Published in final edited form as:
J Org Chem. 2011 June 17; 76(12): 5092–5103. doi:10.1021/jo200780x.

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

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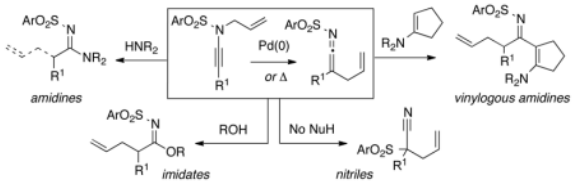
Abstract



A detailed study of amidine synthesis from *N*-allyl-*N*-sulfonyl ynamides is described here. Mechanistically, this is a fascinating reaction consisting of diverging pathways that could lead to deallylation or allyl transfer depending upon the oxidation state of palladium catalysts, the nucleophilicity of amines, and the nature of the ligands. It essentially constitutes a Pd(0)-catalyzed *aza*-Claisen rearrangement of *N*-allyl ynamides, which can also be accomplished thermally. An observation of *N-to-C* 1,3-sulfonyl shift was made when examining these *aza*-Claisen rearrangements thermally. This represents a useful approach to nitrile synthesis. While attempts to render this 1,3-sulfonyl shift stereoselective failed, we uncovered another set of tandem sigmatropic rearrangements, leading to vinyl imidate formation. Collectively, this work showcases the rich array of chemistry one can discover using these ynamides.

Introduction

Amidines[1,2] represent a prolific functional group in medicinal chemistry and an important pharmacophore in drug discovery.[3–6] One notable example is the DNA and RNA binding di-amidine Diminazene, which is found in drugs like Azidin, Berenil, or Pirocide to treat the parasitic protozoan that causes Trypanosoniasis for which African sleeping sickness and Chagas disease are a form.[7] There are several different variations of amidines depending on the substituents on the nitrogen or the sp^2-amidinyl carbon[1,2] [Figure 1]. Aliphatic and aromatic amidines are generally prepared in a very similar manner, frequently from amides, nitriles, and thioamides with a nitrogen nucleophile.[1,2,8] The Pinner reaction and modified Pinner transformations,[9,10] which employ nitriles and go through an imidate, are the most common protocols for synthesizing amidines. However, this method is not good for hindered nitriles and it cannot be used for the synthesis of tertiary amidines. Consequently, amides and thioamides are frequently used.[1,2] Activation of the mono-substituted amide by

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chlorinating agents or alkylation of the alkoxy group can yield amidines when the resulting compound is reacted with an amine. Thioamides can more directly yield an amidine by simply reacting it with an amine and a mercury salt to act as a sulfide scavenger [Figure 1]. Whitby[11] recently reported an interesting usage of isonitrile for accessing amidines by reacting with aryl or allyl bromides and an amine using a palladium catalyst. Lastly, there has been extensive development in constructing amidines through decomposing *N*-sulfonyl triazoles [not shown here].[12–15]

We recently found that ynamides[16–18] could serve as excellent precursors for synthesizing amidines via a Pd(0)-catalyzed *N-to-C* allyl transfer.[19] As shown in Scheme 1, the oxidative addition [O.A.] of *N*-allyl-ynamides **1** would lead to novel ynamido-π-allyl complexes **2a** and ketenimino-π-allyl complexes **2b**. The subsequent formation of amidines **4** would occur in the presence of an amine either through trapping of ketenimines **3**, which is derived from **2b** via reductive elimination [R.E.]; or through π-allyl complex **5**, which is a result of the amine addition to complexes **2b** prior to R. E. We also found that while amidines **4** represent a successful *N-to-C* allyl transfer, the reaction did not always lead to transfer of the allyl group. Instead, a diverging pathway would lead to amidines **6** that could be prepared with concomitant de-allylation depending upon the amine and the nature of the palladium catalyst and ligands. Although it is quite reasonable to presume that this de-allylation could have occurred through amine attacking the palladium π-allyl complexes **2b**, it could also be envisioned from keteniminium intermediate **7** generated from **1** with the Pd(II) species serving as a π-Lewis acid. We recognized that not only does this signify a *de novo* transformation of ynamides with an invaluable opportunity to study ynamido-metal complexes,[12–16,20,21] but also an excellent method for synthesizing amidines especially given that ynamides are now synthetic readily available substrates.[22–24] We report here details of our investigation in developing this amidine synthesis.

Results and Discussion

1. Deallylative Amidine Formation

We made our initial discovery of the deallylation of ynamides when treating *N*-allyl-ynamide **8a** with 5 mol% of $PdCl_2(PPh_3)_2$ with an original intent to hydroaminate the alkyne [Scheme 2]. Instead, we found that amidine **9** was formed in high yield when using 10.0 equiv of H_2N-*t*-Bu, and that the allyl group was missing. Intriguingly, when lowering the amount of the amine to 3.0 equiv, the allyl resonances visibly reappeared in the proton NMR and no longer on the nitrogen atom but on the formerly the β-carbon of the ynamide after isolating **10** in 37% yield. We recognized this unexpected transformation represents an excellent protocol for synthesizing amidines, and to avoid complication with the allyl group issue, we initially focused on deallylation via using 5.0 equiv of the amine. The generality and the effectiveness of this amidine synthesis could be thoroughly captured in Table 1 through using a wide range of primary amines, and demonstrated in Table 2 via employing a diverse array of secondary amines as well as varying the *N*-allyl-ynamide substitutions. It is noteworthy that based on NOE experiments, these amidines adopt an *E*-geometry with respect to the C=N bond.[19]

2. Deallylation Mechanism and Allyl Transfer

While this is an interesting amidine synthesis, we were fascinated by its possible mechanism. Because of their basicity, polarity, and/or volatility, the respective allyl amine byproducts [R_2N-CH_2CH=CH_2] from deallylation were difficult to isolate. Nevertheless, as shown in Scheme 3, a mechanistically revealing experiment involved the use of piperizine, which led to the *N*-allylated amine **36** in 63% yield. Consequently, deallylation could be either a Pd(0)- or Pd(II)-catalyzed process. The former would require oxidative addition of

Pd(0) to *N*-allyl ynamide **8a**, leading to **5** through an *N-to-C* allyl transfer from ynamido-palladium π–allyl complex **2a**; while the latter would involve a palladium(II)-substituted keteniminium ion **7** with Pd(II) serving to activate the alkynyl motif. Deallylation could take place either in an intramolecular manner as shown in **5**; or an intermolecular manner as shown in **7.** Although attempts were made, these reactions were too fast to allow NMR studies to be revealing of possible ynamido-π-allyl complexes even at 25 °C. Only the starting ynamide, silyl-ketenimine such as **3** and respective amidine product [if the reaction was run in the presence of an amine] were clearly in display spectroscopically.

While both pathways could be operative for the deallylation, we suspected that suppression of the Pd(II)-catalyzed pathway through directly using a Pd(0) source could lead to suppression of the deallylation.[25] As shown in Table 3, this predictive assessment turned out to be true. While most Pd(II) sources led to predominantly the deallylation when using 3.0 equiv of *c*-hex-NH_2, $Pd(PPh_3)_4$ gave exclusively the allyl transferred amidine **37** [entry 6]. This preservation of the allyl group turned to be general for a number of primary amines, as evident from amidine products **38a–c**.

However, the use of $Pd(PPh_3)_4$ was not sufficient especially in the case of secondary amines such as pyrrolidine or piperidine, which are more nucleophilic than primary amines, leading to exclusively deallylation.[26] The nature of the ligand also mattered. Those that favored reductive elimination such as xantphos[27,28] allowed the isolation of a range of different allyl transferred amidines such as **39** and **40a–e** [Scheme 4]. X-phos[29] was also examined and was comparable in terms of yield of allylated amidines, but xantphos allowed shorted reaction times.[19]

Furthermore, we found that enamines or vinylogous amides could also be used as nucleophiles under these conditions for allyl transfers. As shown in Table 4, vinylogous amidines **45** and **46** [entries 1 and 2] as well as **47** and **51** [entries 3 and 7] could be accessed utilizing enamine **41** and vinylogous amide **42**, respectively. For reasons unknown to us at this moment, the allyl group did not transfer for vinylogous amidines **48** and **49** [entries 4 and 5], and primary vinylogous amides such as **43** did not work well [entry 6]. Nevertheless, a general trend for the dichotomy of deallylation versus *N-to-C* allyl transfer could be summarized as shown in Figure 2. Deallylation is favored when using excess of amine, or Pd(II) sources, and/or more nucleophilic secondary amines whereas *N-to-C* allyl transfer is favored with less nucleophilic primary amines, Pd(0) sources, and/or R.E. favoring ligands such as xantphos.

3. *Aza*-Claisen Rearrangement and 1,3-Sulfonyl Shift

Our efforts described above allowed us to recognize that these reactions in essence are *aza*-Claisen rearrangements[30–32] promoted by palladium catalysts. In fact, *aza*-Claisen rearrangements could be carried out thermally without any metal catalysts. As shown in Scheme 5, a non-palladium involved pathway would entail an *aza*-Claisen transition state [see **A**], leading to allyl-ketenimine intermediate **B.** Trapping of **B** would then lead to many products, and in the case of an alcohol, imidates could be accessed.[33,34]

Trapping of the allyl-ketenimine intermediate such as **55** with an external amine could also lead to allyl-transferred amidine **39**. This indeed is true not only in the case of **39** but is also highly effective as shown in Table 5 in giving a wide range of amidines **56–60** in good yields.[35] However, this pathway requires much higher temperature and longer reaction time. When carried out at 65 °C to 80 °C in THF, the reaction was sluggish and slow,[36] thereby suggesting that the palladium catalyst was indeed promoting these transformations.

It was during this study that we observed an interesting *N-to-C* 1,3-sulfonyl shift.[37] As shown in Scheme 6, when using ynamides not substituted with TIPS at the terminal position, we observed the formation of quaternary nitriles **61** in the absence of an amine. This observation suggested that allyl ketenimines **3** in which R ≠ TIPS had undergone a *N-to-C* 1,3-sulfonyl shift; whereas this was not the case when R = TIPS. Silyl ketenimines such as **55** were sufficiently stable[38,39] and could be trapped subsequently.

This nitrile formation is very general including a number of different sulfonyl groups as demonstrated in Table 6 [see entries 1–4]. While the 1,3-sulfonyl shift tolerated various substitutions [entries 5 and 6], again when using **8a** containing the TIPS substitution [entry 7], the 1,3-sulfonyl shift only took place only when in conjunction with desilylation. It is also noteworthy that given results in Table 5, the *N-to-C* 1,3-sulfonyl shift most likely took place after the *aza*-Claisen rearrangement. In addition, monitoring the thermal *aza*-Claisen rearrangement of ynamide **8b** using proton NMR did not reveal any respective ketenimine, thereby suggesting that the 1,3-sulfonyl shift was very fast at 110 °C.

We then attempted to extend this interesting 1,3-sulfonyl shift because the formation of tertiary nitriles holds significant merit in synthesis.[40] As shown in Scheme 7, we envisioned that using ynamide **69** containing a propargylic stereocenter could lead to a stereoselective 1,3-sulfonyl shift to give **70** or **70′**. The level of selectivity would depend upon conformational preference of allyl-ketenimine intermediate **72** and **72′**, and in this case, the conformer **72′** could be more preferred given the $A^{1,2}$-*strain* present in **72**. This preference could lead to a facial selective 1,3-sulfonyl shift to give **70′**. In addition, we could vary the P group so that it could lead to the conformational situation shown in **73′** in which anchiomeric assistance could take place, again leading to possible facial selective 1,3-sulfonyl shift.

Unfortunately, after examining a number of such ynamides [**69a–d**], the best ratio was 2:1 using **69c** [entry 3 in Table 7]. Most intriguingly, when exploring ynamide **69e** [P = *N*-dimethyl carbamoyl] and **69d** [P = Piv] with hope of the aforementioned anchiomeric assistance, we obtained α,β-unsaturated imidates **79** and **81**, respectively. The double bond geometry was assured using NOE experiments. In addition, when we went back to crude proton NMR of the reaction using **69b** in which P = Ac, we also saw ~10% of the respective imidate. Intriguingly, no nitrile was found in the case of **69e**, due to the increased electron density in the carbamate. The isolation of these imidates implied a sequence of tandem sigmatropic rearrangement: an *aza*-Claisen followed by another [3,3]-sigmatropic rearrangement through the respective allyl-ketenimine intermediates **78** and **80**.

CONCLUSION

We have described here a detailed study of amidine synthesis from *N*-allyl-*N*-sulfonyl ynamides. Mechanistically, this is a fascinating reaction consisting of diverging pathways that could lead to deallylation or allyl transfer depending upon the oxidation state of palladium catalysts, the nucleophilicity of amines, and the nature of the ligands. It essentially constitutes a Pd(0)-catalyzed *aza*-Claisen rearrangement of *N*-allyl ynamides, which can also be accomplished thermally. An observation of *N-to-C* 1,3-sulfonyl shift was made when examining these *aza*-Claisen rearrangements thermally, thereby representing a useful approach to nitrile synthesis. While attempts to render this 1,3-sulfonyl shift stereoselective failed, we uncovered another set of tandem sigmatropic arrangements, leading to vinyl imidate formation, and thereby suggesting rich chemistry one can develop using these ynamides.

EXPERIMENTAL SECTION

General Procedure for the Preparation of Des-Allyl 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 judged to be 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.

11 (87%): 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 (41%): 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 (22%): 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 (22%): 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 (30%): 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 (≥95%): 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 (≥95%): R*f* = 0.36 [2:1 hexanes:EtOAc]; white solid; mp = 143 – 145 °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 (≥95%): 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 (92%): 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 (37%): 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 (39%): 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 (≥95%): 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 (≥95%): 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 (≥95%): 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 (70%): 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 (≥95%): 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 (77%): 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 (≥95%): R*f* = 0.30 [3:1 hexanes:EtOAc]; white solid; mp = 161 – 163 °0C; ^{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 (≥95%): 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 (≥95%): 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* = 7.8 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 (91%): 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 (≥95%): R*f* = 0.80 [1:1 hexanes:EtOAc]; $[\alpha]_D^{23} = -63.5$ (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 (≥95%): R*f* = 0.46 [95:5 CH_2Cl_2:MeOH]; pale yellow oil; ^1H 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 (≥95%): R*f* = 0.50 [2:1 hexanes:EtOAc]; white solid; mp = 126 – 127 °C; ^1H 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 (≥95%): R*f* = 0.59 [1:1 hexanes:EtOAc]; yellow solid; mp = 125 – 126 °C; ^1H 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 (sept, 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 (82%): R*f* = 0.64 [1:1 hexanes:EtOAc]; brown oil; ^1H 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.

General Procedure for the Preparation of *α*-Allyl Amidines from Secondary Amines using $Pd_2(dba)_3$ and 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 °C 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™ 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: R*f* = 0.22 [5:1 hexanes:EtOAc]; white solid; mp 75 – 76 °C; ^1H NMR (400 MHz, CDCl3) delta; 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 Preparation 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 judged to be 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 (71%): 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 (58%): 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* = 8.5 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 (54%): 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 (57%): 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 (62%): 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 *α*-Allyl Amidines via Thermal Aza-Claisen Rearrangement

To a flame dried screw-cap vial was added ynamide **8b** (62.0 mg, 0.20 mmol), cyclohexylamine (69 μL, 0.60 mmol) and anhyd toluene (2.0 mL). The vial was flushed with nitrogen and heated to 110 °C overnight. When the reaction was judged to be complete by TLC, 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* = 7.2 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.

60 (93%): 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 and Unsaturated Imidates via Tandem Thermal Rearrangements

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. When the reaction was judged to be complete by TLC, 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 (53%): 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 (64%): 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 (91%, 1.5:1 dr): 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* = 6.0 Hz), 5.12 – 5.22 (m, 1H), 5.28 (dd, 1H, *J* = 1.2, 17.6 Hz), 5.90 (ddtd, 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, 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 (50%, 1.3:1 dr): 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, 69.3, 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 (≥95%, 2.0:1 dr): R*f* = 0.23 [8:1 hexanes:EtOAc]; colorless oil; ^1H 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-*major* (69% for both, 1.5:1 dr): 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, 130.4, 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 (74%): R*f* = 0.28 [2:1 hexanes:EtOAc]; white solid; mp = 80 – 84 °C; ^1H 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, 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. 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 (30%): 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Authors thank the NIH [GM066055] for financial support. KAD thanks American Chemical Society for a Division of Medical Chemistry Predoctoral Fellowship. HD thanks China Scholarship Council for a Visiting Scholar Fellowship.

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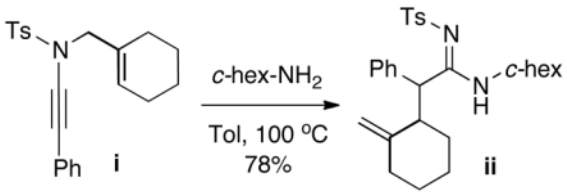
35. Ynamide **i** with substitution along the allyl group was also tolerated, but due to the complication of diastereomers and rotamers of the amidine product **ii**, this effort was not further pursued.



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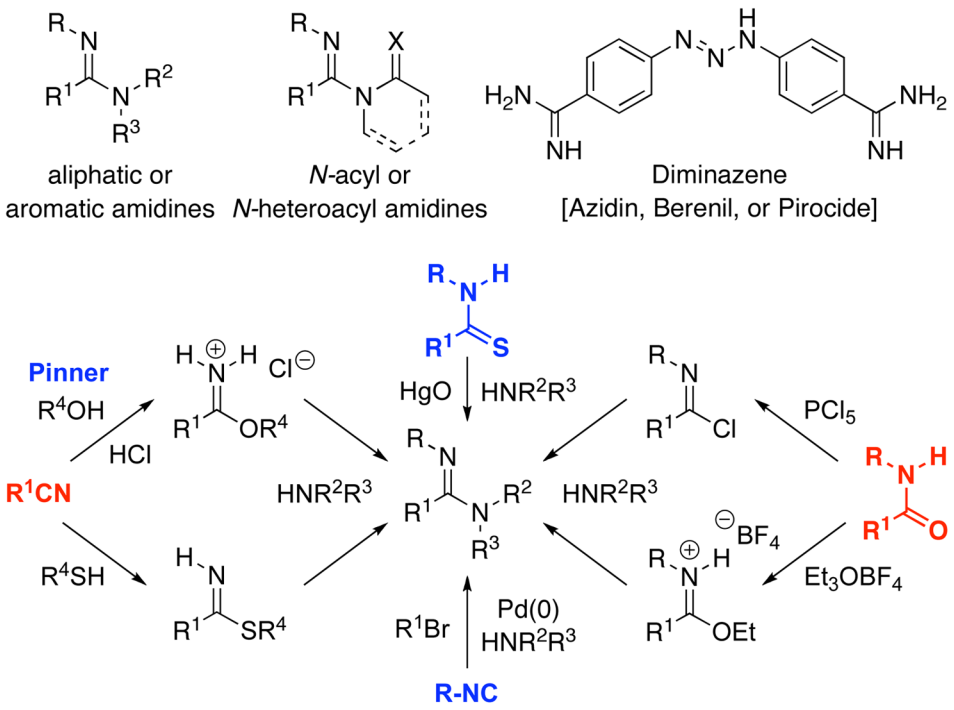


Figure 1.
Amidines and Their General Preparation.

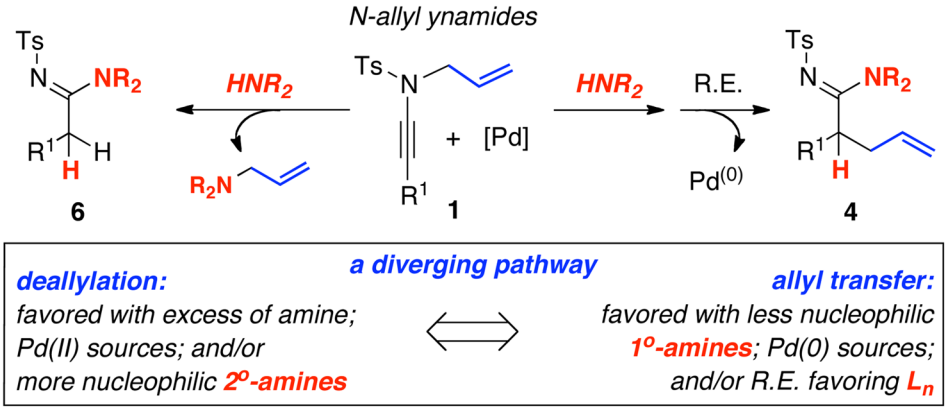
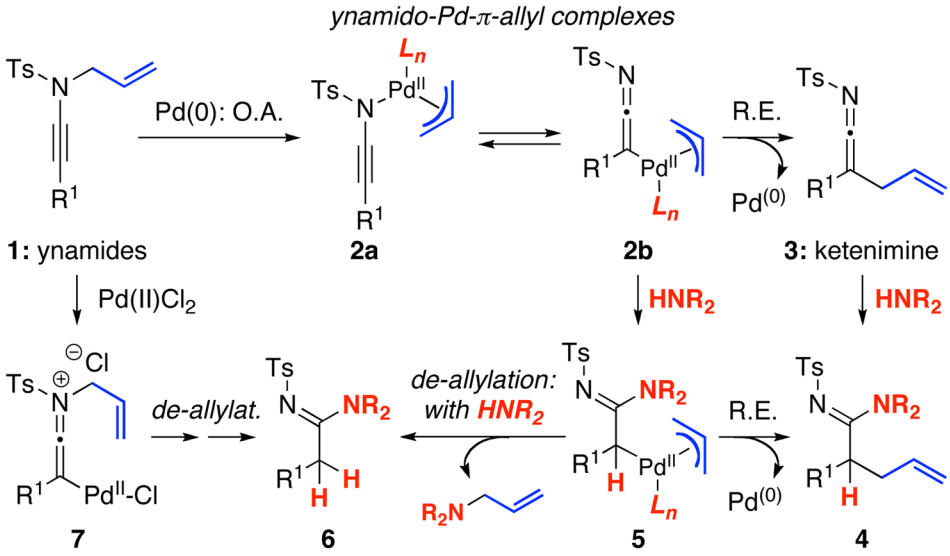
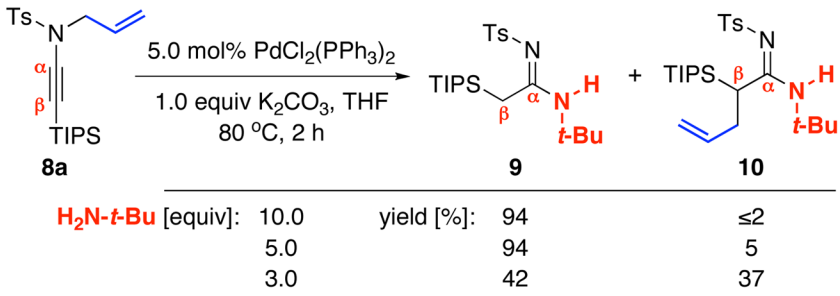


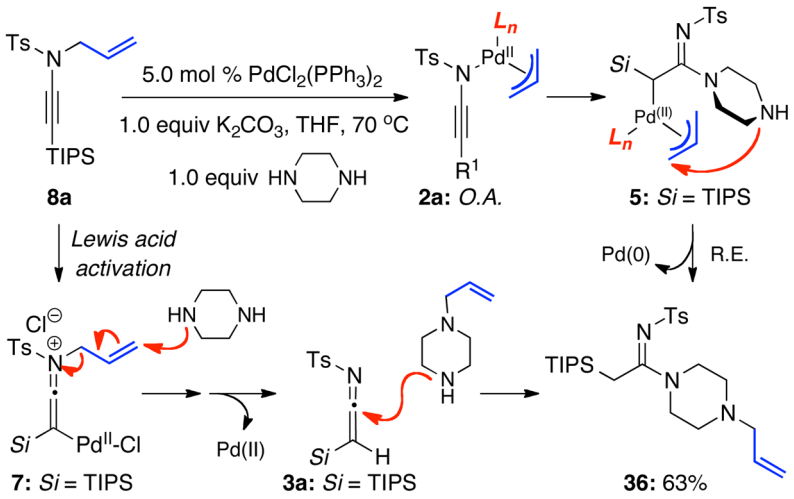
Figure 2.
A Dichotomy of Deallylation and Allyl Transfer.



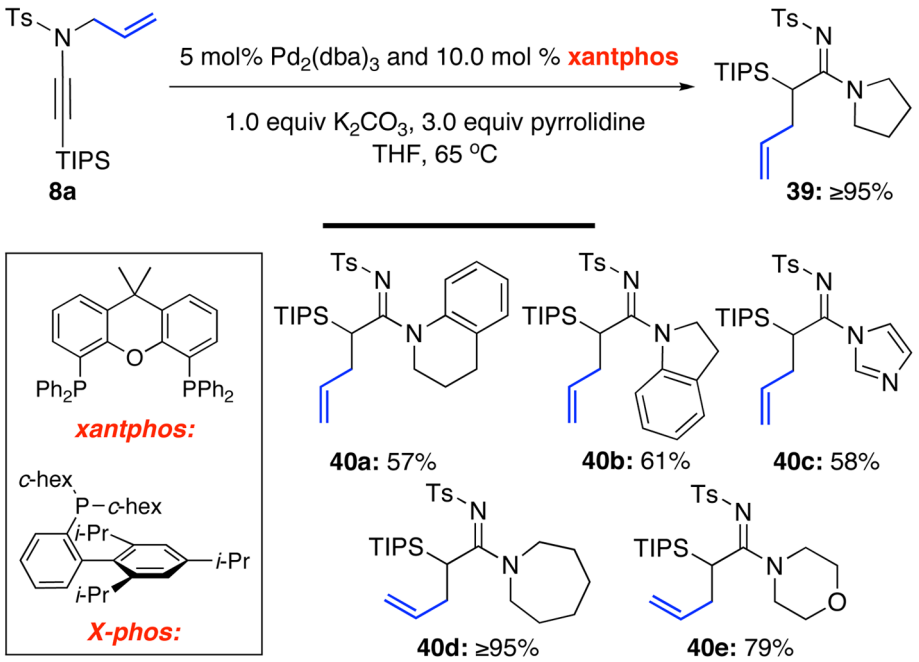
Scheme 1.
Amidine Formation from N-Allyl-Ynamides.



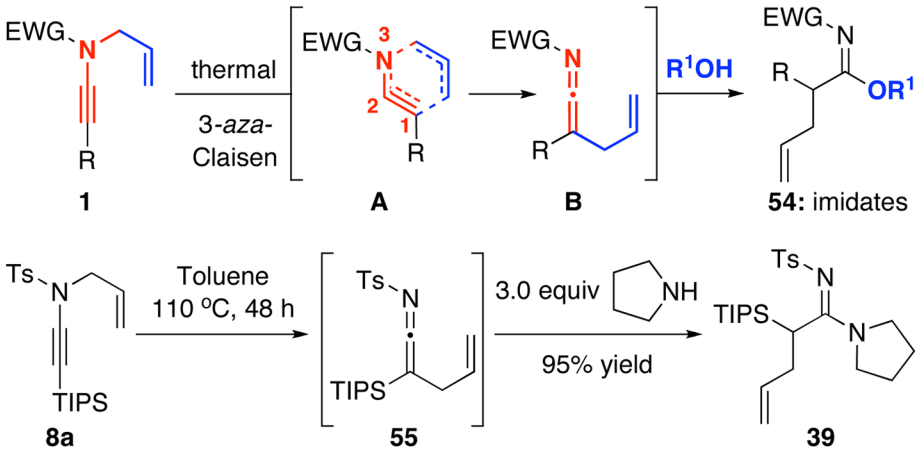
Scheme 2.
Amidine Formation with Pd(II) Catalyst.



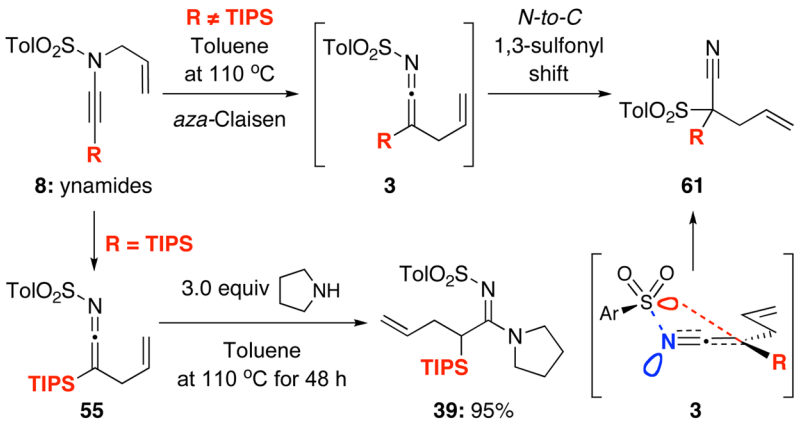
Scheme 3.
Two Possible Deallylation Pathways.



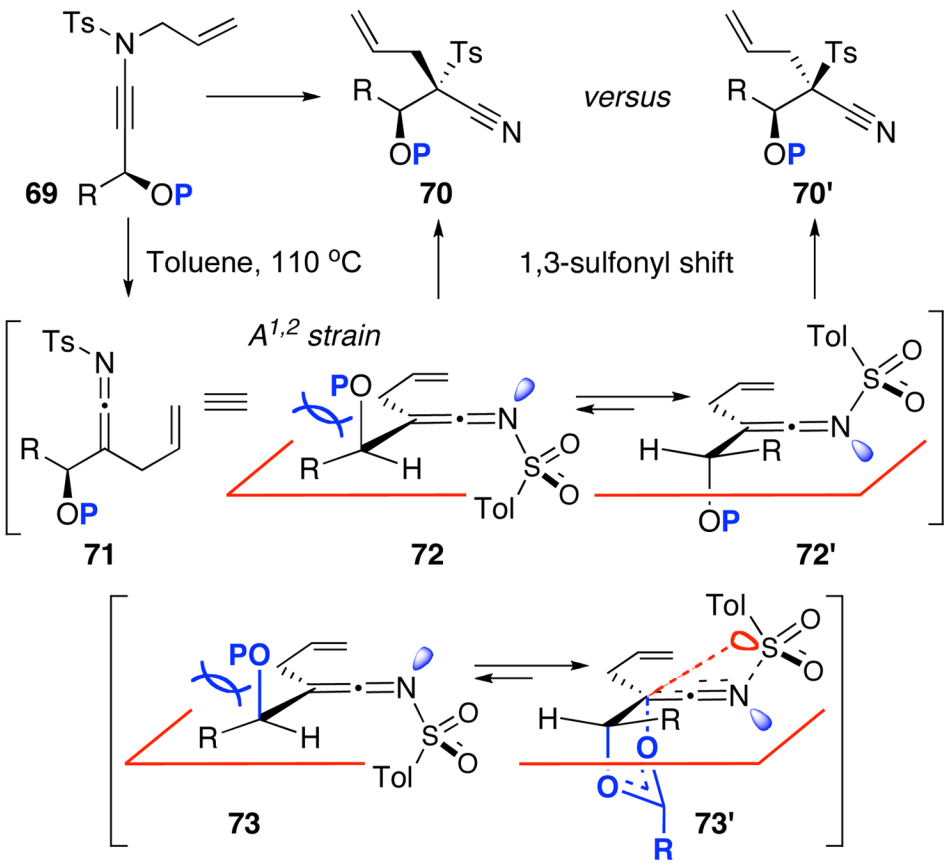
Scheme 4.
The Use of Xantphos Ligand.



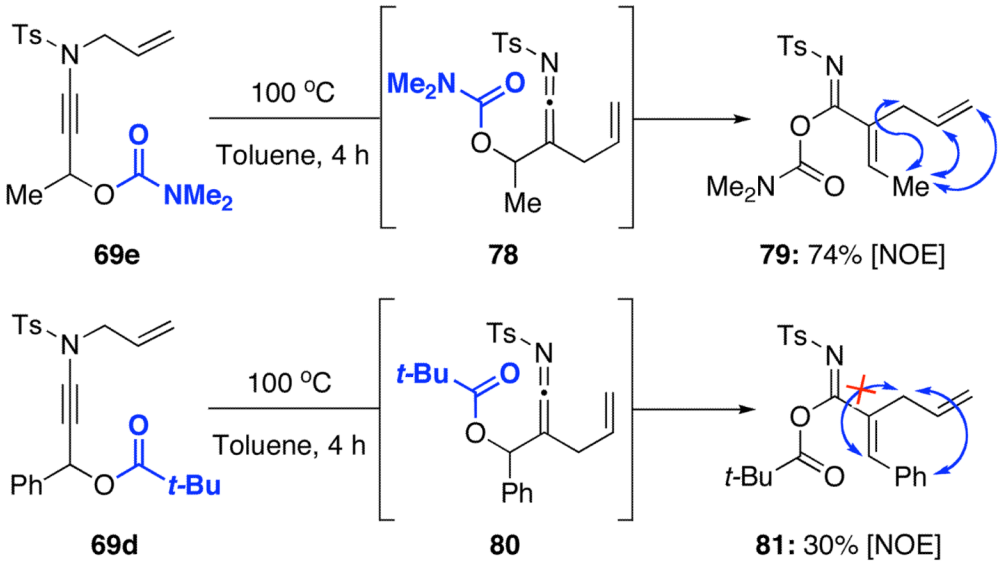
Scheme 5.
Thermal Aza-Claisen Rearrangment.



Scheme 6.
An Unexpected N-to-C 1,3-Sulfonyl Shift.



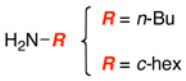
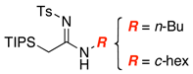
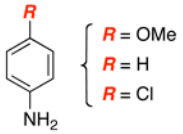
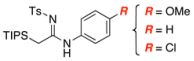
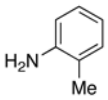
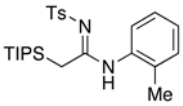
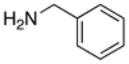
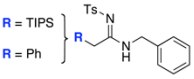
Scheme 7.
Diastereoselective N-to-C 1,3-Sulfonyl Shift.



Scheme 8.
A Tandem Sigmatropic Rearrangement.

Table 1

Deallylative Primary Amidine Formation.

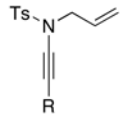
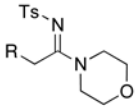
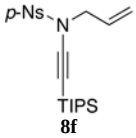
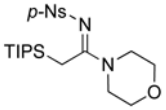
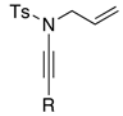
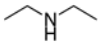
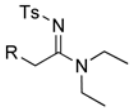
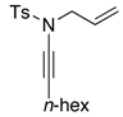
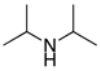
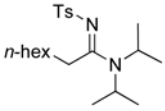
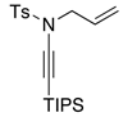
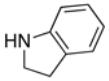
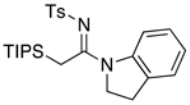
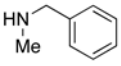
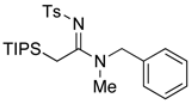
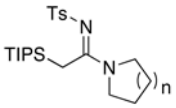
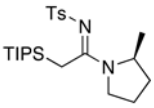
entry	amines [5.0 equiv][a]	amidine products	yield [%][b]
1		 **11**	87
2		**12**	92
3		 **13**	50
4		**14**	71
5		**15**	22
6		 **16**	30
7		 **17**	≥95
8		**18**	≥95

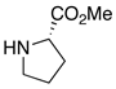
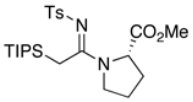
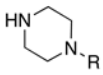
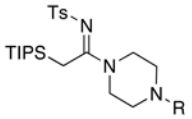
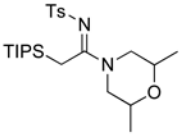
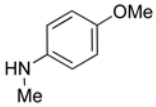
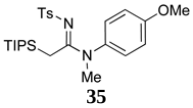
[a] All entries utilized ynamide **8a** except in entry 8, Ph-substituted ynamide **8b** was used. All reactions employed 5.0 mol % $PdCl_2(PPh_3)_2$, 1.0 equiv K_2CO_3, THF [*conc* = 0.05 *M*], 80 °C, 5–8 h.

[b] Isolated yields.

Table 2

Secondary Amidine Formation.

entry	ynamides	amines[a]	amidine products	yield [%][b]
1				≥95
2				≥95
3				92
4	**8a** **8c** **8d** **8e**		**19**: R = TIPS **20**: R = *t*-Bu **21**: R = $(CH_2)_3OTBS$ **22**: R = 2-MeO-Ph	37
5	 **8f**		 **23**	39
6				≥95
7				≥95
8	**8a** **8b** **8g**		**24**: R = TIPS **25**: R = Ph **26**: R = *n*-hex	≥95
9	 **8g**		 **27**	70
10	 **8a**		 **28**	≥95
11			 **29**	77
12				≥95
13				≥95
14			**30a**: *n* = 1 **30b**: *n* = 2 **30c**: *n* = 3	≥95
15			 **31**	91

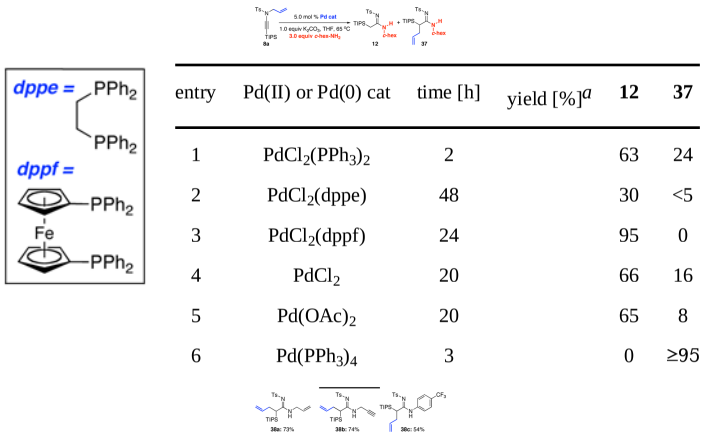
entry	ynamides	amines[a]	amidine products	yield [%][b]
16			 **32**	≥95
17			 **33a**: R = CH_3 **33b**: R = Ph	≥95
18				≥95
19			 **34**	≥95
20			 **35**	82

[a] All reactions utilized 5.0 equiv of the amine, 5.0 mol % $PdCl_2(PPh_3)_2$, and 1.0 equiv K_2CO_3; and were run in THF [*conc* = 0.05 *M*] at 80 °C over 5–8 h.

[b] Isolated yields.

Table 3

Dependence of Deallylation on Palladium Species.

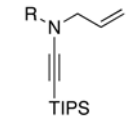
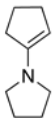
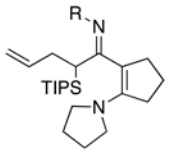
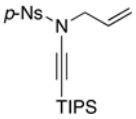
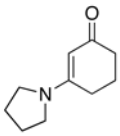
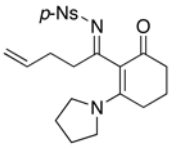
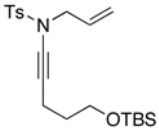
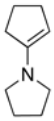
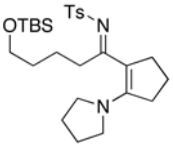
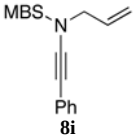
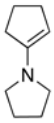
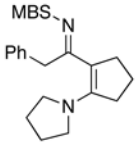
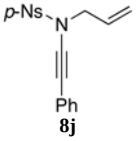
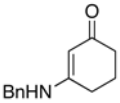
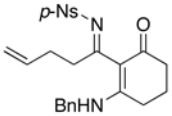
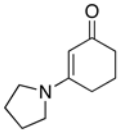
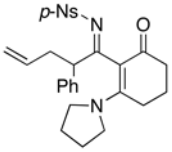


entry	Pd(II) or Pd(0) cat	time [h]	yield [%][a]	**12**	**37**
1	$PdCl_2(PPh_3)_2$	2		63	24
2	$PdCl_2$(dppe)	48		30	<5
3	$PdCl_2$(dppf)	24		95	0
4	$PdCl_2$	20		66	16
5	$Pd(OAc)_2$	20		65	8
6	$Pd(PPh_3)_4$	3		0	≥95

[a] All are isolated yields.

Table 4

Vinylogous Amidine Synthesis.

entry	ynamides	enamines[a]	vinylogous amidines	yield [%][b]
1	 **8a**: R = Ts **8h**: R = MBS	 **41**	 **45** **46**	52[c]
2				71[d]
3	 **8f**	 **42**	 **47**	58[e]
4	 **8d**	 **41**	 **48**	54[f]
5	 **8i**	 **41**	 **49**	57[g]
6	 **8j**	 **43**	 **50**	--
7		 **42**	 **51**	62[h]

[a] Unless otherwise noted, all reactions utilized 3.0 equiv of the enamine, 5.0 mol% $Pd_2(dba)_3$, and 10.0 mol% of xantphos; and were run in THF [*conc* = 0.05 *M*].

[b] Isolated yields.

[c] 2 h at 70°C.

[d] 2 h at 50 °C with 1.5 equiv of K_2CO_3.

[e] 12 h at 70°C with 1.5 equiv of **42;** 2.0 mol % $Pd_2(dba)_3$; and 4.0 mol% of xantphos.

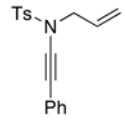
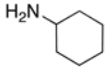
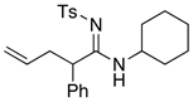
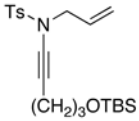
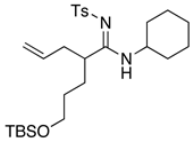
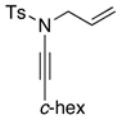
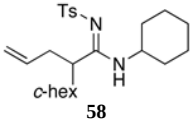
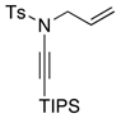
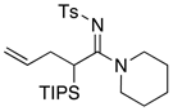
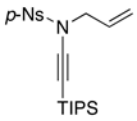
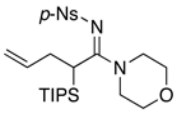
[f] 30 min at 50 °C.

[g] 2 h at RT.

[h] 2 h at 75 °C with 1.5 equiv of K_2CO_3 and 1.5 equiv of **44.**

Table 5

Amidine Synthesis via Aza-Claisen Rearrangement.

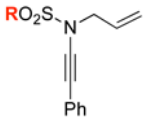
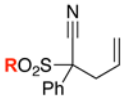
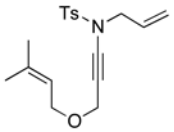
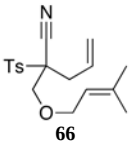
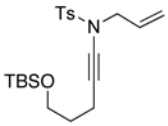
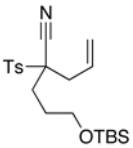
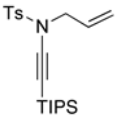
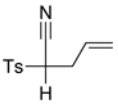
entry	ynamides	amines[a]	amidine products	yield [%][b]
1	 **8b**		 **56**	94
2	 **8d**		 **57**	58
3	 **8k**		 **58**	77
4	 **8a**		 **59**	≥95
5	 **8f**		 **60**	93

[a] All reactions utilized 3.0 equiv of the amine and were run in toluene [*concn* = 0.05 *M*] at 110 °C over 24 h except it was 48 h for entry 4.

[b] Isolated yields.

Table 6

Tandem Aza-Claisen - 1,3-Sulfonyl Shift

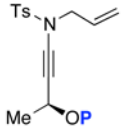
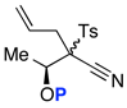
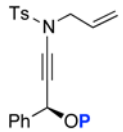
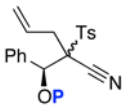
entry	ynamides	nitriles	yield[a,b]
1	 **8b**: R = Ts **8i**: R = 4-MeO-Ph **8j**: R = 4-NO_2-Ph **8l**: R = Me	 **62** **63** **64** **65**	48 53 53 64
5	 **8m**	 **66**	57
6	 **8d**	 **67**	45
7	 **8a**	 **68**	57

[a] Conditions: Toluene, 110 °C, and 14 h.

[b] Isolated yields.

Table 7

Possible Diasteoselective 1,3-Sulfonyl Shift.

entry	ynamides[a]	nitriles	yield[b]	*dr*
1	 (±)-**69a**: P = TIPS (±)-**69b**: P = Ac	 **74** **75**	91	1.5:1
2			50[c]	1.3:1
3	 (±)-**69c**: P = TIPS (±)-**69d**: P = Piv	 **76** **77**	≥95	2.0:1
4			69[c]	1.5:1

[a] Conditions: Toluene, 110 °C, and 2–4 h.

[b] Isolated yields.

[c] See Scheme 8.