(Supporting Information)

Palladium Catalyzed Intramolecular Asymmetric Hydroamination of Alkynes

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Experimental Section

General. The ^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 300 MHz, respectively, using CDCl_3 as solvent and were reported in ppm relative to CHCl_3 ($\delta = 7.26$) for ^1H NMR and relative to the central CDCl_3 ($\delta = 77.00$) resonance for ^{13}C NMR. Coupling constants in ^1H NMR are in Hz. Optical Rotations were measured on a Jasco DIP-1000 digital polarimeter. HPLC was performed on Shimadzu LC9A and SPD-10A using a Daicel CHIRALCEL OD column (4.6 mm x 250 mm).

Optimization of the Reaction Conditions for the Intramolecular Asymmetric Hydroamination

Table 1. Effect of Phosphine Ligands

entry	ligand	yield (%)	ee (%)
1	(S)-BINAP	56	2
2	(S)-MOP	85	10
3	(R,S)-BPPFOAc	91	6
4	(S,R)-BPPFOH	75	0
5	(R,R)-DIOP	100	0
6	(S,S)BPPM	95	15
7	(R,R)-CHIRAPHOS	92	25
8	(R,R)=NORPHOS	<5	98
9	(R,R)-RENORPHOS	65	82 ^a

^a30 mol% of ligand was used.

Neomenthyl(diphenyl)phosphine (NMDPP)

BINAP

MOP

BPPFOAc

BPPFOH

DIOP

BPPM

CHIRAPHOS

NORPHOS

Table 2. Effect of Amino Protecting Groups

entry	R	yield (%)	ee (%)
1	Bn	95	8
2	Ac	0	-
3	Boc	0	-
4	Ts	25	47
5	Tf	65	82
6	Nf	68	88 ^a

^a25 mol% of ligand was used.

General procedure for the intramolecular asymmetric hydroamination of 1.

Conditions A: To Pd₂dba₃·CHCl₃ (6.5 mg, 0.00625 mmol), PhCO₂H (1.5 mg, 0.0125 mmol) and (R,R)-renorphos (14.5 mg, 0.031 mmol) was added the amino alkyne **1** (0.125 mmol) in 1.5 ml of benzene under Ar atmosphere in a pressure vial. After heating at 100°C for 72 hours, the reaction mixture was filtered through a short silica gel column using diethyl ether as an eluent. After evaporation of the solvent, the residue was purified by silica gel column chromatography to afford the product **2**.

Conditions B: To Pd₂dba₃·CHCl₃ (26 mg, 0.025 mmol), PhCO₂H (6.1 mg, 0.05 mmol) and (R,R)-renorphos (58 mg, 0.125 mmol) was added the aminoalkyne **1** (0.125 mmol) in 1.5 ml of benzene/hexane (2:1) under Ar atmosphere in a pressure vial. After heating at 80°C for 72 hours, the reaction mixture was filtered through a short silica gel column using diethyl ether as an eluent. After evaporation of the solvent, the residue was purified by silica gel column chromatography to afford the product **2**.

Unless otherwise noted, the enantiomeric excess values below refer to conditions B.

***N*-triflyl-6-phenyl-5-hexynylamine (1a).** IR (neat) 3322, 2947, 2869, 2234, 1373, 1195, 758 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.24 (m, 5H), 4.95 (br s, 1H), 3.38-3.33 (m, 2H), 2.46 (t, *J* = 6.7 Hz, 2H), 1.82-1.75 (m, 2H), 1.69-1.62 (m, 2H); Anal. Calcd for C₁₃H₁₄F₃NO₂S (305.32): C, 51.14; H, 4.62; N, 4.59; S, 10.50. Found: C, 51.39; H, 4.81; N, 4.64; S, 10.26.

***N*-nonafllyl-6-phenyl-5-hexynylamine (1b).** IR (neat) 3322, 3081, 3053, 3033, 2945, 2870, 2227, 1370, 1355, 1148, 1130, 1079, 1039, 758 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.33-7.18 (m, 5H), 4.49 (br s, 1H), 3.34 (t, *J* = 7.08 Hz, 2H), 2.40 (t, *J* = 6.7 Hz, 2H), 2.09-1.66 (m, 2H), 1.63-1.56 (m, 2H); Anal. Calcd for C₁₆H₁₄F₉NO₂S (455.34): C, 42.20; H, 3.10; N, 3.08; S, 7.03. Found: C, 41.91; H, 3.13; N, 3.01; S, 7.22.

***N*-nonafllyl-6-(4-methoxyphenyl)-5-hexynylamine (1c).** IR (neat) 3301, 2938, 2532, 2049, 1509, 833 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.32-7.24 (m, 2H), 6.82-6.77 (m, 2H), 4.99 (br s, 1H), 3.78 (s, 3H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.44 (t, *J* = 6.6 Hz, 2H), 1.82-1.77 (m, 2H), 1.68-1.63 (m, 2H). Anal. Calcd for C₁₇H₁₆F₉NO₃S (485.37): C, 42.07; H, 3.32; N, 2.89; S, 6.61. Found: C, 42.37; H, 3.62; N, 2.71; S, 6.86.

***N*-nonafllyl-6-(4-trifluoromethylphenyl)-5-hexynylamine (1d).** IR (neat) 3314, 2933, 2870, 2231, 1930, 1615, 1442, 1255 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.45-7.32 (m, 4H), 5.08 (s, 1H),

3.42-3.77 (m, 2H), 2.47 (t, $J = 6.8$ Hz, 2H), 1.82-1.77 (m, 2H), 1.71-1.63 (m, 2H). Anal. Calcd for $C_{17}H_{13}F_{12}NO_2S$ (523.34): C, 39.02; H, 2.50; N, 2.68; S, 6.13. Found: C, 38.83; H, 2.57; N, 2.64; S, 6.28.

***N*-nonafllyl-5-undecynylamine (1e).** IR (neat) 3313, 2935, 2864, 1433, 1376, 1238 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 5.41 (br s, 1H), 3.34 (t, $J = 6.8$ Hz, 2H), 2.20-2.15 (m, 2H), 2.12-2.07 (m, 2H), 1.73-1.66 (m, 2H), 1.56-1.41 (m, 4H), 1.35-1.22 (m, 4H), 0.86 (t, $J = 7.1$ Hz, 3H). Anal. Calcd for $C_{15}H_{20}F_9NO_2S$ (449.38): C, 40.09; H, 4.49; N, 3.12; S, 7.14. Found: C, 39.96; H, 4.41; N, 3.00; S, 7.22.

***N*-nonafllyl-7-phenyl-6-heptynylamine (1f).** IR (neat) 3309, 2943, 2862, 2235, 1355, 1224 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.25 (m, 5H), 4.99 (br s, 1H), 3.36 (t, $J = 7.1$ Hz, 2H), 2.44 (t, $J = 6.8$ Hz, 2H), 1.70-1.50 (m, 6H). Anal. Calcd for $C_{17}H_{16}F_9NO_2S$ (469.37): C, 43.50; H, 3.44; N, 2.98; S, 6.83. Found: C, 43.40; H, 3.41; N, 2.79; S, 6.86.

***N*-nonafllyl-2-(4-phenyl-3-butynyl)benzylamine (1g).** IR (neat) 3287, 3064, 2932, 2232, 1932, 1173 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.21 (m, 9 H), 5.31 (s, 1H), 4.57 (s, 2H), 2.98 (t, $J = 7.1$ Hz, 2H), 2.74 (t, $J = 7.1$ Hz, 2H). Anal. Calcd for $C_{21}H_{16}F_9NO_2S$ (517.41): C, 48.75; H, 3.12; N, 2.71; S, 6.20. Found: C, 48.61; H, 3.18; N, 2.48; S, 6.40.

***N*-triflyl-2-[(*E*)-2-phenylethenyl]pyrrolidine (2a).** IR (neat) 2986, 1378, 1197, 1168, 1090, 1075, 747 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.22 (m, 5H), 6.55 (d, $J = 15.9$ Hz, 1H), 6.08 (dd, $J = 15.6, 7.3$ Hz, 1H), 4.66 (dt, $J = 7.4, 3.9$ Hz, 1H), 3.71-3.57 (m, 2H), 2.28-2.19 (m, 1H), 2.13-1.90 (m, 3H). Anal. Calcd for $C_{13}H_{14}F_3NO_2S$ (305.32): C, 51.14; H, 4.62; N, 4.59; S, 10.50. Found: C, 51.28; H, 4.78; N, 4.62; S, 10.23. $[\alpha]_D^{21} = -81.2$ (c 0.5, $CHCl_3$). The ratio of enantiomers (conditions A, 30 mol% ligand) was determined to be 91.2/8.8 by HPLC analysis (hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): $t_R = 11.9$ min (major enantiomer), $t_R = 15.5$ min (minor enantiomer); 82% ee.

***N*-nonafllyl-2-[(*E*)-2-phenylethenyl]pyrrolidine (2b).** IR (neat) 3025, 2987, 1955, 1887, 1381, 1201, 747 cm^{-1} . 1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.20 (m, 5H), 6.57 (d, $J = 15.6$ Hz, 1H), 6.11 (dd, $J = 15.9, 7.3$ Hz, 1H), 4.76-4.71 (m, 1H), 3.77-3.66 (m, 2H), 2.31-1.94 (m, 4H). Anal. Calcd for $C_{16}H_{14}F_9NO_2S$ (455.34): C, 42.20; H, 3.10; N, 3.08; S, 7.04. Found: C, 42.06; H, 3.29; N, 2.96; S, 7.43. $[\alpha]_D^{23} = -85.0$ (c 0.5, $CHCl_3$). The ratio of enantiomers was determined to be 95.4/4.6 by HPLC analysis (hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): $t_R = 9.6$ min (major enantiomer), $t_R = 12.2$ min (minor enantiomer); 91% ee.

***N*-nonafllyl-2-[(*E*)-2-(4-methoxyphenyl)ethenyl]pyrrolidine (2c).** IR (neat) 2957, 2056, 1606, 1380, 1243 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 7.25 (d, *J* = 8.8 Hz, 2H), (d, *J* = 8.8 Hz, 2H), 6.45 (d, *J* = 15.8 Hz, 1H), 5.91 (dd, *J* = 15.8, 7.4 Hz, 1H), 4.66 (m, 1H), 3.76 (s, 3H), 2.24-1.89 (m, 4H). Anal. Calcd for C₁₇H₁₆F₉NO₃S (485.37): C, 42.07; H, 3.32; N, 2.89; S, 6.61. Found: C, 42.32; H, 3.64; N, 2.70; S, 6.83. [α]_D²² = -66.5 (c 0.5, CHCl₃). The ratio of enantiomers was determined to be 9.5/90.5 by HPLC analysis (hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): t_R = 10.8 min (minor enantiomer), t_R = 12.2 min (major enantiomer); 81% ee.

***N*-nonafllyl-2-[(*E*)-2-(4-trifluoromethylphenyl)ethenyl]pyrrolidine (2d).** IR (neat) 2988, 2919, 2295, 1384, 1227, 1033 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.55 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 6.58 (d, *J* = 15.6 Hz, 1H) 6.19 (dd, *J* = 15.8, 7.3 Hz, 1H), 4.72 (dt, *J* = 7.3, 3.9 Hz, 1H), 3.76-3.65 (m, 2 H), 2.32-2.24 (m, 1H) 2.14-1.91 (m, 3H). Anal. Calcd for C₁₇H₁₃F₁₂NO₂S (523.34): C, 39.02; H, 2.50; N, 2.68; S, 6.13. Found: C, 38.93; H, 2.41; N, 2.56; S, 6.16. [α]_D²² = -62.4 (c 0.6, CHCl₃). The ratio of enantiomers was determined to be 93.8/6.2 by HPLC analysis (hexane/*i*-PrOH = 500/1, flow rate = 1.0 mL/min): t_R = 10.9 min (major enantiomer), t_R = 11.8 min (minor enantiomer); 88% ee.

***N*-nonafllyl-2-[(*E*)-2-pentylethenyl]pyrrolidine (*trans*-(2e)).** IR (neat) 2960, 2931, 1392, 1238, 1140, 1072 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 5.60 (dt, *J* = 15.4, 6.6 Hz, 1H), 5.31 (dd, *J* = 15.1, 7.3 Hz, 1H), 4.45 (dt, *J* = 7.2, 3.9 Hz, 1H), 2.16-1.75 (m, 6H), 1.34-1.15 (m, 6H), 0.81 (t, *J* = 6.9 Hz, 3H). Anal. Calcd for C₁₅H₂₀F₉NO₂S (449.38): C, 40.09; H, 4.49; N, 3.12; S, 7.14. Found: C, 40.06; H, 4.56; N, 3.20; S, 7.22. [α]_D¹⁹ = -19.3 (c 0.5, CHCl₃).

***N*-nonafllyl-2-[(*Z*)-2-pentylethenyl]pyrrolidine (*cis*-(2e)).** IR (neat) 2935, 1391, 1238, 1200, 1140 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 5.67-5.42 (m, 2H), 4.60 (m, 1H), 3.76 (m, 1H), 3.22 (m, 1H) 2.05 (m, 2H), 1.80-1.54 (m, 6H), 1.35-1.25 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 3H). Anal. Calcd for C₁₅H₂₀F₉NO₂S (449.38): C, 40.09; H, 4.49; N, 3.12; S, 7.14. Found: C, 39.97; H, 4.49; N, 2.99; S, 7.02. [α]_D¹⁹ = +13.5 (c 0.5, CHCl₃).

***N*-nonafllyl-2-[(*E*)-2-phenylethenyl]piperidine (2f).** IR (neat) 2956, 1957, 1352, 1257, 1074 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.19 (m, 5 H), 6.6 (d, *J* = 15.8 Hz, 1H), 6.18 (m, 1H), 4.80 (m, 1H), 3.83 (m, 1H), 3.29 (m, 1H), 1.95 (m, 2H), 1.69-1.61 (m, 4H). Anal. Calcd for C₁₇H₁₆F₉NO₂S (469.37): C, 43.50; H, 3.44; N, 2.98; S, 6.83. Found: C, 43.35; H, 3.37; N, 2.70; S, 6.91; [α]_D²⁵ = -85.8 (c 1.0, CHCl₃). The ratio of enantiomers was determined to be 94.9/5.1 by HPLC analysis

(hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): t_R = 5.9 min (major enantiomer), t_R = 7.1 min (minor enantiomer); 90% ee.

***N*-nonafllyl-3-(2-phenylethenyl)-1,2,3,4-tetrahydroisoquinoline (2g).** IR (neat) 3026, 2943, 1384, 1232, 1174 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.24-7.02 (m, 7H) 6.60 (m, 1H), 6.11 (m, 1H), 5.07 (m, 1H) 4.91-4.61 (m, 2H), 3.36 (m, 1H), 2.98 (m, 1H). Anal. Calcd for $\text{C}_{21}\text{H}_{16}\text{F}_9\text{NO}_2\text{S}$ (517.41): C, 48.75; H, 3.12; N, 2.71; S, 6.20. Found: C, 48.54; H, 3.20; N, 2.41; $[\alpha]_D^{21}$ = -11.4 (c 0.5, CHCl_3). The ratio of enantiomers was determined to be 6.3/93.7 by HPLC analysis (hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): t_R = 7.5 min (minor enantiomer), t_R = 8.2 min (major enantiomer); 87% ee.

2-phenethylpyrrolidine (3). The ^1H NMR and ^{13}C NMR spectra of **3** were identical with the literature data, see: Secor, V. H.; Seeman, I. J. *Heterocycles*, **1986**, 24, 1687-1698.

***N*-nonafllyl-6-phenyl-3(*E*),5(*E*)-hexadienylamine (7).** IR (neat) 3325, 3083, 3021, 2919, 1433, 1368, 1241 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.39-7.22 (m, 5H), 6.73 (dd, J = 15.6, 10.2 Hz, 1H), 6.52 (d, J = 15.8 Hz, 1H), 6.31 (dd, J = 15.1, 10.3 Hz, 1H), 5.66 (dt, J = 15.2, 7.3 Hz, 1H), 5.02 (s, 1H), 3.46-3.40 (m, 2H), 2.44 (dt, J = 6.8, 6.6 Hz, 2H). Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{F}_9\text{NO}_2\text{S}$ (455.34): C, 42.20; H, 3.10; N, 3.08; S, 7.04. Found: C, 42.00; H, 3.03; N, 2.89; S, 7.10.

***N*-(*p*-tolylsulfonyl)-4,5-undecadienylamine (8).** The spectral data (IR, ^1H NMR and ^{13}C NMR) of **8** were identical with those reported in the literature, see: Jonasson, C.; Horváth, A.; Bäckvall, J-E. *J. Am. Chem. Soc.* **2000**, 122, 9600-9609.

***N*-(*p*-tolylsulfonyl)-2-[(*E*)-2-pentylethenyl]pyrrolidine (9).** IR (neat) 2955, 2926, 2857, 1457, 1348, 1160, 1094 cm^{-1} . ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, J = 8.3, 2H), 7.20 (d, J = 8.3 Hz, 2H), 5.55 (ddt, J = 15.1, 6.6, 1 Hz, 1H), 5.26 (ddt, J = 15.4, 6.5, 1.5 Hz, 1H), 4.03 (m, 1H), 3.32 (m, 1H), 3.16 (m, 1H), 2.33 (s, 3H), 1.90 (m, 2H), 1.78-1.50 (m, 4H), 1.29-1.12 (m, 6H), 0.80 (t, J = 6.9 Hz, 3H); The ratio of enantiomers was determined to be 49.8/50.2 by HPLC analysis (hexane/*i*-PrOH = 100/1, flow rate = 1.0 mL/min): t_R = 14.7 min (minor enantiomer), t_R = 16.0 min (major enantiomer); 0% ee.

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COMMT
DATIM Sun Oct 26 19:33:32 2003
OBNUC 1H
EXMOD NON
OBFRQ 399.65 MHz
OBSET 124.00 KHz
OBSIN 10500.0 Hz
POINT 32768
FREQU 8000.0 Hz
SCANS 8
ACQIM 4.096 sec
PD 2.904 sec
PW1 5.8 us
IRNUC 1H
CTEMP 23.5 c
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EXREF 0.00 ppm
BF 0.00 Hz
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