Supplementary Information

Diastereo- and Enantioselective Reductive Amination of Cycloaliphatic Ketones by Preformed Chiral Palladium Complexes

Armando Cabrera*ª, Pankaj Sharmaª, F. Javier Pérez-Flores, Luis Velascoª, J. Luis Ariasª and Laura Rubio-Pérezª*

ªInstituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, México, 04510, D. F., México.

ªFacultad de Estudios Superiores Cuautitlán, Departamento de Química, UNAM, Cuautitlán Izcalli, Estado de México 54700

arcaor1@unam.mx and laurarpz@unam.mx

Table of contents:
General and materials………………………………………………………………………………………………S2
Crystal structure of Pd[(R)-Tol-BINAP]Br2 (1e)……………………………………………………………………S3
Preparation of complex and crystal structure of 1h…………………………………………………………………S3
Preparation of complex and crystal structure of 1i…………………………………………………………………S4
Preparation of complex 1j…………………………………………………………………………………………….S6
General procedure for reductive amination of cyclic ketones………………………………………………………S6
General procedure for asymmetric reductive amination of 2-methylcyclopentanone……………………………S10
General procedure for asymmetric reductive amination of 2-methylcyclohexanone……………………………S16
General procedure for asymmetric reductive amination of (R)-3-methylcyclohexanone…………………………S19
General procedure for asymmetric reductive amination of other substituted rings………………………….S21
References…………………………………………………………………………………………………………………..S23
Scanned spectra of NMR and GC-MS (EI) or HPLC for all compounds……………………………………..S24

S1
General:
All reactions and manipulations were carried out by using Schlenk-type techniques. Flash column chromatography was performed on silica gel (70-230 mesh). $^1$H NMR, $^{13}$C NMR and $^{31}$P NMR spectra were obtained on a JEOL GX-300, Bruker-Avance 300, Varian Unity 300 (300, 75 and 121 MHz respectively), and Varian Inova Plus 500 (500 for $^1$H and 125 MHz for $^{13}$C) spectrometers using TMS as the internal reference in CDCl$_3$ as solvent. All chemical shifts (δ) are reported in ppm and coupling constants (J) are reported in Hz to apparent peak multiplications. 2D NOESY, DEPT and $^1$H/$^{13}$C HSQC sequences were used for help the assignments of the $^1$H and $^{13}$C spectra. IR spectra were recorded on a Nicolet FTIR Magna 750 spectrophotometer and the characteristic absorption frequencies are reported in cm$^{-1}$. Optical rotations were performed on a Perkin-Elmer 343 spectropolarimeter (589 nm). Mass spectra were obtained using a JEOL JMS-SX102A instrument with $m$-nitrobenzyl alcohol as the matrix (FAB$^+$ mode), and a JEOL JMS-AX505-A (EI mode at 70 eV). Elemental compositions were calculated within an uncertainty of 5 ppm by using the program installed in the computer system. The enantiomeric excess were determined by GC-MS analyses employing a Hewlett Packard 5890 (series II) instrument coupled with a JEOL JMS-AX505-A GC/MS-EI and Agilent Technologies 6890N coupled with JMS-GC/MS at 70 eV instruments employing a chiral capillary column Cyclodex-β (0.32 mm x 0.32 mm x 50 m) and He as a carrier gas. HPLC analyses were performed on a Hewlett Packard 1100 system with UV-DAD. Separations were achieved on a Daicel Chiracel OD-H (25 x 4.6mm) column. X-ray determination was collected on a Bruker SMART APEX CCD area diffractometer by the o-scan method.

Materials:
All reagents were obtained from commercial suppliers and used without further purification. Diethyl ether and benzene were distilled from sodium-benzophenone and chloroform was distilled from P$_2$O$_5$ under nitrogen. Other solvents were HPLC grade. The Pd(MeCN)$_2$Br$_2$, Pd[(R)-BINAP]Cl$_2$ (1b), Pd[(R)-BINAP]Br$_2$ (1c), Pd[(S)-BINAP]Br$_2$ (1d), Pd[(R)-Tol-BINAP]Br$_2$ (1e), Pd[(S)-Tol-BINAP]Br$_2$ (1f) and Pd[(S,S)-CHIRAPHOS]Br$_2$ (1g) complexes were prepared according to the literature procedures.$^{1-3}$
Crystal structure of Pd[(R)-Tol-BINAP]Br₂ (1e):

Figure S1. X-Ray diffraction structure of catalyst Pd[(R)-Tol-BINAP]Br₂ (1e). Selected bond lengths (Å): Pd(1)–Br(1) 2.4918(5); Pd(1)–Br(2) 2.4898(5); Pd(1)–P(1) 2.2473(1); Pd(1)–P(2) 2.2613(9); selected angles (°): P(1)-Pd(1)-Br(2) 158.08(3); P(2)-Pd(1)-Br(1) 159.00(3); P(1) -Pd(1)-P(2) 94.14(3); P(1)-Pd(1)-Br(1) 90.27(3); P(2)-Pd(1)-Br(2) 88.80(3); Br(2)-Pd(1)-Br(1) 94.733(1).

Preparation of complex 1h:

This complex was synthesized by modified method described for the synthesis of PdCl₂[(S)-P˚N] reported in the literature.⁴ In a Schlenk tube, PdBr₂(MeCN)₂ (174 mg, 0.5 mmol) was suspended in 10 mL of benzene. (R)-2-(2-(diphenylphosphino)phenyl)-4-isopropyl-1,3-oxazoline (186.5 mg, 0.5 mmol) was added. The suspension was stirred at room temperature for overnight. The yellow precipitate was collected by filtration, washed several times with diethyl ether and dried in vacuum. The complex was pure enough for further purposes, but it can be crystallized by the slow diffusion of diethyl ether into a concentrated solution of the solid in a mixture of dichloromethane:acetone (1:1) to obtain orange
crystals (yield: 82%). The presence of crystallization solvent in the product was ascertained by $^1$H NMR spectroscopy. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.16-8.12 (m, 1H, ArH), 7.75-7.29 (m, 12H, ArH), 6.98-6.92 (m, 1H, ArH), 5.71-5.68 (m, 1H, -CHN), 4.51 (t, 1H, $J = 9.3$ Hz, -CH$_2$O), 4.36 (q, 1H, $J = 4.4$ Hz, -CH$_2$O), 2.60-2.54 (m, 1H, CH(CH$_3$)$_2$), 0.78 (d, 3H, $J = 7.1$ Hz, -CH(CH$_3$)$_2$), -0.03 (d, 3H, $J = 7.1$ Hz, -CH(CH$_3$)$_2$); $^{31}$P NMR (121 MHz, CDCl$_3$) $\delta$ 26.7 (s, 1P, {(R)-P=N}); IR (dissolution in CHCl$_3$, cm$^{-1}$) 1624, 1570, 1247, 1100; MS (FAB) $m/z$: 638 [M + 1]$^+$, 560 (100), 478 (13), 402 (18); HRMS (FAB) $m/z$ calcd for C$_{24}$H$_{25}$Br$_2$NOP$_2$Pd [M +1]$^+$ 637.9075, found 637.9076; $[\alpha]_{20}^{\text{D}}$ -258.5 (c 0.4, acetone).

Figure S2. X-Ray diffraction structure of catalyst Pd[(R)-PHOX]Br$_2$.CH$_2$Cl$_2$(1h); selected bond lengths (Å): Pd(1)–Br(1) 2.511(1); Pd(1)–Br(2) 2.414(1); Pd(1)–P(1) 2.223(1); Pd(1)–N(1) 2.048(3); selected angles (°): N(1)-Pd(1)-P(1) 88.40(9); N(1)-Pd(1)-Br(2) 174.42(9); P(1)-Pd(1)-Br(2) 89.79(3); N(1)-Pd(1)-Br(1) 92.61(9); P(1)-Pd(1)-Br(1) 175.06(3); Br(2)-Pd(1)-Br(1) 89.645(1).

Preparation of complex 1i:
Complex 1i was prepared by modified method described for the synthesis of Pd[(R)-BINAP]Cl2 reported in the literature. In a Schlenk tube, [(MeCN)2]PdBr2 (174 mg, 0.5 mmol) and (R)-(H8)-BINAP (315 mg, 0.5 mmol) were suspended in 10 mL of benzene. The suspension was stirred at room temperature for overnight. The yellow-orange precipitate was collected by filtration, washed several times with diethyl ether and dried in vacuum. Yield: 75%. 31P NMR (121 MHz, CDCl3) δ 24.40 (s, 2P, BINAP); 1H NMR (300 MHz, CDCl3) δ 7.87-7.74 (m, 8H, ArH), 7.36-7.18 (m, 12H, ArH), 6.99-6.93 (m, 2H, ArH), 6.65 (d, 2H, J = 8.1 Hz, ArH), 2.48-2.40 (m, 2H, -CH2), 2.23-2.18 (m, 2H, -CH2), 1.85-1.77 (m, 2H, -CH2), 1.51-1.20 (m, 10H, -CH2); FAB MS (positive ion mode): m/z: 815 [M+ - Br]; HRMS-FAB (m/z): calcd for C44H40BrP2Pd [M –Br]+ 815.0823, found: 815.0827; [α]20D +364 (c 0.2, CHCl3).

(a) (b)
Figure S3. X-Ray diffraction structure of catalyst Pd\([\text{H}_8\text{-BINAP}])\text{Br}_2\text{COMe}_2\ (1\text{h}); selected bond lengths (Å): (a) Pd(2)–Br(3) 2.4778(9); Pd(2)–Br(4) 2.4784(9); Pd(2)–P(3) 2.2731(1); Pd(2)–P(4) 2.2586(1); selected angles (°): P(4)-Pd(1)-Br(3) 169.15(5); P(3)-Pd(1)-Br(4) 163.97(5); P(4)-Pd(1)-P(3) 92.94(6); P(3)-Pd(2)-Br(3) 90.46(5); P(4)-Pd(2)-Br(4) 89.76(5); Br(3)-Pd(2)-Br(4) 89.81(4).

(b) Pd(1)–Br(1) 2.4842(8); Pd(1)–Br(2) 2.4948(8); Pd(1)–P(1) 2.2536(1); Pd(1)–P(2) 2.2632(1); selected angles (°): P(1)-Pd(1)-Br(2) 163.04(4); P(2)-Pd(1)-Br(1) 160.57(5); P(1)-Pd(1)-P(2) 93.00(6); P(1)-Pd(1)-Br(1) 88.95(5); P(2)-Pd(1)-Br(2) 90.66(5); Br(2)-Pd(1)-Br(1) 93.08(3).

Preparation of complex 1j:

In a Schlenk tube, [(MeCN)$_2$]PdBr$_2$ (174 mg, 0.5 mmol) and (R)-QUINAP (219.5 mg, 0.5 mmol) were suspended in 10 mL of benzene. The suspension was stirred at room temperature for overnight. The yellow precipitate was collected by filtration, washed several times with diethyl ether and dried in vacuum. Yield: 68%. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 9.57 (d, 1H, $J$ = 8.0 Hz, ArH), 8.05 (d, 2H, $J$ = 8.0 Hz, ArH), 7.95 (d, 1H, $J$ = 8.4 Hz, ArH), 7.61 (d, 1H, $J$ = 8.5 Hz, ArH), 7.59-7.52 (m, 5H, ArH), 7.41-7.37 (m, 4H, ArH), 7.31-7.19 (m, 4H, ArH), 6.99-6.91 (m, 3H, ArH); $^{31}$P NMR (121 MHz, CDCl$_3$) $\delta$ 35.43 (s, 1P, BINAP); FAB MS (positive ion mode): $m$/z: 706 [M$^+$]; HRMS-FAB (m/z): calcd for C$_{44}$H$_{40}$BrP$_2$Pd [M$^+$] 706.9204, found: 706.9209; $\lbrack\alpha\rbrack_{D}^{20}$ +468 (c 0.21, CHCl$_3$).

General procedure for reductive amination of cyclic ketones.

1.0 mmol of cycloaliphatic ketone and 1.3 mmol of aniline derivative were added to a stirred solution of 0.025 mmol of Pd\([\text{rac}-\text{BINAP})\text{Br}_2\), 1k, in 10 mL of dry chloroform (in a Schlenk tube) and stirred for 10 minutes. The solution was transferred to a 45 ml stainless steel autoclave (PARR) previously purged with vacuum-N$_2$ and containing 50 mg of MS 5Å. Subsequently, the reaction was taken to the desired pressure (800 psi H$_2$), stirred in an oil bath at 80°C for 24 h. At the end of this period, the gas was liberated. The solution was analyzed by GC-MS to quantify the remaining substrate, and was later
concentrated under reduced pressure, affording a crude residue, which was purified by column chromatography over silica gel (70-230 mesh), and eluted with hexane-ethyl acetate (99/1) to isolate the corresponding product.

**N-cyclobutyl-3-(trifluoromethyl)benzenamine (3a).** Prepared according to the general procedure from 2-cyclobutanone (75 µL, 1.0 mmol), m-trifluoromethyl aniline (162 µL, 1.3 mmol) and Pd\([\text{(rac)-BINAP}]\Br_2, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (95%). \(^1\H NMR (300 MHz, CDCl_3) \delta 7.14 (t, 2H, J = 7.8 Hz, ArH), 6.82 (d, 1H, J = 7.5 Hz, ArH), 6.64 (s, 1H, ArH), 6.57 (d, 1H, J = 8.1 Hz, ArH), 3.89-3.78 (m, 2H, -NHCH + -NHCH), 2.39-2.30 (m, 2H, -CH_2), 1.80-1.67 (m, 4H, -CH_2); \(^1\C NMR (75 MHz, CDCl_3) \delta 147.3, 131.5 (q, J = 31.6 Hz), 129.6, 124.5 (d, J = 272.0 Hz), 115.8, 113.5 (q, J = 3.9 Hz), 108.9 (q, J = 3.9 Hz), 48.7 (-NHCH), 31.0 (-2CH_2), 15.2 (-CH_2); IR (film, cm\(^{-1}\)) 3418, 2926, 2855, 1615, 1517; MS (EI) \(m/z\): 215 (M\(^+\)), 187 (100), 166 (29), 145 (21); HRMS (EI) \(m/z\) calcld for C\(_{11}\)H\(_{12}\)NF\(_3\) (M\(^+\)) 215.0922, found 215.0922.

**N-cyclopentyl-3,5-bis(trifluoromethyl)benzenamine (3b).** Prepared according to the general procedure from cyclopentanone (88 µL, 1.0 mmol), 3,5-bis(trifluoromethyl)aniline (203 µL, 1.3 mmol) and Pd\([\text{(rac)-BINAP}]\Br_2, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (93%). \(^1\H NMR (300 MHz, CDCl_3) \delta 7.14 (s, 1H, ArH), 6.95 (s, 2H, ArH), 4.14 (bs, 1H, -NHCH), 3.87 – 3.83 (m, 1H, -NHCH), 2.14-2.05 (m, 2H, -CH_2), 1.82-1.67 (m, 4H, -CH_2), 1.57-1.48 (m, 2H, -CH_2); \(^1\C NMR (75 MHz, CDCl_3) \delta 148.4, 132.3 (q = 32.4 Hz), 129.6, 124.5 (d, J = 272.5 Hz), 112.0 (q = 3.0 Hz), 109.5 (q = 3.9 Hz), 54.5 (-NHCH), 33.2 (-CH_2), 23.9 (CH_2); IR (film, cm\(^{-1}\)) 3414, 2924, 2848, 1615, 1517; MS (EI) \(m/z\): 297 (M\(^+\)), 78 (13), 268 (100), 255 (16), 242 (11), 213 (14); HRMS (EI) \(m/z\) calcld for C\(_{13}\)H\(_{13}\)NF\(_6\) (M\(^+\)) 297.0957, found 297.0952.

**N-cyclohexylbenzenamine (3c).** Prepared according to the general procedure from cyclohexanone (103 µL, 1.0 mmol), 3,5-bis(trifluoromethyl)aniline (203 µL, 1.3 mmol) and Pd\([\text{(rac)-BINAP}]\Br_2, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (89%). \(^1\H NMR (300 MHz, CDCl_3) \delta 7.17-7.10 (m, 2H, ArH), 6.67-6.55 (m, 3H, ArH), 3.48 (bs, 1H, -NHCH), 3.28-3.19 (m, 1H, -NHCH), 2.08-2.01 (m, 2H, -CH_2), 1.79-1.72 (m, 2H, -CH_2), 1.67-1.61 (m, 1H, -CH_2), 1.43-1.07 (m, 5H, -CH_2); \(^1\C NMR (75 MHz, CDCl_3) \delta 147.3, 116.7, 113.1, 51.6 (-NHCH), 33.4 (-CH_2), 25.9 (-CH_2), 25.0 (-CH_2); EM-IE (70 eV)
4-bromo-2-chloro-N-cyclohexylbenzenamine (3d). Prepared according to the general procedure from cyclohexanone (103 μL, 1.0 mmol), 4-bromo-2-chloroaniline (266.5 mg, 1.3 mmol) and Pd[(rac)-BINAP]Br₂, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (74%). ¹H NMR (300 MHz, CDCl₃) δ 7.38 (s, 1H, ArH), 7.22 (dd, 1H, J = 8.7 Hz, ArH), 6.55 (s, 1H, ArH), 4.23 (d, 1H, J = 6.60 Hz, -NHCH), 3.33-3.24 (m, 2H, -NHCH₂), 2.07-1.84 (m, 2H, -CH₂), 1.82-1.78 (m, 2H, -CH₂), 1.71-1.64 (m, 1H, -CH₂), 1.48-1.17 (m, 5H, -CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 142.3, 131.4, 130.4, 119.5, 112.6, 106.7, 51.5 (-NHCH), 33.0 (-CH₂), 25.8 (CH₂), 24.8 (CH₂); IR (film, cm⁻¹) 3415, 2927, 2850, 1615, 1517; MS (EI) m/z: 287 (M⁺), 187 (100), 166 (29), 145 (21); HRMS (EI) m/z calcd for C₁₂H₁₇N₁ (M⁺) 287.0076, found 287.0070.

N-phenylcycloheptanamine (3e). Prepared according to the general procedure from cycloheptanone (126 μL, 1.0 mmol), aniline (120 μL, 1.3 mmol) and Pd[(rac)-BINAP]Br₂, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (92%). ¹H NMR (300 MHz, CDCl₃) δ 7.24-7.18 (m, 2H, ArH), 6.73-6.69 (m, 1H, ArH), 6.65-6.58 (m, 2H, ArH), 3.63 (bs, 1H, -NHCH), 3.54-3.47 (m, 1H, -NHCH), 2.09-2.01 (m, 2H, -CH₂), 1.76-1.45 (m, 10H, -CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 147.4, 29.4, 116.9, 113.3, 53.7 (-NHCH), 39.9 (-CH₂), 28.5 (-CH₂), 24.5 (-CH₂); IR (film, cm⁻¹) 3404, 2925, 2854, 1602, 1503; MS (EI) m/z: 189 (M⁺), 146 (14), 132 (100), 120 (38); HRMS (EI) m/z calcd for C₁₃H₁₉N₁(M⁺) 189.1517, found 189.1520.

N-p-tolylcycloheptanamine (3f). Prepared according to the general procedure from cycloheptanone (126 μL, 1.0 mmol), p-toluidine (139 mg, 1.3 mmol) and Pd[(rac)-BINAP], Br₂1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (91%). ¹H NMR (300 MHz, CDCl₃) δ 6.97 (d, 2H, J = 7.9 Hz, ArH), 6.51 (d, 2H, J = 8.2 Hz, ArH), 3.76 (bs, 1H, -NHCH), 3.45-3.38 (m, 1H, -NHCH), 2.23 (s, 3H, -Me), 2.03-1.95 (m, 2H, -CH₂), 1.70-1.39 (m, 10H, -CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 144.6, 129.8, 126.5, 113.9, 54.4 (-NHCH), 34.7 (-CH₂), 28.4 (-CH₂), 24.4 (-CH₂), 20.4 (-Me); IR (film, cm⁻¹) 3400, 2924, 2855, 1617, 1517; MS (EI) m/z: 203 (M⁺), 160 (5), 146 (25), 68 (100); HRMS (EI) m/z calcd for C₁₄H₂₁N₁(M⁺) 203.1674, found 203.1678.
**N-(2-(trifluoromethyl)phenyl)cycloheptanamine (3g).** Prepared according to the general procedure from cycloheptanone (118 µL, 1.0 mmol), o-trifluoromethyl aniline (163 µL, 1.3 mmol) and Pd[(rac)-BINAP]Br₂, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (86%). ¹H NMR (300 MHz, CDCl₃) δ 7.45 (dd, 1H, \( J = 7.96, 1.20 \) Hz, ArH), 7.37 (t, 1H, \( J = 7.81 \) Hz, ArH), 6.71-6.66 (m, 2H, ArH), 4.32 (bs, 1H, -NHCH), 3.59-3.56 (m, 1H, -NHC₇H), 2.07-2.00 (m, 2H, -CH₂), 1.76-1.55 (m, 10H, -C₇H₂); ¹³C NMR (75 MHz, CDCl₃) δ 144.8, 132.9, 126.7 (q = 5.5 Hz), 125.3 (d = 272.1 Hz), 115.1, 113.1 (q = 29.0 Hz), 53.3 (-NHCH), 34.5 (-CH₂), 28.2 (CH₂), 24.2 (CH₂); IR (film, cm⁻¹) 3414, 2925, 2849, 1615, 1517; MS (EI) m/z: 257 (M⁺, 83), 238 (13), 228 (14), 214 (24), 200 (100); HRMS (EI) m/z calcd for C₁₄H₁₈NF₃ (M⁺) 257.1391, found 257.1389.

**N-(3-(trifluoromethyl)phenyl)cycloheptanamine (3h).** Prepared according to the general procedure from cycloheptanone (118 µL, 1.0 mmol), m-trifluoromethylaniline (162 µL, 1.3 mmol) and Pd[(rac)-BINAP]Br₂, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (88%). ¹H NMR (300 MHz, CDCl₃) δ 7.25 (t, 1H, \( J = 7.9 \) Hz, ArH), 6.91 (d, 1H, \( J = 7.7 \) Hz, ArH), 6.76 (s, 1H, ArH), 6.68 (dd, 1H, \( J = 8.3, 2.2 \) Hz, ArH), 3.84 (bs, 1H, -NHCH), 3.53-3.46 (m, 1H, -NHCH), 2.05-1.97 (m, 2H, -CH₂), 1.74-1.50 (m, 10H, -C₇H₂), 147.5, 131.6 (q, \( J = 32.4 \) Hz), 129.7, 124.5 (d, \( J = 272.2 \) Hz), 116.0, 113.1 (q, \( J = 3.4 \) Hz), 109.3 (q, \( J = 3.4 \) Hz), 53.6 (-NHCH), 34.7 (-CH₂), 28.4 (-CH₂), 24.3 (-CH₂); IR (film, cm⁻¹) 3425, 2929, 2849, 1614, 1515; MS (EI) m/z: 257 (M⁺), 228 (3), 214 (24), 200 (100), 187 (19). HRMS (EI) m/z calcd for C₁₄H₁₈NF₃ (M⁺) 257.1391, found 257.1389.

**N-(3-(trifluoromethyl)phenyl)cyclooctanamine (3i).** Prepared according to the general procedure from cyclooctanone (132 µL, 1.0 mmol), m-trifluoromethyl aniline (162 µL, 1.3 mmol) and Pd[(rac)-BINAP]Br₂, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (88%). ¹H NMR (300 MHz, CDCl₃) δ 7.13 (dd, 1H, \( J = 7.8 \) Hz, ArH), 6.78 (d, 1H, \( J = 7.8 \) Hz, ArH), 6.64 (s, 1H, ArH), 6.57 (dd, 1H, \( J = 8.1, 2.0 \) Hz, ArH), 3.70 (bs, 1H, -NHCH), 3.45-3.38 (m, 1H, -NHCH), 1.83-1.76 (m, 2H, -CH₂), 1.66-1.44 (m, 12H, -CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 147.4, 131.5 (q, \( J = 31.5 \) Hz), 129.6, 124.0 (d, \( J = 272.0 \) Hz), 115.9, 112.9 (q, \( J = 3.8 \) Hz), 109.2 (q, \( J = 3.8 \) Hz), 52.4 (-NHCH), 32.3 (-CH₂), 27.1 (-CH₂), 25.8 (-CH₂), 23.9 (-CH₂); IR (film, cm⁻¹) 3416, 2926, 2850, 1614, 1515; MS (EI) m/z: 271 (M⁺), 252 (5), 228 (3), 214 (24), 200 (100), 187 (19). HRMS (EI) m/z calcd for C₁₄H₁₈NF₃ (M⁺) 257.1391, found 257.1389.
N-(3,4-difluorophenyl)cyclododecanamine (3j). Prepared according to the general procedure from cyclododecanone (182 mg, 1.0 mmol), 3,4-difluoromethyl aniline (130 µL, 1.3 mmol) and Pd[(rac)-BINAP]Br₂, 1k, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (81%). 

\[
\text{δ} (6.92, \text{ddd}, 1H, J_H-H = 9.0, J_H-F = 9.0, 1.5 Hz, \text{ArH}), 6.35 (\text{ddd}, 1H, J_H-H = 9.5, J_H-F = 6.5, 3.0 Hz, \text{ArH}), 6.23-6.19 (m, 1H, \text{ArH}), 3.39-3.35 (m, 2H, -NHCH + -NHCH), 1.63-1.57 (m, 1H, -CH₂), 1.49-1.24 (m, 21H, -CH₂), 1.49 (d = 8.7Hz), 142.5 (dd = 233.7, 12.5 Hz), 117.3 (d = 12.5 Hz), 108.0 (d = 12.5 Hz), 101.3 (d = 25.0 Hz), 50.2 (-NHCH), 40.3 (-CH₂), 29.5 (-CH₂), 24.3 (-CH₂), 24.0 (-CH₂), 23.2 (-CH₂), 23.1 (-CH₂), 21.1 (-CH₂); IR (film, cm⁻¹) 3475, 2955, 2873, 1614, 1518; MS (EI) m/z: 295 (M⁺, 100), 266 (3), 252 (8), 238 (4), 224 (8), 168 (71); HRMS (EI) m/z calcld for C₁₈H₂₇F₂N (M⁺) 295.2112, found 295.2115.

**General procedure for asymmetric reductive amination of 2-methylcyclopentanone.**

1.0 mmol of rac-4 and 1.3 mmol of aniline derivative were added to a stirred solution of 0.025 mmol of preformed chiral palladium complex in 10 mL of dry chloroform (in a Schlenk tube) and stirred under nitrogen atmosphere for 10 minutes. The solution was transferred to a 45 ml stainless steel autoclave (PARR) previously purged with vacuum-N₂. Subsequently, the reaction was taken to the desired pressure (900 psi H₂), stirred in an oil bath at 80°C for 24 h. At the end of this period, the gas was liberated. The solution was analyzed by NMR to quantify the remaining substrate and d.r. respectively, and was later concentrated under reduced pressure, affording a crude residue, which was purified by column chromatography over silica gel (70-230 mesh), and eluted with hexane-ethyl acetate (99/1) to isolate the corresponding product.

cis-N-(phenyl)-2-methylcyclopentaneamine (5a). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), aniline (120 µL, 1.3
mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (90%). ¹H NMR (500 MHz, CDCl₃) δ 7.16-7.12 (m, 2H, ArH), 6.64 (t, 1H, J = 7.8 Hz, ArH), 6.60 (dd, 2H, J = 1.0, 7.8 Hz, ArH), 3.72 (m, 1H, -NHCH₂), 3.56 (bs, 1H, -NHCH), 2.31-2.22 (m, 1H, -CHCH₃), 2.02-1.36 (m, 6H, -CH₂), 0.88 (d, 3H, J = 7.0 Hz, -CHCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 148.2, 129.1, 116.6, 112.9, 57.2 (-NHCH), 35.8 (-CHCH₃), 32.0 (-CH₂), 31.5 (-CH₂), 21.2 (-CH₂), 14.3 (-CHCH₃); IR (film, cm⁻¹) 3412, 2957, 2871, 1603, 1507; MS (EI) m/z: 175 (M⁺), 146 (19), 132 (100), 119 (21); HRMS (EI) m/z calcd for C₁₂H₁₇N(M⁺) 175.1361, found 175.1364; [α]²⁰_D +9.2 (c 0.5, CHCl₃); ee = 98% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1⁰/min; t_R = 31.3 min (minor), t_R = 32.2 min (major)]. The relative stereochemistry was assigned by NOE analysis.

Interactions observed by NOE.

With Pd/C the selectivity cis/trans was 62/38.

With catalyst Pd[(R)-BINAP]Cl₂, 1b: [α]²⁰_D +7.8 (c 0.48, CHCl₃); ee = 92% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1⁰/min; t_R = 33.1 min (minor), t_R = 34.3 min (major)].

With catalyst Pd[(S)-BINAP]Br₂, 1d: [α]²⁰_D -11.2 (c 0.5, CHCl₃); ee = 95% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1⁰/min; t_R = 31.4 min (major), t_R = 32.3 min (minor)].

With catalyst Pd[(R)-Tol-BINAP]Br₂, 1e: [α]²⁰_D +8.1 (c 0.5, CHCl₃); ee = 89% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1⁰/min; t_R = 32.2 min (minor), t_R = 33.3 min (major)].

With catalyst Pd[(S)-Tol-BINAP]Br₂, 1f: [α]²⁰_D -10.9 (c 0.51, CHCl₃); ee = 93% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1⁰/min; t_R = 33.2 min (major), t_R = 34.3 min (minor)].
With catalyst Pd[(S,S)-CHIRAPHOS]Br$_2$, 1g: $[\alpha]^{20}_D +8.6$ (c 0.49, CHCl$_3$); ee = 96% by GC-MS (EI) [chiral column: Cyclodex-β]; conditions: $T_{\text{inj}} = 280$ °C; $T_{\text{det}} = 280$ °C; $T_{\text{initial}} = 30$ °C for 3 min; $T_{\text{final}} = 200$ °C; rate = 1°/min; $t_R = 33.4$ min (minor), $t_R = 34.5$ min (major).

With catalyst Pd[(R)-PHOX]Br$_2$, 1h: $[\alpha]^{20}_D -7.2$ (c 0.53, CHCl$_3$); ee = 87% by GC-MS (EI) [chiral column: Cyclodex-β]; conditions: $T_{\text{inj}} = 280$ °C; $T_{\text{det}} = 280$ °C; $T_{\text{initial}} = 30$ °C for 3 min; $T_{\text{final}} = 200$ °C; rate = 1°/min; $t_R = 31.3$ min (minor), $t_R = 32.2$ min (major).

With catalyst Pd[(R)-H$_8$BINAP]Br$_2$, 1i: $[\alpha]^{20}_D +9.0$ (c 0.5, CHCl$_3$); ee = 98% by GC-MS (EI) [chiral column: Cyclodex-β]; conditions: $T_{\text{inj}} = 280$ °C; $T_{\text{det}} = 280$ °C; $T_{\text{initial}} = 30$ °C for 3 min; $T_{\text{final}} = 200$ °C; rate = 1°/min; $t_R = 31.3$ min (minor), $t_R = 32.2$ min (major).

With catalyst Pd[(R)-QUINAP]Br$_2$, 1b: $[\alpha]^{20}_D -8.5$ (c 0.51, CHCl$_3$); ee = 89% by GC-MS (EI) [chiral column: Cyclodex-β]; conditions: $T_{\text{inj}} = 280$ °C; $T_{\text{det}} = 280$ °C; $T_{\text{initial}} = 30$ °C for 3 min; $T_{\text{final}} = 200$ °C; rate = 1°/min; $t_R = 32.4$ min (minor), $t_R = 33.8$ min (major).

cis-$N$-(3-methylphenyl)-2-methylcyclopentaneamine (5b). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), m-toluidine (140 µL, 1.3 mmol) and Pd[(R)-BINAP]Br$_2$, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (90%). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.10 (t, 1H, $J = 7.9$ Hz, ArH), 6.55-6.47 (m, 3H, ArH), 3.77 (m, 1H, -NHC$_2$H), 3.63 (bs, 1H, -NHCH), 2.37-2.27 (m, 4H, -CH$_2$CH$_3$ + -Me), 2.10-1.39 (m, 6H, -CH$_2$), 0.93 (d, 3H, $J = 6.8$ Hz, -CH$_2$CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 148.3, 139.0, 129.2, 117.8, 113.8, 110.2, 57.2 (-NHCH), 35.8 (-CHMe), 32.1 (-CH$_2$), 31.6 (-CH$_2$), 21.8 (-CH$_3$), 21.3 (-CH$_2$), 14.5 (-CH$_2$CH$_3$); IR (film, cm$^{-1}$) 3410, 2955, 2868, 1604, 1511; MS (EI) $m/z$: 189 (M$^+$), 160 (12), 146 (100), 133 (22); HRMS (EI) $m/z$ calcd for C$_{13}$H$_{19}$N(M$^+$) 189.1517, found 189.1515; $[\alpha]^{20}_D +8.2$ (c 0.5, CHCl$_3$); ee = 93% by GC-MS (EI) [chiral column: Cyclodex-β]; conditions: $T_{\text{inj}} = 280$ °C; $T_{\text{det}} = 280$ °C; $T_{\text{initial}} = 30$ °C for 3 min; $T_{\text{final}} = 200$ °C; rate = 1°/min; $t_R = 30.2$ min (minor), $t_R = 31.2$ min (major).

cis-$N$-(4-methylphenyl)-2-methylcyclopentaneamine (5c). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), p-toluidine (139 mg, 1.3 mmol) and Pd[(R)-BINAP]Br$_2$, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as yellow oil (91%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.95 (d, 2H, $J = 8.0$ Hz, ArH), 6.53 (d, 2H, $J = 8.5$ Hz, ArH), 3.69 (m, 1H, -NHCH), 3.35 (bs, 1H, -NHCH), 2.29-2.21 (m, 4H, -CH$_2$CH$_3$ + -Me), 2.00-1.35 (m, 6H, -CH$_2$), 0.87 (d, 3H, $J = 7.0$ Hz, -CH$_2$CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 148.3, 139.0, 129.2, 117.8, 113.8, 110.2, 57.2 (-NHCH), 35.8 (-CHMe), 32.1 (-CH$_2$), 31.6 (-CH$_2$), 21.8 (-CH$_3$), 21.3 (-CH$_2$), 14.5 (-CH$_2$CH$_3$); IR (film, cm$^{-1}$) 3410, 2955, 2868, 1604, 1511; MS (EI) $m/z$: 189 (M$^+$), 160 (12), 146 (100), 133 (22); HRMS (EI) $m/z$ calcd for C$_{13}$H$_{19}$N(M$^+$) 189.1517, found 189.1515; $[\alpha]^{20}_D +8.2$ (c 0.5, CHCl$_3$); ee = 93% by GC-MS (EI) [chiral column: Cyclodex-β]; conditions: $T_{\text{inj}} = 280$ °C; $T_{\text{det}} = 280$ °C; $T_{\text{initial}} = 30$ °C for 3 min; $T_{\text{final}} = 200$ °C; rate = 1°/min; $t_R = 30.2$ min (minor), $t_R = 31.2$ min (major).
NMR (125 MHz, CDCl$_3$) δ 145.9, 129.6, 125.8, 113.1, 57.5 (-NHCH$_3$), 35.7 (-CHCH$_3$), 31.9 (-CH$_2$), 31.5 (-CH$_2$), 21.1 (-CH$_2$), 20.3 (-CH$_3$), 14.3 (-CHCH$_3$); IR (film, cm$^{-1}$) 3409, 2955, 2868, 1618, 1518; MS (El) m/z: 189 (M$^+$), 160 (17), 146 (100), 133 (37); HRMS (El) m/z calcd for C$_{13}$H$_{19}$N(M$^+$) 189.1517, found 189.1521; [α]$D^0$ +5.2 (c 0.5, CHCl$_3$); ee = 95% by GC-MS (El) [chiral column: Cyclodex-β; conditions: T$_{inj}$ = 280 °C; T$_{det}$ = 280 °C; T$_{initial}$ = 30 °C for 3 min; T$_{final}$ = 200 °C; rate = 1°/min; t$_R$ = 39.0 min (minor), t$_R$ = 40.2 min (major)].

cis-N-(4-ethylphenyl)-2-methylcyclopentaneamine (5d). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), p-ethylaniline (160 µL, 1.3 mmol) and Pd[(R)-BINAP]Br$_2$, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as yellow oil (86%). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.00 (d, 2H, J = 7.9 Hz, ArH), 6.57 (d, 2H, J = 7.9 Hz, ArH), 3.73-3.56 (m, 2H, -NHC$H_2$ + -NHC$H_3$), 2.53 (q, 2H, J = 7.5 Hz, -$CH_2CH_3$), 2.33-2.22 (m, 1H, -CH$CH_3$), 1.99-1.39 (m, 6H, -CH$_2$), 1.19 (t, 3H, J = 7.5 Hz, -CH$_2CH_3$), 0.88 (d, 3H, J = 7.1 Hz, -CHCH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 146.1, 132.6, 128.5, 113.1, 57.6 (-NHCH$_3$), 35.8 (-CHCH$_3$), 32.0 (-CH$_2$), 31.5 (-CH$_2$), 27.9 (-CH$_2CH_3$), 21.2 (-CH$_2$), 16.9 (-CH$_2CH_3$), 14.4 (-CHCH$_3$); IR (film, cm$^{-1}$) 3413, 2958, 2869, 1616, 1517; MS (El) m/z: 203 (M$^+$), 174 (11), 160 (65), 147 (21), 106 (100); HRMS (El) m/z calcd for C$_{14}$H$_{21}$N(M$^+$) 203.1674, found 203.1674; [α]$D^0$ +5.9 (c 0.17, CHCl$_3$); ee = 83% by GC-MS (El) [chiral column: Cyclodex-β; conditions: T$_{inj}$ = 280 °C; T$_{det}$ = 280 °C; T$_{initial}$ = 30 °C for 3 min; T$_{final}$ = 200 °C; rate = 1°/min; t$_R$ = 51.8 min (minor), t$_R$ = 53.1 min (major)].

cis-N-(4-methoxyphenyl)-2-methylcyclopentaneamine (5f). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), p-anisidine (160 mg, 1.3 mmol) and Pd[(R)-BINAP]Br$_2$, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as yellow oil (78%). $^1$H NMR (300 MHz, CDCl$_3$) δ 6.76 (d, 2H, J = 8.8 Hz, ArH), 6.60 (d, 2H, J = 8.8 Hz, ArH), 3.74 (s, 4H, -OMe), 3.66 (m, 1H, -NHC$H_3$), 3.21 (bs, 1H, -NHCH$_3$), 2.30-2.21 (m, 1H, -CHCH$_3$), 1.99-1.34 (m, 6H, -CH$_2$), 0.88 (d, 3H, J = 6.9 Hz, -CHCH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 142.3, 114.9, 114.4, 111.7, 58.3 (-NHCH$_3$), 55.9 (-OCH$_3$), 35.7 (-CHCH$_3$), 32.0 (-CH$_2$), 31.3 (-CH$_2$), 21.2 (-CH$_2$), 14.3 (-CHCH$_3$); IR (film, cm$^{-1}$) 3398, 2954, 2869, 1615, 1512; MS (El) m/z: 205 (M$^+$), 190 (10), 176 (18), 162 (100), 149 (38); HRMS (El) m/z calcd for C$_{13}$H$_{19}$NO(M$^+$) 205.1473, found 205.1467; [α]$D^0$ +8.4 (c 0.5, CHCl$_3$); ee = 96% by GC-MS (El) [chiral column: Cyclodex-β; conditions: T$_{inj}$ = 280 °C; T$_{det}$ = 280 °C; T$_{initial}$ = 30 °C for 3 min; T$_{final}$ = 200 °C; rate = 1°/min; t$_R$ = 54.6 min (minor), t$_R$ = 56.2 min (major)].
cis-N-(3-trifluoromethylphenyl)-2-methylcyclopentaneamine (5g). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), m-trifluomethylaniline (162 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (80%). ¹H NMR (300 MHz, CDCl₃) δ 7.22 (t, 1H, J = 7.7 Hz, ArH), 6.88 (d, 1H, J = 7.7 Hz, ArH), 6.81 (s, 1H, ArH), 6.74 (dd, 1H, J = 2.0, 7.7 Hz, ArH), 3.90 (bs, 1H, -NHCH), 3.78-3.71 (m, 1H, -NHC₃H), 2.36-2.22 (m, 1H, -CHCH₃), 2.05-1.38 (m, 6H, -C₃H₂), 0.89 (d, 3H, J = 7.1 Hz, -C₃H₂); ¹³C NMR (75 MHz, CDCl₃) δ 148.3, 131.5 (q, J = 31.3 Hz), 129.6, 124.5 (d, J = 272.2 Hz), 115.9, 113.1 (q, J = 3.6 Hz), 109.0 (q, J = 3.6 Hz), 57.2 (-NHCH), 35.8 (-CHCH₃), 32.0 (-CH₂), 31.5 (-CH₂), 21.2 (-CH₂), 14.4 (-CHCH₃); IR (film, cm⁻¹) 3436, 2960, 2873, 1615, 1517; MS (EI) m/z: 243 (M⁺), 214 (16), 200 (100), 187 (15); HRMS (EI) m/z calcd for C₁₃H₁₆NF₃(M⁺) 243.1235, found 243.1239; [α]²⁰°D +7.2 (c 0.58, CHCl₃); ee = 98% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 17.2 min (minor), t_R = 17.6 min (major)].

With Pd[(S)-BINAP]Br₂, 1d, [α]²⁰°D -10.9 (c 0.55, CHCl₃).

cis-N-(3-chlorophenyl)-2-methylcyclopentaneamine (5h). Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), m-chloroaniline (136 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (86%). ¹H NMR (300 MHz, CDCl₃) δ 7.05 (t, 1H, J = 7.8 Hz, ArH), 6.63 (s, 1H, ArH), 6.60-6.58 (m, 1H, ArH), 6.47 (dd, 1H, J = 1.8, 7.8 Hz, ArH), 3.83 (bs, 1H, -NHCH), 3.73-3.66 (m, 1H, -NHCH), 2.35-2.21 (m, 1H, -CHCH₃), 2.05-1.34 (m, 6H, -CH₂), 0.88 (d, 3H, J = 7.2 Hz, -CHCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 149.1, 134.9, 130.0, 116.5, 112.4, 111.3, 57.1 (-NHCH), 35.6 (-CHCH₃), 31.8 (-CH₂), 31.4 (-CH₂), 21.1 (-CH₂), 14.3 (-CHCH₃); IR (film, cm⁻¹) 3423, 2957, 2870, 1598, 1501; MS (EI) m/z: 209 (M⁺), 180 (21), 166 (100), 153 (22); HRMS (EI) m/z calcd for C₁₃H₁₆NCl(M⁺) 209.0971, found 209.0969; [α]²⁰°D +7.9 (c 0.58, CHCl₃); ee = 91% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 39.8 min (minor), t_R = 41.0 min (major)].
**cis-N-(4-chlorophenyl)-2-methylcyclopentanamine (5i).** Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), p-chloroaniline (165 mg, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (88%). \(^1\)H NMR (300 MHz, CDCl₃) δ 7.09 (d, 2H, J = 8.7 Hz, ArH), 6.53 (d, 2H, J = 8.7 Hz, ArH), 3.90 (bs, 1H, -NHCH), 3.71-3.65 (m, 1H, -NHC₃H), 2.37-2.22 (m, 1H, -CHCH₃), 2.03-1.34 (m, 6H, -CH₂), 0.87 (d, 3H, J = 7.2 Hz, -CHC₃H₃); \(^1\)3C NMR (75 MHz, CDCl₃) δ 146.6, 128.9, 121.2, 114.0, 57.4 (-NHCH), 35.6 (-CHCH₃), 31.9 (-CH₂), 31.4 (-CH₂), 21.1 (-CH₂), 14.3 (-CHCH₃); IR (film, cm⁻¹) 3421, 2957, 2870, 1599, 1499; MS (EI) m/z: 209 (M⁺), 180 (16), 166 (100), 153 (27); HRMS (EI) m/z calcd for C₁₂H₁₆NCl (M⁺) 209.0971, found 209.0968; [α]₂₀° = 10.4 (c 0.5, CHCl₃); ee = 84% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 32.3 min (minor), t_R = 33.7 min (major)].

**cis-N-(2-bromophenyl)-2-methylcyclopentanamine (5j).** Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), o-bromoaniline (147 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (75%). \(^1\)H NMR (300 MHz, CDCl₃) δ 7.40 (d, 1H, J = 8.1 Hz, ArH), 7.15 (td, 1H, J = 1.5, 8.1 Hz, ArH), 6.70 (dd, 1H, J = 1.3, 8.2 Hz, ArH), 6.53 (td, 1H, J = 1.5, 8.0 Hz, ArH), 4.13 (bs, 1H, -NHCH), 3.80-3.73 (m, 1H, -NHC₃H), 2.37-2.21 (m, 1H, -CHCH₃), 2.07-1.41 (m, 6H, -CH₂), 0.93 (d, 3H, J = 6.9 Hz, -CHC₃H₃); \(^1\)3C NMR (75 MHz, CDCl₃) δ 144.6, 132.3, 128.3, 117.2, 112.0, 109.8, 57.4 (-NHCH), 35.9 (-CHCH₃), 31.9 (-CH₂), 31.5 (-CH₂), 21.3 (-CH₂), 14.4 (-CHCH₃); IR (film, cm⁻¹) 3423, 2957, 2870, 1598, 1501; MS (EI) m/z calcd for C₁₂H₁₆NB₃r (M⁺) 253.0466, found 253.0467; [α]₂₀° = -2.2 (c 0.23, CHCl₃); ee = 18% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 32.3 min (minor), t_R = 32.5 min (major)].

**cis-N-(2-trifluoromethylphenyl)-2-methylcyclopentanamine (5l).** Prepared according to the general procedure from 2-methylcyclopentanone (106 µL, 1.0 mmol), o-trifluoromethylaniline (163 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (69%). \(^1\)H NMR (300 MHz, CDCl₃) δ 7.37 (dd, 1H, J = 7.96, 1.20 Hz, ArH), 7.28 (t, 1H, J = 7.81 Hz, ArH), 6.84-6.76 (m, 2H, ArH), 3.90 (bs, 1H, -NHCH), 3.79-3.72 (m, 1H, -NHCH), 2.36-2.22 (m, 1H, -CHCH₃), 2.05-1.38 (m,
6H, -CH₂), 0.90 (d, 3H, J = 7.8 Hz, -CHCH₃); IR (film, cm⁻¹) 3440, 2960, 2877, 1615, 1516; MS (EI) m/z: 243 (M⁺), 214 (16), 200 (100); HRMS (EI) m/z calcd for C₁₃H₁₆NF₃(M⁺) 243.1235, found 243.1239; ee = 95% by GC-MS (El) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 37.7 min (minor), t_R = 38.2 min (major)].

**General procedure for asymmetric reductive amination of 2-methylcyclohexanone.**

The procedure was the same as 2-methylcyclopentanone.

**cis-N-(phenyl)-2-methylcyclohexaneamine (7a).** Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), aniline (120 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (91%). ¹H NMR (300 MHz, CDCl₃) δ 7.18-7.13 (m, 2H, ArH), 6.67-6.56 (m, 3H, ArH), 3.64 (bs, 1H, -NHCH), 3.52-3.47 (m, 1H, -NHCH), 2.06-1.98 (m, 1H, -CHCH₃), 1.80-1.35 (m, 8H, -CH₂), 0.92 (d, 3H, J = 6.9 Hz, -CHCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 147.6, 129.2, 116.5, 113.1, 53.1 (-NHCH), 33.0 (-CHCH₃), 30.3 (-CH₂), 28.5 (-CH₂), 22.9 (-CH₂), 22.7 (-CH₂), 15.4 (-CHCH₃); IR (film, cm⁻¹) 3415, 2926, 2854, 1601, 1504; MS (EI) m/z: 189 (M⁺), 160 (4), 146 (27), 132 (100); HRMS (El) m/z calcd for C₁₃H₁₉N(M⁺) 189.1517, found 189.1520; [α]²⁰D -13.3 (c 0.18, CHCl₃); ee = 79% by GC-MS (El) [chiral column: Cyclodex-β; conditions: t_inj = 280°; t_initial = 30° for 3 min; rate = 1.2°/min; t_R = 39.3 min (minor), t_R = 40.3 min (major)]. The relative stereochemistry of the product was assigned by comparison of ¹H NMR spectral data reported in the literatura for non chiral compound.⁵

With Pd[(R)-Tol-BINAP]Br₂, 1e, [α]²⁰D -11.5 (c 0.53, CHCl₃); ee = 73% by GC-MS (El) [chiral column: Cyclodex-β; conditions T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1.2°/min; t_R = 39.4 min (minor), t_R = 40.3 min (major)].
**cis-N-(4-methylphenyl)-2-methylcyclohexanamine (7b).** Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), p-toluidine (139 mg, 1.3 mmol) and Pd[(S)-BINAP]Br2, 1d, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (91%). $^1$H NMR (300 MHz, CDCl3) $\delta$ 6.98 (d, 2H, $J = 8.2$ Hz, ArH), 6.55 (d, 1H, $J = 8.5$ Hz, ArH), 3.49-3.38 (m, 2H, -NHCH + -NHCH), 2.24 (s, 3H, -CH3), 2.06-2.00 (m, 1H, -CH2CH3), 1.80-1.35 (m, 8H, -CH2), 0.92 (d, 3H, $J = 7.1$ Hz, -CH2CH3); $^{13}$C NMR (75 MHz, CDCl3) $\delta$ 145.5, 129.8, 125.8, 113.4, 53.5 (-NHCH), 33.1 (-CH2), 30.5 (-CH2), 28.7 (-CH2), 23.0 (-CH2), 15.5 (-CH2); IR (film, cm$^{-1}$) 3412, 2924, 2855, 1617, 1518; MS (EI) $m/z$: 203 (M$^+$), 174 (9), 160 (22), 146 (100); HRMS (EI) $m/z$ calcd for C14H21N(M$^+$) 203.1670, found 203.1674; $\left[\alpha\right]_D^{20}$ +7.6 (c 0.5, CHCl3); ee = 75% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T$_{inj}$ = 280 °C; T$_{det}$ = 280 °C; T$_{initial}$ = 30 °C for 3 min; T$_{final}$ = 200 °C; rate = 1.0 °C/min; t$_R$ = 138.6 min (minor), t$_R$ = 139.9 min (major)].

**cis-N-(4-ethylphenyl)-2-methylcyclohexanamine (7c).** Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), p-ethylaniline (160 µL, 1.3 mmol) and Pd[(R)-BINAP]Br2, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as yellow oil (74%). $^1$H NMR (300 MHz, CDCl3) $\delta$ 7.02 (d, 2H, $J = 8.4$ Hz, ArH), 6.58 (d, 1H, $J = 8.7$ Hz, ArH), 3.51-3.47 (m, 2H, -NHCH + -NHCH), 2.56 (q, 2H, $J = 7.6$ Hz, -CH2CH3), 2.08-1.99 (m, 1H, -CH2), 1.80-1.31 (m, 8H, -CH2), 1.2 (t, 3H, $J = 7.5$ Hz, -CH2CH3), 0.94 (d, 3H, $J = 6.9$ Hz, -CH2); $^{13}$C NMR (75 MHz, CDCl3) $\delta$ 145.6, 132.4, 128.5, 113.2, 53.4 (-NHCH), 33.1 (-CH2), 30.3 (-CH2), 28.6 (-CH2), 27.8 (-CH2CH3), 22.9 (-CH2), 22.7 (-CH2), 15.8 (-CH2CH3), 15.5 (-CH2); IR (film, cm$^{-1}$) 3418, 2926, 2855, 1615, 1517; MS (EI) $m/z$: 217 (M$^+$), 188 (5), 174 (29), 160 (100); HRMS (EI) $m/z$ calcd for C15H23N(M$^+$) 217.1830, found 217.1832; $\left[\alpha\right]_D^{20}$ -8.8 (c 0.42, CHCl3); ee = 62% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: t$_{inj}$ = 280 °C; t$_{initial}$ = 30 °C for 3 min; rate = 1.2 °C/min; t$_R$ = 49.8 min (minor), t$_R$ = 51.4 min (major)].

**cis-N-(2-methoxyphenyl)-2-methylcyclohexanamine (7d).** Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), o-anisidine (150 µL, 1.3 mmol) and Pd[(R)-BINAP]Br2, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (83%). $^1$H NMR (300 MHz, CDCl3) $\delta$ 6.87 (td, 1H, $J = 1.3$, 7.15 Hz, ArH), 6.79 (d, 1H, $J = 7.7$ Hz, ArH), 6.66-6.61 (m, 2H, ArH), 4.34 (bs, 1H, -NHCH), 3.87 (s, 3H, -OMe), 3.55-3.51 (m, 1H, -NHCH), 2.10-2.00 (m, 1H, -CH2CH3), 1.76-1.38 (m, 8H, -CH2), 0.95 (d, 3H, $J = 6.8$ Hz, -CH2); $^{13}$C NMR (75 MHz, CDCl3) $\delta$ 146.9, 137.8, 121.3, 115.5, 110.2.
cis-N-(4-methoxyphenyl)-2-methylcyclohexaneamine (7e). Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), p-anisidine (160 mg, 1.3 mmol) and Pd[(R)-BINAP]Br2, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (85%). ¹H NMR (300 MHz, CDCl₃) δ 6.76 (d, 2H, J = 8.7 Hz, ArH), 6.58 (d, 2H, J = 8.7 Hz, ArH), 4.14 (bs, 1H, -NHCH), 3.74 (s, 3H, -OMe), 3.43-3.38 (m, 1H, -NHCH), 2.06-1.97 (m, 1H, -CHCH₃), 2.06-1.97 (m, 1H, -CHCH₃), 1.65-1.35 (m, 8H, -CH₂), 0.91 (d, 3H, J = 7.2 Hz, -CHCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 151.6, 141.9, 114.9, 114.6, 55.8 (-OHCH), 54.2 (-NHCH), 33.0 (-CHCH₃), 30.4 (-CH₂), 28.5 (-CH₂), 22.9 (-CH₂), 22.8 (-CH₂), 15.2 (-CHCH₃); IR (film, cm⁻¹) 3393, 2925, 2853, 1617, 1512; MS (EI) m/z: 219 (M⁺), 190 (4), 176 (22), 162 (100); HRMS (EI) m/z calcd for C₁₄H₂₁NO(M⁺) 219.1623, found 219.1625; [α]²⁰D -7.8 (c 0.54, CHCl₃); ee = 98% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1.0⁰/min; t_R = 156.1 min (minor), t_R = 157.5 min (major)].

cis-N-(3-chlorophenyl)-2-methylcyclohexaneamine (7f). Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), m-chloroaniline (136 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (90%). ¹H NMR (300 MHz, CDCl₃) δ 7.07-7.00 (m, 1H, ArH), 6.62-6.57 (m, 2H, ArH), 6.46 (dd, 1H, J = 1.0, 8.3 Hz ArH), 3.70 (bs, 1H, -NHCH), 3.48-3.44 (m, 1H, -NHCH), 2.04-1.96 (m, 1H, -CHCH₃), 1.83-1.35 (m, 8H, -CH₂), 0.91 (d, 3H, J = 6.6 Hz, -CHCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 148.8, 134.9, 130.0, 116.2, 112.4, 111.3, 53.0 (-NHCH), 32.9 (-CHCH₃), 30.2 (-CH₂), 28.5 (-CH₂), 22.9 (-CH₂), 22.6 (-CH₂), 15.6 (-CHCH₃); IR (film, cm⁻¹) 3425, 2927, 2855, 1597, 1502; MS (EI) m/z: 223 (M⁺), 194 (5), 180 (32), 166 (100); HRMS (EI) m/z calcd for C₁₃H₁₈NCl(M⁺) 223.1128, found 223.1123; [α]²⁰D -9.3 (c 0.4, CHCl₃); ee = >99% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1.0⁰/min; t_R = 143.8 min (minor), t_R = 144.9 min (major)].
cis-N-(4-chlorophenyl)-2-methylcyclohexanamine (7g). Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), p-chloroaniline (165 mg, 1.3 mmol) and Pd[(R)-BINAP]Br2, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (82%). 1H NMR (300 MHz, CDCl3) δ 7.09 (d, 2H, J = 8.8 Hz, ArH), 6.51 (d, 2H, J = 8.8 Hz, ArH), 3.59 (bs, 1H, -NHCH), 3.46-3.41 (m, 1H, -NCH2), 2.04-1.97 (m, 1H, -CH3CH), 1.75-1.36 (m, 8H, -CH2), 0.90 (d, 3H, J = 7.2 Hz, -CH3CH3); 13C NMR (75 MHz, CDCl3) δ 146.4, 129.1, 121.0, 114.2, 53.4 (-NHCH), 33.1 (-CH3CH), 30.3 (-CH2), 28.6 (-CH2), 23.0 (-CH2), 22.8 (-CH2), 15.5 (-CH3CH3); IR (film, cm⁻¹) 3423, 2927, 2856, 1599, 1500; MS (EI) m/z: 223 (M⁺), 194 (6), 180 (37), 166 (100); HRMS (EI) m/z calcd for C13H18NCl(M⁺) 223.1128, found 223.1135; [α]20 D -6.4 (c 0.5, CHCl3); ee = 89% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: Tinj = 280 °C; Tdet = 280 °C; Tinitial = 30 °C for 3 min; Tfinal = 200 °C; rate = 1.0⁰/min; tR = 157.1 min (minor), tR = 157.8 min (major)].

cis-N-(4-bromophenyl)-2-methylcyclohexanamine (7h). Prepared according to the general procedure from 2-methylcyclohexanone (121 µL, 1.0 mmol), p-bromoaniline (222 mg, 1.3 mmol) and Pd[(S)-BINAP]Br2, 1d, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (71%). 1H NMR (300 MHz, CDCl3) δ 7.21 (d, 2H, J = 8.8 Hz, ArH), 6.48 (d, 2H, J = 8.8 Hz, ArH), 3.67 (bs, 1H, -NHCH), 3.46-3.41 (m, 1H, -NHCH), 2.02-1.97 (m, 1H, -CH3CH), 1.77-1.22 (m, 8H, -CH2), 0.90 (d, 3H, J = 7.2 Hz, -CH3CH3); 13C NMR (75 MHz, CDCl3) δ 146.8, 132.0, 114.7, 108.0, 53.4 (-NHCH), 33.0 (-CH3CH), 30.3 (-CH2), 28.6 (-CH2), 23.0 (-CH2), 22.8 (-CH2), 15.5 (-CH3CH3); IR (film, cm⁻¹) 3434, 2926, 2854, 1600, 1515; MS (EI) m/z: 267 (M⁺), 240 (2), 226 (19), 212 (100); HRMS (EI) m/z calcd for C13H18NBr(M⁺) 267.0623, found 267.0631; [α]20 D +6.5 (c 0.52, CHCl3); ee = 83% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: Tinj = 280 °C; Tdet = 280 °C; Tinitial = 30 °C for 3 min; Tfinal = 200 °C; rate = 1.0⁰/min; tR = 167.3 min (minor), tR = 168.0 min (major)].

General procedure for asymmetric reductive amination of (R)-3-methylcyclohexanone.

The procedure was the same as 2-methylcyclopentanone.
trans-N-(phenyl)-3-methylcyclohexaneamine (9a). Prepared according to the general procedure from (R)-(+)3-methylycyclohexanone (122 µL, 1.0 mmol), aniline (120 µL, 1.3 mmol) and Pd[(S)-BINAP]Br₂, 1d, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (87%). ¹H NMR (500 MHz, CDCl₃) δ 7.17-7.14 (m, 2H, ArH), 6.68 (t, 1H, J = 7.2 Hz, ArH), 6.63 (d, 2H, J = 8.0 Hz, ArH), 4.21 (bs, 1H, -NHCH), 3.68-3.64 (m, 1H, -NHCH), 1.78-1.50 (m, 7H, -C(CH₃) + -C₂H), 1.38-1.33 (m, 1H, -CH₂), 1.09-1.01 (m, 1H, -CH₂), 0.91 (d, 3H, J = 6.5 Hz, -CHCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 146.8, 129.2, 117.2, 113.6, 48.1 (-NHCH), 38.6 (-CH₂), 33.8 (-CH₂), 30.3 (-CH₂), 27.1 (-CH₂CH₃), 21.5 (-CH₂CH₃), 20.5 (-CH₂); IR (film, cm⁻¹) 3415, 2923, 2850, 1602, 1504; MS (EI) m/z: 189 (M⁺), 174 (8), 160 (5), 146 (100), 132 (87); HRMS (EI) m/z calcd for C₁₃H₁₉N(M⁺) 189.1517, found 189.1514; [α]₂⁰D -13.3 (c 0.48, CHCl₃); ee = 91% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: Tᵢₙᵢⱼ = 280 °C; Tᵩᵡᵣ = 280 °C; Tᵢₐᵣᵢᵢ = 30 °C for 3 min; Tᵢₚᵩᵣᵢᵢ = 200 °C; rate = 1°/min; tᵣ = 132.7 min (major), tᵣ = 133.2 min (minor)]. The relative configuration was confirmed by NOE experiment and compared with a similar reported compound.⁶

trans-N-(p-ethylphenyl)-3-methylcyclohexaneamine (9b). Prepared according to the general procedure from (R)-(+)3-methylycyclohexanone (122 µL, 1.0 mmol), p-ethylaniline (160 µL, 1.3 mmol) and Pd[(S)-BINAP]Br₂, 1e, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (90%). ¹H NMR (500 MHz, CDCl₃) δ 6.99 (d, 2H, J = 8.5 Hz, ArH), 6.54 (d, 2H, J = 8.5 Hz, ArH), 4.02 (bs, 1H, -NHCH), 3.65-3.62 (m, 1H, -NHCH), 2.52 (q, 2H, J = 7.5 Hz, -CH₂CH₃), 1.76-1.49 (m, 7H, -C(CH₃) + -C₂H), 1.36-1.30 (m, 1H, -CH₂), 1.18 (t, 3H, J = 7.5 Hz, -CH₂CH₃), 1.07-1.00 (m, 1H, -CH₂), 0.90 (d, 3H, J = 6.5 Hz, -CH₂CH₃); ¹³C NMR (125 MHz, CDCl₃) δ 145.3, 132.6, 128.5, 113.2, 47.8 (-NHCH), 38.9 (-CH₂), 33.9 (-CH₂), 30.5 (-CH₂), 27.8 (-CH₂CH₃), 27.1 (-CH₂CH₃), 21.6 (-CH₂CH₃), 20.5 (-CH₂), 15.8 (-CH₂CH₃); IR (film, cm⁻¹) 3411, 2924, 2864, 1615, 1517; MS (EI) m/z: 217 (M⁺), 202 (9), 173 (3), 160 (100), 146 (82); HRMS (EI) m/z calcd for C₁₅H₂₃N(M⁺) 217.1830, found 217.1829; [α]₂⁰D -8.4 (c 0.48, CHCl₃); ee = 95% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: Tᵢₙᵢⱼ = 280 °C; Tᵩᵡᵣ = 280 °C; Tᵢₐᵣᵢᵢ = 30 °C for 3 min; Tᵢₚᵩᵣᵢᵢ = 200 °C; rate = 1°/min; tᵣ = 149.8 min (major), tᵣ = 150.5 min (minor)].
**trans-N-(3-trifluoromethylphenyl)-3-methylcyclohexaneamine (9c).** Prepared according to the general procedure from (R)-(+) -3-methylcyclohexanone (122 µL, 1.0 mmol), m-trifluoromethyl aniline (162 µL, 1.3 mmol) and Pd[(S)-BINAP]Br₂, **1d**, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (84%). ¹H NMR (500 MHz, CDCl₃) δ 7.21 (t, 1H, J = 8.0 Hz, ArH), 6.87 (d, 1H, J = 7.5 Hz, ArH), 6.77 (s, 1H, ArH), 6.70 (d, 1H, J = 8.0 Hz, ArH), 4.06 (bs, 1H, -NHCH), 3.70-3.66 (m, 1H, -NHCH), 1.76-1.45 (m, 7H, -CH₂CH₃ + -CH₂), 1.38-1.32 (m, 1H, -CH₂), 1.09-1.01 (m, 1H, -CH₂), 0.92 (d, 3H, J = 7.0 Hz, -CHCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 147.4, 131.6 (q, J = 31.4 Hz), 129.6, 124.6 (d, J = 271.0 Hz), 115.9, 113.1 (q, J = 3.7 Hz), 109.1 (q, J = 3.8 Hz), 47.6 (-NHCH), 38.6 (-CH₂), 33.8 (-CH₂), 30.2 (-CH₂), 27.1 (-CHCH₃), 21.6 (-CHCH₃), 20.4 (-CH₂); IR (film, cm⁻¹) 3443, 2926, 2857, 1614, 1515; MS (EI) m/z: 257 (M⁺), 242 (7), 214 (100), 228 (2), 200 (74); HRMS (EI) m/z calcd for C₁₄H₁₈NF₃(M⁺) 257.1391, found 257.1389; [α]²⁰D -13.1 (c 0.48, CHCl₃); ee = >99% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 135.8 min (major)].

**trans-N-(3-chlorophenyl)-3-methylcyclohexaneamine (9d).** Prepared according to the general procedure from (R)-(+) -3-methylcyclohexanone (122 µL, 1.0 mmol), m-chloroaniline (136 µL, 1.3 mmol) and Pd[(S)-BINAP]Br₂, **1d**, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (89%). ¹H NMR (500 MHz, CDCl₃) δ 7.02 (t, 1H, J = 8.2 Hz, ArH), 6.62 (d, 1H, J = 8.0 Hz, ArH), 6.54 (s, 1H, ArH), 6.43 (d, 1H, J = 8.5 Hz, ArH), 3.90 (bs, 1H, -NHCH), 3.63-3.60 (m, 1H, -NHCH), 1.72-1.43 (m, 7H, -CHCH₃ + -CH₂), 1.35-1.29 (m, 1H, -CH₂), 1.07-0.99 (m, 1H, -CH₂), 0.91 (d, 3H, J = 6.5 Hz, -CHCH₃); ¹³C NMR (125 MHz, CDCl₃) δ 148.4, 135.0, 130.1, 116.5, 112.5, 111.3, 47.6 (-NHCH), 38.6 (-CH₂), 33.8 (-CH₂), 30.2 (-CH₂), 27.1 (-CHCH₃), 21.5 (-CHCH₃), 20.4 (-CH₂); IR (film, cm⁻¹) 3425, 2924, 2861, 1598, 1500; MS (EI) m/z: 223 (M⁺), 208 (7), 180 (100), 166 (73), 153 (17); HRMS (EI) m/z calcd for C₁₃H₁₈NCl(M⁺) 223.1128, found 223.1129; [α]²⁰D -12.7 (c 0.47, CHCl₃); ee = >99% by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 189.4 min (major)].

**General procedure for asymmetric reductive amination of other substituted rings.**

The procedure was the same as 2-methylcyclopentanone.
cis-N-[2-(3-methoxyphenyl)cyclohexyl]benzenamine (11). Prepared according to the general procedure from 2-(3-methoxyphenyl)cyclohexanone (185 µL, 1.0 mmol), aniline (120 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as light yellow oil (77%). ¹H NMR (500 MHz, CDCl₃) δ 7.16 (t, 1H, J = 7.5 Hz, ArH), 7.03 (dd, 2H, J = 8.5 Hz, ArH), 6.84 (dt, 1H, J = 8.5, 1.0 Hz, ArH), 6.80 (t, 1H, J = 8.5 Hz, ArH), 6.68 (dd, 1H, J = 8.0, 2.5 Hz, ArH), 6.56 (tt, 1H, J = 7.5, 1.0 Hz, ArH), 6.41(d, 2H, J = 8.0 Hz, ArH), 3.82-3.79 (m, 1H, -NHC₃H), 3.70 (s, 3H, -OMe), 3.66 (bs, 1H, -NHCH), 2.98-2.92 (dd, 1H, J = 11.5, 4.0, 4.0 Hz, -C₆H₄ArH), 2.12 -2.08 (m, 1H, -C₆H₂), 1.92-1.82 (m, 3 H, -C₆H₂), 1.61-1.42 (m, 4H, -C₆H₂) ; ¹³C NMR (125 MHz, CDCl₃) δ 159.5, 147.8, 145.4, 129.1, 128.9, 119.9, 116.6, 113.7, 113.2, 111.3, 55.0 (-OMe), 53.2 (-NHCH), 46.1 (-CHArH), 30.1 (-CH₂), 25.87 (-CH₂), 25.83 (-CH₂), 20.3 (-CH₂); IR (film, cm⁻¹) 3424, 2926, 2861, 1598, 1502; MS (EI) m/z: 281 (M⁺), 252 (3), 238 (18), 224 (3), 159 (19), 132 (100); HRMS (EI) m/z calcd for C₁₉H₂₃NO (M⁺) 281.1780, found 281.1784; [α]₂⁰D -36.6 (c 0.21, CHCl₃); ee = 80 % by GC-MS (EI) [chiral column: Cyclodex-β; conditions: T_inj = 280 °C; T_det = 280 °C; T_initial = 30 °C for 3 min; T_final = 200 °C; rate = 1°/min; t_R = 147.0 min (minor), t_R = 148.4 min (major)].

N-(2-(trifluoromethyl)phenyl)bicyclo[2.2.1]heptan-2-amine (15). Prepared according to the general procedure from norcamphor (110 mg, 1.0 mmol), o-trifluoromethyl aniline (163 µL, 1.3 mmol) and Pd[(R)-BINAP]Br₂, 1c, (22 mg, 0.025 mmol) at 80 °C for 24 h, to provide the title compound as colorless oil (74%). ¹H NMR (500 MHz, CDCl₃) δ 7.41 (d, 1H, J = 8.0 Hz, ArH), 7.32 (t, 1H, J = 7.5 Hz, ArH), 6.71(d, 1H, J = 8.5 Hz, ArH), 6.67 (t, 1H, J = 7.5 Hz, ArH), 4.51 (bs, 1H, -NHCH), 3.76-3.73 (m, 1H, -NHCH), 2.55-2.53 (m, 1H, -CH), 2.32-2.26 (m,
1H, -CH), 2.20-2.14 (m, 1H, -CH₂), 1.68-1.55 (m, 2H, -CH₂), 1.50-1.47 (m, 1H, -CH₂), 1.42-1.35 (m, 2H, -CH₂), 1.30-1.16 (m, 1H, -CH₂), 0.84-0.80 (m, 1H, -CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 145.6, 132.9, 126.8 (q, J = 5.3 Hz), 119.8 (d = 272.1 Hz), 115.3, 113.2 (q, J = 29.4 Hz), 112.6, 54.2 (-NHCH), 39.7 (-CH), 38.9 (-CH₂), 38.1 (-CH₂), 36.8 (-CH), 29.7 (-CH₂), 21.2 (-CH₂); IR (film, cm⁻¹) 3476, 2956, 2873, 1615, 1519; MS (EI) m/z: 255 (M⁺, 100), 226 (23), 214 (12), 200 (29), 187 (57), 174 (21); HRMS (EI) m/z calc'd for C₁₄H₁₆NF₃(M⁺) 255.1235, found 235.1239; [α]²₀D -15.7 (c 0.50, CHCl₃); ee = 87% by HPLC (Daicel Chiracel OD-H, eluent hexane-iPrOH = 99 1, flow rate = 1mL min, tstral = 6.58 min (major), tR = 7.58 min (minor)].

References:

Scanned spectra of NMR and GC-MS (EI) or HPLC for all compounds:
UNAM. Instituto de Química.
Dr. A. Cabrera/Laura R. P.
Clave: Reacc352
No. Registro: 896
Experimento: NOESY
Disolvente: CDCl3
Variante: NOESY 500 MHz (O)
Abril 14-2009
Pulse Sequence: noesy
### TIC

**Data:** Dr-Cabrera-Armando-137  
**Date:** 17-Oct-120 10:08  
**Sample:** 2435 G2 Reac 321 y JeolAX505HA  
**Note:** 5 horas  
**Inlet:** GC  
**Ion Mode:** EI+  
**Ion Species:** Normal Ion  
**TIC Range:** m/z 33 to 650

#### No. RT[min] Area Area% Height Height% Width[sec] INTEG

<table>
<thead>
<tr>
<th>No.</th>
<th>RT[min]</th>
<th>Area</th>
<th>Area%</th>
<th>Height</th>
<th>Height%</th>
<th>Width[sec]</th>
<th>INTEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51.86</td>
<td>376.07</td>
<td>8.32</td>
<td>22.97</td>
<td>6.39</td>
<td>15.37</td>
<td>BB</td>
</tr>
<tr>
<td>2</td>
<td>53.16</td>
<td>4143.46</td>
<td>91.68</td>
<td>336.27</td>
<td>93.61</td>
<td>11.57</td>
<td>BB</td>
</tr>
</tbody>
</table>

### Mass Spectrum

**RT:** 51.86 min  
**Scan #:** 4465-4453-4491  
**Temp.:** 8.8 deg.C  
**Ion Mode:** EI+  
**Int.:** 4.97

### Mass Spectrum

**RT:** 53.16 min  
**Scan #:** 4577-4552-4609  
**Temp.:** 8.8 deg.C  
**Ion Mode:** EI+  
**Int.:** 69.20
U.N.A.M. Instituto de Química
ICH
Dr. A. Cabrera/Laura R. P
Clave: Reacc51561516
Disolvente: CDCl3
Experimento 1H
Varian Unity 300 MHz (D)
No. de Registro 0175
20-01-09

Spectrum 3.84, 3.78 ppm

Chemical structure image
[ TIC ]
Data: Dr-Cabrera-Armando-916
Sample: 31 G Reacc 511 AX505HA
Note:
Inlet: GC
Ion Species: Normal Ion
Ion Mode: EI+
TIC Range: m/z 5 to 650

<table>
<thead>
<tr>
<th>No.</th>
<th>RT [min]</th>
<th>Area</th>
<th>Area%</th>
<th>Height</th>
<th>Height%</th>
<th>Width [sec]</th>
<th>INTEGRATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37.77</td>
<td>112.96</td>
<td>2.27</td>
<td>16.64</td>
<td>5.94</td>
<td>6.37</td>
<td>BV</td>
</tr>
<tr>
<td>2</td>
<td>38.21</td>
<td>4858.82</td>
<td>97.73</td>
<td>263.57</td>
<td>94.06</td>
<td>17.31</td>
<td>VB</td>
</tr>
</tbody>
</table>

[ Mass Spectrum ]
RT: 37.77 min
Ion Mode: EI+
Scan#: 2838-2821-2803
Temp: 0.0 deg.C
Int.: 6.02

[ Mass Spectrum ]
RT: 30.21 min
Ion Mode: EI+
Scan#: 2863-2821-2803
Temp: 0.0 deg.C
Int.: 79.31

S79
INSTITUTO DE QUÍMICA, UNAM/ EHS
Dr. A. Cabrer/ Laura R. P.
Clave: Renac309
Disolvente: CDC33
Carbono–13
Eclipse 300 MHz Jeol (E)
27–01–09
No. de registro: 0286
INSTITUTO DE QUÍMICA, UNAM/ EHS
Dr. A. Cabrera/ Luisa R. P.
Clave: Reacc309
Disolvente: CDCl3
DEPT
Eclipse 300 MHz Joes (E)
27-01-09
No. de registro: 0296

Site 6a
(Table 2, entry 11)

CH, CH3

130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0
X: parts per Million : 13C

130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0
X: parts per Million : 13C

123.202 116.683 114.117
123.202 116.683 114.117
123.202 116.683 114.117

CH

CH2
Peak Table

<table>
<thead>
<tr>
<th>Peak Label</th>
<th>RIC</th>
<th>Scan Range</th>
<th>Baseline at</th>
<th>Total Area</th>
<th>Background</th>
<th>Peak Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>138.62</td>
<td>TIC</td>
<td>6793-6829</td>
<td>6784-6788</td>
<td>1438850</td>
<td>8469663</td>
<td>5919187</td>
</tr>
<tr>
<td>139.95</td>
<td>TIC</td>
<td>6905-6941</td>
<td>6895-6899</td>
<td>49880378</td>
<td>8273759</td>
<td>41606619</td>
</tr>
</tbody>
</table>

S86
INSTITUTO DE QUIMICA, UNAM / EHS

Dr. A. Cabrera/ Laura R. P.
Clave: Reacc341
Disolvente: CDCl3
Carbono-13
Eclipse 300 MHz Joel (E)
10-03-08
No. de registro: 0957

X : parts per Million / 13C
No. RT [min] Area Area% Height Height% Width [sec] INTEGR
1 28.48 443.20 3.40 35.05 11.12 11.87 BV
2 29.72 12604.04 96.60 280.19 88.88 42.24 VB
**File:** 1211-REACC382  
**Date Run:** 05-28-2009  
**Time Run:** 19:16:44  
**Sample:** De-Cabralera  
**Instrument:** JEOL GCmate  
**Inlet:** GC  
**Ionization mode:** E1+  

**Peak Table**

<table>
<thead>
<tr>
<th>Peak Label</th>
<th>RIC</th>
<th>Scan Range</th>
<th>Baseline at</th>
<th>Total Area</th>
<th>Background</th>
<th>Peak Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>157.17</td>
<td>TIC</td>
<td>8397-8423</td>
<td>8385-8389</td>
<td>3639883</td>
<td>3372220</td>
<td>250663</td>
</tr>
<tr>
<td>157.83</td>
<td>TIC</td>
<td>8455-8481</td>
<td>8480-8494</td>
<td>7812256</td>
<td>3305930</td>
<td>4506326</td>
</tr>
</tbody>
</table>
SI03

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2
0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2
180.0 190.0 200.0 210.0 220.0 230.0 240.0 250.0 260.0 270.0 280.0 290.0 300.0
X : parts per Million : 13C

Br

7h
File: Carbon
Pulse Sequence: s2pu1
trans-8c

(Table 3, entry 3)

<table>
<thead>
<tr>
<th>Peak Label</th>
<th>RIC</th>
<th>Scan Range</th>
<th>Baseline at</th>
<th>Total Area</th>
<th>Background</th>
<th>Peak Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>135.88</td>
<td>TIC</td>
<td>6557-6581</td>
<td>6547-6551</td>
<td>478247767</td>
<td>4150451</td>
<td>474097316</td>
</tr>
</tbody>
</table>
file: Carbon
Pulse Sequence: s2pul
File: REACC-537
Sample: Dr-Cabrera
Instrument: JEOL GCmate
Inlet: GC
Ionization mode: EI+

Scan: 11201  R.T.: 189.4
Base: m/z 223; 99.6% FS  TIC: 53914192  #Ions: 153
U.N.A.M. Instituto de Química ICH
Dr. A. Cabrera
Clase: Reacc 708F31
Disolvente: CDCl3
Experimento NOESY
Varian Inova 500 MHz (6)
No. de registro 672
10-64-15

Pulse Sequence: noesy
Area Percent Report

Sorted By: Signal
Multiplier: 1.0000
Dilution: 1.0000

Signal 1: DAD1 E, Sig=330,16 Ref=off
Results obtained with enhanced integrator!

<table>
<thead>
<tr>
<th>Peak</th>
<th>RetTime</th>
<th>Type</th>
<th>Width</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.584</td>
<td>BV</td>
<td>0.2941</td>
<td>1.23782e4</td>
<td>568.26147</td>
<td>93.2883</td>
</tr>
<tr>
<td>2</td>
<td>7.585</td>
<td>VP</td>
<td>0.1931</td>
<td>890.56598</td>
<td>76.88500</td>
<td>6.7117</td>
</tr>
</tbody>
</table>

Totals:
1.32688e4  645.14648

*** End of Report ***

ee = 86.57 ~ 87%