Supporting Information

On the Stereoselective Bicyclization of Aminodienes Catalyzed by Chelating Diamide Complexes of the Group 3 Metals. A Direct Comparison of Sc(III) and Y(III) Bis(amide)s with an Application to the Synthesis of Alkaloid 195F.

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Contents

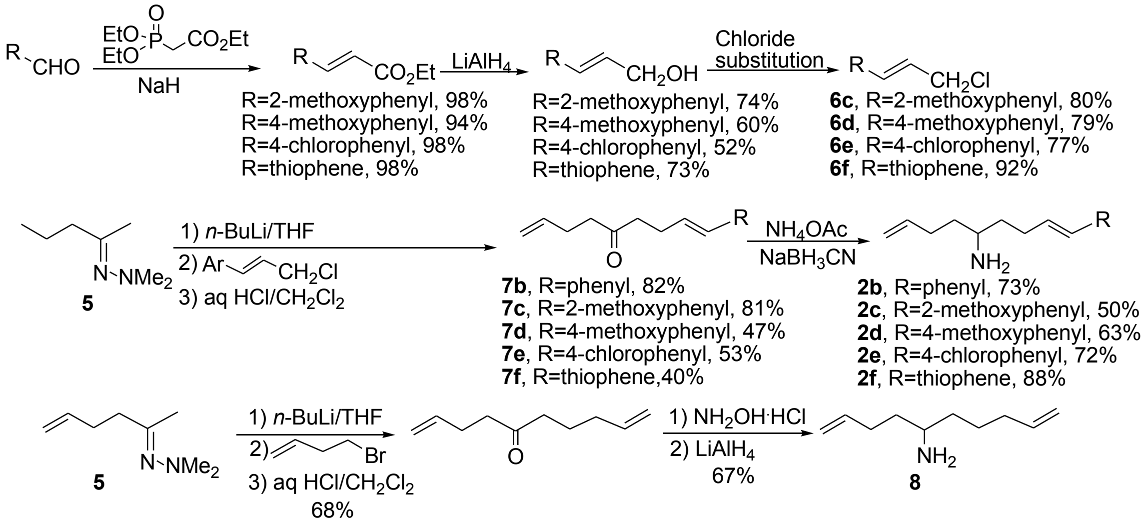
General

Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. THF and diethyl ether were distilled from sodium/benzophenone under nitrogen. CH_2Cl_2 was distilled from CaH_2 under nitrogen. All other materials were used as received from commercial sources and all reactions were carried out under nitrogen unless otherwise noted. Thin-layer chromatography (TLC) employed 0.25 mm glass silica gel plates with UV indicator. Flash chromatographic columns were packed with Merck silica gel 60 or basic alumina as slurry in the initial elution solvent. Nuclear magnetic resonance (NMR) data were obtained from Bruker DPX-300 (300 MHz) and Bruker DPX-500 (500 MHz). Infrared spectra (IR) were obtained from JASCO FTIR-4100. High-resolution mass spectra (HRMS) were obtained from Bruker MicroTOF with an Agilent 1100 HPLC.

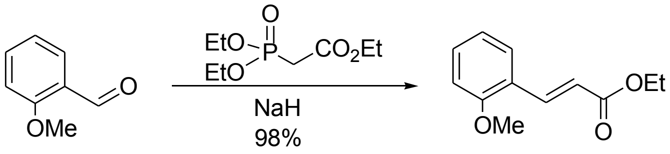
Materials: Aminodiene substrates were synthesized as previously described for 5-amino-1,8-nonadiene, **2a**.[1] Catalysts $Y[N(TMS)_2]_3$ and $Sc[N(TMS)_2]_3$ were obtained by method of Bradley; et. al.[2] All other materials were obtained from commercial sources and used as received.

Experimental procedures and characterization data for new compounds

1. Aminodiene syntheses and characterization data.

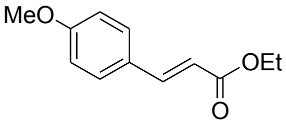


1.1 General Hornor-Wadsworth-Emmons procedure: Ethyl (*E*)-3-(2-methoxyphenyl) acrylate



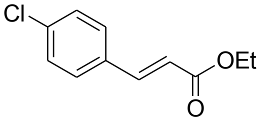
A 250-mL, round-bottomed flask equipped with a magnetic stirring bar and a N_2 inlet was charged with NaH (60% in oil, 2.03 g, 50.7 mmol) and anhydrous THF (20 mL) was subsequently added via syringe. The resulting mixture was stirred for 10 min. The solvent was removed by syringe after the solid NaH precipitated. This whole process was repeated three times to fully remove the mineral oil. Then anhydrous THF (100 mL) was added. After cooling to 0 ºC, triethyl phosphonoacetate (10.3 mL, 50.7 mmol) was slowly added dropwise. The reactant mixture was stirred at 0 ºC for 30 min. Next 2-methoxybenzaldehyde (5.0 mL, 40.6 mmol) was slowly added dropwise and the reactant mixture was stirred for 30 min. The reactant mixture was diluted with diethyl ether (200 mL), washed with saturated $NaHCO_3$ (50 mL), brine (50 mL), and the ether layer was subsequently dried with Na_2SO_4. Concentration in vacuo followed by bulb-to-bulb distillation afforded ethyl (*E*)-3-(2-methoxyphenyl) acrylate (8.4 g, 40.6 mmol, 98%) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 7.49 (d, *J*=7.5 Hz, 1H, Ar-**H**), 7.33 (t, *J*=7.0 Hz, 1H, Ar-**H**), 6.94 (t, *J*=7.5 Hz, 1H, Ar-**H**), 6.90 (d, *J*=8.5 Hz, 1H, Ar-**H**), 6.51 (d, *J*=16.0 Hz, 1H, Ar-C=C**H**), 4.24 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 3.87 (s, 3H, OC**H₃**), 1.32 (dd, apparent triplet, *J*=7.5 Hz, 3H, CH_2C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 167.5, 158.3, 140.0, 131.4, 128.9, 120.7, 118.8, 111.1, 60.3, 55.4, 14.4; IR (film) 2983, 1709, 1631, 1491, 1317, 1247, 1173, 1033, 751 cm^{-1}.

Ethyl (*E*)-3-(4-methoxyphenyl) acrylate



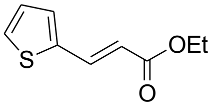
The title compound ethyl (*E*)-3-(4-methoxyphenyl) acrylate (7.76 g, 37.7 mmol, 94%) was obtained from 4-methoxybenzaldehyde (5 mL, 40.3 mmol) by the general Hornor-Wadsworth-Emmons procedure as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 7.46 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.88 (d, *J*=9.0 Hz, 2H, 2Ar-**H**), 6.29 (d, *J*=16.0 Hz, 1H, Ar-C=C**H**), 4.23 (ddd, apparent quartet, *J*=7.5 Hz, 2H, C**H₂**), 3.82 (s, 3H, OC**H₃**), 1.31 (dd, apparent triplet, *J*=7.0 Hz, 3H, CH_2C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 161.3, 144.2, 129.7, 127.2, 115.7, 114.3, 60.3, 55.4, 14.3; IR (film):2979, 1705, 1605, 1517, 1251, 1169, 1029, 825 cm^{-1}.

Ethyl (*E*)-3-(4-chlorophenyl) acrylate



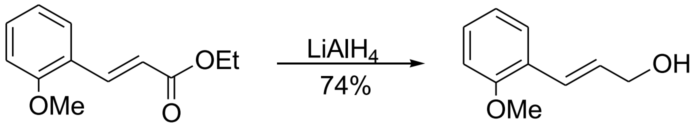
The title compound ethyl (*E*)-3-(4-chlorophenyl) acrylate (4.04 g, 19.0 mmol, 98%) was obtained from 4-chlorobenzaldehyde (2.68 g, 19.0 mmol) by the general Hornor-Wadsworth-Emmons procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 7.43 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 7.33 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.38 (d, *J*=16.0 Hz, 1H, Ar-C=C**H**), 4.24 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 1.31 (dd, apparent triplet, *J*=7.0 Hz, 3H, CH_2C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 166.7, 143.1, 136.1, 132.9, 129.2, 129.1, 118.8, 60.6, 14.3; IR (film):2979, 1719, 1638, 1491, 1309, 1269, 1173, 1088, 1033, 981, 822, 744 cm^{-1}.

Ethyl (*E*)-3-(2-thienyl) acrylate



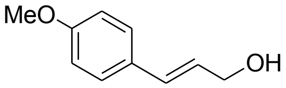
The title compound ethyl (*E*)-3-(2-thienyl) acrylate (19.1 g, 105 mmol, 98%) was obtained from thiophene-2-carboxaldehyde (10 mL, 105 mmol) by the general Hornor-Wadsworth-Emmons procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 7.35 (d, *J*=4.5 Hz, 1H, Ar-**H**), 7.24 (m, 1H, Ar-**H**), 7.04 (m, 1H, Ar-**H**), 6.22 (d, *J*=15.5 Hz, 1H, Ar-C=C**H**), 4.23 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 1.31 (dd, apparent triplet, *J*=7.0 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 166.9, 139.6, 137.0, 130.8, 128.3, 128.0, 117.0, 60.5, 14.3; IR (film) 2978, 1712, 1628, 1306, 1261, 1202, 1162, 1043, 703 cm^{-1}.

1.2 General $LiAlH_4$ reduction procedure: (*E*)-3-(2-Methoxyphenyl)-prop-2-en-1-ol



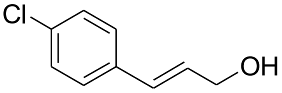
A 100-mL, round-bottomed flask equipped with a magnetic stirring bar and a N_2 inlet was charged with $LiAlH_4$ (0.44 g, 11.7 mmol) and anhydrous diethyl ether (60 mL) was subsequently added. The resulting mixture was cooled to 0 ºC with an ice-water bath. (*E*)-3-(2-Methoxyphenyl) acrylate (3.0 g, 14.6 mmol) in anhydrous ether (10 mL) was slowly added at 0 ºC. The reactant mixture was stirred at 0 ºC for 30 min when judged complete by TLC. Water was slowly added until no more hydrogen was evolved. The reactant mixture was diluted with diethyl ether (30 mL) and subsequently was dried with Na_2SO_4. The white solid was removed by vacuum filtration. Concentration in vacuo followed by flash chromatography on silica gel (2:1 hexane/EtOAc for elution) afforded (*E*)-3-(2-methoxyphenyl)-prop-2-en-1-ol (1.76 g, 10.7 mmol, 74%) as a white solid. ^1H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J*=7.0 Hz, 1H, Ar-**H**), 7.22 (t, *J*=8.0 Hz, 1H, Ar-**H**), 6.91 (d, *J*=15.0 Hz, 1H, Ar-C**H**=C), 6.91 (t, *J*=7.0 Hz, 1H, Ar-**H**), 6.86 (d, *J*=8.0 Hz, 1H, Ar-**H**), 6.37 (ddd, apparent dt, *J*=16.0, 5.5 Hz, 1H, Ar-C=C**H**), 4.31 (dd, apparent triplet, *J*=6.0 Hz, 2H, C$\mathbf{H_2}$), 3.84 (s, 3H, OC$\mathbf{H_3}$), 1.41 (dd, apparent triplet, *J*=6.0 Hz, 1H, O**H**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 129.2, 128.8, 127.0, 126.2, 120.7, 110.8, 64.3, 55.4; IR (film) 3338, 2935, 1594, 1487, 1243, 1029, 977, 751 cm^{-1}.

(*E*)-3-(4-Methoxyphenyl)-prop-2-en-1-ol



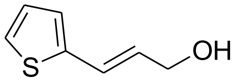
The title compound (*E*)-3-(4-methoxyphenyl)-prop-2-en-1-ol (2.14 g, 13.0 mmol, 60%) was obtained from ethyl (*E*)-3-(4-methoxyphenyl) acrylate (4.45 g, 21.6 mmol) by the general $LiAlH_4$ reduction procedure as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.84 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.54 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.22 (ddd, apparent dt, *J*=15.5, 6.0 Hz, 1H, Ar-C=C**H**), 4.28 (d, *J*=6.0 Hz, 2H, C**H₂**), 3.79 (s, 3H, OC**H₃**), 1.44 (s, 1H, O**H**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 159.3, 131.0, 129.4, 127.7, 126.2, 114.0, 63.9, 55.3; IR (film): 3268, 2844, 1513, 1247, 1025, 969, 836 cm^{-1}.

(*E*)-3-(4-Chlorophenyl)-prop-2-en-1-ol



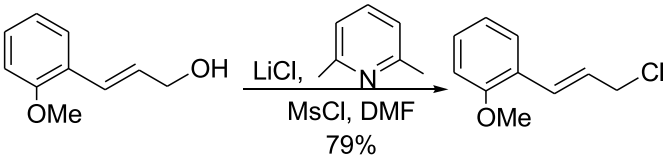
The title compound (*E*)-3-(4-chlorophenyl)-prop-2-en-1-ol (0.83 g, 4.93 mmol, 52%) was obtained from ethyl (*E*)-3-(4-chlorophenyl) acrylate (2.0 g, 9.5 mmol) by the general $LiAlH_4$ reduction procedure as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.22 (m, 4H, 4Ar-**H**), 6.55 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.32 (ddd, apparent dt, *J*=16.0, 5.5 Hz, 1H, Ar-C=C**H**), 4.31 (m, 2H, C**H₂**), 1.48 (s, 1H, O**H**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 129.8, 129.1, 128.8, 127.6, 63.6; IR (film): 3324, 1491, 1406, 1092, 1011, 966, 848 cm^{-1}.

(*E*)-3-(2-Thienyl)-prop-2-en-1-ol



The title compound (*E*)-3-(2-thienyl)-prop-2-en-1-ol (2.70 g, 19.3 mmol, 73%) was obtained from ethyl (*E*)-3-(2-thienyl) acrylate (4.80 g, 26.4 mmol) by the general $LiAlH_4$ reduction procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (t, *J*=3.0 Hz, 1H, Ar-**H**), 6.94 (d, *J*=3.0 Hz, 2H, 2Ar-**H**), 6.73 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.19 (ddd, apparent dt, *J*=15.5, 6.0 Hz, 1H, Ar-C=C**H**), 4.27 (dd, apparent triplet, *J*=5.5 Hz, 2H, C**H₂**), 1.51 (dd, apparent triplet, *J*=5.5 Hz, 1H, O**H**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 128.1, 127.4, 125.9, 124.4, 124.3, 63.4; IR (film) 3316, 2858, 1088, 1007, 955, 700 cm^{-1}.

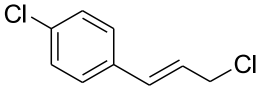
1.3 General allylic chloride preparation procedure:[3] (*E*)-1-(3-Chloroprop-1-enyl)-2-methoxybenzene (**6c**)



A 15-mL, round-bottomed flask equipped with a magnetic stirring bar and a N_2 inlet was charged with LiCl (71 mg, 1.67 mmol) and anhydrous DMF (2.5 mL) was subsequently added. The resulting mixture was stirred at 0 ºC for 10 min until the LiCl had dissolved. (*E*)-3-(2-Methoxyphenyl)-prop-2-en-1-ol (0.25 g, 1.51 mmol) and anhydrous 2,6-lutidine (0.2 mL, 1.66 mmol) were added in succession. Then MsCl (0.13 mL, 1.66 mmol) was slowly added dropwise. The reactant mixture was stirred for 2 h until judged complete by TLC. The reactant mixture was diluted with diethyl ether (10 mL), washed with water (3 mL), brine (3 mL), and the ether layer was subsequently dried with Na_2SO_4.

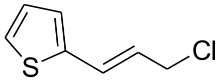
Concentration in vacuo followed by flash chromatography on silica gel (100:10:1 hexane/EtOAc/Et_3N) afforded (*E*)-1-(3-chloroprop-1-enyl)-2-methoxybenzene (**6c**) (0.22 g, 1.19 mmol, 79%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J*=7.5 Hz, 1H, Ar-**H**), 7.24 (t, *J*=7.0 Hz, 1H, Ar-**H**), 6.97 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.92 (t, *J*=7.5 Hz, 1H, Ar-**H**), 6.86 (d, *J*=8.0 Hz, 1H, Ar-**H**), 6.34 (ddd, apparent dt, *J*=15.5, 7.0 Hz, 1H, Ar-C=C**H**), 4.25 (d, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 3.84 (s, 3H, OC$\mathbf{H_3}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.9, 129.4, 129.2, 127.3, 125.5, 120.7, 110.8, 55.4, 46.2; IR (film) 2957, 1598, 1487, 1461, 1243, 1029, 969, 751 cm^{-1}.

(*E*)-1-(3-Chloroprop-1-enyl)-4-chlorobenzene (**6e**)



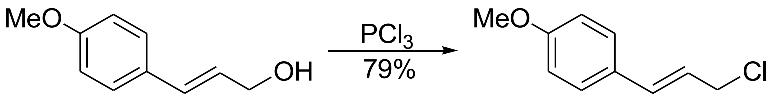
The title compound (*E*)-1-(3-Chloroprop-1-enyl)-4-chlorobenzene (**6e**) (0.71 g, 3.82 mmol, 77%) was obtained from (*E*)-3-(4-chlorophenyl)-prop-2-en-1-ol (0.83 g, 4.93 mmol) by the general allylic chloride preparation procedure followed by bulb-to-bulb distillation from CaH_2 as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (m, 4H, 4Ar-**H**), 6.59 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.28 (ddd, apparent dt, *J*=15.5, 7.5 Hz, 1H, Ar-C=C**H**), 4.21 (d, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 132.8, 128.8, 127.9, 125.5, 45.2; IR (film): 1491, 1406, 1302, 1247, 1092, 1011, 966, 799, 744, 714, 692, 656 cm^{-1}.

(*E*)-1-(3-Chloroprop-1-enyl)-2-thiophene (**6f**)



The title compound (*E*)-1-(3-chloroprop-1-enyl)-2-thiophene (**6f**) (2.11 g, 13.3 mmol, 92%) was obtained from (*E*)-3-(2-thienyl)-prop-2-en-1-ol (2.02 g, 14.4 mmol) by the general allylic chloride preparation procedure without flash chromatography as a light yellow oil, which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, *J*=4.5 Hz, 1H, Ar-**H**), 6.98 (m, 1H, Ar-**H**), 6.96 (d, *J*=3.5 Hz, 1H, Ar-**H**), 6.77 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.13 (ddd, apparent dt, *J*=15.0, 7.0 Hz, 1H, Ar-C=C**H**), 4.20 (d, *J*=7.0 Hz, 2H, C**H₂**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 127.5, 127.3, 126.9, 125.3, 124.2, 45.3; IR (film) 2954, 1646, 1247, 958, 700 cm^{-1}.

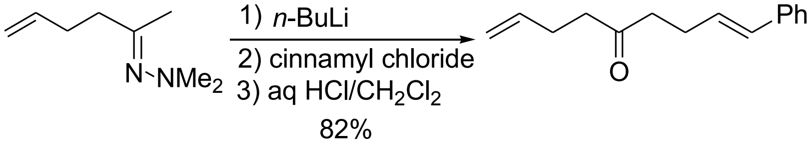
(*E*)-1-(3-Chloroprop-1-enyl)-4-methoxybenzene (**6d**)



A 100-mL, round-bottomed flask equipped with a magnetic stirring bar with a N_2 inlet was charged with (*E*)-3-(4-methoxyphenyl)-prop-2-en-1-ol (1.71 g, 10.4 mmol) and anhydrous THF (60 mL) was subsequently added. After cooling to 0 ºC, PCl_3 (0.93 mL, 10.4 mmol) was slowly added dropwise. The reactant mixture was stirred for 5 min until judged complete by TLC. The reactant mixture was diluted with diethyl ether (50 mL), washed with saturated $NaHCO_3$ (20 mL), brine (15 mL), and the organic layer was subsequently dried with Na_2SO_4. Concentration in vacuo afforded (*E*)-1-(3-chloroprop-1-enyl)-4-methoxybenzene (**6d**) (1.50 g, 8.22 mmol, 79%) as a white solid, which was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, *J*=8.5 Hz, 2H, 2Ar-

H), 6.85 (d, *J*=9.0 Hz, 2H, 2Ar-**H**), 6.58 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.17 (ddd, apparent dt, *J*=15.5, 7.5 Hz, 1H, Ar-C=C**H**), 4.22 (d, *J*=7.0 Hz, 2H, C**H**$_2$), 3.80 (s, 3H, OC**H**$_3$); ^{13}C NMR (500 MHz, CDCl$_3$): δ 159.6, 133.8, 129.5, 128.6, 128.0, 122.6, 114.0, 55.3, 46.0; IR (film): 2957, 2840, 1605, 1513, 1287, 1247, 1176, 1029, 969, 807, 656 cm^{-1}.

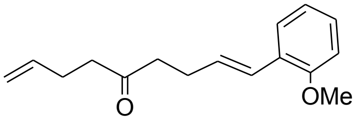
1.4 General alkylation procedure: (*E*)-1-Phenyl-nona-1,8-dien-5-one (**7b**)



A 50-mL, round-bottomed flask equipped with a magnetic stirring bar and a N$_2$ inlet was charged with 5-hexen-2-one-*N,N*-dimethylhydrazone (**5**) (1.50 g, 10.7 mmol) and anhydrous THF (20 mL) was subsequently added. The resulting solution was cooled to −78 ºC with a dry ice-acetone bath and *n*-BuLi (5.2 M, 2.0 mL, 10.4 mmol) was slowly added dropwise. The reactant mixture was warmed up to −15 ºC and stirred for 30 min, and then re-cooled back to −78 ºC. Cinnamyl chloride (1.0 mL, 7.14 mmol) in THF (3 mL) was added and the reactant mixture was stirred for 30 min at −78 ºC. The reactant mixture was diluted with diethyl ether (50 mL), washed with saturated NaHCO$_3$ (10 mL), brine (10 mL) and concentrated in vacuo. The CH$_2$Cl$_2$ (12 mL) and diluted HCl (3.0 M, 3 mL, 9.0 mmol) were added in succession and the reactant mixture was stirred for 10 h at room temperature. The organic phase was separated, washed with saturated NaHCO$_3$ (3 mL), brine (3 mL), and subsequently dried with Na$_2$SO$_4$. Concentration in vacuo followed by flash chromatography on silica gel (20:1 hxane/EtOAc for elution) afforded (*E*)-1-phenyl-nona-1,8-dien-5-one (**7b**) (1.25 g, 5.84 mmol, 82%) as a colorless oil. ^{1}H

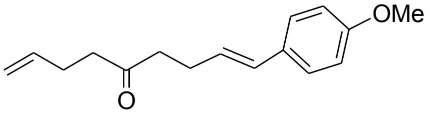
NMR (500 MHz, $CDCl_3$): δ 7.31-7.17 (m, 5H, 5Ar-**H**), 6.38 (d, *J*=15.5 Hz, 1H, Ph-C**H**=C), 6.18 (ddd, apparent dt, *J*=14.0, 7.0 Hz, 1H, Ph-C=C**H**), 5.79 (dddd, apparent ddt, *J*=16.5, 10.0, 6.5 Hz, 1H, CH_2=C**H**), 5.02 (d, *J*=17.0 Hz, 1H, C$\mathbf{H}_2$=CH), 4.97 (d, *J*=10.0 Hz, 1H, C$\mathbf{H}_2$=CH), 2.58 (dd, apparent triplet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 2.52 (dd, apparent triplet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 2.47 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 2.33 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 209.3, 137.4, 137.1, 130.7, 128.9, 128.5, 127.1, 126.0, 115.3, 42.3, 41.9, 27.7, 27.1; IR (film): 2921, 1713, 966, 914, 744, 692 cm^{-1}; HRMS (ESI): Calcd for $C_{15}H_{19}O$ $[M+H]^+$: 215.1430, found: 215.1374.

(*E*)-1-(2-Methoxyphenyl)-nona-1,8-dien-5-one (**7c**)



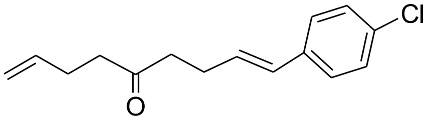
The title compound (*E*)-1-(2-methoxyphenyl)-nona-1,8-dien-5-one (**7c**) (1.16 g, 4.75 mmol, 81%) was obtained from (*E*)-1-(3-chloroprop-1-enyl)-2-methoxybenzene (**6c**) (1.08 g, 5.91 mmol) by the general alkylation procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, *J*=7.0 Hz, 1H, Ar-**H**), 7.17 (t, *J*=8.0 Hz, 1H, Ar-**H**), 6.88 (t, *J*=7.5 Hz, 1H, Ar-**H**), 6.83 (d, *J*=8.5 Hz, 1H, Ar-**H**), 6.71 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.17 (ddd, apparent dt, *J*=16.0, 7.0 Hz, 1H, Ar-C=C**H**), 5.79 (dddd, apparent ddt, *J*=16.5, 10.0, 6.5 Hz, 1H, CH_2=C**H**), 5.02 (d, *J*=17.0 Hz, 1H, C$\mathbf{H}_2$=CH), 4.96 (d, *J*=10.5 Hz, 1H, C$\mathbf{H}_2$=CH), 3.82 (s, 3H, OC$\mathbf{H_3}$), 2.59 (dd, apparent triplet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 2.54-2.46 (m, 4H, 2C$\mathbf{H_2}$), 2.32 (ddd, apparent quartet, *J*=6.5 Hz, 2H, C$\mathbf{H_2}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 209.5, 156.3, 137.1, 129.6, 128.1, 126.5, 125.3, 120.6, 115.2, 110.7, 55.4, 42.5, 41.9, 27.7, 27.5; IR (film): 2939, 1716, 1487, 1247, 755 cm^{-1}, HRMS (ESI): Calcd for $C_{16}H_{21}O_2$ $[M+H]^+$: 245.14636, found: 245.14540.

(*E*)-1-(4-Methoxyphenyl)-nona-1,8-dien-5-one (**7d**)



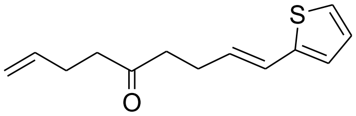
The title compound (*E*)-1-(4-methoxyphenyl)-nona-1,8-dien-5-one (**7d**) (0.94 g, 3.84 mmol, 47%) was obtained from (*E*)-1-(3-chloroprop-1-enyl)-4-methoxybenzene (**6d**) (1.50 g, 8.22 mmol) by the general alkylation procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (d, *J*=6.5 Hz, 2H, 2Ar-**H**), 6.81 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 6.32 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.02 (ddd, apparent dt, *J*=15.5, 7.0 Hz, 1H, Ar-C=C**H**), 5.78 (dddd, apparent ddt, *J*=16.5, 10.5, 6.5 Hz, 1H, CH_2=C**H**), 5.01 (d, *J*=17.0 Hz, 1H, C$\mathbf{H}_2$=CH), 4.96 (d, *J*=10.0 Hz, 1H, C$\mathbf{H}_2$=CH), 3.77 (s, 3H, OC$\mathbf{H_3}$), 2.56 (dd, apparent triplet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 2.51 (dd, apparent triplet, *J*=7.5 Hz, 2H, C$\mathbf{H_2}$), 2.44 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$), 2.32 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C$\mathbf{H_2}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 209.5, 158.8, 137.1, 130.2, 130.1, 127.1, 126.7, 115.3, 113.9, 55.3, 42.5, 41.9, 27.7, 27.1; IR (film): 2913, 1712, 1605, 1509, 1251, 1173, 1033 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{21}O_2$ $[M+H]^+$: 245.1464, found: 245.1437.

(*E*)-1-(4-Chlorophenyl)-nona-1,8-dien-5-one (**7e**)



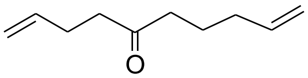
The title compound (*E*)-1-(4-chlorophenyl)-nona-1,8-dien-5-one (**7e**) (0.50 g, 2.01 mmol, 53%) was obtained from (*E*)-1-(3-chloroprop-1-enyl)-4-chlorobenzene (**6e**) (0.80 g, 5.73 mmol) by the general alkylation procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (m, 4H, 4Ar-**H**), 6.32 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.15 (ddd, apparent dt, *J*=15.5, 7.0 Hz, 1H, Ar-C=C**H**), 5.78 (dddd, apparent ddt, *J*=17.0, 10.5, 6.5 Hz, 1H, CH_2=C**H**), 5.01 (d, *J*=17.0 Hz, 1H, C**H**$_2$=CH), 4.96 (d, *J*=10.0 Hz, 1H, C**H**$_2$=CH), 2.57 (dd, apparent triplet, *J*=7.0 Hz, 2H, C**H₂**), 2.51 (dd, apparent triplet, *J*=7.0 Hz, 2H, C**H₂**), 2.45 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 2.32 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 209.2, 137.0, 135.9, 132.6, 129.7, 129.6, 128.6, 127.2, 115.3, 42.2, 41.9, 27.7, 27.0; IR (film): 2917, 1712, 1491, 1406, 1368, 1088, 1011, 969, 918, 848, 803 cm^{-1}, HRMS (ESI): Calcd for $C_{15}H_{17}ClO$ $[M+H]^+$: 248.09657, found: 248.09590.

(*E*)-1-Thiophen-2-yl-nona-1,8-dien-5-one (**7f**)



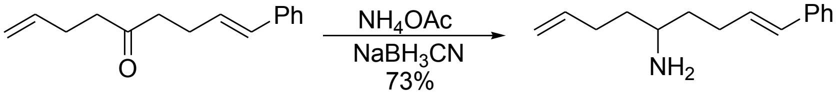
The title compound (*E*)-1-thiophen-2-yl-nona-1,8-dien-5-one (**7f**) (1.67 g, 7.59 mmol, 40%) was obtained from (*E*)-1-(3-chloroprop-1-enyl)-2-thiophene (**6f**) (3.15 g, 19.8 mmol) by the general alkylation procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.06 (d, *J*=4.5 Hz, 1H, Ar-**H**), 6.90 (dd, *J*=4.5, 3.5 Hz, 1H, Ar-**H**), 6.85 (m, 1H, Ar-**H**), 6.50 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.00 (ddd, apparent dt, *J*=15.0, 6.5 Hz, 1H, Ar-C=C**H**), 5.78 (dddd, apparent ddt, *J*=16.5, 10.0, 6.5 Hz, 1H, CH_2=C**H**), 5.01 (d, *J*=17.0 Hz, 1H, C**H**$_2$=CH), 4.96 (d, *J*=10.0 Hz, 1H, C**H**$_2$=CH), 2.54 (dd, apparent triplet, *J*=7.0 Hz, 2H, C**H₂**), 2.49 (dd, apparent triplet, *J*=6.5 Hz, 2H, C**H₂**), 2.42 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 2.32 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 209.1, 142.6, 137.1, 128.8, 127.3, 124.7, 124.0, 123.4, 115.3, 42.1, 41.9, 27.7, 26.8; IR (film) 2917, 1716, 1435, 955, 918, 696 cm^{-1}; HRMS (ESI): Calcd for $C_{13}H_{17}SO$ [M+H]$^+$: 221.0995, found: 221.0988.

Deca-1,9-dien-5-one



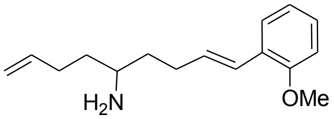
The title compound deca-1,9-dien-5-one (0.77 g, 5.07 mmol, 68%) was obtained from 4-bromo-1-butene (0.75 mL, 7.41 mmol) by the general alkylation procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.75 (m, 2H, 2C**H**=CH_2), 4.98 (m, 4H, 2C**H**$_2$=C), 2.47 (dd, apparent triplet, *J*=7.0 Hz, 2H, C**H₂**), 2.39 (dd, apparent triplet, *J*=7.5 Hz, 2H, C**H₂**), 2.29 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 2.02 (ddd, apparent quartet, *J*=7.0 Hz, 2H, C**H₂**), 1.65 (dddd, apparent quintet, *J*=7.0 Hz, 2H, C**H₂**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 210.1, 138.0, 137.1, 115.2, 41.9, 41.8, 33.1, 27.8, 22.7; IR (film) 3080, 2979, 2935, 1712, 1638, 1439, 1413, 1368, 995, 910 cm^{-1}, HRMS (ESI): Calcd for $C_{10}H_{16}O$ [M+H]$^+$: 152.06377, found: 152.01998.

1.5 General reductive amination procedure: (*E*)-1-But-3-enyl-5-phenyl-pent-4-enylamine (**2b**)



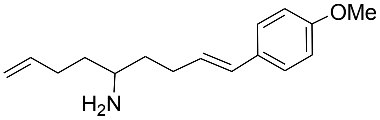
A 50-mL, round-bottomed flask equipped with a magnetic stirring bar and a N_2 inlet was charged with (*E*)-1-phenyl-nona-1,8-dien-5-one (**7b**) (1.51 g, 7.06 mmol) and anhydrous methanol (27 mL) was subsequently added. Then NH_4OAc (5.43 g, 70.6 mmol) and $NaBH_3CN$ (0.44 g, 7.05 mmol) were added in succession. The reactant mixture was stirred at room temperature for 24 h when judged complete by TLC. Aqueous 10% NaOH was slowly added dropwise until pH=10. The reactant mixture was extracted with diethyl ether (60 mL), and the organic phase was dried with Na_2SO_4. Concentration in vacuo followed by bulb-to-bulb distillation from CaH_2 afforded (*E*)-1-but-3-enyl-5-phenyl-pent-4-enylamine (**2b**) (1.11 g, 5.16 mmol, 73%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.16 (m, 5H, 5Ar-**H**), 6.39 (d, *J*=16.0 Hz, 1H, Ph-C**H**=C), 6.21 (ddd, apparent dt, *J*=15.0, 6.5 Hz, 1H, Ph-C=C**H**), 5.81 (m, 1H, CH_2=C**H**), 5.03 (d, *J*=17.0 Hz, 1H, C$\mathbf{H}_2$=CH), 4.96 (d, *J*=10.0 Hz, 1H, C$\mathbf{H}_2$=CH), 2.76 (m, 1H, C**H**-NH_2), 2.32-2.07 (m, 4H, 2C$\mathbf{H_2}$), 1.59-1.32 (m, 4H, 2C$\mathbf{H_2}$), 1.17 (s, 2H, N$\mathbf{H_2}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 138.7, 137.7, 130.5, 130.0, 128.5, 126.9, 125.9, 114.6, 50.3, 37.6, 37.3, 30.5, 29.8; IR (film): 2925, 1576, 1446, 966, 914, 744, 692 cm^{-1}; HRMS (ESI): Calcd for $C_{15}H_{22}N$ $[M+H]^+$: 216.17468, found: 216.17446.

(*E*)-1-But-3-enyl-5-(2-methoxyphenyl)-pent-4-enylamine (**2c**)



The title compound (*E*)-1-but-3-enyl-5-(2-methoxyphenyl)-pent-4-enylamine (**2c**) (0.55 g, 2.24 mmol, 50%) was obtained from (*E*)-1-(2-methoxyphenyl)-nona-1,8-dien-5-one (**7c**) (1.09 g, 4.47 mmol) by the general reductive amination procedure as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.39 (d, *J*=7.5 Hz, 1H, Ar-**H**), 7.16 (t, *J*=7.5 Hz, 1H, Ar-**H**), 6.89 (t, *J*=7.5 Hz, 1H, Ar-**H**), 6.82 (d, *J*=8.0 Hz, 1H, Ar-**H**), 6.72 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.19 (ddd, apparent dt, *J*=14.5, 6.5 Hz, 1H, Ar-C=C**H**), 5.80 (m, 1H, CH$_2$=C**H**), 5.02 (d, *J*=17.0 Hz, 1H, C**H**$_2$=CH), 4.94 (d, *J*=10.5 Hz, 1H, C**H**$_2$=CH), 3.81 (s, 3H, OC**H$_3$**), 2.76 (m, 1H, C**H**-NH$_2$), 2.34-2.06 (m, 4H, 2C**H$_2$**), 1.60-1.32 (m, 4H, 2C**H$_2$**), 1.29 (s, 2H, N**H$_2$**); ^{13}C NMR (500 MHz, CDCl$_3$): δ 156.2, 138.7, 131.2, 127.9, 126.7, 126.4, 124.6, 120.6, 114.6, 110.7, 55.4, 50.3, 37.7, 37.1, 30.5, 30.2; IR (film): 2932, 1594, 1491, 1461, 1239, 1033, 973, 910, 747 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.18524, found: 246.18614.

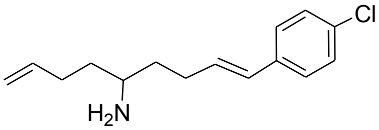
(*E*)-1-But-3-enyl-5-(4-methoxyphenyl)-pent-4-enylamine (**2d**)



The title compound (*E*)-1-but-3-enyl-5-(4-methoxyphenyl)-pent-4-enylamine (**2d**) (0.6 g, 2.43 mmol, 63%) was obtained from (*E*)-1-(4-methoxyphenyl)-nona-1,8-dien-5-one (**7d**) (0.94 g, 3.84 mmol) by the general reductive amination procedure as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.25 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.81 (d, *J*=8.0 Hz, 2H, 2Ar-

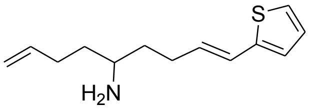
H), 6.32 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.05 (ddd, apparent dt, *J*=15.0, 7.0 Hz, 1H, Ar-C=C**H**), 5.82 (dddd, apparent ddt, *J*=17.0, 10.0, 7.0 Hz, 1H, CH_2=C**H**), 5.02 (d, *J*=17.0 Hz, 1H, C**H**$_2$=CH), 4.94 (d, *J*=10.0 Hz, 1H, C**H**$_2$=CH), 3.78 (s, 3H, OC**H**$_3$), 2.76 (m, 1H, C**H**-NH_2), 2.38-2.06 (m, 4H, 2C**H**$_2$), 1.61-1.30 (m, 4H, 2C**H**$_2$), 1.25 (s, 2H, N**H**$_2$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 158.7, 138.7, 130.5, 129.3, 128.3, 127.0, 114.6, 113.9, 55.3, 50.3, 37.8, 37.3, 30.5, 29.7; IR (film): 2921, 1605, 1513, 1251, 1176, 1033, 966 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.18524, found: 246.18620.

(*E*)-1-But-3-enyl-5-(4-chlorophenyl)-pent-4-enylamine (**2e**)



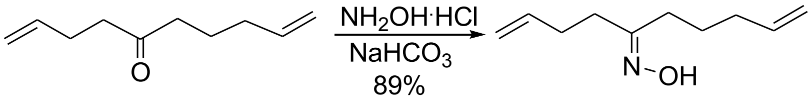
The title compound (*E*)-1-but-3-enyl-5-(4-chlorophenyl)-pent-4-enylamine (**2e**) (0.36 g, 1.44 mmol, 72%) was obtained from (*E*)-1-(4-chlorophenyl)-nona-1,8-dien-5-one (**7e**) (0.50 g, 2.01 mmol) by the general reductive amination procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (m, 4H, 4Ar-**H**), 6.33 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.18 (ddd, apparent dt, *J*=15.0, 6.5 Hz, 1H, Ar-C=C**H**), 5.79 (dddd, apparent ddt, *J*=17.0, 10.5, 7.0 Hz, 1H, CH_2=C**H**), 5.02 (d, *J*=17.0 Hz, 1H, C**H**$_2$=CH), 4.94 (d, *J*=10.0 Hz, 1H, C**H**$_2$=CH), 2.76 (m, 1H, C**H**-NH_2), 2.34-2.06 (m, 4H, 2C**H**$_2$), 1.62-1.33 (m, 4H, 2C**H**$_2$), 1.23 (s, 2H, N**H**$_2$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 138.6, 131.3, 128.8, 128.6, 127.1, 114.6, 50.3, 37.5, 37.3, 30.5, 29.7; IR (film): 2925, 2846, 1638, 1491, 1450, 1092, 1011, 966, 914, 848, 803 cm^{-1}; HRMS (ESI): Calcd for $C_{15}H_{20}ClN$ $[M+H]^+$: 250.13570, found: 250.13536.

(*E*)-1-But-3-enyl-5-thiophen-2-yl-pent-4-enylamine (**2f**)



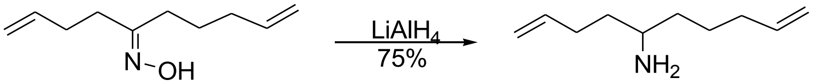
The title compound (*E*)-1-but-3-enyl-5-thiophen-2-yl-pent-4-enylamine (**2f**) (0.15 g, 0.69 mmol, 88%) was obtained from (*E*)-1-thiophen-2-yl-nona-1,8-dien-5-one (**7f**) (0.17 g, 0.79 mmol) by the general reductive amination procedure as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.06 (d, *J*=4.5 Hz, 1H, Ar-**H**), 6.92 (dd, *J*=4.5, 3.5 Hz, 1H, Ar-**H**), 6.84 (d, 1H, *J*=2.5 Hz, Ar-**H**), 6.51 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 6.04 (ddd, apparent dt, *J*=15.0, 7.0 Hz, 1H, Ar-C=C**H**), 5.80 (dddd, apparent ddt, *J*=16.5, 10.0, 6.5 Hz, 1H, CH_2=C**H**), 5.02 (d, *J*=17.0 Hz, 1H, C**H**$_2$=CH), 4.95 (d, *J*=10.0 Hz, 1H, C**H**$_2$=CH), 2.75 (m, 1H, C**H**-NH_2), 2.29-2.06 (m, 4H, 2C**H₂**), 1.61-1.33 (m, 4H, 2C**H₂**), 1.25 (s, 2H, N**H₂**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 138.6, 130.5, 127.2, 124.3, 123.3, 123.2, 114.6, 50.2, 37.4, 37.2, 30.5, 29.5; IR (film) 2921, 1642, 1450, 958, 910, 696 cm^{-1}; HRMS (ESI): Calcd for $C_{13}H_{20}NS$ $[M+H]^+$: 222.13110, found: 222.13118.

Deca-1,9-dien-5-one oxime



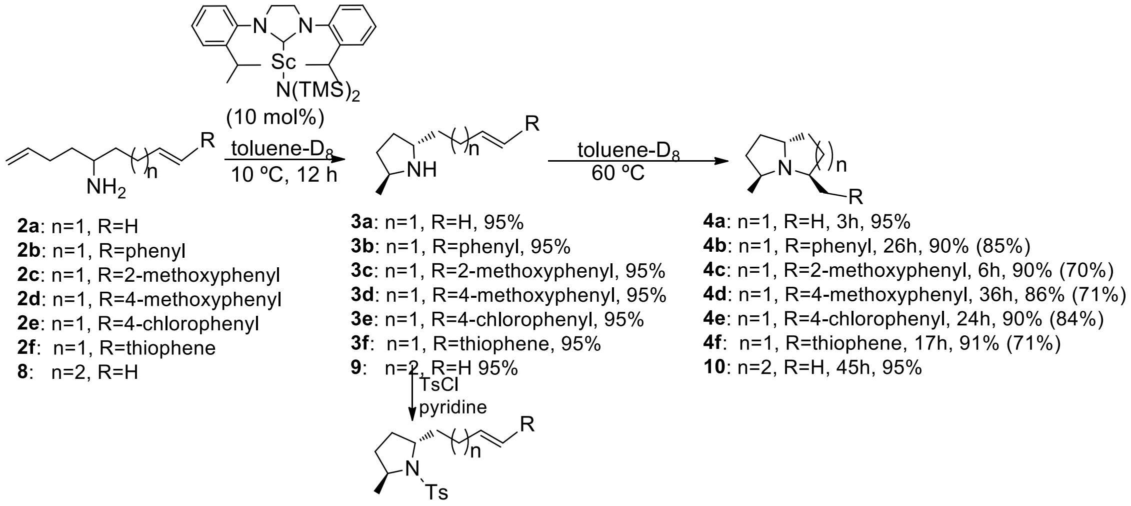
A 25-mL, round-bottomed flask equipped with a magnetic stirring bar and a N_2 inlet was charged with deca-1,9-dien-5-one (0.77 g, 5.1 mmol) and EtOH/THF/H_2O (volume ratio 4:2:1, 10 mL) was subsequently added. Then $NH_2OH{\cdot}HCl$ (0.70 g, 10.1 mmol) and $NaHCO_3$ (0.85 g, 10.1 mmol) were added in succession. The reactant mixture was stirred at room temperature for 10 h when judged complete by TLC. The reactant mixture was diluted with EtOAc (30 mL), washed with water (10 mL), brine (10 mL), and the organic phase was subsequently dried with Na_2SO_4. Concentration in vacuo followed by flash chromatography on silica gel (10:1 hexane/EtOAc for elution) afforded deca-1,9-dien-5-one oxime (0.75 g, 4.50 mmol, 89%) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.86 (s, 1H, O**H**), 5.79 (m, 2H, 2C**H**=CH_2), 5.00 (m, 4H, 2C**H₂**=C), 2.43-2.00 (m, 8H, 4C**H₂**), 1.60 (m, 2H, C**H₂**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 160.9, 138.1, 137.6, 137.4, 115.2, 15.1, 115.0, 33.8, 33.6, 33.5, 33.3, 30.2, 29.6, 27.3, 27.0, 25.3, 24.8; IR (film): 3239, 3080, 2932, 1638, 1439, 991, 914 cm^{-1}; HRMS (ESI): Calcd for $C_{10}H_{18}NO$ $[M+H]^+$: 168.13829, found: 163.13708.

1-But-3-enyl-hex-5-enylamine (**8**)



A 50-mL, round-bottomed flask equipped with a magnetic stirring bar and a N_2 inlet was charged with $LiAlH_4$ (0.34 g, 9.0 mmol) and anhydrous diethyl ether (18 mL) was subsequently added. The resulting mixture was cooled to 0 ºC with an ice-water bath. Deca-1,9-dien-5-one oxime (0.75 g, 4.5 mmol) in anhydrous diethyl ether (3 mL) was then added at 0 ºC. The reactant mixture was stirred under reflux for 10 h when judged complete by TLC. Water was slowly added dropwise until no more hydrogen was evolved. The reactant mixture was diluted with diethyl ether (30 mL) and was subsequently dried with Na_2SO_4. The white solid was removed by vacuum filtration. The organic filtrate was concentrated in vacuo. Bulb-to-bulb distillation from CaH_2 afforded 1-but-3-enyl-hex-5-enylamine (**8**) (0.52 g, 3.39 mmol, 75%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.77 (m, 2H, 2C**H**=CH_2), 4.95 (m, 4H, 2C$\mathbf{H_2}$=C), 2.68 (m, 1H, C**H-**NH$_2$), 2.13-2.02 (m, 4H, 2C$\mathbf{H_2}$), 1.55-1.32 (m, 8H, 3C$\mathbf{H_2}$ and N$\mathbf{H_2}$); ^{13}C NMR (500 MHz, CDCl$_3$): δ 138.8, 138.7, 114.5, 50.6, 37.5, 37.2, 33.8, 30.5, 25.4; IR (film): 2928, 2854, 1642, 1579, 1450, 995, 910 cm^{-1}; HRMS (ESI): Calcd for $C_{10}H_{19}N$ [M+H]$^+$: 154.1593, found: 154.1590.

2. General hydroamination procedure:

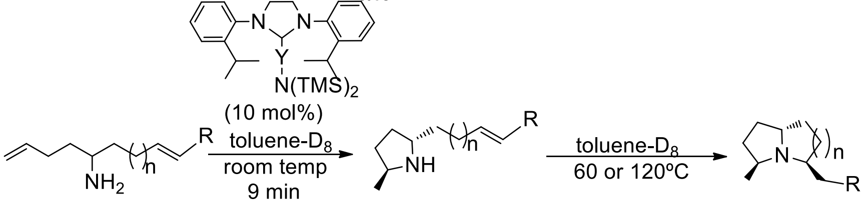


2a: n=1, R=H
2b: n=1, R=phenyl
2c: n=1, R=2-methoxyphenyl
2d: n=1, R=4-methoxyphenyl
2e: n=1, R=4-chlorophenyl
2f: n=1, R=thiophene
8: n=2, R=H

3a: n=1, R=H, 95%
3b: n=1, R=phenyl, 95%
3c: n=1, R=2-methoxyphenyl, 95%
3d: n=1, R=4-methoxyphenyl, 95%
3e: n=1, R=4-chlorophenyl, 95%
3f: n=1, R=thiophene, 95%
9: n=2, R=H 95%

4a: n=1, R=H, 3h, 95%
4b: n=1, R=phenyl, 26h, 90% (85%)
4c: n=1, R=2-methoxyphenyl, 6h, 90% (70%)
4d: n=1, R=4-methoxyphenyl, 36h, 86% (71%)
4e: n=1, R=4-chlorophenyl, 24h, 90% (84%)
4f: n=1, R=thiophene, 17h, 91% (71%)
10: n=2, R=H, 45h, 95%

3a$_{\mathbf{NTs}}$: n=1, R=H, dr 50:1
3b$_{\mathbf{NTs}}$: n=1, R=phenyl, dr 50:1
3c$_{\mathbf{NTs}}$: n=1, R=2-methoxyphenyl, dr 50:1
3d$_{\mathbf{NTs}}$: n=1, R=4-methoxyphenyl, dr 50:1
3f$_{\mathbf{NTs}}$: n=1, R=4-chlorophenyl, dr 50:1
3e$_{\mathbf{NTs}}$: n=1, R=thiophene, dr 50:1
9$_{\mathbf{NTs}}$: n=2, R=H, dr 50:1



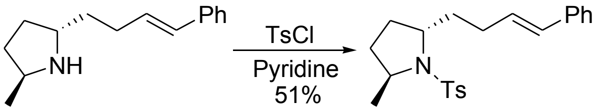
2a: n=1, R=H
2b: n=1, R=phenyl
2c: n=1, R=2-methoxyphenyl
2d: n=1, R=4-methoxyphenyl
2e: n=1, R=4-chlorophenyl
2f: n=1, R=thiophene
8: n=2, R=H

3a: n=1, R=H, 95%, dr 18:1
3b: n=1, R=phenyl, 95%, dr 18:1
3c: n=1, R=2-methoxyphenyl,
95%, dr 18:1
3d: n=1, R=4-methoxyphenyl,
95%, dr 18:1
3e: n=1, R=4-chlorophenyl,
95%, dr 18:1
3f: n=1, R=thiophene, 95%, dr 18:1
9: n=2, R=H, 95%, dr 18:1

4a: n=1, R=H, 60°C, 3h, 95%
4b: n=1, R=phenyl, 60°C, 44h, 87% (73%)
4c: n=1, R=2-methoxyphenyl,
60°C,11h, 91% (81%)
4d: n=1, R=4-methoxyphenyl,
120°C, 48h, 70% (64%)
4e: n=1, R=4-chlorophenyl,
60°C, 30h, 84% (75%)
4f: n=1, R=thiophene, 60°C, 60h, 82% (74%)
10: n=2, R=H, 60°C, 144h, 80%

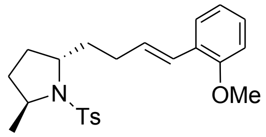
In an argon-filled glove box, $Sc[N(TMS)_2]_3$[2] (10.52 mg, 0.02 mmol) and *N*,*N'*-bis-(2-isopropylphenyl)-ethane-1,2-diamine (5.93 mg, 0.02 mmol) were introduced into a J. Young NMR tube equipped with teflon screw cap, and toluene-D_8 (0.5 mL) was subsequently added. The homogeneous reactant mixture was heated in an oil bath maintained at 120 ºC for 48 h to effect ligand exchange as indicated by ^1H NMR spectroscopy. The aminodienes **2a-2f, 8** (0.2 mmol) were added to the preformed complex and the reactant mixture was subsequently held at 10 ºC in a cooling bath for 12 h until the first ring closure was judged complete (≥95% by ^1H NMR integration). The reactant mixture was subsequently heated at 60 ºC in an oil bath until the hydroamination for second ring closure was judged complete (≥90% by ^1H NMR integration). Concentration in vacuo followed by flash chromatography on basic alumina afforded the pure bicyclic targets **4b-4f**. Similarly, $Y[N(TMS)_2]_3$[2] (11.4 mg, 0.02 mmol) and *N*,*N'*-bis-(2-isopropylphenyl)-ethane-1,2-diamine (5.93 mg, 0.02 mmol) were introduced into a J. Young NMR tube equipped with teflon screw cap, and toluene-D_8 (0.5 mL) was subsequently added. The homogeneous reactant mixture was heated in an oil bath maintained at 150 ºC for 5 h to effect ligand exchange as indicated by ^1H NMR spectroscopy. The aminodienes **2a-2f, 8** (0.2 mmol) were added to the preformed complex and the first ring closure was judged complete immediately (≥95%, dr 18:1 by ^1H NMR integration). The reactant mixture was subsequently heated at 60 ºC (**3a, 3b, 3c, 3e**, **3f**, **9**) and 120 ºC (**3d**) in an oil bath until the hydroamination for second ring closure was judged complete as indicated by ^1H NMR spectroscopy. Concentration in vacuo followed by flash chromatography on basic alumina afforded the pure bicyclic targets **4b-4f**.

General *p*-toluenesulfonamide preparation procedure: 2-Methyl-5-[(*E*)-4-phenyl-but-3-enyl]-1-(toluene-4-sulfonyl)-2αH,5βH-tetrahydropyrrole (**3b**$_{\boldsymbol{N}\mathbf{Ts}}$)



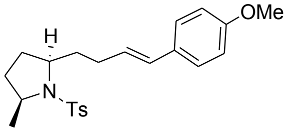
The tetrahydropyrrole **3b** was obtained from (*E*)-1-but-3-enyl-5-phenyl-pent-4-enylamine (**2b**) (34 mg, 0.16 mmol) by the general hydroamination procedure for the first ring closure. Following pyrrolidine formation, the teflon screw cap was removed and crude **3b** was diluted with anhydrous CH_2Cl_2 (3 mL). TsCl (45 mg, 0.24 mmol) and pyridine (0.02 mL, 0.25 mmol) were added in succession. The reactant mixture was stirred at room temperature for 12 h. The reactant mixture was diluted with diethyl ether (10 mL), washed with saturated $NaHCO_3$ (3 mL) and brine (3 mL). The organic phase was subsequently dried with Na_2SO_4. Concentration in vacuo followed by flash chromatography on silica gel (10:1 to 5:1 hexane/EtOAc for elution) afforded 2-methyl-5-[(*E*)-4-phenyl-but-3-enyl]-1-(toluene-4-sulfonyl)-2αH,5βH-tetrahydropyrrole (**3b**$_{\boldsymbol{N}\mathbf{Ts}}$) (30 mg, 0.08 mmol, 51%) as a colorless oil (dr 50:1 by ^{1}H NMR integration). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.32-7.19 (m, 5H, 5Ar-**H**), 7.16 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.32 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.14 (ddd, apparent dt, *J*=15.5, 6.5 Hz, 1H, Ar-C=C**H**), 4.05 (m, 1H, C**H**-N), 3.82 (m, 1H, C**H**-N), 2.36 (s, 3H, ArC$\mathbf{H_3}$), 2.17-1.47 (m, 8H, 4C$\mathbf{H_2}$), 1.16 (d, *J*=6.0 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 142.6, 137.6, 130.3, 129.7, 129.4, 128.5, 127.0, 126.9, 125.9, 59.7, 56.6, 33.6, 31.4, 29.8, 27.9, 21.5, 20.8; IR (film): 2969, 1335, 1154, 662, 596 cm^{-1}; HRMS (ESI): Calcd for $C_{22}H_{28}NO_2S$ $[M+H]^+$: 370.18353, found: 370.18290; Calcd for $C_{22}H_{27}NNaO_2S$ $[M+Na]^+$: 392.16547, found: 392.16515.

2-[(*E*)-4-(2-Methoxyphenyl)-but-3-enyl]-5-methyl-1-(toluene-4-sulfonyl)-2βH,5αH-tetrahydropyrrole (**3c**$_{\textit{N}\textbf{Ts}}$)



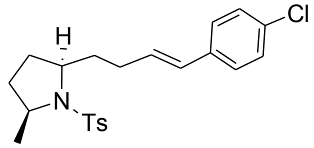
The title compound 2-[(*E*)-4-(2-methoxyphenyl)-but-3-enyl]-5-methyl-1-(toluene-4-sulfonyl)-2βH,5αH-tetrahydropyrrole (**3c**$_{\textit{N}\textbf{Ts}}$) (34 mg, 0.09 mmol, 46%) was obtained from (*E*)-1-but-3-enyl-5-(2-methoxyphenyl)-pent-4-enylamine (**2c**) (45 mg, 0.18 mmol) by the general hydroamination and *p*-toluenesulfonamide preparation procedure as a colorless oil (dr 50:1 by ^{1}H NMR integration). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J=8.0 Hz, 2H, 2Ar-**H**), 7.38 (d, J=7.5 Hz, 1H, Ar-**H**), 7.18 (m, 3H, 3Ar-**H**), 6.90 (t, J=7.5 Hz, 1H, Ar-**H**), 6.85 (d, J=8.0 Hz, 1H, Ar-**H**), 6.65 (d, J=16.0 Hz, 1H, Ar-C**H**=C), 6.13 (ddd, apparent dt, J=13.5, 6.5 Hz, 1H, Ar-C=C**H**), 4.04 (m, 1H, C**H**-N), 3.82 (m, 1H, C**H**-N), 3.82 (s, 3H, OC$\mathbf{H_3}$), 2.36 (s, 3H, ArC$\mathbf{H_3}$), 2.14-1.46 (m, 8H, 4C$\mathbf{H_2}$), 1.17 (d, J=6.5 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 156.3, 142.6, 130.4, 129.5, 129.4, 128.0, 127.3, 127.0, 126.4, 124.9, 120.7, 110.8, 59.9, 56.5, 55.4, 33.7, 31.4, 30.3, 27.8, 21.4, 20.8; IR (film): 2965, 1491, 1332, 1242, 1154, 1098, 755, 666, 596 cm^{-1}; HRMS (ESI): Calcd for $C_{23}H_{30}NO_3S$ $[M+H]^+$: 400.19409, found: 400.19341; Calcd for $C_{23}H_{29}NNaO_3S$ $[M+Na]^+$: 422.17604, found: 422.17491.

2-[(*E*)-4-(4-Methoxyphenyl)-but-3-enyl]-5-methyl-1-(toluene-4-sulfonyl)-2βH,5αH-tetrahydropyrrole (**3d$_{NTs}$**)



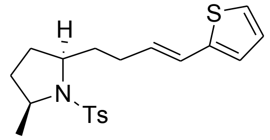
The title compound 2-[(*E*)-4-(4-methoxyphenyl)-but-3-enyl]-5-methyl-1-(toluene-4-sulfonyl)-2βH,5αH-tetrahydropyrrole (**3d$_{NTs}$**) (44 mg, 0.11 mmol, 55%) was obtained from (*E*)-1-but-3-enyl-5-(4-methoxyphenyl)-pent-4-enylamine (**2d**) (49 mg, 0.2 mmol) by the general hydroamination and *p*-toluenesulfonamide preparation procedure as a colorless oil (dr 50:1 by ^{1}H NMR integration). ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.70 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.25 (d, *J*=7.0 Hz, 2H, 2Ar-**H**), 7.17 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 6.83 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.26 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 5.99 (ddd, apparent dt, *J*=15.5, 6.5 Hz, 1H, Ar-C=C**H**), 4.05 (m, 1H, C**H**-N), 3.82 (m, 1H, C**H**-N), 3.79 (s, 3H, OC**H$_3$**), 2.36 (s, 3H, ArC**H$_3$**), 2.13-1.43 (m, 8H, 4C**H$_2$**), 1.16 (d, *J*=6.5 Hz, 3H, C**H$_3$**); ^{13}C NMR (500 MHz, CDCl$_3$): δ 158.7, 142.6, 130.4, 129.7, 129.4, 127.5, 127.0, 113.9, 59.7, 56.5, 55.3, 33.8, 31.4, 29.8, 27.9, 21.5, 20.8; IR (film) 2965, 1513, 1332, 1251, 1154, 670, 596 cm^{-1}; HRMS (ESI): Calcd for $C_{23}H_{30}NO_3S$ [M+H]$^+$: 400.19409, found: 400.19380; Calcd for $C_{23}H_{29}NNaO_3S$ [M+Na]$^+$: 422.17604, found: 422.17534.

2-[(*E*)-4-(4-Chlorophenyl)-but-3-enyl]-5-methyl-1-(toluene-4-sulfonyl)-2βH,5αH-tetrahydropyrrole (**3e*NTs***)



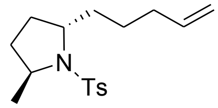
The title compound 2-[(*E*)-4-(4-chlorophenyl)-but-3-enyl]-5-methyl-1-(toluene-4-sulfonyl)-2βH,5αH-tetrahydropyrrole (**3e*NTs***) (21 mg, 0.05 mmol, 42%) was obtained from (*E*)-1-but-3-enyl-5-(4-chlorophenyl)-pent-4-enylamine (**2e**) (31 mg, 0.12 mmol) by the general hydroamination and *p*-toluenesulfonamide preparation procedure as a colorless oil (dr 50:1 by ^{1}H NMR integration). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.24 (m, 4H, 4Ar-**H**), 7.18 (d, *J*=7.0 Hz, 2H, 2Ar-**H**), 6.28 (d, *J*=16.0 Hz, 1H, Ar-C**H**=C), 6.13 (m, 1H, Ar-C=C**H**), 4.05 (m, 1H, C**H**-N), 3.81 (m, 1H, C**H**-N), 2.36 (s, 3H, ArC**H₃**), 2.16-1.48 (m, 8H, 4C**H₂**), 1.15 (d, *J*=6.5 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 142.7, 136.1, 130.5, 129.4, 129.1, 128.6, 127.1, 127.0, 59.7, 56.5, 33.6, 31.4, 29.8, 27.9, 21.5, 20.7; IR (film) 2969, 1491, 1332, 1154, 1092, 966, 811, 666, 596, 548 cm^{-1}; HRMS (ESI): Calcd for $C_{22}H_{26}ClNO_2S$ $[M+H]^+$: 404.14455, found: 404.14518.

2-Methyl-5-[(*E*)-4-thiophen-2-yl-but-3-enyl]-1-(toluene-4-sulfonyl)-2αH,5βH-tetrahydropyrrole (**3f**$_{\boldsymbol{N}\mathbf{Ts}}$)



The title compound 2-methyl-5-[(*E*)-4-thiophen-2-yl-but-3-enyl]-1-(toluene-4-sulfonyl)-2αH,5βH-tetrahydropyrrole (**3f**$_{\boldsymbol{N}\mathbf{Ts}}$) (14 mg, 0.04 mmol, 37%) was obtained from (*E*)-1-but-3-enyl-5-thiophen-2-yl-pent-4-enylamine (**2f**) (22 mg, 0.10 mmol) by the general hydroamination and *p*-toluenesulfonamide preparation procedure as a colorless oil (dr 50:1 by ^{1}H NMR integration). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.19 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.09 (d, *J*=5.0 Hz, 1H, Ar-**H**), 6.92 (dd, *J*=5.0, 3.5 Hz, 1H, Ar-**H**), 6.85 (d, *J*=3.0 Hz, 1H, Ar-**H**), 6.44 (d, *J*=15.5 Hz, 1H, Ar-C**H**=C), 5.97 (ddd, apparent dt, *J*=15.0, 6.5 Hz, 1H, Ar-C=C**H**), 4.06 (m, 1H, C**H**-N), 3.80 (m, 1H, C**H**-N), 2.37 (s, 3H, ArC**H₃**), 2.11-1.44 (m, 8H, 4C**H₂**), 1.17 (d, *J*=6.0 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 142.6, 129.6, 129.4, 127.2, 127.0, 124.4, 123.6, 123.3, 59.5, 56.6, 33.5, 31.4, 29.5, 27.9, 21.5, 20.8; IR (film) 2965, 1335, 1158, 666, 596 cm^{-1}; HRMS (ESI): Calcd for $C_{20}H_{26}NO_2S_2$ $[M+H]^+$: 376.13995, found: 376.13792; Calcd for $C_{20}H_{25}NNaO_2S_2$ $[M+Na]^+$: 398.12189, found: 398.11863.

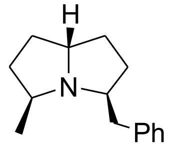
2-Methyl-5-pent-4-enyl-1-(toluene-4-sulfonyl)-2αH,5βH-tetrahydropyrrole (**9**$_{\boldsymbol{N}\mathbf{Ts}}$)



The title compound 2-methyl-5-pent-4-enyl-1-(toluene-4-sulfonyl)-2αH,5βH-tetrahydropyrrole (**9**$_{\boldsymbol{N}\mathbf{Ts}}$) (13 mg, 0.04 mmol, 36%) was obtained from 1-but-3-enyl-hex-5-

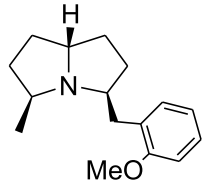
enylamine (**8**) (18 mg, 0.12 mmol) by the general hydroamination and *p*-toluenesulfonamide preparation procedure as a colorless oil (dr 50:1 by ^{1}H NMR integration). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.24 (m, 2H, 2Ar-**H**), 5.72 (dddd, apparent ddt, *J*=17.0, 10.5, 7.0 Hz, 1H, C**H**=CH_2), 4.94 (d, *J*=18.5 Hz, 1H, C$\mathbf{H_2}$=C), 4.91 (d, *J*=11.0 Hz, 1H, C$\mathbf{H_2}$=C), 4.00 (m, 1H, C**H**-N), 3.80 (m, 1H, C**H**-N), 2.39 (s, 3H, ArC$\mathbf{H_3}$), 2.07-1.21 (m, 10H, 5C$\mathbf{H_2}$), 1.15 (d, *J*=6.5 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 142.6, 138.5, 129.4, 126.9, 114.6, 60.5, 56.3, 33.7, 33.6, 31.5, 27.8, 25.7, 21.5, 21.1; IR (film) 2969, 2928, 1332, 1154, 1095, 1055, 814, 662, 596, 548 cm^{-1}; HRMS (ESI): Calcd for $C_{17}H_{25}NO_2S$ $[M+H]^+$: 308.1679, found: 308.1699.

3-Benzyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4b**)



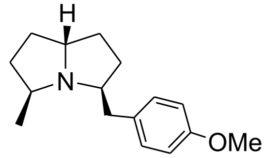
The bicycle compound 3-benzyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4b**) was obtained from (*E*)-1-but-3-enyl-5-phenyl-pent-4-enylamine (**2b**) (25.7 mg, 0.12 mmol) by the general hydroamination procedure (first ring closure: 10 ºC, 12 h, 95%, second ring closure: 60 ºC, 12 h, 90% based on ^{1}H NMR integration). Following the completion of the second ring closure, the teflon screw cap was removed and crude **4b** was concentration in vacuo. Flash chromatography on basic alumina (1:1 hexane/CH_2Cl_2 followed by 10:1 hexane/EtOAc for elution) afforded 3-benzyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4b**) (22 mg, 0.1 mmol, 85%) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.16 (m, 5H, 5Ar-**H**), 3.67 (dddd, apparent quintet, *J*=7.0 Hz, 1H, CH_2-C**H-**CH_2), 2.94 (dd, *J*=13.0, 4.5 Hz, 1H, Ar-C**H**), 2.91-2.84 (m, 1H, ArCH_2C**H**), 2.81 (ddddd, apparent sextet, *J*=6.0 Hz, 1H, C**H**CH_3), 2.54 (dd, *J*=12.5, 9.5 Hz, 1H, Ar-C**H**), 1.98-1.72 (m, 4H, 2C**H₂**), 1.58-1.28 (m, 4H, 2C**H₂**), 1.09 (d, *J*=6.5 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 140.4, 129.2, 128.2, 125.8, 68.5, 65.2, 61.7, 43.7, 34.4, 32.3, 31.9, 22.0; IR (film): 2954, 1453, 1092, 696 cm^{-1}. The ^{1}H NMR, ^{13}C NMR and IR spectra were consistent with those reported in the literature.[4]

3-(2-Methoxybenzyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4c**)



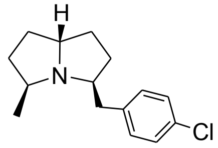
The title compound 3-(2-methoxybenzyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4c**) (16 mg, 0.07 mmol, 70%) was obtained from (*E*)-1-but-3-enyl-5-(2-methoxyphenyl)-pent-4-enylamine (**2c**) (25 mg, 0.10 mmol) by the general hydroamination procedure (first ring closure: 10 ºC, 12 h, 95%, second ring closure: 60 ºC, 6 h, 90% based on ^{1}H NMR integration) followed by flash chromatography on basic alumina (1:1 hexane/CH_2Cl_2 followed by 3:1 hexane/EtOAc for elution) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (t, *J*=8.0 Hz, 1H, Ar-**H**), 7.11 (d, *J*=7.0 Hz, 1H, Ar-**H**), 6.86-6.80 (m, 2H, 2Ar-**H**), 3.80 (s, 3H, OC**H₃**), 3.67 (dddd, apparent quintet, *J*=7.0 Hz, 1H, CH_2-C**H-**CH_2), 3.01 (dd, *J*=12.5, 4.0 Hz, 1H, Ar-C**H**), 2.95-2.87 (m, 1H, ArCH_2C**H**), 2.82 (ddddd, apparent sextet, *J*=6.0 Hz, 1H, C**H**CH_3), 2.50 (dd, *J*=12.5, 10.0 Hz, 1H, Ar-C**H**), 1.98-1.25 (m, 8H, 4C**H₂**), 1.12 (d, *J*=6.0 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 157.5, 130.9, 129.0, 127.1, 120.2, 110.2, 66.5, 65.1, 61.6, 55.2, 38.0, 34.5, 32.2, 32.1, 31.9, 21.8; IR (film): 2957, 1495, 1239, 751 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.18524, found: 246.18604.

3-(4-Methoxybenzyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4d**)



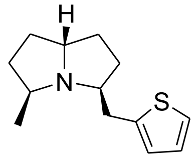
The title compound 3-(4-methoxybenzyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4d**) (15 mg, 0.06 mmol, 71%) was obtained from (*E*)-1-but-3-enyl-5-(4-methoxyphenyl)-pent-4-enylamine (**2d**) (21 mg, 0.09 mmol) by the general hydroamination procedure (first ring closure: 10 ºC, 12 h, 95%, second ring closure: 60 ºC, 36 h, 80% based on ^{1}H NMR integration) followed by flash chromatography on basic alumina (1:1 hexane/CH_2Cl_2 followed by 3:1 hexane/EtOAc for elution) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 6.80 (d, *J*=8.5 Hz, 2H, 2Ar-**H**), 3.77 (s, 3H, OC**H$_3$**), 3.66 (dddd, apparent quintet, *J*=6.5 Hz, 1H, CH_2-C**H-**CH_2), 2.88 (dd, *J*=12.5, 4.5 Hz, 1H, Ar-C**H**), 2.84-2.78 (m, 2H, ArCH$_2$C**H** and C**H**CH$_3$), 2.47 (dd, *J*=12.5, 9.5 Hz, 1H, Ar-C**H**), 1.98-1.26 (m, 8H, 4C**H$_2$**), 1.08 (d, *J*=6.5 Hz, 3H, C**H$_3$**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 157.8, 132.6, 130.0, 113.6, 68.7, 65.2, 61.7, 55.2, 42.7, 34.4, 32.3, 31.9, 22.0; IR (film):2953, 1514, 1246, 1173, 1037 cm^{-1}; HRMS (ESI): Calcd for $C_{16}H_{24}NO$ $[M+H]^+$: 246.18524, found: 246.18643.

3-(4-Chlorobenzyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4e**)



The title compound 3-(4-chlorobenzyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4e**) (31.8 mg, 0.13 mmol, 84%) was obtained from (*E*)-1-but-3-enyl-5-(4-chlorophenyl)-pent-4-enylamine (**2e**) (38 mg, 0.15 mmol) by the general hydroamination procedure (first ring closure: 10 ºC, 12 h, 95%, second ring closure: 60 ºC, 15 h, 90% based on ^{1}H NMR integration) followed by flash chromatography on basic alumina (1:1 hexane/CH_2Cl_2 followed by 5:1 hexane/EtOAc for elution) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 7.10 (d, *J*=8.0 Hz, 2H, 2Ar-**H**), 3.64 (dddd, apparent quintet, *J*=7.0 Hz, 1H, CH_2-C**H-**CH_2), 2.89-2.75 (m, 3H, 2N-C**H** and ArC**H**, 2.49 (dd, *J*=12.5, 9.0 Hz, 1H, Ar-C**H**), 1.97-1.74 (m, 4H, 2C**H₂**), 1.53-1.27 (m, 4H, 2C**H₂**),1.08 (d, *J*=6.5 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 138.9, 131.6, 130.5, 128.2, 68.3, 65.2, 61.7, 42.9, 34.4, 32.3, 31.8, 25.0, 22.0; IR (film):2957, 2866, 1491, 1446, 1372, 1095, 1017, 844, 803 cm^{-1}; HRMS (ESI): Calcd for $C_{15}H_{20}ClN$ $[M+H]^+$: 250.13570, found: 250.13757.

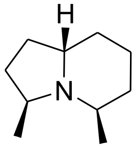
3-(Thiophen-2-ylmethyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4f**)



The title compound 3-(thiophen-2-ylmethyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4f**) (22 mg, 0.10 mmol, 71%) was obtained from (*E*)-1-but-3-enyl-5-

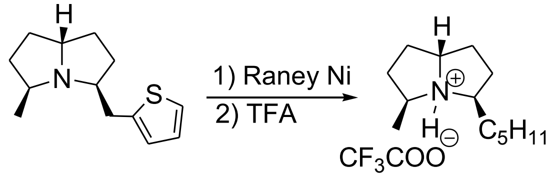
thiophen-2-yl-pent-4-enylamine (**2f**) (31 mg, 0.14 mmol) by the general hydroamination procedure (first ring closure: 10 ºC, 12 h, 95%, second ring closure: 60 ºC, 17 h, 90% based on ^{1}H NMR integration) followed by flash chromatography on basic alumina (1:1 hexane/CH_2Cl_2 followed by 10:1 hexane/EtOAc for elution) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10 (d, *J*=5.0 Hz, 1H, Ar-**H**), 6.90 (t, *J*=4.5 Hz, 1H, Ar-**H**), 6.79 (m, 1H, Ar-**H**), 3.65 (dddd, apparent quintet, *J*=7.0 Hz, 1H, CH_2-C**H-**CH_2), 3.08 (dd, *J*=14.0, 4.0 Hz, 1H, Ar-C**H**), 2.96-2.89 (m, 1H, ArCH_2C**H**), 2.85-2.76 (m, 2H, C**H**CH_3 and Ar-C**H**), 2.00-1.30 (m, 8H, 4C**H₂**), 1.08 (d, *J*=6.5 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 142.6, 126.5, 125.1, 123.4, 68.2, 65.3, 61.8, 37.4, 34.5, 32.4, 32.0, 31.8, 22.0; IR (film) 2957, 1446, 1372, 1106, 688 cm^{-1}; HRMS (ESI): Calcd for $C_{13}H_{20}NS$ $[M+H]^+$: 222.13110, found: 222.13220.

3,5-Dimethyl-3αH,5βH,8aαH-1*H*-octahydro-indolizine (**10**)



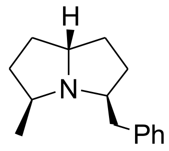
The title compound 3,5-dimethyl-3αH,5βH,8aαH-1*H*-octahydro-indolizine (**10**) was obtained from 1-but-3-enyl-hex-5-enylamine (**8**) (20 mg, 0.15 mmol) by the general hydroamination procedure (first ring closure: 10 ºC, 12 h, 95%, second ring closure: 60 ºC, 45 h, 95% based on ^{1}H NMR integration). ^{1}H NMR (500 MHz, toluene-D_8): δ 3.22 (m, 1H, N-C**H**), 2.95 (m, 1H, N-C**H**), 2.88 (m, 1H, N-C**H**), 1.92-1.20 (m, 10H, 5C**H₂**), 1.17 (d, *J*=7.0 Hz, 3H, C**H₃**), 1.03 (d, *J*=6.0 Hz, 3H, C**H₃**); ^{13}C NMR (500 MHz, toluene-D_8): δ 54.3, 53.2, 47.4, 31.1, 28.9, 27.4, 24.9, 21.5, 19.3. The ^{1}H NMR and ^{13}C NMR spectra were consistent with those reported in the literature.[5,6]

2.7 3-Pentyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine, trifluoroacetate salt (**11**)



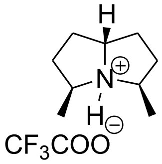
A 25-mL, round-bottomed flask equipped with a magnetic stirring bar and a H_2 balloon inlet was charged with 3-(thiophen-2-ylmethyl)-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4e**) (20 mg, 0.1 mmol), anhydrous THF (1.0 mL) and MeOH (1.0 mL) were subsequently added. Freshly prepared Raney Ni (100 mg as a slurry in 1.0 mL MeOH) was subsequently added. The reactant mixture was stirred for 24 h at room temperature until judged complete by TLC. The reactant mixture was diluted with diethyl ether (10 mL), washed with 10% aqueous NaOH (3.0 mL) and subsequently dried with Na_2SO_4. Following concentration in vacuo, TFA (1M in CH_2Cl_2, 1.0 mL, 1.0 mmol) was added. The reactant mixture was stirred for 2 h at room temperature until judged complete by TLC. The reactant mixture was concentrated in vacuo and washed with hexane (3×1 mL) to afford 3-pentyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine, trifluoroacetate salt (**11**) (17 mg, 0.06 mmol, 64%) as a light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.5 (s, 1H, $^+$N**H**), 4.62 (m, 1H, N-C**H**), 3.31 (m, 1H, N-C**H**), 3.11 (m, 1H, N-C**H**), 2.40-1.60 (m, 10H, 5C**H₂**), 1.50 (d, *J*=6.0 Hz, 3H, C**H₃**), 1.30 (m, 6H, 3C**H₂**), 0.86 (m, 3H, C**H₃**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 69.4, 67.8, 65.0, 33.3, 31.6, 31.3, 31.1, 30.5, 30.2, 26.4, 22.4, 16.6, 13.9; IR (film) 2957, 2935, 2872, 1741, 1672, 1461, 1390, 1202, 799, 718, 703 cm^{-1}; HRMS (-CF_3COOH): Calcd for $C_{13}H_{25}N$ $[M+H]^+$: 196.2060, found: 196.2114.

General large scale (≥1mmol) hydroamination procedure: 3-Benzyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4b**)



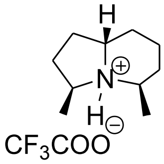
In an argon-filled glove box, Sc[N(TMS)$_2$]$_3$ (11.28 mg, 0.02 mmol) and *N*,*N*'-bis-(2-isopropylphenyl)-ethane-1,2-diamine (6.36 mg, 0.02 mmol) were introduced into a J. Young NMR tube equipped with teflon screw cap, and toluene-D$_8$ (0.5 mL) was subsequently added. The homogeneous reactant mixture was heated in an oil bath maintained at 150 ºC for 3 h to effect ligand exchange as indicated by ^{1}H NMR spectroscopy. (*E*)-1-But-3-enyl-5-phenyl-pent-4-enylamine (**2b**) (231 mg, 1.07 mmol) and *p*-xylene (30 mg) were added to the preformed complex and the reactant mixture was subsequently held at 10 ºC in a cooling bath for 5 d until the first ring closure was judged complete (≥95% by ^{1}H NMR integration). The reactant mixture was subsequently heated at 90 ºC in an oil bath for 14 h until the hydroamination for second ring closure was judged complete (≥95% by ^{1}H NMR integration). Concentration in vacuo followed by flash chromatography on basic alumina (1:1 hexane/CH$_2$Cl$_2$ followed by 10:1 hexane/EtOAc for elution) afforded 3-benzyl-5-methyl-3αH,5αH,7aβH-1*H*-hexahydropyrrolizine (**4b**) (170 mg, 0.79 mmol, 74%) as a light yellow oil. The ^{1}H NMR spectrum was consistent with that previously reported.[4]

3,5-Dimethyl-3αH,5βH,7aβH-1*H*-hexahydropyrrolizine, trifluoroacetate salt (**4a**)



The bicyclic target compound 3,5-dimethyl-3αH,5βH,7aβH-1*H*-hexahydropyrrolizine was obtained from 1-but-3-enylpent-4-enylamine (**2a**) (140 mg, 1.0 mmol) by the general large scale (≥1mmol) hydroamination procedure (first ring closure: 10 ºC, 5 d, ≥95%, second ring closure: 90 ºC, 10 h, ≥95% based on ^{1}H NMR integration). The teflon screw cap was removed and crude product was diluted with anhydrous CH_2Cl_2 (3 mL). After cooling to 0 ºC, TFA (0.08 mL, 1.0 mmol) was added in dropwise and the reactant mixture was stirred at 0 ºC for 1.5 h. The reactant mixture was concentrated in vacuo and washed with hexane (3×1 mL) to afford 3,5-dimethyl-3αH,5βH,7aβH-1*H*-hexahydropyrrolizine, trifluoroacetate salt (**4a**) (250 mg, 1.0 mmol, 98%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.4 (s, 1H, $^+$N**H**), 4.64 (m, 1H, N-C**H**), 3.27 (m, 2H, 2N-C**H**), 2.32 (m, 2H, C$\mathbf{H_2}$), 2.16 (m, 2H, C$\mathbf{H_2}$), 1.96 (m, 2H, C$\mathbf{H_2}$), 1.66 (m, 2H, C$\mathbf{H_2}$), 1.50 (d, *J*=6.5 Hz, 6H, 2C$\mathbf{H_3}$); ^{13}C NMR (500 MHz, $CDCl_3$): δ 67.6, 64.6, 33.9, 30.6, 16.6; IR (film) 2983, 1675, 1394, 1199, 1128, 829, 795, 718 cm^{-1}.

3,5-Dimethyl-3αH,5βH,8aαH-1*H*-octahydro-indolizine, trifluoroacetate salt (**10**)



The bicyclic target compound 3,5-dimethyl-3αH,5βH,8aαH-1*H*-octahydro-indolizine was obtained from 1-but-3-enyl-hex-5-enylamine (**8**) (180 mg, 1.19 mmol) by the general large scale (≥1mmol) hydroamination procedure (first ring closure: 10 ºC, 6 d, ≥95%, second ring closure: 90 ºC, 10.5 d, ≥90% based on ^{1}H NMR integration). The teflon screw cap was removed and crude product was diluted with anhydrous CH_2Cl_2 (3 mL). After cooling to 0 ºC, TFA (0.11 mL, 1.41 mmol) was added in dropwise and the reactant mixture was stirred at 0 ºC for 1.5 h. The reactant mixture was concentrated in vacuo and washed with hexane (3×1 mL) to afford 3,5-dimethyl-3αH,5βH,8aαH-1*H*-octahydro-indolizine, trifluoroacetate salt (**10**) (311 mg, 1.16 mmol, 98%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.2 (s, 1H, $^+$N**H**), 4.06 (m, 1H, N-C**H**), 3.67 (m, 1H, N-C**H**), 3.25 (m, 1H, N-C**H**), 2.32-1.56 (m, 10H, 5C**H$_2$**), 1.49 (d, *J*=6.0 Hz, 3H, C**H$_3$**), 1.47 (d, *J*=6.5 Hz, 3H, C**H$_3$**); ^{13}C NMR (500 MHz, $CDCl_3$): δ 59.7, 58.5, 53.1, 29.2, 27.3, 26.7, 25.0, 17.8, 17.1, 16.7; IR (film) 2954, 1672, 1450, 1199, 1140, 799, 722, 703 cm^{-1}.

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