Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 62 (2006) 6312–6320
Tetrahedron

Sequential addition reaction of lithium acetylides and Grignard reagents to thioiminium salts from thiolactams leading to 2,2-disubstituted cyclic amines

Toshiaki Murai,* Rie Toshio and Yuichiro Mutoh

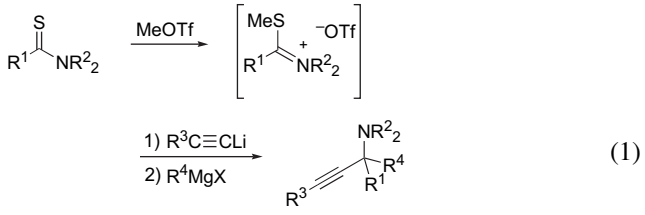
Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-1193, Japan

Received 20 March 2006; revised 13 April 2006; accepted 14 April 2006
Available online 12 May 2006

Abstract—The reaction of thioiminium salts derived from γ- and δ-thiolactams with lithium acetylides and Grignard reagents proceeded sequentially to give 2,2-disubstituted pyrrolidines and piperidines in moderate to high yields. In the initial step of the reaction, 2-(methylthio)-pyrrolidines and -piperidines may be formed. The use of lithium (trimethylsilyl)acetylide gave the products most effectively. Aryl-, alkyl-, and allylmagnesium halides were used as Grignard reagents. Silylcarbocyclization of *N*-allyl 2-ethynyl cyclic amines with $HSiMe_2Ph$ in the presence of a catalytic amount of $Rh_4(CO)_{12}$ was carried out to give trisubstituted hexahydro-1*H*-pyrrolizines and octahydroindolizines.

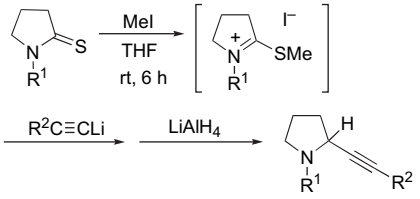
1. Introduction

The development of new carbon–carbon bond-forming reactions, in which multiple components are coupled in one operation, is needed.[1] In this context, we have recently reported the sequential addition reactions of lithium acetylides and Grignard reagents to thioiminium salts derived from acyclic thioamides[2] (Eq. 1) during the course of our studies on thioamides.[3]



(1)

In those studies, two different carbon nucleophiles were selectively introduced to thioiminium salts, and no products, to which the same carbon nucleophiles were doubly introduced, were observed. Cyclic thioamides, i.e., γ- and δ-thiolactams, can be used as a substrate in Eq. 1. In fact, the methylation of γ-thiolactams with methyl iodide has been reported to take place.[4] Alkynylation of the resulting thioiminium salts followed by reduction gives 2-alkynyl pyrrolidines (Eq. 2).[4a]



(2)

In this case, about 6 h was necessary for methylation of the thiolactams. Due to the higher reactivity of MeOTf, the methylation of thiolactams is expected to be complete within a shorter reaction time. Furthermore, the introduction of two different carbon nucleophiles to thioiminium salts derived from thiolactams can lead to 2-alkynyl-2-substituted pyrrolidines and piperidines, which are not readily available by ordinary synthetic methods. Several examples of the alkynylation of cyclic imines and iminium salts leading to 2-alkynyl pyrrolidines[5] and piperidines[6] are known, but reactions leading to 2-alkynyl-2-substituted pyrrolidines[7] and piperidines[7a,8] are rare. We report here sequential addition reactions of lithium acetylides and Grignard reagents to thioiminium salts derived from γ- and δ-thiolactams. Additionally, silylcarbocyclization was applied to the obtained *N*-allyl 2-ethynyl-2-substituted cyclic amines.

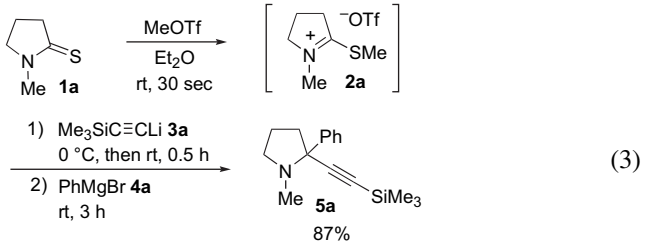
2. Results and discussion

Initially, methylation of *N*-methyl γ-thiolactam **1a** with methyl triflate (MeOTf) was carried out (Eq. 3). This reaction went to completion almost instantly to give thioiminium salt **2a**. Lithium (trimethylsilyl)acetylide (**3a**) (1.5 equiv) and phenylmagnesium bromide (**4a**) (2 equiv) were then added to an Et_2O solution of **2a** to give

Keywords: Thiolactams; Thioiminium salts; Lithium acetylides; Grignard reagents; 2,2-Disubstituted cyclic amines; Silylcarbocyclization.
* Corresponding author. Tel.: +81 58 293 2614; fax: +81 58 230 1893; e-mail: mtoshi@cc.gifu-u.ac.jp

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.04.065

N-methyl-2-alkynyl-2-phenylpyrrolidine **5a** in 87% yield. 2-(Methylthio)pyrrolidine **6a**[9] is probably formed in the step of the addition of **3a**. In the next step, the substitution reaction occurs at the carbon atom bearing nitrogen and sulfur atoms with Grignard reagent **4a**. As expected, products derived from 2 equiv of the identical carbon nucleophiles were not observed, and 2 equiv or one more equiv of Grignard reagent **4a** was enough to efficiently substitute the MeS group in **6a**. In the first step, thioiminium salt **2a** appears to react with more ionic organolithium reagents, whereas in the second step, the coordination of the sulfur atom to the Lewis acidic magnesium metal may facilitate the reaction of Grignard reagents.

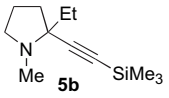
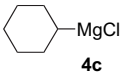
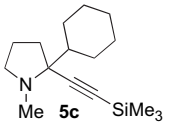
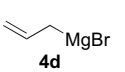
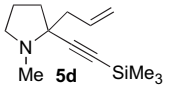
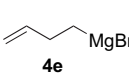
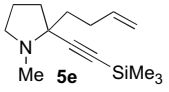
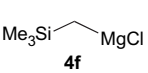
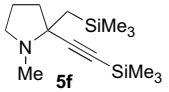


(3)

Next, a variety of Grignard reagents **4** were used for the sequential reaction. The results are summarized in Table 1. Ethyl-, cyclohexyl-, 2-propenyl-, 3-butenyl-, and silylmethylmagnesium halides **4b**–**4f** were used as aliphatic Grignard reagents. In all cases, the reaction proceeded smoothly to give the corresponding 2-alkynyl-2-alkylpyrrolidines **5b**–**5f** in good to high yields. The usual aqueous workup of the reaction mixture followed by concentration of the organic layers gave products **5** with high purity except for the reaction with **4f**.

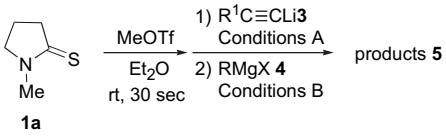
Lithium acetylides **3b**–**3e** derived from phenylacetylene, 2-methyl-1-butene-3-yne, 1-hexyne, and 1-ethynylcyclohexene were also used for the sequential addition reaction to **2a** (Eq. 4). The results are summarized in Table 2. As in the reaction with lithium silylacetylide **3a**, thioiminium salt **2a** was stirred with lithium phenylacetylide (**3b**) at 0 °C–room temperature for 30 min. To the reaction mixture was then added Grignard reagents **4a**, **4b**, and **4f**, and the mixture was stirred at room temperature for 3 h, but the desired products **5g**–**5i** were obtained in at most 40% yield (entries 1, 3, and 4). To confirm the efficiency of the generation of 2-(methylthio)pyrrolidine **6b** from **2a** and **3b**, the reduction of in situ-generated **6b** was carried out with $LiAlH_4$ to give 2-phenylethynylpyrrolidine (**5j**) in 59% yield (entry 5). Thus, the addition of **3b** to **2a** occurs efficiently, and lower yields in entries 1, 3, and 4 may be due to a less efficient reaction of **6b** with Grignard reagents **4**. Attempts to enhance the yields of **5g**–**5i** by raising the reaction temperature or by using a large excess of Grignard reagents **4** were not successful, but the reaction with **4a** under reflux in THF gave the product **5g** in slightly better yield (entry 2). The use of lithium acetylides **3c**–**3e** gave 2-alkynyl-2-alkyl or -aryl

Table 1. Sequential reaction of thiolactam **1a** with MeOTf, lithium silylacetylide **3a**, and Grignard reagents **4**[a]

Grignard reagent **4**	Product **5**	Yield (%)[b]
EtMgBr, **4b**		58
 **4c**		70
 **4d**		96[c]
 **4e**		88[c]
 **4f**		51[d]

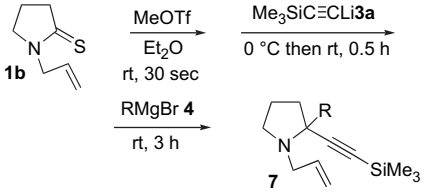
[a] Reaction was carried out as follows, unless otherwise noted: to thiolactam **1a** (1 mmol) in Et_2O (5 mL) were added MeOTf (1 equiv), lithium silylacetylide **3a** (1.5 equiv), and Grignard reagents **4** (2 equiv).
[b] Yields of crude product **5** with purity higher than 95%.
[c] Thiolactam **1a** (5 mmol) was used.
[d] Product **5f** was purified by column chromatography on silica gel, and the isolated yield is shown.

pyrrolidines **5k**–**5m** and **5o**, albeit in low to moderate yields (entries 6–8 and 10). The sequential reaction of **2a** with **3d** and $LiAlH_4$ gave the product **5n** in 59% yield, which suggested the efficient formation of **6d** and the lower efficiency of the reaction of **6d** with Grignard reagents **4**.



(4)

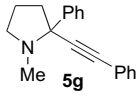
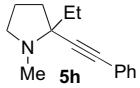
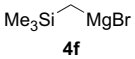
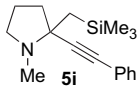
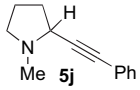
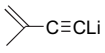
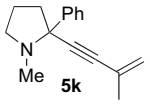
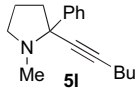
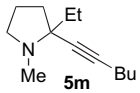
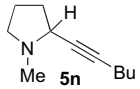
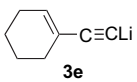
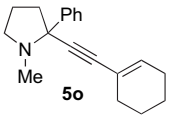
Instead of γ-thiolactam **1a**, *N*-allyl γ-thiolactam **1b** was chosen as a starting material (Eq. 5). As in the reaction of **1a**, the corresponding pyrrolidines **7** were obtained in good to high yields by reacting with lithium acetylide **3a** and Grignard reagents **4**.



(5)

[a] after the purification by column chromatography on silica gel

Table 2. Sequential reaction of thiolactam **1a** with MeOTf, lithium acetylides **3**, and Grignard reagents **4** or $LiAlH_4$[a]

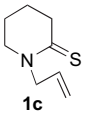
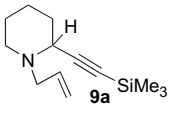
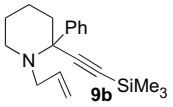
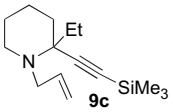
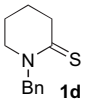
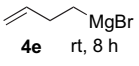
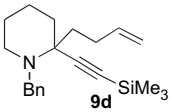
Entry	$R^1C{\equiv}CLi$ **3**	Conditions A	RMgBr **4** or $LiAlH_4$	Conditions B	Product **5**	Yield (%)[b]
1	PhC≡CLi, **3b**	0 °C, then rt, 0.5 h	PhMgBr, **4a**	rt, 3 h	 **5g**	30
2[c]				Reflux, 12 h		44
3	**3b**	0 °C, then rt, 0.75 h	EtMgBr, **4b**	rt, 3 h	 **5h**	40
4	**3b**	0 °C, then rt, 0.5 h	 **4f**	rt, 3 h	 **5i**	36
5[d]	**3b**	0 °C, then rt, 0.5 h	$LiAlH_4$	−10 °C, 3 h	 **5j**	59
6	 **3c**	0 °C, then rt, 0.5 h	**4a**	rt, 3 h	 **5k**	18
7	BuC≡CLi, **3d**	−78 °C, 1 h	**4a**	−78 °C, then rt, 3 h	 **5l**	40
8	**3d**	−30 °C, 0.5 h	**4b**	Reflux, 3 h	 **5m**	40
9[d]	**3d**	0 °C, 0.5 h	$LiAlH_4$	−10 °C, 3 h	 **5n**	59
10	 **3e**	−78 °C, 1 h	**4a**	−78 °C, then rt, 3 h	 **5o**	41

[a] Reaction was carried out as follows, unless otherwise noted: to thiolactam **1a** (1 mmol) in Et_2O (5 mL) were added MeOTf (1 equiv), lithium acetylide (1.5 equiv), and Grignard reagent **4** (2 equiv). Products **5** were purified by column chromatography on silica gel.
[b] Isolated yields.
[c] Lithium phenylacetylide **3b** (3 equiv) and phenylmagnesium bromide **4a** (4 equiv) were used in THF.
[d] $LiAlH_4$ (2.6 equiv) was used.

The above results clearly show that the 2-(methylthio)pyrrolidine **6a** derived from **2a** and lithium silylacetylide **3a** undergoes a substitution reaction at the carbon atom adjacent to the nitrogen atom with Grignard reagents **4** with better efficiency. This may be partly due to the electron-withdrawing ability of the silicon atom enabling the carbon atom bearing the sulfur and nitrogen atoms in **6a** more electropositive.

δ-Thiolactams **1c** and **1d** were also used as a starting material. The results are summarized in Table 3. To confirm the efficient generation of 2-(methylthio)piperidine **8**,[10] the reaction mixture obtained from δ-thiolactam **1c**, MeOTf, and lithium silylacetylide **3a** was treated with $LiAlH_4$ to give 2-silylethynylpiperidine **9a** in good yield (entry 1). The use of phenylmagnesium bromide (**4a**) produced the corresponding product **9b** in low yield (entry 2), whereas the

Table 3. Sequential reaction of thiolactam **1c** and **1d** with MeOTf, lithium silylacetylide **3a**, and $LiAlH_4$ or Grignard reagents **4**[a]

Entry		$LiAlH_4$ or R′MgBr **4** Conditions[b]	Product **9**	Yield (%)[c]
1	 **1c**	$LiAlH_4$, −10 °C, 3 h	 **9a**	67[d]
2	**1c**	PhMgBr **4a**, rt, 5 h	 **9b**	21
3	**1c**	EtMgBr **4b**, rt, 8 h	 **9c**	77
4	 **1d**	 **4e** rt, 8 h	 **9d**	48

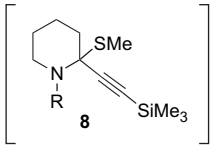
[a] Reaction was carried out unless otherwise noted: to thiolactam **1** (1 mmol) in Et_2O (5 mL) were added MeOTf (1 equiv), lithium silylactylide **3a** (1.5 equiv), and Grignard reagents **4** (2 eqiuv). Products **9** were purified by column chromatography on silica gel.

[b] Reaction conditions of the reaction with $LiAlH_4$ or Grignard reagents **4** are shown.

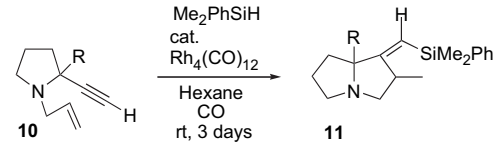
[c] Isolated yields.

[d] $LiAlH_4$ (2.6 equiv) was used.

reaction with ethylmagnesium bromide (**4b**) led to the product **9c** in better yield (entry 3).



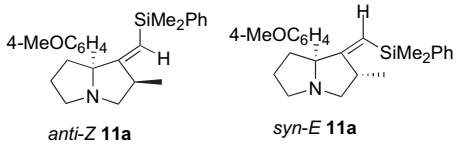
Finally, 2-alkynyl-2-substituted pyrrolidines and piperidines obtained above were subjected to silylcarbocyclization developed by Ojima and his co-workers.[11] *N*-Allyl-2-ethynylpyrrolidines **10**, obtained by the desilylation of cyclic amines **7** and **9**, were reacted with $HSiPhMe_2$ in the presence of $Rh_4(CO)_{12}$ under a CO atmosphere (Eq. 6). The silylcarbocyclization of acyclic amines has been reported to be complete within 1 min, but in the reaction of **10a**, only a starting cyclic amine **10a** was observed after 1 min. To efficiently complete the cyclization, the reaction was carried out under various reaction conditions. Consequently, the reaction at room temperature for 3 days gave 1,2,7a-trisubstituted hexahydro-1*H*-pyrrolizine[12] **11a** as a mixture of four diastereomers (67:26:6:1) in 85% yield. The stereochemistry of the two major diastereomers was estimated to be *anti-Z*-**11a**[15] and *syn-E*-**11a** by phase-sensitive NOESY spectroscopy. A similar reaction of **10b** took place to give the corresponding pyrrolizine **11b**, whereas 2-ethynyl-2-alkylpyrrolidines **10c** and **10d** did not react at all under identical reaction conditions. In contrast, the silylcarbocyclization of 2-ethynyl-2-ethylpiperidine **12** proceeded in a similar manner to give 1,2,8a-trisubstituted octahydroindolizine[12] **13** as a mixture of two diastereomers.[16]

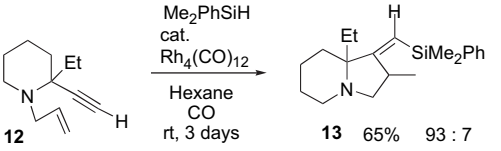


(6)

10a R = C_6H_4-OMe-4
10b R = Ph
10c R = Me
10d R = Et

11a 85% (67 : 26 : 6 : 1)
11b 88% (70 : 26 : 3 : 1)





(7)

In summary, we have demonstrated the sequential reaction of γ- and δ-thiolactams with MeOTf, lithium acetylides, and Grignard reagents to give 2-alkynyl-2-substituted pyrrolidines and piperidines in low to high yields. The synthesis of trisubstituted pyrrolizines and indolizines was achieved by $Rh_4(CO)_{12}$-catalyzed silylcarbocyclization.

3. Experimental

3.1. General methods

The IR spectra were obtained on a JASCO FTIR 410 spectrophotometer. ^1H (399.7 MHz) and ^{13}C (100.4 MHz) NMR spectra were measured on a JEOL α-400 spectrometer. The ^1H and the ^{13}C chemical shifts are reported in δ values referred to Me_4Si and $CHCl_3$ as an internal standard, respectively. All spectra were acquired in the proton-decoupled mode. Phase-sensitive NOESY spectra were measured with a Varian Inova 500 NMR spectrometer. The mass spectra (MS) were taken on SHIMADZU GCMS QP1000 and JEOL MStation 700 spectrometers. The high-resolution mass spectra (HRMS) were measured on JEOL GC-mate II and JEOL MStation 700 mass spectrometers.

3.2. General procedure for the sequential addition reaction of lithium acetylides and Grignard reagents to thioiminium salts derived from γ-thiolactams

In a typical example, to an Et_2O (5 mL) solution of 1-methyl-2-pyrrolidinethione (0.115 g, 1.0 mmol) was added methyl triflate (0.115 mL, 1.0 mmol) at room temperature, and the mixture was stirred at this temperature for 30 s. To this was added an Et_2O solution (5 mL) of the alkynyllithium

prepared from (trimethylsilyl)acetylene (0.21 mL, 1.5 mmol) and BuLi (1.6 M solution in hexane, 0.94 mL, 1.5 mmol) at 0 °C, and this was stirred for 0.5 h at room temperature. To this was added phenylmagnesium bromide (1.0 M solution in THF, 2.0 mL, 2.0 mmol) at room temperature, and the mixture was stirred at this temperature for 3 h. The resulting mixture was poured into a saturated aqueous solution of NH_4Cl, and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to give the amine **5a** (0.206 g, 87%) as an orange oil.

3.2.1. 1-Methyl-2-phenyl-2-(2-trimethylsilyl)ethynylpyrrolidine (5a). IR (neat) 3060, 3026, 2959, 2902, 2878, 2843, 2817, 2787, 2156, 1621, 1601, 1447, 1250, 880, 843, 759 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.22 (s, 9H), 1.89–2.02 (m, 3H), 2.09 (s, 3H), 2.23–2.29 (m, 1H), 2.61 (q, J=8.4 Hz, 1H), 3.13–3.18 (m, 1H), 7.02 (t, J=6.3 Hz, 1H), 7.10 (t, J=6.8 Hz, 2H), 7.45 (d, J=7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.41, 21.4, 35.8, 44.5, 53.6, 68.9, 92.1, 104.0, 127.0, 127.4, 128.3, 142.5; MS (EI) m/z 257 (M^+); HRMS Calcd for $C_{16}H_{23}NSi$: 257.1600 (M^+). Found: 257.1582.

3.2.2. 1-Methyl-2-ethyl-2-(2-trimethylsilyl)ethynylpyrrolidine (5b). Orange oil: IR (neat) 2966, 2880, 2844, 2811, 2787, 2153, 1460, 1378, 1306, 1251, 1082, 1031, 971, 920, 879, 842, 760, 689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.10 (s, 9H), 0.93 (t, J=7.6 Hz, 3H), 1.22–1.31 (m, 1H), 1.59–1.75 (m, 4H), 1.93–1.99 (m, 1H), 2.18 (s, 3H), 2.38–2.44 (m, 1H), 2.89–2.94 (m, 1H); ^{13}C (NMR) δ 0.39, 9.8, 20.3, 31.4, 35.5, 37.4, 54.1, 65.1, 89.6, 105.7; MS (EI) m/z 180 ($M^+-CH_2CH_3$); HRMS Calcd for $C_{12}H_{23}NSi$: 209.1600 (M^+). Found: 209.1585.

3.2.3. 1-Methyl-2-cyclohexyl-2-(2-trimethylsilyl)ethynylpyrrolidine (5c). Orange oil: IR (neat) 2927, 2852, 2788, 2671, 2153, 1649, 1578, 1449, 1408, 1345, 1299, 1250, 1213, 1164, 1105, 1045, 1000, 877, 842, 760, 689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.08 (s, 9H), 0.84–0.92 (m, 2H), 1.05–1.21 (m, 4H), 1.44–1.45 (m, 1H), 1.57–1.74 (m, 7H), 1.93–1.96 (m, 1H), 2.10 (s, 3H), 2.33–2.38 (m, 1H), 2.87 (dt, J=8.5, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.45, 20.4, 25.5, 26.4, 26.9, 27.2, 29.8, 32.8, 35.2, 42.8, 53.9, 67.6, 88.8, 107.1; MS (EI) m/z 263 (M^+), 180 ($M^+-C_6H_{11}$); HRMS Calcd for $C_{16}H_{29}NSi$: 263.2069 (M^+). Found: 263.2082.

3.2.4. 1-Methyl-2-(2-propenyl)-2-(2-trimethylsilyl)ethynylpyrrolidine (5d). Orange oil: IR (neat) 3077, 2960, 2907, 2845, 2813, 2788, 2677, 2154, 1641, 1449, 1416, 1347, 1251, 1201, 1167, 1110, 1045, 994, 949, 913, 843, 760, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9H), 1.71–1.84 (m, 3H), 1.92–1.98 (m, 1H), 2.16 (dd, J=13.5, 7.6 Hz, 1H), 2.27 (s, 3H), 2.44–2.52 (m, 2H), 2.97 (dt, J=8.5, 3.2 Hz, 1H,), 5.01–5.13 (m, 2H), 5.90 (dddd, J=17.1, 10.3, 7.8, 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.36, 20.3, 35.5, 37.5, 42.9, 54.0, 63.6, 89.8, 105.7, 117.4, 134.3; MS (EI) m/z 221 (M^+); HRMS Calcd for $C_{13}H_{23}NSi$: 221.1600 (M^+). Found: 221.1620.

3.2.5. 1-Methyl-2-(3-butenyl)-2-(2-trimethylsilyl)ethynylpyrrolidine (5e). Orange oil: IR (neat) 3078, 2959, 2847, 2788, 2153, 1641, 1451, 1346, 1250, 1165, 1109, 1031, 910, 843, 760, 698 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (s, 9H), 1.35 (dt, J=12.7, 4.9 Hz, 1H), 1.66–1.82 (m, 4H), 1.99–2.08 (m, 2H), 2.21–2.26 (m, 4H), 2.39–2.43 (m, 1H), 2.89–2.94 (m, 1H), 4.91 (d, J=10.3 Hz, 1H), 4.99 (d, J=17.1 Hz, 1H), 5.82 (dddd, J=17.0, 12.7, 10.2, 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.35, 20.4, 29.8, 35.5, 37.8, 38.0, 53.9, 64.1, 89.9, 105.6, 114.3, 138.7; MS (EI) m/z 235 (M^+); HRMS Calcd for $C_{14}H_{25}NSi$: 235.1756 (M^+). Found: 235.1750.

3.2.6. 1-Methyl-2-(1-trimethylsilyl)methyl-2-(2-trimethylsilyl)ethynylpyrrolidine (5f). Yellow oil: IR (neat) 2958, 2903, 2843, 2813, 2785, 2153, 1450, 1415, 1345, 1250, 1207, 1138, 1101, 1018, 986, 925, 842, 760, 697 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.09 (s, 9H), 0.15 (s, 9H), 0.67 (d, J=14.2 Hz, 1H), 1.29 (d, J=14.2 Hz, 1H), 1.66–1.76 (m, 3H), 2.06–2.10 (m, 1H), 2.24 (s, 3H), 2.37–2.43 (m, 1H), 2.91–2.95 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 0.21, 0.23, 20.2, 27.4, 34.9, 39.8, 52.8, 62.3, 89.0, 106.5; MS (EI) m/z 267 (M^+); HRMS Calcd for $C_{14}H_{29}NSi$: 267.1839 (M^+). Found: 267.1841.

3.2.7. 1-Methyl-2-phenyl-2-(2-phenyl)ethynylpyrrolidine (5g). Yellow oil: IR (neat) 3060, 3031, 2963, 2906, 2816, 2787, 1947, 1599, 1489, 1445, 1414, 1260, 1027, 865, 796, 756, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88–2.08 (m, 3H), 2.13 (s, 3H), 2.28–2.34 (m, 1H), 2.67 (q, J=8.8 Hz, 1H), 3.13–3.18 (m, 1H), 7.16–7.69 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 21.5, 36.0, 44.6, 53.8, 68.9, 87.9, 88.3, 123.5, 126.8, 127.2, 127.3, 128.2, 128.3, 131.8, 142.8; MS (EI) m/z 261 (M^+), 184 ($M^+-C_6H_5$); HRMS Calcd for $C_{19}H_{19}N$: 261.1517 (M^+). Found: 261.1488.

3.2.8. 1-Methyl-2-ethyl-2-(2-phenyl)ethynylpyrrolidine (5h). Yellow oil: IR (neat) 3055, 2968, 2877, 2786, 1600, 1573, 1489, 1443, 1345, 1231, 1147, 1031, 914, 755, 596 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (t, J=7.6 Hz, 3H,), 1.40–1.49 (m, 1H), 1.78–1.95 (m, 4H), 2.12–2.17 (m, 1H), 2.36 (s, 3H), 2.57–2.64 (m, 1H), 3.03–3.08 (m, 1H), 7.26–7.32 (m, 3H), 7.40–7.44 (m, 2H); ^{13}C NMR δ 9.9, 20.4, 31.7, 35.7, 37.6, 54.4, 65.2, 86.2, 89.2, 123.6, 127.7, 128.2, 131.7; MS (EI) m/z 184 ($M^+-CH_2CH_3$); HRMS Calcd for $C_{13}H_{14}N$: 184.1126 ($M^+-CH_2CH_3$). Found: 184.1114.

3.2.9. 1-Methyl-2-(1-trimethylsilyl)methyl-2-(2-phenyl)-ethynylpyrrolidine (5i). Yellow oil: IR (neat) 3080, 3056, 3033, 2952, 2904, 2841, 2810, 2784, 1945, 1742, 1598, 1573, 1545, 1490, 1248, 846, 755, 691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.10 (s, 9H), 0.73 (d, J=13.9 Hz, 1H), 1.37 (d, J=13.9 Hz, 1H), 1.73–1.80 (m, 3H), 2.13–2.18 (m, 1H), 2.30 (s, 3H), 2.45–2.53 (m, 1H), 2.95–3.00 (m, 1H), 7.22–7.27 (m, 3H), 7.34–7.37 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 0.2, 20.3, 27.6, 35.1, 40.0, 53.1, 62.4, 85.8, 90.1, 123.6, 127.7, 128.2, 131.5; MS (EI): m/z 271 (M^+); HRMS Calcd for $C_{17}H_{25}NSi$: 271.1756 (M^+). Found: 271.1779.

3.2.10. 1-Methyl-2-(2-phenyl)ethynylpyrrolidine (5j). Yellow oil: IR (neat) 2975, 2877, 2838, 2777, 1739, 1599, 1490, 1444, 1355, 1241, 1046, 757, 691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77–1.83 (m, 1H), 1.90–2.06 (m, 2H), 2.15–2.24 (m, 1H), 2.39 (q, J=8.8 Hz, 1H), 2.48 (s, 3H), 2.94 (dt, J=8.8, 3.9 Hz, 1H), 3.30 (t, J=7.1 Hz, 1H), 7.26–7.29 (m, 3H), 7.41–7.45 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 22.4,

32.2, 39.9, 54.8, 57.0, 84.1, 88.8, 123.3, 127.8, 128.1, 131.6; MS (EI) *m/z* 185 (M^+); HRMS Calcd for $C_{13}H_{15}N$: 185.1204 (M^+). Found: 185.1179.

3.2.11. 1-Methyl-2-phenyl-2-(3-methyl-3-buten-1-ynyl)-pyrrolidine (5k). Yellow oil: IR (neat) 3423, 3060, 3030, 2969, 2843, 2816, 2787, 2514, 2346, 1946, 1794, 1600, 1483, 1446, 1299, 1173, 895, 738, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.82–2.01 (m, 6H), 2.05 (s, 3H), 2.18–2.24 (m, 1H), 2.58 (q, J=8.6 Hz, 1H), 3.08–3.13 (m, 1H), 5.15 (quint, J=1.23 Hz, 1H), 5.26 (quint, J=1.23 Hz, 1H), 7.15–7.19 (m, 1H), 7.24–7.28 (m, 2H), 7.59–7.61 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 24.1, 35.9, 44.5, 53.7, 68.7, 86.8, 89.5, 121.1, 126.8, 127.2, 128.1, 128.8, 142.9; MS (EI) *m/z* 225 (M^+); HRMS Calcd for $C_{16}H_{19}N$: 225.1518 (M^+). Found: 225.1530.

3.2.12. 1-Methyl-2-phenyl-2-hexynylpyrrolidine (5l). Yellow oil: IR (neat) 2934, 2861, 2785, 1601, 1487, 1447, 1299, 1244, 1172, 1055, 913, 756, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, J=7.3 Hz, 3H), 1.36–1.53 (m, 4H), 1.80–1.98 (m, 3H), 2.02 (s, 3H), 2.12–2.18 (m, 1H), 2.26 (t, J=6.8 Hz, 2H), 2.55 (q, J=8.7 Hz, 1H), 3.06–3.11 (m, 1H), 7.16 (t, J=7.3 Hz, 1H), 7.25 (t, J=7.3 Hz, 2H), 7.62 (d, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.7, 18.5, 21.5, 22.0, 31.4, 35.8, 44.7, 53.6, 68.4, 77.7, 88.3, 126.9, 127.0, 128.0, 143.4; MS (EI) *m/z* 241 (M^+); HRMS Calcd for $C_{17}H_{23}N$: 241.1830 (M^+). Found: 241.1831.

3.2.13. 1-Methyl-2-ethyl-2-hexynylpyrrolidine (5m). Yellow oil: IR (neat) 2964, 2934, 2875, 2786, 1460, 1378, 1260, 1231, 1083, 1031, 909, 806, 404 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (t, J=7.3 Hz, 3H), 0.95 (t, J=7.6 Hz, 3H), 1.21–1.31 (m, 1H), 1.35–1.46 (m, 4H), 1.62–1.75 (m, 4H), 1.91–1.96 (m, 1H), 2.16 (t, J=6.8 Hz, 2H), 2.20 (s, 3H), 2.43 (q, J=8.6 Hz, 1H), 2.90–2.95 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 9.9, 13.7, 18.3, 20.2, 21.9, 31.4, 31.8, 35.5, 37.7, 54.2, 64.6, 78.9, 85.8; MS (EI) *m/z* 164 ($M^+-CH_2CH_3$); HRMS Calcd for $C_{11}H_{18}N$: 164.1439 ($M^+-CH_2CH_3$). Found: 164.1406.

3.2.14. 1-Methyl-2-hexynylpyrrolidine (5n). Yellow oil: IR (neat) 2958, 2873, 2775, 2235, 1641, 1458, 1353, 1321, 1219, 1159, 1115, 1039, 904, 733, 407 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (t, J=7.3 Hz, 3H), 1.30–1.46 (m, 4H), 1.62–1.71 (m, 1H), 1.75–1.84 (m, 2H), 1.98–2.05 (m, 1H), 2.14 (td, J=7.3, 1.8 Hz, 2H), 2.19–2.25 (m, 1H), 2.33 (s, 3H), 2.79–2.85 (m, 1H), 2.94 (t, J=6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.6, 18.4, 21.9, 22.2, 31.0, 32.4, 39.8, 54.8, 56.8, 79.2, 84.2; MS (EI) *m/z* 165 (M^+); HRMS Calcd for $C_{11}H_{19}N$: 165.1517 (M^+). Found: 165.1493.

3.2.15. 1-Methyl-2-phenyl-2-(1-cyclohexenyl)ethynylpyrrolidine (5o). Yellow oil: IR (neat) 3060, 2935, 2840, 2785, 2204, 1948, 1810, 1741, 1600, 1488, 1446, 1346, 1297, 1241, 1173, 1055, 918, 756, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.51–1.63 (m, 4H), 1.82–1.89 (m, 2H), 1.94–2.07 (m, 6H), 2.12–2.23 (m, 3H), 2.58 (dd, J=17.1, 8.8 Hz, 1H), 3.08–3.13 (m, 1H), 6.08 (quint, J=2.0 Hz, 1H), 7.16 (t, J=7.3 Hz, 1H), 7.25 (t, J=7.8 Hz, 2H), 7.62 (d, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 21.6, 22.4, 25.6, 29.9, 35.9, 44.6, 53.7, 68.8, 84.7, 90.2, 120.7, 126.8, 127.1, 128.1, 134.0, 143.1; MS (EI) *m/z* 265 (M^+); HRMS Calcd for $C_{19}H_{23}N$: 265.1830 (M^+). Found: 265.1810.

3.2.16. 1-(2-Propenyl)-2-phenyl-2-(2-trimethylsilyl)ethynylpyrrolidine (7a). Orange oil: IR (neat) 3389, 3063, 2959, 2815, 2155, 1737, 1598, 1447, 1249, 1167, 1098, 916, 841, 759, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (s, 9H), 1.78–1.92 (m, 3H), 2.13–2.19 (m, 1H), 2.38–2.44 (m, 1H), 2.65 (dd, J=13.7, 7.8 Hz, 1H), 2.94–2.98 (m, 1H), 3.20 (dt, J=8.8, 3.1 Hz, 1H), 4.94 (d, J=10.3 Hz, 1H), 5.09 (d, J=17.1 Hz, 1H), 5.76 (dddd, J=17.6, 10.3, 7.8, 4.9 Hz, 1H), 7.16 (t, J=7.3 Hz, 1H), 7.24 (t, J=7.6 Hz, 2H), 7.63 (d, J=8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.39, 21.4, 44.4, 50.7, 53.5, 68.6, 91.6, 104.6, 115.8, 126.7, 127.2, 128.1, 136.9, 143.0; MS (EI) *m/z* 206 ($M^+-C_6H_5$); HRMS Calcd for $C_{18}H_{25}NSi$: 283.1756 (M^+). Found: 283.1741.

3.2.17. 1-(2-Propenyl)-2-methyl-2-(2-trimethylsilyl)ethynylpyrrolidine (7b). Orange oil: IR (neat) 3080, 2961, 2812, 2155, 1718, 1644, 1418, 1350, 1251, 1098, 1020, 843, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.13 (s, 9H), 1.33 (s, 3H), 1.68–1.79 (m, 3H), 2.02–2.07 (m, 1H), 2.30–2.36 (m, 1H), 2.79 (dd, J=13.2, 7.8 Hz, 1H), 2.98–3.04 (m, 1H), 3.30 (dd, J=13.2, 5.9 Hz, 1H), 5.05 (d, J=9.8 Hz, 1H), 5.18 (d, J=17.1 Hz, 1H), 5.89 (dddd, J=17.6, 9.8, 7.8, 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.37, 20.2, 25.6, 40.4, 51.5, 53.5, 60.1, 88.2, 107.2, 116.6, 136.9; MS (EI) *m/z* 221 (M^+), 206 (M^+-CH_3); HRMS Calcd for $C_{13}H_{23}NSi$: 221.1600 (M^+). Found: 221.1569.

3.2.18. 1-(2-Propenyl)-2-ethyl-2-(2-trimethylsilyl)ethynylpyrrolidine (7c). Orange oil: IR (neat) 3079, 2967, 2879, 2811, 2153, 1643, 1460, 1417, 1378, 1350, 1250, 1144, 995, 842, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.14 (s, 9H), 0.96 (t, J=7.6 Hz, 3H), 1.32–1.41 (m, 1H), 1.66–1.81 (m, 4H), 1.97–2.01 (m, 1H), 2.31–2.37 (m, 1H), 2.77 (dd, J=13.2, 7.8 Hz, 1H), 3.02–3.07 (m, 1H), 3.31 (dd, J=13.7, 5.4 Hz, 1H), 5.04 (d, J=10.2 Hz, 1H), 5.18 (d, J=17.1 Hz, 1H), 5.88 (dddd, J=17.6, 10.3, 8.3, 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.41, 9.6, 20.3, 31.7, 37.4, 51.8, 53.5, 64.8, 89.1, 106.6, 116.3, 137.1; MS (EI) *m/z* 206 ($M^+-CH_2CH_3$); HRMS Calcd for $C_{12}H_{20}NSi$: 206.1365 ($M^+-CH_2CH_3$). Found: 206.1354.

3.2.19. 1-(2-Propenyl)-2-(4-methoxyphenyl)-2-(2-trimethylsilyl)ethynylpyrrolidine (7d). Yellow oil: IR (neat) 3076, 2957, 2813, 2155, 1643, 1611, 1582, 1509, 1464, 1415, 1349, 1250, 1172, 1038, 843, 760, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, 9H), 1.84–1.96 (m, 3H), 2.16–2.22 (m, 1H), 2.41–2.47 (m, 1H), 2.67 (dd, J=13.7, 7.8 Hz, 1H), 2.98–3.03 (m, 1H), 3.24 (dt, J=8.3, 2.9 Hz, 1H), 3.79 (s, 3H), 5.00 (d, J=10.2 Hz, 1H), 5.15 (dd, J=17.1, 0.98 Hz, 1H), 5.80 (dddd, J=17.6, 10.2, 7.8, 4.9 Hz, 1H), 6.85 (d, J=8.8 Hz, 2H), 7.59 (d, J=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.41, 21.3, 44.2, 50.6, 53.4, 55.3, 68.1, 91.5, 104.7, 113.4, 115.8, 127.9, 134.9, 136.9, 158.8; MS (EI) *m/z* 313 (M^+); HRMS Calcd for $C_{19}H_{27}NOSi$: 313.1862 (M^+). Found: 313.1836.

3.2.20. 1-(2-Propenyl)-2-(2-trimethylsilyl)ethynylpiperidine (9a). Yellow oil: IR (neat) 3080, 2937, 2861, 2814, 2157, 1745, 1643, 1442, 1420, 1319, 1250, 1124, 955, 920, 843, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (s, 9H), 1.36–1.61 (m, 4H), 1.66–1.70 (m, 2H), 2.39–2.44 (m, 2H), 2.96 (dd, J=7.3, 5.9 Hz, 1H), 3.06–3.11 (m, 1H), 3.50 (s,

1H), 5.07 (d, J=10.2 Hz, 1H), 5.15 (d, J=17.1 Hz, 1H), 5.78 (dddd, J=17.1, 13.2, 10.3, 6.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.25, 20.6, 25.6, 31.2, 48.9, 52.1, 59.3, 90.6, 103.5, 118.0, 135.2; MS (EI) m/z 221 (M^+); HRMS Calcd for $C_{13}H_{23}NSi$: 221.1600 (M^+). Found: 221.1569.

3.2.21. 1-(2-Propenyl)-2-phenyl-2-(2-trimethylsilyl)ethynylpiperidine (9b). Yellow oil: IR (neat) 3062, 2935, 2860, 2817, 2724, 2156, 1642, 1601, 1488, 1446, 1347, 1250, 1222, 1131, 1012, 915, 843, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.19 (s, 9H), 1.47–1.71 (m, 6H), 2.28–2.38 (m, 2H), 2.84–2.90 (m, 2H), 4.94 (d, J=10.3 Hz, 1H), 5.04 (d, J=17.1 Hz, 1H), 5.65 (dddd, J=17.6, 10.2, 7.8, 4.4 Hz, 1H), 7.16 (t, J=7.3 Hz, 1H), 7.24 (t, J=7.6 Hz, 2H), 7.67 (d, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.48, 22.3, 25.9, 43.3, 48.2, 55.8, 65.5, 93.4, 103.6, 116.0, 126.6, 127.1, 128.1, 136.8, 145.6; MS (EI) m/z 297 (M^+); HRMS Calcd for $C_{19}H_{27}NSi$: 297.1913 (M^+). Found: 297.1888.

3.2.22. 1-(2-Propenyl)-2-ethyl-2-(2-trimethylsilyl)ethynylpiperidine (9c). Orange oil: IR (neat) 2935, 2810, 2154, 1641, 1444, 1250, 1161, 1085, 992, 905, 859, 842, 760, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H), 0.87 (t, J=7.8 Hz, 3H), 1.19–1.73 (m, 8H), 2.18 (dt, J=11.7, 2.4 Hz, 1H), 2.50 (dd, J=13.7, 7.8 Hz, 1H), 2.70 (d, J=12.2 Hz, 1H), 3.34 (dt, J=14.2, 2.4 Hz, 1H), 5.00 (d, J=10.2 Hz, 1H), 5.09 (d, J=17.1 Hz, 1H), 5.78 (dddd, J=17.5, 10.3, 8.3, 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.46, 8.0, 21.6, 25.8, 32.4, 35.4, 48.6, 54.1, 59.3, 89.8, 106.7, 116.4, 137.1; MS (EI) m/z 220 ($M^+-CH_2CH_3$); HRMS Calcd for $C_{13}H_{22}NSi$: 220.1522 ($M^+-CH_2CH_3$). Found: 220.1528.

3.2.23. 1-Phenylmethyl-2-(3-butenyl)-2-(2-trimethylsilyl) ethynylpiperidine (9d). Yellow oil: IR (neat) 3063, 3028, 2935, 2861, 2804, 2153, 1640, 1603, 1495, 1452, 1360, 1250, 1162, 1067, 991, 842, 728, 640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 9H), 1.25–1.41 (m, 2H), 1.50–1.64 (m, 4H), 1.73–1.85 (m, 2H), 2.13–2.23 (m, 3H), 2.47 (d, J=11.7 Hz, 1H), 2.94 (d, J=14.2 Hz, 1H), 3.93 (d, J=14.2 Hz, 1H), 4.85 (d, J=10.3 Hz, 1H), 4.93 (d, J=17.1 Hz, 1H), 5.74 (dddd, J=17.0, 12.7, 10.2, 6.3 Hz, 1H), 7.11–7.28 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 0.53, 21.8, 25.9, 27.7, 36.1, 39.2, 48.6, 55.0, 58.8, 89.9, 106.6, 114.3, 126.5, 128.2, 128.6, 138.9, 140.5; MS (EI) m/z 325 (M^+); HRMS Calcd for $C_{21}H_{31}NSi$: 325.2226 (M^+). Found: 325.2215.

3.3. General procedure for the desilylation of cyclic amines 7 and 9 with K_2CO_3 in MeOH

In a typical experiment, a mixture of 1-(2-propenyl)-2-phenyl-2-(2-trimethylsilyl)ethynylpyrrolidine **7a** (0.603 g, 2.1 mmol) and K_2CO_3 (0.290 g, 2.1 mmol) in MeOH (10 mL) was stirred at room temperature for 5 h, and then treated with an aqueous solution of NH_4Cl, extracted with ether, washed with brine, dried over $MgSO_4$ and concentrated in vacuo to give the amine **10b** (0.415 g, 93%) as a yellow oil.

3.3.1. 1-(2-Propenyl)-2-(4-methoxyphenyl)-2-ethynylpyrrolidine (10a). Yellow oil: IR (neat) 3296, 3075, 2955, 2815, 1643, 1609, 1581, 1509, 1463, 1416, 1349, 1249, 1172, 1037, 919, 831, 794 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.87–2.00 (m, 3H), 2.20–2.26 (m, 1H), 2.44–2.51 (m, 1H), 2.56 (s, 1H), 2.72 (dd, J=13.7, 8.3 Hz, 1H), 3.01–3.06 (m, 1H), 3.27 (dt, J=8.5, 3.2 Hz, 1H), 3.79 (s, 3H), 5.01 (dt, J=11.2, 1.5 Hz, 1H), 5.17 (dq, J=17.1, 1.5 Hz, 1H), 5.81 (dddd, J=17.1, 10.2, 8.3, 4.9 Hz, 1H), 6.85 (d, J=8.8 Hz, 2H), 7.62 (d, J=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.2, 44.3, 50.5, 53.2, 55.2, 67.5, 75.1, 82.5, 113.4, 115.9, 127.8, 134.6, 136.7, 158.8; MS (EI) m/z 241 (M^+); HRMS Calcd for $C_{16}H_{19}NO$: 241.1467 (M^+). Found: 241.1458.

3.3.2. 1-(2-Propenyl)-2-phenyl-2-ethynylpyrrolidine (10b). Yellow oil: IR (neat) 3300, 3062, 3025, 2977, 2878, 2816, 1642, 1600, 1488, 1446, 1418, 1350, 1262, 1098, 918, 758, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.88–2.03 (m, 3H), 2.24–2.30 (m, 1H), 2.48–2.55 (m, 1H), 2.57 (s, 1H), 2.76 (dd, J=13.7, 8.3 Hz, 1H), 3.04–3.09 (m, 1H), 3.31 (dt, J=8.6, 3.1 Hz, 1H), 5.03 (d, J=10.3 Hz, 1H), 5.19 (dq, J=17.1, 1.5 Hz, 1H), 5.84 (dddd, J=17.1, 10.2, 7.8, 4.4 Hz, 1H), 7.25 (t, J=7.3 Hz, 1H), 7.33 (t, J=7.6 Hz, 2H), 7.72 (d, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.3, 44.5, 50.6, 53.4, 68.0, 75.1, 82.4, 116.0, 126.6, 127.3, 128.2, 136.7, 142.7; MS (EI) m/z 211 (M^+), 170 ($M^+-CH_2CH{=}CH_2$); HRMS Calcd for $C_{15}H_{17}N$: 211.1361 (M^+). Found: 211.1375.

3.3.3. 1-(2-Propenyl)-2-methyl-2-ethynylpyrrolidine (10c). Yellow oil: IR (neat) 3303, 2975, 2814, 1643, 1443, 1370, 1351, 1260, 1143, 995, 919, 636 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3H), 1.67–1.77 (m, 3H), 2.02–2.06 (m, 1H), 2.23 (s, 1H), 2.26–2.33 (m, 1H), 2.77 (dd, J=13.2, 7.8 Hz, 1H), 2.97–3.02 (m, 1H), 3.28 (dd, J=13.2, 4.9 Hz, 1H), 5.00 (d, J=9.8 Hz, 1H), 5.15 (d, J=17.1 Hz, 1H), 5.83 (dddd, J=17.6, 9.8, 7.8, 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.1, 25.6, 40.4, 51.4, 53.3, 59.5, 72.1, 84.7, 116.6, 136.7; MS (EI) m/z 149 (M^+); HRMS Calcd for $C_9H_{12}N$: 134.0970 (M^+-CH_3). Found: 134.0937.

3.3.4. 1-(2-Propenyl)-2-ethyl-2-ethynylpyrrolidine (10d). Yellow oil: IR (neat) 3303, 3079, 2971, 2936, 2880, 2813, 2362, 2095, 1643, 1460, 1351, 1260, 1143, 997, 918, 635 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97 (t, J=7.3 Hz, 3H), 1.34–1.43 (m, 1H), 1.68–1.81 (m, 4H), 1.97–2.02 (m, 1H), 2.26 (s, 1H), 2.31–2.37 (m, 1H), 2.77 (dd, J=13.2, 7.8 Hz, 1H), 3.03–3.08 (m, 1H), 3.31 (dd, J=13.2, 5.4 Hz, 1H), 5.02 (d, J=9.8 Hz, 1H), 5.17 (dd, J=17.1, 0.98 Hz, 1H), 5.85 (dddd, J=17.1, 10.2, 8.3, 5.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 9.4, 20.2, 31.7, 37.3, 51.7, 53.3, 64.1, 72.8, 84.1, 116.4, 136.8; MS (EI) m/z 134 ($M^+-CH_2CH_3$); HRMS Calcd for $C_9H_{12}N$: 134.0970 ($M^+-CH_2CH_3$). Found: 134.0956.

3.3.5. 1-(2-Propenyl)-2-ethyl-2-ethynylpiperidine (12). Yellow oil: IR (neat) 3305, 2935, 2812, 2095, 1643, 1443, 1347, 1261, 1166, 1019, 918, 805, 637 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J=7.8 Hz, 3H), 1.37–1.78 (m, 8H), 2.23 (td, J=11.7, 2.9 Hz, 1H), 2.30 (s, 1H), 2.56 (dd, J=14.2, 8.3 Hz, 1H), 2.77 (dt, J=12.2, 2.9 Hz, 1H), 3.41 (d, J=14.2 Hz, 1H), 5.04 (d, J=10.2 Hz, 1H), 5.14 (d, J=17.1 Hz, 1H), 5.81 (dddd, J=17.5, 10.3, 8.3, 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.9, 21.5, 25.7, 32.6, 35.4, 48.6, 54.0, 58.8, 73.4, 84.1, 116.5, 136.9; MS (EI) m/z 148

($M^+-CH_2CH_3$); HRMS Calcd for $C_{12}H_{19}N$: 177.1517 (M^+). Found: 177.1507.

3.4. General procedure for the silylcarbocyclization of cyclic amines 10 and 12

In a typical example, a two-necked flask equipped with a stirring bar and a CO inlet was charged with $Rh_4(CO)_{12}$ (1.9 mg, 0.0025 mmol). After the flask was purged with CO, hexane (1 mL) was added to dissolve the catalyst. Me_2PhSiH (0.038 mL, 0.25 mmol) was added via a syringe. After the reaction mixture was stirred for 5 min at room temperature, it was then cannulated into a flask containing a solution of 1-(2-propenyl)-2-phenyl-2-ethynylpyrrolidine **10b** (0.106 g, 0.5 mmol), Me_2PhSiH (0.077 mL, 0.5 mmol) in hexane (1 mL) via CO pressure without stirring. The resulting mixture was stirred for 72 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (SiO_2, hexane/EtOAc/Et_3N=3:1:1 vol %) to give a mixture of four diastereomers of the bicyclic compound **11b** (0.153 g, 88%, 70:26:3:1) as a yellow oil.

3.4.1. *anti*-1-[*Z*-(Dimethylsilyl)methylidene]-7a-(4-methoxyphenyl)-2-methylhexahydro-1*H*-pyrrolizine (11a). Yellow oil: IR (neat) 3067, 2955, 2833, 1609, 1508, 1462, 1427, 1375, 1302, 1247, 1176, 1114, 1038, 836, 774, 639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.27 (s, 3H), 0.29 (s, 3H), 1.03 (d, J=6.8 Hz, 3H), 1.62–1.71 (m, 1H), 1.87–1.96 (m, 1H), 2.00–2.06 (m, 1H), 2.24–2.30 (m, 1H), 2.38 (dd, J=10.3, 6.8 Hz, 1H), 2.68–2.73 (m, 1H), 2.76–2.82 (m, 1H), 2.90–2.96 (m, 1H), 3.24 (dd, J=10.3, 8.3 Hz, 1H), 3.73 (s, 3H), 5.36 (d, J=2.4 Hz, 1H), 6.79 (d, J=8.8 Hz, 2H), 7.22–7.29 (m, 3H), 7.37–7.40 (m, 4H); ^{13}C NMR ($CDCl_3$) δ −0.52, 22.0, 24.8, 37.3, 38.6, 53.5, 55.2, 60.2, 82.2, 113.2, 117.9, 127.7, 127.8, 128.7, 133.7, 138.8, 139.9, 158.0, 173.4; MS (EI) m/z 377 (M^+); HRMS Calcd for $C_{24}H_{31}NOSi$: 377.2175 (M^+). Found: 377.2165.

3.4.2. *syn*-1-[*E*-(Dimethylsilyl)methylidene]-7a-(4-methoxyphenyl)-2-methylhexahydro-1*H*-pyrrolizine. ^1H NMR ($CDCl_3$) δ 0.35 (t, J=4.6 Hz, 6H), 0.84 (d, J=6.8 Hz, 3H), 1.63–1.72 (m, 1H), 1.74–1.84 (m, 1H), 1.97–2.03 (m, 1H), 2.08–2.15 (m, 1H), 2.58–2.65 (m, 1H), 2.68–2.78 (m, 3H), 3.00–3.06 (m, 1H), 3.73 (s, 3H), 5.56 (s, 1H), 6.77 (d, J=9.3 Hz, 2H), 7.28–7.30 (m, 2H), 7.43–7.50 (m, 4H), 7.54–7.56 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −0.82, −0.66, 21.4, 24.8, 38.6, 40.2, 53.8, 55.2, 59.0, 80.7, 113.2, 117.3, 127.2, 127.8, 128.9, 133.7, 139.2, 139.8, 158.0, 171.7.

3.4.3. *anti*-1-[*Z*-(Dimethylsilyl)methylidene]-7a-phenyl-2-methylhexahydro-1*H*-pyrrolizine (11b). Yellow oil: IR (neat) 3066, 2956, 1620, 1487, 1444, 1427, 1248, 1113, 1028, 836, 762, 730, 700, 641 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.26 (s, 3H), 0.29 (s, 3H), 1.03 (d, J=7.3 Hz, 3H), 1.61–1.71 (m, 1H), 1.87–1.96 (m, 1H), 2.03–2.10 (m, 1H), 2.27–2.33 (m, 1H), 2.41 (dd, J=10.7, 6.8 Hz, 1H), 2.67–2.74 (m, 1H), 2.77–2.84 (m, 1H), 2.93–2.99 (m, 1H), 3.26 (dd, J=10.7, 8.3 Hz, 1H), 5.39 (d, J=2.4 Hz, 1H), 7.09–7.16 (m, 1H), 7.20–7.29 (m, 5H), 7.36–7.39 (m, 2H), 7.46–7.49 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −0.49, 22.0, 25.0, 37.8, 38.8, 53.9, 60.4, 82.6, 118.1, 126.2, 126.7, 127.7, 127.9, 128.7, 133.7, 139.9, 146.9, 173.2; MS (EI) m/z 347 (M^+); HRMS Calcd for $C_{23}H_{29}NSi$: 347.2069 (M^+). Found: 347.2041.

3.4.4. *syn*-1-[*E*-(Dimethylsilyl)methylidene]-7a-phenyl-2-methylhexahydro-1*H*-pyrrolizine. ^1H NMR ($CDCl_3$) δ 0.33 (s, 3H), 0.35 (s, 3H), 0.81 (d, J=6.8 Hz, 3H), 1.62–1.71 (m, 1H), 1.74–1.84 (m, 1H), 1.97–2.04 (m, 1H), 2.10–2.17 (m, 1H), 2.61–2.67 (m, 1H), 2.72–2.76 (m, 3H, CH_2), 3.01–3.07 (m, 1H), 5.60 (s, 1H), 7.10–7.13 (m, 1H), 7.19–7.24 (m, 2H), 7.27–7.29 (m, 3H), 7.45–7.48 (m, 2H), 7.54–7.56 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −0.81, −0.65, 21.3, 25.0, 39.0, 40.6, 54.1, 59.2, 80.9, 117.4, 126.0, 127.8, 127.9, 128.9, 133.8, 139.8, 147.4, 171.5.

3.4.5. Major isomer of 1-[*E*-(dimethylsilyl)methylidene]-8a-ethyl-2-methyloctahydroindolizine (13). Yellow oil: IR (neat) 3067, 2927, 2797, 1619, 1483, 1427, 1372, 1329, 1248, 1113, 974, 832, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.29 (s, 3H), 0.31 (s, 3H), 0.71 (t, J=7.3 Hz, 3H), 0.96 (t, J=6.8 Hz, 3H), 1.08–1.11 (m, 2H), 1.30 (sext, J=7.3 Hz, 1H), 1.42–1.65 (m, 4H), 1.95 (sext, J=7.3 Hz, 1H), 2.49 (sext, J=7.3 Hz, 1H), 2.65–2.73 (m, 2H), 2.78–2.84 (m, 1H), 2.91 (t, J=8.3 Hz, 1H), 5.15 (d, J=2.4 Hz, 1H), 7.24–7.26 (m, 3H), 7.45–7.48 (m, 2H); ^{13}C NMR ($CDCl_3$) δ −0.63, −0.45, 7.8, 18.9, 21.2, 21.5, 24.0, 30.8, 36.6, 43.9, 56.2, 67.0, 113.2, 127.7, 128.7, 133.8, 140.1; MS (EI) m/z 313 (M^+); HRMS Calcd for $C_{20}H_{31}NSi$: 313.2226 (M^+). Found: 313.2249.

Acknowledgements

This work was supported in part by a Grant-in-Aid for Scientific Research on Priority Area (No. 18037024, 'Advanced Molecular Transformations of Carbon Resources') from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References and notes

1. For example, (a) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168–3210; (b) Bienaymé, H.; Hulme, C.; Oddon, G.; Schmitt, P. *Chem.—Eur. J.* **2000**, *6*, 3321–3329; (c) Collins, I. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1921–1940; (d) Balme, G.; Bossharth, E.; Monteiro, N. *Eur. J. Org. Chem.* **2003**, 4101–4111; (e) Balme, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 6238–6241; (f) Ramón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602–1634.
2. Murai, T.; Mutoh, Y.; Ohta, Y.; Murakami, M. *J. Am. Chem. Soc.* **2004**, *126*, 5968–5969.
3. (a) Murai, T.; Aso, H.; Tatematsu, Y.; Itoh, Y.; Niwa, H.; Kato, S. *J. Org. Chem.* **2003**, *68*, 8514–8519; (b) Murai, T.; Niwa, H.; Kimura, T.; Shibahara, F. *Chem. Lett.* **2004**, *33*, 508–509; (c) Murai, T.; Ohta, Y.; Mutoh, Y. *Tetrahedron Lett.* **2005**, *46*, 3637–3640; (d) Murai, T.; Sano, H.; Kawai, H.; Aso, H.; Shibahara, F. *J. Org. Chem.* **2005**, *70*, 8148–8153.
4. (a) Takahata, H.; Takahashi, K.; Wang, E.-C.; Yamazaki, T. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1211–1214; (b) Michael, J. P.; de Koning, C. B.; Malefetse, T. J.; Yillah, I. *Org. Biomol. Chem.* **2004**, *2*, 3510–3517.
5. (a) Mori, S.; Iwakura, H.; Takechi, S. *Tetrahedron Lett.* **1988**, *29*, 5391–5394; (b) Nagasaka, T.; Nishida, S.; Adachi, K.; Kawahara, T.; Sugihara, S.; Hamaguchi, F. *Heterocycles* **1993**, *36*, 2657–2662; (c) Katritsky, A. R.; Luo, Z.; Fang, Y.

Tetrahedron Lett. **2000**, *41*, 9691–9693; (d) Suga, S.; Okajima, M.; Yoshida, J.-i. *Tetrahedron Lett.* **2001**, *42*, 2173–2174; (e) Zhang, J.; Chunmei, L.; Li, C.-J. *Tetrahedron Lett.* **2002**, *43*, 5731–5733; (f) Goti, A.; Cicchi, S.; Mannucci, V.; Cardona, F.; Guarna, F.; Merino, P.; Tejero, T. *Org. Lett.* **2003**, *5*, 4235–4238; (g) Pilli, R. A.; Robello, L. G. *Synlett* **2005**, 2297–2300.

6. (a) Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 1719–1722; (b) Kuznetsov, S. G.; Libman, N. M.; Gorchakov, V. S.; Golikov, S. N.; Zatsepin, E. P. *Khim.-Farm. Zh.* **1984**, *18*, 435–440.
7. (a) Easton, N. R.; Henderson, F. G.; McMurray, W. J.; Leonard, N. J. *J. Med. Chem.* **1966**, *9*, 465–468; (b) Baracz, N. M.; Hankovszky, O. H.; Sar, C. P.; Jerkovich, G.; Hideg, K. *Synthesis* **1996**, 204–208; (c) Sar, C. P.; Jeko, J.; Fajer, P.; Hideg, K. *Synthesis* **1999**, 1039–1045.
8. Ryan, C. W.; Ainsworth, C. *J. Org. Chem.* **1961**, *26*, 1547–1550.
9. Unlike acyclic *S*,*N*-acetals,[2] 2-(methylthio)pyrrolidines **6** were highly labile, and they could not be detected even by NMR spectroscopy.
10. Joshi, K.; Rao, V. A.; Anand, N. *Indian J. Chem.* **1973**, *11*, 1222–1224.
11. Ojima, I.; Vu, A. T.; Lee, S.-Y.; McCullagh, J. V.; Moralee, A. C.; Fujiwara, M.; Hoang, T. H. *J. Am. Chem. Soc.* **2002**, *124*, 9164–9174.
12. Syntheses of 1,2,7a-trisubstituted hexahydro-1*H*-pyrrolizines[13] and 1,2,8a-trisubstituted octahydroindolizines[14] are rare.
13. (a) Stavinoha, J. L.; Mariano, P. S.; Leone-Bay, A.; Swanson, R.; Bracken, C. *J. Am. Chem. Soc.* **1981**, *103*, 3148–3160; (b) Imai, N.; Terao, Y.; Achiwa, K.; Sekiya, M. *Tetrahedron Lett.* **1984**, *25*, 1579–1582; (c) Imai, N.; Nemoto, M.; Terao, Y.; Achiwa, K.; Sekiya, M. *Chem. Pharm. Bull.* **1986**, *34*, 1080–1088; (d) Bureau, R.; Mortier, J.; Joucla, M. *Bull. Soc. Chim. Fr.* **1993**, *130*, 584–596; (e) Crich, D.; Ranganathan, K.; Neelamkavil, S.; Huang, X. *J. Am. Chem. Soc.* **2003**, *125*, 7942–7947.
14. (a) Joucla, M.; Mortier, J.; Hamelin, J. *Tetrahedron Lett.* **1985**, *26*, 2775–2778; (b) Joucla, M.; Mortier, J.; Hamelin, J.; Toupet, L. *Bull. Soc. Chim. Fr.* **1988**, 143–150; (c) Epperson, M. T.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 1778–1780; (d) Pearson, W. H.; Stoy, P.; Mi, Y. *J. Org. Chem.* **2004**, *69*, 1919–1939.
15. For example, in phase-sensitive NOESY spectroscopy of *anti*-*Z*-**11a**, cross peaks were observed among the protons at the *ortho*-positions of 4-methoxyphenyl group and at the proton attached to the carbon atom bearing a methyl group.
16. The stereochemistry of **13** was not determined, but the geometry of the carbon–carbon double bond was estimated to be *E* on the basis of phase-sensitive NOESY spectroscopy.