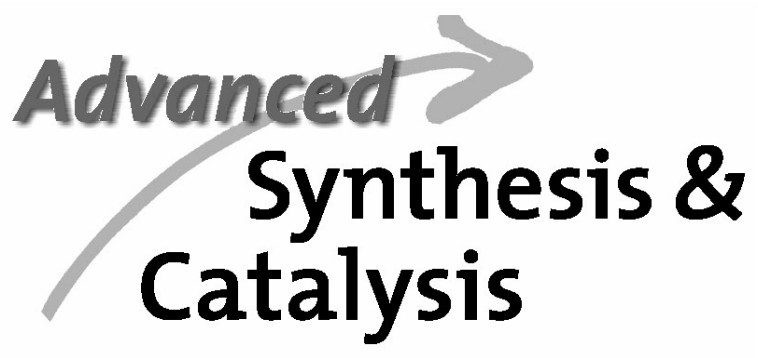

Supporting Information

Niobium-catalyzed Highly Enantioselective Aza Diels-Alder Reactions

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Supporting Information

General experimental

^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECX400, JNM-ECX500, and JNM-ECX600 spectrometer in $CDCl_3$, unless otherwise noted. Tetramethylsilane (TMS) served as internal standard (0 ppm) for ^{1}H NMR, and $CDCl_3$ was used as internal standard (77.0 ppm) for ^{13}C NMR. IR spectra were measured using a JASCO FT/IR-610 spectrometer. Optical rotations were measured with a JASCO P-1010 polarimeter. High-performance liquid chromatography was carried out using following apparatus: SHIMADZU LC-10AT (liquid chrmatograph), SHIMADZU SPD-10A (UV detecter), and SHIMADZU C-R6A Chromatopac. ESI high-resolution mass spectra (ESI-HRMS) were measured with BRUKER DALTONICS BioTOF II. Melting points were measured with Buchi B-545 and are uncorrected. Column chromatography was conducted on Silica gel 60 (Merk) and preparative thin-layer chromatography was carried out using Wacogel B-5F. All solvents were distilled and dried over MS 4A. Niobium alkoxides were purchased from High Purity Chemical Laboratory Co. Ltd. and Aldrich. Molecular sieves used in the reactions were dried under reduced pressure at 200 ^{o}C for 8 h for two times.

Ligand **2** was prepared according literature procedure.[1]

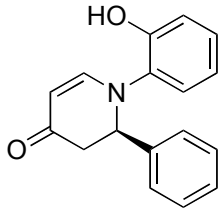
Imines were prepared by reactions of 2-amino-phenol and aldehydes in water and dried in vacuo over P_2O_5 at 60 °C.

Danishefsky's dienes were prepared according literature procedures[2] and purified by distillation. Aldehydes were distilled prior to use.

Typical procedure for the aza Diels-Alder reaction catalyzed by niobium

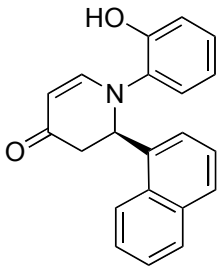
To a solution of a ligand (7.8 mg, 0.016 mmol) in PhMe (1.0 mL), NMI (1.5 μL, 0.016 mmol) was added. After 5 minutes stirring, $Nb(OMe)_5$ (3.7 mg, 0.015 mmol) was added as a solid in argon. The traces of $Nb(OMe)_5$ which remained on the walls were washed down with additional portion of PhMe (0.5 mL). The reaction mixture was heated at 60 °C for 3 h. After cooling to room temperature, 3Å molecular sieves (25 mg) were added. The catalyst solution was cooled to an appropriate temperature, and a solution of an imine (0.3 mmol) in DCM (1.5 mL) was added, followed by a diene (0.4 mmol, 100 μL). After 48 h, the reaction mixture was quenched with sat. $NaHCO_3$ (3 mL) and the resulting mixture was extracted with EtOAc (4 x 5 mL). The combined organic fractions were dried over Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was cooled to 0 °C and treated with 0.1 M HCl in THF (10 mL). After 15 min, the mixture was basified by addition of sat. $NaHCO_3$ and the product was extracted with EtOAc (4 x 5 mL). The combined organic fractions were dried over Na_2SO_4 and the solvents were removed under reduced pressure. The crude mixture was purified by preparative TLC (Hex/EtOAc, 1/1) to give the desired product as a solid.

(*R*)-1-(2-Hydroxyphenyl)-2-phenyl-2,3-dihydropyridin-4(1H)-one (5a):



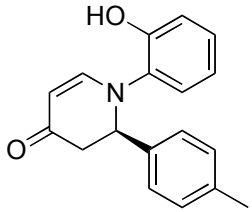
Spectral data were consistent with literature values.[3] HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{major} = 14.04 min, t_{minor} = 16.83 min.

(*R*)-1-(2-Hydroxyphenyl)-1-(naphthalen-2-yl)-2,3-dihydropyridin-4(1H)-one (5b):



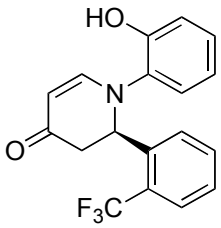
White solid. mp 201 °C; $[\alpha]^{22}_{D}$: −11.3 (c 0.285, MeOH, 92% *ee*); IR (KBr) 1599s, 1558vs, 1510s, 1458m, 1290m, 1092s, 775m, 754m cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-*d6*) δ = 10.1 (bs, 1 H), 8.06 (d, *J*= 8.4 Hz, 1 H), 7.89 (d, *J*= 8.4 Hz, 1 H), 7.78 (d, *J*= 8.0 Hz, 1 H), 7.75-7.70 (m, 2 H), 7.57-7.47 (m, 2 H), 7.40 (t, *J*= 7.6 Hz, 1 H), 7.15 (d, *J*= 8.0 Hz, 1 H), 6.95-6.87 (m, 1 H), 6.85-6.80 (m, 1 H), 6.62 (t, *J*= 8.0 Hz, 1 H), 6.27-6.23 (m, 1 H), 4.95 (d, *J* = 8.0 Hz, 1 H), 3.20 (dd, *J* = 16.4 Hz, 6.8 Hz, 1 H), 2.72 (d, *J* = 16.0 Hz); ^{13}C-NMR (100 MHz, DMSO-d_6) δ = 188.7, 154.3, 151.1, 133.8, 133.6, 131.9, 129.5, 129.0, 128.0, 127.2, 126.5, 125.7, 125.5, 125.2, 124.1, 122.7, 119.3, 116.8, 97.9, 58.0, 42.7. HRMS (ESI) calculated for $C_{21}H_{18}NO_2^+$: 316.1332, found: 316.1342. HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{major} = 14.28 min, t_{minor} = 17.28 min.

(*R*)-1-(2-Hydroxyphenyl)-2-p-tolyl-2,3-dihydropyridin-4(1H)-one (5c):



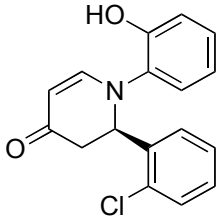
White solid. mp 165 °C; $[\alpha]^{22}_{D}$: −160.9 (*c* 0.29, DCM, 94% *ee*); IR (KBr) 1558vs, 1512s, 1461s, 1290s, 1230s, 816s, 754s cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ = 7.35 (d, *J*= 6.6 Hz, 1 H), 7.10-7.05 (m, 2 H), 6.95-6.90 (m, 3 H), 6.90-6.85 (m, 1 H), 6.81-6.77 (m, 1 H), 6.63-5.57 (m, 1 H), 5.23-5.15 (m, 2 H), 3.16 (dd, *J*= 16.5 Hz, 6.8 Hz, 1 H), 2.77 (dd, *J*= 16.5 Hz, 6.2 Hz, 1 H), 2.16 (s, 3 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 192.4, 155.8, 151.9, 137.8, 135.6, 131.7, 129.4, 128.5, 127.0, 126.4, 119.8, 117.3, 98.7, 62.2, 42.9, 21.2. HRMS (ESI) calculated for $C_{18}H_{18}NO_2^+$ 280.1332, found: 280.1335. HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{minor} = 13.78 min, t_{major} = 16.47 min.

(*R*)-1-(2-Hydroxyphenyl)-2-(2-(trifluoromethyl)phenyl)-2,3-dihydropyridin-4(1H)-one (5d):



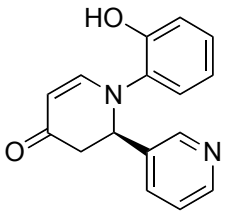
Yellow solid. mp 93 °C; $[\alpha]^{22}_{D}$: –227.6 (*c* 0.25, DCM, 99% *ee*); IR (KBr) 1565vs, 1456s, 1311vs, 1159s, 1114s, 1037s 755s cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.84 bs (1 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 7.53 (d, *J* = 7.6 Hz, 1 H), 7.50-7.47 (m, 2 H), 7.33-7.22 (m, 1 H), 7.00-6.80 (m, 3 H), 6.70-6.60 (m, 1 H), 5.79 (t, *J* = 8.0 Hz, 1 H), 5.30 (d, *J* = 7.6 Hz, 1 H), 3.19 (dd, *J* = 17.2 Hz, 7.6 Hz, 1 H), 2.60 (dd, *J* = 16.4 Hz, 8.4 Hz, 1 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 191.3, 156.8, 151.5, 138.5, 132.3, 131.1, 128.4, 128.0, 127.3, 127.0, 126.1 (q, *J* = 3.9 Hz, 1 H), 126.07, 125.9, 119.9, 117.1, 98.8, 58.1, 43.5. HRMS (ESI) calculated for $C_{18}H_{15}F_3NO_2^+$: 334.1049, found: 334.1041. HPLC: 2xAD-H, Hex/EtOH (9/1), 1mL/min, t_{minor} = 62.01 min, t_{major} = 65.78 min.

(*R*)-2-(2-Chlorophenyl)-1-(2-hydroxyphenyl)-2,3-dihydropyridin-4(1H)-one (5e):



Yellow oil. $[\alpha]^{22}_{D}$: –93.2 (*c* 0.37, DCM, 91% *ee*); IR (KBr) 1562vs, 1291m, 1199m, 1092s, 669m cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ = 9.75 (s, 1 H), 7.42 =(d, *J* = 7.4 Hz, 1 H), 7.20 (s, 1 H), 7.10-7.05 (m, 3 H), 6.96-6.91 (m, 1 H), 6.85-6.81 (m, 2 H), 6.67-6.61 (m, 1 H), 5.25-5.20 (m, 1 H), 5.17 (d, *J* = 7.6 Hz, 1 H), 3.20 (dd, *J* = 16.4 Hz, 6.8 Hz, 1 H), 2.72 (dd, *J* = 17.2 Hz, 6.2 Hz, 1 H); ^{13}C-NMR (150 MHz, $CDCl_3$) δ = 191.6, 155.7, 151.6, 140.5, 134.3, 131.1, 129.9, 128.6, 128.1, 127.0, 126.1, 125.1, 119.9, 117.2, 98.7, 61.6, 42.4. HRMS (ESI) calculated for $C_{17}H_{15}ClNO_2^+$: 300.0786, found: 300.0790. HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{minor} = 10.62 min, t_{major} = 12.08 min.

(*R*)-1-(2-Hydroxyphenyl)-2-(pyridin-3-yl)-2,3-dihydropyridin-4(1H)-one (5f):

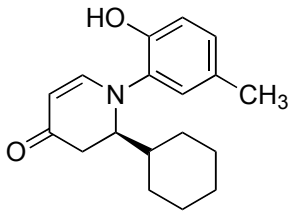


Yellow oily solid. mp 99 °C; $[\alpha]^{22}_{D}$: –204.2 (*c* 0.28, DCM, 90% *ee*); IR (KBr) 1629s, 1565vs, 1512m, 1461m, 1290s, 1227s, 1195s, 1097s, 756m cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ = 11.1 (bs, 1 H), 8.53 (s, 1 H), 8.40-8.30 (m, 1 H), 7.75-7.65 (m, 1 H), 7.37 (d, J = 7.6 Hz, 1 H), 7.25-7.15 (m, 1 H, H-Ar), 6.95-6.83 (m, 2 H), 6.80-6.70 (m, 1 H), 6.70-6.60 (m, 1 H), 5.45-5.35 (m, 1 H), 5.20-5.10 (m, 1 H), 3.10-3.00 (m, 1 H), 2.85-2.75 (m, 1 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 190.7, 154.6, 152.1, 148.1, 147.9, 135.8, 135.1, 131.1, 128.6, 126.6, 123.9, 119.7, 117.0, 99.5, 60.1, 42.9. HRMS (ESI) calculated for $C_{16}H_{15}N_2O_2^+$ 267.1128, found: 267.1120. HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{minor} = 55.07 min, t_{major} = 67.51 min.

Three-component Aza Diels-Alder reaction:

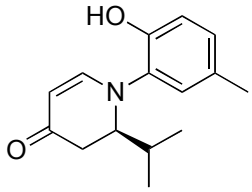
The reaction was conducted in the same manner as described in the typical procedure. The imine was generated in DCM or PhMe (1.0 mL) from 2-amino-*m*-cresol (0.30 mmol) and an aldehyde (0.30 mmol) using $MgSO_4$ as a drying agent. After stirred for 2 h at room temperature, $MgSO_4$ was filtered off by inverse filtration using cotton wool on the top of a syringe needle, and a solution of the imine was added to the cooled solution of the catalyst. Another portion of the solvent (0.5 mL) was used to wash $MgSO_4$ and then was added to the reaction mixture. Diene (0.40 mmol) was added. After 48 h, the reaction was quenched and worked up in the same manner as in the typical procedure.

(*R*)-2-Cyclohexyl-1-(2-hydroxy-5-methylphenyl)-2,3-dihydropyridin-4(1H)-one (5g):



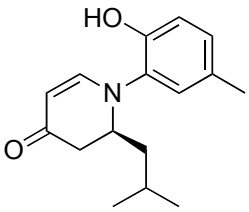
Yellow solid. mp 180°C; $[\alpha]^{22}_{D}$: −120.4 (*c* 0.20, DCM, 90% *ee*); IR (KBr) 2928s, 1561vs, 1380m, 1081vs cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 9.62 (bs, 1 H), 7.30-7.26 (m, 1 H), 7.00-6.80 (m, 3 H), 5.03 (d, *J* = 7.6 Hz), 4.17-4.00 (m, 1 H), 3.18 (dd, *J* = 8.0 Hz, 8.0 Hz, 1 H), 2.60 (dd, *J* = 17.2 Hz, 3.2 Hz, 1 H), 2.26 (s, 3 H), 2.00-1.40 (m, 6 H), 1.20-0.90 (m, 5 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 192.8, 155.9, 149.5, 131.6, 129.2, 128.9, 126.9, 117.2, 97.0, 62.9, 40.1, 36.0, 29.5, 28.3, 26.13, 26.07, 26.03, 20.4. HRMS (ESI) calculated for $C_{18}H_{24}NO_2^+$, 286.1802 found: 286.1796. HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{minor} = 9.18 min, t_{major} = 11.07 min.

(*R*)-1-(2-Hydroxy-5-methylphenyl)-2-isopropyl-2,3-dihydropyridin-4(1H)-one (5h):



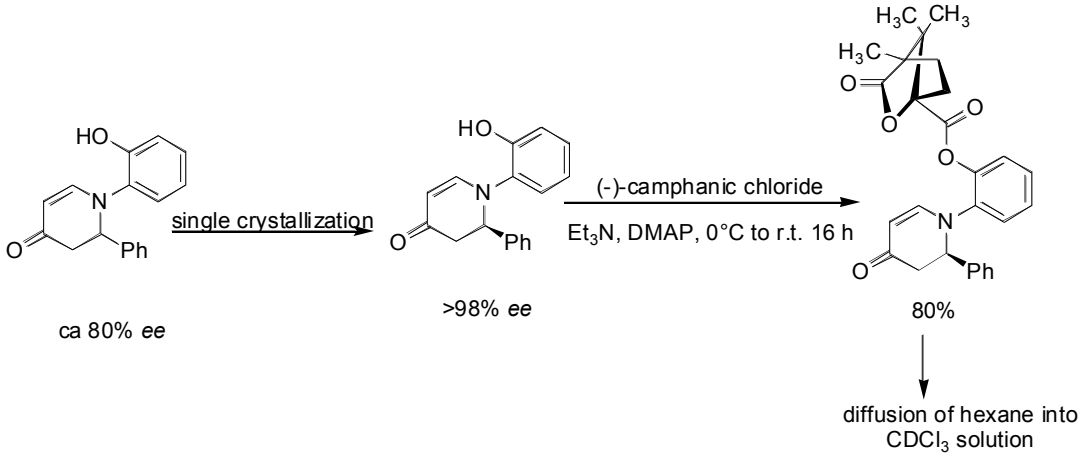
Brown oil which solidified upon standing. mp 73 °C; $[\alpha]^{22}_{D}$ −133.3 (*c* 0.20, DCM, 92% *ee*); IR (KBr) 1620s, 1561vs, 1512s, 1246s, 1251s, 1092s cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.26 (d, *J* = 7.6 Hz, 1 H), 7.00-6.75 (m, 3 H), 5.04 (d, *J* = 7.2 Hz, 1 H), 4.17-4.07 (m, 1 H), 3.00-2.89 (m, 1 H), 2.65-2.55 (m, 1 H), 2.25 (s, 3 H), 2.15-2.00 (m, 1 H), 0.90 (d, *J* = 7.2 Hz, 3 H), 0.81 (d, *J* = 7.2 Hz, 3 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 193.2, 156.2, 149.9, 131.4, 129.3, 129.1, 127.3, 117.3, 97.2, 63.2, 35.4, 29.8, 20.5, 19.6, 17.6. HRMS (ESI) calculated for $C_{15}H_{19}NNaO_2^+$ 268.1308, found: 268.1294. HPLC: AD-H, Hex/EtOH (9/1), 1mL/min, t_{minor} = 7.08 min, t_{major} = 8.12 min.

(*S*)-1-(2-Hydroxy-5-methylphenyl)-2-isobutyl-2,3-dihydropyridin-4(1H)-one (5i):



Yellow oil which solidified upon standing. mp 53 °C; $[\alpha]^{22}_{D}$: −85.3 (*c* 0.25, DCM, 78% *ee*); IR (KBr) 1620s, 1561vs, 1511s, 1218s, 1090s, 817m cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.25-7.20 (m, 1 H), 6.97-6.90 (m, 2 H), 6.85 (s, 1 H), 5.11 (d, *J* = 8.0 Hz, 1 H), 4.25-4.15 (m, 1 H), 3.47 (dd, *J* = 16.8 Hz, 6.4 Hz, 1 H), 2.60 (dd, *J* = 16.8 Hz, 3.2 Hz, 1 H), 2.26 (s, 3 H), 1.85-1.75 (m, 1 H), 1.60-1.45 (m, 1 H), 1.40-1.30 (m, 1 H), 0.78 (d, *J* = 6.4 Hz, 3 H), 0.72 (d, *J* = 6.4 Hz, 3 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 192.3, 154.5, 149.6, 131.2, 129.5, 129.2, 127.2, 117.2, 97.7, 56.9, 39.1, 37.6, 24.3, 23.5, 21.4, 20.5. HRMS (ESI) calculated for $C_{16}H_{22}NO_2^+$: 260.1645, found: 260.1649. HPLC: AD-H, Hex/EtOH (9/1), 0.35mL/min, t_{major} = 19.31 min, t_{minor} = 20.58 min.

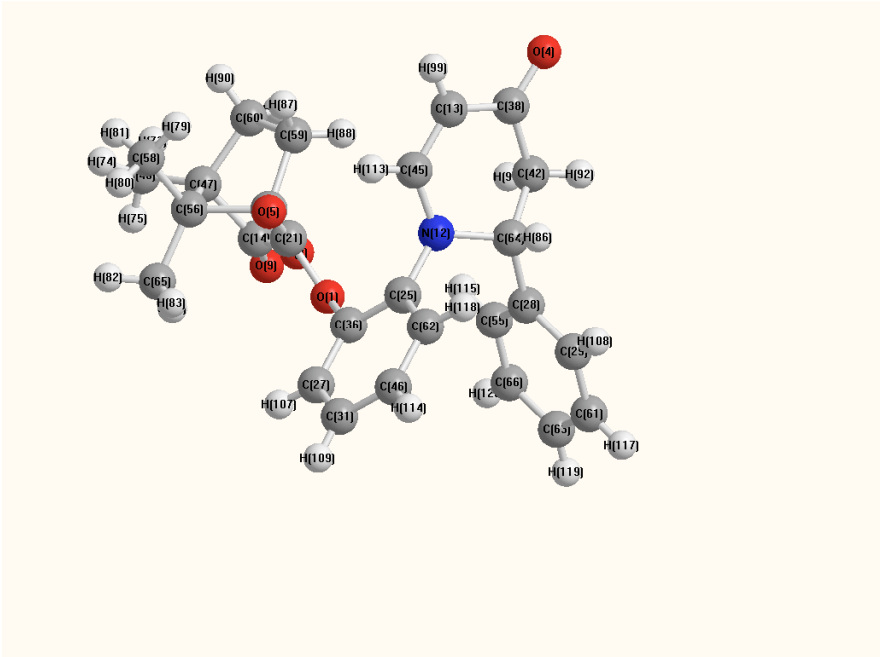
Determination of the absolute configuration (*1R*)-2-(4-Oxo-2-phenyl-3,4-dihydropyridin-1(2H)-yl)phenyl 4,7,7-trimethyl-3-oxo-2-oxa-bicyclo[2.2.1]heptane-1-carboxylate:



(*R*)-1-(2-Hydroxyphenyl)-2-phenyl-2,3-dihydropyridin-4(1H)-one (**5a**) (265.3 mg, 1.00 mmol) was disolved in DCM (20 mL), in which DMAP (5 mg) and Et_3N (153 μL, 1.10 mmol) were added. After 5 minutes, the reaction mixture was cooled to 0 °C and the solution of (*1S*)-(-)-camphanic chloride (237 mg, 1.10 mmol) in DCM (5.00 mL) was added. The reaction mixture was stirred at 0 °C overnight. The solvents were removed under reduced pressure, and the crude mixture was purrified by column chromatography to give the corresponding ester as a white solid (446 mg,

80%). White solid. mp 155 °C; $[\alpha]^{22}_{D}$: +46.5 (*c* 0.275, DCM, 99% *ee*); IR (KBr) 1792vs, 1650vs, 1578vs, 1495s, 1260s, 1092s, 1044s cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.35-7.17 (m, 7 H), 7.15-7.05 (m, 2 H), 7.00-6.95 (m, 1 H), 5.25 (d, *J* = 7.6 Hz, 1 H), 5.08 (t, *J* = 6.4 Hz, 1 H), 3.12-3.05 (m, 1H), 2.82-2.75 (m, 1 H), 2.60-2.40 (m, 1 H), 2.20-2.10 (m, 1 H), 2.05-1.90 (m, 1 H), 1.80-1.70 (m, 1 H), 1.17 (s, 3 H), 1.13 (s, 3 H), 1.11 (s, 3 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 190.3, 177.5, 165.9, 151.6, 144.0, 138.4, 137.5, 128.9, 128.1, 127.6, 127.4, 126.7, 125.4, 123.3, 101.9, 90.5, 63.7, 54.9, 54.8, 44.1, 31.4, 28.9, 16.8, 16.7, 9.6. HRMS-(ESI) calculated for: $C_{27}H_{27}NNaO_5^{+}$: 468.1781, found 468.1770.

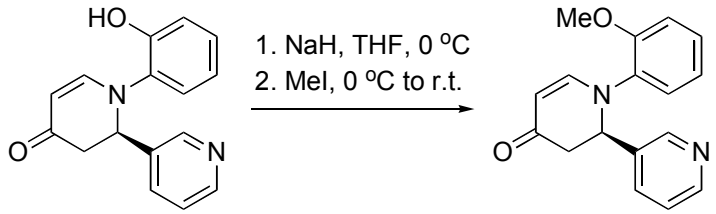
X-Ray suitable crystals were obtained by slow diffusion of the hexane to the solution of the ester in $CDCl_3$(CCDC 667042).



Synthesis of anabasine

(R)-1-(2-Hydroxyphenyl)-2-(pyridin-3-yl)-2,3-dihydropyridin-4(1H)-one (**5f**) was prepared in the same manner as mentioned in general procedure. Reaction was conducted on 1.50 mmol scale.

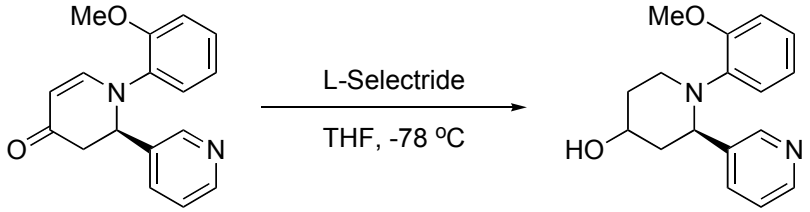
(*R*)-1-(2-Methoxyphenyl)-2-(pyridin-3-yl)-2,3-dihydropyridin-4(1H)-one:



Caution: Methyl iodide is human carcinogen. All operations were performed in the fume hood. (*R*)-1-(2-Methoxyphenyl)-2-(pyridin-3-yl)-2,3-dihydropyridin-4(1H)-one (267 mg, 1.00 mmol) was dissolved in dry THF (15 mL) and mixture was cooled to 0 °C. NaH (43.6 mg of 55% suspension in minaral oil, 1.00 mmol) was added. After stirring at 0 °C for 30 min, MeI (125 μL, 2.00 mmol) was added and the reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was diluted with water (10 mL) and the aqueous layer was extracted with DCM (3x15 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purrified using PTLC (DCM/MeOH = 1/1), giving the corresponding product as a white solid (185 mg, 65%).

mp 135 °C, $[\alpha]^{22}_{D}$: –474 (*c* 0.135, MeOH); IR (KBr) 1620s, 1564vs, 1452m, 1501s, 1289m, 1199m, 1039m, 753m ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.48-8.42 (m, 2 H), 7.60-7.54 (m, 1 H), 7.10 (d, *J* = 7.6 Hz, 1 H), 7.12-7.06 (m, 2 H), 6.95-6.90 (m, 1 H), 6.80-6.72 (m, 2 H), 5.21-5.16 (m, 1 H), 5.13 (d, *J* = 8.0 Hz, 1 H), 3.71 (s, 3 H), 3.00 (dd, *J* = 16.4 Hz, 5.4 Hz, 1 H), 2.72 (dd, *J* = 16.0 Hz, 8.0 Hz, 1 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 190.1, 153.6, 153.1, 149.0, 148.5, 134.4, 134.3, 132.4, 128.3, 126.7, 123.0, 120.8, 111.7, 100.0, 60.3, 55.3, 43.0. HRMS (ESI) calculated for: $C_{17}H_{17}N_2O_2^+$: 281.1285, found: 281.1476.

(*R*)-1-(2-Methoxyphenyl)-2-(pyridin-3-yl)piperidin-4-ol:



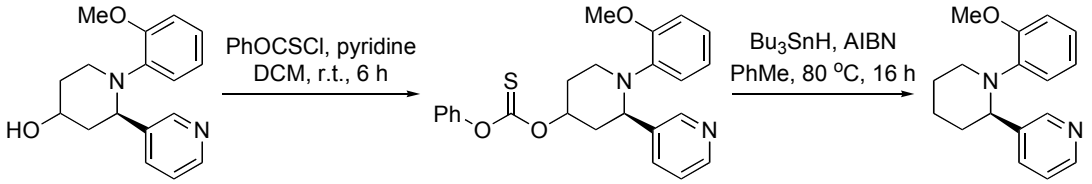
(*R*)-1-(2-Methoxyphenyl)-2-(pyridin-3-yl)-2,3-dihydropyridin-4(1H)-one (165 mg, 0.59 mmol) was dissolved in THF (3 mL), and the mixture was cooled to -78 °C. A 1M solution of L-Selectride (1.76 mL, 3 eq.) was added dropwise and the mixture was stirred at -78 °C for additional 4 h. At this temperature (-78 °C), the reaction mixture was quenched with H_2O (1.00 mL) and warmed to 0 °C. 10% NaOH (1.4

mL) and 30% H_2O_2 (1.00 mL) were added in order to destroy formed borane intermediates, and the reaction mixture was stirred overnight. The reaction mixture was extracted with DCM (3x10 mL), the combined organic layers were washed with sat. $Na_2S_2O_5$, brine, dried over Na_2SO_4, and the solvents were removed under reduced pressure. The crude product was purrified by PTLC giving the title compound as an oily solid (137 mg, 82 % mixture of *syn* and *anti*).

major:^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.43 (s, 1 H), 8.24-8.19 (m, 1 H), 7.54-7.50 (m, 1 H), 7.00-6.95 (m, 1 H), 6.84-6.80 (m, 2 H), 6.70-6.50 (m, 2 H), 4.75-4.60 (m, 1 H), 4.15-4.12 (m, 1 H), 3.76 (s, 3 H), 3.15-3.11 (m, 2 H), 2.20-1.60 (m, 4 H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 154.4, 148.7, 147.4, 139.8, 135.0, 134.9, 124.4, 124.3, 123.2, 120.4, 111.4, 64.2, 56.1, 55.3, 47.8, 42.7, 33.3. HRMS calculated for $C_{17}H_{21}N_2O_2^+$: 285.1598, found: 285.1630.

Signals of the minor isomer were not assigned due to overlap with the signals of the major one. The mixture of diastereomers was used directly in the subsequent steps.

(*R*)-3-(1-(2-Methoxyphenyl)piperidin-2-yl)pyridine:



(*R*)-1-(2-Methoxyphenyl)-2-(pyridin-3-yl)piperidin-4-ol (126 mg, 0.44 mmol) was disolved in DCM (6 mL), in which pyridine (142 μL, 1.76 mmol) and PhOSCCl (178 μL, 1.32 mmol) were added successively. The reaction mixture was stirred at room temperature for 14 h. The reaction was quenched with addition of sat. $NaHCO_3$ (5 mL) and the aqueous layer was extracted with DCM (4x5 mL). The combined organic fractions were dried over Na_2SO_4 and the solvents were removed under reduced pressure. The crude product was purrified by preparative TLC (DCM/MeOH, 9/1) to give the corresponding *O*-phenyl thionocarbonate as a white solid. Purification was essential for the next step.

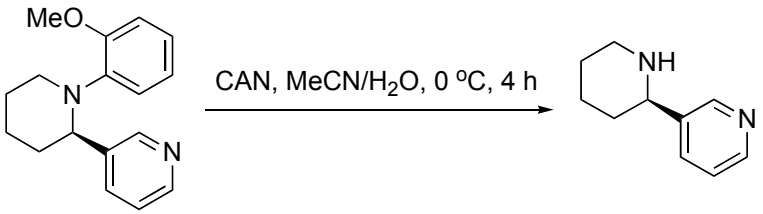
major:^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.50 (s, 1 H), 8.31 (d, J = 4.4 Hz, 1 H), 7.59 (d, J = 8.0 Hz, 1 H), 7.44 (t, J = 8.0 Hz, 2 H), 7.35-7.30 (m, 1 H), 7.20-7.15 (m, 2 H), 7.10-7.00 (m, 1 H), 6.95-6.85 (m, 2 H), 6.77-6.65 (m, 2 H), 5.67-5.64 (m, 1 H), 4.58-4.53 (m, 1 H), 3.82 (s, 3 H), 3.28-3.23 (m, 1 H), 3.12-3.08 (m, 1 H), 2.20-2.05 (m, 4 H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 193.7, 154.6, 153.2, 149.1, 148.1, 139.4, 138.6, 134.7, 129.5, 126.5, 124.77, 124.76, 123.1, 121.9, 120.4, 111.4, 60.3, 56.8, 55.3, 48.5, 39.1, 29.6.

minor:^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.48 (bs, 1 H), 8.31 (bs, 1 H), 7.65-6.60 (m, 11 H), 5.60-5.40 (m, 1 H), 4.50-4.40 (m, 1 H), 3.83 (s, 3 H), 3.55-3.40 (m, 1 H), 3.12-3.00 (m, 1 H), 2.60-2.00 (m, 4 H) ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 194.1, 155.6, 153.4, 153.2, 149.1, 148.3, 138.5, 138.4, 134.9, 129.5, 126.5, 125.6, 123.2, 121.9, 120.5, 111.5, 81.6, 60.0, 55.2, 51.7, 40.6, 31.3.

Caution: Because of the irritating odour of the tributyltin hydride, all operations were performed in the fume hood. Material obtained from the previous step was disolved in PhMe and Bu_3SnH (244 μL, 0.88 mmol) was added, followed by AIBN (14.4 mg, 0.088 mmol). The mixture was heated at 80°C for 16 h. After cooling down to r.t., the solvents were removed under reduced pressure, and the crude mixture was purrified by preparative TLC (1st DCM/MeOH = 9/1, then Hex/EtOAc = 1/1) to give the title compound as colorless oil.

$[\alpha]^{22}_{D}$: −85.5 (*c* 0.115, MeOH); IR (KBr) 2932 vs, 2844s, 1587s, 1494vs, 1243vs, 1106vs, 1025vs, 750s cm^{-1} ^{1}H-NMR (400 MHz, $CDCl_3$) δ = 8.45 (bs, 1 H), 7.26 (dd, J = 4.4 Hz, 1.2 Hz, 1 H), 7.54 (d, J = 8.0 Hz, 1 H), 7.05-6.98 (m, 1 H), 6.90-6.80 (m, 2 H), 6.75-6.70 (m, 1 H), 6.65-6.60 (m, 1 H), 4.19 (dd, J = 10.4, 2.4 Hz, 1 H), 3.82 (s, 3 H), 3.42-3-37 (m, 1 H), 2.78-2.65 (m, 1 H), 2.00-1.50 (m, 6 H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ = 154.8, 148.0, 147.6, 140.35, 140.27, 134.7, 124.9, 124.4, 123.1, 120.4, 111.5 62.0, 55.3, 54.6, 36.9, 26.3, 24.7. HRMS (ESI) calculated for: $C_{17}H_{21}N_2O^+$: 269.1648, found: 269.1641.

(*R*)-3-(Piperidin-2-yl)pyridine ((+)-anabasine):



(*R*)-3-(1-(2-Methoxyphenyl)piperidin-2-yl)pyridine (40 mg, 0.15 mmol) was disolved in a mixture of MeCN (2.00 mL) and water (0.50 mL), and the mixture was cooled to 0 °C. Cerium ammonium nitrate (540 mg, 1.04 mmol) was added and the reaction mixture was stirred at 0 °C for 4 h. The reaction mixture was diluted with water (5.00 mL) and EtOAc (20 mL), and the water phase was basified by solid K_2CO_3. The mixture was filtered through pad of celite and the aqueous phase was extrated with EtOAc (3 x 15 mL). The combined organic layers were dried over K_2CO_3 and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (DCM/MeOH = 9/1) to give (+)-anabasine as colorless liquid which turns yellow upon standing (14.5 mg, 60%). The spectral data were consistent with the values of the authentic sample.[4] The enantiomeric purity was determined by HPLC analysis: OJ-H, Hex/EtOH/Et_2N/CF_3COOH = 97/3/0.1/0.1, 1 mL/min. t_S = 22.4 min. t_S = 26.15 min. The retention times were in agreement with literature values.[5]

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4. See Aldrich prod. no. 284599.
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