Stereocontrolled Synthesis of 5-Acyl-3,4-dihydro-2*H*-pyrroles and Related Heterocycles via Intramolecular 2-Propylidene-1,3-bis(silane)−Acylnitrilium Ion Cyclizations†

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2-Propylidene-1,3-bis(silane)s have been shown to be highly effective terminators in heteroannulations initiated by *C*-acylnitrilium ions. These cyclizations proceed under exceedingly mild reaction conditions with good to excellent levels of substrate-derived stereocontrol to provide the corresponding Δ^1-pyrrolines possessing a functionalizable allylsilane moiety. Sequential reduction/*N*-tosylation of these products leads to the stereoselective formation of *cis*-pyrrolidine derivatives.

Background

The intramolecular interception of nitrogen-stabilized carbocations by appropriately situated nucleophiles constitutes a particularly versatile method for heterocycle synthesis.[2] Previous accounts from these laboratories have documented the successful trapping of *C*-acylnitrilium ions by various arenes and silyl enol ethers to provide advanced intermediates en route to several polycyclic alkaloids.[3] In principle, a variety of alternative carbon-based nucleophiles could be utilized in conjunction with these electrophiles for the synthesis of structurally diverse heterocycles in a stereocontrolled manner. We have recently shown that 2-propylidene-1,3-bis(silane) moieties can serve as highly effective terminators in *trans*-selective cyclizations initiated by metalloiminium ions.[4] In addition to high regio- and stereochemical control, another appealing aspect connected with the use of the 2-propylidene-1,3-bis(silane) terminator resides in the simultaneous liberation of a functionalizable allylsilane moiety upon monocyclization.[5−7] The comparatively high nucleophilicity of 2-propylidene-1,3-bis(silane)s raised the issue of the prospective compatibility of these terminators with reaction conditions which are required for the initiation of other cyclization sequences.[8] Herein we report the facile generation of *C*-acylnitrilium ions tethered to 2-propylidene-1,3-bis(silane)s and the stereocontrolled coupling of these components to furnish highly functionalized Δ^1-pyrrolines.[9] We further show that the product Δ^1-pyrrolines are convertible to 2,3-*cis*-pyrrolidine derivatives which stereochemically complement those available from the corresponding metalloiminium cyclizations (Scheme 1).

Isonitrile Synthesis

We began this investigation by developing methods for the synthesis of 2-propylidene-1,3-bis(silane) bearing isonitriles. Treatment of imide **7a**[10] with CBr_4 and Ph_3P (CH_2Cl_2, 0 °C) provided imide **8a** in 86% isolated yield. Exposure of **8a** to $(Me_3SiCH_2)_2Zn$ (1.5 equiv, prepared from $Me_3SiCH_2MgCl + ZnCl_2$ *in-situ*) in the presence of 7 mol % $PdCl_2(PPh_3)_2$ (THF, rt) furnished **9a** in 96% yield after purification which, upon PHT cleavage with $N_2H_4 \cdot H_2O$ (EtOH, reflux), afforded amine **1a** (78% *overall* from **7a**).[11] Sequential *N*-formylation of **1a** (EtOCHO) followed by dehydration of the corresponding formamide ($POCl_3/Et_3N$, THF, 0 °C) furnished **2a** in 85% overall yield. Gratifyingly, products resulting from electrophilic desilylation were not observed during the course of the formylation−dehydration sequence. Isonitriles **2b**, **2c**, and **2d** were efficiently synthesized in an analogous manner from imides **7b**, **7c**, and **7d** which were prepared, in turn, by either DBU- or sodium ethoxide-mediated addition of phthalimide to the requisite α,β-unsaturated aldehydes (5% DBU, PHTNH, DMF, rt *or* 10%, NaOEt, PHTNH, EtOH, rt) (Schemes 2 and 3). For the sterically hindered amine **1d**, optimal conversion to the corresponding formamide was effected using formic acetic anhydride[12] (Et_2O, −78 °C).

† This manuscript is dedicated to the memory of Professor William S. Johnson.

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(1) Fellow of the Alexander von Humboldt Foundation, 1993−1995.

(2) Overman, L. E.; Ricca, D. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 4.4 and references therein.

(3) (a) Luedtke, G.; Livinghouse, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2369. (b) Hughes, D. J.; Livinghouse, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2373. (c) Lee, C. H.; Westling, M.; Livinghouse, T.; Williams, A. C. *J. Am. Chem. Soc.* **1992**, *114*, 4089. (d) Luedtke, G.; Westling, M.; Livinghouse, T. *Tetrahedron* **1992**, *48*, 2209. (e) Westling, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1987**, *109*, 590. (f) Westing, M.; Smith, R.; Livinghouse, T. *J. Org. Chem.* **1986**, *51*, 1159. (g) Westling, M.; Livinghouse, T. *Tetrahedron Lett.* **1985**, *26*, 5389.

(4) Kercher, T.; Livinghouse, T. *J. Am. Chem. Soc.* **1996**, *118*, 4200.

(5) For a comprehensive account dealing with the synthetic utility of allylsilanes and related compounds see: The Electrophilic Substitution of Allylsilanes and Vinylsilanes. Fleming, I.: Dunogués. J.; Smithers, R. in *Organic Reactions*, Kende, A. S., Ed.; John Wiley and Sons: New York, 1989, Vol. 37, Chapter 2, p 57.

(6) Several additional examples of stereocontrolled allylsilane-iminium ion cyclizations have appeared: (a) Heerding, D. A.; Hong, C. Y.; Kado, N.; Look, G. C.; Overman L. E. *J. Org. Chem.* **1993**, *58*, 6947. (b) Hong, C. Y.; Kado, N.; Overman, L. E. *J. Am. Chem. Soc.* **1993**, *115*, 11028. (c) Hiemstra, H.; Forgens, H. P.; Speckamp, W. N. *Tetrahedron Lett.* **1985**, *26*, 3155. (d) Hiemstra. H.; Sno, M. H. A. M.; Vijn, R. J.; Speckamp, W. N. *J. Org. Chem.* **1985**, *50*, 4014.

(7) (a) Larsen, S. D.; Grieco, P. A.; Fobare, W. F. *J. Am Chem Soc.* **1986**, *108*, 3512. (b) Grieco, P. A.; Fobare, W. F. *Tetrahedron Lett.* **1986**, *27*, 5067.

(8) In contrast to allylsilanes, 2-propylidene-1,3-bis(silane)s have seen relatively little use in synthesis. For pertinent references concerning the use of these compounds as well as related methodology, see: (a) Rubiralt, M.; Diez, A.; Miguel, D. *Syn. Commun.* **1992**, *22*, 359. (b) Guyot, B.; Pornet, J.; Miginiac, L. *J. Organomet. Chem.* **1990**, *386*, 19. (c) Guyot, B.; Pornet, J.; Miginiac, L. *Tetrahedron* **1991**, *47*, 3981.

(9) An account addressing stereoselective cyclizations of allylsilanes with nitrilium ions generated by a Beckmann rearrangement has appeared, see: Schinzer, D.; Bo, *Y. Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 687.

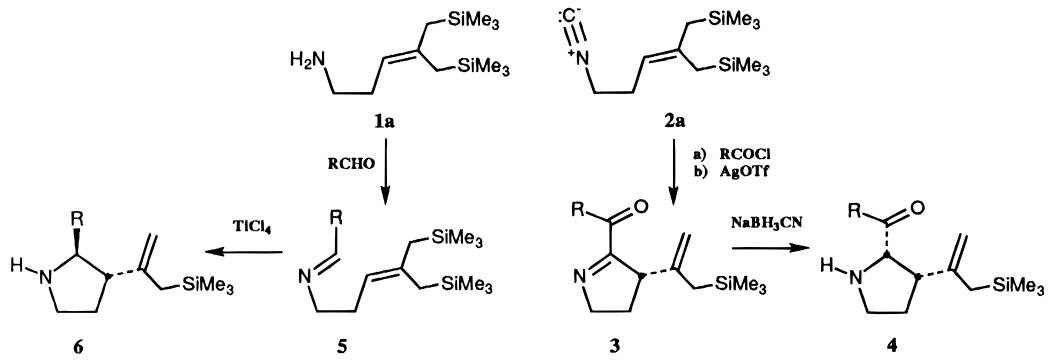
(10) Danishefsky, S.; McKee, R.; Singh, R. K. *J. Am. Chem. Soc.* **1977**, *99*, 771.

(11) All new compounds have been fully characterized by ^1H and ^{13}C NMR, IR and possess satisfactory combustion analyses or exact mass.

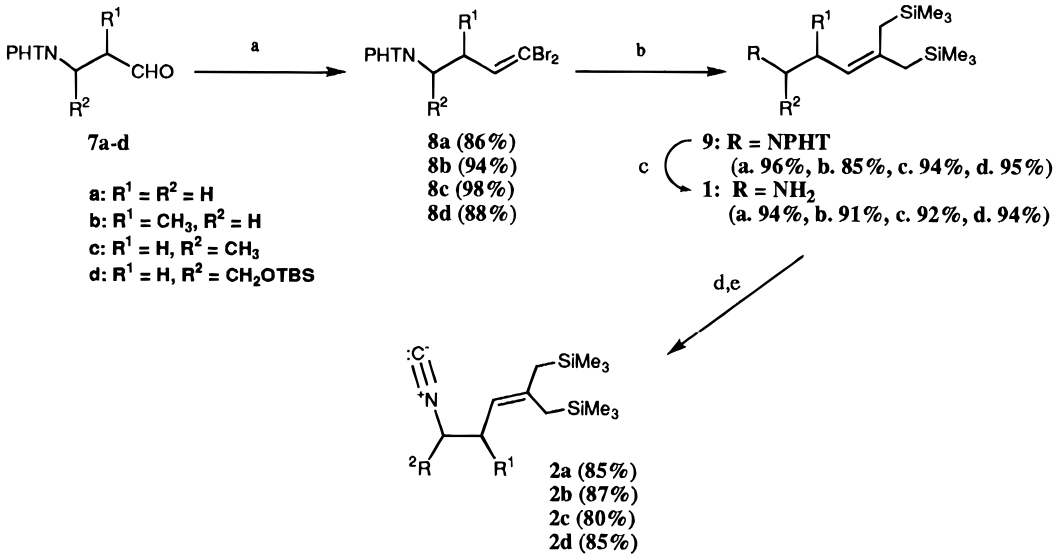
(12) Krimen, L. I. in *Organic Syntheses*; Breslow, R., Ed.; John Wiley and Sons: New York, 1970; Vol. 50, p 1.

S0022-3263(96)01452-1 CCC: $14.00

Scheme 1

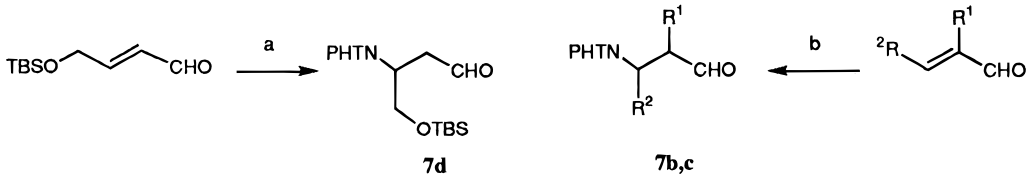


Scheme 2[a]



[a] (a) CBr_4, Ph_3P, CH_2Cl_2, 0 °C; (b) $(TMSCH_2)_2Zn$ (1.5 equiv), $PdCl_2(Ph_3P)_2$ (7 mol %), THF, rt; (c) $N_2H_4 \cdot H_2O$, EtOH, reflux; (d) EtOCHO, reflux, or CH_3CO_2CHO, Et_2O, −78 °C for **1d**; (e) $POCl_3/Et_3N$, THF, 0 °C.

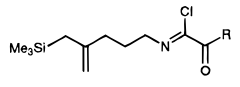
Scheme 3[a]



[a] (a) 5% DBU, PHTNH, DMF, rt; (b) 10% NaOEt, PHTNH, EtOH, rt.

Cyclization Studies

The acylative cyclization of **2a** with a variety of simple as well as functionalized acyl chlorides was subsequently examined. Treatment of **2a** with various acyl chlorides (1.1 equiv, CH_2Cl_2, rt) resulted in *chemospecific* functionalization of the isonitrile moiety to generate the corresponding α-ketoimido chlorides **10a**−**e** in quantitative yields as determined by ^{1}H-NMR. Immediate exposure of the unpurified adducts **10a**−**e** to AgOTf (1.5 equiv, $CH_2Cl_2/ClCH_2CH_2Cl$, −78 °C → −20 °C) led to smooth cyclization to provide the 2-acyl-Δ^1-pyrrolines **3a**−**e** in 61% to 91% isolated yields (Scheme 4) after neutralization of the reaction mixture by careful *inverse* addition to vigorously stirred aqueous $KHCO_3$ at 0 °C followed by chromatographic purification (Table 1). It is noteworthy in a preparative context that quenching via *direct* addition of $KHCO_{3(aq)}$ sometimes led to the formation of products derived from protodesilylation of the pendant allylsilane moiety. In addition, the use of $AgBF_4$ (−78 °C)[3] in place of AgOTf resulted in diminished yields (<20−70%) of the desired Δ^1-pyrrolines with protodesilylated materials of type **11** frequently being isolated.



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Diastereoselective Cyclizations

In principle, the cyclization of isonitriles possessing sites of resident asymmetry could give rise to 2-acyl-Δ^1-pyrrolines with a high degree of substrate derived stereocontrol.[13] To investigate this possibility, the isonitriles **2b**, **2c**, and **2d** were prepared (*vide supra*) and subjected to AgOTf-mediated acylative cyclization. Silver ion-

Scheme 4

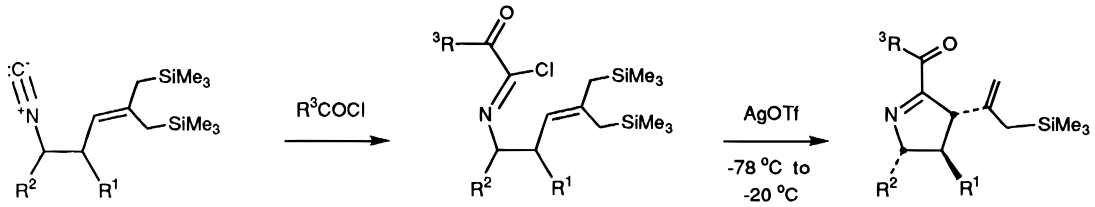
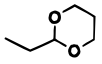
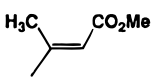


Table 1. Acylative Cyclizations of Isonitrile 2a

Pyrroline	R^3COCl ($-R^3$)	Yield[1] (%)	Pyrroline	R^3COCl ($-R^3$)	Yield[1] (%)
3a	$-C(CH_3)_3$	82	**3d**	$-CH_2CH_2CH_2Cl$	61
3b	$-CH(CH_3)_2$	68	**3e**		91
3c	$-CH_2CH(CH_3)_2$	77			

[1] All yields are from **2a** and correspond to isolated, chromatographically purified products.

Table 2. Stereocontrolled Acylative Cyclizations of Isonitriles 2b−d

Pyrroline	R^3COCl ($-R^3$)	Isonitrile	$3_{trans} : 3_{cis}$[2]	Yield[1] (%)
3f	$-C(CH_3)_3$	**2b**	>50 : 1	41
3g	$-CH_2CH_3$	**2b**	>50 : 1	40
3h	$-C(CH_3)_3$	**2c**	1 : 4.6	90(65[3])
3i	$-CH_2CH_3$	**2c**	1 : 3.8	78(49[3])
3j	$-C(CH_3)_3$	**2d**	1 : 2.6	87(56[3])
3k	$-CH_2CH_2CO_2Me$	**2d**	1 : 4.5	77(48[3])
3l		**2d**	1 : 3.0	76(47[3])

[1] All yields are from the isonitrile and correspond to isolated, chromatographically purified products. [2] Obtained from integration of the expanded olefinic region of 300 ^1H NMR spectra of crude Δ^1-pyrrolines. [3] Isolated yield of chromatographically purified *cis*-isomer from isonitrile.

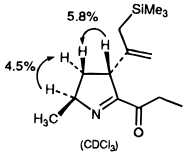
induced cyclizations of representative α-ketoimidoyl chlorides **10f** and **10g** derived from **2b** [AgOTf (1.5 equiv), $CH_2Cl_2/ClCH_2CH_2Cl$, −78 °C → −20 °C] were found to proceed with excellent levels of internal stereoselection [*trans*:*cis* ≥ 50:1 (NMR)] but with lower overall efficiency than those observed for acyl chloride derivatives of **2a**. By way of contrast, cyclization of α-ketoimidoyl chlorides derived from **2c** and **2d** gave rise to Δ^1-pyrrolines **3h**−**l** in 76% to 90% isolated yields but with diminished stereoselectivity in favor of the *cis* isomers (Table 2). In these instances, the major diastereomers **3h**−**l**$_{cis}$ could be readily separated by column chromatography on silica gel (see Table 2). The stereochemical outcome of the foregoing cyclizations can be rationalized on the basis of conformational control involving minimization of nonbonded interactions. Accordingly, *trans* selective cyclization of *C*-acylnitrilium ions **12f** and **12g**, corresponding to isonitrile **2b**, should occur via a conformer in which energetically unfavorable $A^{1,3}$-interactions are suppressed. In the case of the *C*-acylnitrilium ions **12h**−**l**, derived from isonitriles **2c** and **2d**, the origin of the comparatively lower levels of 1,3-stereoinduction favoring the corresponding *cis*-Δ^1-pyrrolines **3h**−**l** can be ascribed to the avoidance of an allylic through-space interaction that is less profound than in the cases of **12f** and **12g** (Figure 1). In all of the preceding examples, stereochemical assignments were based on rigorous NOE spectroscopic studies. Several representative NOE enhancements for the Δ^1-pyrrolines **3f**, **3k**, and **3h** are shown in Figure 2. For the *cis*-Δ^1-pyrrolines, the observance of a large NOE interaction from the C-4 and C-2 methine hydrogens to the *same* hydrogen of the centrally located C-3 methylene was particularly diagnostic. Analogous experiments performed on the minor *trans* isomers revealed NOE enhancements that complimented these stereochemical assignments.[14]

Diastereoselective Reductions

Reduction of the imine moiety of representative Δ^1-pyrrolines in this series could be readily accomplished by treatment with $NaBH_3CN$ (4.00 equiv) and TFA (1.05 equiv) in CH_3OH at −78 °C. As expected, kinetic delivery of hydride occurred predominantly in an *anti* sense with respect to the 1-[(trimethylsilyl)methyl]ethylidene substituent to provide crude *cis*-pyrrolidines **4a**−**c**$_{cis}$ which were not purified but immediately subjected to *N*-tosylation [TsCl, DMAP, CH_2Cl_2, −78 °C → −20 °C] to furnish the sulfonamide derivatives **13a**−**c**$_{cis}$ (Scheme 5). In this fashion, higher overall yields of pure materials were obtained, and, for the case of **13b**, removal of the minor diastereomer was readily accomplished by fractional crystallization of the major diastereomer from petroleum ether. In addition, *N*-tosylation of the basic pyrrolidines **4a**−**c** retarded facile epimerization at the labile C-2 stereocenter.[15] As before, stereochemical assignments were based on a series of NOE experiments after definitive assignments had been established by

(13) For a recent review see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.

(14) In contrast to the *cis*-pyrrolines, the only significant NOE enhancements which were observed upon irradiation of the C-4 and C-2 methine hydrogens in the minor trans isomers were to *different* hydrogens on the central C-3 methylene:



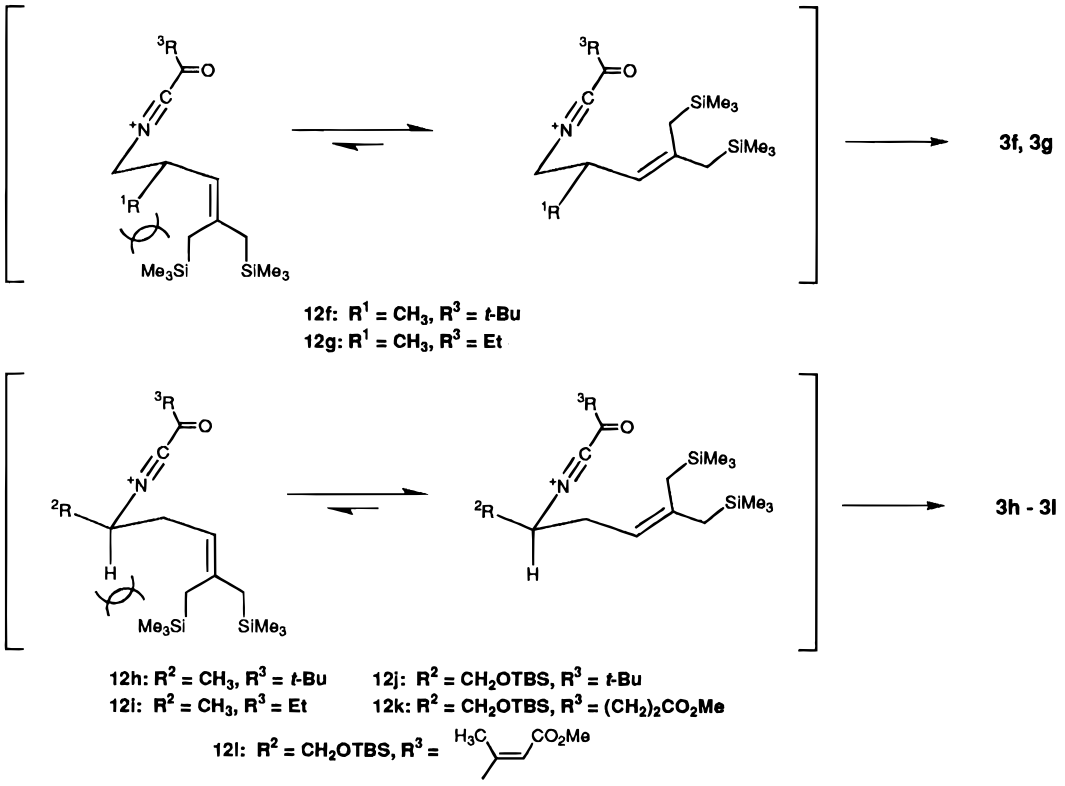


Figure 1.

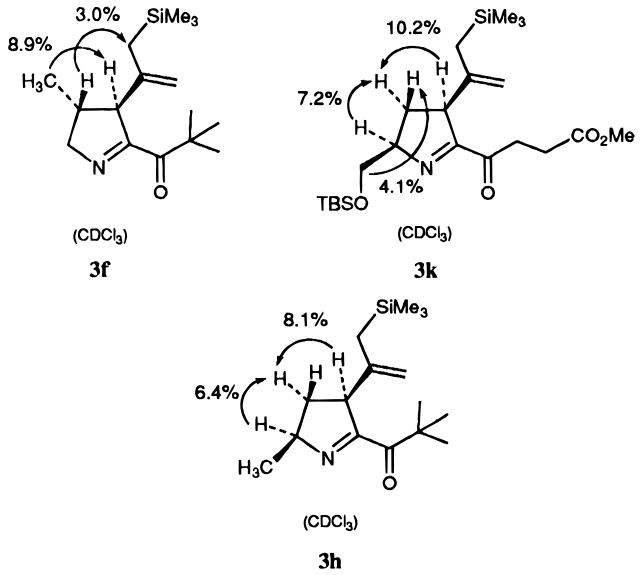


Figure 2.

homonuclear decoupling (Figure 3). The anti approach of hydride in the reduction step was clearly evident in the large (9.2−13.1%) NOE enhancement between the C-2 and C-3 methine hydrogens. The results of these spectroscopic studies are consistent with, and therefore serve to support, the initial stereochemical assignments of pyrrolines **3f**−**3l**.

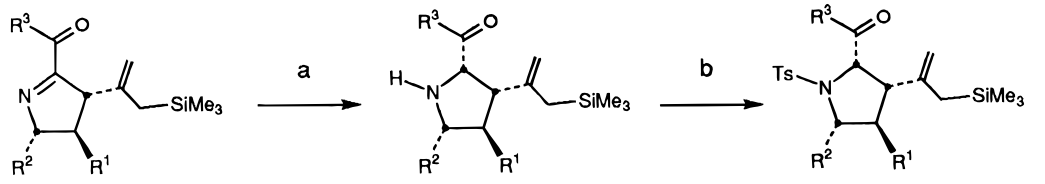
(15) In related pyrrolidine systems, Overman has observed epimerization upon exposure to silica gel during chromatography: Deng, W.; Overman, L. E. *J. Am. Chem. Soc* **1994**, *116*, 11241.

In conclusion, this study has shown that *C*-acylnitrilium ion−2-propylidene-1,3-bis(silane) cyclizations are useful for providing a range of functionally diverse Δ^1-pyrrolines in a highly convergent manner. The product Δ^1-pyrrolines may be readily isolated in stereochemically pure form and in reasonable to good overall yield. Subsequent reduction of these unsaturated heterocycles can provide rapid access to the corresponding *cis*-2-acylpyrrolidines which bear synthetically useful allylsilane moieties. In addition, the flexible and efficient synthesis of requisite amino-2-propylidene 1,3-bis(silane)s could, in principle, be extended to longer, carbon chain homologs, enabling the preparation of larger ring heterocycles by this methodology.

Experimental Section

General Experimental Details. Tetrahydrofuran (THF) was distilled from potassium, and diethyl ether (Et_2O) was distilled from sodium−benzophenone. Dichloromethane (CH_2Cl_2), 1,2-dichloroethane ($ClCH_2CH_2Cl$), ethyl formate, triethylamine, and commercially purchased acid chlorides were distilled from CaH_2. Methanol (CH_3OH) was distilled from $Mg(OCH_3)_2$. Silver trifluoromethanesulfonate (AgOTf) was purchased from Aldrich Chemical Company, Inc. and was used without additional purification. Acetic formic anhydride was prepared following known literature procedure.[12] Compounds **8a**−**d**, **9a**−**d**, and **1a**−**d** were prepared using previously described procedures.[4] All reactions were carried out under an atmosphere of argon in flamed, oven-dried vessels utilizing standard syringe-septum techniques. ^{1}H NMR and ^{13}C NMR spectra were measured at 300 and 75 MHz, respectively, with a Bruker AC-300 spectrometer. ^{1}H NMR and ^{13}C NMR chemical shifts are reported as δ values in ppm relative to residual proton signals in $CDCl_3$ (δ = 7.24, 77.0) or C_6D_6 (δ = 7.15, 128.7). ^{1}H NMR coupling constants are reported in hertz and refer to apparent multiplicities. Infrared spectra were recorded with a Bruker IFS 25 IR spectrometer. High resolution mass spectra were recorded on a VG Instruments 70E-HF spectrometer. Melting points were obtained using a Mel-

Scheme5[a]



a: $R^1 = R^2 = H$, $R^3 = t$-Bu
b: $R^1 = CH_3$, $R^2 = H$, $R^3 = t$-Bu
c: $R^1 = H$, $R^2 = CH_2OTBS$, $R^3 = t$-Bu

[a] (a) $NaBH_3CN$ (4.00 equiv), TFA (1.05 equiv), CH_3OH, −78 °C; (b) TsCl (1.2 equiv), DMAP (1.3 equiv), CH_2Cl_2, −78 °C → −20 °C.

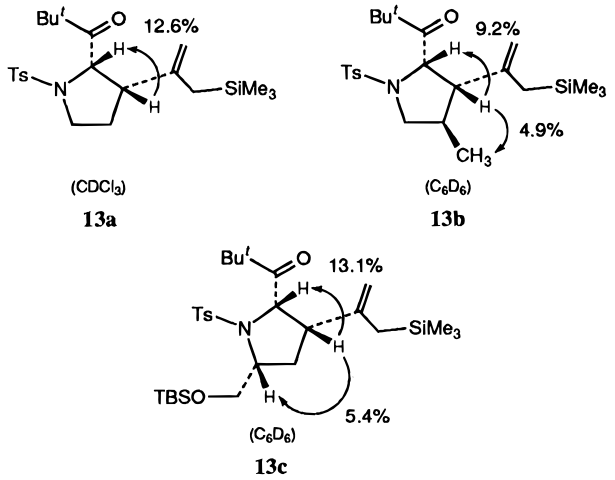


Figure 3.

Temp II apparatus equipped with a digital thermometer and are uncorrected. Column chromatography was performed with Merck silica gel 60, and reduced pressure concentrations were conducted with a Büchi rotary evaporator.

1-Isocyano-2-methyl-5-(trimethylsilyl)-4-[(trimethylsilyl)methyl]pent-3-ene (2b). A solution of amine **1b** (2.00 g, 7.76 mmol) in freshly distilled ethyl formate (6.0 mL) was heated at reflux for 14 h. Upon cooling to room temperature, the reaction mixture was concentrated under reduced pressure, and the residue was filtered through a silica gel plug (Et_2O for elution) to furnish the corresponding formamide as a viscous, colorless oil. A solution of the formamide and triethylamine (5.15 mL, 38.8 mmol) in THF (20 mL) was cooled to 0 °C, and phosphorus oxychloride (800 μL, 8.54 mmol) in THF (2 mL) was added dropwise over 15 min. During the time of addition, the internal reaction temperature was not permitted to exceed 5 °C. The reaction mixture was stirred for 2 h at 0 °C and was poured into chilled water (40 mL). The organic layer was separated, and the remaining aqueous phase was extracted with Et_2O (3 × 15 mL). The combined organic fractions were washed with brine (40 mL) and dried over anhydrous $MgSO_4$. The solvents were evaporated in vacuo, and the residue was subjected to silica gel chromatography (5% EtOAc/hexane for elution) to yield isonitrile **2b** (1.80 g, 87% from **1b**) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.56 (d, J = 9.7 Hz, 1H, C=C*H*), 3.16 (m, 2H, $^-\ddot{C}{\equiv}N^+CH_2$), 2.57 (m, 1H, C*H*), 1.57 (d, J = 13.5 Hz, 1H, SiC*H*H), 1.38 (q, J = 13.0 Hz, 3H, SiCH*H* and $SiCH_2$), 1.03 (d, J = 6.6 Hz, 3H, CH_3), 0.02 (s, 9H, $(CH_3)_3Si$), −0.01 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 156.2, 137.6, 120.1, 47.9 (t, J = 5.4 Hz), 32.9, 29.6, 24.7, 18.5, −0.7, −1.2; IR (film) 2956, 2897, 2145, 1645, 1417, 1249, 1156, 1068, 961, 853, 700, 625 cm^{-1}; HRMS calcd for $C_{14}H_{29}NSi_2$ (M^+) 267.1839, found 267.1845.

2-Isocyano-6-(trimethylsilyl)-5-[(trimethylsilyl)methyl]hex-4-ene (2c). Sequential formylation/dehydration of amine **1c** (2.00 g, 7.76 mmol) using the procedure described for the preparation of **2b** provided isonitrile **2c** (1.65 g, 80%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.80 (t, J = 7.3 Hz, 1H, C=C*H*), 3.53 (app tsx, J = 6.4, 1.4 Hz, 1H, $CHN^+{\equiv}\ddot{C}^-$), 2.21 (m, 2H, CH_2), 1.47 (d, J = 3.7 Hz, 2H, $SiCH_2$), 1.42 (s, 2H, $SiCH_2$), 1.32 (ddd, J = 8.9, 4.4, 2.3 Hz, 3H, CH_3), 0.01 (s, 9H, $(CH_3)_3Si$), 0.00 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 154.7, 139.7, 113.1, 51.0 (t, J = 5.4 Hz), 36.4, 30.2, 24.6, 21.5, −0.3, −0.7; IR (film) 2983, 2955, 2897, 2137, 1646, 1415, 1248, 1153, 1065, 851, 699, 625 cm^{-1}; HRMS calcd for $C_{14}H_{29}NSi_2$ (M^+) 267.1839, found 267.1831.

1-Isocyano-5-(trimethylsilyl)-4-[(trimethylsilyl)methyl]pent-3-ene (2a). Sequential formylation/dehydration of amine **1a** (2.00 g, 8.21 mmol) using the procedure described for the preparation of **2b** provided isonitrile **2a** (1.77 g, 85%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.75 (t, J = 7.0 Hz, 1H, C=C*H*), 3.28 (app tt, J = 6.9, 1.8 Hz, 2H, $CH_2N^+{\equiv}\ddot{C}^-$), 2.28 (app tq, J = 6.9, 1.8 Hz, 2H, CH_2), 1.47 (s, 2H, $SiCH_2$), 1.41 (s, 2H, $SiCH_2$), 0.01 (s, 9H, $(CH_3)_3Si$), −0.01 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR ($CDCl_3$, 75 MHz, ^{1}H decoupled) δ 155.7, 139.2, 113.1, 41.8, 29.7, 28.8, 24.0, −0.8, −1.3; IR (film) 2985, 2954, 2896, 2146, 1647, 1415, 1247, 1153, 1063, 852, 699, 625 cm^{-1}; HRMS calcd for $C_{13}H_{27}NSi_2$ (M^+) 253.1682, found 253.1675.

1-[(*tert*-Butyldimethylsilyl)oxy]-2-isocyano-6-(trimethylsilyl)-5-[(trimethylsilyl)methyl]hex-4-ene (2d). A solution of amine **1d** (1.50 g, 3.87 mmol) in Et_2O (25 mL) was cooled to −78 °C, and freshly prepared formic acetic anhydride (360 mg, 4.06 mmol) was added dropwise via a syringe. The reaction mixture was stirred for 45 min at −78 °C and was then transferred slowly by cannula into vigorously stirred, saturated aqueous $KHCO_3$ (40 mL). The resulting biphasic mixture was stirred for 30 min, and the layers were separated. The aqueous phase was extracted with Et_2O (2 × 15 mL), and the combined organic fractions were washed once with brine (35 mL), dried over $MgSO_4$, and filtered through a silica gel pad (Et_2O for elution) to afford the corresponding formamide as a colorless viscous oil. Dehydration of the formamide with $POCl_3$ in the manner previously described for the preparation of **2b** gave the title isonitrile (1.26 g, 85% from **1d**) as a colorless oil after purification of the crude product by filtration through a silica gel plug (5% EtOAc/hexane for elution): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.81 (t, J = 7.3 Hz, 1H, C=C*H*), 3.65 (d, J = 4.6 Hz, 2H, OCH_2), 3.47 (p, J = 6.1 Hz, 1H, C*H*), 2.27 (m, 2H, CH_2), 1.49 (s, 2H, $SiCH_2$), 1.42 (s, 2H, $SiCH_2$), 0.89 (s, 9H, $(CH_3)_3CSi$), 0.07 (s, 6H, $OSi(CH_3)_2$), 0.01 (s, 18H, $Si(CH_3)_3$ × 2); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 156.0, 139.5, 112.4, 64.3, 57.1, 30.6, 29.9, 25.8, 24.2, 18.2, −0.7, −1.1, −5.4; IR (film) 2955, 2897, 2858, 2139, 1646, 1472, 1464, 1412, 1362, 1249, 1129, 836, 778, 700, 626 cm^{-1}; HRMS calcd for $C_{20}H_{43}NOSi_3$ (M^+) 397.2652, found 397.2641.

5-(Trimethylacetyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3a). The following procedure, employed for the preparation of pyrroline **3a**, constitutes the general procedure used for the silver ion-mediated cyclization of ketoimidoyl chlorides. To a solution of isonitrile **2a** (200 mg, 0.79 mmol) in CH_2Cl_2 (500 μL) was added trimethylacetyl

chloride (117 μL, 0.95 mmol), and the mixture was stirred for 12 h at room temperature. The volatile components were removed under reduced pressure during which time exposure of the reaction mixture to air was kept at a minimum. The residue was dissolved in a 1:1 mixture of CH_2Cl_2 and $ClCH_2CH_2Cl$ (800 μL), and the resulting solution of the crude keto imidoyl chloride was used *immediately* in the next step.

A suspension of AgOTf (304 mg, 1.18 mmol) in 1:1 CH_2Cl_2/$ClCH_2CH_2Cl$ (4 mL) was cooled to −78 °C, and the freshly prepared solution of the crude ketoimidoyl chloride was added dropwise via a gas-tight syringe. The mixture was stirred at a temperature range of −78 °C to −65 °C for 2 h during which time a white solid precipitated. Stirring was continued at −20 °C for an additional 6 h after which time the cold reaction mixture was transferred dropwise via cannula into vigorously stirred, aqueous saturated $KHCO_3$ (8 mL) at 0 °C. The biphasic mixture was stirred for 15 min at room temperature, decanted into a separatory funnel, and the organic layer was separated. The remaining aqueous phase was extracted with Et_2O (2 × 4 mL), and the combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was subjected to chromatography on silica gel (5% EtOAc/hexane for elution) to furnish pyrroline **3a** (171 mg, 82% from **2a**) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.51 (s, 1H, C=C*H*H), 4.31 (s, 1H, C=CH*H*), 4.06 (m, 2H, CH_2N=C), 3.60 (ddd, J = 10.0, 4.3, 2.2 Hz, 1H, C=CC*H*), 2.12 (m, 1H, C*H*H), 1.71 (dddd, J = 17.0, 12.2, 6.9, 4.7 Hz, 1H, CH*H*), 1.65 (d, J = 14.0 Hz, 1H, SiC*H*H), 1.50 (d, J = 13.8 Hz, 1H, SiCH*H*), 1.29 (s, 9H, (CH_3)$_3$C), 0.05 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 205.0, 173.9, 147.8, 107.3, 61.4, 55.3, 44.0, 30.5, 28.2, 27.0, −1.3; IR (film) 3077, 2955, 2870, 1684, 1630, 1482, 1459, 1249, 1162, 1055, 982, 848, 694 cm^{-1}; HRMS calcd for $C_{15}H_{27}NOSi$ (M^+) 265.1862, found 265.1856.

5-(2-Methylpropanoyl)-4-[1-[(trimethylsilyl)methyl]-ethenyl]-3,4-dihydro-2*H*-pyrrole (3b). Using isonitrile **2a** (100 mg, 0.39 mmol) and isobutyryl chloride (62 μL, 0.59 mmol) in the general procedure described above provided the title pyrroline (67 mg, 68%) as a light yellow oil after silica gel chromatography (5% EtOAc/hexane for elution): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.50 (s, 1H, C=C*H*H), 4.24 (s, 1H, C=CH*H*), 4.06 (m, 2H, CH_2N=C), 3.60 (m, 1H, C*H*(CH$_3$)$_2$), 3.57 (dd, J = 8.9, 1.9 Hz, 1H, C=CC*H*), 2.18 (dq, J = 8.8, 3.6 Hz, 1H, C*H*H), 1.81 (ddd, J = 16.4, 7.6, 3.7 Hz, 1H, CH*H*), 1.69 (d, J = 13.4 Hz, 1H, SiC*H*H), 1.52 (d, J = 13.7 Hz, 1H, SiCH*H*), 1.10 (dd, J = 7.0, 3.4 Hz, 6H, (CH_3)$_2$C), 0.06 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 203.0, 174.7, 147.5, 106.9, 60.9, 53.4, 35.8, 31.3, 28.1, 18.6, 17.9, −1.4; IR (film) 3076, 2955, 2875, 1698, 1630, 1468, 1383, 1299, 1159, 1052, 983, 694 cm^{-1}; HRMS calcd for $C_{14}H_{25}NOSi$ (M^+) 251.1705, found 251.1705.

5-(3-Methylbutanoyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3c). The standard procedure was followed using isonitrile **2a** (100 mg, 0.39 mmol) and isovaleryl chloride (72 μL, 0.59 mmol) to provide the title pyrroline (81 mg, 77%) as a light yellow oil after purification of the product by chromatography on silica gel (5% EtOAc/hexane for elution): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (s, 1H, C=C*H*H), 4.20 (s, 1H, C=CH*H*), 4.03 (m, 2H, CH_2N=C), 3.57 (dt, J = 10.0, 2.6 Hz, 1H, C=CC*H*), 2.76 (app t, J = 7.6 Hz, 2H, O=CCH_2), 2.17 (m, 2H, C*H*(CH$_3$)$_2$ and C*H*H), 1.81 (ddd, J = 12.6, 7.5, 3.7 Hz, 1H, CH*H*), 1.69 (d, J = 13.4 Hz, 1H, SiC*H*H), 1.51 (d, J = 13.5 Hz, 1H, SiCH*H*), 0.90 (app t, J = 6.2 Hz, 6H, (CH_3)$_2$CH), 0.06 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 199.1, 175.7, 147.5, 107.0, 60.8, 53.3, 47.6, 31.3, 28.1, 24.4, 22.7, 22.4, −1.3; IR (film) 3075, 2956, 1696, 1630, 1466, 1369, 1249, 1023, 989, 845, 693 cm^{-1}; HRMS calcd for $C_{15}H_{27}NOSi$ (M^+) 265.1862, found 265.1852.

5-(4-Chlorobutanoyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3d). Utilization of isonitrile **2a** (100 mg, 0.39 mmol) and 4-chlorobutyryl chloride (66 μL, 0.59 mmol) in the general procedure furnished the title pyrroline (69 mg, 61%) as a light yellow oil after purification by silica gel chromatography (5% EtOAc/ hexane for elution): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (s, 1H, C=C*H*H), 4.18 (s, 1H, C=CH*H*), 4.03 (m, 2H, CH_2N=C), 3.54 (t, J = 6.4 Hz, 3H, CH_2Cl and C=CC*H* (overlap)), 3.20 (dt, J = 18.4, 7.2 Hz, 1H, O=CC*H*H), 2.95 (dt, J = 18.2, 7.2 Hz, 1H, O=CCH*H*), 2.17 (dq, J = 12.5, 9.9 Hz, 1H, C*H*H), 2.07 (dp, J = 7.0, 2.0 Hz, 2H, CH_2CH$_2$Cl), 1.81 (ddd, J = 16.6, 7.6, 3.8 Hz, 1H, CH*H*), 1.68 (d, J = 13.7 Hz, 1H, SiC*H*H), 1.51 (d, J = 13.6 Hz, 1H, SiCH*H*), 0.05 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 198.1, 175.1, 147.35, 107.0, 60.8, 53.4, 44.2, 35.9, 31.2, 28.0, 26.4, −1.3; IR (film) 3075, 2954, 1739, 1699, 1629, 1405, 1248, 1158, 1051, 983, 845, 695 cm^{-1}; HRMS calcd for $C_{14}H_{24}ClNOSi$ (M^+) 285.1316, found 285.1306.

5-[2-(1,3-Dioxolanyl)acetyl]-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3e). To a 5-mL tear drop flask containing a solution of 2-(1,3-dioxolanyl)acetyl chloride (61 mg, 0.37 mmol) in CH_2Cl_2 (200 μL) was added isonitrile **2a** (94 mg, 0.37 mmol) via syringe. The flask was sealed, and the reaction mixture was stirred at 40 °C for 14 h. Upon cooling the mixture to room temperature, 1:1 CH_2Cl_2/$ClCH_2CH_2Cl$ (0.5 mL) was added and the resulting solution of the crude ketoimidoyl chloride was treated with AgOTf (143 mg, 0.56 mmol) as described in the general procedure. Isolation and purification of the crude product was achieved by the methods described previously to furnish **3e** (105 mg, 91%) as a colorless viscous oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.05 (dd, J = 5.6, 5.2 Hz, 1H, OC*H*O), 4.47 (s, 1H, C=C*H*H), 4.20 (s, 1H, C=CH*H*), 4.03 (m, 4H, C=NCH_2 and OC*H*H × 2), 3.74 (ddd, J = 12.8, 2.3, 1.1 Hz, 2H, OCH*H* × 2), 3.53 (dt, J = 10.1, 2.9 Hz, 1H, C=CC*H*), 3.27 (dd, J = 15.7, 5.8 Hz, 1H, O=CC*H*H), 3.10 (dd, J = 15.8, 4.7 Hz, 1H, O=CCH*H*), 2.11 (m, 2H, $^-$C≡N$^+$CH$_2$C*H*H and OCH$_2$C*H*H), 1.80 (dddd, J = 12.7, 11.2, 7.4, 3.6 Hz, 1H, NCH$_2$CH*H*), 1.66 (d, J = 13.5 Hz, 1H, SiC*H*H), 1.47 (d, J = 13.6 Hz, 1H, SiCH*H*), 1.27 (app dt, J = 13.5, 1.1 Hz, 1H, OCH$_2$CH*H*), 0.04 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 195.0, 175.2, 146.9, 107.2, 99.0, 66.9, 60.8, 53.2, 44.6, 31.3, 27.8, 25.5, −1.3; IR (film) 3075, 2954, 2855, 1739, 1702, 1631, 1248, 1136, 1017, 847 cm^{-1}; HRMS calcd for $C_{16}H_{27}NO_3Si$ (M^+) 309.1760, found 309.1754.

***trans*-3-Methyl-5-(trimethylacetyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3f$_{trans}$).** The previously described procedure was followed employing isonitrile **2b** (144 mg, 0.54 mmol) and trimethylacetyl chloride (83 μL, 0.67 mmol) to provide **3f$_{trans}$** (61 mg, 41%) as a colorless oil after purification by silica gel chromatography (1% EtOAc/hexane for elution): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.47 (s, 1H, C=C*H*H), 4.29 (s, 1H, C=CH*H*), 4.15 (ddd, J = 17.1, 7.1, 2.2 Hz, 1H, C*H*HN=C), 3.67 (dd, J = 17.1, 3.0 Hz, 1H, CH*H*N=C), 3.20 (t, J = 2.7 Hz, 1H, C=CC*H*), 2.11 (m, 1H, C*H*CH$_3$), 1.59 (d, J = 13.7 Hz, 1H, SiC*H*H), 1.43 (d, J = 13.7 Hz, 1H, SiCH*H*), 1.29 (s, 9H, (CH_3)$_3$C), 0.99 (d, J = 7.0 Hz, 3H, CH_3), 0.05 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 205.1, 173.4, 146.3, 107.2, 68.8, 63.9, 44.1, 38.3, 27.3, 27.1, 20.9, −1.2; IR (film) 3075, 2956, 2871, 1683, 1631, 1482, 1419, 1249, 1161, 1093, 955, 846, 696 cm^{-1}; HRMS calcd for $C_{16}H_{29}NOSi$ (M^+) 279.2018, found 279.2011.

***trans*-3-Methyl-4-[1-[(trimethylsilyl)methyl]ethenyl]-5-propanoyl-3,4-dihydro-2*H*-pyrrole (3g$_{trans}$).** The previously described procedure was followed employing isonitrile **2b** (241 mg, 0.87 mmol) and propionyl chloride (84 μL, 0.96 mmol) to provide **3g$_{trans}$** (86 mg, 40%) as a colorless oil after purification by silica gel chromatography (1% to 5% EtOAc/hexane for elution): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.44 (s, 1H, C=C*H*H), 4.16 (s, 1H, C=CH*H*), 4.12 (ddd, J = 17.4, 6.9, 2.4 Hz, 1H, C*H*HN=C), 3.67 (dd, J = 17.5, 2.4 Hz, 1H, CH*H*N=C), 3.17 (t, J = 2.1 Hz, 1H, C=CC*H*), 3.05 (dq, J = 18.1, 7.5 Hz, 1H, C*H*HCH$_3$), 2.78 (dq, J = 18.8, 7.4 Hz, 1H, CH*H*CH$_3$), 2.19 (m, 1H, CH$_3$C*H*), 1.64 (d, J = 13.5 Hz, 1H, SiC*H*H), 1.45 (d, J = 13.7 Hz, 1H, SiCH*H*), 1.08 (t, J = 7.4 Hz, 3H, CH$_2$CH_3), 1.00 (d, J = 7.5 Hz, 3H, CH_3), 0.07 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 200.1, 174.6, 146.0, 106.8, 68.2, 62.1, 39.1, 32.0, 27.3, 21.3, 7.6, −1.2; IR (film) 3076, 2956, 1700, 1631, 1460, 1377, 1249, 1159, 1096, 950, 848, 698 cm^{-1}; HRMS calcd for $C_{14}H_{25}NOSi$ (M^+) 251.1705, found 251.1705.

***cis*- and *trans*-2-Methyl-5-(trimethylacetyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3h$_{trans}$ and 3h$_{cis}$).** Utilizing isonitrile **2c** (200 mg, 0.75 mmol) and trimethylacetyl chloride (110 μL, 0.90 mmol) in the procedure outlined for the preparation of **3a**, a mixture of pyrrolines **3h$_{cis}$** and **3h$_{trans}$** (4.7:1.0, 189 mg, 90%) was obtained

as a light yellow oil after filtration of the crude product mixture through a plug of silica gel (5% EtOAc/hexane for elution). The mixture of diastereomeric pyrrolines was subjected to column chromatography on silica gel (1% to 5% EtOAc/hexane for elution) to afford the more polar major pyrroline **3h**$_{cis}$ (131 mg, 63% from **2c**) as a colorless oil:

3h$_{cis}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.56 (s, 1H, C=C*H*H), 4.39 (s, 1H, C=CH*H*), 4.19 (sx, J = 6.7 Hz, 1H, CH_3CHN=C), 3.58 (dt, J = 9.6, 1.5 Hz, 1H, C=CC*H*), 2.41 (ddd, J = 18.0, 9.9, 8.1 Hz, 1H, C*H*H), 1.65 (d, J = 13.5 Hz, 1H, SiC*H*H), 1.52 (d, J = 13.4 Hz, 1H, SiCH*H*), 1.35 (d, J = 6.9 Hz, 3H, CH_3) 1.29 (m, 1H, CH*H*), 1.27 (s, 9H, $(CH_3)_3C$), 0.03 (s, 9H, $(CH_3)_3$-Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 206.3, 172.1, 149.3, 108.2, 68.8, 56.7, 44.0, 38.3, 28.5, 27.1, 22.2, −1.3; IR (film) 3077, 2957, 2871, 1685, 1630, 1482, 1457, 1364, 1249, 1161, 1050, 841, 695, cm^{-1}; HRMS calcd for $C_{16}H_{29}NOSi$ (M^+) 279.2018, found 279.2012.

3h$_{trans}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.47 (s, 1H, C=C*H*H), 4.32 (m, 1H, CH_3CHN=C), 4.31 (s, 1H, C=CH*H*), 3.66 (dt, J = 9.9, 2.9 Hz, 1H, C=CC*H*), 1.91 (ddd, J = 12.9, 7.2, 3.5 Hz, 1H, C*H*H), 1.64 (d, J = 13.0 Hz, 1H, SiC*H*H), 1.63 (ddd, J = 17.7, 9.9, 7.3 Hz, 1H, CH*H*), 1.48 (d, J = 13.0 Hz, 1H, SiC*H*H), 1.29 (s, 9H, $(CH_3)_3C$), 0.04 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 205.2, 171.7, 147.4, 106.9, 68.8, 55.9, 44.2, 38.7, 29.9, 27.7, 21.6, −1.3; IR (film) 3077, 2954, 2858, 1687, 1630, 1472, 1463, 1361, 1250, 1161, 1125, 1004, 840, 777, 696 cm^{-1}.

***cis*- and *trans*-3-Methyl-4-[1-[(trimethylsilyl)methyl]-ethenyl]-5-propanoyl-3,4-dihydro-2*H*-pyrrole (3i**$_{cis}$ **and 3i**$_{trans}$**).** The above procedure was followed using isonitrile **2c** (215 mg, 0.78 mmol) and propionyl chloride (80 μL, 0.92 mmol) to furnish a mixture of pyrrolines **3i**$_{cis}$ and **3i**$_{trans}$ (3.9:1.0, 152 mg, 78%) which was isolated as a light yellow-green oil after elution of the crude material through a silica gel plug (5% EtOAc/hexane for elution). The mixture of isomeric pyrrolines was subjected to chromatography on silica gel (1% to 5% EtOAc/hexane for elution) to provide the more polar major diastereomer **3i**$_{cis}$ (95 mg, 49% from **2c**) as a colorless oil.

3i$_{cis}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.52 (s, 1H, C=C*H*H), 4.26 (s, 1H, C=CH*H*), 4.21 (sx, J = 7.0 Hz, 1H, CH_3CHN=C), 3.53 (dd, J = 9.5, 6.9 Hz, 1H, C=CC*H*), 3.05 (dq, 18.1, 7.3 Hz, 1H, C*H*HCH$_3$), 2.72 (dq, J = 18.1, 7.4 Hz, 1H, CH*H*CH$_3$), 2.48 (ddd, J = 18.6, 10.4, 8.6 Hz, 1H, C*H*H), 1.68 (d, J = 13.5 Hz, 1H, SiC*H*H), 1.51 (d, J = 13.5 Hz, 1H, SiCH*H*), 1.35 (q, J = 6.3 Hz, 1H, CH*H*), 1.33 (d, J = 6.9 Hz, 3H, C*H*$_3$), 1.06 (t, J = 7.4 Hz, 3H, CH_2CH_3), 0.04 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 200.7, 173.3, 149.7, 107.8, 68.4, 54.8, 38.8, 32.5, 28.3, 22.1, 7.5, −1.3; IR (film) 3074, 2967, 2896, 1701, 1631, 1451, 1410, 1374, 1321, 1249, 1159, 1111, 919, 854, 696 cm^{-1}; HRMS calcd for $C_{14}H_{25}NOSi$ (M^+) 251.1705 found 251.1701.

3i$_{trans}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.46 (s, 1H, C=C*H*H), 4.26 (dsx, J = 6.7, 1.8 Hz, 1H, CH_3CHN=C), 4.21 (s, 1H, C=CH*H*), 3.64 (dt, J = 9.9, 2.3 Hz, 1H, C=CC*H*), 3.06 (dq, J = 18.2, 7.2 Hz, 1H, C*H*HCH$_3$), 2.77 (dq, J = 18.1, 7.4 Hz, 1H, CH*H*CH$_3$), 2.00 (ddd, J = 12.6, 6.9, 2.6 Hz, 1H, C*H*H), 1.67 (dd, J = 18.3, 12.8 Hz, 1H, CH*H*), 1.67 (d, J = 13.1 Hz, 1H, SiC*H*H), 1.49 (d, J = 13.8 Hz, 1H, SiCH*H*), 1.35 (d, J = 6.9 Hz, 3H, C*H*$_3$), 1.08 (t, J = 7.3 Hz, 3H, CH_2CH_3), 0.06 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 200.3, 173.5, 147.0, 106.6, 68.1, 54.2, 39.4, 32.1, 27.9, 21.5, 7.5, −1.3; IR (film) 3075, 2960, 2890, 1701, 1654, 1631, 1449, 1376, 1308, 1249, 1158, 1099, 854, 695 cm^{-1}.

***cis*- and *trans*-2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-5-(trimethylacetyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3j**$_{cis}$ **and 3j**$_{trans}$**).** Isonitrile **2d** (205 mg, 0.51 mmol) and trimethylacetyl chloride (76 μL, 0.62 mmol) were used in the general procedure outlined for the preparation **3a** to yield a mixture of diastereomeric pyrrolines **3j**$_{cis}$ and **3j**$_{trans}$ (2.8:1.0, 184 mg, 87%) as a light gold oil after purification of the crude material via filtration through a silica gel plug (5% EtOAc/hexane for elution). Separation of the mixture by column chromatography on silica gel (1% to 5% EtOAc/hexane for elution) furnished the more polar major diastereomer **3j**$_{cis}$ (118 mg, 56% from **2d**) as a light yellow oil.

3j$_{cis}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (s, 1H, C=C*H*H), 4.49 (s, 1H, C=CH*H*), 4.17 (m, 1H, C*H*N=C), 3.86 (d, J = 4.8 Hz, 2H, CH_2O), 3.59 (dt, J = 10.7, 2.1 Hz, 1H, C=CC*H*), 2.26 (ddd, J = 18.1, 9.2, 8.2, 1H, C*H*H), 1.65 (dd, J = 16.2, 12.8 Hz, 1H, CH*H*), 1.59 (ABq, ν = 33.4 Hz, J = 13.6 Hz, 2H, SiCH_2), 1.27 (s, 9H, $(CH_3)_3C$), 0.87 (s, 9H, $(CH_3)_3CSi$), 0.05 (s, 3H, $CH_3SiC(CH_3)_3$), 0.04 (s, 3H, $CH_3SiC(CH_3)_3$), 0.03 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 206.5, 173.9, 148.9, 108.8, 74.9, 65.5, 56.3, 43.9, 32.7, 28.4, 27.0, 25.9, 18.4, −1.3, −5.3; IR (film) 3077, 2954, 2859, 1687, 1630, 1482, 1472, 1463, 1391, 1361, 1250, 1160, 1123, 1037, 1001, 940, 837, 776 cm^{-1}; HRMS calcd for $C_{22}H_{43}NO_2Si_2$ (M^+) 409.2832, found 409.2826.

3j$_{trans}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (s, 1H, C=C*H*H), 4.38 (m, 1H, C*H*N=C), 4.34 (s, 1H, C=CH*H*), 3.80 (dd, J = 4.2, 2.4 Hz, 2H, OCH_2), 3.66 (ddd, J = 9.8, 4.2, 2.3 Hz, 1H, C=CC*H*), 2.04 (ddd, J = 16.4, 10.0, 6.4 Hz, 1H, C*H*H), 1.75 (ddd, J = 12.5, 7.8, 4.6 Hz, 1H, CH*H*), 1.65 (d, J = 13.5 Hz, 1H, SiC*H*H), 1.50 (d, J = 13.3 Hz, 1H, SiCH*H*), 1.29 (s, 9H, $(CH_3)_3C$), 0.84 (s, 9H, $(CH_3)_3CSi$), 0.06 (s, 3H, $CH_3SiC(CH_3)_3$), 0.04 (s, 9H, $(CH_3)_3Si$), 0.02 (s, 3H, $CH_3SiC(CH_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 205.3, 173.6, 148.2, 107.2, 75.1, 65.5, 56.1, 44.1, 33.2, 28.2, 27.1, 25.8, 18.3, −1.2, −5.4; IR (film) 3076, 2954, 2858, 1686, 1630, 1482, 1472, 1463, 1391, 1361, 1250, 1161, 1125, 1004, 840, 777, 696, 627 cm^{-1}.

***cis*- and *trans*-2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-5-(3-carbomethoxypropanoyl)-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3k**$_{cis}$ **and 3k**$_{trans}$**).** Using the procedure outlined for the preparation of **3a**, isonitrile **2d** (188 mg, 0.47 mmol) and 3-carbomethoxypropionyl chloride (85 mg, 0.57 mmol) were converted into a mixture of diastereomeric pyrrolines **3k**$_{cis}$ and **3k**$_{trans}$ (4.3:1.0, 160 mg, 77%). In this instance, exposure of the crude ketoimidoyl chloride to AgOTf was performed at −78 °C for 2 h followed by an abbreviated reaction time of 2 h at −25 °C. Isolation of the more polar major pyrroline **3k**$_{cis}$ (99 mg, 48% from **2d**) was achieved by separation of the mixture by silica gel chromatography (5% EtOAc/hexane for elution).

3k$_{cis}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.55 (s, 1H, C=C*H*H), 4.33 (s, 1H, C=CH*H*), 4.24 (m, 1H, C=NC*H*), 3.88 (dd, J = 10.1, 4.6 Hz, 1H, SiOC*H*H), 3.77 (dd, J = 10.2, 6.1 Hz, 1H, SiOCH*H*), 3.64 (s, 3H, CH_3O), 3.54 (ddd, J = 9.5, 7.3, 1.5 Hz, 1H, C=CC*H*), 3.44 (dt, J = 18.8, 6.8 Hz, 1H, O=CC*H*H), 2.97 (dt, J = 18.9, 6.6 Hz, 1H, O=CCH*H*), 2.61 (t, J = 6.7 Hz, 2H, O=CCH_2CH_2), 2.35 (ddd, J = 18.7, 10.0, 8.7 Hz, 1H, C*H*H), 1.70 (dd, J = 19.9, 6.8 Hz, 1H, CH*H*), 1.68 (d, J = 13.9 Hz, 1H, SiC*H*H), 1.52 (d, J = 13.6 Hz, 1H, SiCH*H*), 0.88 (s, 9H, $(CH_3)_3CSi$), 0.06 (s, 3H, $(CH_3)_3CSiCH_3$), 0.05 (s, 3H, $(CH_3)_3$-$CSiCH_3$), 0.04 (s, 9, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 197.8, 174.6, 172.9, 149.1, 108.4, 74.7, 65.7, 54.4, 51.6, 34.3, 33.6, 28.2, 27.6, 25.9, 18.4, −1.3, −5.2; IR (film) 2954, 2929, 2857, 1744, 1705, 1632, 1472, 1437, 1361, 1250, 1212, 1162, 1123, 1006, 841, 777 cm^{-1}; HRMS calcd for $C_{22}H_{41}$-NO_4Si_2 (M^+) 439.2574, found 439.2563.

3k$_{trans}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.20 (d, J = 1.0 Hz, 1H, C=C*H*H), 4.08 (m, 1H, C=NC*H*), 3.93 (m, 4H, SiOCH_2, C=CC*H* and C=CH*H*), 3.63 (s, 3H, OCH_3), 3.34 (dt, J = 19.0, 6.8 Hz, 1H, O=CC*H*H), 3.01 (dt, J = 18.9, 6.8 Hz, 1H, O=CCH*H*), 2.60 (dt, J = 7.0, 1.8 Hz, 2H, O=CH_2CH_2), 2.08 (ddd, J = 16.5, 9.5, 8.6 Hz, 1H, C*H*H), 1.70 (ddd, J = 19.4, 9.8, 9.8 Hz, 1H, CH*H*), 1.39 (dd, J = 15.1, 1.3 Hz, 1H, SiC*H*H), 1.10 (d, J = 15.2 Hz, 1H, SiCH*H*), 0.89 (s, 9H, $(CH_3)_3CSi$), 0.11 (s, 6H, $(CH_3)_3CSi(CH_3)_2$), −0.01 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 197.3, 174.4, 172.9, 152.8, 126.2, 73.8, 65.4, 57.2, 51.6, 34.0, 31.5, 27.5, 26.0, 24.0, 18.5, −0.5, −5.2; IR (film) 2954, 2898, 2858, 1744, 1705, 1599, 1472, 1438, 1373, 1360, 1249, 1168, 1125, 1047, 1015, 837, 779, 734, 690 cm^{-1}.

***cis*- and *trans*-2-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-5-[(*E*)-3-carbomethoxy-2-methylpropenoyl]-4-[1-[(trimethylsilyl)methyl]ethenyl]-3,4-dihydro-2*H*-pyrrole (3l**$_{cis}$ **and 3l**$_{trans}$**).** Employing isonitrile **2d** (259 mg, 0.65 mmol) and (*E*)-3-carbomethoxy-2-methylpropenoyl chloride (127 mg, 0.78 mmol) in the general procedure provided a mixture of diastereomeric pyrrolines **3l**$_{cis}$ and **3l**$_{trans}$ (3.0:1.0, 225 mg, 76%) after elution of the crude material through a silica gel plug (5%

EtOAc/hexane for elution). Separation of the diastereomers was achieved by subjecting the mixture to column chromatography on silica gel (1% to 5% EtOAc/hexane for elution) to afford the more polar **3l**$_{cis}$ (138 mg, 47% from **2d**) as a light yellow oil.

3l$_{cis}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (d, J = 1.3 Hz, 1H, C=C*H*), 4.57 (s, 1H, C=C*H*H), 4.52 (s, 1H, C=CH*H*), 4.18 (m, 1H, C=NC*H*), 4.06 (dd, J = 10.2, 4.1 Hz, 1H, SiOC*H*H), 3.81 (dd, J = 10.2, 3.5 Hz, 1H, SiOCH*H*), 3.73 (dt, J = 9.3, 2.5 Hz, 1H, C=CC*H*), 3.72 (s, 3H, OCH_3), 2.34 (ddd, J = 17.9, 9.7, 8.3 Hz, 1H, C*H*H), 2.25 (d, J = 1.5 Hz, 3H, C=CCH_3), 1.81 (ddd, J = 17.0, 8.6, 8.6 Hz, 1H, CH*H*), 1.56 (ABq, ν = 28.6 Hz, J = 13.6 Hz, 2H, SiCH_2), 0.88 (s, 9H, $(CH_3)_3$CSi), 0.06 (s, 6H, $(CH_3)_3$CSi$(CH_3)_2$), 0.03 (s, 9H, $(CH_3)_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 193.6, 174.0, 166.4, 148.8, 148.1, 130.2, 109.3, 74.8, 64.9, 56.4, 51.4, 32.6, 28.2, 25.9, 18.4, 13.2, −1.3, −5.5; IR (film) 3076, 2953, 2897, 2858, 1729, 1667, 1635, 1472, 1436, 1361, 1251, 1206, 1119, 1041, 840, 777 cm^{-1}; HRMS calcd for $C_{23}H_{41}NO_4Si_2$ (M^+) 451.2574, found 451.2571.

3l$_{trans}$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (d, J = 1.3 Hz, 1H, C=C*H*), 4.53 (s, 1H, C=C*H*H), 4.44 (m, 1H, C=NC*H*), 4.38 (s, 1H, C=CH*H*), 3.80 (m, 3H, SiOCH_2 and C=CC*H*), 3.74 (s, 3H, OCH_3), 2.26 (d, J = 1.2 Hz, 3H, C=CCH_3), 2.23 (ddd, 15.3, 9.9, 5.4 Hz, 1H, C*H*H), 1.84 (ddd, J = 13.4, 8.1, 5.8 Hz, 1H, CH*H*), 1.55 (ABq, ν = 37.1 Hz, J = 13.5 Hz, 2H, SiCH_2), 0.83 (s, 9H, $(CH_3)_3$CSi), 0.03 (s, 9H, $(CH_3)_3$Si), 0.00 (s, 3H, $(CH_3)_3$CSiCH_3), −0.02 (s, 3H, $(CH_3)_3$CSiCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 193.1, 174.1, 166.4, 149.3, 147.8, 129.2, 107.7, 75.0, 65.2, 56.2, 51.5, 33.5, 28.0, 25.8, 18.2, 13.6, −1.3, −5.5; IR (film) 3075, 2954, 2858, 1727, 1667, 1631, 1472, 1436, 1361, 1251, 1203, 1119, 1035, 1005, 837, 777 cm^{-1}.

***cis,cis-N*-Tosyl-5-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2-(trimethylacetyl)-3-[1-[(trimethylsilyl)methyl]ethenyl]-pyrrolidine (13c).** To a solution of pyrroline **3j**$_{cis}$ (66 mg, 0.16 mmol) in MeOH (1.1 mL) was added $NaBH_3CN$ (41 mg, 0.65 mmol) in one portion, and the resulting solution was cooled to −78 °C. Trifluoroacetic acid (13 μL, 0.17 mmol) was immediately added in a dropwise manner, and the mixture was stirred for 1 h at −78 °C. The cold reaction mixture was poured into pH 7 buffer (3 mL), and the aqueous solution was stirred for 30 min at rt. The solution was saturated with NaCl and extracted with three portions of CH_2Cl_2 (1.5 mL), and the combined CH_2Cl_2 extracts were thoroughly dried over Na_2SO_4. The solution was filtered and then concentrated in vacuo to afford the crude pyrrolidine as a viscous, colorless oil which was used immediately in the next step.

A solution of DMAP (24 mg, 0.19 mmol) in CH_2Cl_2 (1.0 mL) was cooled to 0 °C, and TsCl (34 mg, 0.18 mmol) was added in one portion. The mixture was stirred at 0 °C for 30 min, cooled to −78 °C, and treated dropwise with a solution of the crude pyrrolidine in CH_2Cl_2 (0.20 mL) via syringe. The reaction mixture was stirred for 2 h at −78 °C then for an additional 12 h at −20 °C. Water (2.0 mL) was added to the cold mixture, and the resulting biphasic mixture was stirred for 1 h at room temperature. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 1.0 mL). The organic phases were combined and dried over Na_2SO_4. Removal of solvent in vacuo afforded the crude product which was purified by chromatography on silica gel (5% EtOAc/hexane for elution) to provide the title compound (60 mg, 67% from **3j**$_{cis}$) as a colorless, viscous oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.2 Hz, 2H, Ar*H*), 7.35 (d, J = 8.1 Hz, 2H, Ar*H*), 4.86 (d, J = 7.4 Hz, O=CC*H*N), 4.55 (d, J = 5.3 Hz, 2H, C=CH_2), 4.08 (dd, J = 9.0, 4.7 Hz, 1H, SiOC*H*H), 3.91 (dd, J = 9.7, 9.3 Hz, 1H, SiOCH*H*), 3.60 (m, 1H, SiOCH_2C*H*N), 2.42 (s, 3H, ArCH_3), 2.27 (dt, J = 13.1, 8.8 Hz, 1H, C*H*H), 1.85 (ddd, J = 12.8, 6.5, 6.5 Hz, 1H, CH*H*), 1.54 (ddd, J = 13.6, 7.7, 7.7 Hz, 1H, C=CC*H*), 1.53 (d, J = 13.2 Hz, SiC*H*H), 1.10 (s, 9H, $(CH_3)_3$CC=O), 1.03 (d, J = 12.5 Hz, SiCH*H*), 0.89 (s, 9H, $(CH_3)_3$CSi), 0.09 (s, 6H, $(CH_3)_3$CSi$(CH_3)_2$), −0.23 (s, 9H, $(CH_3)_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 213.4, 143.9, 141.0, 134.8, 129.9, 127.6, 110.5, 67.1, 62.3, 61.8, 49.3, 44.6, 33.6, 29.7, 26.3, 26.0, 21.4, 18.3, −1.9, −5.2; IR (film) 2956, 2929, 2887, 2857, 1711, 1633, 1597, 1473, 1354, 1250, 1165, 1090, 991, 838, 776 cm^{-1}; HRMS calcd for $C_{28}H_{48}NO_4SSi_2$ (M^+ − CH_3) 550.2843, found 550.2842.

***cis-N*-Tosyl-2-(trimethylacetyl)-3-[1-[(trimethylsilyl)methyl]ethenyl]pyrrolidine (13a).** Utilizing pyrroline **3a** (100 mg, 0.38 mmol) in the procedure described for the preparation of **13c** furnished the title compound (87 mg, 55% from **3a**) which was obtained as a white, crystalline solid: mp 112.3−114.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H, Ar*H*), 7.30 (d, J = 8.1 Hz, 2H, Ar*H*), 5.02 (d, J = 7.4 Hz, 1H, O=CC*H*N), 4.60 (d, J = 7.0 Hz, 2H, C=CH_2), 3.59 (dt, J = 9.9, 1.4 Hz, 1H, NC*H*H), 3.36 (ddd, J = 16.9, 9.6, 7.4 Hz, 1H, NCH*H*), 2.45 (ddd, J = 15.8, 12.6, 3.3 Hz, 1H, C=CC*H*), 2.40 (s, 3H, ArCH_3), 2.06 (ddd, J = 13.5, 6.8, 6.8 Hz, 1H, C*H*H), 1.72 (ddd, J = 12.1, 6.0, 6.0 Hz, 1H, CH*H*), 1.61 (d, J = 13.1 Hz, 1H, SiC*H*H), 1.24 (d, J = 13.0 Hz, 1H, SiCH*H*), 1.10 (s, 9H, $(CH_3)_3$C), −0.13 (s, 9H, $(CH_3)_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 214.2, 143.5, 141.3, 135.9, 129.7, 127.3, 110.8, 61.7, 50.3, 47.5, 44.4, 29.8, 28.4, 26.4, 21.4, −1.8; IR (film) 2956, 2922, 1709, 1631, 1595, 1478, 1351, 1248, 1163, 1093, 992, 849, 663 cm^{-1}; HRMS calcd for $C_{22}H_{36}NO_3SSi$ (MH^+) 422.2185, found 422.2167.

***trans,cis-N*-Tosyl-4-methyl-3-[1-[(trimethylsilyl)methyl]ethenyl]-2-(trimethylacetyl)pyrrolidine (13b).** The procedure used for the preparation of **13c** was employed using pyrroline **3f**$_{trans}$ (109 mg, 0.39 mmol) and a reaction time of 2 h at -78 °C for the reduction with $NaBH_3CN$/TFA to provide a mixture of diastereomeric *N*-tosyl pyrrolidines (4.4:1.0, 106 mg, 63% from **3f**) which was obtained as a white solid after filtration of the crude material through a silica gel plug (5% EtOAc/hexane for elution). Recrystallization of the mixture (petroleum ether) provided a pure sample of the major *N*-tosyl pyrrolidine isomer **13b** as a crystalline white solid: mp 136.0−137.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.1 Hz, 2H, Ar*H*), 7.30 (d, J = 8.0 Hz, 2H, Ar*H*), 5.09 (d, J = 7.4 Hz, 1H, O=CC*H*N), 4.66 (s, 1H, C=C*H*H), 4.52 (s, 1H, C=CH*H*), 3.69 (t, J = 7.5 Hz, 1H, NC*H*H), 2.91 (dd, J = 15.8, 7.4 Hz, 1H, NCH*H*), 2.90 (m, 1H, NCH_2C*H*CH_3), 2.40 (s, 3H, ArCH_3), 1.70 (dd, J = 11.4, 7.6 Hz, 1H, C=CC*H*), 1.63 (d, J = 13.2 Hz, 1H, SiC*H*H), 1.23 (d, J = 13.1 Hz, 1H, SiCH*H*), 1.10 (s, 9H, $(CH_3)_3$CC=O), 0.80 (d, J = 6.2 Hz, 3H, CH_3), −0.11 (s, 9H, $(CH_3)_3$Si); ^{13}C NMR (75 MHz, $CDCl_3$, ^{1}H decoupled) δ 214.2, 143.5, 139.9, 135.7, 129.6, 127.3, 111.1, 62.8, 57.0, 54.8, 44.3, 34.4, 30.4, 26.5, 21.4, 15.7, −1.4; IR (film) 3068, 2958, 2884, 1706, 1631, 1596, 1481, 1343, 1243, 1154, 1058, 1041, 852, 661 cm^{-1}; HRMS calcd for $C_{23}H_{38}NO_3SSi$ (MH^+) 436.2342, found 436.2340.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for all isonitriles and products (38 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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