**Rhodium-Catalyzed Intramolecular, Anti-Markovnikov Hydroamination.
Synthesis of 3-Arylpiperidines**

Supporting Information

Akihiro Takemiya and John F. Hartwig*

*Yale University, Department of Chemistry,
P.O. Box 208107, New Haven, CT, 06520-8107*

General Comments. All reactions were performed under nitrogen atmosphere using standard Schlenk and drybox techniques. THF was dried by passing it through column of activated alumina. 1, 4-dioxane was purchased from commercial sources and was used under nitrogen without further purification. $[\text{Rh}(\text{COD})(\text{DPPB})]\text{BF}_4$, $[\text{Rh}(\text{COD})_2]\text{BF}_4$, and DPPB were purchased from commercial sources and were used without further purification. NMR spectra were recorded on a 400 MHz instrument. GC-MS data were obtained with an Alltech EC-1 capillary column.

Synthesis of Methyl-(4-phenylpent-4-enyl)-amine:

4-Phenylpent-4-enoic acid

To a suspension of methyltriphenylphosphonium bromide (39.1 g, 109.5 mmol) in THF (200 mL) was added sodium *tert*-butoxide (21.0 g, 218.9 mmol) at 0 °C. The mixture was then stirred for 30 min. 3-benzoylpropionic acid (15.0 g, 84.2 mmol) was then added to the reaction mixture at 0 °C. The mixture was allowed to warm to room temperature, and was then stirred for 16 h. After evaporation of THF, dichloromethane and 1 N NaOH were added. The aqueous layer was washed with dichloromethane. 12 N HCl was then added until pH of the aqueous layer was *ca.* 2. The aqueous layer was then extracted with dichloromethane twice and dried over magnesium sulfate. Concentration of the organic layer gave the title compound as a white solid (14.8 g, 84.2 mmol, quant.). The product was used for next step without further purification. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.53 (t, 2H, $J = 7.4$ Hz), 2.85 (t, 2H, $J = 7.4$ Hz), 5.11 (s, 1H), 5.32 (s, 1H), 7.25-7.41 (m, 5H), 10.7 (br, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 30.1, 32.9, 112.9, 126.1, 127.7, 128.4, 140.4, 146.5, 179.4; MS, m/e : 176 $[\text{M}^+]$, 131 $[\text{PhC}(\text{=CH}_2)\text{CH}_2\text{CH}_2]^+$, 77 $[\text{Ph}^+]$.

4-Phenylpent-4-en-1-ol

4-Phenylpent-4-enoic acid (5.0 g, 28.4 mmol) was dissolved in THF (56 mL). Lithium aluminum hydride (2.27 g, 59.8 mmol) was added portionwise at 0 °C. The reaction mixture was stirred for 30 min. The reaction was then quenched with 2 N NaOH and filtered through a pad of Celite. The organic layer was extracted with diethyl ether and dried over magnesium sulfate. Concentration of the organic layer gave the title compound as a clear oil. (4.19 g, 25.8 mmol, 91%). The product was used for the next step without further purification. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 1.59 (br, 1H), 1.67-1.73 (m, 2H), 2.57 (t, 2H, $J = 6.5$ Hz), 5.09 (d, 2H, $J = 1.3$ Hz), 5.29 (d, 2H, $J = 1.3$ Hz), 7.26-7.33 (m, 3H), 7.35-7.43 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 31.1, 31.5, 62.3, 112.5, 126.1, 127.3, 128.2, 140.9, 147.9; MS, m/e : 162 $[\text{M}^+]$, 117 $[\text{PhC}(\text{=CH}_2)\text{CH}_2]^+$, 103 $[\text{PhC}(\text{=CH}_2)^+]$.

4-Phenylpent-4-enal

4-Phenylpent-4-en-1-ol (3.24 g, 18.4 mmol), triethylamine (7.7 mL, 55 mmol) and dimethylsulfoxide (3.9 mL, 55 mmol) were dissolved in dichloromethane (40 mL). Sulfur trioxide pyridine complex (8.79 g, 55.2 mmol) was added at 0 °C. The reaction mixture was allowed to warm to room temperature, and was then stirred for 12 h. After quenching with cold water, the organic layer was extracted with dichloromethane and dried over magnesium sulfate. Silica gel chromatography (4% EtOAc/hexane) gave the title compound as a clear oil. (2.04 g, 11.7 mmol, 64%) ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.59 (t, 2H, $J = 7.2$ Hz), 2.84 (t, 2H, $J = 7.2$ Hz), 5.08 (s, 1H), 5.31 (s, 1H), 7.27-7.39 (m, 5H), 9.76 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 27.6, 42.3, 113.0, 126.0, 127.7, 128.4, 140.3, 146.5, 201.6; MS, m/e: 160 [M^+], 117 [$\text{PhC}(\text{=CH}_2)\text{CH}_2^+$].

Methyl-(4-phenylpent-4-enyl)-amine

To a solution of 4-phenylpent-4-enal (1.30 g, 8.11 mmol) in MeOH (16 mL) was added methylamine (2.0 M in MeOH, 8.1 mL, 16.2 mmol) at room temperature. The resulting mixture was stirred for 2 h. The reaction mixture was then cooled to 0 °C. Sodium borohydride (154 mg, 4.06 mmol) was added to the reaction mixture and stirred at 0 °C for 30 min. The reaction was quenched by addition of water. The organic layer was extracted with dichloromethane and dried over potassium carbonate. Silica gel (Chromatorex NH-DU3050 aminopropyl-capped silica, purchased from FUJI SYLYSISA Co. Ltd., Japan) chromatography (50% EtOAc/hexane) gave the title compound as a pale yellow oil. (1.02 g, 5.82 mmol, 72%) ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.64-1.683 (m, 2H), 1.82 (br, 1H), 2.42 (s, 3H), 2.56 (t, 2H, $J = 7.6$ Hz), 2.61 (t, 2H, $J = 7.2$ Hz), 5.08 (s, 1H), 5.28 (s, 1H), 7.28-7.34 (m, 3H), 7.39-7.42 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.4, 33.0, 36.5, 51.8, 112.2, 126.0, 127.3, 128.2, 141.1, 148.2; MS, m/e: 175 [M^+], 160 [$\text{PhC}(\text{=CH}_2)\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}^+$], 103 [$\text{PhC}(\text{=CH}_2)^+$], 77 [Ph^+].

Synthesis of [3-(4-methoxyphenyl)-but-3-enyl]-methylamine

4-(4-Methoxyphenyl)-pent-4-enoic acid

The procedure for 4-phenylpent-4-enoic acid was followed with 4-(4-methoxyphenyl)-4-oxopropionic acid (5.00 g, 24.0 mmol). The title compound was obtained as a pale yellow solid (4.95 g, 24.0 mmol,

quant.). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.53 (t, 2H, $J = 7.7$ Hz), 2.82 (t, 2H, $J = 7.7$ Hz), 3.82 (s, 3H), 5.02 (s, 1H), 5.26 (s, 1H), 6.87 (d, 2H, $J = 8.6$ Hz), 7.35 (d, 2H, $J = 8.6$ Hz), 11.0 (br, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 30.2, 32.9, 55.3, 111.4, 113.8, 127.2, 132.8, 145.8, 159.2, 178.8; MS, m/e: 206 [M^+], 191 [$\text{M}^+ - \text{Me}$], 135 [$\text{MeOC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+ - \text{Me}$].

4-(4-Methoxyphenyl)-pent-4-en-1-ol

The procedure for 4-phenylpent-4-en-1-ol was followed with 4-(4-methoxyphenyl)-pent-4-enoic acid (4.95 g, 24.0 mmol). The title compound was obtained as a white solid (4.60 g, quant.). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.25 (br, 1H), 1.56-1.75 (m, 2H), 2.57 (t, 2H, $J = 7.6$ Hz), 3.65 (t, 2H, $J = 6.4$ Hz), 3.80 (s, 3H), 5.01 (d, 2H, $J = 1.2$ Hz), 5.22 (d, 2H, $J = 1.2$ Hz), 6.86 (dd, 2H, $J = 6.8, 2.1$ Hz), 7.35 (dd, 2H, $J = 6.8, 2.1$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, $\text{DMSO}-d_6$) δ 31.1, 31.3, 55.1, 60.3, 110.3, 113.7, 126.9, 132.6, 146.9, 158.7; MS, m/e: 192 [M^+], 177 [$\text{M}^+ - \text{Me}$], 161 [$\text{MeOC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2\text{CH}_2^+$].

4-(4-Methoxyphenyl)-pent-4-enal

The procedure for 4-phenylpent-4-en-1-enal was followed with 4-(4-methoxy-phenyl)-pent-4-en-1-ol (4.60 g, 24.0 mmol). The title compound was obtained as a white solid (2.94 g, 65%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.61 (t, 2H, $J = 7.6$ Hz), 2.82 (t, 2H, $J = 7.6$ Hz), 3.82 (s, 3H), 5.01 (s, 1H), 5.26 (s, 1H), 6.87 (d, 2H, $J = 8.7$ Hz), 7.34 (d, 2H, $J = 8.7$ Hz), 9.78 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, $\text{DMSO}-d_6$) δ 27.6, 42.4, 55.2, 111.5, 113.7, 127.1, 132.7, 145.8, 159.2, 201.9; MS, m/e: 190 [M^+], 161 [$\text{MeOC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2\text{CH}_2^+$], 147 [$\text{MeOC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+$], 133 [$\text{MeOC}_6\text{H}_4\text{C}(\text{=CH}_2)^+$].

[3-(4-Methoxyphenyl)-but-3-enyl]-methylamine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 4-(4-methoxyphenyl)-pent-4-enal (2.94 g, 15.5 mmol). The title compound was obtained as a pale yellow oil (2.29 g, 72%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.02 (br, 1H), 1.60-1.68 (m, 2H), 2.41 (s, 3H), 2.52 (t, 2H, $J = 8.3$ Hz), 2.59 (t, 2H, $J = 7.2$ Hz), 4.99 (d, 2H, $J = 1.3$ Hz), 5.21 (d, 2H, $J = 1.3$ Hz), 6.86 (d, 2H, $J = 8.8$ Hz), 7.35 (d, 2H, $J = 8.8$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.4, 33.1, 36.45, 51.7, 55.3, 110.8, 113.6, 127.1, 133.5, 147.4, 159.0; MS, m/e: 206 [M^+], 190 [$\text{M}^+ - \text{Me}$], 147 [$\text{MeOC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+$], 57 [$\text{CH}_2\text{CH}_2\text{NHMe}^+ - \text{H}$].

Synthesis of [3-(4-fluorophenyl)-but-3-enyl]-methylamine

4-(4-fluorophenyl)-pent-4-enoic acid

The procedure for 4-phenylpent-4-enoic acid was followed with 4-(4-fluorophenyl)-4-oxopropionic acid (5.00 g, 25.5 mmol). The title compound was obtained as a pale yellow solid (4.96 g, 25.5 mmol, quant.). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.51 (t, 2H, $J = 7.7$ Hz), 2.81 (t, 2H, $J = 7.7$ Hz), 5.09 (s, 1H), 5.26 (s, 1H), 7.02 (t, 2H, $J = 8.7$ Hz), 7.36 (dd, 2H, $J = 8.7, 5.4$ Hz), 10.7 (br, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 30.2, 32.9, 113.0, 115.3 (d, $J = 21.2$ Hz), 127.7 (d, $J = 7.9$ Hz), 136.5 (d, $J = 3.1$ Hz), 145.6, 162.4 (d, $J = 245.1$ Hz), 179.4; MS, m/e: 194 [M^+], 149 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2\text{CH}_2^+$].

4-(4-Fluorophenyl)-pent-4-en-1-ol

The procedure for 4-phenylpent-4-en-1-ol was followed with 4-(4-fluorophenyl)-pent-4-enoic acid (4.95 g, 25.5 mmol). The title compound was obtained as a clear oil (4.60 g, 25.5 mmol, quant.). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.68-1.75 (m, 2H), 1.95 (br, 1H), 2.58 (t, 2H, $J = 7.4$ Hz), 3.67 (t, 2H, $J = 6.4$ Hz), 5.00 (s, 1H), 5.22 (s, 1H), 6.85 (d, 2H, $J = 8.8$ Hz), 7.35 (d, 2H, $J = 8.8$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 31.0, 31.6, 62.2, 112.4, 115.1 (d, $J = 21.0$ Hz), 127.6 (d, $J = 7.7$ Hz), 137.0 (d, $J = 3.4$ Hz), 146.9, 162.2 (d, $J = 244.7$ Hz); MS, m/e: 180 [M^+], 135 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+$], 121 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)^+$].

4-(4-Fluorophenyl)-pent-4-enal

The procedure for 4-phenylpent-4-en-1-enal was followed with 4-(4-fluorophenyl)-pent-4-en-1-ol (4.60 g, 25.5 mmol). The title compound was obtained as a clear oil (3.00 g, 16.8 mmol, 66%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.60 (t, 2H, $J = 7.2$ Hz), 2.80 (t, 2H, $J = 7.6$ Hz), 5.07 (s, 1H), 5.27 (s, 1H), 7.02 (t, 2H, $J = 8.7$ Hz), 7.35 (t, 2H, $J = 8.7$ Hz), 9.78 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 27.6, 42.2, 113.0, 115.2 (d, $J = 21.3$ Hz), 127.6 (d, $J = 7.8$ Hz), 136.4 (d, $J = 3.4$ Hz), 145.5, 162.4 (d, $J = 245.4$ Hz); MS, m/e: 178 [M^+], 149 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2\text{CH}_2^+$], 135 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+$], 121 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)^+$].

[3-(4-Fluorophenyl)-but-3-enyl]-methylamine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 4-(4-fluorophenyl)-pent-4-enal (3.00 g, 16.8 mmol). The title compound was obtained as a pale yellow oil (3.11 g, 16.1 mmol, 96%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.11 (br, 1H), 1.59-1.66 (m, 2H), 2.41 (s, 3H), 2.52 (t, 2H, $J = 7.3$ Hz), 2.58 (t, 2H, $J = 7.3$ Hz), 5.06 (s, 1H), 5.22 (s, 1H), 7.00 (t, 2H, $J = 8.8$ Hz), 7.37 (t, 2H, $J = 8.8$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.3, 33.2, 36.5, 51.7, 112.3, 115.1 (d, $J = 21.1$ Hz), 127.7 (d, $J = 7.8$ Hz), 137.2 (d, $J = 3.4$ Hz), 147.2, 162.2 (d, $J = 241.2$ Hz); MS, m/e: 193 [M^+], 178 [$\text{M}^+ - \text{Me}$], 135 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+$], 121 [$\text{FC}_6\text{H}_4\text{C}(\text{=CH}_2)\text{CH}_2^+$], 57 [$\text{CH}_2\text{CH}_2\text{NHMe}^+ - \text{H}$].

Synthesis of [3-(3, 4-dimethoxyphenyl)-but-3-enyl]-methylamine

4-(3, 4-dimethoxyphenyl)-pent-4-enoic acid

The procedure for 4-phenylpent-4-enoic acid was followed with 4-(3, 4-dimethoxyphenyl)-4-oxopropionic acid (6.82 g, 28.6 mmol). The title compound was obtained as a pale yellow solid (5.91 g, 25.0 mmol, 87%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.54 (t, 2H, $J = 7.6$ Hz), 2.82 (t, 2H, $J = 7.6$ Hz), 3.88 (s, 3H), 3.90 (s, 3H), 5.04 (s, 1H), (s, 1H), 5.27 (s, 1H), 6.82-6.84 (m, 1H), 6.95-6.97 (m, 2H), 10.8 (br, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 30.2, 33.0, 55.9, 55.9, 109.4, 110.9, 111.7, 133.2, 146.1, 148.8, 148.8, 179.5; MS, m/e: 236 [M^+], 191 [$\text{M}^+ - \text{COOH}$].

4-(3, 4-Dimethoxyphenyl)-pent-4-en-1-ol

The procedure for 4-phenylpent-4-en-1-ol was followed with 4-(3, 4-dimethoxyphenyl)-pent-4-enoic acid (5.91g, 25.0 mmol). The title compound was obtained as a clear oil (3.51 g, 16.9 mmol, 68%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.70-1.74 (m, 2H), 2.05 (br, s, 1H), 2.57 (t, 2H, $J = 7.5$ Hz), 3.66 (t, 2H, $J = 6.4$ Hz), 3.89 (s, 3H), 3.90 (s, 3H), 5.04 (s, 1H), 5.24 (s, 1H), 6.83 (d, 1H, $J = 8.1$ Hz), 6.97-6.99 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 31.0, 31.6, 55.7, 55.7, 62.1, 109.3, 110.1, 111.0, 118.3, 133.7, 147.3, 148.4, 148.9; MS, m/e: 222 [M^+], 207 [$\text{M}^+ - \text{Me}$], 191 [$\text{M}^+ - \text{CH}_2\text{OH}$].

4-(3, 4-Dimethoxyphenyl)-pent-4-enal

The procedure for 4-phenylpent-4-en-1-enal was followed with 4-(3, 4-dimethoxyphenyl)-pent-4-en-1-ol (3.35 g, 15.1 mmol). The title compound was obtained as a clear oil (1.47g, 6.67 mmol, 44%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.61 (t, 2H, $J = 7.3$ Hz), 2.82 (t, 2H, $J = 7.3$ Hz), 3.88 (s, 3H), 3.89 (s, 3H), 5.02 (s, 1H), 5.26 (s, 1H), 6.83 (d, 1H, $J = 8.2$ Hz), 6.93-6.95 (m, 2H), 9.78 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR

(100 MHz, CDCl₃) δ 27.5, 42.3, 55.7, 55.7, 109.2, 110.7, 111.6, 118.2, 133.0, 146.0, 148.6, 148.6, 210.6; MS, m/e: 220 [M⁺], 161 [M⁺ - CHO, Me, Me].

[3-(3, 4-Dimethoxyphenyl)-but-3-enyl]-methylamine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 4-(3, 4-dimethoxyphenyl)-pent-4-enal (1.47 g, 6.67 mmol). The title compound was obtained as a pale yellow oil (1.20 g, 5.10 mmol, 77%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.24 (br, 1H), 1.62-1.69 (m, 2H), 2.42 (s, 3H), 2.60 (t, 2H, *J* = 7.2 Hz), 2.53 (t, 2H, *J* = 7.6 Hz), 3.88 (s, 3H), 3.89 (s, 3H), 5.01 (d, 1H, *J* = 1.1 Hz), 5.22 (d, 1H, *J* = 1.1 Hz), 6.82 (d, 1H, *J* = 8.0 Hz), 6.95-6.98 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 28.5, 33.1, 36.5, 51.7, 55.9, 55.9, 109.5, 110.8, 111.1, 118.4, 134.0, 147.8, 148.5, 148.6; MS, m/e: 235 [M⁺], 220 [M⁺ - Me], 57 [CH₂CH₂NHMe⁺ - H].

Synthesis of [3-(3, 4-Difluorophenyl)-but-3-enyl]-methylamine

4-(3, 4-Difluorophenyl)-pent-4-enoic acid

The procedure for 4-phenylpent-4-enoic acid was followed with 4-(3, 4-difluorophenyl)-4-oxopentanoic acid (3.74 g, 17.5 mmol). The title compound was obtained as a pale yellow solid (3.07 g, 14.5 mmol, 83%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 2.53 (t, 2H, *J* = 7.7 Hz), 2.79 (t, 2H, *J* = 7.7 Hz), 5.13 (s, 1H), 5.30 (s, 1H), 7.10-7.23 (m, 3H), 11.0 (br, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 29.9, 32.3, 113.9, 115.1 (d, *J* = 17.0 Hz), 117.1 (d, *J* = 17.0 Hz), 122.0 (dd, *J* = 6.0, 3.6 Hz), 137.5 (t, *J* = 4.7 Hz), 144.6, 149.9 (dd, *J* = 247.3, 12.7 Hz), 150.2 (dd, *J* = 246.3, 12.7 Hz); MS, m/e: 212 [M⁺], 167 [M⁺ - COOH].

4-(3, 4-Difluorophenyl)-pent-4-en-1-ol

The procedure for 4-phenylpent-4-en-1-ol was followed with 4-(3, 4-fluorophenyl)-pent-4-enoic acid (3.07 g, 14.5 mmol). The title compound was obtained as a clear oil (2.68 g, 13.5 mmol, 93%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.66-1.70 (m, 2H), 2.52 (t, 2H, *J* = 7.6 Hz), 3.62 (t, 2H, *J* = 6.4 Hz), 5.09 (s, 1H), 5.25 (s, 1H), 7.04-7.19 (m, 3H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 30.8, 31.2, 61.8, 113.2, 114.8 (d, *J* = 17.4 Hz), 116.8 (d, *J* = 17.4 Hz), 121.9 (dd, *J* = 6.0, 3.5 Hz), 138 (t, *J* = 4.8 Hz), 145.8, 149.5 (dd, *J* = 246.7, 12.7 Hz), 149.9 (dd, *J* = 245.7, 12.7 Hz); MS, m/e: 198 [M⁺], 139 [M⁺ - CH₂OH].

4-(3, 4-Difluorophenyl)-pent-4-enal

The procedure for 4-phenylpent-4-en-1-enal was followed with 4-(3,4-difluorophenyl)-pent-4-en-1-ol (2.68 g, 13.5 mmol). The title compound was obtained as a clear oil (1.24 g, 6.32 mmol, 47%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.62 (t, 2H, $J = 7.2$ Hz), 2.79 (t, 2H, $J = 7.2$ Hz), 5.11 (s, 1H), 5.30 (s, 1H), 7.10-7.22 (m, 3H), 9.79 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 27.4, 42.2, 114.0, 115.1 (d, $J = 17.4$ Hz), 117.2 (d, $J = 17.4$ Hz), 137.6 (t, $J = 4.9$ Hz), 144.7, 149.9 (dd, $J = 247.3$, 12.7 Hz), 150.2 (dd, $J = 246.3$, 12.7 Hz), 201.2; MS, m/e: 196 [M^+], 167 [$\text{M}^+ - \text{CHO}$].

[3-(3,4-Difluorophenyl)-but-3-enyl]-methylamine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 4-(3,4-difluorophenyl)-pent-4-enal (1.24 g, 6.32 mmol). The title compound was obtained as a pale yellow oil (780 mg, 3.69 mmol, 58%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.59-1.66 (m, 2H), 2.42 (s, 3H), 2.50 (t, 2H, $J = 7.6$ Hz), 2.59 (t, 2H, $J = 7.2$ Hz), 5.10 (s, 1H), 5.24 (s, 1H), 7.08-7.22 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.3, 32.9, 36.5, 51.6, 113.2, 115.1 (d, $J = 17.2$ Hz), 116.9 (d, $J = 17.2$ Hz), 122.1 (dd, $J = 60.0$, 3.2 Hz), 138.3 (t, $J = 4.4$ Hz), 146.3, 149.7 (dd, $J = 246.8$, 12.7 Hz), 151.1 (dd, $J = 245.9$, 12.7 Hz); MS, m/e: 211 [M^+], 196 [$\text{M}^+ - \text{Me}$], 57 [$\text{CH}_2\text{CH}_2\text{NHMe}^+ - \text{H}$].

Synthesis of methyl-(2-methyl-4-phenylpent-4-enyl)-amine

2-Methyl-4-phenylpent-4-enoic acid

The procedure for 4-phenylpent-4-enoic acid was followed with 2-methyl-4-oxo-4-phenylbutyric acid (5.0 g, 26.0 mmol). The title compound was obtained as a clear oil (4.95 g, 26.0 mmol, quant.). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.15 (d, 3H, $J = 6.8$ Hz), 2.48-2.61 (m, 2H), 3.00 (dd, 1H, $J = 13.8$, 5.7 Hz), 5.12 (d, 1H, $J = 0.8$ Hz), 5.33 (d, 1H, $J = 0.8$ Hz), 7.27-7.41 (m, 5H), 11.1 (br, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 16.3, 37.8, 39.1, 114.8, 126.3, 127.7, 128.4, 140.3, 145.6, 182.5; MS, m/e: 190 [M^+], 145 [$\text{M}^+ - \text{COOH}$].

2-Methyl-4-phenylpent-4-en-1-ol

The procedure for 4-phenylpent-4-en-1-ol was followed with 2-methyl-4-phenylpent-4-enoic acid (4.95 g, 26.0 mmol). The title compound was obtained as a clear oil (4.22 g, 23.7 mmol, 91%). ^1H NMR (400

MHz, CDCl₃, TMS) δ 0.88 (d, 3H, J = 6.7 Hz), 1.56 (br, 1H), 1.74 (m, 1H), 2.28 (dd, 1H, J = 14.1, 8.2 Hz), 2.71 (dd, 1H, J = 14.1, 6.3 Hz), 3.41-3.50 (m, 2H), 5.07 (d, 1H, J = 1.38 Hz), 5.30 (d, 1H, J = 1.38 Hz), 7.23-7.41 (m, 5H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 16.5, 34.0, 39.5, 67.9, 114.0, 126.3, 127.4, 128.3, 141.0, 147.1; MS, m/e: 176 [M⁺], 145 [M⁺ - CH₂OH], 103 [PhC(=CH₂)⁺], 77 [Ph⁺].

2-Methyl-4-phenylpent-4-enal

The procedure for 4-phenylpent-4-enal was followed with 2-methyl-4-phenylpent-4-en-1-ol (4.22 g, 23.7 mmol). The title compound was obtained as a clear oil (2.98 g, 17.1 mmol, 72%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 1.05 (d, 3H, J = 6.8 Hz), 2.38-2.48 (m, 2H), 3.02-3.06 (m, 1H), 5.10 (d, 1H, J = 0.9 Hz), 5.33 (d, 1H, J = 0.9 Hz), 7.29-7.39 (m, 5H), 9.63 (s, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 13.1, 36.4, 44.4, 114.8, 126.2, 127.7, 128.4, 140.2, 145.4, 204.3; MS, m/e: 174 [M⁺], 145 [M⁺ - CHO], 130 [PhC(=CH₂)CH⁺].

Methyl-(2-methyl-4-phenylpent-4-enyl)-amine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 2-methyl-4-phenylpent-4-enal (2.98 g, 17.1 mmol). The title compound was obtained as a clear oil (2.59 g, 13.7 mmol, 80%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.87 (d, 3H, J = 6.6 Hz), 1.09 (br, 1H), 1.66-1.76 (m, 1H), 2.24 (dd, 1H J = 13.9, 8.6 Hz), 2.36-2.41 (m, 4H), 2.50 (dd, 1H, J = 11.6, 5.9 Hz), 2.69 (dd, 1H, J = 13.9, 5.9 Hz), 5.05 (s, 1H), 5.28 (s, 1H), 7.25-7.33 (m, 3H), 7.39 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 17.9, 31.3, 36.7, 41.2, 58.5, 113.4, 126.2, 127.3, 128.2, 141.1, 147.3; MS, m/e: 189 [M⁺], 174 [M⁺ - Me], 57 [CH₂CH₂NHMe⁺ - H].

Synthesis of (2-Methoxymethyl-4-phenylpent-4-enyl)-methylamine

4-Phenylpent-4-enoic acid *tert*-butyl ester

To a THF (40 mL) solution of 4-phenylpent-4-enoic acid (4.77 g, 20.5 mmol), trifluoroacetic anhydride (6.40 mL, 45.1 mmol) was added dropwise at 0 °C. After stirring for 30 min at 0 °C, *tert*-butanol (20 mL) was added and was stirred at room temperature for 12 h. After the reaction, saturated sodium bicarbonate solution was added. Organic layer was extracted with diethyl ether and dried over sodium sulfate. Concentration of the organic layer and silicagel chromatography (5% EtOAc in hexane) gave the title compound as a pale yellow oil (4.32 g, 91%). ¹H NMR (400 MHz, CDCl₃, TMS)

δ 1.43 (s, 9H), 2.39 (t, 2H, $J = 7.8$ Hz), 2.79 (t, 2H, $J = 7.8$ Hz), 5.08 (d, 2H, $J = 1.3$ Hz), 5.29 (d, 2H, $J = 1.3$ Hz), 7.25-7.35 (m, 3H), 7.38-7.41 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.1, 30.6, 34.4, 80.3, 112.7, 126.1, 127.5, 128.3, 140.8, 147.2, 172.4; MS, m/e : 232 [M^+], 131 [$\text{PhC(=CH}_2\text{)CH}_2\text{CH}_2^+$].

2-Methoxymethyl-4-phenylpent-4-enoic acid *tert*-butyl ester

To a THF (20 mL) solution of 4-phenylpent-4-enoic acid *tert*-butyl ester (2.00 g, 8.61 mmol) was added lithium diisopropylamide (2.0 M solution in heptane/THF/ethylbenzene, 5.6 mL, 11.2 mmol) dropwise at -78°C . After stirring for 20 min, chloromethyl methyl ether (980 μL , 12.9 mmol) was added at the same temperature dropwise, and the resulting mixture was then allowed to warm to 0°C over 2 h. After this time, saturated aqueous ammonium chloride was added to the reaction mixture. The organic layer was extracted with diethyl ether and dried over sodium sulfate. Concentration of the organic layer and silica gel chromatography (5% EtOAc in hexane) gave the title compound as a pale yellow oil (2.00 g, 7.24 mmol, 84%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.43 (s, 9H), 2.63-2.72 (m, 2H), 2.76-2.82 (m, 1H), 3.29 (s, 3H), 3.43 (dd, $J = 9.3, 5.0$ Hz), 3.52 (dd, $J = 9.3, 6.9$ Hz), 5.12 (d, 1H, $J = 1.2$ Hz), 5.30 (d, 1H, $J = 1.2$ Hz), 7.26-7.34 (m, 3H), 7.39 (d, 2H, $J = 8.1$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.1, 34.5, 45.2, 58.9, 73.0, 80.5, 114.4, 126.3, 127.5, 128.3, 140.6, 145.7, 173.1; MS, m/e : 276 [M^+].

2-Methoxymethyl-4-phenylpent-4-en-1-ol

The procedure for 4-phenylpent-4-en-1-ol was followed with 2-methoxymethyl-4-phenylpent-4-enoic acid *tert*-butyl ester (2.00 g, 7.24 mmol). The title compound was obtained as a clear oil (1.49 g, 7.24 mmol, quant.). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.90-1.97 (m, 1H), 2.49-2.56 (m, 3H), 3.30 (s, 3H), 3.37-3.42 (m, 1H), 3.48-3.51 (m, 1H), 3.59-3.64 (m, 1H), 3.69-3.75 (m, 1H), 5.10 (d, 1H, $J = 1.7$ Hz), 5.33 (d, 1H, $J = 1.7$ Hz), 7.27-7.35 (m, 3H), 7.39-7.41 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 34.1, 38.6, 59.1, 65.7, 75.7, 114.3, 126.2, 127.6, 128.4, 140.6, 146.3; MS, m/e : 191 [$\text{M}^+ - \text{Me}$], 117 [$\text{PhC(=CH}_2\text{)CH}_2^+$], 103 [$\text{PhC(=CH}_2\text{)}^+$].

2-Methoxymethyl-4-phenylpent-4-enal

The procedure for 4-phenylpent-4-en-1-enal was followed with 2-methoxymethyl-4-phenylpent-4-en-1-ol (1.49 g, 7.24 mmol). The title compound was obtained as a

clear oil (940 mg, 4.63 mmol, 64%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 2.56-2.63 (m, 1H), 2.69 (ddd, 1H, $J=14.4$, 8.3, 0.8 Hz), 3.01 (ddd, 1H, $J=14.4$, 6.3, 1.0 Hz), 3.29 (s, 3H), 3.55 (dd, 1H, $J=10.1$, 4.3 Hz), 3.61 (dd, 1H, $J=10.1$, 5.8 Hz), 5.13 (d, 1H, $J=1.1$ Hz), 5.36 (d, 1H, $J=1.1$ Hz), 7.28-7.41 (m, 5H), 9.72 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 31.4, 50.3, 59.1, 70.3, 114.9, 126.2, 127.8, 128.5, 140.1, 145.2, 203.2; MS, m/e : 204 $[\text{M}^+]$, 117 $[\text{PhC}(\text{=CH}_2)\text{CH}_2^+]$, 103 $[\text{PhC}(\text{=CH}_2)^+]$.

(2-Methoxymethyl-4-phenylpent-4-enyl)-methylamine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 2-methoxymethyl-4-phenylpent-4-enal (940 mg, 4.60 mmol). The title compound was obtained as a pale yellow oil (614 mg, 2.81 mmol, 61%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.27 (br, 1H), 1.85-1.91 (m, 1H), 2.35 (s, 3H), 2.52-2.63 (m, 4H), 3.27 (s, 3H), 3.30-3.35 (m, 2H), 5.08 (d, 1H, $J=1.4$ Hz), 5.32 (d, 1H, $J=1.4$ Hz), 7.23-7.34 (m, 3H), 7.40-7.43 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 36.0, 36.8, 36.9, 54.2, 58.9, 74.5, 114.1, 126.3, 127.4, 128.3, 140.9, 146.8; MS, m/e : 219 $[\text{M}^+]$, 204 $[\text{M}^+ - \text{Me}]$, 189 $[\text{M}^+ - \text{NHMe}]$, 144 $[\text{PhC}(\text{=CH}_2)\text{CH}_2\text{CHCH}_2^+]$; Anal. Calcd. for $\text{C}_{14}\text{H}_{21}\text{NO}$: C, 76.56; H, 9.85; N, 6.32. Found: C, 76.35; H, 9.76; N, 6.23.

Synthesis of [2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-4-phenyl-pent-4-enyl]-methylamine

2-Hydroxymethyl-4-phenylpent-4-enoic acid *tert*-butyl ester

To a THF (28.0 mL) solution of 4-phenylpent-4-enoic acid *tert*-butyl ester (3.30 g, 14.2 mmol) was added lithium diisopropylamide (2.0 M in heptane/THF/ethylbenzene solution, 9.3 mL, 19 mmol) dropwise at -78°C . After stirring for 20 min, ethyl formate (2.3 mL, 28.4 mmol) was added dropwise at the same temperature, and the resulting solution was then stirred for 1 h. After the reaction, saturated aqueous ammonium chloride was added. The organic layer was extracted with diethyl ether and dried over magnesium sulfate. After evaporation of the solvent, the residue was dissolved in methanol (28.0 mL). Sodium borohydride (537 mg, 14.2 mmol) was added to this solution at 0°C . After stirring for 20 min at 0°C , water was added to the reaction mixture. The organic layer was extracted with ethyl acetate and dried over magnesium sulfate. Evaporation of the solvent and silica gel chromatography (15% EtOAc in hexane) gave the title compound as a clear oil (2.32 g, 8.80 mmol, 62%). ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.45 (s, 9H), 2.25 (br, 1H), 2.53-2.59 (m, 1H), 2.69 (dd, 1H, $J=14.4$, 7.8 Hz), 2.94 (dd, 1H, $J=14.4$, 6.8 Hz), 3.69 (t, 2H, $J=4.9$ Hz), 5.14 (d, 1H, $J=1.1$ Hz), 5.33 (d, 1H, $J=1.1$ Hz), 7.27-7.42 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 28.1, 34.4, 46.3, 62.6, 81.2, 114.8, 126.3, 127.7, 128.4, 140.2, 145.4, 174.2; MS, m/e : 189 $[\text{M}^+ - \text{O}^t\text{Bu}]$, 117 $[\text{PhC}(\text{=CH}_2)\text{CH}_2^+]$, 103 $[\text{PhC}(\text{=CH}_2)^+]$, 77

[Ph⁺], 57 [^tBu⁺].

2-(*tert*-Butyl-dimethyl-silyloxyethyl)-4-phenylpent-4-enoic acid *tert*-butyl ester

To a DMF (18 mL) solution of 2-hydroxymethyl-4-phenylpent-4-enoic acid *tert*-butyl ester (2.32 g, 8.84 mmol) were added imidazole (906 mg, 13.3 mmol) and *tert*-butyldimethylsilyl chloride (1.73 g, 11.5 mmol) at 0 °C. The reaction mixture was stirred overnight. After the reaction, ice water was added. The organic layer was extracted with diethyl ether and washed with water. After drying over magnesium sulfate, evaporation of solvent and silica gel chromatography (3% EtOAc in hexane) gave the title compound as a clear oil (3.03 g, 8.04 mmol, 91%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.02 (s, 6H), 0.87 (s, 9H), 1.41 (s, 9H), 2.52-2.59 (m, 1H), 2.73-2.75 (m, 2H), 3.65 (dd, 1H, *J* = 9.6, 5.3 Hz), 3.73 (dd, 1H, *J* = 9.6, 6.8 Hz), 5.11 (d, 1H, *J* = 1.2 Hz), 5.30 (d, 1H, *J* = 1.2 Hz), 7.26-7.34 (m, 3H), 7.34-7.41 (m, 2H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ -5.60, 18.2, 25.8, 28.1, 34.1, 47.5, 63.6, 80.3, 114.3, 126.3, 127.5, 128.3, 140.6, 145.8, 173.3; MS, *m/e*: 303 [M⁺ - O^tBu], 287 [M⁺ - CO₂^tBu], 245 [M⁺ - OTBS], 103 [PhC(=CH₂)⁺], 57 [^tBu⁺].

2-(*tert*-Butyl-dimethyl-silyloxyethyl)-4-phenylpent-4-enal

2-(*tert*-Butyl-dimethyl-silyloxyethyl)-4-phenylpent-4-enoic acid *tert*-butyl ester (3.03 g, 7.97 mmol) was dissolved in dichloromethane (20 mL). To this solution was added diisobutylaluminum hydride (1.0 M in toluene, 15.9 mL, 15.9 mmol) dropwise at -78 °C. After stirring for 1 h, saturated aqueous ammonium chloride was added. The organic layer was extracted with dichloromethane and dried over magnesium sulfate. Evaporation of the solvent and silica gel chromatography (8% EtOAc in hexane) gave the title compound as a clear oil (737 mg, 30%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.02 (s, 6H), 0.87 (s, 9H), 2.47-2.51 (m, 1H), 2.70 (dd, 1H, *J* = 14.6, 8.7 Hz), 2.99 (dd, 1H, *J* = 14.6, 6.1 Hz), 3.74-3.79 (m, 1H), 3.84-3.90 (m, 1H), 5.12 (d, 1H, *J* = 1.2 Hz), 5.34 (d, 1H, *J* = 1.2 Hz), 7.24-7.36 (m, 3H), 7.36-7.40 (m, 2H), 9.72 (s, 1H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ -5.67, 18.1, 25.7, 30.9, 51.9, 60.9, 114.7, 126.1, 127.7, 128.4, 140.0, 145.2, 203.9; MS, *m/e*: 247 [M⁺ - TBS], 173 [M⁺ - OTBS], 103 [PhC(=CH₂)⁺].

[2-(*tert*-Butyl-dimethyl-silyloxyethyl)-4-phenylpent-4-enyl]-methylamine

The procedure for methyl-(4-phenylpent-4-enyl)-amine was followed with 2-(*tert*-butyl-dimethyl-silyloxyethyl)-4-phenylpent-4-enal (737 mg, 2.42 mmol). The title compound was obtained as a clear oil (630 mg, 1.96 mmol, 81%). ¹H NMR (400 MHz, CDCl₃, TMS) δ 0.09 (s, 6H), 0.89 (s, 9H), 1.40 (br, 1H), 1.74-1.80 (m, 1H), 2.35 (s, 3H), 2.44-2.66 (m, 4H), 3.54 (d, 2H,

$J = 5.3$ Hz), 5.07 (d, 1H, $J = 1.2$ Hz), 5.30 (d, 1H, $J = 1.2$ Hz), 7.23-7.36 (m, 3H), 7.41-7.43 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ -5.51, 18.2, 25.9, 35.7, 36.8, 38.8, 54.1, 64.5, 113.9, 126.3, 127.4, 128.3, 140.9, 146.7; MS, m/e : 319 [M^+], 144 [$\text{PhC(=CH}_2\text{)CHCH}_2^+$], 131 [OTBS^+], 115 [TBS^+]; Anal. Calcd. for $\text{C}_{19}\text{H}_{33}\text{NOSi}$: C, 71.41; H, 10.41; N, 4.38. Found: C, 71.52; H, 10.54; N, 4.47.

General Procedure for the Intramolecular Hydroamination.

In a dry box, the aminoolefin reactant (1 mmol) was added by pipette to a suspension of $[\text{Rh}(\text{COD})(\text{DPPB})]\text{BF}_4$ (36.2 mg, 0.05 mmol) in THF (0.6 mL) in a screw-capped vial. The pipette was rinsed with THF (0.4 mL). The vial was sealed with a cap containing a PTFE septum and removed from the dry box. The reaction mixture was stirred at 70 °C for 48 h. After the reaction, the yield of enamine byproduct was determined by NMR spectra of the crude mixture containing 1, 1, 2, 2-tetrachloroethane as an internal standard. After determination of NMR yield of enamine, the crude reaction mixture was absorbed onto silicagel and purified by flash silicagel (Chromatorex NH-DU3050, aminopropylcapped silicagel, purchased from FUJI SYLYSISA Co. Ltd., Japan) chromatography.

1-Methyl-3-phenylpiperidine¹.

The general procedure was followed with methyl-(4-phenyl-pent-4-enyl)-amine. The reaction mixture was purified by flash silica gel chromatography (3% EtOAc in hexane) to give 133.3 mg (74%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.42 (dddd, 1H, $J = 12.4, 12.4, 12.4, 4.5$ Hz), 1.74-1.79 (m, 2H), 1.89-2.04 (m, 3H), 2.30 (s, 3H), 2.83 (dddd, 1H, $J = 15.4, 7.9, 3.6, 3.6$ Hz), 2.89-2.98 (m, 2H), 7.18-7.32 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 25.9, 30.9, 43.1, 46.6, 55.9, 63.3, 126.3, 127.2, 128.4, 144.6; MS, m/e : 175 [M^+].

3-(4-Methoxyphenyl)-1-methylpiperidine².

The general procedure was followed with methyl-[4-(4-methoxyphenyl)-pent-4-enyl]-amine. The reaction mixture was purified by flash silica gel chromatography (4% EtOAc in hexane) to give 161 mg (78%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.38 (dddd, 1H, $J = 12.4, 12.4, 12.4, 4.4$ Hz), 1.66-1.82 (m, 2H), 1.87-1.94 (m, 3H), 2.29 (s, 3H), 2.78 (dddd, 1H, $J = 15.7, 7.9, 3.5, 3.5$ Hz), 2.88-2.95 (m, 2H), 3.78 (s, 3H), 6.84 (d, 2H, $J = 8.7$ Hz), 7.15 (d, 2H, $J = 8.7$ Hz); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 25.8, 31.0, 42.0, 46.5, 55.1, 55.8, 63.4, 113.6, 127.9, 136.7, 157.9; MS, m/e : 205 [M^+].

3-(4-Fluorophenyl)-1-methylpiperidine.

The general procedure was followed with methyl-[4-(4-fluorophenyl)-pent-4-enyl]-amine. The reaction mixture was purified by flash silica gel chromatography (3% EtOAc in hexane) to give 150.0 mg (78%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.38 (dddd, 1H, $J = 12.4, 12.4, 12.4, 4.5$ Hz), 1.74-1.79 (m, 2H), 1.89-1.94 (m, 3H), 2.29 (s, 3H), 2.78 dddd, 1H, $J = 15.4, 7.9, 3.8, 3.8$ Hz), 2.88-2.94 (m, 2H), 6.94-7.00 (m, 2H), 7.15-7.20 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 25.8, 31.1, 42.3, 46.6, 55.8, 63.4, 115.7 (d, $J = 20.7$ Hz), 128.5 (d, $J = 7.7$ Hz), 140.3 (d, $J = 3.2$ Hz), 161.4 (d, $J = 242.5$ Hz); MS, m/e : 193 [M^+]; Anal. Calcd. for $\text{C}_{12}\text{H}_{16}\text{FN}$: C, 74.58; H, 8.34; N, 7.25. Found: C,

74.47; H, 8.55; N, 7.04.

3-(3, 4-Dimethoxyphenyl)-1-methylpiperidine.

The general procedure was followed with methyl-[4-(3, 4-dimethoxyphenyl)-pent-4-enyl]-amine. The reaction mixture was purified by flash silica gel chromatography (6% EtOAc in hexane) to give 193.8 mg (82%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.39 (dddd, 1H, $J = 12.4, 12.4, 12.4, 4.4$ Hz), 1.66-1.83 (m, 2H), 1.89-1.95 (m, 3H), 2.30 (s, 3H), 2.77 (dddd, 1H, $J = 15.4, 7.8, 3.6, 3.6$ Hz), 2.89-2.97 (m, 2H), 3.86 (s, 3H), 3.88 (s, 3H), 6.75-6.82 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 25.5, 30.8, 42.3, 46.2, 55.4, 55.5, 55.5, 63.2, 110.3, 110.8, 118.5, 137.0, 147.1, 148.4; MS, m/e : 253 $[\text{M}^+]$.

3-(3, 4-Difluorophenyl)-1-methylpiperidine.

The general procedure was followed with methyl-[4-(3, 4-difluorophenyl)-pent-4-enyl]-amine. The reaction mixture was purified by flash silicagel chromatography (3% EtOAc in hexane) to give 150.0 mg (71%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.35 (dddd, 1H, $J = 12.4, 12.4, 12.4, 4.3$ Hz), 1.65-1.83 (m, 2H), 1.87-1.96 (m, 3H), 2.30 (s, 3H), 2.79 (dddd, 1H, $J = 15.1, 7.6, 3.5, 3.5$ Hz), 2.87-2.93 (m, 2H), 6.92-6.95 (m, 1H), 7.00-7.08 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 25.6, 31.0, 42.2, 46.5, 55.7, 63.0, 115.9 (d, $J = 16.8$ Hz), 117.0 (d, $J = 16.8$ Hz), 123.5 (dd, $J = 5.9, 3.4$ Hz), 141.6 (t, $J = 4.4$ Hz), 148.9 (dd, $J = 244.5, 12.6$ Hz), 150.2 (dd, $J = 245.8, 12.6$ Hz); MS, m/e : 211 $[\text{M}^+]$.

cis-1,3-Dimethyl-5-phenylpiperidine.

The general procedure was followed with methyl-(2-methyl-4-phenylpent-4-enyl)-amine. The reaction mixture was purified by flash silica gel chromatography (3% EtOAc in hexane) to give 148.2 mg (78%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 0.94 (d, 3H, $J = 6.5$ Hz), 1.10 (ddd, $J = 12.1, 12.1, 12.1$ Hz, 1H), 1.56 (dd, 1H, $J = 10.8, 10.8$ Hz), 1.81-1.93 (m, 3H), 2.30 (s, 3H), 2.83-2.91 (m, 2H), 2.94-2.98 (m, 1H), 7.18-7.31 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 19.6, 31.4, 39.8, 43.0, 46.3, 62.8, 63.6, 126.4, 127.2, 128.4, 144.4; MS, m/e : 189 $[\text{M}^+]$; Anal. Calcd. for $\text{C}_{13}\text{H}_{19}\text{N}$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.11; H, 10.44; N, 7.23.

cis-3-Methoxymethyl-1-methyl-5-phenylpiperidine.

The general procedure was followed with (2-methoxymethyl-4-phenylpent-4-enyl)-methylamine. The reaction mixture was purified by flash silica gel chromatography (3% EtOAc in hexane) to give 190.9 mg (87%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.20 (ddd, 1H, $J = 12.4, 12.4, 12.4$ Hz), 1.71 (dd, 1H, $J = 11.1, 11.1$ Hz), 1.91-1.97 (m, 2H), 2.08-2.19 (m, 1H), 2.33 (s, 3H), 2.92 (dddd, 1H, $J = 15.7, 8.0, 3.6, 3.6$ Hz), 2.98-3.06 (m, 2H), 3.28-3.32 (m, 2H), 3.34 (s, 3H), 7.19-7.32 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 34.1, 36.8, 42.3, 46.2, 58.6, 58.9, 62.9, 76.0, 126.2, 126.9, 128.2, 143.9; MS, m/e : 219 $[\text{M}^+]$, 204 $[\text{M}^+ - \text{Me}]$, 174 $[\text{M}^+ - \text{CH}_2\text{OMe}]$; Anal. Calcd. for $\text{C}_{14}\text{H}_{21}\text{NO}$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.35; H, 9.76; N, 6.23.

cis-3-(tert-Butyl-dimethyl-silanyloxymethyl)-1-methyl-5-phenylpiperidine.

The general procedure was followed with [2-(tert-Butyl-dimethyl-silanyloxymethyl)-4-phenylpent-4-enyl]-methylamine on 0.5 mmol scale. The reaction mixture was purified by flash silica gel

chromatography (3% EtOAc in hexane) to give 118.7 mg (74%) of the product as a clear oil. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 0.05 (s, 6H), 0.90 (s, 9H), 1.16 (ddd, 1H, $J = 12.3, 12.3, 12.3$ Hz), 1.66 (dd, 1H, $J = 11.0, 11.0$ Hz), 1.87-2.04 (m, 3H), 2.32 (s, 3H), 2.89 (dddd, 1H, $J = 15.6, 8.1, 3.8, 3.8$ Hz), 2.96-3.05 (m, 2H), 3.48 (dd, 1H, $J = 10.1, 6.8$ Hz), 3.55 (dd, 1H, $J = 10.1, 5.4$ Hz), 7.18-7.32 (m, 5H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ -5.4, 18.3, 25.9, 33.9, 42.5, 46.4, 59.1, 63.3, 66.4, 126.4, 127.2, 128.4, 144.3; MS, m/e : 319 $[\text{M}^+]$, 262 $[\text{M}^+ - \text{tBu}]$, 174 $[\text{M}^+ - \text{CH}_2\text{OTBS}]$; Anal. Calcd. for $\text{C}_{19}\text{H}_{33}\text{NOSi}$: C, 71.41; H, 10.41; N, 4.38. Found: C, 71.64; H, 10.64; N, 4.39.

Synthesis of phenyl-(3-phenyl-piperidin-1-yl)-methanone³.

To a 1, 2-dichloroethane (1.0 mL) solution of 1-methyl-3-phenylpiperidine (55.0 mg, 0.314 mmol), sodium carbonate (50.0 mg, 0.471 mmol) and 1-chloroethyl chloroformate (50.8 μL , 0.471 mmol) were added at room temperature. The reaction mixture was heated at 70 $^\circ\text{C}$. After 1 h, methanol (1.0 mL) was added, and the resulting mixture was heated at 70 $^\circ\text{C}$ for 1 h. After this time, the precipitate was removed by filtration. The filtrate was evaporated and dissolved in DMF (1.5 mL). To this solution was added benzoic acid (57.5 mg, 0.471 mmol), EDC HCl (90.3 mg, 0.471 mmol), and triethylamine (65.6 μL , 0.471 mmol), and the resulting solution was stirred at room temperature for 12 h. After this time, 1 N aqueous NaOH was added. The organic layer was extracted with diethyl ether and washed with 1 N aqueous NaOH and water. After drying over magnesium sulfate and evaporation of solvent, the crude product was purified by flash silicagel chromatography (11% EtOAc in hexane) to give 74.5 mg (90%) of the product as a white solid. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 1.59-1.64 (m, 4H), 2.82 (br, 2H), 3.02 (br, 1H), 3.81 (br, 1H), 4.84 (br, 1H), 7.10-7.41 (m, 10H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, $\text{DMSO}-d_6$, 90 $^\circ\text{C}$) δ 24.8, 30.9, 41.8, 44.2, 50.3, 126.0, 126.1, 126.3, 127.8, 127.9, 128.7, 136.2, 142.8, 168.7; MS, m/e : 265 $[\text{M}^+]$, 160 $[\text{M}^+ - \text{PhCO}^+]$, 105 $[\text{PhCO}^+]$, 77 $[\text{Ph}^+]$.

Attempts at analogous intramolecular hydroaminations catalyzed by *n*-butyl lithium⁴

In dry box, the aminoolefin (175 mg, 1.00 mmol) was dissolved in THF (2 mL) in a screw-capped vial. To this solution, *n*-butyl lithium (1.6 M in hexane, 63 μL , 0.10 mmol) was added and was stirred for 10 min at room temperature. The vial was sealed with a cap containing a PTFE septum and removed from the dry box. The reaction mixture was heated at 120 $^\circ\text{C}$ for 24 h. After this time, the reaction mixture was allowed to cool to room temperature and was quenched with methanol (0.5 mL). The solvent was removed under vacuum. No piperidine product was observed by ^1H -NMR spectroscopy. After flash

silicagel (Chromatorex NH-DU3050, aminopropylcapped silicagel, purchased from FUJI SYLYSISA Co. Ltd., Japan) chromatography, the starting material was recovered (164.0 mg, 0.936 mmol, 94% recovery).

The reaction of aminoolefins containing substituents in the 2-position of the chain was also conducted with *n*-butyllithium as a catalyst at the temperature and time of the rhodium-catalyzed reactions. The aminoolefin reactant (189 mg, 1.00 mmol) was dissolved in THF (1 mL) in a screw-caped vial. To this solution, *n*-butyl lithium (1.6 M in hexane, 63 μ L, 0.10 mmol) was added and was stirred for 10 min at room temperature. The vial was sealed with a cap containing a PTFE septum and removed from the dry box. The reaction mixture was heated at 70 $^\circ$ C for 48 h. After this time, the reaction mixture was allowed to cool to room temperature and was quenched with methanol (0.5 mL). The solvent was removed under vacuum. No reaction was observed by ^1H -NMR spectroscopy.

References

- (1) Sumiya, F.; Shirai, N.; Sato, Y. *Chem. Pharm. Bull.* **1991**, *39*, 36-40.
- (2) Julia, M.; Siffert, O.; Bagot, J. *Bull. Soc. Chim. Fr.* **1968**, 1000-1007.
- (3) Hasebe, M.; Tsuchiya, T. *Tetrahedron Lett.* **1986**, *27*, 3239-3242.
- (4) Kumar, K.; Michalik, D.; Castro, I. G.; Tillack, A.; Zapf, A.; Arlt, M.; Heinrich, T.; Bottcher, H.; Beller, M. *Chem.Eur. J.* **2004**, *10*, 746-757.

NAME	Nov08-2005-Tak
EXPNO	30
PROCNO	1

Date_ 20051108

INSTRUM spect

PULPROG z930

SOLVENT	CDC13
CH ₂ Cl ₂	0.9
CH ₃ OH	0.8
CH ₃ COOH	0.7
H ₂ O	0.6
EtOH	0.5
MeCN	0.4
DMSO	0.3
NMP	0.2
THF	0.1
BzPh	0.0

DS 0570 4 16 2

FIGURES

0.126314
3 9581243

DE	0.00
TE	0.00E

0
0
0
0
0
0
0
0
0
0

NUC1 1H

PL1 -6.00

SI 32768

WDW

LB 0.30

PC 1.00

10	parameters	00
CY		20 00

FIP	11,000
E1	4400 40

1.000
-400.04

HZCM	240.02161
------	-----------

Current Data Parameters
NAME Oct11-2005-Tsk
EXPNO 40
PROCNO 1

F2 - Acquisition Parameters
Date_ 20051011
Time 14.33
INSTRUM spect
PROBHD 5mm_GNP_H-F-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 201
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 6.55 usec
PL1 -3.00 dB
SF01 100.6001570 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 18.00 dB
PL13 18.00 dB
SF02 400.0376001 MHz

F2 - Processing parameters
SI 32768
SF 100.5891395 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

10 NMR plot parameters
CX 20.00 cm
FIP 220.000 ppm
F1 22129.61 Hz
F2P -10.000 ppm
F2 -1005.89 Hz
PPMCM 11.50000 ppm/cm
HZCM 1156.77515 Hz/cm

SM, 4-F

0.0000

2.6073
2.5895
2.5714
2.5400
2.5214
2.5030
2.4110
1.6452
1.6261
1.6079

5.2189
5.0580
5.0549

7.3832
7.3697
7.3612
7.3478
7.0237
7.0021
6.9803

Current Data Parameters
NAME Nov08-2005-Tak
EXPNO 40
PROCNO 1

F2 - Acquisition Parameters
Date_ 20051108
Time 18.36
INSTRUM spect
PROBHD 5mm_QNP_H-F-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.958243 sec
RG 80.6
DM 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 6.40 usec
PL1 -6.00 dB
SFO1 400.0384704 MHz

F2 - Processing parameters
SI 32768
SF 400.0360111 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
F1P 11.000 ppm
F1 4400.40 Hz
F2P -1.000 ppm
F2 -400.04 Hz
PPMCM 0.60000 ppm/cm
HZCM 240.02161 Hz/cm

Integral

1.8957
1.8658
1.0000
1.0057
2.0200
2.0946
3.0571
2.0801
0.9781

Current Data Parameters
NAME Oct26-2005-Tak
EXPNO 20
PROCNO 1

F2 - Acquisition Parameters
Date_ 20051026
Time 13.49
INSTRUM spect
PROBHD 5mm_QNP_H-F-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 170
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 2048
DW 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 6.55 usec
PL1 -3.00 dB
SF01 100.6001570 MHz

===== CHANNEL f2 =====
CPOPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 18.00 dB
PL13 18.00 dB
SF02 400.0375001 MHz

F2 - Processing parameters
SI 32768
SF 100.5691326 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ID NMR plot parameters
CX 20.00 cm
F1P 220.000 ppm
F1 22129.61 Hz
F2P -10.000 ppm
F2 -1005.89 Hz
PPMCM 11.50000 ppm/cm
HZCM 1156.77502 Hz/cm

SM, 3, 4-OMe

Current Data Parameters

NAME Nov09-2005-Tak
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters

Date_ 20051109
Time 18.06
INSTRUM spect
PROBHD 5mm_QNP_HF-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9584243 sec
RG 114
DW 60.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== CHANNEL f1 =====

NUC1 1H
P1 6.40 usec
PL1 -6.00 dB
SF01 400.0384704 MHz

F2 - Processing parameters

SI 32768
SF 400.0360103 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

CX 20.00 cm
F1P 11.000 ppm
F1 4400.40 Hz
F2P -1.000 ppm
F2 -400.04 Hz
PPMCM 0.60000 ppm/cm
HZCM 240.02161 Hz/cm

Current Data Parameters
NAME Oct28-2005-Tak
EXPNO 50
PROCNO 1

F2 - Acquisition Parameters
Date_ 20051028
Time 19.03
INSTRUM spect
PROBHD 5mm_QNP_H-F-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 931
DS 4
SWH 25125.629 Hz
FIDRES 0.383367 Hz
AQ 1.3042164 sec
RG 16384
DM 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.0002000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 6.55 usec
PL1 -3.00 dB
SF01 100.6001570 MHz

===== CHANNEL f2 =====
CPOPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -6.00 dB
PL12 18.00 dB
PL13 18.00 dB
SF02 400.0376001 MHz

F2 - Processing parameters
SI 32768
SF 100.5891369 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 220.000 ppm
F1 22129.61 Hz
F2P -10.000 ppm
F2 -1005.89 Hz
PPMCM 11.50000 ppm/cm
HZCM 1156.77502 Hz/cm

3, 4-F