 °C; $[\alpha]_D^{22}$ +206° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3052, 2976, 1719, 1507, 1437, 1366, 1293, 1219, 1148, 1118; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.02-7.91 (4H, m), 7.60 (1H, d, *J*= 8.3 Hz), 7.54 (1H, d, *J*= 8.4 Hz), 7.48-7.44 (2H, m), 7.40 (1H, d, *J*= 8.6 Hz), 7.34 (1H, d, *J*= 8.3 Hz), 7.26–7.22 (2H, m), 4.67 (1H, t, *J*= 7.6 Hz), 3.84 (1H, d, *J*= 12.2 Hz), 3.74 (1H, d, *J*= 12.2 Hz), 1.82 (1H, dd, *J*= 15.3, 7.6 Hz), 1.72 (1H, dd, *J*= 15.2, 7.7 Hz), 1.18 (9H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 171.4, 137.5, 136.7, 135.0, 133.8, 133.2, 133.1, 132.1, 129.3, 129.1, 128.8, 128.5, 128.4, 128.1, 127.5, 127.4, 127.0, 125.9, 125.7, 125.6, 125.5, 80.2, 59.1, 48.8, 43.0, 27.9; HRMS (CI+) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{28}NO_2]^+$ 410.2120; Found 410.2114.

**(+)-2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetic acid (+)-32**

*tert*-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (660 mg, 1.6 mmol) was dissolved in dichloromethane (30 mL), and trifluoroacetic acid (1.5 mL, 19.3 mmol, 12 equiv.) added. The mixture was stirred until consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using $H_2O$ (15 mL)and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue recrystallized ($CH_2Cl_2$ and light petroleum ether) to yield the title compound as a colourless solid (535 mg, 94%).

m.p. 228–230 °C; $[\alpha]_D^{22}$ +264 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3345, 3072, 2971, 1719, 1597, 1507, 1375, 1204, 1152; $^1$H NMR (400 MHz, *d6*-DMSO) δ 8.10 (2H, d, *J* = 8.3 Hz), 8.07 (2H, d, *J* = 8.3 Hz), 7.73 (1H, d, *J* = 8.3 Hz), 7.62 (1H, d, *J* = 8.4 Hz), 7.57-7.48 (2H, m), 7.37-7.28 (2H, m), 7.24 (1H, d, *J* = 8.5 Hz), 7.16 (1H, d, *J* = 8.4 Hz), 4.66 (1H, dd, *J* = 10.5, 5.8 Hz), 3.97 (1H, d, *J* = 12.0 Hz), 3.52 (1H, d, *J* = 11.9 Hz), 1.73 (1H, dd, *J* = 16.2, 5.8 Hz), 1.30 (1H, dd, *J* = 16.2, 5.8 Hz); $^{13}$C NMR (101 MHz, *d6*-DMSO) δ 176.4, 136.5, 135.2, 133.4, 133.3, 133.2, 131.8, 131.7, 131.59, 129.67, 129.52, 129.28, 129.02, 128.77, 128.02, 126.90, 126.85, 126.81, 126.59, 126.43, 126.42, 57.12, 46.75, 38.32; HRMS ($Cl^+$) *m/z*: $[M+H]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1487.

**(+)-2-((3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetic acid (+)-32.HCl**

*tert*-Butyl 2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (481 mg, 1.2 mmol) was dissolved in dichloromethane (20 mL), and trifluoroacetic acid (1.3 mL, 16.4 mmol, 14 equiv.) added. The mixture was stirred until consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using $H_2O$ (10 mL) and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. Aqueous HCl

 

(37%, 3 drops) was added, and the mixture stirred for 10 min. The solvent was removed under reduced pressure and the residue recrystallized (hot $CHCl_3$) to yield the title compound as a colourless solid (398 mg, 85%).
m.p. 293-295 °C; $[\alpha]_D^{23}$ +378 ° (*c* 0.5, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 2916, 2811, 2720, 2433, 1723, 1587, 1413, 1398, 1289, 1191, 899; $^1$H NMR (500 MHz, *d6*-DMSO) δ 12.46 (1H, s), 10.21 (1H, s), 9.53 (1H, s) 8.21 (2H, dd, *J*= 19.0, 8.4 Hz), 8.14 (2H, dd, *J*= 13.0, 8.5 Hz), 7.79 (1H, d, *J*= 8.0 Hz), 7.72 (1H, d, *J*= 8.5 Hz), 7.62 (2H, dd, *J*= 15.6, 8.3 Hz), 7.46-7.34 (2H, m), 7.26-7.16 (2H, dd, *J*= 13.5, 8.5 Hz), 5.11 (1H, t, *J*= 7.0 Hz), 4.30 (1H, d, *J*= 13.0 Hz), 3.78 (1H, d, *J*= 13.0 Hz), 1.94 (2H, m); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ 171.3, 135.5, 134.00, 133.98, 133.8, 132.9, 131.6, 131.5, 130.0, 129.78, 129.76, 129.6, 129.1, 128.9, 128.68, 128.67, 127.41, 127.35, 127.1, 127.0, 126.9, 56.6, 46.1, 36.8; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{24}H_{19}ClNO_2]^-$ 388.1104; Found 388.1118.

**(+)-*tert*-Butyl 2-((3R,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoate (+)-29**

A mixture of zinc dust (2.0 g, 30.6 mmol, 10 equiv.), anhydrous THF (40 mL), and TMSCl (0.4 mL, 3.06 mmol, 1 equiv.) was heated at reflux for 30 min. tert-Butyl α-bromoisobutyrate (0.57 mL, 3.06 mmol, 1 equiv.) was added, and the mixture heated at reflux for a further 30 min. The mixture was cooled to –78 °C. (*S*)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (2.0 g, 3.06 mmol) was dissolved in anhydrous THF (40 mL), and transferred into the activated zinc slurry using a cannula. The mixture was stirred for 1 h at –78 °C. *tert*-Butyl α-isobromobutyrate (5.7 mL, 30.6 mmol, 10 equiv.) was added in small portions over 20 min, maintaining the temperature at –78 °C. The mixture was allowed to reach room temperature and monitored by TLC. Saturated aqueous ammonium chloride (5 mL) and $Et_2O$ (50 mL) were added, and the mixture filtered through a pad of celite. The filtrate was washed with $H_2O$ (3 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified using column chromatography on silica gel (9:1 light petroleum ether/EtOAc) to yield the title compound as a colourless oil (1.1 g, 76%). $[\alpha]_D^{19}$ +102.8° (*c* 1.3, $CHCl_3$); $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 2977, 2934, 2872, 1722, 1475, 1458, 1391, 1367, 1254, 1141, 1119, 918, 850, 819, 755, 667; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.89-7.86 (4H, m), 7.54 (1H, d, *J*= 10.0 Hz), 7.45 (1H, d, *J*= 10.0 Hz), 7.42–7.36 (3H, m), 7.31 (1H, d, *J*= 10.0 Hz), 7.21 (1H, ddd, *J*= 8.3, 6.8, 1.5 Hz), 7.15 (1H, ddd, *J*= 8.3, 6.8, 1.5 Hz), 5.83-5.93 (1H, m), 5.24-5.20 (1H, m), 5.14-5.11 (1H, m), 4.55 (1H, s), 3.65 (1H, d, *J*= 11.5 Hz), 3.49-3.48 (2H, m), 3.41 (1H, d, *J*= 11.5 Hz), 1.29 (9H, s), 0.44 (3H, s), 0.30 (3H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 176.9, 136.5, 136.1, 136.0, 135.8, 134.2, 133.0, 133.0, 132.8, 132.2, 128.7, 128.3, 128.2, 128.2, 128.0, 127.8, 127.6, 125.8, 125.6, 125.3, 125.2, 117.1, 80.6, 79.8, 64.6, 55.1, 51.1, 28.0, 22.6, 22.4; HRMS ($Cl^+$) *m/z*: $[M+H]^+$ Calcd for $[C_{33}H_{36}NO_2]^+$ 478.2746; Found 478.2735.

**(+)-*tert*-Butyl 2-((3R,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoate (+)-31**

*tert*-Butyl 2-((3R,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoate (1.12 g, 2.3 mmol) was dissolved in anhydrous dichloromethane (70 mL). 1,3-Dimethylbarbituric acid (1.08 g, 6.9 mmol, 3 equiv.) and $Pd(PPh_3)_4$ (0.05 g, 0.046 mmol, 0.02 equiv.) were added, and the mixture was heated at reflux overnight or until complete consumption of the starting material was observed by TLC. The reaction was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was redissolved in $Et_2O$ (60 mL), and the solution washed with 1M NaOH (2 x 15 mL), $H_2O$ (2 x 20 mL), and saturated brine (2 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and column chromatography on silica gel (1:1 light petroleum ether/EtOAc) yielded the title compound as a colourless foam (623 mg, 62%).
m.p. 87-89 °C; $[\alpha]_D^{20}$ +314.0 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3019, 2980, 2935, 2400, 1710, 1598, 1509, 1437, 1420, 1366, 1215, 1153, 1132, 1031, 928, 849, 819; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.88 (4H, dd, *J*= 8.0, 5.0 Hz), 7.49 (1H, d, *J*= 8.0 Hz), 7.45 (1H, d, *J*= 8.0 Hz), 7.42-7.38 (2H, m), 7.26-7.24 (2H, m), 7.20 (1H, ddd, *J*= 8.2, 6.7, 1.5 Hz), 7.15 (1H, ddd, *J*= 8.2, 6.7, 1.5 Hz), 4.89 (1H, s), 3.95 (1H, d, *J*= 12.5 Hz), 3.73 (1H, d, *J*= 12.5 Hz), 1.35 (9H, s), 0.73 (3H, s), 0.23 (3H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 176.8, 138.9, 136.4, 134.8, 134.6, 133.4, 132.9, 132.8, 132.7, 132.4, 128.8, 128.4, 128.1, 127.9, 127.7, 127.5, 126.7, 125.8, 125.7, 125.4, 125.0, 80.1, 70.3, 50.7, 49.4, 28.0, 23.7, 19.6; HRMS ($Cl^+$) *m/z*: $[M+H]^+$ Calcd for $[C_{30}H_{32}NO_2]^+$ 438.2433; Found 438.2424.

**(+)-2-((3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoic acid hydrochloride (+)-33.HCl**

*tert*-Butyl 2-((3R,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methyl propanoate (643 mg, 1.47 mmol) was dissolved in dichloromethane (20 mL). Trifluoroacetic acid (1.3 mL, 17.6 mmol, 12 equiv.) was added, and the mixture stirred until complete consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed with $H_2O$ (15 mL) and saturated brine solution (2 x 15 mL), and dried over anhydrous $MgSO_4$. The residue was subjected to column chromatography on silica gel (EtOAc). Aqueous HCl (37%, 3 drops) was added, and the mixture stirred for 10 min. The solvent was then removed under reduced pressure and the residue recrystallized ($Et_2O$/light petroleum ether) to yield the title compound as a colourless solid (469 mg, 76%).
m.p. 222-225 °C; $[\alpha]_D^{23}$ +283° (*c* 0.5, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3500, 2928, 2833, 2728, 1703, 1566, 1460, 1189, 1154, 1134, 1034, 726; $^1$H NMR (500 MHz, *d6*-DMSO) δ 13.01 (1H, s), 10.92 (1H, s), 9.05 (1H, s), 8.13 (2H, t, *J*= 8.5 Hz), 8.07 (2H, dd, *J*= 8.0, 4.5 Hz), 7.75 (1H, d, *J*= 8.5 Hz), 7.69 (1H, dd, *J*= 8.0, 3.3 Hz), 7.59-7.55 (2H, m), 7.35 (1H, t, *J*= 8.5 Hz), 7.27 (1H, t, *J*= 8.5 Hz), 7.15 (1H, d, *J*= 8.5 Hz), 7.08 (1H, d, *J*= 8.5 Hz), 5.24 (1H, s), 4.25 (1H, d, *J*= 13.5 Hz), 3.88 (1H, d, *J*= 13.0 Hz), 0.82 (3H, s), 0.18 (3H, s); $^{13}$C NMR (126 MHz, DMSO) δ 176.6, 135.2, 133.4, 133.4, 133.2, 132.1, 131.6, 131.5, 129.5, 129.4, 129.1, 128.9, 128.7, 128.5, 128.5, 128.2, 127.2, 126.9, 126.7, 126.5, 126.3, 66.5, 47.4, 47.0, 25.0, 19.3; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{26}H_{24}NO_2]^+$ 382.1807; Found 382.1791.

**(+)-2-((3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoic acid (+)-33**

*tert*-Butyl2-((3R,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2- methylpropanoate (300 mg, 0.69 mmol) was dissolved in dichloromethane (20 mL), and trifluoroacetic acid (0.63

mL, 8.2 mmol, 12 equiv.) added. The mixture was stirred until complete consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using $H_2O$ (20 mL) and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue subjected to column chromatography (EtOAc). Recrystallization ($CHCl_3$/light petroleum ether) yielded the title compound as a beige solid (161 mg, 61%).

m.p. 192-194 °C; $[\alpha]_D^{25}$ +138.1°(*c* 0.9, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3400, 3054, 2979, 2850, 1673, 1598, 1470, 1200, 1135, 821, 751; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.98 (1H, d, *J*= 8.5 Hz), 7.94 (1H, d, *J*= 8.2 Hz), 7.89 (1H, d, *J*= 8.2 Hz), 7.78 (1H, d, *J*= 7.8 Hz), 7.58 (5H, d, *J*= 8.1 Hz), 7.56-7.46 (3H, m), 7.26-7.30 (2H, m), 7.24-7.17 (2H, m), 5.35 (5H, s), 4.39 (2H, d, *J* = 12.9 Hz), 4.09 (2H, d, *J* = 12.8 Hz), 1.16 (3H, s), 0.01 (3H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 179.6, 136.1, 133.9, 133.9, 133.6, 132.9, 132.4, 131.7, 131.8, 129.6, 129.4, 129.2, 128.7, 128.1, 128.0, 127.6, 127.5, 126.8, 126.6, 126.3, 126.1, 77.2, 67.8, 47.2, 27.6, 26.6; HRMS ($Cl^+$) *m/z*: $[M+H]^+$ Calcd for $[C_{26}H_{24}NO_2]^+$ 382.1807; Found 382.1803.

**(–)-(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (–)-13**

**Method A:** (*S*)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine (1.32 g, 4.5 mmol) was dissolved in warmed *t*-BuOH (30 mL). A solution of di-*tert*-butyl dicarbonate (1.02 g, 4.7 mmol, 1.05 equiv.) in *t*-BuOH (10 mL) was added, and the mixture stirred at room temperature for 3 h. A further portion of di-*tert*-butyl dicarbonate (0.12 equiv.) was added, and the mixture stirred until full consumption of the starting material was observed by TLC. EtOAc (50 mL) was added, and the solution washed with $H_2O$ (2 x 20 mL) and saturated brine (20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield the product as a pale yellow solid (1.65 g, 92%).

**Method B:** (*S*)-2,2'-Bis-bromomethyl-[1,1']binaphthalene (600 mg, 1.36 mmol) was dissolved in anhydrous DMF (30 mL). The pale yellow solution was cooled to 0 °C, and NaH (130 mg, 5.45 mmol, 4 equiv.) added in one portion. *t*-Butyl carbamate (160 mg, 1.36 mmol, 1 equiv.) was added slowly in small portions. The mixture was stirred for 4 days or until full consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (10 mL) added. The majority of the solvent was removed under reduced pressure. $Et_2O$ (100 mL) was added, and the mixture washed with $H_2O$ (5 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified by recrystallization (acetone) to yield the title compound as a colourless solid (469 mg, 87%).

m.p. 219- 221 °C; $[\alpha]_D^{23}$ −7.0° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3057, 2979, 2933, 2253, 1819, 1682, 1508, 1464, 1405, 1367, 1275, 1252, 1219, 1163, 1106, 908, 867, 819;$^1$H NMR (500 MHz, $CDCl_3$) δ 7.99-7.91 (4H, m), 7.60 (2H, d, *J*= 8.0 Hz), 7.47 (2H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.43 (2H, d, *J*= 8.5 Hz), 7.26 (2H, ddd, *J*= 8.5, 7.0, 1.0 Hz), 4.93 (2H, br s), 3.65 (2H, d, *J*= 13.0 Hz), 1.51 (9H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 154.4, 135.0, 133.33, 133.28, 131.5, 129.2, 128.3, 127.51, 127.47, 126.0, 125.8, 85.2, 80.0, 28.6, 27.4; ; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{27}H_{26}NO_2]^+$ 396.1964; Found 396.1955.

**(–)-(3R,11cS)-4-*tert*-Butyl 3-ethyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (–)-15**

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (200 mg, 0.51 mmol) was dissolved in anhydrous $Et_2O$ (20 mL), and the solution cooled to −78 °C. *sec*-BuLi (1.4 M solution in cyclohexane, 0.47 mL, 0.66 mmol, 1.3 equiv.) was added dropwise; the pale yellow solution instantly turned black on addition. The mixture was stirred at −78 °C for 1 h. Ethyl chloroformate (0.15 mL, 1.53 mmol, 3 equiv.) was added in one portion, causing the solution to turn from black to bright yellow. The mixture was allowed to reach room overnight, or until full consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (10 mL) added. The mixture was washed with $H_2O$ (3 x 10 mL) and saturated brine (3 x 10 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (7:3 light petroleum ether/EtOAc) to yield the title compound as a colourless solid (174 mg, 73%).

m.p. 101-103 °C; $[\alpha]_D^{22}$ −17.6 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3052, 2976, 2931, 1748, 1695, 1508, 1475, 1461, 1392, 1366, 1297, 1252, 1243, 1217, 1164, 1155, 1107, 1027, 945, 911, 897, 864, 825, 814; 1H NMR (500 MHz, $CDCl_3$) δ 8.02 (2H, d, *J* = 8.2 Hz), 8.00–7.94 (4H, m), 7.89 (2H, d, *J* = 8.2 Hz), 7.69–7.60 (3H, m), 7.56 (1H, d, *J* = 8.3 Hz), 7.53–7.46 (3H, m), 7.42 (4H, ddd, *J* = 11.9, 8.3, 5.1 Hz), 7.33 (2H, dd, *J* = 8.3, 3.5 Hz), 7.30–7.27 (1H, m), 7.24 (2H, dd, *J* = 8.2, 7.2 Hz), 5.95 (1H, s), 5.69 (1H, s), 5.26 (1H, d, *J* = 13.4 Hz), 5.03 (1H, d, *J* = 13.3 Hz), 3.75 (2H, d, *J* = 13.3 Hz), 3.64 (1H, d, *J* = 13.4 Hz), 3.08 (2H, m), 2.93 – 2.64 (2H, m), 1.55 (9H, s), 1.47 (9H, s), 0.98–0.79 (6H, m), 0.53 (3H, t, *J* = 7.1 Hz), 0.47 (3H, t, *J* = 7.1 Hz); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 169.9, 169.6, 154.3, 154.0, 134.7, 134.32, 134.31, 134.28, 133.88, 133.37, 133.34, 133.32, 133.17, 133.13, 133.10, 131.64, 131.52, 131.50, 131.40, 129.6, 129.3, 129.2, 128.7, 128.6, 128.23, 128.20, 128.1, 127.8, 127.47, 127.39, 127.3, 127.2, 126.3, 126.2, 126.1, 126.02, 126.97, 125.8, 125.7, 80.6, 80.5, 62.2, 61.0, 60.84, 60.82, 47.8, 46.5, 28.5, 28.4, 13.3, 13.2; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{30}H_{30}NO_4]^+$ 468.2175; Found 468.2165.

**(+)-(3R,11cS)-Ethyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate (+)-17**

(3R,11cS)-4-*tert*-Butyl 3-ethyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (90 mg, 0.2 mmol) was dissolved in dichloromethane (5 mL). Trifluoroacetic acid (0.2 mL, 2.8 mmol, 14 equiv.) was added, and the mixture stirred until complete consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the pH of the solution to neutral. The solvent was removed reduced pressure and the residue redissolved in EtOAc (5 mL). The solution was washed with $H_2O$ (3 x 5 mL) and saturated brine (3 x 5 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc), to yield the product as a yellow oil (60 mg, 81%).

$[\alpha]_D^{23}$ +386.0° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3583, 2980, 2253, 1742, 1710, 1394, 1366, 1222, 1156, 1109, 1027, 909, 826;$^1$H NMR (500 MHz, $CDCl_3$) δ 8.01 (1H, d, *J*= 8.5 Hz), 7.98–7.91 (2H, m), 7.89 (1H, d, *J*= 8.5 Hz), 7.63 (1H, d, *J*= 8.5 Hz), 7.51-7.44 (2H, m), 7.44–7.34 (3H, m), 7.29-7.20 (2H, m), 4.59 (1H, s), 3.83 (1H, d, *J*= 13.5 Hz), 3.55 (1H, d, *J*= 13.5 Hz), 3.36 (1H, s), 3.22 (1H, dq, *J*= 10.7, 7.1 Hz), 2.58

 

(1H, dq, *J*= 10.7, 7.2 Hz), 0.49 (3H, t, *J*= 7.5 Hz); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.1, 137.5, 134.9, 134.0, 133.4, 133.3, 132.9, 131.60, 131.57, 129.6, 129.0, 128.8, 128.34, 128.28, 127.4, 127.2, 126.9, 125.98, 125.95, 125.9, 125.4, 62.5, 61.1, 48.5, 13.3; HRMS (ESI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{25}H_{22}NO_2]^+$ 368.1651; Found 368.1645.

**(+)-(3R,11cS)-Ethyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate hydrochloride (+)-17.HCl**

(3R,11cS)-4-*tert*-butyl 3-ethyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (300 mg, 0.64 mmol) was dissolved in acetone (30 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($Et_2O$ and light petroleum ether) to yield the title compound as a yellow solid (260 mg, 100%).

m.p.* 219-221 °C (*decomp); $[\alpha]_D^{23}$ +340° (*c* 1.03, $CHCl_3$); $\nu_{max}$ (solid)/cm$^{-1}$ 3394, 2928, 2661, 1736, 1671, 1595, 1545, 1443, 1369, 1299, 1236, 1195, 1055, 1027, 961, 897, 820, 796, 749, 705, 624; $^1$H NMR (500 MHz, *d6*-DMSO) δ 8.02 (1H, d, *J*= 8.4 Hz), 7.94 (2H, dd, *J*= 8.3, 4.8 Hz), 7.88 (1H, d, *J*= 8.2 Hz), 7.58 (1H, d, *J*= 8.4 Hz), 7.48 (1H, d, *J*= 8.4 Hz), 7.45-7.40 (1H, m), 7.37 (1H, t, *J*= 7.5 Hz), 7.24-7.14 (2H, m), 7.03 (1H, d, *J*= 8.6 Hz), 6.96 (1H, d, *J*= 8.5 Hz), 5.63 (1H, s), 4.14 (1H, d, *J*= 13.5 Hz), 3.46 (1H, d, *J*= 13.0 Hz), 3.03 (1H, dq, *J*= 10.8, 7.1 Hz), 2.38 (1H, dq, *J*= 10.8, 7.1 Hz), 0.16 (3H, t, *J*= 7.1 Hz); $^{13}$C NMR (126 MHz, DMSO) δ 167.76, 134.57, 134.13, 133.92, 131.16, 131.08, 130.38, 130.23, 129.93, 129.70, 129.61, 128.99, 128.44, 127.57, 127.30, 127.26, 127.19, 127.05, 127.02, 62.29, 59.18, 45.84, 13.23; HRMS (ESI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{25}H_{22}NO_2]^+$ 368.1651; Found 368.1645.

**(–)-(3R,11cS)-4-tert-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (–)-14**

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (900 mg, 2.3 mmol) was dissolved in anhydrous $Et_2O$ (50 mL). The solution was cooled to −78 °C, and *sec*-BuLi (1.3 M in cyclohexane, 2.3 mL, 3.0 mmol, 1.3 equiv.) added dropwise, causing the pale yellow solution to turn black. The mixture was stirred at −78 °C for 1 h. Methyl chloroformate (0.53 mL, 6.8 mmol, 3 equiv.) was added, causing the solution to turn bright yellow. The mixture was allowed to reach room temperature over 12 h, or until complete consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (5 mL) added. The mixture was washed with $H_2O$ (2 x 20 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (9:1 light petroleum ether/EtOAc) to yield title compound as a colourless fluffy solid (845 mg, 81%).

m.p. 124-126 °C; $[\alpha]_D^{23}$ −20.8° (*c* 0.5, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/cm$^{-1}$ 3053, 2975, 2946, 2884, 1751, 1696, 1508, 1456, 1392, 1366, 1296, 1164, 960, 823; $^1$H NMR (500 MHz, *d6*-DMSO at 380 K) δ 8.13 (1H, d, *J*= 8.3 Hz), 8.08 (1H, d, *J*= 8.2 Hz), 8.04 (1H, d, *J*= 8.3 Hz), 8.01 (1H, d, *J*= 8.2 Hz), 7.76 (1H, d, *J*= 8.3 Hz), 7.60 (1H, d, *J*= 8.3 Hz), 7.56 (1H, ddd, *J*= 8.1, 6.6, 1.3 Hz), 7.51 (1H, ddd, *J*= 8.1, 6.8, 1.1 Hz), 7.37-7.32 (1H, m), 7.32–7.28 (2H, m), 7.19 (1H, d, *J*= 8.5 Hz), 5.85 (1H, s), 5.10 (1H, d, *J*= 13.3 Hz), 3.61 (1H, d, *J*= 13.4 Hz), 2.54 (3H, s), 1.50 (9H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO at 380 K) δ 169.9, 153.9, 134.5, 134.3, 134.2, 133.7, 133.6, 133.5, 131.63, 131.58, 129.8, 129.7, 128.9, 128.7, 128.6, 128.3, 127.1, 126.9, 126.73, 126.67, 126.4, 126.2, 80.5, 79.6, 51.2, 28.7, 28.6; HRMS (ESI-FTMS) *m/z*: $[M+Na]^+$ Calcd for $[C_{29}H_{27}NNaO_4]^+$ 476.1838; Found 476.1832.

**(+)-(3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate (+)-16**

(3*R*,11cS)-4-*tert*-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (600 mg, 1.32 mmol) was dissolved in dichloromethane (10 mL), and trifluoroacetic acid (1.4 mL, 18.5 mmol, 14 equiv.) added. The mixture was stirred for 30 min. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure and the residue redissolved in EtOAc (30 mL). The solution was washed with $H_2O$ (3 x 20 mL) and saturated brine (3 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$ and light petroleum ether) to yield the title compound as a colourless solid (364 mg, 78%).

m.p. 214-216 °C; $[\alpha]_D^{21}$ +420 ° (*c* 1.03, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/cm$^{-1}$ 3318, 3050, 2947, 2874, 1730, 1508, 1448, 1432, 1223, 1207, 1110, 992, 866, 822; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.02 (1H, d, *J*= 8.0 Hz), 7.97-7.93 (2H, m), 7.91 (1H, d, *J*= 8.0 Hz), 7.64 (1H, d, *J*= 8.5 Hz), 7.52-7.47 (2H, m), 7.44-7.42 (2H, m), 7.36 (1H, d, *J*= 8.5 Hz), 7.28 (1H, d, *J*= 7.6 Hz), 7.24 (1H, d, *J*= 7.5 Hz), 4.62 (1H, s), 3.84 (1H, d, *J*= 14.0 Hz), 3.57 (1H, d, *J*= 13.7 Hz), 2.49 (3H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.4, 137.4, 135.0, 133.7, 133.4, 133.3, 132.9, 131.5, 131.4, 129.7, 129.1, 128.4, 128.34, 128.29, 127.3, 127.0, 126.8, 126.1, 126.0, 125.9, 125.5, 62.2, 51.6, 48.4; HRMS (ESIFTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1479.

**(+)-(3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate hydrochloride (+)-16.HCl**

(3R,11cS)-4-*tert*-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (258 mg, 0.57 mmol) was dissolved in acetone (30 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by recrystallization (MeOH and $Et_2O$) to yield the title compound as a beige solid (222 mg, 100%).

m.p. 220-230 °C; $[\alpha]_D^{21}$ + 296.0 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ (solid)/cm$^{-1}$ 3406, 3053, 2950, 2673, 1746, 1596, 1508, 1439, 1371, 1248, 1212, 1058, 864, 822; $^1$H NMR (500 MHz, *d6*-DMSO) δ 9.67 (1H, s), 8.26 (1H, d, *J*= 8.0 Hz), 8.17-8.15 (2H, m), 8.12 (1H, d, *J*= 8.5 Hz), 7.81 (1H, d, *J*= 8.5 Hz), 7.71 (1H, d, *J*= 8.3 Hz), 7.65 (1H, ddd, *J*= 8.0, 6.6, 1.0 Hz), 7.61 (1H, ddd, *J*= 8.1, 6.8, 1.0 Hz), 7.42-7.37 (2H, m), 7.27 (1H, d, *J*= 8.4 Hz), 7.16 (1H, d, *J*= 8.5 Hz), 5.86 (1H, s), 4.36 (1H, d, *J*= 13.2 Hz), 3.70 (1H, d, *J*= 13.2 Hz), 2.45 (3H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ 167.8, 134.2, 134.1, 133.6, 133.4, 130.74, 130.66, 130.5, 130.0, 129.9, 129.5, 129.2, 128.8, 128.5, 127.9, 127.1, 126.9, 126.8, 126.5, 126.3 58.6, 52.0, 45.4; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1488.

**(–)-(3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (–)-18a and (+)-(3S,11cS)-4-(*tert*-butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (+)-18b**

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (500 mg, 1.26 mmol) was dissolved in anhydrous $Et_2O$ (30 mL) under a positive pressure of argon, and the mixture was cooled to −78 °C. *sec*-BuLi (1.4 M solution in cyclohexane, 1.2 mL, 1.6 mmol, 1.3 equiv.) was added, causing the solution to turn from a pale yellow to a black colour. The mixture was stirred at −78 °C for 1 h. $CO_2$ gas was bubbled directly into the solution *via* a drying tube filled with $CaCl_2$. The mixture was stirred overnight at −78 °C under an atmosphere of argon. Saturated aqueous ammonium chloride (10 mL) and EtOAc (20 mL) were added. The organic layer was washed with $H_2O$ (2 x 20 mL) and saturated brine (2 x 20 mL), dried over anhydrous $Na_2SO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (4:1 light petroleum ether/EtOAc).

For the first eluting diastereoisomer **18a**: isolated as a colourless solid (188 mg, 34%), m.p. 164-167 °C; $[\alpha]_D^{24}$ −47.2 ° (*c* 1.00, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3056, 2976, 2937, 1754, 1694, 1393, 1367, 1303, 1245, 1156, 912, 819, 749; $^1$H NMR (500 MHz, *d6*-DMSO, 363 K) δ 8.07 (1H, d, *J*= 8.7 Hz), 8.02 (1H, d, *J*= 8.7 Hz), 7.98–7.94 (2H, m), 7.70 (1H, d, *J*= 8.6 Hz), 7.57 (1H, d, *J*= 8.2 Hz), 7.49 (1H, ddd, *J*= 8.1, 6.8, 1.5 Hz), 7.44 (1H, ddd, *J*= 8.1, 6.8, 1.5 Hz), 7.25 (2H, m), 7.20-7.15 (2H, m), 5.72 (1H, s), 5.07 (1H, d, *J*= 15.5 Hz), 3.56 (1H, d, *J*= 15.5 Hz), 1.45 (9H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO, 363 K) δ 170.5, 154.0, 134.3, 133.5, 131.8, 131.7, 129.5, 129.4, 128.7, 128.6, 128.4, 127.4, 127.2, 126.5, 126.2, 126.0, 80.2, 62.1, 47.4, 28.7; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{26}NO_4]^+$ 440.1862; Found 440.1854.

For the first eluting diastereoisomer **18b**: isolated as a colourless solid (170 mg, 31%), m.p. 255-257 °C; $[\alpha]_D^{24}$ +58.4 ° (*c* 1.00, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3052, 3006, 2976, 2927, 1751, 1725, 1696, 1395, 1367, 1251, 1219, 1151, 820, 772, 759, 677; $^1$H NMR (500 MHz, *d6*-DMSO, 353 K) δ 8.07 (2H, d, *J*= 8.3 Hz), 8.02 (2H, dd, *J*= 11.6, 8.3 Hz), 7.66 (1H, d, *J*= 9.0 Hz), 7.58 (1H, d, *J*= 9.0 Hz), 7.52-7.48 (2H, m), 7.35-7.31 (2H, m), 7.27-7.24 (1H, m), 7.16 (1H, d, *J*= 8.7 Hz), 4.95 (1H, d, *J* =15.0 Hz), 4.36 (1H, s), 3.55 (1H, d, *J* =15.0 Hz), 1.40 (9H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO, 353 K) δ 171.4, 155.75, 136.3, 135.1, 133.5, 133.4, 132.6, 132.3, 131.7, 131.5, 129.8, 129.2, 128.9, 128.7, 127.21, 127.16, 126.8, 126.8, 126.7, 126.3, 126.1, 125.2, 81.1, 62.7, 48.7, 28.4; ; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{26}NO_4]^+$ 440.1862; Found 440.1852.

**(+)-(3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid hydrochloride (+)-19a.HCl**

3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (230 mg, 0.52 mmol) was dissolved in acetone (20 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. The residue was purified by recrystalization (MeOH and light petroleum ether) to yoeld the title compound as a pale yellow solid (197 mg, 100%).

m.p. 265-267 °C; $[\alpha]_D^{22}$ +294 ° (*c* 1.00, MeOH); $\nu_{max}$ $(CH_2Cl_2)/cm^{-1}$ 3019, 2400, 1741, 1528, 1425, 1215, 928, 757, 669, 625; $^1$H NMR (500 MHz, *d6*-DMSO) δ 13.26 (1H, s), 11.10 (1H, s), 9.43 (1H, s), 8.23 (1H, d, *J*= 8.4 Hz), 8.15 (2H, dd, *J*= 8.3, 3.7 Hz), 8.09 (1H, d, *J*= 8.2 Hz), 7.80 (1H, d, *J*= 8.4 Hz), 7.71 (1H, d, *J*= 8.4 Hz), 7.66-7.54 (2H, m), 7.43-7.34 (2H, m), 7.18 (2H, t, *J*= 8.0 Hz), 5.71 (1H, s), 4.34 (1H, d, *J*= 13.1 Hz), 3.67 (1H, d, *J*= 13.1 Hz); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ 168.9, 134.7, 134.6, 134.1, 134.0, 131.34, 131.25, 130.2, 129.9, 129.8, 129.68, 129.65, 129.6, 129.0, 128.9, 128.4, 127.4, 127.3, 127.2, 127.1, 127.0, 59.4, 46.0; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1333.

**(+)-(3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (+)-19a**

(3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (1.55g, 3.53 mmol) was dissolved in dichloromethane (30 mL), trifluoroacetic acid (3.8 mL, 49.4 mmol, 14 equiv.) added, and the solution stirred for 30 min. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (30 mL). The solution was washed with $H_2O$ (3 x 20 mL) and saturated brine (3 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$ and light petroleum ether) to yield the title compound (983 mg, 82%).

m.p. 269-271 °C; $[\alpha]_D^{25}$ +272.8 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$(solid)/$cm^{-1}$ 3400, 3067, 2926, 2876, 2521, 1722, 1670, 1367, 1367, 1194, 1139, 820, 749; $^1$H NMR (500 MHz, *d6*-DMSO) δ 8.21 (1H, d, *J*= 8.0 Hz), 8.13 (2H, dd, *J*= 8.0, 2.0 Hz), 8.08 (1H, d, *J*= 8.0 Hz), 7.77 (1H, d, *J*= 8.0 Hz), 7.69 (1H, d, *J*= 8.0 Hz), 7.60 (2H, dt, *J*= 15.9, 7.5), 7.37 (2H, ddd, *J*= 8.0, 6.5, 1.0 Hz), 7.17 (2H, dd, *J*= 8.5, 5.3 Hz), 5.49 (1H, s), 4.30 (1H, d, *J*= 13.1 Hz), 3.63 (1H, d, *J*= 13.1 Hz); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ 168.9, 134.7, 134.4, 133.92, 133.86, 131.4, 131.3, 131.1, 130.5, 129.9, 129.8, 129.7, 128.9, 128.8, 128.3, 127.4, 127.2, 127.0, 126.92, 126.86, 60.1, 46.1; HRMS (NSI-FTMS) *m/z* $[M-H]^-$ Calcd for $[C_{23}H_{16}NO_2]^-$ 338.1181; Found 338.1181.

**(+)-(3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid hydrochloride (+)-19b.HCl**

(3S,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (346 mg, 0.79 mmol) was dissolved in acetone (35 mL), concentrated aqueous HCl (3 drops) added., and the reaction mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by recrystalization (diethyl ether and light petroleum ether) to yield the title compound as a yellow solid (296 mg, 100%). m.p.* 290-292 °C (*decomp); $[\alpha]_D^{22}$ +282 ° (*c* 1.00, MeOH); $\nu_{max}$(solid)/$cm^{-1}$ 3247, 2737, 1961, 1714, 1594, 1461, 1430, 1310, 1276, 1235, 1028, 816, 780, 665, 640; $^1$H NMR (500 MHz, *d6*-DMSO) δ 10.51 (1H, s), 10.09 (1H, s), 8.29 (1H, d, *J*= 8.5 Hz), 8.24 (1H, d, *J*= 8.0 Hz), 8.17 (2H, d, *J*= 8.0 Hz), 7.79 (1H, d, *J*= 8.5 Hz), 7.68–7.62 (2H, m), 7.54 (1H, d, *J*= 8.5 Hz), 7.47-7.42 (2H, m), 7.35 (1H d, *J*= 8.5 Hz), 7.29 (1H, d, *J*= 8.6 Hz), 4.61 (1H, s), 4.41 (1H, d, *J*= 13.0 Hz), 3.45 (1H, d, *J*= 13.0 Hz); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ 169.1, 135.7, 134.5, 134.3, 134.1, 131.1, 130.8, 130.4, 130.1, 129.7, 129.1, 128.5, 127.8, 127.6, 127.5, 127.41, 127.34, 127.3, 127.1, 124.6, 58.3, 46.2; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1336.

**(+)-(3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (+)-19b**

(3S,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (1.60 g, 3.64 mmol) was dissolved in dichloromethane (30 mL), trifluoroacetic acid (3.9 mL, 50.96 mmol,

 

14 equiv.) added, and the solution stirred for 30 min. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (30 mL). The solution was washed with $H_2O$ (3 x 20 mL) and saturated brine solution (3 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$ and light petroleum ether) to yield the title compound (877 mg, 71%) as a colourless solid.

m.p. 276-280 °C; $[\alpha]_D^{25}$ +196.0 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3408, 3053, 3009, 2974, 2974, 2784, 2595, 1760, 1633, 1400, 1392, 1340, 1201, 1029, 820, 739; $^1$H NMR (500 MHz, *d6*-DMSO) δ 8.09 (4H, m), 7.70 (2H, d, *J*= 8.3 Hz), 7.58 (2H, m), 7.42–7.26 (3H, m), 7.22 (1H, d, *J*= 8.6 Hz), 4.10 (1H, d, *J*= 12.7 Hz), 3.85 (1H, s), 3.35 (1H, d, *J*= 12.7 Hz); $^{13}$C NMR (126 MHz, DMSO) δ 134.7, 134.5, 133.3, 133.1, 132.2, 131.0, 130.6, 130.3, 129.0, 128.7, 128.6, 128.4, 127.6, 126.63, 126.59, 126.5, 126.32, 126.28, 126.24, 126.21, 60.2, 45.8; HRMS (NSI-FTMS) *m/z* $[M+H]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1335.

**(S)-(+)-6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (+)-21** [30]

NaOH (5.88 g, 147 mmol) and 2-amino-3-methylbenzoic acid (17 g, 113 mmol) were dissolved in water, and the solution cooled to 0 °C. $NaNO_2$ (7.8 g, 113 mol) was added. The mixture was stirred until homogeneous. Aqueous HCl (4M, 240 mL) was added dropwise, keeping the temperature below 8 °C. After addition, the mixture was stirred at 0 °C for 30 min. A solution of $CuSO_4.5H_2O$ (48 g, 192 mmol) in water (150 mL) was cooled to 0 °C, and aqueous ammonium hydroxide (95 mL, 215 mmol) was added. $NH_2OH$ was added (prepared from $(NH_2OH)_2.H_2SO_4$ (17.6 g, 107 mmol) with 3M NaOH (75 mL)). The diazonium salt was added in 40 mL portions *via* syringe, with the needle kept below the surface of the reaction medium, while maintaining the temperature below 8 °C. The mixture was heated under reflux for 30 minutes, allowed to cool to room temperature, and aqueous HCl (12M, 80 mL) added. The mixture was allowed to stand overnight, and the precipitate removed by filtration. The residue (17.5 g) was dried at 60 °C for 12 h, and recrystallized (ethanol) to give a yellow solid. The solvents were removed from the filtrate under reduced pressure, and the residue purified by recrystallization (ethanol-$H_2O$) to yield (±)-6,6'-dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid as a red-brown solid (8.2 g, 30.3 mmol, 54%).

(±)-6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (3.5 g, 12.9 mmol) was dissolved in boiling EtOH (16 mL), and quinine (4.2 g, 12.9 mmol, 1 equiv.) added in one portion. The solution was allowed to cool to room temperature, and the colourless precipitate of the quinine monohydrate salt (4.90 g) removed by filtration. The salt was dissolved in EtOAc (70 mL), and 3 M HCl (80 mL) added. The solution was washed with $H_2O$ (3 x 20 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and the solution concentrated under reduced pressure to yield the title compound as an orange solid (1.3 g, 37%).

$[\alpha]_D^{21}$ +20.8 ° [(*c* 1.00, MeOH) (Lit[30] $[\alpha]_D^{25}$ +19.2 °, *c* 1.00, MeOH)]; m.p. 225-227 °C (Lit[30] 220-230 °C), $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3054, 2986, 2923, 2832, 2685, 2560, 2411, 2305, 1702, 1682, 1592, 1579, 1421, 1296, 1264, 1187, 1159, 1111, 934, 896, 819; $^1$H NMR (500 MHz, *d6*-DMSO) δ 12.39 (2H, s), 7.72 (2H, d, *J*= 7.6 Hz), 7.46 (2H, d, *J*= 7.4 Hz), 7.33 (2H, t, *J*= 7.6 Hz ), 1.83 (6H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ 168.5, 141.1, 136.4, 133.3, 130.9, 127.7, 127.1, 20.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{16}H_{13}O_4]^-$ 269.0814; Found 269.0812.

**(S)- (–)-(6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-diyl)dimethanol (–)-22** [30]

6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (144 mg, 0.48 mmol) was dissolved in anhydrous $Et_2O$ (10 mL), and the solution cooled to 0 °C. $LiAlH_4$ (73 mg, 1.93 mmol, 4 equiv.) was added. After 5 h the mixture was quenched with $H_2O$ (10 mL). The mixture was filtered through a pad of celite, washed with $H_2O$ (3 x 15 mL) and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield the product as an orange solid (117 mg, 100%), used without further purification.

m.p. 208-210 °C (Lit[30] 116-118 °C); $[\alpha]_D^{22}$ −74.7 ° [(*c* 1.00, $CHCl_3$); Lit[30] $[\alpha]_D$ −30 ° (*c* 0.4, $CHCl_3$)]; $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3064, 3018, 2970, 2918, 2856, 1459, 1437, 1381, 1246, 1210, 1166, 788, 755, 735, 626, 613; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.36 (2H, dd, *J*= 7.4, 1.0 Hz), 7.31 (2H, t, *J*= 7.5 Hz), 7.26 (2H, t, *J*= 6.1 Hz), 4.29 (2H, d, *J*= 11.5 Hz), 4.14 (2H, d, *J*= 11.5 Hz), 2.27 (2H, br s, O*H*), 1.87 (6H, s, ArC$H_3$); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 138.4, 138.2, 136.0, 129.8, 127.9, 127.5, 63.0, 20.1.

**(+)-2,2'-bis(Bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (+)-20**

(6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-diyl)dimethanol (500 mg, 2.1 mmol) and pyridine (19 µL, 0.23 mmol, 0.11 equiv.) were dissolved in anhydrous toluene (50 mL). Phosphorus tribromide (0.6 mL, 6.3 mmol, 3 equiv.) was added dropwise. The mixture was heated at 60 °C for 3 h. $H_2O$ (50 mL) was added, and the mixture washed with saturated aqueous sodium hydrogen carbonate (20 mL). The organic layer was dried over anhydrous $MgSO_4$, decolourized with carbon black, filtered, and the solvent removed under reduced pressure to yield the title compound as an orange solid (677 mg, 88%), used without further purification.

m.p. 45-47 °C; $[\alpha]_D^{19.4}$ +35.2 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3064, 3018, 2970, 2918, 2856, 1593, 1459, 1437, 1381, 1246, 1210, 1166, 1005, 935, 788, 755, 735, 626, 613; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.43 (2H, d, *J*= 7.6 Hz), 7.32 (2H, t, *J*= 7.6 Hz), 7.26 (2H, d, *J*= 7.6 Hz), 4.15 (4H, q, *J*= 10.1 Hz), 1.98 (6H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 137.7, 136.7, 135.4, 130.5, 128.6, 128.4, 32.4, 20.2.

**(–)-(*S*)-*tert*-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (–)-23**

2,2'-bis(Bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (500 mg, 1.36 mmol) was dissolved in anhydrous DMF (30 mL), and NaH (67 mg, 2.78 mmol, 2.05 equiv.) added. The mixture was cooled to 0 °C, and *tert*-butyl carbamate (159 mg, 1.36 mmol, 1 equiv.) added in one portion. On completion of the reaction (TLC), DMF was removed under reduced pressure and the residue redissolved in EtOAc (60 mL). The solution was washed with $H_2O$ (5 x 10 mL) and saturated brine (2 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography (9:1 light petroleum ether/EtOAc) to yield the product as a colourless oil (385 mg, 88%).

$[\alpha]_D^{22}$ −238 ° (*c* 1.50, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3063, 2974, 2927, 2866, 1691, 1459, 1400, 1364, 1036, 1247, 1216, 1158, 1100, 869; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.42-7.10 (6H, m), 4.71 (2H, d, *J*= 9.7 Hz), 3.45 (2H, d, *J*= 13.1 Hz), 2.18 (6H, s), 1.48 (9H, s); $^{13}$C NMR (126 MHz,

$CDCl_3$) δ 154.3, 138.2, 136.1, 134.9, 130.0, 127.9, 126.5, 79.7, 47.8, 28.6, 19.7; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{21}H_{26}NO_2]^+$ 324.1964; Found 324.1960.

**(–)-(5R,11bS)-6-tert-Butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (–)-24**

*tert*-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (645 mg, 1.99 mmol) was dissolved in anhydrous $Et_2O$ (60 mL), and the solution cooled to −78 °C. *s*-BuLi (1.4 M in cyclohexane, 2.85 mL, 3.99 mmol, 2 equiv.) was added, and the mixture stirred for 1 h. Methyl chloroformate (0.23 mL, 2.99 mmol, 1.5 equiv.) was added, and the mixture stirred for 1 h at −78 °C. Saturated aqueous ammonium chloride was added. The mixture was washed with $H_2O$ (2 x 30 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and the solvents removed under reduced pressure. The residue was purified by column chromatography (9:1 light petroleum ether/EtOAc) to yield the product as a colourless fluffy solid (600 mg, 79%).

m.p. 74-76 °C; $[\alpha]_D^{23}$ −248 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3065, 3002, 2975, 2948, 2930, 2872, 2250, 1752, 1686, 1600, 1474, 1458, 1433, 1392, 1366, 1355, 1308, 1255, 1221, 1206, 1161, 1105, 1004, 912, 875; $^1$H NMR (500 MHz, *d6*-DMSO, 373 K) δ 7.42-7.16 (6H, m), 5.61 (1H, s), 4.85 (1H, d, *J*= 13.3 Hz), 3.38 (1H, d, *J*= 13.1 Hz), 3.10 (3H, s), 2.13 (3H s), 2.07 (3H, s), 1.47 (9H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ $^3$C NMR (126 MHz, $CDCl_3$) δ 170.8, 170.5, 154.3, 153.9, 137.5, 137.5, 137.3, 137.2, 136.9, 136.7, 136.6, 136.4, 135.2, 134.9, 134.7, 134.6, 130.6, 130.4, 129.8, 129.7, 128.50, 128.47, 128.2, 128.1, 128.04, 128.01, 127.3, 127.1, 80.5, 80.4, 62.1, 60.8, 51.7, 47.7, 46.4, 28.5, 28.4, 19.52, 19.46; $^1$HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{23}H_{28}NO_4]^+$ 382.2018; Found 382.2013.

**(+)-(5R,11bS)-Methyl 1,11-dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylate (+)-25**

(5R,11bS)-6-tert-Butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (100 mg, 0.26 mmol) was dissolved in dichloromethane (8 mL), trifluoroacetic acid (0.28 mL, 3.64 mmol, 14 equiv.) added in one portion, and the solution stirred for 30 minutes. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (10 mL). The solution was washed with $H_2O$ (3 x 10 mL) and saturated brine (3 x 5 mL), and dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$) to yield the title compound as a colourless solid (55 mg, 75%).

$[\alpha]_D^{26}$ +37.7 ° (*c* 0.70, $CHCl_3$); $\nu_{max}$ ($CH_2Cl_2$)/$cm^{-1}$ 3316, 3062, 3017, 2948, 2926, 2867, 1732, 1493, 1432, 1378, 1302, 1265, 1228, 1211, 1122, 1099, 994, 785, 770, 741, 680; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.36-7.29 (2H, m), 7.29-7.22 (2H, m), 7.18 (1H, d, *J*= 7.4 Hz), 7.11 (1H, d, *J*= 7.3 Hz), 4.44 (1H, s), 3.64 (1H, d, *J*= 13.6 Hz), 3.35 (1H, d, *J*= 13.6 Hz), 3.22 (3H, s), 2.64 (1H, s), 2.15 (3H, s), 2.12 (3H, s); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.3, 138.3, 137.9, 136.9, 136.6, 136.3, 135.1, 130.3, 129.2, 128.5, 128.0, 127.9, 125.6, 62.4, 51.9, 48.3, 19.5, 19.4; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{18}H_{20}NO_2]^+$ 282.1494; Found 282.1489.

**(–)-(5R,11bS)-6-(*tert*-Butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5Hdibenzo[c,e]azepine-5-carboxylic acid (–)-26**

*tert*-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (645 mg, 1.99 mmol) was dissolved in anhydrous $Et_2O$ (60 mL), and the solution cooled to −78 °C. *s*-BuLi (1.4 M in cyclohexane, 2.85 mL, 4.00 mmol, 2 equiv.) was added. After stirring for 1 h at −78 °C, $CO_2$ gas was bubbled into the mixture through a drying tube of $CaCl_2$ over 1 h. The mixture was allowed to reach ambient temperature overnight. Saturated aqueous ammonium chloride was added at 0 °C. The mixture was washed with $H_2O$ (2 x 20 mL) and saturated brine (2 x 10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (4:1 light petroleum ether/EtOAc) to yield the title compound as a colourless solid (330 mg, 45%).

m.p. 117-119 °C; $[\alpha]_D^{24}$ −250 ° (*c* 1.00, $CHCl_3$); $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3066, 3009, 2976, 2928, 2782, 1751, 1717, 1601, 1456, 1394, 1367, 1310, 1254, 1219, 1160, 883, 760, 744; $^1$H NMR (500 MHz, *d6*-DMSO, 380 K) δ 11.35 (1H, s), 7.37-7.32 (2H, m), 7.29-7.21 (3H, m), 7.17 (1H dd, *J*= 6.7, 2.0 Hz), 5.52 (1H, s), 4.84 (1H, d, *J*= 13.1 Hz), 3.39 (1H, d, *J*= 13.2 Hz), 2.13 (3H, s), 2.08 (3H, s), 1.47 (9H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO, 380 K) δ 170.7, 153.9, 137.8, 137.7, 136.9, 136.3, 135.7, 135.2, 130.5, 130.0, 128.6, 128.4, 128.3, 127.4, 80.0, 63.4, 28.7, 28.7, 19.7, 19.5; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{22}H_{24}NO_4]^-$ 366.1705; Found 366.1702.

**(–)-(5R,11bS)-1,11-Dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylic acid trifluoroacetic acid (–)-27.TFA**

(5R,11bS)-6-(*tert*-Butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5H dibenzo[c,e]azepine-5-carboxylic acid (250 mg, 0.68 mmol) was dissolved in dichloromethane (10 mL), trifluoroacetic acid (0.71 mL, 9.53 mmol, 14 equiv.) added in one portion, and the solution stirred for 30 minutes. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (10 mL). The solution was washed with $H_2O$ (3 x 10 mL) and saturated brine (3 x 5 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$) to yield the title compound as a colourless solid (128 mg, 50%).

m.p. 250-252 °C; $[\alpha]_D^{24}$ −34.8 ° (*c* 1.02, MeOH); $\nu_{max}$ (solid)/$cm^{-1}$ 3169, 2800, 1729, 1643, 1566, 1433, 1379, 1348, 1285, 1249, 1150, 1136, 1059, 839, 786, 725, 675; $^1$H NMR (500 MHz, *d6*-DMSO) δ 13.49 (1H, s), 10.10 (1H, s), 9.13 (1H, s), 7.52-7.28 (6H, m), 5.43 (1H, s), 4.09 (1H, d, *J* = 12.9 Hz), 3.43 (1H, d, *J* = 12.9 Hz), 2.11 (3H, s), 2.08 (3H, s); $^{13}$C NMR (126 MHz, *d6*-DMSO) δ $^{13}$C NMR (126 MHz, DMSO) δ 168.7, 137.2, 136.9, 136.7, 136.4, 131.8, 131.48, 130.45, 130.0, 129.3, 128.5, 128.2, 128.0, 59.0, 45.6, 19.2, 19.0; HRMS (NSI-FTMS) *m/z*: $[M-CF_3CO_2H_2]^-$ Calcd for $[C_{17}H_{16}NO_2]^-$ 266.1181; Found 266.1187.

**General procedure for the organocatalytic Diels-Alder reaction**

The catalyst (10 mol%) was dissolved in MeOH:$H_2O$ (95:5, 1 mL), and an α-β unsaturated aldehyde (1.0 mmol) was added. After 5 minutes the diene was added (3 mmol, 3 equiv.). The reaction was monitored by TLC, and upon complete consumption of cinnamaldehyde the mixture was diluted with $Et_2O$ (5 mL), washed with $H_2O$ (3 x 5 mL) and saturated brine (2 x 5 mL), and concentrated under reduced pressure. Hydrolysis of the dimethyl acetal adduct was performed by stirring in TFA:$H_2O$:$CHCl_3$ (1:1:2) for 2 h. The mixture was neutralized with aqueous sodium hydrogen carbonate, and extracted with $Et_2O$ (2 x 10 mL). The combined organic layers were washed with

 

saturated brine (2 x 5 mL), dried over anhydrous $MgSO_4$, and the solvents were removed under reduced pressure. The residue was purified by column chromatography. Reduction to the corresponding alcohol was performed using $LiAlH_4$ in anhydrous $Et_2O$ to allow separation on HPLC media.

**(1R,2S,3S,4S)-3-Phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde** and **(1S,2S,3S,4R)-3-phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [42]

The reaction was performed according to the general procedure using (*E*)-cinnamaldehyde (126 µL, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.86 (1H, d, *J*= 2.0 Hz); *endo* δ 9.59 (1H, d, *J*= 2.2 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3059, 3026, 2970, 2950, 2898, 2828, 1718, 1600, 1496, 1450, 1333, 1131, 1059, 720, 699; $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 203.5, 202.8, 143.6, 142.6, 139.2, 136.6, 136.3, 133.8, 128.6, 128.2, 127.9, 127.4, 126.3, 126.2, 60.9, 59.5, 48.5, 48.4, 47.6, 47.2, 45.7, 45.48, 45.50, 45.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{14}H_{13}O]^-$ 197.0966; Found 197.0960.

For the *exo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.86 (1H, d, *J*= 2.0 Hz), 7.30-7.10 (5H, m), 6.29 (1H, dd, *J*= 5.5, 3.5 Hz), 6.03 (1H, dd, *J*= 5.5, 3.0 Hz), 3.69 (1H, dd, *J*= 5.0, 3.5 Hz), 3.18-3.16 (2H, m), 2.55 (1H, m), 1.61-1.54 (2H, m).
For the *endo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.55 (1H, d, *J*= 2.2 Hz), 7.30-7.10 (5H, m), 6.37 (1H, dd, *J*= 5.7, 3.2 Hz), 6.13 (1H, dd, *J*= 5.7, 2.8 Hz), 3.30-3.26 (1H, m), 3.08- 3.07 (1H, m), 3.06 (1H, dd, *J*= 4.5, 1.0 Hz), 2.93-2.90 (1H, m), 1.79-1.74 (1H, m), 1.51 (1H, m).

**((1R,2S,3S,4S)-3-Phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol** and **((1S,2S,3S,4R)-3-phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol** [36]

Following purification, the adduct (150 mg, 0.76 mmol) was dissolved in anhydrous $Et_2O$ (10 mL). $LiAlH_4$ (30 mg, 0.76 mmol) was added, and the mixture stirred until completion of the reaction was observed by TLC. Purification by column chromatography (4:1 light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3339 (br), 3058, 2965, 2872, 1030, 717, 698; $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.32-7.14 (10H, m), 6.37 (1H, dd, *J*= 5.5, 3.0 Hz), 6.34 (1H, dd, *J*= 5.5, 3.0 Hz), 6.16 (1H, dd, *J*= 5.7, 3.0 Hz), 5.94 (1H, dd, *J*= 5.5, 3.0 Hz), 3.90 (1H, dd, *J*= 10.5, 6.0 Hz), 3.70- 3.62 (2H, m), 3.40 (1H, dd, *J*= 10.5, 9.0 Hz), 3.03 (2H, br m), 2.87 (2H, br m) 2.84 (1H, dd, *J*= 5.0, 3.5 Hz), 2.40-2.32 (1H, m), 2.14 (1H, dd, *J*= 5.5, 2.0 Hz), 1.94-1.90 (1H, m), 1.80-1.77 (1H, m), 1.66-1.64 (1H, m), 1.61-1.57 (1H, m), 1.54 (2H, m); $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 145.0, 144.0, 138.7, 137.6, 134.6, 134.3, 128.5, 128.0, 127.5, 126.0, 125.9, 66.9, 66.5, 50.3, 49.9, 49.0, 48.7, 48.4, 47.8, 47.08, 47.10, 44.8, 44.1; HRMS (NSI-FTMS) *m/z*: $[M+NH_4]^+$ Calcd for $[C_{14}H_{20}NO]^+$ 218.1545; Found 218.1541. Enantiomeric excesses were determined using HPLC with Chiralcel® OJ column (hexane/iPrOH=90:10, λ=222 nm), 1.0 mL; *endo* isomer ($t_R$1 15 min, 35 min); *exo* isomer ($t_R$1 47 min, 65 min)).

**(1R,2S,3S,4S)-3-(2-Methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** and **(1S,2S,3S,4R)-3-(2-methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [36]

The reaction was performed according to the general procedure using (*E*)-2-methoxycinnamaldehyde (162 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.93 (1H, d, *J*= 3.0 Hz); *endo* δ 9.50 (1H, d, *J*= 4.0 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 2969, 2716, 1717, 1490, 1243, 1111, 1028, 753, 719; $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 206.3, 204.2, 157.6, 157.5, 138.5, 136.9, 136.4, 134.2, 132.4, 131.0, 127.3, 127.2, 127.2, 125.6, 120.4, 120.0, 110.0, 109.9, 59.7, 58.0, 55.0, 54.9, 47.8, 47.4, 47.0, 46.3, 46.2, 45.6, 40.8, 40.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{15}H_{15}O_2]^-$ 227.1072; Found 227.1065.

For the *exo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.93 (1H, d, *J*= 3.0 Hz), 7.26-6.79 (4H, m), 6.27 (1H, dd, *J*= 6.0, 3.5 Hz), 6.17 (1H, dd, *J*= 6.0, 3.0 Hz), 3.88 (1H, dd, *J*= 5.5, 3.0 Hz), 3.78 (3H, s), 3.29 (1H, m), 3.10-3.07 (1H, m), 2.38-2.31 (1H, m), 1.61 (1H, ddd, *J*= 8.5, 3.5, 1.5 Hz), 1.55 (1H, ddd, *J*= 8.5, 3.5, 1.5 Hz).
For the *endo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.50 (1H, d, *J*= 4.0 Hz), 7.26 – 6.79 (4H, m), 6.42 (1H, dd, *J*= 6.0, 3.5 Hz), 6.17 (1H, dd, *J*= 6.0, 3.0 Hz), 3.73 (3H, s), 3.26-3.22 (1H, m), 3.20 (1H, s), 3.16 (1H, d, *J*= 4.0 Hz), 2.55 (1H, dt, *J*= 5.0, 3.8 Hz), 1.72 (1H, s) 1.57-1.55 (1H, m).

**((1R,2S,3S,4S)-3-(2-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol** and **((1S,2S,3S,4R)-3-(2-methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol**

Following purification, the adduct (210 mg, 0.92 mmol) was dissolved in anhydrous $Et_2O$ (10 mL). $LiAlH_4$ (35 mg, 0.92 mmol) was added, and the mixture stirred until completion of the reaction was observed by TLC. Purification by column chromatography (4:1 light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3368, 2962, 2941, 1598, 1490, 1463, 1242, 1029, 752, 736, 716; $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.32 (1H, dd, *J*= 8.0, 1.5 Hz), 7.22-7.16 (1H, m), 7.16-7.12 (1H, m), 7.05 (1H, dd, *J*= 8.0, 2.0 Hz), 6.96 (1H, td, *J*= 7.5, 1.0 Hz), 6.86 (1H, dd, *J*= 8.2, 1.0 Hz), 6.83-6.80 (2H, m), 6.36 (2H, dt, *J*= 5.8, 3.0 Hz), 6.13 (1H, dd, *J*= 6.0, 3.0 Hz), 5.84 (1H, dd, *J*= 6.0, 3.0 Hz), 3.84 (6H, s), 3.83 (1H, m), 3.80 (1H, m) 3.62 (1H, dd, *J*= 10.6, 8.5 Hz), 3.54 (1H, dd, *J*= 10.8, 7.5 Hz), 3.45 (1H, dd, *J*= 10.8, 6.8 Hz), 3.27 (1H, dd, *J*= 5.4, 3.2 Hz), 3.00 (1H, s), 2.96 (1H, s), 2.86 (2H, s), 2.50 (1H, dd, *J*= 5.0, 1.0 Hz), 2.24-2.15 (1H, m), 1.97-1.89 (1H, m), 1.82 (1H, d, *J*= 8.4 Hz), 1.73 (1H, br s), 1.68 (1H, d, *J*= 8.6 Hz), 1.58 (1H, ddd, *J*= 8.4, 3.3, 1.6 Hz), 1.50 (1H, ddd, *J*= 8.6, 3.4, 1.5 Hz); $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 157.6, 156.80, 138.7, 137.3, 134.9, 134.6, 133.7, 131.8, 127.5, 126.8, 126.8, 126.6, 121.1, 120.0, 110.4, 109.9, 67.2, 67.0, 55.4, 50.89, 48.7, 48.6, 47.6, 47.5, 47.4, 44.9, 44.8, 40.9, 40.3; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{15}H_{19}O_2]^+$ 231.1385; Found 231.1380. Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=98:2, λ=222 nm), 0.5 mL; *endo* isomer ($t_R$1 65 min, 80 min); *exo* isomer ($t_R$1 57 min, 69 min)).

**(1R,2S,3S,4S)-3-(4-Methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-**

**carbaldehyde and (1S,2S,3S,4R)-3-(4-methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [36]

The reaction was performed according to the general procedure using (*E*)-4-methoxycinnamaldehyde (162 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.88 (1H, d, *J*= 2.0 Hz); *endo* δ 9.56 (1H, d, *J*= 2.3 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 2968, 2835, 2718, 1715, 1611, 1513, 1463, 1247, 1180, 1035, 726; $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 203.7, 202.9, 158.2, 158.0, 139.3, 136.6, 136.3, 135.6, 134.7, 133.7, 128.8, 128.3, 114.0, 113.6, 61.0, 59.7, 55.3, 55.2, 48.7, 48.6, 47.6, 47.1, 45.5, 45.07, 45.10, 44.7.

For the *exo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.88 (1H, d, *J*= 2.0 Hz), 7.08-7.03 (2H, m), 6.79-6.76 (2H, m), 6.31 (1H, dd, *J*= 5.6, 3.0 Hz), 6.05 (1H, dd, *J*= 5.6, 3.0 Hz), 3.75 (3H, s), 3.64 (1H, dd, *J*= 5.2, 3.5 Hz), 3.19-3.16 (1H, m), 3.16-3.14 (1H, m), 2.51 (1H, dt, *J*= 5.3, 2.0 Hz), 1.61-1.56 (1H, m), 1.53 (1H, m);

For the *endo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.56 (1H, d, *J*= 2.3 Hz), 7.19-7.15 (2H, m), 6.87-6.82 (2H, m), 6.39 (1H, dd, *J*= 5.6, 3.0 Hz), 6.14 (1H, dd, *J*= 5.6, 3.0 Hz), 3.76 (3H, s), 3.31-3.28 (1H, m), 3.06-3.03 (1H, m), 3.02-2.99 (1H, m), 2.91 (1H, ddd, *J*= 5.0, 3.4, 2.4 Hz), 1.78-1.76 (1H, m), 1.61-1.58 (1H, m).

**((1S,2S,3S,4R)-3-(4-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol**

Following purification, the adduct (158 mg, 0.69 mmol) was dissolved in anhydrous $Et_2O$ (10 mL). $LiAlH_4$ (26 mg, 0.69 mmol) was added, and the mixture stirred until competition of the reaction was observed by TLC. Purification by column chromatography (9:1, light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3400, 3056, 2964, 1611, 1580, 1511, 1464, 1265, 1246, 1034, 910, 743; $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.25-7.07 (4H, m), 6.90-6.73 (4H, m), 6.37- 6.32 (1H, m), 6.14 (1H, dd, *J*= 5.7, 2.8 Hz), 5.94 (1H, dd, *J*= 5.7, 2.8 Hz), 3.88 (1H, dd, *J*= 10.5, 6.0 Hz), 3.79 (3H, m), 3.76 (3H, m), 3.66 (1H, dd, *J*= 10.5, 9.0 Hz) 3.61 (1H, dd, *J*= 10.5, 6.0 Hz), 3.38 (1H, dd, *J*= 10.5, 9.0 Hz), 3.01 (2H, br d, *J*= 17.5 Hz), 2.84 (1H, dd, *J*= 14.6, 1.5 Hz), 2.79 (1H, dd, *J*= 5.0, 3.5 Hz), 2.37-2.27 (1H, m), 2.11-2.07 (1H, m), 1.88-1.84 (2H, m), 1.75 (1H, d, *J*= 8.5 Hz), 1.63 (1H, d, *J*= 8.5 Hz), 1.59-1.54 (2H, m), 1.54-1.50 (1H, m), 1.26 (1H, s), 1.21 (1H, d, *J*= 6.1 Hz); $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 157.9, 157.8, 138.7, 137.5, 137.0, 136.1, 134.6, 134.1, 129.0, 128.9, 128.4, 113.8, 113.4, 66.9, 66.6, 55.3, 55.2, 50.8, 50.4, 50.1, 49.4, 49.2, 48.8, 47.5, 47.1, 47.06, 47.09, 44.8, 44.1. HRMS (NSI-FTMS) *m/z*: $[M+NH_4]^+$ Calcd for $[C_{15}H_{22}NO_2]^+$ 248.1651; Found 248.1646. Enantiomeric excesses were determined using Chiralcel® AS-3 column (hexane/iPrOH=95:5, λ=222 nm), 0.5 mL; *endo* isomer ($t_R$1 35 min, 59 min); *exo* isomer ($t_R$1 39 min, 56 min)).

**(1R,2S,3S,4S)-3-(2-Nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and (1S,2S,3S,4R)-3-(2-nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [37]

The reaction was performed according to the general procedure using (*E*)-2-nitrocinnamaldehyde (177 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.80 (1H, d, *J*= 2.2 Hz); *endo* δ 9.40 (1H, d, *J*= 3.5 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a yellow oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3054, 2986, 2825, 2305, 2254, 1717, 1687, 1527, 1421, 1351, 1263, 746, 705; $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 203.6, 201.5, 139.2, 137.3, 137.0, 136.3, 136.1, 134.2, 132.8, 131.8, 128.9, 127.9, 127.4, 127.3, 124.8, 124.0, 59.3, 59.0, 49.8, 49.2, 48.2, 47.2, 46.6, 46.3, 41.7, 40.1; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{14}H_{12}NO_3]^-$ 242.0817; Found 242.0811.

For the *exo* compound $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.81 (1H, d, *J*= 2.2 Hz), 7.72 (1H, dd, *J*= 8.0, 1.5 Hz), 7.45-7.41 (1H, m), 7.36-7.30 (1H, m), 7.18 (1H, dd, *J*= 8.0, 1.0 Hz), 6.47 (1H, dd, *J*= 5.6, 3.2 Hz), 6.02 (1H, dd, *J*= 5.6, 3.0 Hz), 4.09 (1H, dd, *J*= 5.2, 3.3 Hz), 3.37 (1H, br s), 3.31-3.26 (1H, m), 2.63-2.58 (1H, m), 1.67-1.60 (1H, m), 1.60-1.57 (1H, m).

For the *endo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.40 (1H, d, *J*= 3.5 Hz), 7.82 (1H, dd, *J*= 8.0, 1.5 Hz), 7.59-7.52 (2H, m), 7.39 (1H, ddd, *J*= 8.4, 7.3, 1.5 Hz), 6.50 (1H, dd, *J*= 5.6, 3.2 Hz), 6.22 (1H, dd, *J*= 5.7, 2.8 Hz), 3.44 (1H, dd, *J*= 5.0, 1.0 Hz), 3.34-3.30 (1H, m), 3.13-3.11 (1H, m), 2.95 (1H, dt, *J*= 5.2, 3.6 Hz), 1.84 (1H, dt, *J*= 9.0, 1.5 Hz), 1.69-1.68 (1H, m).

**((1R,2S,3S,4S)-3-(2-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol compound and ((1S,2S,3S,4R)-3-(2-nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol**

Following purification, the adduct (140 mg, 0.58 mmol) was dissolved in anhydrous $Et_2O$ (10 mL). $LiAlH_4$ (22 mg, 0.58 mmol, 1 equiv.) was added, and the mixture stirred until competition of the reaction was observed by TLC. Purification by column chromatography (9:1, light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a pale yellow oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3064, 2973, 1717, 1523, 1351, 723; $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.70 (1H, dd, *J* = 8.0, 1.4 Hz), 7.63 (2H, ddd, *J* = 8.0, 3.5, 1.1 Hz), 7.54 (1H, td, *J* = 7.8, 1.4 Hz), 7.40 (1H, dd, *J* = 7.3, 1.0 Hz), 7.36-7.26 (3H, m), 6.47 (1H, dd, *J* = 5.6, 3.2 Hz), 6.42 (1H, dd, *J* = 5.6, 3.1 Hz), 6.15 (1H, dd, *J* = 5.7, 2.9 Hz), 5.89 (1H, dd, *J* = 5.6, 2.9 Hz), 3.76 (1H, dd, *J* = 10.6, 6.3 Hz), 3.63 (1H, dd, *J* = 10.5, 8.2 Hz), 3.45 (1H, dd, *J* = 10.6, 6.0 Hz), 3.35 (1H, dd, *J* = 10.6, 8.0 Hz), 3.18 (1H, dd, *J* = 5.2, 3.2 Hz), 3.11 (2H, dd, *J* = 7.5, 1.8 Hz), 2.91 (1H, d, *J* = 1.4 Hz), 2.80 (1H, d, *J* = 1.4 Hz), 2.58-2.50 (2H, m), 2.00-1.93 (2H, m), 1.77 (2H, d, *J* = 8.9 Hz), 1.69 (2H, d, *J* = 8.8 Hz), 1.58-1.52 (2H, m); $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 138.3, 137.4, 134.0, 131.5, 129.1, 126.8, 123.4, 66.5, 50.7, 49.3, 48.0, 45.1, 42.6, 14.2; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{14}H_{16}NO_3]^+$ 246.1130; Found 246.1124. Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=95:5, λ=254 nm), 0.5 mL: *endo* isomer ($t_R$1 37 min, 39 min); *exo* isomer ($t_R$1 41 min, 50 min)).

**(1R,2S,3S,4S)-3-(4-Nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and (1S,2S,3S,4R)-3-(4-nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [36]

The reaction was performed according to the general procedure using (*E*)-4-nitrocinnamaldehyde (177 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and

 

assignment of the diastereoisomeric ratio (*exo* δ 9.92 (1H, d, *J*= 2.0 Hz); *endo* δ 9.65 (1H, d, *J*= 2.0 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a yellow oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 2972, 1715, 1596, 1515, 1495, 1345, 1107, 721; $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 202.1, 201.6, 171.1, 151.7, 150.6, 146.5, 146.3, 139.0, 137.0, 135.9, 134.0, 128.7, 128.2, 123.7, 123.3, 61.1, 60.3, 59.5, 48.4, 47.9, 47.6, 47.1, 45.6, 45.5, 45.1, 45.0, 21.0, 14.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{14}H_{12}NO_3]^-$ 242.0817; Found 242.0811.

For the *exo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.92 (1H, d, *J*= 2.0 Hz), 8.12-8.01 (2H, m), 7.36-7.26 (2H, m), 6.41 (1H, dd, *J*= 5.5, 3.0 Hz), 6.05 (1H, dd, *J*= 5.5, 3.0 Hz), 3.89 (1H, dd, *J*= 5.0, 3.5 Hz), 3.34-3.29 (1H, m), 3.26 (1H, br s), 2.64 (1H, d, *J*= 5.2 Hz), 1.62-1.59 (2H, m).

For the *endo* compound: $^1H$ NMR (500 MHz, $CDCl_3$) δ 9.65 (1H, d, *J*= 2.0 Hz), 8.22-8.12 (2H, m), 7.48-7.35 (2H, m), 6.44 (1H, dd, *J*= 6.0, 3.5 Hz), 6.20 (1H, dd, *J*= 6.0, 3.0 Hz), 3.44 (1H, br s), 3.21-3.19 (2H, m), 2.98 (1H, ddd, *J*= 5.0, 3.5, 1.7 Hz), 1.78-1.68 (2H, m).

**((1R,2S,3S,4S)-3-(4-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol and ((1S,2S,3S,4R)-3-(4-nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol**

Following purification, the adduct (210 mg, 0.86 mmol) was dissolved in anhydrous $Et_2O$ (10 mL). $LiAlH_4$ (32 mg, 0.86 mmol, 1 equiv.) was added, and the mixture stirred until competition of the reaction was observed by TLC. Purification by column chromatography (9:1, light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. $\nu_{max}$ ($CHCl_3$)/$cm^{-1}$ 3418, 3054, 2986, 1265, 739; $^1H$ NMR (500 MHz, $CDCl_3$) δ 8.18-8.12 (2H, m), 8.10-8.06 (2H, m), 7.51-7.46 (2H, m), 7.38-7.34 (2H, m), 6.40-6.37 (2H, m), 6.19 (1H, dd, *J*= 6.0, 3.0 Hz), 5.91 (1H, dd, *J*= 6.0, 3.0 Hz), 3.85 (1H, dd, *J*= 10.5, 7.0 Hz), 3.75 (1H, dd, *J*= 10.5, 8.0 Hz), 3.58 (1H, dd, *J*= 10.5, 7.0 Hz), 3.51 (1H, dd, *J*= 10.5, 8.0 Hz), 3.09 (1H, s), 3.07 (1H, s), 3.04-2.98 (1H, m), 2.97-2.95 (1H, br m), 2.90-2.89 (1H, br m), 2.38-2.31 (1H, m), 2.31-2.28 (1H, br m), 1.98-1.92 (1H, m), 1.72 (2H, br dd, *J*= 15.5, 8.5 Hz), 1.64 (1H, ddd, *J*= 8.8, 3.3, 1.7 Hz), 1.59 (1H, ddd, *J*= 8.8, 3.3, 1.6 Hz), 1.53 (2H, br s); $^{13}C$ NMR (126 MHz, $CDCl_3$) δ 153.3, 152.2, 146.4, 146.2, 138.3, 138.3, 134.8, 134.0, 128.8, 128.3, 123.6, 123.2, 66.7, 66.4, 50.8, 50.0, 48.9, 48.8, 48.7, 48.1, 47.4, 47.1, 45.0, 44.4; HRMS (NSI-FTMS) *m/z*: $[M+NH_4]^+$ Calcd for $[C_{14}H_{19}N_2O_3]^+$ 263.1396; Found 263.1390. Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=90:10, λ=254 nm), 0.5 mL; *endo* isomer ($t_R$1 49 min, 57 min); *exo* isomer ($t_R$1 43 min, 53 min)).

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

This investigation has enjoyed the support of EU Interreg IVA (project 4061) and the University of East Anglia. We are also indebted to the EPSRC National Mass Spectrometry Facility at Swansea University.

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