SUPPORTING INFORMATION

for
the
communication
entitled

Synthesis of Amidines Using *N*-Allyl Ynamides A Palladium-Catalyzed Allyl Transfer Through an Ynamido-π-Allyl Complex.

authored by

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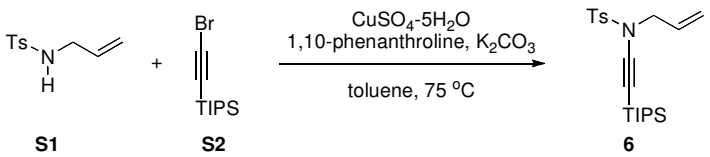
GENERAL EXPERIMENTAL INFORMATION

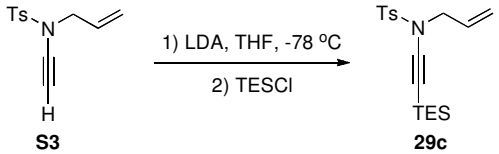
All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased from Aldrich, Acros, Alfa Aesar, or TCI) unless otherwise noted. Chromatographic separations were performed using Silicycle 43-60 Å SiO_2. ^1H and ^{13}C NMR spectra were obtained on Varian VI-400 and VI-500 spectrometers using $CDCl_3$ with TMS or residual solvent as standard unless otherwise noted. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained on Bruker EQUINOX 55 FTIR. TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and $KMnO_4$ stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD and are APCI. High-resolution mass spectral analysis performed at University of Wisconsin School of Pharmacy and Department of Chemistry Mass Spectrometry Laboratories. All spectral data obtained for new compounds are reported here.

General Procedures for Preparation of Ynamides via Cu(I)-catalyzed Cross-Coupling.[1,2]



S1 **S2** **6**

To a flame-dried 100-mL RB-flask was added *N*-allyl tosyl amine **S1** (2.07 g, 9.80 mmol), $CuSO_4$-$5H_2O$ (368.0 mg, 1.47 mmol), phenanthroline (529.0 mg, 2.94 mmol) and K_2CO_3 (3.38 g, 24.5 mmol), followed by anhyd toluene (15 mL) and acetylenic bromide **S2** (3.20 g, 12.3 mmol). The flask was filled with Argon by three vacuum-flush cycles and the solution was heated in a 75 °C-oil bath overnight. When complete, the crude reaction mixture was cooled to rt, filtered through Celite™, and concentrated *in vacuo*. Purification of the crude residue using silica gel flash column chromatography (isocratic eluent: 25:5:1 hexane/CH_2Cl_2/EtOAc) gave the pure ynamide **6**[3] (3.03 g, 7.70 mmol) in 79% yield.

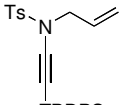


S3 **29c**

To a flame-dried 25-mL RB-flask filled with Nitrogen was added ynamide[3] **S3** (200.0 mg, 0.85 mmol) and anhyd THF (3 mL). To this solution was added a solution of LDA [prepared from di-isopropylamine (108.0 mg, 1.07 mmol) and 2.5 *M n*-BuLi (0.41 mL, 1.02 mmol) in THF (2 mL)] via syringe slowly at -78 °C. The resulting solution was stirred at -78 °C for 20 min, and was then allowed to warm briefly to 0 °C before being cooled to -78 °C. TESCl (256.0 mg, 1.07 mmol) was added at -78 °C, and the resulting solution was warmed to rt and stirred for 2 h before being quenched with H_2O. The mixture was extracted with CH_2Cl_2 (equal volume), dried over Na_2SO_4, and

concentrated *in vacuo*. Purification of the crude residue using silica gel flash column chromatography (isocratic eluent) gave the pure ynamide **29c** (202.0 mg, 0.58 mmol) in 68% yield.

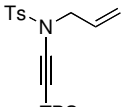
29c: R_f = 0.38 [1:9 EtOAc/hexanes]; colorless oil;
^{1}H NMR (500 MHz, $CDCl_3$) δ 0.56 (q, 6H, *J* = 8 Hz), 0.94 (t, 9H, *J* = 8 Hz), 2.44 (s, 3H), 3.95 (d, 2H, *J* = 6.5 Hz), 5.19 (dd, 1H, *J* = 1.0, 10.0 Hz), 5.22 (dd, 1H, *J* = 1, 17.0 Hz), 5.72 (ddt, 1H, *J* = 6.5, 10.0, 17.0 Hz), 7.32 (d, 2H, *J* = 8.0 Hz), 7.79 (d, 2H, *J* = 8.5 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 4.7, 7.6, 21.8, 54.4, 70.9, 95.5, 120.1, 128.1, 129.8, 130.9, 134.8, 144.8;
IR (thin film) cm^{-1} 2954m, 2165m, 1368s, 1168s, 1016s;
mass spectrum (APCI): m/e (% relative intensity) 350 (100) $(M+H)^+$.



29a

Ynamide **29a** (325.0 mg, 0.69 mmol) was prepared in 80% yield from **S3** according to the general procedure described for **29c**.

29a: R_f = 0.30 [1:13 EtOAc/hexanes]; white solid; mp 46-48 °C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 9H), 2.43 (s, 3H), 4.07 (d, 2H, *J* = 6.4 Hz), 5.24-5.32 (m, 2H), 5.81 (ddt, 1H, *J* = 6.4, 10.4, 16.8 Hz), 7.27 (d, 2H, *J* = 8.4 Hz), 7.32-7.39 (m, 6H), 7.72-7.75 (m, 4H), 7.81 (d, 2H, *J* = 8.4 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 21.9, 27.2, 54.4, 69.4, 98.6, 120.5, 127.8, 128.1, 129.6, 129.9, 131.0, 133.7, 134.8, 135.7, 144.9;
IR (thin film) cm^{-1} 2930m, 2858m, 2167s, 1370s, 1169s, 1108s;
mass spectrum (APCI): m/e (% relative intensity) 474 (100) $(M+H)^+$.

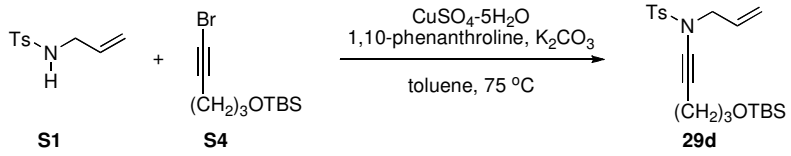


29b

Ynamide **29b** (246.0 mg, 0.70 mmol) was prepared in 83% yield from **S3** according to the general procedure described for **29c**.

29b: R_f = 0.34 [1:9 EtOAc/hexanes]; white solid; mp 66-68 °C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.88 (s, 9H), 2.45 (s, 3H), 3.95 (d, 2H, *J* = 6.4 Hz), 5.18 (dd, 1H, *J* = 1.2, 10.0 Hz), 5.22 (dd, 1H, *J* = 1.0, 16.8 Hz), 5.71 (ddt, 1H, *J* = 6.4, 10, 16.8 Hz), 7.32 (d, 2H, *J* = 8.4 Hz), 7.78 (d, 2H, *J* = 8.4 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) δ -4.3, 16.9, 22.1, 26.2, 54.4, 71.8, 95.4, 120.2, 128.1, 129.6, 130.0, 134.9, 144.8;
IR (thin film) cm^{-1} 2928m, 2856m, 2166s, 1361s, 1169s, 1088s;

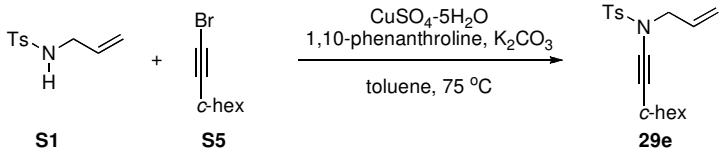
mass spectrum (APCI): m/e (% relative intensity) 350 (100) $(M+H)^+$.



S1 **S4** **29d**

To a flame-dried 100-mL RB-flask was added *N*-allyl sulfonamide **S1** (853.0 mg, 4.00 mmol), $CuSO_4$-$5H_2O$ (150.0 mg, 0.60 mmol), 1,10-phenanthroline (216.0 mg, 1.20 mmol) and K_2CO_3 (1.38 g, 10.0 mmol), anhyd toluene (12 mL), and acetylenic bromide **S4** (1.45 g, 5.26 mmol). The flask was filled with Argon by three vacuum-flush cycles and the solution was heated in a 75 °C-oil bath for 18 h. When complete, the reaction mixture was cooled to rt and filtered through Celite™, and concentrated *in vacuo*. Purification of the crude residue using silica gel flash column chromatography (isocratic eluent: 60:10:2 hexane/CH_2Cl_2/EtOAc) gave the pure ynamide **29d** (1.09 g, 2.69 mmol) in 67% yield.

29d: R_f = 0.21 [60:10:2 hexane/CH_2Cl_2/EtOAc]; colorless oil;
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.0 (s, 6H), 0.85 (s, 9H), 1.63 (quintet, 2H, *J* = 6.4 Hz), 2.30 (t, 2H, *J* = 6.8), 2.41 (s, 3H), 3.6 (t, 2H, *J* = 6.4 Hz), 3.88 (td, 2H, *J* = 1.2, 6.4 Hz), 5.13-5.21 (m, 2H), 5.69 (tdd, *J* = 6.4, 10.4, 16.8 Hz), 7.29 (d, 2H, *J* = 8.2 Hz), 7.74 (d, 2H, *J* = 8.2 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) δ -5.4, 14.8, 18.2, 21.6, 25.9, 32.0, 54.2, 61.4, 69.9, 73.0, 119.5, 127.7, 129.5, 131.1, 134.7, 144.3;
IR (thin film) cm^{-1} 2930m, 2859m, 2256m, 1367s, 1188s;
mass spectrum (APCI): m/e (% relative intensity) 408 (100) $(M+H)^+$.

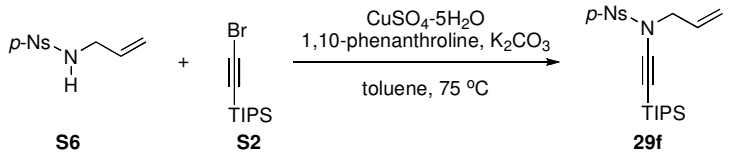


S1 **S5** **29e**

To a flame-dried 50-mL RB-flask was added *N*-allyl sulfonamide **S1** (810.0 mg, 4.35 mmol), $CuSO_4$-$5H_2O$ (126.0 mg, 0.50 mmol), 1,10-phenanthroline (181.0 mg, 1.01 mmol), K_2CO_3 (1.15 g, 8.33 mmol) followed by dry toluene (8 mL) and acetylenic bromide **S5** (707.0 mg, 3.35 mmol). The flask was filled with Argon by three vacuum-flush cycles and the solution was heated in 80 °C oil bath overnight. When complete, the reaction mixture was cooled to rt and filtered through Celite™, and concentrated *in vacuo*. Purification of the crude residue using silica gel flash column chromatography (isocratic eluent: 24:2:1 hexane/CH_2Cl_2/EtOAc) gave **29e** (505.0 mg, 1.60 mmol) in 48% yield.

29e: R_f = 0.22 [1:2:24 EtOAc/CH_2Cl_2/hexanes]; pale yellow oil;
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22-1.52 (m, 6H), 1.58-1.78 (m, 4H), 2.44-2.48 (m, 1H), 2.45 (s, 3H), 3.91 (dt, 2H, *J* = 1.2, 6.4 Hz), 5.15-5.25 (m, 2H), 5.72 (ddt, 1H, *J* = 6.4, 10.0, 16.8 Hz), 7.33 (d, 2H, *J* = 8.4 Hz), 7.80 (d, 2H, *J* = 8.4 Hz);

^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 24.8, 26.1, 28.9, 33.0, 54.5, 73.6, 74.6, 119.8, 128.0, 129.7, 131.38, 134.9, 144.5;
IR (film) cm^{-1} 2929m, 2854m, 2248w, 1364s, 1167s;
mass spectrum (APCI): m/e (% relative intensity) 350 (100) $(M+MeOH+H)^+$.



S6 **S2** **29f**

To a flame-dried 25-mL RB-flask was added *N*-allyl sulfonamide **S6** (500.0 mg, 2.05 mmol), $CuSO_4$-$5H_2O$ (51.0 mg, 0.205 mmol), 1,10-phenanthroline (74.0 mg, 0.41 mmol), K_2CO_3 (707.0 mg, 5.13 g), anhyd toluene (4 mL), and acetylenic bromide **S2** (670.0 mg, 2.56 mmol). The flask was filled with Argon by three vacuum-flush cycles and the solution was then heated in a 80 ^{o}C-oil bath overnight. When complete, solution was then cooled to rt, filtered through Celite^{TM}, and concentrated *in vacuo*. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 15:1 hexane/CH_2Cl_2 to 25:5:1 hexane/CH_2Cl_2/EtOAc) gave **29f** (665.0 mg, 1.57 mmol) in 77% yield.

29f: R_f = 0.35 [1:5 EtOAc/hexanes]; mp 54-55 ^{o}C;
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (s, 21H), 4.05 (d, 2H, J = 6.5 Hz), 5.23-5.20 (m, 2H), 5.73 (ddt, 1H, J = 6.5, 10.0, 16.5 Hz), 8.11 (d, 2H, J = 9.0 Hz), 8.38 (d, 2H, J = 8.5 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.4, 18.7, 54.8, 71.0, 95.0, 121.0, 124.4, 129.3, 130.2, 143.3, 150.8;
IR (thin film) cm^{-1} 2942s, 2865s, 2171s, 1603s, 1403s, 1169s;
mass spectrum (APCI): m/e (% relative intensity) 423 (100) $(M+H)^+$.

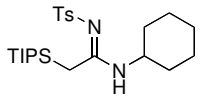
General Procedure for Preparations of Amidines Using Primary Amines.

To a flame-dried 25-mL RB-flask filled with Argon or Nitrogen was added a respective ynamide (0.20 mmol, 1.00 equiv), $Pd(PPh_3)_4$ (0.010 mmol, 0.050 equiv), K_2CO_3 (0.20 mmol, 1.00 equiv), and a respective primary amine (0.60 mmol, 3.00 equiv), followed by anhyd THF (4 mL). The resulting reaction mixture was stirred under argon at a 70 ^oC-oil bath for 5-8 h. The progress of the reaction was monitored by TLC. After complete consumption of the starting ynamide, the crude reaction mixture was allowed to cool to rt, filtered through Celite™, and concentrated *in vacuo*. Purification of the crude residue via silica gel flash column chromatography afforded the desired amidine product.

General Procedure for Preparations of Amidine Using Secondary Amines.

To a flame-dried 25-mL RB-flask filled with Argon or Nitrogen was added $Pd_2(dba)_3$ (0.010 mmol, 0.050 equiv), xantphos (0.020 mmol, 0.10 equiv), and anhyd THF (4 mL). The resulting solution was stirred at rt for 10 min. Subsequently, a respective ynamide (0.20 mmol, 1.00 equiv), K_2CO_3 (0.20 mmol, 1.00 equiv), and a respective secondary amine (0.60 mmol, 3.00 equiv) were added. The reaction mixture was stirred under Argon at in a 70 ^oC-oil bath for 2-6 h. The progress of the reaction was monitored by TLC. After complete consumption of the starting ynamide, the crude reaction mixture was allowed to cool to rt, filtered through Celite™, and concentrated *in vacuo*. Purification of the crude residue via silica gel flash column chromatography afforded the desired amidine product.

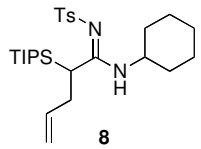
Characterizations of Amidines.



7

Amidine **7** (85.0 mg, 0.20 mmol) was prepared in 63% yield from ynamide **6** (117.0 mg, 0.30 mmol) and cyclohexylamine (89.0 mg, 0.90 mmol) following the general procedure *but with $Pd(PPh_3)_2Cl_2$ (10.5 mg, 0.015 mmol) as the catalyst.*

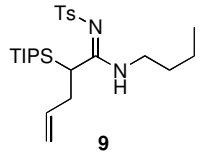
7: R_f = 0.22 [1:9 EtOAc/hexanes]; white solid, mp 112-114 °C;
^{1}H NMR (400 MHz, $CDCl_3$) *(showing as two rotamers in 3:1 ratio)* major rotamer δ 0.96-1.15 (m, 21H), 1.24-1.91 (m, 10H), 2.39 (s, 3H), 2.39 (s, 2H), 3.36-3.88 (m, 1H), 7.22 (d, 2H, J = 8.0 Hz), 7.75 (d, 2H, J = 8.4 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) major rotamer δ 11.4, 17.8, 18.4, 21.4, 24.4, 25.0, 33.3, 53.3, 126.2, 128.8, 140.2, 142.0, 168.2;
IR (film) cm^{-1} 3314m, 2931m, 1524s, 1260s, 1159s;
mass spectrum (APCI): m/e (% relative intensity) 451 (100) $(M+H)^+$.



8

Amidine **8** (98.0 mg, 0.20 mmol) was prepared in ≥95% yield from ynamide **6** (78.0 mg, 0.20 mmol) and cyclohexylamine (59.5 mg, 0.60 mmol) following the general procedure.

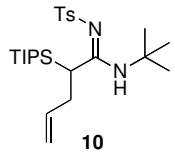
8: R_f = 0.23 [1:5 EtOAc/hexanes]; colorless oil;
^{1}H NMR (400 MHz, $CDCl_3$) *(showing as two rotamers in 10:1 ratio)* major rotamer δ 1.03 (d, 9H, *J* = 7.0 Hz), 1.04 (d, 9H, *J* = 7.0 Hz), 1.08-1.17 (m, 3H), 1.21-1.89 (m, 10H), 2.14 (dd, 1H, *J* = 2.4, 12.0 Hz), 2.25 (dd, 1H, *J* = 7.8, 13.5 Hz), 2.38 (s, 3H), 2.70 (dt, *J* = 6.8, 12.8 Hz), 3.39-3.42 (m, 1H), 4.76-4.81 (m, 2H), 5.46-5.56 (m, 1H), 7.21 (d, 2H, *J* = 8.2 Hz), 7.75 (d, 2H, *J* = 8.2 Hz), 8.38 (d, 1H, *J* = 8.6 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) major rotamer δ 11.4, 18.9, 18.9, 21.4, 24.5, 25.0, 31.3, 32.8, 34.6, 34.7, 52.8, 115.8, 126.3, 128.8, 137.4, 140.2, 142.0, 170.2;
IR (film) cm^{-1} 3274m, 2931m, 2865s, 1588s, 1271s, 1136s;
mass spectrum (APCI): m/e (% relative intensity) 491 (100) $(M+H)^+$.



9

Amidine **9** (91.0 mg, 0.196 mmol) was prepared in ≥95% yield from ynamide **6** (78.0 mg, 0.20 mmol) and *n*-butylamine (44.0 mg, 0.60 mmol) following the general procedure.

9: R_f = 0.25 [1:9 EtOAc/hexanes]; colorless oil;
^{1}H NMR (400 MHz, $CDCl_3$) *(showing as two rotamers in 1.2:1 ratio)* major rotamer δ 0.80 (t, 3H, *J* = 7.4 Hz), 1.10 (s, 9H), 1.12 (s, 9H), 1.16-1.21 (m, 3H), 1.31-1.57 (m, 4H), 2.36 (s, 3H), 2.60 (s, 1H), 2.62 (sbr, 1H), 3.29-3.33 (m, 2H), 3.89-3.91 (m, 2H); 5.07-5.24 (m, 2H), 5.67-5.77 (m, 1H), 7.19 (d, 2H, *J* = 8.0 Hz), 7.76 (d, 2H, *J* = 8.0 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) for both rotamers δ 12.3, 13.6, 13.8, 16.5, 18.7, 18.8, 20.1, 20.3, 21.4, 28.8, 30.3, 48.5, 49.5, 51.6, 51.7, 117.7, 118.6, 125.8, 125.9, 128.8, 128.8, 131.5, 132.6, 141.1, 141.1, 142.4, 168.0, 168.5 *(three sp^3 and one sp^2 signals missing due to overlap or line-broadening)*;
IR (film) cm^{-1} 2941m, 2867m, 1524s, 1272s, 1197s;
mass spectrum (APCI): m/e (% relative intensity) 465 (100) $(M+H)^+$.

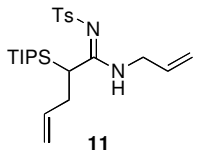


10

Amidine **10** (84.0 mg, 0.18 mmol) was prepared in ≥95% yield from ynamide **6** (78.0 mg, 0.20 mmol) and *tert*-butylamine (44.0 mg, 0.60 mmol) following the general procedure.

10: R_f = 0.25 [1:10 EtOAc/hexanes]; white solid; mp 107-110 ^oC;

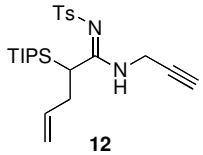
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (d, 9H, *J* = 7.4 Hz), 1.15 (d, 9H, *J* = 7.2 Hz), 1.25 (s, 9H), 1.21-1.35 (m, 3H), 2.18 (ddd, 1H, *J* = 8.8, 14, 14 Hz), 2.35 (s, 3H), 2.56-2.62 (m, 1H), 3.80 (dd, 1H, *J* = 3.7, 12.9 Hz), 4.89-4.96 (m, 2H), 5.02 (sbr, 1H), 5.67-5.77 (m, 1H), 7.19 (d, 2H, *J* = 8.0 Hz), 7.76 (d, 2H, *J* = 8.0 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 19.1, 19.1, 21.4, 28.5, 31.5, 36.0, 53.1, 115.9, 126.1, 128.8, 136.5, 141.3, 141.8, 168.6;
IR (film) cm^{-1} 3408m, 2943m, 2867s, 1524s, 1271s, 1142s;
mass spectrum (APCI): m/e (% relative intensity) 465 (100) $(M+H)^+$.



11

Amidine **11** (65.0 mg, 0.145 mmol) was prepared in 73% yield from ynamide **6** (78.0 mg, 0.60 mmol) and allylamine (34.0 mg, 0.60 mmol) following the general procedure.

11: R_f = 0.23 [1:7 EtOAc/hexanes]; colorless oil;
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (d, 9H, *J* = 7.0 Hz), 1.03 (d, 9H, *J* = 7.0 Hz), 1.09-1.18 (m, 3H), 2.19 (dd, 1H, *J* = 2.4, 11.9 Hz), 2.28 (dd, 1H, *J* = 7.4, 12.6 Hz), 2.38 (s, 3H), 2.66 (ddd, 1H, *J* = 7.2, 12.8, 12.8 Hz), 3.81-3.98 (m, 2H), 4.74-4.79 (m, 2H), 5.22-5.30 (m, 2H), 5.51 (tdd, 1H, *J* = 7.2, 10.1, 16.8 Hz), 5.79 (tdd, 1H, *J* = 6.4, 10.5, 17.2 Hz), 7.21 (d, 2H, *J* = 8.0 Hz), 7.75 (d, 2H, *J* = 8.2 Hz), 8.42 (sbr, 1H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 18.8, 18.9, 21.4, 31.0, 34.7, 46.4, 115.9, 118.2, 126.3, 128.8, 132.2, 137.1, 140.0, 142.1, 171.5;
IR (film) cm^{-1} 3367m, 2944m, 2867s, 1530s, 1136s;
mass spectrum (APCI): m/e (% relative intensity) 449 (100) $(M+H)^+$.

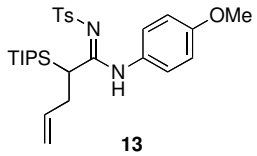


12

Amidine **12** (68.0 mg, 0.152 mmol) was prepared in 76% yield from ynamide **6** (78.0 mg, 0.20 mmol) and propargyl amine (33.0 mg, 0.60 mmol) following the general procedure.

12: R_f = 0.24 [1:6 EtOAc/hexanes]; colorless oil;
^{1}H NMR (400 MHz, $CDCl_3$) *(showing as two rotamers in 4:1 ratio)* major rotamer δ 1.03 (d, 9H, *J* = 7.0 Hz), 1.04 (d, 9H, *J* = 7.0 Hz), 1.09-1.20 (m, 3H), 2.21 (dd, 1H, *J* = 2.5, 11.9 Hz), 2.28-2.35 (m, 1H), 2.36 (t, 1H, *J* = 2.4 Hz), 2.40 (s, 3H), 2.64 (ddd, 1H, *J* = 7.2, 12.8, 12.8 Hz), 4.06 (dd, 2H, *J* = 2.6, 5.4 Hz), 4.78-4.83 (m, 2H), 5.56-5.63 (m, 1H), 7.24 (d, 2H, *J* = 8.0 Hz), 7.78 (d, 2H, *J* = 8.2 Hz), 8.57 (t, 1H, *J* = 4.5 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) major rotamer δ 11.3, 18.8, 18.9, 21.4, 31.1, 33.6, 35.0, 73.8, 77.5, 116.2, 126.4, 128.9, 136.8, 139.7, 142.4, 171.4;
IR (film) cm^{-1} 2944m, 2868m, 1464s, 1163s;

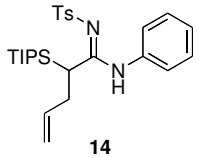
mass spectrum (APCI): m/e (% relative intensity) 447 (100) $(M+H)^+$.



13

Amidine **13** (69.0 mg, 0.134 mmol) was prepared in 67% yield from ynamide **6** (78.0 mg, 0.20 mmol) and *p*-anisidine (74.0 mg, 0.60 mmol) following the general procedure.

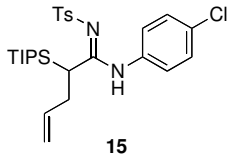
13: R_f = 0.40 [1:6 EtOAc/hexanes]; white solid; mp 78-81 ^oC;
^1H NMR (500 MHz, $CDCl_3$) δ 0.89 (d, 9H, *J* = 7.3 Hz), 0.97 (d, 9H, *J* = 7.3 Hz), 1.02-1.10 (m, 3H), 2.24 (dd, 1H, *J* = 7.5, 13 Hz), 2.42 (s, 3H), 2.76 (ddd, 1H, *J* = 7.5, 12.5, 12.5 Hz), 3.81 (s, 3H), 4.83-4.91 (m, 2H), 5.63 (ddt, 1H, *J* = 7.5, 10.0, 17.0 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 7.07 (d, 2H, *J* = 8.8 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 7.84 (d, 2H, *J* = 8.0 Hz), 9.91 (s, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.4, 18.7, 18.8, 21.5, 30.8, 34.8, 55.5, 114.3, 116.1, 126.5, 128.3, 129.0, 129.5, 137.3, 139.8, 142.4, 158.8, 171.2;
IR (film) cm^{-1} 3240m, 2941m, 2866m, 1509s, 1251s;
mass spectrum (APCI): m/e (% relative intensity) 513 (100) $(M-H)^-$.



14

Amidine **14** (82.0 mg, 0.17 mmol) was prepared in 85% yield from ynamide **6** (78.0 mg, 0.20 mmol) and aniline (22.3.0 mg, 0.24 mmol) following the general procedure.

14: R_f = 0.26 [1:10 EtOAc/hexanes]; white solid; mp 102-104 ^oC;
^1H NMR (500 MHz, $CDCl_3$) δ 0.91 (d, 9H, *J* = 7.0 Hz), 1.01 (d, 9H, *J* = 7.0 Hz), 1.07-1.12 (m, 3H), 2.30 (m, 1H), 2.46 (s, 3H), 2.56 (d, 1H, *J* = 11.5 Hz), 2.83 (dt, *J* = 7.3, 12.6 Hz), 4.90-4.98 (m, 2H), 5.71 (ddt, 1H, *J* = 7.3, 9.8, 17.0 Hz), 7.21 (d, 2H, *J* = 7.8 Hz), 7.30-7.34 (m, 3H), 7.40-7.43 (m, 2H), 7.89 (d, 2H, *J* = 8.0 Hz), 10.11 (s, 1H);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.4, 18.6, 18.7, 21.4, 30.9, 34.6, 116.2, 126.5, 126.7, 127.4, 129.0, 129.3, 136.8, 127.2, 139.7, 142.4, 170.9;
IR (film) cm^{-1} 3270m, 2941m, 2864m, 1579s, 1275s;
mass spectrum (APCI): m/e (% relative intensity) 485 (100) $(M+H)^+$.

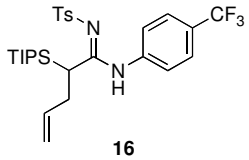


15

Amidine **15** (81.0 mg, 0.156 mmol) was prepared in 78% yield from ynamide **6** (78.0 mg, 0.20 mmol) and *p*-chloroaniline (77.0 mg, 0.60 mmol) following the general procedure.

15: R_f = 0.24 [1:9 EtOAc/hexanes]; white solid; mp 136-138 ^oC;

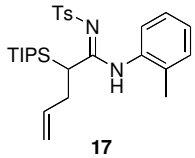
^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (d, 9H, *J* = 6.8 Hz), 0.97 (d, 9H, *J* = 7.0 Hz), 1.05-1.06 (m, 3H), 2.24-2.28 (m, 1H), 2.42 (s, 3H), 2.42-2.45 (m, 1H), 2.74-2.77 (m, 1H), 4.87-4.94 (m, 2H), 5.66 (ddt, 1H, *J* = 7.0, 9.5, 17.0 Hz), 7.11 (d, 2H, *J* = 8.5 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.34 (d, 2H, *J* = 8.5 Hz), 7.83 (d, 2H, *J* = 8.0 Hz), 10.0 (brs, 1H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.6, 18.7, 21.4, 31.1, 34.6, 116.5, 126.5, 128.0, 129.0, 129.4, 133.2, 135.4, 137.1, 139.5, 142.6, 170.6;
IR (film) cm^{-1} 3263m, 2939m, 2864m, 1601s, 1574s, 1269s, 1137s;
mass spectrum (APCI): m/e (% relative intensity) 519 (100) $(M+H)^+$.



16

Amidine **16** (55.0 mg, 0.107 mmol) was prepared in 54% yield from ynamide **6** (78.0 mg, 0.20 mmol) and 4-trifluoromethyl-aniline (96.0 mg, 0.60 mmol) following the general procedure.

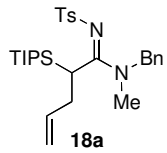
16: R_f = 0.22 [1:9 EtOAc/hexanes]; white solid; mp 106-109 °C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, 9H, *J* = 6.8 Hz), 0.96 (d, 9H, *J* = 6.8 Hz), 1.04-1.05 (m, 3H), 2.23-2.28 (m, 1H), 2.41 (s, 3H), 2.41 (brs, 1H), 2.75-2.83 (m, 1H), 4.90-4.96 (m, 2H), 5.70 (ddt, 1H, *J* = 7.2, 10.0, 17.0 Hz), 7.26, (d, 2H, *J* = 7.8 Hz), 7.30 (d, 2H, *J* = 8.3 Hz), 7.62 (d, 2H, *J* = 8.4 Hz), 7.82 (d, 2H, *J* = 8.2 Hz), 10.12 (brs, 1H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.5, 18.7, 21.5, 31.3, 34.6, 116.7, 126.4, 126.4, 126.5, 126.7 (q, $J_{C\text{-}F}$ = 272 Hz), 129.1, 137.0, 139.3, 140.2, 140.2, 142.8, 170.3;
IR (film) cm^{-1} 3264m, 2950m, 2866m, 1579s, 1323s;
mass spectrum (APCI): m/e (% relative intensity) 553 (100) $(M+H)^+$.



17

Amidine **17** (52.0 mg, 0.104 mmol) was prepared in 52% yield from ynamide **6** (78.0 mg, 0.20 mmol) and *o*-toluidine (64.0 mg, 0.60 mmol) following the general procedure.

17: R_f = 0.28 [1:9 EtOAc/hexanes]; white solid; mp 74-76 °C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, 9H, *J* = 7.0 Hz), 0.98 (d, 9H, *J* = 7.0 Hz), 1.00-1.10 (m, 3H), 2.25-2.28 (m, 1H), 2.32 (s, 3H), 2.41 (s, 3H), 2.67 (d, 1H, *J* = 12.0 Hz), 2.79 (dt, *J* = 7.0, 12.0 Hz), 4.84-4.89 (m, 2H), 5.62 (ddt, 1H, *J* = 7.2, 10.0, 17.0 Hz), 7.14-7.23 (m, 4H), 7.26 (d, 2H, *J* = 8.4 Hz), 7.84 (d, 2H, *J* = 8.4 Hz), 10.04 (brs, 1H);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 18.0, 18.6, 18.8, 21.4, 30.3, 34.9, 116.3, 126.3, 126.4, 127.1, 129.0, 131.2, 132.9, 135.5, 137.2, 139.7, 142.4, 170.8 *(one aryl carbon missing due to overlap or line-broadening)*;
IR (film) cm^{-1} 2938m, 2863m, 1578s, 1273s;
mass spectrum (APCI): m/e (% relative intensity) 499 (100) $(M+H)^+$.



18a

Amidine **18a** (95.2 mg, 0.19 mmol) was prepared in 93% yield from ynamide **6** (78.0 mg, 0.20 mmol) and *N*-methyl-benzylamine (120.0 mg, 1.00 mmol) with $Pd_2(dba)_3$ (18.0 mg, 0.022 mmol) and xantphos (23.0 mg, 0.040 mmol) as the catalyst system following the general procedure.

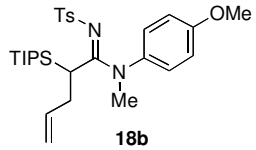
18a: R_f = 0.43 [1:5 EtOAc/hexanes]; white solid; mp 103-105 ºC

^{1}H NMR (500 MHz, toluene-d_8, 75 ºC) *(due to rotamers, many of the signals were not well-resolved and/or line-broadened)* δ 1.05-1.22 (brs, 18H), 1.22-1.43 (brs, 3H), 2.01 (s, 3H), 2.40 (brs, 1H), 2.55 (brs, 1H), 2.80-3.12 (brs, 3H), 4.23 (brs, 1H), 4.78 (brs, 1H), 4.85-4.96 (m, 2H), 5.96 (brs, 1H), 6.89 (d, 2H, *J* = 7.6 Hz), 7.01-7.22 (m, 5H), 7.93 (d, 2H, *J* = 7.6 Hz);

^{13}C NMR (100 MHz, $CDCl_3$): Not recorded due to complications of rotamers;

IR (film) cm^{-1} 2944m, 1538s, 1302s, 1140s, 873s;

mass spectrum (APCI): m/e (% relative intensity) 513 (100) $(M+H)^+$.



18b

Amidine **18b** (41.0 mg, 0.078 mmol) was prepared in 41% yield from ynamide **6** (75.0 mg, 0.192 mmol) and 4-methoxy-*N*-methylaniline (79.0 mg, 0.58 mmol) with $Pd_2(dba)_3$ (8.80 mg, 0.010 mmol) and xantphos (11.1 mg, 0.020 mmol) as the catalyst system following the general procedure.

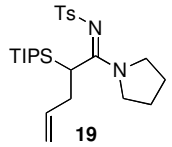
18: R_f = 0.40 [1:3 EtOAc/hexanes]; pale yellow oil;

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (d, 9H, *J* = 7.5 Hz), 0.99 (d, 9H, *J* = 7.5 Hz), 1.12-1.16 (m, 3H), 1.26 (brs, 1H), 2.02-2.03 (m, 1H), 2.18-2.21 (m, 1H), 2.40 (s, 3H), 3.82 (s, 3H), 3.83 (s, 3H), 4.83 (d, 1H, *J* = 16.9 Hz), 4.95 (d, 1H, *J* = 10.2 Hz), 5.65 (m, 1H), 6.89 (d, 2H, *J* = 8.4 Hz), 7.17 (d, 2H, *J* = 8.4 Hz), 7.24 (d, 2H, *J* = 8.0 Hz), 7.86 (d, 2H, *J* = 8.0 Hz);

^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 19.2, 21.7, 29.97, 35.4, 35.9, 46.7, 55.8, 114.8, 116.0, 126.26, 129.1, 137.9, 138.2, 141.4, 143.1, 159.4, 170.8 *(one sp^2 carbon missing due to overlap or line-broadening)*;

IR (film) cm^{-1} 2944m, 2868m, 1540s, 1509s, 1142s;

mass spectrum (APCI): m/e (% relative intensity) 529 (100) $(M+H)^+$.

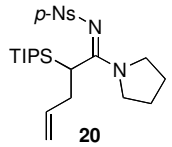


19

Amidine **19** (95.0 mg, 0.202 mmol) was prepared in ≥95% yield from ynamide **6** (79.0 mg, 0.202 mmol) and pyrrolidine (41.0 mg, 0.6 mmol) with $Pd_2(dba)_3$ (8.90 mg, 0.010 mmol) and xantphos (11.2 mg, 0.020 mmol) as the catalyst system following the general procedure.

19: R_f = 0.22 [1:5 EtOAc/hexanes]; white solid; mp 75-76 ^{o}C;

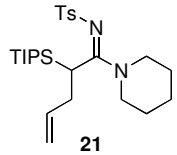
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, 18H, *J* = 6.0 Hz), 1.16 (m, 3H), 1.76-1.82 (m, 1H), 1.92-2.08 (m, 3H), 2.17-2.22 (m, 1H), 2.26-2.29 (m, 1H), 2.38 (s, 3H), 2.44-2.52 (m, 1H), 3.56 (q, 1H, *J* = 8.0 Hz), 3.68 (td, 1H, *J* = 8.0, 2.4 Hz), 4.22 (brs, 2H), 4.97 (d, 1H, *J* = 10.8 Hz), 5.02 (d, 1H, *J* = 17.6 Hz), 5.81 (m, 1H), 7.20 (d, 2H, *J* = 8.4 Hz), 7.78 (d, 2H, *J* = 8.4 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.5, 19.1, 21.5, 25.4, 25.8, 35.8, 35.9, 51.8, 53.2, 116.0, 126.1, 128.8, 137.8, 140.9, 143.2, 167.1;
IR (neat) cm^{-1} 2924ms, 2863m, 1547s, 1414s, 1274s, 1139s;
mass spectrum (APCI): m/e (% relative intensity) 463 (100) $(M+H)^+$.



20

Amidine **20** (100.0 mg, 0.202 mmol) was prepared in 95% yield from ynamide **29f** (90.0 mg, 0.212 mmol) and pyrrolidine (45.0 mg, 0.638 mmol) with $Pd_2(dba)_3$ (9.70 mg, 0.011 mmol) and xantphos (12.3 mg, 0.021 mmol) as the catalyst system following the general procedure.

20: R_f = 0.12 [1:4 EtOAc/hexanes]; white solid; mp 84-85 °C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (d, 18H, *J* = 6.8 Hz), 1.08-1.17 (m, 3H), 1.80-1.86 (m, 1H), 1.99-2.09 (m, 3H), 2.19-2.24 (m, 1H), 2.30-2.38 (m, 2H), 3.60 (qt, 1H, *J* = 10.4 Hz), 3.72 (td, 1H, *J* = 10.4, 2.8 Hz), 4.18-4.20 (m, 2H), 5.00-5.04 (m, 2H), 5.78-5.82 (m, 1H), 8.07 (d, 2H, *J* = 8.8 Hz), 8.28 (d, 2H, *J* = 9.2 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 19.0, 25.4, 25.7, 35.7, 36.0, 52.0, 53.4, 116.4, 123.8, 127.2, 137.3, 149.0, 151.3, 168.2;
IR (thin film) cm^{-1} 2944m, 2865m, 2176s, 1726s, 1529s, 1287s, 1145s;
mass spectrum (APCI): m/e (% relative intensity) 494 (100) $(M+H)^+$.

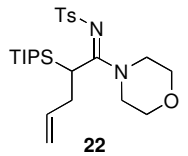


21

Amidine **21** (94.3 mg, 0.198 mmol) was prepared in 99% yield from ynamide **6** (78.0 mg, 0.20 mmol) and piperidine (116.0 mg, 0.990 mmol) with $Pd_2(dba)_3$ (18.0 mg, 0.020 mmol) and xantphos (23.0 mg, 0.040 mmol) as the catalyst system following the general procedure.

21: R_f = 0.40 [1:5 EtOAc/hexanes]; pale yellow solid; mp 114-118 ºC
^{1}H NMR (400 MHz, $CDCl_3$) *(due to rotamers, many of the signals were not well-resolved and/or line-broadened)* δ 0.85-1.16 (brs, 18H), 1.16-1.38 (brs, 5H), 1.53-1.87 (brs, 6H), 2.26-2.48 (brs, 5H), 3.43-3.84 (m, 3H,), 4.89-5.02 (m, 2H), 5.76 (m, 1 H), 7.20 (d, 2 H, *J* = 8.0 Hz), 7.78 (d, 2 H, *J* = 8.1 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.8, 19.3, 19.4, 21.7, 24.3, 26.0, 30.0, 35.4, 116.0, 126.2, 129.0, 138.1, 141.2, 143.0, 169.9;
IR (film) cm^{-1} 2927s, 2863s, 1731m, 1538s, 1270s;

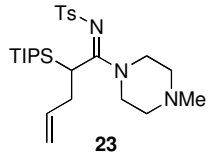
mass spectrum (APCI): m/e (% relative intensity) 477 (100) $(M+H)^+$.



22

Amidine **22** (76.0 mg, 0.159 mmol) was prepared in 79% yield from ynamide **6** (78.0 mg, 0.20 mmol) and morpholine (52.0 mg, 0.60 mmol) with $Pd(PPh_3)_4$ (11.5 mg, 0.010 mmol) as the catalyst system following the general procedure.

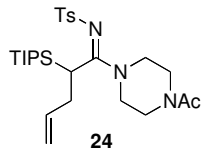
22: R_f = 0.26 [1:3 EtOAc/hexanes]; white solid; mp 122-124 °C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 9H), 1.05 (s, 9H), 1.10-1.17 (m, 3H), 2.22-2.42 (brs, 3H), 2.39 (s, 3H), 3.66 (m, 6H), 3.93 (brs, 2H), 4.95-4.98 (m, 2H), 5.72-5.76 (m, 1H), 7.22 (d, 2H, J = 8.0 Hz), 7.78 (d, 2H, J = 8.0 Hz);
^{13}C NMR (100 MHz, $CDCl_3$) δ 11.4, 18.9, 19.0, 21.4, 34.9, 66.5, 116.1, 125.9, 128.8, 137.4, 141.3, 142.2, 169.4 *(two sp^3 carbon missing due to overlap or line-broadening)*;
IR (film) cm^{-1} 2946m, 2867m, 1638s, 1269s, 1134s;
mass spectrum (APCI): m/e (% relative intensity) 479 (100) $(M+H)^+$.



23

Amidine **23** (120.0 mg, 0.243 mmol) was prepared in ≥95% yield from ynamide **6** (100.0 mg, 0.26 mmol) and 1-methylpiperazine (77.0 mg, 0.77 mmol) with $Pd_2(dba)_3$ (11.7 mg, 0.013 mmol) and xantphos (14.8 mg, 0.026 mmol) as the catalyst system following the general procedure.

23: R_f = 0.33 [1:1 EtOAc/hexanes + 5% MeOH];
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (brs, 18H), 1.23-1.25 (m, 3H), 2.32 (s, 3H), 2.37 (s, 3H), 2.41-2.65 (brm, 5H), 3.67 (brs, 2H), 4.92-4.98 (m, 2H), 5.74 (m, 1H), 7.20 (d, 2H, J = 8.0 Hz), 7.76 (d, 2H, J = 8.0 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 14.3, 19.2, 19.3, 21.6, 22.8, 31.8, 35.1, 45.8, 54.8, 116.1, 126.1, 129.0, 137.8, 141.3, 142.6, 169.6;
IR (thin film) cm^{-1} 2942m, 2866m, 1527s, 1457s, 1273s, 1138s, 1089s;
mass spectrum (APCI): m/e (% relative intensity) 492 (100) $(M+H)^+$.

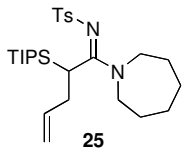


24

Amidine **24** (52.0 mg, 0.10 mmol) was prepared in 77% yield from ynamide **6** (49.8 mg, 0.13 mmol) and 1-acetylpiperazine (49.2 mg, 0.38 mmol) with $Pd_2(dba)_3$ (5.80 mg, 0.0060 mmol) and xantphos (7.40 mg, 0.013 mmol) as the catalyst system following the general procedure.

24: R_f = 0.29 [EtOAc]; orange-brown solid; mp 118-122 ºC

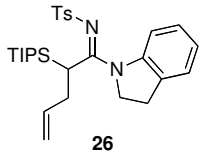
^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (brs, 18H), 1.14-1.29 (m, 3H), 2.12 (s, 3H), 2.32-2.41 (m, 3H), 2.39 (s, 3H), 3.64-3.79 (brm, 8H), 4.95-5.02 (m, 2H), 5.75 (m, 1 H), 7.23 (d, 2 H, *J* = 8.2 Hz), 7.75 (d, 2 H, *J* = 8.2 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 19.3, 21.5, 21.7, 35.3, 41.4, 45.8, 50.2, 116.6, 126.2, 129.2, 137.6, 141.8, 142.2, 169.6, 170.2;
IR (film) cm^{-1} 2927s, 2864s, 1729 m, 1657s, 1426s, 1140s;
mass spectrum (APCI): m/e (% relative intensity) 520 (100) $(M+H)^+$.



25

Amidine **25** (100.0 mg, 0.20 mmol) was prepared in ≥95% yield from ynamide **6** (80.0 mg, 0.20 mmol) and hexamethyleneimine (61.0 mg, 0.61 mmol) with $Pd_2(dba)_3$ (9.30 mg, 0.010 mmol) and xantphos (11.8 mg, 0.020 mmol) as the catalyst system following the general procedure.

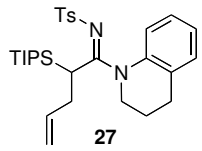
25: R_f = 0.33 [1:5 EtOAc/hexanes]; white solid, mp 87-89 °C;
^{1}H NMR (500 MHz, d_8-toluene, 90 °C) δ 1.09 (s, 18H), 1.3`2-1.36 (m, 8H), 1.51-1.52 (m, 4H), 2.02 (s, 3H), 2.42 (brs, 1H), 2.67 (brs, 1H), 3.48-3.50 (m, 4H), 4.97 (d, 1H, *J* = 10.0 Hz), 5.06 (d, 1H, *J* = 17.0 Hz), 6.89 (d, 2H, *J* = 7.5 Hz), 7.94 (d, 2H, *J* = 7.5 Hz);
^{13}C NMR (100 MHz, $CDCl_3$): Not recorded due to complications of rotamers;
IR (thin film) cm^{-1} 2926m, 1514s, 1452s, 1262s, 1136s, 1089s;
mass spectrum (APCI): m/e (% relative intensity) 491 (100) $(M+H)^+$.



26

Amidine **26** (59.0 mg, 0.20 mmol) was prepared in 61% yield from ynamide **6** (75.0 mg, 0.19 mmol) and indoline (68.0 mg, 0.57 mmol) with $Pd_2(dba)_3$ (8.80 mg, 0.010 mmol) and xantphos (11.0 mg, 0.020 mmol) as the catalyst system following the general procedure.

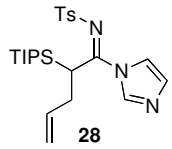
26: R_f = 0.31 [1:5 EtOAc:hexanes]; pale yellow solid; mp 136-137 ºC;
^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78-0.94 (m, 9H), 0.94-1.03 (m, 9H), 1.09 (brs, 3H), 2.22-2.26 (m, 1H), 2.41 (s, 3H), 2.58-2.62 (m, 1H), 2.94 (dd, 1H, *J* = 15.5, 8.7 Hz), 3.12-3.15 (m, 1H), 3.36 (d, 1H, *J* = 8.8 Hz), 4.61-4.86 (m, 2H), 4.96-5.11 (m, 2H), 5.90-5.96 (m, 1H), 7.07-7.30 (m, 2H), 7.25 (d, 2H, *J* = 8.2 Hz), 7.24-7.26 (m, 1H), 7.48 (d, 1 H, *J* = 6.4 Hz), 7.84 (d, 2 H, *J* = 8.2 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 11.9, 18.9, 19.2, 21.7, 29.3, 32.4, 35.4, 58.8, 116.6, 118.1, 125.7, 126.1, 126.3, 127.1, 129.2, 135.3, 138.3, 141.7, 142.5, 143.3, 168.2;
IR (film) cm^{-1} 2942m, 2866m, 1518s, 694s;
mass spectrum (APCI): m/e (% relative intensity) 509 (100) $(M-H)^-$.



27

Amidine **27** (38.0 mg, 0.073 mmol) was prepared in 57% yield from ynamide **6** (50.2 mg, 0.13 mmol) and 1,2,3,4-tetrahydroquinoline (51.0 mg, 0.38 mmol) with $Pd_2(dba)_3$ (5.80 mg, 0.0060 mmol) and xantphos (7.40 mg, 0.013 mmol) as the catalyst system following the general procedure.

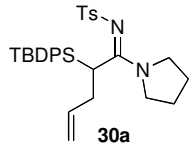
27: R_f = 0.43 [1:3 EtOAc:hexanes]; brown solid; mp 122-125 ºC;
^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (d, 9 H, *J* = 5.9 Hz), 1.00-1.10 (m, 12 H), 1.28-1.46 (m, 1H), 1.90 (m, 1H), 2.25-2.29 (m, 1H), 2.40 (s, 3H), 2.51-2.57 (m, 1H), 2.70-2.75 (m, 1H), 2.77-2.81 (m, 1H), 2.99 (brs, 1H), 4.05 (brs, 1H), 4.59 (brs, 1H), 4.87 (d, 1H, *J* = 17.1 Hz), 5.02 (d, 1H, *J* = 9.2 Hz), 5.83-5.92 (m, 1H), 7.08-7.16 (m, 3H), 7.24 (d, 2H, *J* = 8.2 Hz), 7.30 (d, 1H, *J* = 6.5 Hz), 7.84 (d, 2H, *J* = 8.2 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 18.8, 19.0, 21.7, 24.9, 26.3, 33.8, 35.4, 38.9, 116.3, 126.3, 126.6, 128.9, 129.1, 131.1, 132.7, 134.0, 138.3, 139.8, 141.5, 142.6, 170.9;
IR (film) cm^{-1} 2929, 1729m, 1518s, 1280s, 1142s, 1089s
mass spectrum (APCI): m/e (% relative intensity) 525 (100) $(M+H)^+$.



28

Amidine **28** (52.0 mg, 0.11 mmol) was prepared in 58% yield from ynamide **6** (75.0 mg, 0.19 mmol) and imidazole (40.0 mg, 0.588 mmol) with $Pd_2(dba)_3$ (8.80 mg, 0.010 mmol) and xantphos (11.0 mg, 0.020 mmol) as the catalyst system following the general procedure.

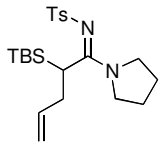
28: R_f = 0.63 [EtOAc]; pale yellow oil;
^{1}H NMR (400 MHz, $CDCl_3$) *(showing as two rotamers in 10:1 ratio)* major rotamer δ 0.95-1.16 (m, 21H), 2.29-2.42 (m, 1H), 2.44 (s, 3H), 2.61-2.67 (m, 1H), 2.74 (brs, 1H), 4.81 (d, 1H, *J* = 17.2 Hz), 4.96 (m, 1H), 5.72-5.77 (m, 1H), 7.15 (s, 1H), 7.31 (d, 2H, *J* = 8.1 Hz), 7.59 (s, 1H), 7.80 (d, 2H, *J* = 8.1 Hz), 8.21 (s, 1H);
^{13}C NMR (100 MHz, $CDCl_3$) major rotamer δ 12.1, 18.8, 18.9, 21.9, 34.7, 40.3, 117.3, 120.0, 127.1, 129.7, 130.9, 136.6, 138.1, 138.7, 143.9, 163.9;
IR (film) cm^{-1} 2947m, 2869m, 1962m, 1597s, 1157s;
mass spectrum (APCI): m/e (% relative intensity) 461 (30) $(M+H)^+$, 392 (100) $(M+H\text{-Imidazole})^+$.



30a

Amidine **30a** (104.0 mg, 0.19 mmol) was prepared in 95% yield from ynamide **29a** (95.0 mg, 0.20 mmol) and pyrrolidine (43.0 mg, 0.60 mmol) with $Pd_2(dba)_3$ (9.20 mg, 0.010 mmol) and xantphos (11.5 mg, 0.020 mmol) as the catalyst system following the general procedure.

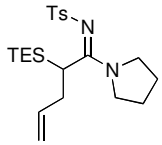
30a: R_f = 0.10 [1:5 EtOAc/hexanes]; amorphous solid, mp 58-63 °C;
^{1}H NMR (500 MHz, d_8-toluene, -6 °C) δ 1.08 (s, 9H), 2.00 (s, 3H), 2.09-2.15 (m, 2H), 2.49 (dd, 1H, *J* = 12.0, 8.0 Hz), 2.65-2.75 (m, 2H), 2.91 (td, 1H, *J* = 12.0, 6.5 Hz), 3.02 (t, 1H, *J* = 7.5 Hz), 3.10-3.22 (m, 1H), 4.05-4.09 (m, 1H), 4.20 (td, 1H, *J* = 12.0, 6.5 Hz), 5.02 (d, 1H, *J* = 10.0 Hz), 5.14 (d, 1H, *J* = 17.0 Hz), 5.95-6.04 (m, 1H), 6.82 (d, 2H, *J* = 8.0 Hz), 7.11-7.21 (m, 6H), 7.63-7.67 (m, 4H), 7.96 (d, 2H, *J* = 8.0 Hz);
^{13}C NMR (100 MHz, $CDCl_3$): Not recorded due to complications of rotamers;
IR (thin film) cm^{-1} 2973m, 2860m, 1542s, 1274s, 1136s, 1086s;
mass spectrum (APCI): m/e (% relative intensity) 545 (100) $(M+H)^+$.



30b

Amidine **30b** (84.0 mg, 0.20 mmol) was prepared in 94% yield from ynamide **29b** (75.0 mg, 0.21 mmol) and pyrrolidine (45.8 mg, 0.64 mmol) with $Pd_2(dba)_3$ (9.80 mg, 0.011 mmol) and xantphos (12.4 mg, 0.020 mmol) as the catalyst system following the general procedure.

30b: R_f = 0.13 [1:5 EtOAc/hexanes]; white solid, mp 74-76 °C;
^{1}H NMR (500 MHz, $CDCl_3$) δ -0.04 (s, 6H), 0.92 (s, 9H), 1.82-1.99 (m, 4H), 2.12 (dd, 1H, *J* = 7.5, 13.5 Hz), 2.25 (dd, 1H, *J* = 2.0, 13.5 Hz), 2.38 (s, 3H), 2.43-2.54 (m, 1H), 3.46-3.49 (m, 1H), 3.61-3.63 (m, 1H), 4.15-4.16 (m, 2H), 4.89-4.95 (m, 2H), 5.74-5.79 (m, 1H), 7.21 (d, 2H, *J* = 8.0 Hz), 7.81 (d, 2H, *J* = 8.0 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ -7.6, -6.7, 17.9, 21.5, 25.5, 25.7, 27.1, 34.7, 35.2, 51.3, 52.6, 115.5, 125.8, 128.9, 138.0, 140.8, 143.4, 166.8;
IR (thin film) cm^{-1} 2926m, 2854m, 1739s, 1531s, 1260s, 1061s;
mass spectrum (APCI): m/e (% relative intensity) 421 (100) $(M+H)^+$.

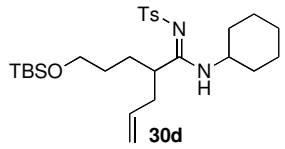


30c

Amidine **30c** (78.0 mg, 0.19 mmol) was prepared in 87% yield from ynamide **29c** (75.0 mg, 0.21 mmol) and pyrrolidine (46.0 mg, 0.643 mmol) with $Pd_2(dba)_3$ (9.80 mg, 0.011 mmol) and xantphos (12.4 mg, 0.021 mmol) as the catalyst system following the general procedure.

30c: R_f = 0.12 [1:5 EtOAc/hexanes]; colorless oil;
^{1}H NMR (500 MHz, d_8-toluene at 75 °C) *(showing as two rotamers in 1.1:1 ratio)* major rotamer δ 0.70 (brs, 6H), 0.96 (brs, 9H), 1.29-1.37 (m, 5H), 2.02 (s, 3H), 2.23 (sbr, 1H), 3.19 (brs, 3H), 4.92-5.07 (m, 2H), 5.91-5.96 (m, 1H), 6.90 (d, 2H, *J* = 8.0 Hz), 7.99 (d, 2H, *J* = 8.0 Hz) *(2 protons missing due to line-broadening)*;

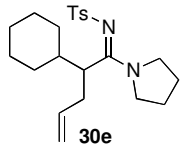
^{13}C NMR (125 MHz, d_8-toluene at -10 ^{o}C) *(for both rotamers)* δ 3.7, 4.7, 8.3, 8.4, 23.8, 25.7, 25.8, 27.0, 32.8, 33.5, 35.0, 36.4, 48.4, 50.2, 51.3, 52.7, 115.6, 116.2, 126.9, 127.0, 127.2, 127.4, 138.5, 139.0, 140.9, 141.2, 144.2, 145.1, 166.1, 168.1 *(two sp^3 carbon missing due to overlap or line-broadening)*;
IR (thin film) cm^{-1} 2952m, 2875m, 1519s, 1270s, 1136s, 1087s;
mass spectrum (APCI): m/e (% relative intensity) 421 (100) $(M+H)^+$.



30d

Amidine **30d** (38.0 mg, 0.075 mmol) was prepared in 41% yield from ynamide **29d** (75.5 mg, 0.19 mmol) and cyclohexylamine (79.0 mg, 0.55 mmol) with $Pd_2(dba)_3$ (8.40 mg, 0.010 mmol) and xantphos (10.6 mg, 0.020 mmol) as the catalyst system following the general procedure.

30d: R_f = 0.41 [1:5 EtOAc/hexanes]; yellow oil;
^{1}H NMR (500 MHz, $CDCl_3$) *(showing as two rotamers in 3:1 ratio)* major rotamer δ 0.00 (brs, 6H), 0.86 (s, 9H), 1.20-1.35 (m, 7H), 1.55-1.90 (m, 7H), 2.13-2.22 (m, 1H), 2.25-2.36 (m, 2H), 2.38 (s, 3H), 2.47-2.51 (m, 1H), 3.35-3.59 (m, 2H), 4.82-4.89 (m, 2H), 5.48-5.54 (m, 1H), 7.24 (d, 2H, *J* = 7.6 Hz), 7.76 (d, 2H, *J* = 7.6 Hz), 8.43 (d, 1H, *J* = 7.6 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) major rotamer δ -5.2, 18.5, 21.6, 24.4, 25.1, 26.1, 29.9, 30.4, 34.0, 38.0, 41.9, 52.5, 63.0, 117.5, 126.4, 129.2, 135.2, 140.1, 142.5, 170.4;
IR (film) cm^{-1} 3319w, 2929s, 2856s, 1538s, 1258s, 1087s, 834s;
mass spectrum (APCI): m/e (% relative intensity) 507 (100) $(M+H)^+$.

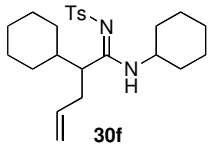


30e

Amidine **30e** (41.0 mg, 0.106 mmol) was prepared in 54% yield from ynamide **29e** (62.3 mg, 0.195 mmol) and pyrolidine (79.0 mg, 0.59 mmol) with $Pd_2(dba)_3$ (9.00 mg, 0.010 mmol) and xantphos (11.5 mg, 0.020 mmol) as the catalyst system following the general procedure.

30e: R_f =0.22 [1:3 EtOAc/hexanes]; yellow oil;
^{1}H NMR (500 MHz, $CDCl_3$) *(showing as two rotamers in 1:1 ratio)* both rotamers δ 1.01-2.07 (m, 32H), 2.20-2.25 (m, 1H), 2.38 (s, 6H), 2.47-2.51 (m, 1H), 2.62-2.66 (m, 1H), 2.72-2.76 (m, 1H), 3.38-3.84 (m, 6H), 3.90-3.95 (m, 2H), 4.88-5.05 (m, 3H), 5.06-5.14 (m, 1H), 5.71-5.78 (m, 1H), 5.83-5.85 (m, 1H), 7.22 (d, 4H, *J* = 7.9 Hz), 7.83 (d, 4H, *J* = 7.9 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) for both rotamers δ 14.4, 21.7, 22.9, 23.2, 25.1, 25.9, 26.3, 26.3, 26.6, 26.7, 27.0, 30.9, 31.4, 32.0, 32.2, 34.6, 34.7, 40.2, 40.4, 48.2, 49.6, 50.5, 50.7, 51.1, 52.2, 116.0, 117.3, 126.1, 126.6, 129.1, 136.3, 136.5, 141.2, 141.6, 142.6, 143.6, 166.5, 167.6 *(one sp^3 and one sp^2 carbon missing due to overlap or line-broadening)*;
IR (film) cm^{-1} 2927m, 2852m, 1530s, 1139s, 1087s;

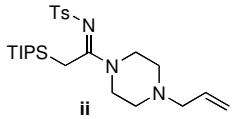
mass spectrum (APCI): m/e (% relative intensity) 389 (100) $(M+H)^+$.



30f

Amidine **30f** (67.0 mg, 0.161 mmol) was prepared in 69% yield from ynamide **29e** (74.0 mg, 0.234 mmol) and cyclohexylamine (81.0 mg, 71.0 mmol) with $Pd_2(dba)_3$ (10.9 mg, 0.010 mmol) and xantphos (11.5 mg, 0.020 mmol) as the catalyst system following the general procedure.

30f: R_f = 0.40 [1:3 EtOAc/hexanes]; white solid; mp 53-57 ºC;
^{1}H NMR (500 MHz, $CDCl_3$) *(showing as two rotamers in 3:1 ratio)* major rotamer δ 0.98-1.44 (m, 10H), 1.45-1.96 (m, 11H), 2.16-2.21 (m, 1H), 2.29-2.33 (m, 1H), 2.39 (s, 3H), 2.38-2.46 (m, 1H), 3.41 (brs, 1H), 4.81-4.89 (m, 2H), 5.46-5.56 (m, 1H), 7.23 (d, 2H, J = 8.0 Hz), 7.78 (d, 2H, J = 8.0 Hz), 8.50 (d, 1H, J = 8.0 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) major rotamer δ 21.7, 24.5, 24.6, 25.2, 26.5, 26.6, 30.6, 31.8, 33.9, 34.2, 35.3, 41.2, 48.1, 52.7, 117.4, 126.6, 129.3, 135.6, 140.1, 142.6, 170.4 *(one sp^3 carbon missing due to overlap or line-broadening)*;
IR (film) cm^{-1} 3316w, 2925m, 2852m, 1640s, 1136s, 1086s;
mass spectrum (APCI): m/e (% relative intensity) 415 (100) $(M-H)^-$.



ii

Amidine **ii** (30.0 mg, 0.063 mmol) was prepared in 63% yield from ynamide **6** (40.0 mg, 0.10 mmol) and piperazine (8.60 mg, 0.10 mmol) with $PdCl_2(PPh_3)_2$ (4.00 mg, 0.0050 mmol) as the catalyst following the general procedure.

Footnote compound ii: R_f = 0.25 [2:1 EtOAc/hexanes]; white solid, mp 112-114 ^{o}C;
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (d, 18H, J = 8.4 Hz), 1.32-1.38 (m, 3H), 2.38 (s, 3H), 2.38 (sbr, 2H), 2.45 (sbr, 2H), 2.68 (s, 2H), 2.98 (d, 2H, J = 6.8 Hz), 3.50 (sbr, 2H), 3.73 (sbr, 2H), 5.16-5.21 (m, 2H), 5.80 (ddt, 1H, J = 6.6, 10.4, 16.8 Hz), 7.21 (d, 2H, J = 8.0 Hz), 7.78 (d, 2H, J = 8.0 Hz);
^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 16.4, 18.7, 21.4, 44.7, 46.5, 52.3, 52.6, 61.2, 118.6, 125.9, 128.9, 134.2, 141.3, 142.2, 168.1;
IR (thin film) cm^{-1} 2869m, 1524s, 1268s, 1162s, 1086s;
mass spectrum (APCI): m/e (% relative intensity) 478 (100) $(M+H)^+$.

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