NEW ANIONIC CYCLIZATION OF 4- AND 5-ALKYNYLAMINES : SYNTHESIS OF 2-BENZYLIDENE PYRROLIDINES AND PIPERIDINES

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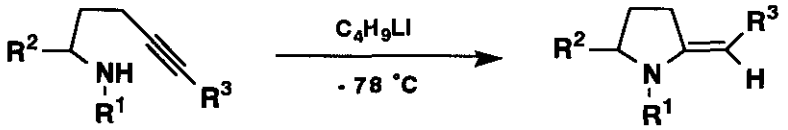
Abstract - Treatment of 4- and 5-alkynylamines with 0.5-1.2 equiv. of butyllithium brought about a facile anionic cyclization, giving the corresponding enamine pyrrolidines and piperidines having an exo double bond in high yields. Treatment of 4-alkynamides with lithium aluminum hydride also gave the similar enamine pyrrolidines in high yields.

We previously reported that the neutral aminyl radicals generated by anodic oxidation of the lithium amides of 4-alkenylamines undergo a regio- and stereoselective cyclization to give *cis*-1-methyl-2,5-disubstituted pyrrolidines.[1] In the course of our continuing studies on aminyl radical cyclizations, we have found a new facile anionic cyclization of 4-alkynylamines to give enamine pyrrolidines having an exo double bond.[2] This anionic cyclization is noteworthy from both mechanistic and synthetic viewpoints since the nucleophilic addition of amines to simple alkynes is usually difficult and requires an assistance of metal ions such as mercuric sulfate. On the other hand, although several methods for the preparation of enamine pyrrolidines having an endo double bond, namely 2-pyrrolines, are available,[3] only a few methods have been reported for the synthesis of enamine pyrrolidines having an exo double bond.[4] Most of these methods, however, were limited to a synthesis of enamine pyrrolidines carrying an electron-withdrawing group at the terminal carbon of the exo double bond, probably because those studies were mainly carried out in order to prepare part of the corrin system.[4a]

In this paper we report the results of a detailed and further study on a new, facile cyclization of alkynylamines and alkynamides to give enamine pyrrolidines and piperidines having a benzylidene group at the C-2 position.

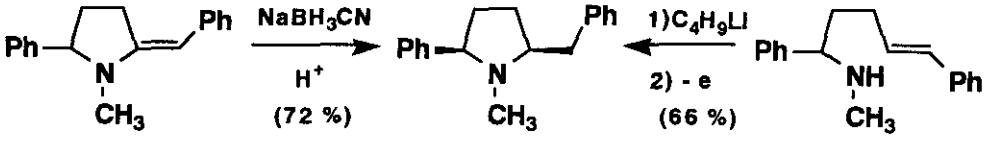
Treatment of *N*-methyl-1,5-diphenyl-4-pentynylamine (**1a**) in tetrahydrofuran with 1.2 equiv. of butyllithium at -78 °C under a nitrogen atmosphere gave (*E*)-2-benzylidene-1-methyl-5-phenylpyrrolidine (**2a**) in a 85% yield (Scheme 1). The pyrrolidine (**2a**) was not stable and gradually decomposed upon heating or exposure to air. The structure of **2a** was confirmed by both spectroscopic analysis and its transformation into a known pyrrolidine. The ir spectrum of **2a** exhibited a strong absorption ascribable to the enamine double bond at 1632 cm^{-1}. The ^1H nmr spectrum exhibited a singlet at δ 5.17 attributable to a vinylic proton, which is exchangable



1a : R^1=CH_3, R^2=R^3=Ph — **2a (85 %)**
1b : R^1=R^2=CH_3, R^3=Ph — **2b (95 %)**
1c : R^1= $CH_2CH=CH_2$, R^2=R^3=Ph — **2c (82 %)**
1d : R^1= $CH_2CH=CH_2$, R^2=CH_3, R^3=Ph — **2d (80 %)**
1e : R^1=CH_3, R^2=Ph, R^3=H
1f : R^1=CH_3, R^2=Ph, R^3=$Si(CH_3)_3$

Scheme 1

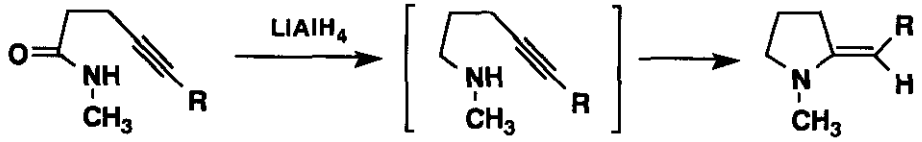
with deuterium by the addition of D_2O.[4f] Moreover, an *NOE* enhancement (8.5%) was observed between the signal due to the vinylic proton and that due to the *N*-methyl protons, indicating the (*E*)-configuration of the double bond of **2a**. A reduction of **2a** with sodium cyanoborohydride under acidic conditions gave *cis*-2-benzyl-1-methyl-5-phenylpyrrolidine (**3**), which was fully identical to the pyrrolidine (**3**) prepared by anodic cyclization of *N*-methyl-1,5-diphenylpent-4-enylamine (**4**) (Scheme 2).[1c] Similar treatment of 4-alkynylamines (**1b**), (**1c**), and (**1d**) with butyllithium gave the corresponding enaminopyrrolidines (**2b**), (**2c**), and (**2d**) in high yields (Scheme 1).



2a **3** **4**

Scheme 2

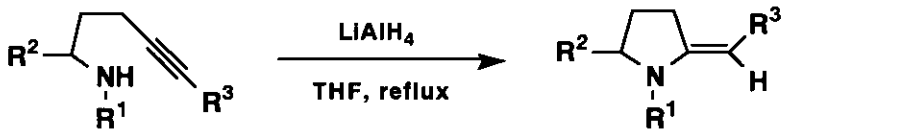
We subsequently found that 2-benzylidene-1-methylpyrrolidine (**7a**) was obtained in 82% yield by treatment of 4-alkynamide (**5a**) with lithium aluminum hydride (Scheme 3). The role of lithium aluminum hydride



5a : R=Ph — **6a, 6b** — **7a (82 %)**
5b : R=H

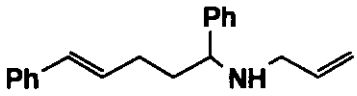
Scheme 3

$LiAlH_4$ in this reaction is apparently to reduce amide (**5a**) into alkynylamine (**6a**) and to generate a nitrogen anion which attacks the acetylenic carbon intramolecularly to give **7a**. Anionic cyclization of 4-alkynylamines with $LiAlH_4$ was found to be entirely general. Treatment of alkynylamines (**1a**), (**1b**), and (**1d**) with $LiAlH_4$ gave 2-benzylidenepyrrolidines (**2a**), (**2b**), and (**2d**) in high yields (Scheme 4). However, treatment of amine (**1c**) with $LiAlH_4$ resulted in the formation of *N*-allyl-1,5-diphenylpent-4-enylamine (**8**) (82%), which arose from a preferential reduction of the carbon-carbon triple bond rather than a proton abstraction of **1c**. The failure of the cyclization in pentynylamine (**1c**) may be attributable to a steric factor.



1a, 1b, 1d **2a (86%); 2b (98%); 2d (82%)**

Scheme 4



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The presence of 5-phenyl group in 4-alkynylamines is necessary for a facile anionic cyclization since treatment of amines (**1e**) and (**1f**) with butyllithium or $LiAlH_4$ gave no enaminopyrrolidines (**2e**) and (**2f**), and unreacted amines (**1e**) and (**1f**) were recovered unchanged. Similarly, treatment of *N*-methyl-4-pentynamide (**5b**) with $LiAlH_4$ gave simply *N*-methyl-4-pentynylamine (**6b**) in quantitative yield and no cyclization product (Scheme 3).

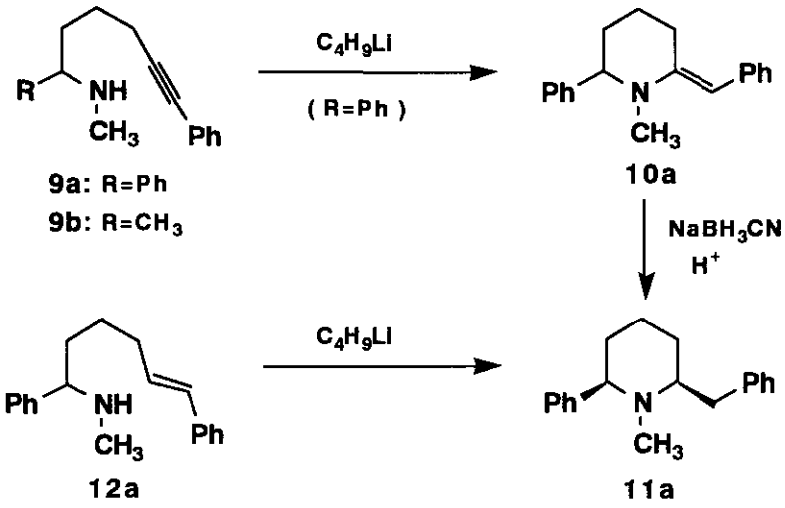
Several different bases were then examined whether they are effective in the cyclization of 4-alkynylamines. The results in the cyclization of **1a** with various bases are summarized in Table 1. Although potassium *t*-butoxide was effective in the cyclization, sodium borohydride, sodium amide, and sodium ethoxide were all ineffective and the starting amine was recovered. The anionic cyclization of 4-alkynylamine to enamine pyrrolidine was subsequently found to take place with a catalytic amount of butyllithium; treatment of **1a** with 0.5 equiv. of butyllithium gave **2a** in a 85% yield (Table 1, Entry 2).

The present anionic cyclization was found to take place in the formation of six-membered nitrogen heterocycles. Thus, treatment of 5-alkynylamine (**9a**) with butyllithium afforded the corresponding enamine piperidine (**10a**) having a benzylidene substituent at the C-2 position. Since enamine piperidine (**10a**) was rather unstable, it was immediately converted into 2-benzyl-1-methyl-6-phenylpiperidine (**11a**)

Table 1. Anionic Cyclization of 4-Alkynylamine (**1a**) with Various Bases[a)]

Entry	Base	Yield of **2a** (%)[b)]
1	BuLi	85
2	BuLi[c)]	85
3	$LiAlH_4$	86
4	*t*-BuOK	62
5	$NaBH_4$	0[d)]
6	$NaNH_2$	0[d)]
7	NaOEt	0[d)]

a) Base (1.2 equiv.) was reacted with **1a** in THF at -78 °C (BuLi) or at a refluxing temperature (other bases).
b) Isolated yields by tlc.
c) Butyllithium (0.5 equiv.) was used as a base.
d) Starting amine (**1a**) was recovered unchanged.

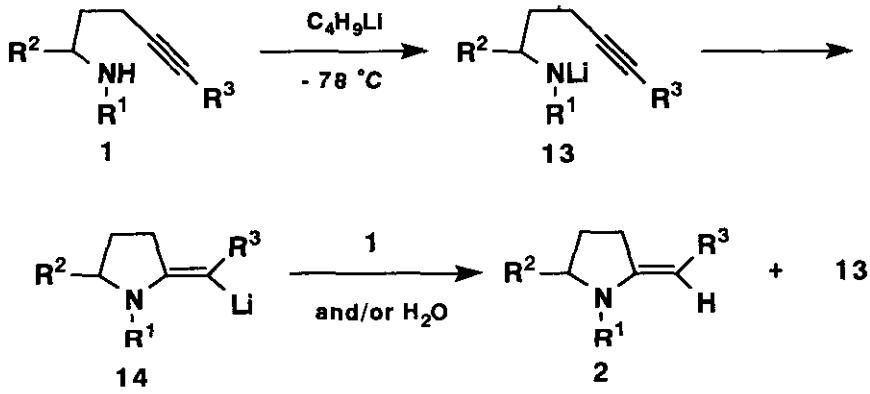


Scheme 5

(33% from **9a**) by reduction with sodium cyanoborohydride under acidic conditions in methanol (Scheme 5). No enamine piperidine, on the other hand, was obtained by treatment of amine (**9b**) with butyllithium. The structures of **10a** and **11a** were determined by both spectroscopic analysis and comparison with related compounds. The ir spectrum of **10a** exhibited a strong absorption at 1672 cm^{-1}, which indicated the presence of enamine double bond. The ^1H nmr spectrum exhibited a singlet at δ 5.42 attributable to a vinylic proton.

On the other hand, the ^{1}H nmr spectrum of **11a** exhibited two absorptions at δ 2.27 and δ 2.98 attributable to two methine protons at the C-2 and C-6 positions. An *NOE* enhancement (6.0%) was observed between two signals at δ 2.27 and δ 2.98, indicating that **11a** was *cis*-2-benzyl-1-methyl-6-phenylpiperidine. Piperidine (**11a**) was identical to the product which was obtained in a 18% yield by anionic cyclization of 5-hexenylamine (**12a**) (Scheme 5).[5] We have already reported that treatment of various 4-alkenylamines with butyllithium gave stereoselectively *cis*-2,5-disubstituted pyrrolidines in good yields.[6]

The present cyclization of 4-alkynylamines (**1**) probably proceeds *via* the reaction pathways outlined in Scheme 6. Thus, a deprotonation of 4-alkynylamine (**1**) with butyllithium gives lithium amide (**13**), which undergoes a facile anionic cyclization to produce a lithiobenzylidenepyrrolidine (**14**). The intermediate vinyllithium (**14**) abstracts a proton from the starting amine (**1**) or water to afford the product (**2**) with a regeneration of lithium amide (**13**). Both the cyclization to **14** and the following protonation to give **2** should be very fast, since all attempts to trap the intermediate amide (**13**) and vinyllithium (**14**) with various electrophiles failed.



Scheme 6

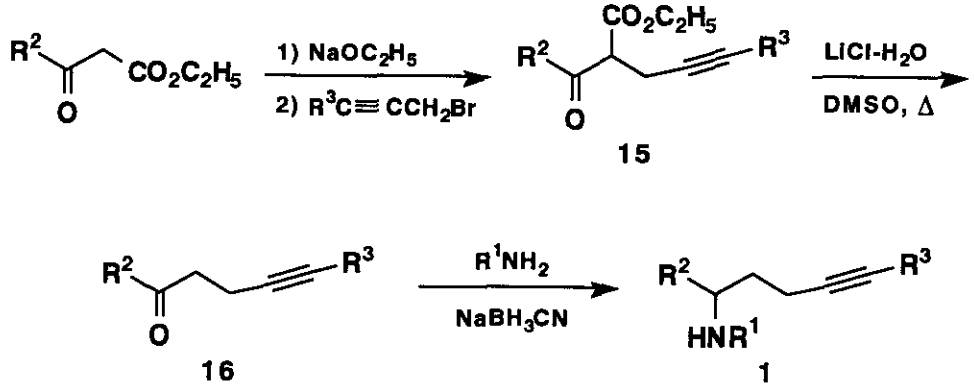
EXPERIMENTAL SECTION

Mps were measured with a Yanagimoto Melting Point apparatus. The ^{1}H nmr spectra were measured in $CDCl_3$ with a JEOL JNM-EX 400 spectrometer (400 MHz) or a JEOL JNM-EX 270 spectrometer (270 MHz) using tetramethylsilane as an internal standard. The ir spectra were measured with a JASCO IR-810 spectrophotometer. The high and low resolution mass spectra were measured with a JEOL JMS-D300 mass spectrometer (70 eV). Merck silica gel 60 PF_{254} and Merck silica gel 60 were used for tlc and column chromatography, respectively.

Preparation of 4-Alkynylamines

4-Alkynylamines (**1a~1f**) were prepared according to the sequences outlined in Scheme[7]. Thus, an alkylation of ethyl benzoylacetate or ethyl acetoacetate with 1-bromo-2-alkynes gave the keto esters (**15**) (80-97%).

Decarbethoxylation[7] of **15** (74-90%) followed by reductive amination[8] of the resulting ketones (**16**) with methylamine or allylamine gave the desired 4-alkynylamines (**1a~1f**) (70-95%). Typically, to a 20 ml of ethanol solution containing sodium ethoxide (2.2 g, 31.6 mmol) was added dropwise ethyl benzoylacetate (6.1 g, 31.6 mmol) at room temperature, and the solution was heated under reflux for 2 h. 3-Bromo-1-phenyl-1-propyne (6.7 g, 34.4 mmol) was added to the reaction mixture and the solution was stirred overnight. Usual work-up gave almost pure ethyl 2-benzoyl-5-phenyl-4-pentynoate (**15a**) (9.4 g, 97%): Ir (neat) 2242, 1719, and 1691 cm^{-1}; ^1H nmr δ 1.19 (3H, t, *J*=7.0Hz), 3.11 (2H, dd, *J*=7.3 and 13.2Hz), 4.18 (2H, q, *J*=7.0 Hz), 4.65 (1H, t, *J*=7.5 Hz), 7.1-7.5 (8H, m), and 8.0-8.1 (2H, m) ; ms *m/z* (rel intensity) 306 (M^+, 10), 277 (2), 233 (48). HRms Calcd for $C_{20}H_{18}O_3$: *m/z* 306.1256. Found : *m/z* 306.1266. To a 300 ml of dimethyl sulfoxide solution of **15a** (8.5 g, 27.7 mmol) was added 30 ml of aqueous lithium chloride (1.4 g, 33.0 mmol). The mixture was heated under reflux for 10 h. Usual work-up followed by recrystallization from hexane gave 1,5-diphenyl-4-pentyn-1-one (**16a**) (4.8 g, 74%) : Ir (neat) 1684 cm^{-1}; ^1H nmr δ 2.84 (1H, d, *J* = 9.2 Hz), 2.87 (1H, d, *J* = 7.7 Hz), 3.30 (1H, d, *J* = 7.7 Hz), 3.34 (1H, d, *J* =9.2 Hz), 7.2-7.6 (8H, m), and 7.9-8.0 (2H, m) ; ms *m/z* (rel intensity) 234 (M^+, 50), 105 (100). HRms Calcd for $C_{17}H_{14}O$; *m/z* 234.1037. Found: *m/z* 234.1041. Anal. Calcd for $C_{17}H_{14}O$: C, 87.15 ; H, 6.02. Found: C, 87.08 ; H, 6.02. To a saturated solution of methylamine hydrochloride (5.4 g, 80 mmol) in methanol (30 ml) was added ketone (**16a**) (3.6 g, 15.6 mmol) under a nitrogen atmosphere. Sodium cyanoborohydride (980 mg, 15.6 mmol) was added to the mixture and the solution was stirred overnight at room temperature. After evaporation of the solvent, the residue was dissolved in ether (50 ml). The ethereal solution was treated with 4*N* sodium hydroxide (10 ml). The organic phase was separated and the aqueous phase was extracted with ether. The combined extracts were condensed to 10 ml and the condensed ethereal solution was made acidic (pH < 2) with diluted hydrochloric acid at 0 °C. After removing the impurities with ether (2 ml x 5), the aqueous phase was made basic (pH >9) with potasium hydroxide. The solution was saturated with sodium chloride and extracted with ether (10 ml x



a : R^1=CH_3, R^2=R^3=Ph
b : R^1=R^2=CH_3, R^3=Ph
c : R^1= $CH_2CH{=}CH_2$, R^2=R^3=Ph
d : R^1= $CH_2CH{=}CH_2$, R^2=CH_3, R^3=Ph
e : R^1=CH_3, R^2=Ph, R^3=H
f : R^1=CH_3, R^2=Ph, R^3=$Si(CH_3)_3$

Scheme 7

3). The combined extracts were dried over anhydrous sodium sulfate. Filtration and evaporation of the solvent gave almost pure amine, which was subjected to a distillation (138-141 °C/0.08 mmHg) to give *N*-methyl-1,5-diphenyl-4-pentynylamine (**1a**) (3.6 g, 93%). Spectral data of 4-alkynylamines (**1**) thus prepared are described in the followings.

***N*-Methyl-1,5-diphenyl-4-pentynylamine (1a).**

Ir (neat) 3332, and 2232 cm^{-1} ; ^1H nmr δ 1.52 (1H, br s), 1.8-2.0 (1H, m), 2.0-2.1 (1H, m), 2.2-2.4 (2H, m), 2.30 (3H, s), 3.68 (1H, dd, *J* = 5.9 and 7.7 Hz), and 7.2-7.4 (10H, m) ; ms *m/z* (rel intensity) 249 (M^+, 15), 120 (100). HRms calcd for $C_{18}H_{19}N$: *m/z* 249.1497. Found: *m/z* 249.1507.

***N*-Methyl-1-methyl-5-phenyl-4-pentynylamine (1b).**

Bp 89-93 °C/1 mmHg. Ir (neat) 3322 and 2234 cm^{-1}; ^1H nmr δ 1.13 (3H, d,*J*=6.2 Hz), 1.5-1.7 (1H, m), 1.7-1.9(1H, m), 2.40 (1H, br s), 2.45 (3H, s), 2.4-2.5 (2H, m), 2.79 (1H, m), and 7.1-7.4 (5H, m) ; ms*m/z* (rel intensity) 187 (M^+, 11), 98 (100). HRms Calcd for $C_{13}H_{17}N$: *m/z* 187.1379. Found: *m/z* 187.1370.

***N*-Allyl-1,5-diphenyl-4-pentynylamine (1c).**

Ir (neat) 3328, 2234, and 1644 cm^{-1}; ^1H nmr δ 1.65 (1H, br s), 1.8-2.1 (2H, m), 2.2-2.5 (2H, m), 3.10 (2H, m), 3.85 (1H, dd, *J* = 6.2 and 7.7 Hz), 5.0-5.2 (2H, m), 5.8-6.0 (1H, m), and 7.2-7.4 (5H, m); ms*m/z* (rel intensity) 275 (M^+, 17), 146 (100). HRms Calcd for $C_{20}H_{21}N$: *m/z* 275.1636. Found: *m/z* 275.1655.

***N*-Allyl-1-methyl-5-phenyl-4-pentynylamine (1d).**

Bp 86-90 °C/0.06 mmHg. Ir (neat) 3330, 2234, and 1644 cm^{-1} ; ^1H nmr δ 1.11 (3H, d, *J* = 6.2 Hz), 1.5-1.7 (1H, m), 1.7-1.9 (1H, m), 2.3-2.6 (2H, m), 2.8-2.9 (2H, m), 3.2-3.4 (2H, m), 5.0-5.3 (2H, m), 5.8-6.0 (1H, m), and 7.2-7.4 (5H, m) ; ms *m/z* (rel intensity) 213 (M^+, 21), 84 (100). HRms Calcd for $C_{15}H_{19}N$:*m/z* 213.1473. Found: *m/z* 213.1495.

***N*-Methyl-1-phenyl-4-pentynylamine (1e).**

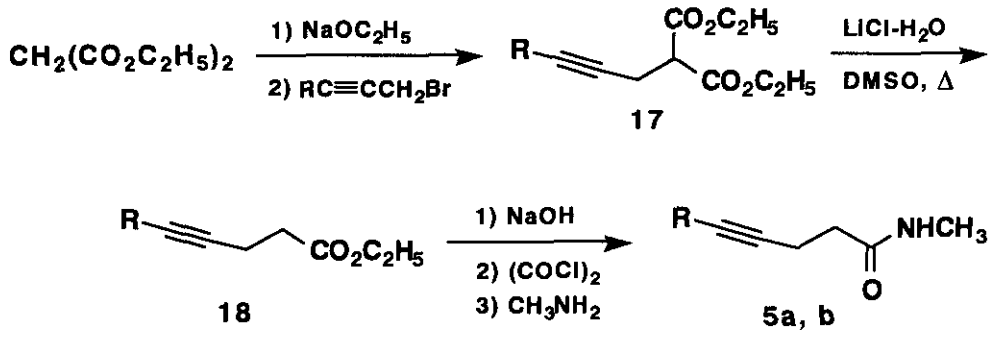
Ir (neat) 3302 and 2116 cm^{-1}; ^1H nmr δ 1.8-2.2 (4H, m), 1.96 (1H, t, *J*=2.6 Hz), 2.30 (3H, s), 2.43 (1H, br s), 3.65 (1H, dd, *J*=5.5 and 7.5 Hz), and 7.2-7.4 (5H, m); ms *m/z* (rel intensity) 173 (M^+, 4), 120 (100). HRms Calcd for $C_{12}H_{15}N$: *m/z* 173.1224. Found: m/z 173.1214.

***N*-Methyl-1-phenyl-5-trimethylsilyl-4-pentynylamine (1f).**

Treatment of **1e** with butyllithium followed by trimethylsilylation with chlorotrimethylsilane gave *N*-methyl-1-phenyl-5-trimethylsilyl-4-pentynylamine (**1f**) (bp 86-90 °C/0.06 mmHg; 99%): Ir (neat) 3330 and 2174 cm^{-1}; ^1H nmr δ 0.15 (9H, s), 1.6 (1H, br s), 1.7-2.2 (4H, m), 2.28 (3H, s), 3.59 (1H, dd, *J*=6.2 and 7.7 Hz), and 7.2-7.4 (5H, m); ms *m/z* (rel intensity) 245 (M^+, 0.8), 120 (100). HRms Calcd for $C_{15}H_{23}NSi$:*m/z* 245.1590. Found: *m/z* 245.1595.

Preparation of 4-Alkynamides

4-Alkynamides (**5a**) and (**5b**) were prepared according to the sequences outlined in Scheme 8. Alkylation of diethyl malonate with 1-bromo-2-alkynes (75 %) followed by decarbethoxylation[7] gave ethyl 4-alkynoates (**18**) (70 %). Hydrolysis of **18** followed by amidation[9] with methylamine gave *N*-methyl-4-alkynamide (**5**) (64 %). Typically, alkylation of diethyl malonate (12.0 g, 75.2 mmol) with 3-bromo-1-phenyl-1-



Scheme 8

propyne (9.8 g, 50.1 mmol) and sodium ethoxide (3.4 g, 50.1 mmol) gave ethyl 2-ethoxycarbonyl-5-phenyl-4-pentynoate (10.3 g, 37.6 mmol, 75%): bp 115-127 °C/0.1 mmHg. Decarbethoxylation[7] of ethyl 2-ethoxycarbonyl-5-phenyl-4-pentynoate (2.8 g, 10 mmol) gave ethyl 5-phenyl-4-pentynoate (**18**) (1.4 g 6.9 mmol, 69 %): bp 97-112 °C/0.08 mmHg; ir (neat) 2240 and 1735 cm^{-1}; ^1H nmr δ 1.28 (3H, t, J = 7.0 Hz), 2.6-2.7 (2H, m), 2.7-2.8 (2H, m), 4.18 (2H, q, J = 7.0 Hz), and 7.2-7.4 (5H, m); ms *m/z* (rel intensity) 202 (M^+, 32), 175 (32), 128 (90). HRms Calcd for $C_{13}H_{14}O_2$: *m/z* 202.0940. Found: *m/z* 202.0967. The ester (**18**) (1.4 g 6.9 mmol) was hydrolyzed with 10% sodium hydroxide in ethanol. The sodium salt of 5-phenyl-4-pentynoic acid was converted to acid chloride by treatment with oxalyl chloride[9] (1.32 g, 10.4 mmol). A gas of methylamine was bubbled into a benzene solution of the acid chloride until the solution became basic. Usual work-up followed by recrystallization from hexane gave *N*-methyl-5-phenyl-4-pentynamide (**5a**) (829.0 mg, 64 %).

***N*-Methyl-5-phenyl-4-pentynamide (5a)**

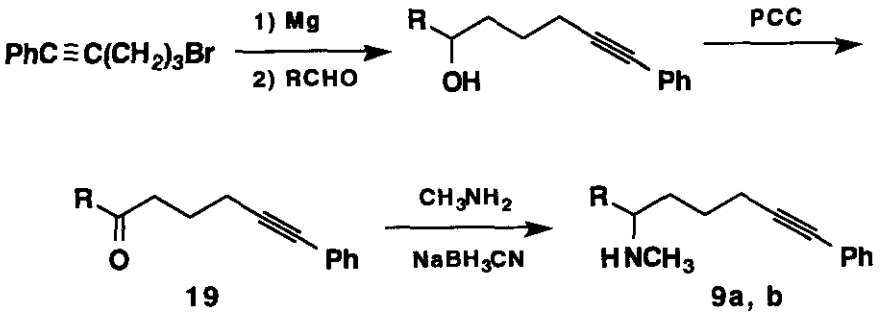
Mp 88-89 °C. Ir (Nujol) 3308, 2242, and 1645 cm^{-1}; ^1H nmr δ 1.69 (1H, br s), 2.3-2.6 (2H, m), 2.6-2.9 (2H, m), 2.84 (3H, d, J = 4.6 Hz), and 7.1-7.3 (5H, m); ms *m/z* (rel intensity) 187 (M^+, 100), 128 (79). HRms Calcd for $C_{12}H_{13}NO$: *m/z* 187.1003. Found: *m/z* 187.1000. Anal. Calcd for $C_{12}H_{13}NO$: C, 76.89: H, 7.00; N, 7.84. Found: C, 76.98: H, 6.96; N, 7.69.

***N*-Methyl-4-pentynamide (5b)**

Mp 120 °C (decomp). Ir (Nujol) 3300, 3256 cm^{-1}; ^1H nmr δ 1.95 (1H, br s), 2.01(1H, t, J=2.6 Hz), 2.3-2.5 (2H, m), 2.5-2.7 (2H, m), and 2.83 (3H, d, J =5.1 Hz); ms *m/z* (rel intensity) 110 (M^+-1, 59), 58 (100). HRms Calcd for C_6H_9NO:*m/z* 111.0631. Found: *m/z* 111.0658.

Preparation of 5-Alkynylamine (9).

5-Alkynylamines (**9a**) and (**9b**) were prepared according to the sequences outlined in Scheme 9. Grignard reaction of 5-bromo-1-phenyl-1-pentyne[10] and benzaldehyde or acetaldehyde followed by oxidation gave ketone (**19**) (38-20 %). Reductive amination of **19** with methylamine gave 5-alkynylamines (**9a**) and (**9b**) (48-70 %). Typically, Grignard reaction of benzaldehyde (1.7 g, 16.5 mmol) and 5-bromo-1-phenyl-1-pentyne[10] (3.7 g 16.5 mmol) in the presence of magnesium (365 mg, 15 mmol) gave 1,6-diphenyl-5-hexyn-1-ol. Oxidation of the crude alcohol with pyridinium chlorochromate gave a crude ketone, which was



Scheme 9

subjected to column chromatography (hexane/ethyl acetate = 20/1) to give 1,6-diphenyl-5-hexyn-1-one (**19a**) (1.6 g, 38% from benzaldehyde): Ir (neat) 2226, 1687, 1599, and 1491 cm^{-1}, ^1H nmr δ 2.0-2.1 (2H, m), 2.55 (2H, t, *J* = 6.9 Hz), 3.18 (2H, t, *J*=7.3 Hz), 7.2-7.6 (8H, m), and 7.9-8.1 (2H, m); ms*m/z* (rel intensity) 248 (M^+, 28), 128 (100), 115 (22), and 105 (81). HRms Calcd for $C_{18}H_{16}O$: *m/z* 248.1201. Found: *m/z* 248.1207. To a saturated solution of methylamine hydrochloride (5.4 g, 80 mmol) in methanol (30 ml) was added ketone (**19a**) (650 mg, 2.6 mmol) under a nitrogen atmosphere. Sodium cyanoborohydride (271 mg, 4.3 mmol) was added to the mixture and the solution was stirred overnight at room temperature. The same work-up as that of **1** gave *N*-methyl-1,6-diphenyl-5-hexynylamine (**9a**) (315.8 mg, 48%).

***N*-Methyl-1,6-diphenyl-5-hexynylamine (9a).**

Ir (neat) 3323, 2232, 1600, and 1491 cm^{-1}, ^1H nmr δ 1.4-1.6 (2H, m), 1.7-1.9 (2H, m), 2.28(3H, s), 2.37 (2H, t, *J*= 6.9 Hz), 3.50 (1H, dd, *J* =5.8 and 8.1 Hz), and 7.1-7.4 (10H, m); ms *m/z* (rel intensity) 263 (M^+, 3), 128 (17), 120 (100), 115 (3). HRms Calcd for $C_{19}H_{21}N$: *m/z* 263.1674. Found: *m/z* 263.1662.

***N*-Methyl-1-methyl-6-phenyl-5-hexynylamine (9b).**

Ir (neat) 3032, 2240, 1600, 1491, 757 cm^{-1}; ^1H nmr δ 1.07 (3H, d, *J*= 6.3 Hz), 1.47 (2H, m), 1.63 (3H, m), 2.41 (3H, s), 2.42 (2H, t, *J*= 7.9 Hz), 2.59 (1H, m), 7.2-7.4 (5H, m); ms *m/z* (rel intensity) 201 (M^+, 2), 186 (6), 129 (11), 115 (11), 58 (100). HRms Calcd for $C_{14}H_{19}N$: *m/z* 201.1518. Found: *m/z* 201.1493.

Anionic Cyclization of 4- (1) and 5-Alkynylamines (9) with Butyllithium.

A typical procedure for anionic cyclization was as follows. To a 6 ml of tetrahydrofuran solution containing *N*-methyl-1,5-diphenyl-4-pentynylamine (**1a**) (99.6 mg, 0.4 mmol) was added dropwise butyllithium (30.7 mg, 0.48 mmol in hexane) at -78 °C under nitrogen atmosphere, and the solution was stirred at -78 °C for 30 min and then at -10 °C for 30 min. A reaction mixture was quenched with 1 ml of water and stirred at room temperature for 30 min. A tetrahydrofuran solution was diluted with 80 ml of ether. The solution was washed with water (5 ml x 3) and brine (5 ml), and then dried over anhydrous sodium sulfate. The usual work-up gave a crude pyrrolidine, which was subjected to a preparative tlc (CH_2Cl_2/MeOH/aq. NH_4OH = 200/10/1) to give 2-benzylidene-1-methyl-5-phenylpyrrolidine (**2a**) (85.7 mg, 85%). Spectral data of the cyclization products are described in the followings.

2-Benzylidene-1-methyl-5-phenylpyrrolidine (2a). (85%)
Ir (neat) 3330 and 1632 cm^{-1}; ^1H nmr δ 1.8-2.0 (1H, m), 2.3-2.5 (1H, m) 2.8-3.0 (1H, m), 2.9-3.1 (1H, m), 2.63 (3H, s), 4.30 (1H, t, *J* = 7.0 Hz), 5.17 (1H, br s), 6.9-7.1 (1H, m), and 7.2-7.4 (9H, m); ms *m/z* (rel intensity) 249 (M^+, 100), 172(30), and 120 (70). HRms Calcd for $C_{18}H_{19}N$: *m/z* 249.1533. Found:*m/z* 249.1548.

2-Benzylidene-1,5-dimethylpyrrolidine (2b). (95%)
Ir (neat) 3318 and 1629 cm^{-1}; ^1H nmr δ 1.15 (3H, d, *J* =6.2 Hz), 2.72 (3H, s), 3.33 (1H, m, *J* = 6.2 Hz), 5.04 (1H, br s), 6.9-7.0 (1H, m), and 7.2-7.4 (4H, m); ms *m/z* (rel intensity) 187 (M^+, 35), 172 (39), and 98 (100). HRms Calcd for $C_{13}H_{17}N$: *m/z* 187.1348. Found: *m/z* 187.1335.

1-Allyl-2-benzylidene-5-phenylpyrrolidine (2c). (82%)
Ir (neat) 3318 and 1631 cm^{-1}; ^1H nmr δ 1.86 (1H, m, *J* = 6.2 Hz), 2.36 (1H, m), 2.88(1H, m), 3.03 (1H, m) 3.40 (1H, dd, *J* = 6.6 and 16.1 Hz), 3.86 (1H, m), 4.45 (1H, t, *J* = 6.6 Hz), 5.0-5.2 (2H, m), 5.26 (1H, br s), 5.7-5.9 (1H, m), 6.9-7.0 (1H, m), and 7.2-7.4 (9H, m); ms *m/z* (rel intensity) 275 (M^+, 92), 146 (73), and 117 (100). HRms Calcd for $C_{20}H_{21}N$: *m/z* 275.1684. Found: *m/z* 275.1694.

1-Allyl-2-benzylidene-5-methylpyrrolidine (2d). (80%)
Ir (neat) 3310 and 1628 cm^{-1}, ^1H nmr δ 1.14 (3H, d, *J* =6.2 Hz,), 2.0-2.2 (1H, m), 2.3-2.5 (1H, m) 2.6-2.8 (1H, m), 2.8-3.0 (1H, m), 3.49 (1H, m), 3.67 (1H, dd, *J* =6.2 and 16.7 Hz), 3.86 (1H, m), 5.09 (1H, br s), 5.1-5.3 (2H, m), 5.8-6.0 (1H, m), 6.8-7.0 (1H, m), and 7.2-7.4 (4H, m); ms *m/z* (rel intensity) 213 (M^+, 15), 124 (100). HRms Calcd for $C_{15}H_{19}N$: *m/z* 213.3237. Found: *m/z* 213.3213.

***cis*-1-Methyl-2,6-diphenylpiperidene (11a).**
Ir (neat) 1672, 1640, 1598, 1494, and 759 cm^{-1}; ^1H nmr δ 2.61 (3H, s), 5.42 (1H, br s). Since this enamine pyrrolidine (**10a**) was unstable, **10a** was immediately reduced with sodium borohydride under acidic conditions to give*cis*-1-methyl-2,6-diphenylpiperidene (**11a**) (33% yield from *N*-methyl-1,6-diphenyl-5-hexynylamine (**9a**): Ir (neat) 1605, 1494, and 746 cm^{-1}; ^1H nmr δ 1.1-1.3 (2H, m), 1.4-1.6 (2H, m), 1.6-1.7 (2H, m), 2.17 (3H, s), 2.27 (1H, m; *NOE* enhancement (6.0 %) was observed when a double-doublet at δ 2.98 was irradiated), 2.53 (1H, dd, *J* = 9.1 and 13.2 Hz), 2.98 (1H, dd, *J* =2.6 and 11.2 Hz; *NOE* enhancement (6.4 %) was observed when a multiplet at δ 2.27 was irradiated), 3.25 (1H, dd, *J* =3.8 and 13.2 Hz), and 7.1-7.4 (10H, m); ms *m/z* (rel intensity) 265 (M^+, 0.8), 174 (100), 118 (10). HRms Calcd for $C_{19}H_{23}N$:*m/z* 265.1831. Found: *m/z* 265.1805.

Reductive Cyclization of 4-Alkynamide (5) and 4-Alkynylamines (1) with Lithium Aluminum Hydride.

A 5 ml of tetrahydrofuran solution of *N*-methyl-5-phenyl-4-pentynamide (**5a**) (300 mg, 1.6 mmol) was carefully added to a stirred suspension of lithium aluminum hydride (121.6 mg, 3.2 mmol) in tetrahydrofuran (10 ml) under reflux. The mixture was heated under reflux for 30 min and it was stirred overnight at room temperature. The usual work-up gave an enamine pyrrolidine, which was subjected to a distillation (81-85 °C/0.09 mmHg) to give 2-benzylidene-1-methylpyrrolidine (**7a**) (225.1 mg, 82 %).

2-Benzylidene-1-methylpyrrolidine (7a).
Ir (neat) 3284 and 1631 cm^{-1}; ^1H nmr δ 1.93 (2H, m), 2.84 (2H, t, *J* =7.7 Hz), 3.19 (2H, t, *J* =7.0 Hz), 2.78

(3H, s), 5.05 (1H, br s), 6.9-7.0 (1H, m), and 7.2-7.4 (4H, m); ms *m/z* (rel intensity) 173 (M^+, 39), 158 (7), 84 (100). HRms Calcd for $C_{12}H_{15}N$: *m/z* 173.1200. Found: *m/z* 173.1196.

Similar treatment of 4-alkynylamines (**1**) with lithium aluminum hydride as that described in the above gave the corresponding enamine pyrrolidines (**2a**) (86 %), (**2b**) (98 %), and (**2d**) (82 %).

Anionic Cyclization of *N*-Methyl-1,5-diphenyl-4-pentynylamine (1a) with Potassium *tert*-Butoxide.

A 5 ml of tetrahydrofuran solution of **1a** (99.6 mg, 0.4 mmol) was carefully added to a refluxed and stirred solution of potassium *tert*-butoxide (53.9 mg, 0.48 mmol) in tetrahydrofuran (10 ml). The mixture was heated under reflux for 2 h and it was stirred overnight at room temperature. The usual work-up gave a crude enamine pyrrolidine, which was subjected to a tlc separation to give 2-benzylidene-1-methyl-5-phenyl-pyrrolidine (**2a**) (62.3 mg, 62 %). Spectral data of the pyrrolidine was completely identical to those of the enamine pyrrolidine (**2a**) obtained in the cyclization of **1a** with butyllithium as a base.

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