SUPPORTING INFORMATION

for the
full paper
entitled

# *N*-Allyl-*N*-Sulfonyl *Ynamides as Synthetic Precursors to Amidines and Vinylogous Amidines. An Unexpected 1,3-Sulfonyl Shift in Nitrile Synthesis*


authored by

Kyle A. DeKorver, Whitney L. Johnson, Yu Zhang, Richard P. Hsung*, Huifang Dai, Jun Deng, Andrew G. Lohse, and Yan-Shi Zhang*

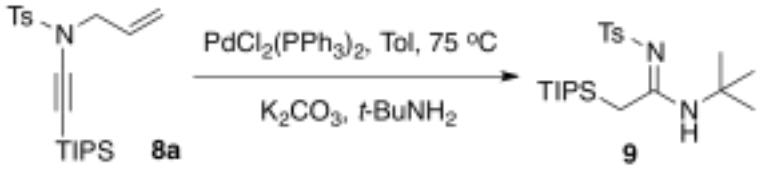
*Division of Pharmaceutical Sciences and Department of Chemistry,*
*7111 Rennebohm Hall, 777 Highland Avenue*
*University of Wisconsin at Madison, Madison, WI 53705-2222*


**TABLE OF CONTENTS**

## GENERAL EXPERIMENTAL INFORMATION

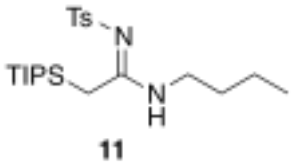
All reactions were performed in flame-dried glassware under a nitrogen atmosphere. Solvents were distilled prior to use. $^{1}H$ and $^{13}C$ NMR spectra were obtained using $CDCl_3$ with TMS or residual solvent as standard unless otherwise noted. Melting points are uncorrected/calibrated. TLC analysis was performed using 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and $KMnO_4$ stains. All spectral data obtained for new compounds are reported here.

**General Procedure for the Preparation of Amidines from *N*-allyl Ynamides.**




To a flame dried screw-cap vial was added ynamide **8a** (117.0 mg, 0.300 mmol), $PdCl_2(PPh_3)_2$ (10.5 mg, 0.015 mmol), THF (6 mL), and *tert*-butyl amine (158.0 μL, 1.50 mmol), then sealed under a dry nitrogen atmosphere and heated to 80 °C for 2 h. After the reaction was complete by TLC, the solvent was removed *in vacuo* and the resulting crude residue was purified via silica gel flash column chromatography (isocratic eluent: 6:1 hexane/EtOAc) to afford amidine **9** as a white solid (119.0 mg, 0.282 mmol, 94%).

**9:** R*f* = 0.27 [4:1 hexanes:EtOAc]; white solid; mp = 134 – 135 °C;
$^{1}H$ NMR (400 MHz, $CDCl_3$) δ 1.11 (d, 18H, *J* = 8.8 Hz), 1.28 (sept, 3H, *J* = 8.8 Hz), 1.31 (s, 9H), 2.39 (s, 3H), 2.45 (s, 2H), 4.91 (brs, 1H), 7.25 (d, 2H, *J* = 10.0 Hz), 7.79 (d, 2H, *J* = 10.0 Hz);
$^{13}C$ NMR (100 MHz, $CDCl_3$) δ 11.5, 18.7, 18.8, 21.6, 28.7, 53.4, 126.3, 129.2, 141.7, 141.8, 167.1;
IR (film) $cm^{-1}$ 3328m, 2942m, 2867m, 1570m, 1530s, 1341m;
mass spectrum (ESI): m/e (% relative intensity) 447 (100) $(M+Na)^+$, 425 (40) $(M+H)^+$;
HRMS (ESI) m/e calcd for $C_{22}H_{40}N_2O_2SSiNa$ 447.2472, found 447.2476.




Amidine **11** (111.0 mg, 0.261 mmol) was prepared in 87% yield following the general procedure from ynamide **8a**.

**11:** R*f* = 0.31 [4:1 hexanes:EtOAc]; white solid; mp = 73 – 76 °C;

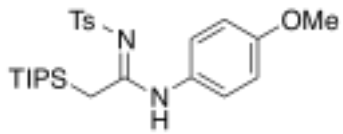
$^1$H NMR (400 MHz, $CDCl_3$) *(showing as two rotamers in 2.3:1 ratio) major rotamer* δ 0.96 (d, 18H, *J* = 6.0 Hz), 0.96 – 1.02 (m, 1H), 1.10 (s, 3H), 1.20 – 1.35 (m, 2H), 1.35 – 1.50 (m, 2H), 1.60 (pent, 2H, *J* = 7.2 Hz), 1.85 (s, 2H), 2.39 (s, 3H), 3.27 (t, 2H, *J* = 7.2 Hz), 7.22 (d, 2H, *J* = 8.0 Hz), 7.76 (d, 2H, *J* = 8.0 Hz), 8.28 (brs, 1H);

$^{13}$C NMR (100 MHz, $CDCl_3$) *major rotamer* δ 11.7, 13.9, 18.0, 18.7, 20.1, 21.7, 31.8, 44.6, 126.5, 129.1, 140.4, 142.4, 169.7;

IR (film) cm$^{-1}$ 3322m, 2942m, 2869m, 1532s, 1465m;

mass spectrum (APCI): m/e (% relative intensity) 425 (50) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{22}H_{40}N_2O_2SSiH$ 425.2653, found 425.2640.




**13**

Amidine **13** (39.0 mg, 0.082 mmol) was prepared in 41% yield following the general procedure from ynamide **8a**.

**13:** R*f* = 0.20 [4:1 hexanes:EtOAc]; white solid; mp = 84 – 87 °C;

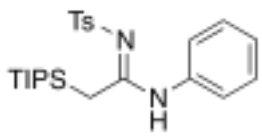
$^1$H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, 18H, *J* = 6.4 Hz), 0.90 (sept, 3H, *J* = 6.4 Hz), 1.88 (s, 2H), 2.42 (s, 3H), 3.82 (s, 3H), 6.90 (d, 2H, *J* = 8.8 Hz), 7.08 (d, 2H, *J* = 8.8 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 7.83 (d, 2H, *J* = 8.0 Hz), 9.80 (s, 1H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 11.5, 18.3, 18.6, 21.7, 55.8, 114.8, 126.6, 128.2, 129.2, 130.3, 140.1, 142.7, 159.1, 169.3;

IR (film) cm$^{-1}$ 3272m, 2943m, 2869m, 1610m, 1573s, 1513m;

mass spectrum (ESI): m/e (% relative intensity) 497 (100) $(M+Na)^+$, 475 (40) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{25}H_{38}N_2O_3SSiNa$ 497.2265, found 497.2258.




**14**

Amidine **14** (20.0 mg, 0.044 mmol) was prepared in 22% yield following the general procedure from ynamide **8a**.

**14:** R*f* = 0.31 [4:1 hexanes:EtOAc]; white solid; mp = 125 – 128 °C;

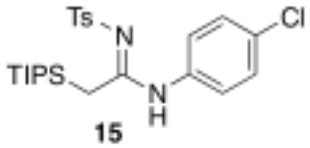
$^1$H NMR (500 MHz, $CDCl_3$) δ 0.85 (d, 18H, *J* = 6.0 Hz), 0.85 – 0.95 (m, 3H), 1.94 (s, 2H), 2.42 (s, 3H), 7.17 (d, 2H, *J* = 7.5 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.31 (t, 1H, *J* = 7.5 Hz), 7.40 (t, 2H, *J* = 7.5 Hz), 7.84 (d, 2H, *J* = 8.0 Hz), 9.96 (s, 1H);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 11.5, 18.4, 18.6, 21.8, 126.7, 126.8, 127.9, 129.3, 129.7, 137.6, 140.0, 142.8, 168.9;

IR (film) cm$^{-1}$ 3338w, 2962m, 2867m, 1608m, 1569m, 1527s, 1441m;

mass spectrum (ESI): m/e (% relative intensity) 467 (100) $(M+Na)^+$, 445 (35) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{36}N_2O_2SSiNa$ 467.2159, found 467.2173.



**15**

Amidine **15** (21.0 mg, 0.044 mmol) was prepared in 22% yield following the general procedure from ynamide **8a**.

**15:** R*f* = 0.30 [4:1 hexanes:EtOAc]; white solid; mp = 147 – 150 °C;

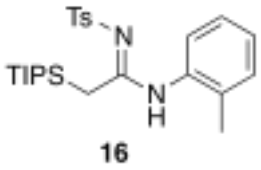
$^1$H NMR (400 MHz, $CDCl_3$) δ 0.87 (s, 18H), 0.90 – 1.20 (m, 3H), 1.90 (brs, 2H), 2.42 (s, 3H), 7.05 – 7.17 (m, 2H), 7.27 (d, 2H, *J* = 8.0 Hz), 7.32 – 7.42 (m, 2H), 7.81 (d, 2H, *J* = 8.0 Hz), 9.91 (brs, 1H);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 11.6, 18.6, 21.7, 29.9, 126.6, 128.1, 129.3, 129.9, 133.7, 136.2, 139.7, 142.9, 168.7;

IR (film) cm$^{-1}$ 3314m, 2943m, 2867m, 1600m, 1569s, 1517s, 1493s;

mass spectrum (ESI): m/e (% relative intensity) 501 (100) $(M+Na)^+$, 479 (45) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{35}ClN_2O_2SSiNa$ 501.1770, found 501.1766.



**16**

Amidine **16** (27.0 mg, 0.060 mmol) was prepared in 30% yield following the general procedure from ynamide **8a**.

**16:** R*f* = 0.33 [4:1 hexanes:EtOAc]; white solid; mp = 74 – 76 °C;

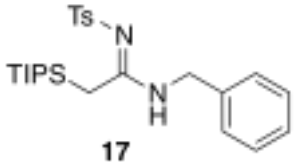
$^1$H NMR (500 MHz, $CDCl_3$) δ 0.87 (d, 18H, $J$ = 7.0 Hz), 0.94 – 0.98 (m, 3H), 1.82 (s, 2H), 2.26 (s, 3H), 2.42 (s, 3H), 7.10 – 7.17 (m, 1H), 7.20 – 7.26 (m, 3H), 7.27 (d, 2H, $J$ = 8.5 Hz), 7.84 (d, 2H, $J$ = 8.5 Hz), 9.79 (brs, 1H);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 11.6, 18.2, 18.2, 18.6, 21.8, 126.7, 127.1, 127.5, 128.2, 129.3, 131.5, 134.7, 136.3, 140.0, 142.7, 169.2;

IR (film) cm$^{-1}$ 3256m, 2941m, 2866m, 1566s, 1461m; 1369m,

mass spectrum (ESI): m/e (% relative intensity) 481 (100) $(M+Na)^+$, 459 (35) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{25}H_{38}N_2O_2SSi$ 481.2316, found 481.2306.




**17**

Amidine **17** (34.0 mg, 0.074 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**17:** R$f$ = 0.19 [4:1 hexanes:EtOAc], colorless oil;

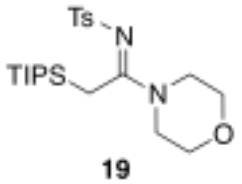
$^1$H NMR (500 MHz, $CDCl_3$) [*showing as two rotamers in a 3:2 ratio*] *major rotamer* δ 0.97 (d, 18H, $J$ = 6.5 Hz), 1.02 (sept, 3H, $J$ = 6.5 Hz), 2.41 (s, 2H), 2.52 (s, 3H), 4.48 (d, 2H, $J$ = 6.0 Hz), 7.24 (d, 2H, $J$ = 7.0 Hz), 7.39 – 7.19 (m, 5H), 7.77 (d, 2H, $J$ = 8.0 Hz), 8.65 (s, 1H);

$^{13}$C NMR (125 MHz, $CDCl_3$) *major rotamer* δ 11.7, 18.3, 18.7, 21.7, 48.5, 126.6, 127.2, 128.4, 129.2, 129.3, 136.3, 140.2, 142.6, 170.0;

IR (film) cm$^{-1}$ 3326brs, 2942m, 2866m, 1537s, 1496m, 1270m;

mass spectrum (APCI): m/e (% relative intensity) 459 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{25}H_{38}N_2O_2SSiH$ 459.2496, found 459.2506.




**19**

Amidine **19** (43.0 mg, 0.096 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**19:** R$f$ = 0.36 [2:1 hexanes:EtOAc]; white solid; mp = 143 − 145 $^o$C;

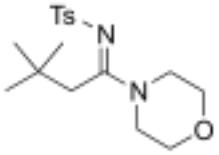
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, 18H, $J$ = 7.5 Hz), 1.38 (sept, 3H, $J$ = 7.5 Hz), 2.40 (s, 3H), 2.70 (s, 2h), 3.57 (brs, 2H), 3.69 (brs, 6H), 7.25 (d, 2H, $J$ = 8.1 Hz), 7.80 (d, 2H, $J$ = 8.1 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.3, 16.3, 18.9, 21.6, 44.1, 47.1, 66.4, 77.6, 126.1, 129.2, 141.7, 142.1, 168.7;

IR (film) cm$^{-1}$ 2966m, 2945m, 2868m, 1519s, 1444m, 1271s, 1089s;

mass spectrum (APCI): m/e (% relative intensity) 439 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{22}H_{38}N_2O_3SSiNa$ 461.2265, found 461.2275.




**20**

Amidine **20** (32.3 mg, 0.096 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8c**.

**20**: R*f* = 0.28 [1:1 hexanes:EtOAc]; white solid; mp = 125 − 132 °C;

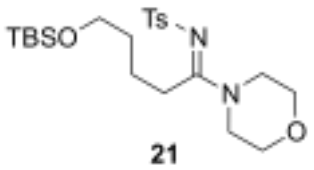
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 9H), 2.39 (s, 3H), 3.09 (s, 2H), 3.66 (brs, 8H), 7.23 (d, 2H, $J$ = 8.4 Hz), 7.78 (d, 2H, $J$ = 8.4 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.6, 31.0, 31.4, 39.9, 66.8, 126.1, 129.3, 141.9, 142.3, 165.8 [*missing one $sp^3$ carbon due to overlap*];

IR (film) cm$^{-1}$ 2960w, 2868w, 1599s, 1459m, 1398m, 1293s, 1141m, 1065s;

mass spectrum (APCI): m/e (% relative intensity) 339 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{17}H_{26}N_2O_3SNa$ 361.1556, found 361.1574.




**21**

Amidine **21** (42.4 mg, 0.093 mmol) was prepared in 92% yield following the general procedure from ynamide **8d**.

**21**: R*f* = 0.36 [1:1 hexanes:EtOAc]; brown oil;

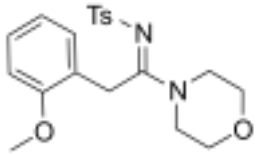
$^1$H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.88 (s, 9H), 1.57 – 1.72 (m, 4H), 2.40 (s, 3H), 2.93 – 2.98 (m, 2H), 3.51 – 3.53 (m, 2H), 3.62 – 3.72 (m, 8H), 7.25 (d, 2H, $J$ = 8.4 Hz), 7.81 (d, 2H, $J$ = 8.4 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ -5.2, 14.3, 18.4, 21.2, 21.6, 23.5, 26.1, 30.4, 32.3, 60.5, 62.1, 66.5, 126.4, 128.6, 129.3, 132.3, 142.1;

IR (film) cm$^{-1}$ 3058m, 2929m, 2856m, 1536s, 1438m, 1388w, 1359w, 1268s, 1143s, 1117s, 1087s;

mass spectrum (APCI): m/e (% relative intensity) 455 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{22}H_{38}N_2O_4SSiNa$ 477.2214, found 477.2222.




22

Amidine **22** (25.4 mg, 0.066 mmol) was prepared in 37% yield following the general procedure from ynamide **8e**.

**22:** R*f* = 0.21 [1:1 hexanes:EtOAc]; yellow foam; mp = 54 − 60 °C;

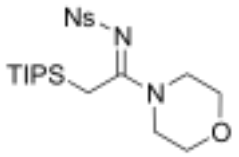
$^1$H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.24 (t, 2H, *J* = 4.8 Hz), 3.33 (t, 2H, *J* = 4.8 Hz), 3.63 (t, 2H, *J* = 5.2 Hz), 3.81 (t, 2H, *J* = 5.2 Hz), 3.83 (s, 3H), 4.35 (s, 2H), 6.84 (d, 1H, *J* = 8.0 Hz), 6.85 (td, 1H, *J* = 1.2, 7.6 Hz), 7.04 (dd, 1H, *J* = 1.2, 7.6 Hz), 7.20 (d, 2H, *J* = 8.0 Hz), 7.21 − 7.23 (m, 1H), 7.80 (d, 2H, *J* = 8.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 21.7, 30.4, 45.2, 46.9, 55.7, 66.5, 66.5, 110.6, 121.2, 122.5, 126.7, 128.5, 128.7, 129.3, 141.1, 142.2, 156.1, 166.4;

IR (film) cm$^{-1}$ 2966w, 2858w, 1540s, 1463m, 1271s, 1069s, 998s;

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

HRMS (ESI) m/e calcd for $C_{20}H_{24}N_2O_4SH$ 389.1530, found 389.1523.




23

Amidine **23** (25.3 mg, 0.055 mmol) was prepared in 39% yield following the general procedure from ynamide **8f**.

**23:** R*f* = 0.50 [1:1 hexanes:EtOAc]; pale yellow solid; mp = 159 − 161 °C;

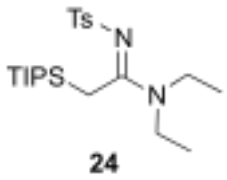
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.15 (d, 18H, *J* = 7.2 Hz), 1.37 (sept, 3H, *J* = 7.2 Hz), 2.71 (s, 2H), 3.53 (brs, 2H), 3.65 (brs, 2H), 3.68 (brs, 2H), 3.73 (brs, 2H), 8.08 (d, 2H, *J* = 9.2 Hz), 8.29 (d, 2H, *J* = 9.2 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.3, 17.0, 18.9, 45.5, 47.3, 66.4, 124.1, 127.4, 149.4, 150.4, 169.2;

IR (film) cm$^{-1}$ 2983w, 2360w, 1740s, 1526m, 1444m, 1374m, 1242s, 1047s;

mass spectrum (APCI): m/e (% relative intensity) 470 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{21}H_{35}N_3O_5SSiH$ 470.2140, found 470.2150.




**24**

Amidine **24** (42.0 mg, 0.098 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**24:** R*f* = 0.32 [4:1 hexanes:EtOAc]; white solid; mp = 129 − 130 °C;

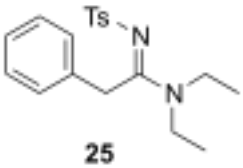
$^1$H NMR (500 MHz, $CDCl_3$) δ 1.08 (t, 3H, *J* = 7.5 Hz), 1.18 (d, 18H, *J* = 7.5 Hz), 1.19 (t, 3H, *J* = 7.0 Hz), 1.39 (sept, 3H, *J* = 7.5 Hz), 2.36 (s, 3H), 2.62 (s, 2H), 3.32 (q, 2H, *J* = 7.0 Hz) 3.42 (q, 2H, *J* = 7.0 Hz), 7.20 (d, 2H, *J* = 8.0 Hz), 7.79 (d, 2H, *J* = 8.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 12.3, 12.4, 13.6, 16.4, 18.9, 21.5, 43.5, 43.6, 125.9, 129.0, 141.2, 142.7, 167.7;

IR (film) cm$^{-1}$ 2941s, 2868m, 2361w, 1548s, 1469s, 1362m, 1261m, 1395s;

mass spectrum (APCI): m/e (% relative intensity) 425 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{22}H_{40}N_2O_2SSiNa$ 447.2472, found 447.2479.

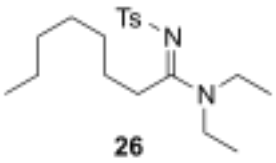



**25**

Amidine **25** (28.6 mg, 0.083 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8b**.

**25:** R*f* = 0.29 [2:1 hexanes:EtOAc]; pale yellow oil;

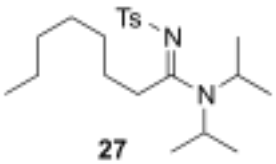
$^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, 3H, *J* = 7.2 Hz), 1.16 (t, 3H, *J* = 7.2 Hz), 2.36 (s, 3H), 3.20 (q, 2H, *J* = 7.2 Hz), 3.50 (q, 2H, *J* = 7.2 Hz), 4.38 (s, 2H), 7.09 − 7.27 (m, 7H), 7.76 (d, 2H, *J* = 8.1 Hz);
$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.0, 13.5, 21.5, 36.6, 43.3, 43.4, 126.2, 126.7, 127.8, 128.8, 129.0, 134.3, 141.4, 141.6, 164.5;
IR (film) $cm^{-1}$ 2978w, 2937w, 2359w, 1650w, 1549s, 1475m, 1274m, 1143m;
mass spectrum (APCI): m/e (% relative intensity) 345 (100) $(M+H)^+$;
HRMS (ESI) m/e calcd for $C_{19}H_{24}N_2O_2SNa$ 367.1451, found 367.1438.



**26**

Amidine **26** (45.0 mg, 0.130 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8g**.

**26**: R*f* = 0.09 [4:1 hexanes:EtOAc]; waxy white solid; mp = 30 – 31 °C;
$^{1}$H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J* = 7.0 Hz), 1.10 (t, 3H, *J* = 7.0 Hz), 1.22 (t, 3H, *J* = 7.0 Hz), 1.24 – 1.32 (m, 6H), 1.35 – 1.40 (m, 2H), 1.58 – 1.63 (m, 2H), 2.39 (s, 3H), 2.81 – 2.86 (m, 2H), 3.34 (q, 2H, *J* = 7.0 Hz), 3.44 (q, 2H, *J* = 7.0 Hz), 7.23 (d, 2H, *J* = 7.5 Hz), 7.82 (d, 2H, *J* = 7.5 Hz);
$^{13}$C NMR (125 MHz, $CDCl_3$) δ 12.3, 14.2, 14.4, 21.6, 22.7, 27.6, 29.0, 30.1, 31.1, 31.8, 43.3, 126.2, 129.1, 141.6, 142.1, 167.8;
IR (film) $cm^{-1}$ 2920m, 2855m, 1550s, 1474s, 1453s, 1434s;
mass spectrum (ESI): m/e (% relative intensity) 375 (100) $(M+Na)^+$, 353 (30) $(M+H)^+$;
HRMS (ESI) m/e calcd for $C_{19}H_{32}N_2O_2SNa$ 375.2077, found 375.2075.



**27**

Amidine **27** (26.2 mg, 0.070 mmol) was prepared in 70% yield following the general procedure from ynamide **8g**.

**27**: R*f* = 0.68 [1:1 hexanes:EtOAc]; yellow solid; mp = 78 − 80 °C;

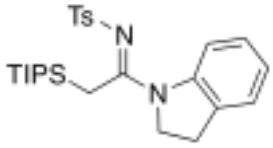
$^1$H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, 3H, $J$ = 8.0 Hz), 1.22 − 1.49 (m, 20H), 1.56 − 1.68 (m, 2H), 2.39 (s, 3H), 2.85 − 2.89 (m, 2H), 3.51 (brs, 1H), 4.03 (sept, 1H, $J$ = 6.4 Hz), 7.24 (d, 2H, $J$ = 8.0 Hz), 7.81 (d, 2H, $J$ = 8.0 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 14.3, 20.3, 20.9, 21.6, 22.8, 27.5, 29.1, 30.0, 31.9, 33.0, 48.1, 50.1, 126.3, 129.2, 141.6, 142.2, 166.7;

IR (film) cm$^{-1}$ 3479w, 2970w, 2932w, 1539s, 1494m, 1449m, 1267m, 1086s;

mass spectrum (APCI): m/e (% relative intensity) 381 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{21}H_{36}N_2O_2SH$ 381.2570, found 381.2561.




**28**

Amidine **28** (47.1 mg, 0.100 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**28**: R*f* = 0.45 [4:1 hexanes:EtOAc]; brown solid; mp = 182 − 184 °C;

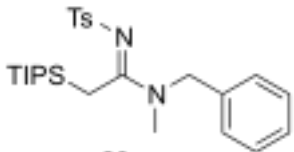
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.15 (d, 18H, $J$ = 7.2 Hz), 1.46 (sept, 3H, $J$ = 7.2 Hz), 2.39 (s, 3H), 2.84 (brs, 2H), 3.14 (t, 2H, $J$ = 8.4 Hz), 4.11 (t, 2H, $J$ = 8.4 Hz), 7.00 (td, 1H, $J$ = 0.8, 7.2 Hz), 7.06 (t, 1H, $J$ = 7.2 Hz), 7.17 (d, 1H, $J$ = 7.2 Hz), 7.25 (dd, 2H, $J$ = 0.4, 8.8 Hz), 7.85 (d, 2H, $J$ = 8.8 Hz), 8.07, (brs, 1H);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.8, 19.0, 20.1, 21.7, 27.7, 50.4, 119.8, 124.8, 124.8, 126.5, 127.7, 129.3, 132.9, 141.6, 141.8, 142.6, 166.3;

IR (film) cm$^{-1}$ 3055w, 2941w, 2867w, 1541m, 1481m, 1265s, 1143m, 1089m;

mass spectrum (APCI): m/e (% relative intensity) 471 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{26}H_{38}N_2O_2SSiNa$ 493.2316, found 493.2340.




**29**

Amidine **29** (36.7 mg, 0.077 mmol) was prepared in 77% yield following the general procedure from ynamide **8a**.

**29:** R*f* = 0.67 [1:1 hexanes:EtOAc]; white solid; mp = 89 − 90 °C;

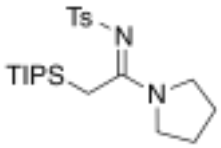
$^1$H NMR (400 MHz, $CDCl_3$) [*showing as two rotamers in 1.7:1 ratio*] *major rotamer* δ 1.13 (d, 18H, *J* = 7.6 Hz), 1.40 (sept, 3H, *J* = 7.6 Hz), 2.37 (s, 3H), 2.75 (s, 2H), 3.01 (s, 3H), 4.68 (s, 2H), 7.06 − 7.11 (m, 3H), 7.17 (d, 2H, *J* = 8.4 Hz), 7.22 − 7.26 (m, 2H), 7.74 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) *major rotamer* δ 12.6, 17.0, 18.9, 21.6, 36.9, 54.2, 126.2, 127.8, 128.5, 128.7, 129.1, 136.1, 141.4, 142.3, 169.4;

IR (film) cm$^{-1}$ 3060w, 2944m, 2867m, 2362w, 1530s, 1454m, 1266s, 1142s, 1088s, 1017m;

mass spectrum (APCI): m/e (% relative intensity) 473 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{26}H_{40}N_2O_2SSiH$ 473.2653, found 473.2676.




**30a**

Amidine **30a** (32.0 mg, 0.075 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**30a**: R*f* = 0.30 [3:1 hexanes:EtOAc]; white solid; mp = 161− 163 °C;

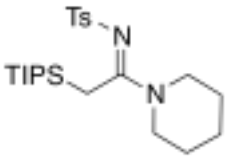
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, 18H, *J* = 7.2 Hz), 1.41 (sept, 3H, *J* = 7.2 Hz), 1.87 (quint, 2H, *J* = 6.6 Hz), 1.98 (quint, 2H, *J* = 6.6 Hz), 2.40 (s, 3H), 2.63 (s, 2H), 3.51 (q, 4H, *J* = 8.7 Hz), 7.23 (d, 2H, *J* = 8.4 Hz), 7.85 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.6 18.3, 18.9, 21.5, 24.4, 26.1, 48.3, 49.0, 126.1, 129.0, 141.3, 142.7, 167.2;

IR (film) cm$^{-1}$2945w, 2868m, 1530s, 1463m, 1421m, 1337w, 1268m, 1139m, 1089s;

mass spectrum (APCI): m/e (% relative intensity) 423 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{22}H_{38}N_2O_2SSiNa$ 445.2316, found 445.2329.




**30b**

Amidine **30b** (44.0 mg, 0.099 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**30b**: R*f* = 0.28 [4:1 hexanes:EtOAc]; white solid; mp = 121 − 122 °C;

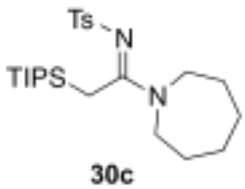
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, 18H, *J* = 7.5 Hz), 1.39 (sept, 3H, *J* = 7.5 Hz), 1.54 (brs, 2H), 1.64 (brs, 4H), 2.39 (s, 3H), 2.69 (s, 2H), 3.45 (brs, 2H), 3.70 (brs, 2H), 7.28 (d, 2H, *J* = 8.4 Hz), 7.80 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.3, 16.5, 18.9, 21.5, 24.3, 25.5, 26.4, 46.3, 48.1, 126.0, 129.0, 141.3, 142.7, 167.9;

IR (film) cm$^{-1}$ 2943m, 2867m, 1526s, 1468m, 1445m, 1271m, 1144s, 1089s;

mass spectrum (APCI): m/e (% relative intensity) 437 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{23}H_{40}N_2O_2SSiNa$ 459.2472, found 459.2461.




**30c**

Amidine **30c** (34.0 mg, 0.075 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**30c**: R*f* = 0.34 [4:1 hexanes:EtOAc]; white solid; mp = 150 − 152 °C;

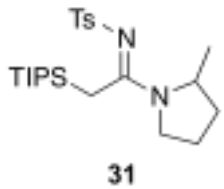
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, 18H, *J* = 7.2 Hz), 1.39 − 1.73 (m, 11H), 2.40 (s, 3H), 2.68 (s, 2H), 3.49 (t, 2H, *J* = 6.0 Hz), 3.61 (t, 2H, *J* = 6.0 Hz), 7.23 (d, 2H, *J* = 8.1 Hz), 7.81 (d, 2H, *J* = 8.1 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.4, 16.4, 18.9, 21.5, 26.3, 26.4, 26.7, 29.0, 50.0, 50.1, 125.9, 129.0, 141.2, 142.6, 168.4;

IR (film) cm$^{-1}$ 2939m, 2866m, 1533s, 1473m, 1370w, 1271m, 1143m, 1089m;

mass spectrum (APCI): m/e (% relative intensity) 451 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{42}N_2O_2SSiNa$ 473.2629, found 473.2643.

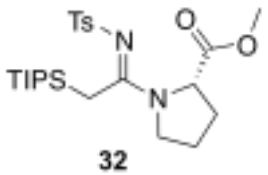



**31**

Amidine **31** (79.7 mg, 0.182 mmol) was prepared in 91% yield following the general procedure from ynamide **8a**.

**31**: R*f* = 0.64 [1:1 hexanes:EtOAc]; pale solid; mp = 92 − 96 °C;

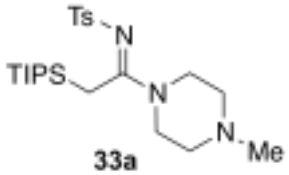
$^{1}$H NMR (400 MHz, $CDCl_3$) [*showing as two rotamers in a 2.0:1 ratio*] *major rotamer* δ 1.10 − 1.24 (m, 21H), 1.33 − 1.40 (m, 3H), 1.86 − 2.04 (m, 4H), 2.36 (s, 3H), 2.43 (d, 1H, *J* = 12.4 Hz), 2.73 (d, 1H, *J* = 12.4 Hz), 3.41 − 3.53 (m, 2H), 4.27 − 4.30 (m, 1H), 7.20 (d, 2H, *J* = 8.4 Hz), 7.79 (d, 2H, *J* = 8.4 Hz);
$^{13}$C NMR (100 MHz, $CDCl_3$) *major rotamer* δ 12.7, 18.4, 19.0, 19.0, 21.6, 23.8, 31.8, 48.6, 55.8, 126.1, 129.1, 141.3, 142.7, 166.9;
IR (film) cm$^{-1}$ 2972m, 2868m, 2839m, 2361m, 1781w, 1738s, 1517s, 1461m, 1240s;
mass spectrum (APCI): m/e (% relative intensity) 437 (100) $(M+H)^+$;
HRMS (ESI) m/e calcd for $C_{23}H_{40}N_2O_2SSiNa$ 459.2472, found 459.2471.



**32**

Amidine **32** (45.4 mg, 0.097 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**32**: R*f* = 0.80 [1:1 hexanes:EtOAc]; $[\alpha]_D^{25}$ = -63.5 (*c* 0.43, dichloromethane); pale yellow oil;
$^{1}$H NMR (400 MHz, $CDCl_3$) δ 1.13 − 1.16 (m, 18H), 1.40 (sept, 3H, *J* = 6.8 Hz), 1.92 − 1.99 (m, 2H), 2.09 − 2.16 (m, 2H), 2.39 (s, 3H), 2.43 (d, 1H, *J* = 12.4 Hz), 2.95 (d, 1H, *J* = 12.4 Hz), 3.34 (s, 3H), 3.59 − 3.60 (m, 1H), 3.66 − 3.72 (m, 1H), 4.45 (dd, 1H, *J* = 4.0, 8.4 Hz), 7.21 (d, 2H, *J* = 8.4 Hz), 7.74 (d, 2H, *J* = 8.4 Hz);
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.6, 18.0, 19.0, 21.6, 24.8, 29.5, 48.7, 52.0, 61.5, 126.4, 129.0, 141.6, 142.0, 167.6, 172.3;
IR (film) cm$^{-1}$ 3058w, 2949m, 2871m, 2364w, 1747s, 1519s, 1459m, 1367w, 1267s, 1142m;
mass spectrum (APCI): m/e (% relative intensity) 481 (100) $(M+H)^+$;
HRMS (ESI) m/e calcd for $C_{29}H_{40}N_2O_4SSiNa$ 503.2370, found 503.2348.



**33a**

Amidine **33a** (34.0 mg, 0.076 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**33a**: R*f* = 0.46 [95:5 $CH_2Cl_2$:MeOH]; pale yellow oil;

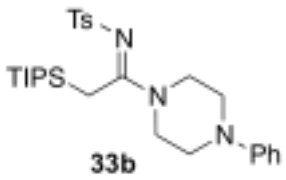
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.15 (d, 18H, *J* = 7.5 Hz), 1.38 (sept, 3H, *J* = 7.5 Hz), 2.30 (s, 3H), 2.39 (brs, 4H), 2.40 (s, 3H), 2.70 (s, 2H), 3.51 (brs, 2H), 3.74 (brs, 2H), 7.24 (d, 2H, *J* = 8.4 Hz), 7.81 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.2, 16.5, 18.9, 21.6, 44.8, 45.9, 46.6, 54.4, 54.9, 77.2, 128.6, 133.2, 141.5, 142.3, 168.4;

IR (film) cm$^{-1}$ 2943m, 2868m, 2796m, 1525s, 1452m, 1363w, 1271m, 1143m, 1092m;

mass spectrum (APCI): m/e (% relative intensity) 452 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{23}H_{41}N_3O_2SSiH$ 452.2672, found 452.2668.



**33b**

Amidine **33b** (39.0 mg, 0.076 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**33b**: R*f* = 0.50 [2:1 hexanes:EtOAc]; white solid; mp = 126 − 127 °C;

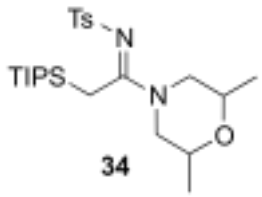
$^1$H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, 18H, *J* = 7.2 Hz), 1.43 (sept, 3H, *J* = 7.2 Hz), 2.42 (s, 3H), 2.77 (s, 2H), 3.17 (brs, 2H), 3.24 (brs, 2H), 3.71 (brs, 2H), 3.92 (brs, 2H), 6.92 − 6.98 (m, 3H), 7.26 − 7.35 (m, 4H), 7.85 (d, 2H, *J* = 8.1 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.0, 16.2, 18.6, 21.3, 44.4, 46.3, 48.5, 49.2, 116.3, 120.6, 125.9, 128.9, 129.2, 141.4, 141.9, 150.3, 168.3;

IR (film) cm$^{-1}$ 3029w, 2945m, 2868m, 1600m, 1525s, 1453m, 1277m, 1143m, 1091m;

mass spectrum (APCI): m/e (% relative intensity) 514 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{28}H_{43}N_3O_2SSiNa$ 536.2738, found 536.2737.



**34**

Amidine **34** (57.6 mg, 0.124 mmol) was prepared in ≥95% yield following the general procedure from ynamide **8a**.

**34**: R*f* = 0.59 [1:1 hexanes:EtOAc]; yellow solid; mp = 125 − 126 °C;

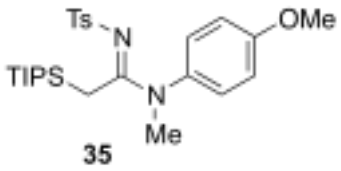
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.12 (d, 18H, *J* = 7.2 Hz), 1.10 – 1.20 (m, 6H), 1.34 (sept, 3H, *J* = 7.2 Hz), 2.28 − 2.31 (m, 1H), 2.37 (s, 3H), 2.62 − 2.74 (m, 2H), 3.47 − 3.68 (m, 3H), 3.37 (sext, 1H, *J* = 4.8 Hz), 4.62 (d, 1H, *J* = 13.2 Hz), 7.20 (d, 2H, *J* = 7.6 Hz), 7.75 (d, 2H, *J* = 7.6 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.3, 12.4, 16.5, 18.9, 19.0, 21.6, 71.6, 126.1, 129.2, 141.7, 142.2, 168.4;

IR (film) cm$^{-1}$ 2973m, 2870m, 1523s, 1463m, 1271m, 1148s, 1093s;

mass spectrum (APCI): m/e (% relative intensity) 467 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{42}N_2O_3SSiH$ 467.2758, found 467.2747.



**35**

Amidine **35** (40.2 mg, 0.082 mmol) was prepared in 82% yield following the general procedure from ynamide **8a**.

**35**: R*f* = 0.64 [1:1 hexanes:EtOAc]; brown oil;

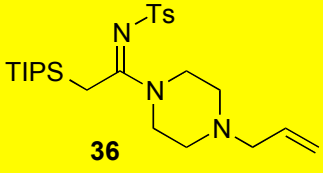
$^1$H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, 18H, *J* = 7.6 Hz), 1.18 (sept, 3H, *J* = 7.6 Hz), 2.42 (s, 3H), 2.73 (s, 2H), 3.27 (s, 3H), 3.82 (s, 3H), 6.92 (d, 2H, *J* = 8.4 Hz), 7.12 (d, 2H, *J* = 8.4 Hz), 7.25 (d, 2H, *J* = 7.6 Hz), 7.88 (d, 2H, *J* = 7.6 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.2, 17.3, 18.6, 18.8, 21.6, 55.9, 113.8, 115.1, 115.2, 126.2, 128.9, 129.2, 141.6, 159.3, 169.9;

IR (film) cm$^{-1}$ 2945m, 2868m, 2252w, 1608m, 1509s, 1463m, 1406m;

mass spectrum (APCI): m/e (% relative intensity) 498 (100) $(M+H)^+$;

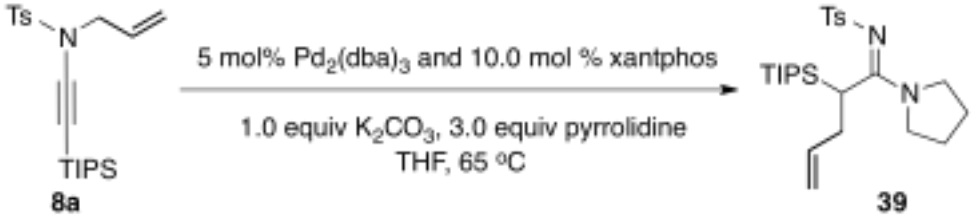
HRMS (ESI) m/e calcd for $C_{26}H_{40}N_2O_3SSiNa$ 511.2421, found 511.2411.



**36**

Amidine **36** (30.0 mg, 0.063 mmol) was prepared in 63% yield following the general procedure from ynamide **8a** and is a known compound.[3]

**General Procedure for the Preparation of $\alpha$-Allyl Amidines from Secondary Amines using Xantphos.**[3]




To a flame-dried vial filled with nitrogen was added $Pd_2(dba)_3$ (8.90 mg, 0.010 mmol), xantphos (11.2 mg, 0.020 mmol), and anhyd THF (4 mL). The resulting solution was stirred at rt for 10 min. Subsequently, a respective ynamide (79.0 mg, 0.20 mmol), $K_2CO_3$ (27.8 mg, 0.20 mmol), and pyrollidine (49.0 µL, 0.60 mmol) were added. The reaction mixture was stirred under nitrogen at 65 $^oC$ for 6 h. The progress of the reaction was monitored by TLC. After complete consumption of the starting ynamide, the crude reaction mixture was filtered through Celite$^{TM}$ and concentrated *in vacuo*. Purification of the crude residue via silica gel flash column chromatography [isocratic eluent: 5:1 hexanes/EtOAc] afforded amidine **39** (95.0 mg, 0.20 mmol, ≥95%).

**39:** *Rf* = 0.22 [5:1 hexanes:EtOAc]; white solid; mp 75-76 $^oC$;

$^1H$ NMR (400 MHz, CDCl3) 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* = 2.4, 8.0 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);

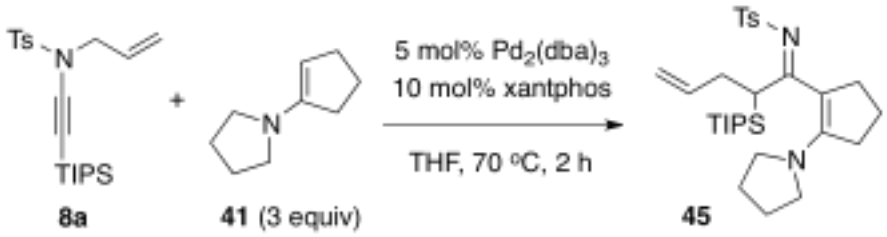
$^{13}C$ NMR (125 MHz, CDCl3) δ 11.5, 19.1, 21.5, 25.4, 25.8, 35.8, 35.9, 51.8, 53.2, 116.0, 126.1, 128.8, 137.8, 140.9, 143.2, 167.1;

IR (neat) $cm^{-1}$ 2924ms, 2863m, 1547s, 1414s, 1274s, 1139s;

mass spectrum (APCI): m/e (% relative intensity) 463 (100) $(M+H)^+$.

HRMS (ESI) m/e calcd for $C_{25}H_{42}N_2O_2SSiNa$ 485.2628, found 486.2630.

**General Procedure for the Synthesis of Vinylogous Amidines.**




To a flame dried screw-cap vial was added ynamide **8a** (75.0 mg, 0.192 mmol), $Pd_2(dba)_3$ (8.8 mg, 0.0096 mmol), xantphos (11.1 mg, 0.019 mmol), THF (2.0 mL), and enamine **41** (77.0 µL, 0.576 mmol), then sealed under a dry nitrogen atmosphere and heated to 70 °C for 2 h. After the reaction was complete by TLC, the solvent was removed *in vacuo* and the resulting crude residue was purified via silica gel flash column chromatography (isocratic eluent: 1:1 hexane/EtOAc + 5% $NEt_3$ buffer) to afford the vinylogous amidine **45** as an orange solid (52.4 mg, 0.099 mmol, 52%).

**45:** R*f* = 0.23 [1:1 hexanes:EtOAc]; orange solid, mp = 95 – 97 °C;

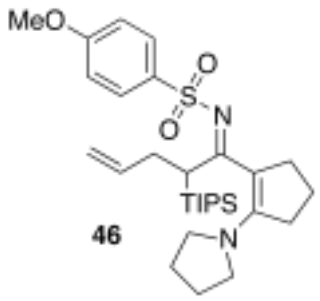
$^1$H NMR (400 MHz, $CDCl_3$) [*spectrum complicated by rotamers*] δ 1.07 (d, 9H, *J* = 6.4 Hz), 1.11 (d, 9H, *J* = 5.2 Hz), 1.10 – 1.20 (m, 3H), 1.83 – 1.90 (m, 2H), 1.90 – 2.01 (m, 3H), 2.01 – 2.15 (m, 2H), 2.25 – 2.35 (m, 1H), 2.34 (s, 3H), 2.50 (d, 1H, *J* = 11.2 Hz), 2.57 – 2.72 (m, 2H), 2.80 (t, 1H, *J* = 4.8 Hz), 2.85 – 2.92 (m, 1H), 3.18 (brs, 2H), 3.89 (brs, 2H), 4.66 (d, 1H, *J* = 18.8 Hz), 4.67 (d, 1H, *J* = 9.2 Hz), 5.51 – 5.62 (m, 1H), 7.14 (d, 2H, *J* = 8.4 Hz), 7.76 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 12.3, 19.3, 19.4, 21.6, 21.7, 25.4, 29.9, 35.2, 36.2, 40.4, 53.0, 111.4, 113.6, 126.0, 128.7, 131.1, 140.0, 140.2, 143.7, 148.1;

IR (film) $cm^{-1}$ 2944m, 2865m, 1736m, 1579m, 1469s, 1445s, 1342m;

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

HRMS (ESI) m/e calcd for $C_{30}H_{48}N_2O_2SSiH$ 529.3279, found 529.3269.



46

Vinylogous amidine **46** (71.3 mg, 0.131 mmol) was prepared in 71% yield following the general procedure from ynamide **8h** in 2 h at 50 °C with the addition of 1.5 equiv of $K_2CO_3$ to the reaction mixture.

**46:** R*f* = 0.18 [1:1 hexanes:EtOAc], orange oil;

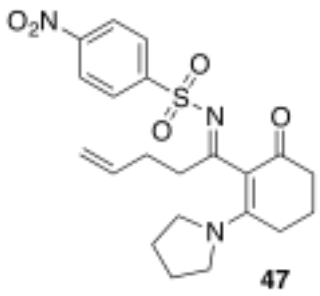
$^1$H NMR (400 MHz, $CDCl_3$) [*spectrum complicated by rotamers*] δ 1.05 (d, 9H, *J* = 6.4 Hz), 1.09 (d, 9H, *J* = 5.2 Hz), 1.09 – 1.15 (m, 3H), 1.70 – 2.10 (m, 9H), 2.32 (brs, 1H), 2.48 (d, 1H, *J* = 11.2 Hz), 2.57 – 2.70 (m, 2H), 2.76 (brs, 1H), 2.80 – 2.90 (m, 1H), 3.13 (brs, 2H), 3.80 (s, 3H), 3.83 (brs, 2H), 4.63 (d, 1H, *J* = 5.6 Hz), 4.65 (d, 1H, *J* = 10.8 Hz), 5.48 – 5.60 (m, 1H), 6.81 (d, 2H, *J* = 8.8 Hz), 7.79 (d, 2H, *J* = 8.8 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 12.3, 19.3, 19.4, 21.7, 25.4, 35.1, 36.2, 40.3, 52.9, 55.5, 113.2, 113.6, 127.9, 139.0, 139.8, 139.9, 160.9 [*missing two $sp^2$ signals due to rotamers*];

IR (film) $cm^{-1}$ 2943m, 2866m, 1596m, 1590m, 1468s, 1249s;

mass spectrum (APCI): m/e (% relative intensity) 545 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{30}H_{48}N_2O_3SSiH$ 545.3228, found 545.3240.



47

Vinylogous amidine **47** (43.3 mg, 0.100 mmol) was prepared in 58% yield following the general procedure from ynamide **8f** in 12 h at 70 °C using 2 mol% $Pd_2(dba)_3$, 4 mol% xantphos, and 1.5 equiv of enaminone **42**.

**47:** R*f* = 0.12 [1:2 hexanes:EtOAc]; orange solid, mp = 69 – 72 °C;

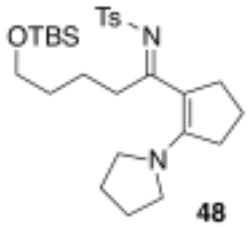
$^{1}$H NMR (500 MHz, $CDCl_3$) δ 1.98 (pent, 2H, *J* = 6.5 Hz), 2.02 (brs, 4H), 2.32 (t, 2H, *J* = 9.0 Hz), 2.34 (t, 2H, *J* = 8.5 Hz), 2.71 (t, 2H, *J* = 6.5 Hz), 3.07 (t, 2H, *J* = 6.5 Hz), 3.30 – 3.55 (m, 4H), 4.92 (dq, 1H, *J* = 1.5, 10.0 Hz), 5.00 (dq, 1H, *J* = 1.5, 17.0 Hz), 5.81 (ddt, 1H, *J* = 6.5, 10.5, 17.0 Hz), 8.30 (d, 2H, *J* = 9.0 Hz), 8.05 (d, 2H, *J* = 9.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 19.3, 25.3, 31.2, 32.1, 38.1, 41.8, 52.5, 109.7, 115.2, 124.1, 128.0, 137.7, 148.6, 149.7, 169.5, 186.5, 193.0;

IR (film) cm$^{-1}$ 3062m, 2954m, 2877m, 1634m, 1608m, 1527s, 1436s, 1349s;

mass spectrum (ESI): m/e (% relative intensity) 454 (100) $(M+Na)^+$, 432 (15) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{21}H_{25}N_3O_5SNa$ 454.1408, found 454.1402.




**48**

Vinylogous amidine **48** (33.6 mg, 0.067 mmol) was prepared in 54% yield following the general procedure from ynamide **8d** in 30 min at 50 °C.

**48:** R*f* = 0.14 [1:1 hexanes:EtOAc]; orange solid; mp = 104 – 107 °C;

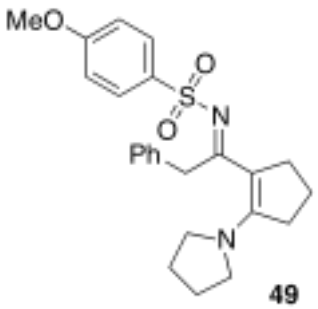
$^{1}$H NMR (500 MHz, $CDCl_3$) δ 0.00 (s, 6H), 0.84 (s, 9H), 1.22 (s, 2H), 1.51 – 1.56 (m, 4H), 1.71 – 1.79 (m, 6H), 2.35 (s, 3H), 2.57 (t, 2H, *J* = 7.5 Hz), 2.61 (t, 2H, *J* = 7.5 Hz), 2.75 – 2.78 (m, 2H), 3.32 (t, 4H, *J* = 6.5 Hz), 3.55 (t, 2H, *J* = 6.5 Hz), 7.19 (d, 2H, *J* = 8.0 Hz), 7.78 (d, 2H, *J* = 8.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ -5.1, 18.5, 21.3, 21.6, 25.0, 25.6, 26.2, 32.8, 33.3, 36.6, 37.1, 53.8, 62.9, 107.0, 126.8, 129.2, 141.6, 142.4, 165.8, 176.9;

IR (film) cm$^{-1}$ 2928m, 2855m, 1569s, 1470s, 1416s;

mass spectrum (ESI): m/e (% relative intensity) 505 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{27}H_{44}N_2O_3SSiH$ 505.2915, found 505.2894.




**49**

Vinylogous amidine **49** (40.8 mg, 0.096 mmol) was prepared in 57% yield following the general procedure from ynamide **8i** in 2 h at rt.

**49:** R*f* = 0.17 [1:2 hexanes:EtOAc]; orange solid; mp = 79 – 83 °C;

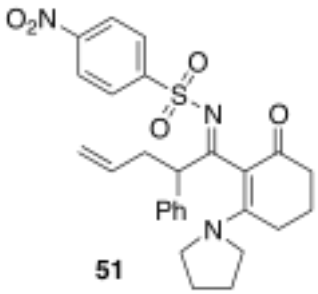
$^1$H NMR (500 MHz, $CDCl_3$) δ 1.69 (pent, 2H, *J* = 7.5 Hz), 1.82 – 1.85 (m, 4H), 2.40 (t, 2H, *J* = 7.5 Hz), 2.53 (t, 2H, *J* = 7.5 Hz), 3.43 (t, 4H, *J* = 7.5 Hz), 3.81 (s, 3H), 4.24 (s, 2H), 6.85 (d, 2H, *J* = 9.0 Hz), 7.13 – 7.22 (m, 5H), 7.84 (d, 2H, *J* = 9.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 21.2, 25.6, 32.8, 36.4, 42.6, 53.8, 55.7, 108.2, 113.7, 126.1, 128.4, 128.7, 129.2, 137.0, 137.6, 161.9, 166.9, 172.6;

IR (film) cm$^{-1}$ 2953m, 2870m, 1665m, 1594m, 1494m, 1412s;

mass spectrum (ESI): m/e (% relative intensity) 425 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{28}N_2O_3SH$ 425.1894, found 425.1897.




**51**

Vinylogous amidine **51** (69.0 mg, 0.136 mmol) was prepared in 62% yield following the general procedure from ynamide **8j** in 3 h at 70 °C using 1.5 equiv of enaminone **42** and 1.5 equiv $K_2CO_3$.

**51:** R*f* = 0.15 [1:1 hexanes:EtOAc]; yellow solid; mp = 177 – 179 °C;

$^1$H NMR (500 MHz, $d_8$-toluene, 90 °C) *spectrum not resolved due to rotamers* δ 1.00 – 1.30 (m, 8H), 1.30 – 1.60 (m, 6H), 1.75 – 1.85 (m, 2H), 1.95 – 2.10 (m, 2H), 2.32 (brs, 4H), 2.55 – 2.62 (m, 3H), 2.83 (brs, 6H), 3.05 – 3.13 (m, 1H), 3.31 (brs, 1H), 3.79 (dd, 1H, *J* = 6.5, 15.0 Hz), 4.65 – 4.75 (m, 2H), 4.76 – 4.85 (m, 2H), 5.52 (brs, 1H), 5.60 – 5.65 (m, 1H), 6.80 – 7.20 (m, 10H), 7.40 (brs, 2H), 7.52 (d, 2H, *J* = 7.5 Hz), 7.65 (d, 2H, *J* = 6.5 Hz), 7.65 – 7.80 (m, 2H).

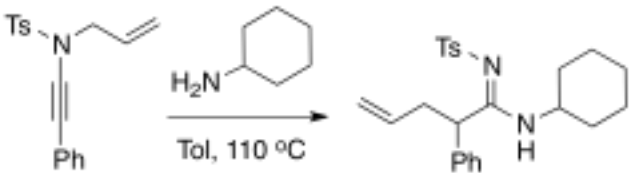
$^{13}$C NMR (125 MHz, $CDCl_3$) *could not obtain spectrum due to rotamers;*

IR (film) $cm^{-1}$ 2970m, 2924w, 1738s, 1621m, 1527s, 1432s, 1350s;

mass spectrum (APCI): m/e (% relative intensity) 508 (100) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{27}H_{29}N_3O_5SH$ 508.1901, found 508.1900.

**General Procedure for the Preparation of $\alpha$-Allyl Amidines via Thermal Aza-Claisen Rearrangement.**




**8b** **56**

To a flame dried screw-cap vial was added ynamide **8b** (62.0 mg, 0.20 mmol), cyclohexylamine (69 µL, 0.60 mmol, 3.0 equiv) and anhyd toluene (2.0 mL). The vial was flushed with nitrogen and heated to 110 °C overnight. Removal of the solvent *in vacuo* followed by purification via silica gel flash column chromatography (isocratic eluent: 5:1 hexanes/EtOAc) afforded the amidine **56** (77.4 mg, 0.19 mmol, 94% yield).

**56:** R*f* = 0.33 [5:1 hexanes:EtOAc]; white solid; mp = 106 – 108 °C;

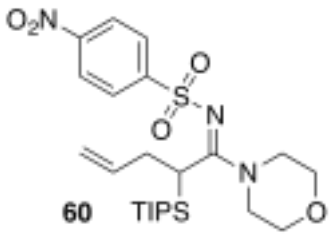
$^1$H NMR (400 MHz, $CDCl_3$) [*showing as two rotamers in 2.5:1 ratio*] *major rotamer* δ 0.80 – 1.40 (m, 6H), 1.40 – 1.70 (m, 3H), 1.70 – 1.95 (m, 2H), 2.41 (s, 3H), 2.82 (pent, 1H, *J* = 7.2 Hz), 3.47 (brs, 1H), 3.64 (t, 1H, *J* = 6.8 Hz), 4.89 (d, 1H, *J* = 11.2 Hz), 4.93 (d, 1H, *J* = 19.2 Hz), 5.55 – 5.68 (m, 1H), 7.21 (brs, 5H), 7.25 (d, 2H, *J* = 7.6 Hz), 7.78 (d, 2H, *J* = 8.4 Hz), 8.34 (d, 1H, *J* = 8.4 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) *major rotamer* δ 21.7, 24.6, 24.7, 25.1, 33.3, 34.3, 39.3, 48.7, 52.6, 117.3, 126.5, 127.7, 128.0, 129.0, 129.3, 135.7, 139.5, 140.0, 142.7, 166.9;

IR (film) $cm^{-1}$ 3320brs, 2933m, 2856m, 1532s, 1451m;

mass spectrum (ESI): m/e (% relative intensity) 844 (30) (2M+Na+H), 433 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{48}H_{60}N_4O_4S_2Na$ (2M+Na) 843.3949, found 843.3962;




Amidine **60** (44.7 mg, 0.088 mmol) was prepared in 93% yield following the general procedure from ynamide **8f**.

**60:** R*f* = 0.12 [4:1 hexanes:EtOAc]; colorless oil;

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 18H), 1.15 – 1.30 (m, 3H), 2.18 – 2.32 (m, 2H), 2.32 – 2.61 (m, 1H), 3.45 – 4.20 (m, 8H), 4.99 (d, 1H, *J* = 16.8 Hz), 5.00 (d, 1H, *J* = 10.0 Hz), 5.65 – 5.85 (m, 1H), 8.06 (d, 2H, *J* = 9.2 Hz), 8.30 (d, 2H, *J* = 9.2 Hz);

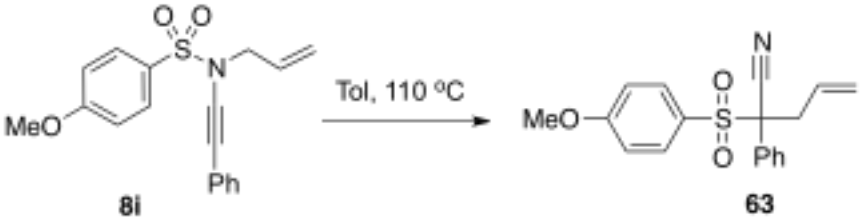
$^{13}$C NMR (125 MHz, $CDCl_3$) δ 11.6, 19.1, 34.0, 35.0, 51.6, 66.7, 116.7, 123.9, 127.3, 137.2, 149.2, 150.6 170.7;

IR (film) cm$^{-1}$2947m, 2869m, 1640w, 1529s, 1425m, 1350m;

mass spectrum (ESI): m/e (% relative intensity) 532 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{39}N_3O_5SSiNa$ 532.2272, found 532.2264.

**General Procedure for the Preparation of Nitriles via Tandem Thermal *Aza*-Claisen Rearrangement – 1,3-Sulfonyl Shift.**




To a flame dried screw-cap vial was added ynamide **8i** (100.0 mg, 0.306 mmol) and anhyd toluene (2.5 mL). The vial was flushed with nitrogen and heated to 110 °C overnight. Removal of the solvent *in vacuo* followed by purification via silica gel flash column chromatography (isocratic eluent: 10:1 hexanes/EtOAc) afforded the nitrile **63** (52.7 mg, 0.161 mmol, 53% yield).

**63:** R*f* = 0.32 [4:1 hexanes:EtOAc]; waxy white solid; mp = 50 – 53 °C;

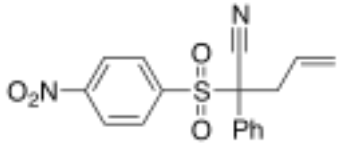
$^1$H NMR (400 MHz, $CDCl_3$) δ 3.32 (dd, 1H, *J* = 7.2, 14.0 Hz), 3.45 (dd, 1H, *J* = 6.8, 14.0 Hz), 3.85 (s, 3H), 5.18 (dd, 1H, *J* = 1.2, 10.0 Hz), 5.30 (dd, 1H, *J* = 1.2, 16.8 Hz), 5.55 (dddd, 1H, *J* = 6.8, 7.2, 10.0, 16.8 Hz), 6.84 (d, 2H, *J* = 9.2 Hz), 7.33 – 7.35 (m, 2H), 7.38 – 7.41 (m, 3H), 7.44 (d, 2H, *J* = 9.2 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 36.1, 56.0, 72.2, 114.2, 116.6, 122.2, 125.1, 128.8, 128.9, 129.0, 129.3, 130.2, 133.2, 164.9;

IR (film) $cm^{-1}$ 2946m, 2843m, 2238w, 1641s, 1592s, 1495s, 1365s;

mass spectrum (ESI): m/e (% relative intensity 350 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{18}H_{17}NO_3SNa$ 350.0822, found 350.0818.



64

Nitrile **64** (51.6 mg, 0.151 mmol) was prepared in 53% yield following the general procedure from ynamide **8j**.

**64:** R*f* = 0.21 [4:1 hexanes:EtOAc]; yellow solid; mp = 125 – 128 °C;

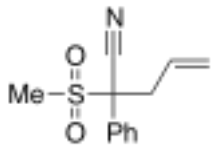
$^1$H NMR (400 MHz, $CDCl_3$) δ 3.39 (dd, 1H, *J* = 7.2, 14.0 Hz,), 3.49 (dd, 1H, *J* = 6.4, 14.0 Hz), 5.24 (d, 1H, *J* = 10.0 Hz), 5.35 (d, 1H, *J* = 16.8 Hz), 5.60 – 5.50 (m, 1H), 7.44 – 7.34 (m, 5H), 7.71 (d, 2H, *J* = 8.4 Hz), 8.22 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 35.7, 72.6, 115.8, 123.1, 123.9, 127.8, 128.4, 128.9, 129.4, 130.9, 132.3, 139.5, 151.6;

IR (film) $cm^{-1}$ 3104m, 2932m, 2850m, 2240w, 1606m, 1530s, 1450m;

mass spectrum (ESI): m/e (% relative intensity) 365 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{17}H_{14}N_2O_4SNa$ 365.0566, found 365.0559.



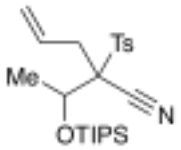
65

Nitrile **65** (31.9 mg, 0.136 mmol) was prepared in 64% yield following the general procedure from ynamide **8l**.

**65:** R*f* = 0.22 [4:1 hexanes:EtOAc]; white solid; mp = 48 – 50 °C;

$^1$H NMR (400 MHz, $CDCl_3$) δ 2.83 (s, 3H), 3.28 – 3.30 (m, 3H), 5.22 (dd, 1H, *J* = 1.2, 10.0 Hz), 5.31 (dd, 1H, *J* = 1.2, 16.8 Hz), 5.55 (ddt, 1H, *J* = 7.2, 10.0, 16.8 Hz), 7.48 – 7.53 (m, 3H), 7.69 – 7.73 (m, 2H);

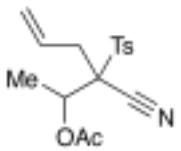
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 35.9, 37.1, 70.8, 116.1, 122.8, 128.4, 128.7, 128.7, 129.7, 130.8;
IR (film) $cm^{-1}$ 3008m, 2930m, 2241w, 1642m, 1599m, 1450s;
mass spectrum (ESI): m/e (% relative intensity) 258 (100) $(M+Na)^+$;
HRMS (ESI) m/e calcd for $C_{12}H_{13}NO_2SNa$ 258.0559, found 258.0552.




**74**

An inseparable 1.5:1 diastereomeric mixture of nitriles **74** (36.4 mg, 0.083 mmol) was prepared in 91% yield following the general procedure from ynamide (±)-**69a**.

**74:** R*f* = 0.41 [6:1 hexanes:EtOAc], colorless oil;
$^1$H NMR (400 MHz, $CDCl_3$) *major isomer* δ 1.06 (s, 18H), 1.05 – 1.08 (m, 3H), 1.50 (d, 3H, *J* = 6.0 Hz), 2.48 (s, 3H), 2.82 – 3.00 (m, 2H), 4.50 (q, 1H, *J* = 5.6 Hz), 5.12 – 5.22 (m, 1H), 5.28 (dd, 1H, *J* = 1.2, 17.6 Hz), 5.90 (dddt, 1H, *J* = 1.2, 7.2, 10.0, 17.2 Hz), 7.41 (d, 2H, *J* = 8.4 Hz), 7.90 (d, 2H, *J* = 8.4 Hz); *minor isomer* δ 0.98 – 1.02 (m, 21H), 1.60 (d, 3H, *J* = 6.4 Hz), 2.48 (s, 3H), 2.82 – 3.00 (m, 2H), 4.73 (q, 1H, *J* = 6.4 Hz), 5.12 – 5.22 (m, 2H), 5.68 – 5.78 (m, 1H), 7.38 (d, 2H, *J* = 8.4 Hz), 7.90 (d, 2H, *J* = 8.4 Hz);
$^{13}$C NMR (125 MHz, $CDCl_3$) *both isomers* δ 12.9, 13.1, 18.2, 18.3, 18.3, 18.4, 19.2, 21.6, 22.0, 22.0, 32.1, 34.8, 69.5, 71.9, 116.4, 116.7, 120.3, 121.0, 130.0, 130.1, 130.6, 131.0, 131.1, 131.3, 132.5, 133.7, 146.4, 146.8;
IR (film) $cm^{-1}$ 2945m, 2868m, 2256w, 1596m, 1493m, 1330m;
mass spectrum (ESI): m/e (% relative intensity) 458 (100) $(M+Na)^+$;
HRMS (ESI) m/e calcd for $C_{23}H_{37}NO_3SSiNa$ 458.2156, found 458.2171.




**75**

An inseparable 1.3:1 diastereomeric mixture of nitriles **75** (19.8 mg, 0.062 mmol) was prepared in 50% yield following the general procedure from ynamide (±)-**69b**.

**75:** R*f* = 0.18 [4:1 hexanes:EtOAc]; colorless oil;

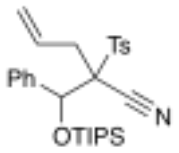
$^1$H NMR (400 MHz, $CDCl_3$) *major diastereomer* δ 1.47 (d, 3H, *J* = 6.4 Hz), 1.90 (s, 3H), 2.49 (s, 3H), 2.81 – 3.04 (m, 2H), 5.25 – 5.30 (m, 2H), 5.46 (q, 1H, *J* = 6.4 Hz), 5.85 – 5.98 (m, 1H), 7.42 (d, 2H, *J* = 8.4 Hz), 7.89 (d, 2H, *J* = 8.4 Hz); *minor diastereomer* δ 1.50 (d, 3H, *J* = 6.4 Hz), 1.97 (s, 3H), 2.49 (s, 3H), 2.81 – 3.04 (m, 2H), 5.25 – 5.30 (m, 2H), 5.46 (q, 1H, *J* = 6.4 Hz), 5.85 – 5.98 (m, 1H), 7.43 (d, 2H, *J* = 8.4 Hz), 7.91 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) *both diastereomers* δ 16.6, 17.8, 21.0, 21.1, 22.1, 31.8, 34.3, 34.7, 68.6, 69.2, 69.3, 71.6, 115.4, 121.7, 121.7, 129.8, 130.0, 130.2, 130.3, 130.8, 131.2, 132.4, 133.2, 147.0, 147.1, 169.1, 169.2 [*missing one sp$^2$ carbon from minor*];

IR (film) cm$^{-1}$ 2923m, 2243w, 1752s, 1642m, 1597m, 1374, 1335s;

mass spectrum (ESI): m/e (% relative intensity) 344 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{16}H_{19}NO_4SNa$ 344.0927, found 344.0914.




**76**

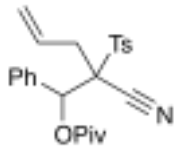
An inseparable 2.0:1 diastereomeric mixture of nitriles **76** (48.0 mg, 0.964 mmol) was prepared in ≥95% yield following the general procedure from ynamide (±)-**69c**.

**76:** R*f* = 0.23 [8:1 hexanes:EtOAc]; colorless oil;

$^1$H NMR (500 MHz, $CDCl_3$) *major diastereomer* δ 0.99 (s, 18H), 1.02 (s, 3H), 2.40 (s, 3H), 3.08 (ddd, 1H, *J* = 1.0, 7.0, 15.0 Hz), 3.18 (ddd, 1H, *J* = 1.0, 7.0, 15.0 Hz), 5.13 (d, 1H, *J* = 9.0 Hz), 5.16 (d, 1H, *J* = 16.0 Hz), 5.54 (s, 1H), 5.74 (ddt, 1H, *J* = 7.0, 9.0, 16.0 Hz), 7.21 (d, 2H, *J* = 8.0 Hz), 7.25 – 7.30 (m, 2H), 7.34 – 7.37 (m, 1H), 7.50 (d, 2H, *J* = 7.0 Hz), 7.63 (d, 2H, *J* = 8.0 Hz); *minor diastereomer* δ 0.99 (s, 18H), 1.02 (s, 3H), 2.44 (ddd, 1H, *J* =1.0, 6.5, 15.5 Hz), 2.45 (s, 3H), 2.64 (ddd, 1H, *J* = 1.0, 6.5, 15.5 Hz), 4.81 (d, 1H, *J* = 17.0 Hz), 4.93 (d, 1H, *J* = 10.0 Hz); 5.45 (ddt, 1H, *J* = 6.5, 10.0, 17.0 Hz), 5.81 (s, 1H), 7.25 – 7.30 (m, 2H), 7.31 (d, 2H, *J* = 8.0 Hz), 7.34 – 7.37 (m, 1H), 7.54 – 7.59 (m, 2H), 7.89 (d, 2H, *J* = 8.0 Hz);

$^{13}$C NMR (125 MHz, $CDCl_3$) *both diastereomers* δ 13.02, 13.12, 18.19, 18.23, 21.95, 22.02, 34.99, 35.38, 72.86, 72.87, 75.50, 75.66, 116.02, 120.06, 120.84, 128.29, 129.14, 129.24, 129.26, 129.43, 129.56, 129.62, 129.65, 129.89, 130.52, 130.89, 130.93, 131.25, 131.31, 133.47, 138.58, 145.94 [*missing two sp$^2$ signals from minor*];

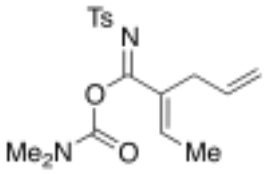
IR (film) $cm^{-1}$ 2945m, 2893m, 2867m, 2240w, 1639w, 1596m, 1494m, 1365m;
mass spectrum (ESI): m/e (% relative intensity) 520 (100) $(M+Na)^+$;
HRMS (ESI) m/e calcd for $C_{28}H_{39}NO_3SSiNa$ 520.2313, found 520.2322.




**77**

A separable 1.5:1 mixture of nitrile diastereomers **77** (29.8 mg, 0.070 mmol) was prepared in 69% yield following the general procedure from ynamide (±)-**69d**.

**77**-*major*: R*f* = 0.28 [6:1 hexanes:EtOAc]; colorless oil;
$^1H$ NMR (500 MHz, $CDCl_3$) δ 1.04 (s, 9H), 2.38 (dd, 1H, *J* = 7.0, 15.5 Hz), 2.48 (s, 3H), 2.64 (dd, 1H, *J* = 7.0, 15.5 Hz), 4.76 (dd, 1H, *J* = 1.5, 17.0), 4.93 (dd, 1H, *J* = 1.5, 10.0 Hz), 5.27 (ddt, 1H, *J* = 7.0, 10.0, 17.0 Hz), 6.30 (s, 1H), 7.35 – 7.38 (m, 3H), 7.41 (d, 2H, *J* = 8.5 Hz), 7.46 – 7.49 (m, 2H), 7.93 (d, 2H, *J* = 8.5 Hz);
$^{13}C$ NMR (125 MHz, $CDCl_3$) δ 22.0, 26.8, 36.1, 38.9, 69.8, 73.6, 114.9, 120.8, 128.5, 129.1, 129.2, 130.1, 130.3, 131.1, 133.3, 134.8, 146.9, 176.0;
IR (film) $cm^{-1}$ 3068w, 2974m, 2934m, 2873w, 2242w, 1739s, 1595m, 1494m, 1336s;
mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+Na)^+$;
HRMS (ESI) m/e calcd for $C_{24}H_{27}NO_4SNa$ 448.1553, found 448.1558.
**77**-*minor*: R*f* = 0.35 [6:1 hexanes:EtOAc]; colorless oil;
$^1H$ NMR (500 MHz, $CDCl_3$) δ 1.27 (s, 9H), 2.46 (s, 3H), 3.03 (dd, 1H, *J* = 7.0, 15.0 Hz), 3.16 (dd, 1H, *J* = 7.0, 15.0 Hz), 5.22 (d, 1H, *J* = 9.0 Hz), 5.23 (d, 1H, *J* = 17.5 Hz), 5.81 – 5.84 (m, 1H), 6.22 (s, 1H), 7.30 – 7.37 (m, 7H), 7.75 (d, 2H, *J* = 8.5 Hz);
$^{13}C$ NMR (125 MHz, $CDCl_3$) δ 22.1, 27.2, 34.7, 39.2, 70.0, 73.0, 115.4, 121.5, 128.5, 128.7, 129.8, 130.0, 130.4, 131.2, 132.2, 134.4, 146.7, 175.8;
IR (film) $cm^{-1}$ 3069w, 2978m, 2937m, 2874w, 2244w, 1746s, 1597m, 1495m, 1338s;
mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+Na)^+$;
HRMS (ESI) m/e calcd for $C_{24}H_{27}NO_4SNa$ 448.1553, found 448.1566.




**79**

Imidate **79** (24.4 mg, 0.070 mmol) was prepared in 74% yield following the same procedure as for nitrile formation from ynamide (±)-**69e**.

**79:** R*f* = 0.28 [2:1 hexanes:EtOAc]; white solid; mp = 80 – 84 °C;

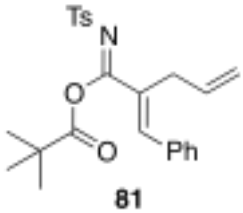
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.70 (d, 3H, *J* = 7.2 Hz), 2.43 (s, 3H), 2.93 (d, 2H, *J* = 6.4 Hz), 3.18 (s, 6H), 4.92 (dq, 1H, *J* = 2.0, 10.2 Hz), 4.95 (dq, 1H, *J* = 2.0, 16.8 Hz), 5.64 (ddt, 1H, *J* = 6.4, 10.2, 16.8 Hz), 6.06 (q, 1H, *J* = 7.2 Hz), 7.31 (d, 2H, *J* = 8.4 Hz), 7.98 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.0, 32.3, 116.4, 129.4, 129.6, 133.4, 134.1, 134.3, 136.3, 145.3, 152.1, 169.0 [*missing $NMe_2$ carbon signal*];

IR (film) cm$^{-1}$ 2927m, 2251w, 1703s, 1641m, 1598m, 1495m, 1448m, 1359s;

mass spectrum (ESI): m/e (% relative intensity) 373 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{17}H_{22}N_2O_4SNa$ 373.1193, found 373.1188.




**81**

Imidate **81** (12.7 mg, 0.299 mmol) was prepared in 30% yield following the general procedure for nitrile formation from ynamide (±)-**69d**.

**81:** R*f* = 0.41 [6:1 hexanes:EtOAc]; white solid; mp = 65 – 67 °C;

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.43 (s, 3H), 3.28 (d, 2H, *J* = 5.6 Hz), 5.08 (d, 1H, *J* = 10.4 Hz), 5.11 (d, 1H, *J* = 17.2 Hz), 5.89 (ddt, 1H, *J* = 5.6, 10.4, 17.2 Hz), 7.31 (d, 2H, *J* = 8.4 Hz), 7.40 (s, 6H), 7.54 (s, 1H), 7.85 (d, 2H, *J* = 8.4 Hz);

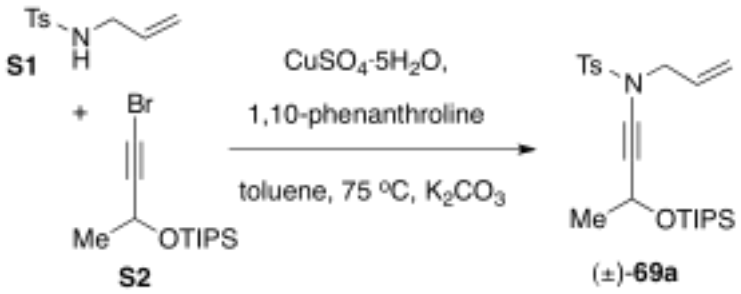
$^{13}$C NMR (125 MHz, $CDCl_3$) δ 21.9, 27.4, 32.2, 39.9, 116.9, 127.4, 128.9, 129.6, 130.0, 130.0, 132.2, 134.4, 134.9, 138.3, 143.7, 144.0, 162.1, 174.4;

IR (film) cm$^{-1}$ 2966m, 1765s, 1740s, 1601s, 1481m, 1326s;

mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{27}NO_4SNa$ 448.1553, found 448.1543.

**General Procedure for the Preparation of Ynamides via Cu(I)-catalyzed Cross-Coupling.**[1-3]




To a flame-dried screw-cap vial was added *N*-allyl sulfonamide **S1** (287.0 mg, 1.36 mmol), $CuSO_4 \cdot 5H_2O$ (34.0 mg, 0.14 mmol), 1,10-phenanthroline (49.0 mg, 0.28 mmol) and $K_2CO_3$ (375.0 mg, 2.72 mmol), followed by anhyd toluene (3 mL) and acetylenic bromide **S2** (500.0 mg, 1.63 mmol). The flask was filled with nitrogen by three vacuum-flush cycles and the solution was heated in a 75 °C oil bath overnight. When complete, the crude reaction mixture was filtered through Celite™ and concentrated *in vacuo*. Purification of the crude residue using silica gel flash column chromatography (isocratic eluent: 8:1 hexane/EtOAc) afforded ynamide (±)-**69a** (107.0 mg, 0.246 mmol, 18% yield).

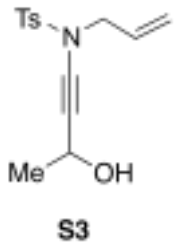
(±)-**69a:** R*f* = 0.37 [8:1 hexanes:EtOAc]; pale yellow oil;

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.00 – 1.07 (m, 21H), 1.42 (d, 3H, *J* = 6.4 Hz), 2.44 (s, 3H), 3.89 – 4.00 (m, 2H), 4.70 (q, 1H, *J* = 6.4 Hz), 5.16 – 5.25 (m, 2H), 5.72 (ddt, 1H, *J* = 6.4, 10.4, 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 12.4, 18.2, 21.9, 26.1, 54.5, 59.4, 73.8, 76.6, 120.0, 128.0, 129.9, 131.3, 135.1, 144.7;

IR (film) $cm^{-1}$ 2944m, 2866m, 2246m, 1737m, 1463m, 1367s;

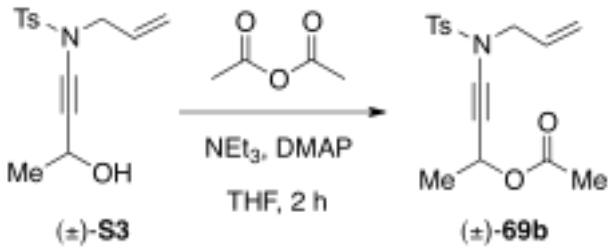
mass spectrum (APCI): m/e (% relative intensity) 294 (100) $(M\text{-OTIPS+MeOH+H})^+$.




Ynamide (±)-**S3 (**134.0 mg, 0.480 mmol) was prepared in 23% yield following the general procedure.

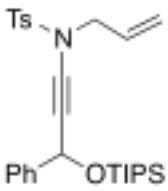
(±)-**S3:** R*f* = 0.22 [2:1 hexanes:EtOAc]; colorless oil;

$^1$H NMR (400 MHz, $CDCl_3$) δ 1.42 (d, 3H, $J$ = 6.8 Hz), 2.45 (3H, s), 3.91 – 3.96 (m, 2H), 4.59 – 4.64 (m, 1H), 5.17 – 5.27 (m, 2H), 5.65 – 5.77 (m, 1H), 7.34 (d, 2H, $J$ = 8.4 Hz), 7.78 (d, 2H, $J$ = 8.4 Hz);
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.8, 24.6, 46.9, 54.2, 58.6, 73.2, 120.2, 127.9, 129.9, 130.9, 134.7, 144.9;
IR (film) cm$^{-1}$ 3502m, 2982m, 2245m, 1567m, 1363s;
mass spectrum (APCI): m/e (% relative intensity) 280 (80) $(M+H)^+$.
HRMS (ESI) m/e calcd for $C_{14}H_{17}NO_3SNa$ 302.0822, found 302.0818.




To a solution of alcohol (±)-**S3** (114.0 mg, 0.407 mmol) and $NEt_3$ (84.0 µL, 0.611 mmol) in $CH_2Cl_2$ (1.4 mL) at 0 °C was added acetic anhydride (58 µL, 0.611 mmol) then DMAP (5.0 mg, 0.041 mmol). After 1.5 h at 0 °C, the reaction mixture was diluted with EtOAc (5 mL) and quenched with sat. $NaHCO_3$. The organic phase extracted with EtOAc (3 x 10 mL), then washed with brine, dried over $Na_2SO_4$, and concentrated *in vacuo*. The crude residue was then purified by flash silica gel column chromatography (isocratic eluent: 8:1:1 hexanes/EtOAc/$CH_2Cl_2$) to afford the ynamide (±)-**69b** (100.2 mg, 0.311 mmol) in 76% yield.

(±)-**69b:** R*f* = 0.24 [4:1 hexanes:EtOAc]; colorless oil;
$^1$H NMR (500 MHz, $CDCl_3$) δ 1.46 (d, 3H, $J$ = 7.0 Hz), 2.03 (s, 3H), 2.45 (s, 3H), 3.89 – 4.00 (m, 2H), 5.20 (dd, 1H, $J$ = 1.5, 10.0 Hz), 5.23 (dd, 1H, $J$ = 1.5, 17.0 Hz), 5.52 (q, 1H, $J$ = 7.0 Hz), 5.71 (ddt, 1H, $J$ = 6.5, 10.0, 17.0 Hz), 7.35 (d, 2H, $J$ = 8.0 Hz), 7.90 (d, 2H, $J$ = 8.0 Hz);
$^{13}$C NMR (75 MHz, $CDCl_3$) δ 21.3, 21.5, 21.8, 54.2, 60.9, 70.4, 78.5, 120.3, 128.0, 129.9, 130.8, 134.7, 144.9, 170.0;
IR (film) cm$^{-1}$ 2989w, 2937w, 2247m, 1737s, 1366s;
mass spectrum (ESI): m/e (% relative intensity) 344 (100) $(M+Na)^+$;
HRMS (ESI) m/e calcd for $C_{16}H_{19}NO_4SNa$ 344.0927, found 344.0932.




(±)-**69c**

Ynamide (±)-**69c** (163.0 mg, 0.327 mmol) was prepared in 66% yield from amide **S1** (105.0 mg, 0.499 mmol) using CuTC (19.0 mg, 0.099 mmol), DMEDA (21.0 µL, 0.199 mmol), and $Cs_2CO_3$ (327.0 mg, 0.996 mmol) following the general procedure.

(±)-**69c:** R*f* = 0.39 [6:1 hexanes:EtOAc]; colorless oil;

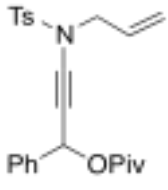
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.03 (d, 9H, *J* = 7.2 Hz), 1.05 (d, 9H, *J* = 7.2 Hz), 1.10 – 1.18 (m, 3H), 2.41 (s, 3H), 3.87 – 3.99 (m, 2H), 5.14 (dd, 1H, *J* = 1.2, 9.0 Hz), 5.17 (dd, 1H, *J* = 1.2, 16.4 Hz), 5.65 (s, 1H), 5.69 (ddt, 1H, *J* = 6.4, 9.0, 16.4 Hz), 7.20 (d, 2H, *J* = 8.0 Hz), 7.26 – 7.30 (m, 1H), 7.34 (t, 2H, *J* = 7.6 Hz), 7.45 (d, 2H,*J* = 7.6 Hz), 7.62 (d, 2H, *J* = 8.0 Hz);

$^{13}$C NMR (75 MHz, $CDCl_3$) δ 12.5, 18.3, 21.9, 54.4, 65.2, 72.8, 79.1, 120.1, 126.2, 127.7, 128.0, 128.4, 129.8, 131.2, 134.8, 142.7, 144.6;

IR (film) cm$^{-1}$ 2943m, 2866m, 2240w, 1597m, 1368s;

mass spectrum (APCI): m/e (% relative intensity) 821 (100) $(2M–HOTIPS+H)^+$, 498 (40) $(M+H)^+$;

HRMS (ESI) m/e calcd for $C_{28}H_{39}NO_3SSiNa$ 520.2312, found 520.2303.




(±)-**69d**

Ynamide (±)-**69d** (146.8 mg, 0.345 mmol) was prepared in 36% yield from amide **S1** (200.0 mg, 0.971 mmol) using CuTC (37.0 mg, 0.193 mmol), DMEDA (42.0 µL, 0.386 mmol), and $Cs_2CO_3$ (663.0 mg, 1.94 mmol) following the general procedure.

(±)-**69d:** R*f* = 0.28 [6:1 hexanes:EtOAc]; pale yellow solid; mp = 51 – 53 °C;

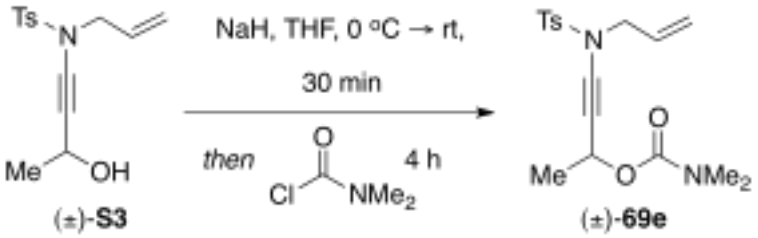
$^1$H NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 9H), 2.42 (s, 3H), 3.97 (dd, 2H, *J* = 6.4, 7.2 Hz), 5.17 – 5.24 (m, 2H), 5.70 (ddt, 1H, *J* = 6.4, 10.4, 16.8 Hz), 6.50 (s, 1H), 7.26 (d, 2H, *J* = 8.4 Hz), 7.34 – 7.39 (m, 3H), 7.46 (dd, 2H, *J* = 2.0, 7.6 Hz), 7.72 (d, 2H, *J* = 8.4 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.9, 27.2, 38.9, 54.3, 66.1, 68.9, 80.7, 120.4, 127.6, 128.0, 128.7, 128.8, 129.9, 130.8, 134.7, 137.6, 144.9, 177.4;

IR (film) cm$^{-1}$ 2971m, 2871m, 2247m, 1725s, 1506m, 1457m, 1362s;

mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{24}H_{27}NO_4SNa$ 448.1553, found 448.1544.




To a solution of alcohol (±)-**S3** (50.0 mg, 0.179 mmol) in THF (0.4 mL) at 0 °C was added NaH (8.6 mg, 0.215 mmol). After 30 min at 0 °C, *N,N*-dimethylcarbamoyl chloride (19.8 µL, 0.215 mmol) was added dropwise, then the cooling bath was removed. After 4 h at rt, the reaction was diluted with EtOAc (5 mL) and quenched with sat. $NH_4Cl$. The organic phase was washed with sat. $NaHCO_3$ and brine then dried over $Na_2SO_4$ and concentrated *in vacuo*. The crude residue was then purified by flash silica gel column chromatography (isocratic eluent: 2:1 hexanes/EtOAc) to afford the ynamide (±)-**69e** (40.0 mg, 0.114 mmol) in 64% yield.

(±)-**69e:** R*f* = 0.28 [2:1 hexanes:EtOAc]; colorless oil;

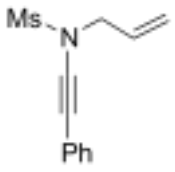
$^1$H NMR (500 MHz, $CDCl_3$) δ 1.47 (d, 3H, *J* = 7.0 Hz), 2.45 (s, 3H), 2.90 (s, 6H), 3.91 – 3.99 (m, 2H), 5.19 (d, 1H, *J* = 10.0 Hz), 5.23 (d, 1H, *J* = 17.5 Hz), 5.49 (q, 1H, *J* = 7.0 Hz), 5.67 – 5.75 (m, 1H), 7.33 (d, 2H, *J* = 8.0 Hz), 7.80 (d, 2H, *J* = 8.0 Hz);

$^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.8, 22.1, 36.1, 36.6, 54.3, 61.8, 71.0, 78.1, 120.2, 128.0, 129.8, 130.9, 134.8, 144.8, 155.7;

IR (film) cm$^{-1}$ 2986w, 2943w, 1702s, 1366m;

mass spectrum (ESI): m/e (% relative intensity) 373 (100) $(M+Na)^+$;

HRMS (ESI) m/e calcd for $C_{17}H_{22}N_2O_4SNa$ 373.1193, found 373.1185.




**8l**

Ynamide **8l** (166.0 mg, 0.704 mmol) was prepared in 64% yield following the general procedure from *N*-mesyl allyl amine.

**8l:** R*f* = 0.27 [4:1 hexanes:EtOAc]; colorless oil;

$^{1}$H NMR (500 MHz, $CDCl_3$) δ 3.14 (s, 3H), 4.17 (d, 2H, *J* = 6.5 Hz), 5.38 (d, 1H, *J* = 10.0 Hz), 5.44 (d, 1H, *J* = 17.0 Hz), 6.00 (ddtd, 1H, *J* = 1.5, 6.5, 10.0, 17.0 Hz), 7.28 – 7.30 (m, 3H), 7.37 – 7.42 (m, 2H);

$^{13}$C NMR (125 MHz, $CDCl_3$) δ 39.2, 54.7, 71.4, 81.8, 120.9, 122.7, 128.3, 128.6, 131.2, 131.8;

IR (film) $cm^{-1}$ 3030w, 2933w, 2241m, 1596w, 1490m, 1344s;

mass spectrum (ESI): m/e (% relative intensity) 258 (100) $(M+Na)^{+}$.

HRMS (ESI) m/e calcd for $C_{12}H_{13}N_2O_2SH$ 236.0740, found 236.0740.

1. Zhang, Y.; Hsung, R. P.; Tracey, M. R.; Kurtz, K. C. M.; Vera, E. L. *Org. Lett.* **2004**, *6*, 1151.
2. Zhang, X.; Zhang, Y.; Huang, J.; Hsung, R. P.; Kurtz, K. C. M.; Oppenheimer, J.; Peterson, M. E.; Sagamanova, I. K.; Shen, L.; Tracey, M. R. *J. Org. Chem.* **2006**, *71*, 4170.
3. Zhang, Y.; DeKorver, K. A.; Lohse, A. G.; Zhang, Y.-S.; Huang, J.; Hsung, R. P. *Org. Lett.* **2009**, *11*, 899.