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Tandem Cyclization of *N*-Allylaminyl Radicals: Stereoselective Synthesis of 1,2,5-Trisubstituted Pyrrolizidines

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Abstract: Radical reaction of *N*-allylalk-4-enylaminyl radicals, generated from the corresponding *N*-chloroamines by treatment with Bu_3SnH-AIBN in refluxing toluene, was carried out. Tandem cyclization of the resulting neutral aminyl radicals readily took place stereoselectively to give 1,2,5-trisubstituted pyrrolizidines and a pyrroloindole derivative as a sole product in good yields. The cyclization products contained only two stereoisomers in each reaction, indicating that both of the consecutive cyclizations proceeded in a stereoselective manner.

Keywords: Radicals and radical reactions; Pyrrolizines/pyrrolizidines; Chain reactions; Cyclisation

Cyclization of aminyl radicals is one of the most useful methods for the construction of a pyrrolidine ring, which is an important skeleton of some alkaloids and nitrogen heterocycles. Although many methods for generating aminyl radicals and their synthetic applications have been reported,[1] the chemistry of nitrogen radicals is not satisfactorily developed, compared to that of carbon radicals.[2,3] From our studies on the use of aminyl radical cyclization for synthesizing of nitrogen heterocycles, we have already reported a new synthesis of *trans*-2,5-disubstituted pyrrolidines by stereoselective cyclization of neutral aminyl radicals generated from *N*-chloroalk-4-enylamines and Bu_3SnH-AIBN in refluxing benzene,[4] and its application for the synthesis of *trans*-*N*-methyl-2-butyl-5-heptylpyrrolidine, an ant venom alkaloid.[5] 2,5-Disubstituted pyrrolidines are very often encountered in living organisms and have potential usefulness as chemotherapeutic agents.[6] We also reported that when *N*-allyl-*N*-chloro-1-methyl-5-phenylpent-4-enylamine was treated with Bu_3SnH-AIBN in refluxing benzene, a tandem radical cyclization of the resulting *N*-allylaminyl radical readily took place stereoselectively to give 1,2,5-trisubstituted pyrrolizidines as a mixture of only two stereoisomers in 53% yield.[4] In the course of our continuing study on stereoselective cyclization of aminyl radicals, we have succeeded in separation and stereochemical assignment of the two stereoisomers obtained in the tandem cyclization. We have also clarified that

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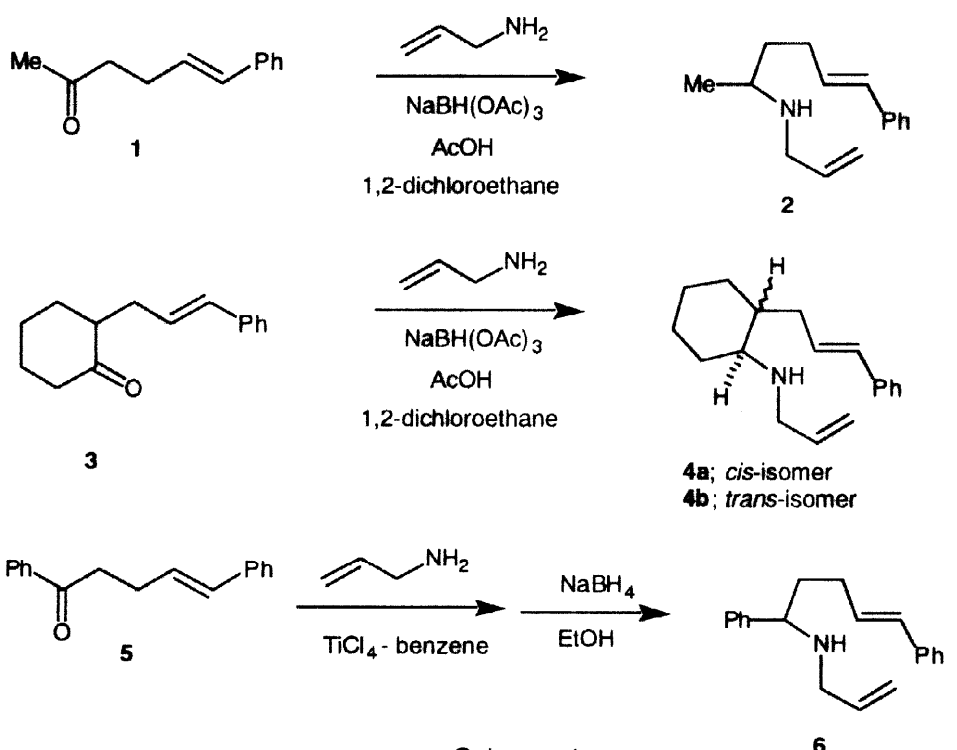
three stereocentered carbons of the tandem cyclization products, 1,2,5-trisubstituted pyrrolizidines, were fixed in one step by two consecutive stereoselective cyclizations. In this paper, we report the results of a new stereoselective tandem cyclization of *N*-allylaminyl radicals to give 1,2,5-trisubstituted pyrrolizidines.

Tandem cyclization of carbon radicals has been widely investigated, and the results of these studies have been summarized in several reviews.[7] There have also been several studies on the tandem cyclization of nitrogen radicals,[8,9] since bicyclic nitrogen heterocycles could be produced in one step. However, most of these studies were on the tandem cyclization of cationic aminium radicals (protonated or metal complexed aminyl radicals),[8] and there have been only a few reports on that of neutral aminyl radicals.[9] Furthermore, there have been no reports on the tandem cyclization of neutral aminyl radicals whose products, pyrrolizidines, were fully assigned in those stereochemistries.

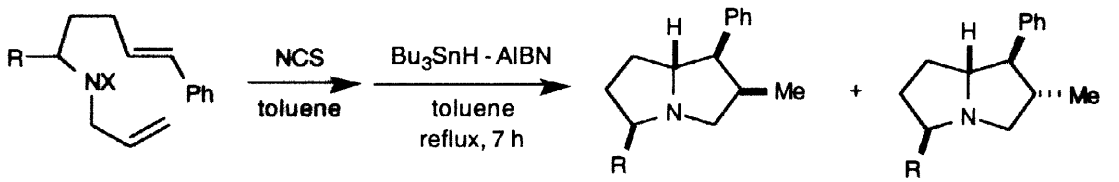
N-Allylalk-4-enylamines **2**, **4a** and **6** as substrates for aminyl radical cyclization were prepared from the corresponding ketones **1**,[10] **3** and **5**[10] by reductive amination[11] with *N*-allylamine, or by a formation of *N*-allylimine using titanium tetrachloride[12] followed by hydride reduction (Scheme 1). Stereochemistries of cyclohexylamines **4a** and **4b** were determined by an NOE experiment. In the ^{1}H NMR spectrum of **4a**, two signals at δ 1.8 and 2.74, assignable to methine protons having a cinnamyl group and an *N*-allylamino group, respectively, have 5.7% and 6.6% of NOE enhancement of each other. On the other hand, no enhancement between two methine protons was observed in an NOE experiment of **4b**. Therefore, we assigned **4a** to a *cis*-isomer and **4b** to a *trans*-isomer.



Scheme 1

We first carried out an aminyl radical cyclization of *N*-allyl-1-methyl-5-phenylpent-4-enylamine, which we had performed previously,[4] under improved reaction conditions.[13] A toluene solution of *N*-allyl-1-methyl-5-phenylpent-4-enylamine (**2**) was treated with *N*-chlorosuccinimide (NCS, 1.0 equiv.) for 30 min at room

temperature to quantitatively form the corresponding *N*-chloroamine **7**. The formation of *N*-chloroamine was readily checked by TLC (SiO_2). In ^1H NMR analysis, other products, except for *N*-chloroamine **7**, were not detected at this stage. The resulting *N*-chloroamine **7** was successively treated with 1.0 equiv. of Bu_3SnH and 0.2 equiv. of AIBN in refluxing toluene for 7 h. After the usual work-up, crude products were separated by TLC (Al_2O_3) to give the two pyrrolizidines **8** and **9** in 30% and 52% yield, respectively (Scheme 2).



2; R = Me, X = H
7; R = Me, X = Cl
6; R = Ph, X = H
10; R = Ph, X = Cl

8; R = Me, 30 %
11; R = Ph, 23 %

9; R = Me, 52 %
12; R = Ph, 36 %

Scheme 2

It should be noted that neither indolizidine, which might be formed by 5-*exo* and the following 6-*endo* cyclization or by 6-*endo* and the following 5-*exo* cyclization, nor quinolizidine, which might be formed by 6-*endo* and the following 6-*endo* cyclization, were obtained. When the conditions in the radical cyclization were improved by carrying out in refluxing toluene using 0.2 equiv. of AIBN,[13] the combined yield of pyrrolizidines **8** and **9** was increased to 82% from 53% in our previous study.[4] Moreover, purification of the reaction mixture with TLC on aluminum oxide, instead of TLC on silica gel, enabled us to separate two diastereoisomers of the resulting pyrrolizidines. A similar radical reaction of *N*-allyl-1,5-diphenylpent-4-enylamine (**6**) also gave pyrrolizidines **11** and **12** in 23% and 36% yield, respectively. *N*-Allylalk-4-enylamines employed in this study carry a phenyl group at the terminal carbon of the double bond. The present tandem cyclization would be applicable to that of *N*-allylalk-4-enylamines carrying an alkyl group at their vinylic terminal carbon (C-5 carbon), since a radical cyclization of *N*-methylalk-4-enylamines having methyl or dimethyl substituents at the C-5 position gave the corresponding pyrrolidines in comparable yields to that of *N*-methyl-5-phenylalk-4-enylamines.[4]

Stereochemical assignments of **8** and **9** were determined by ^1H and ^{13}C NMR, ^1H-^1H and ^1H-^{13}C 2D NMR, and ^1H NOESY. The results of ^1H and ^{13}C NMR spectra are listed in Table 1, and the results of ^1H NOESY spectra are shown in Figure 1. Correlations of NOE in pyrrolizidine **8** were observed between "$H_{1\alpha}$ - $H_{2\alpha}$", "Me($C_{5\beta}$) - $H_{6\beta}$ - $H_{7\beta}$ - $H_{7a\beta}$ - Phenyl($C_{1\beta}$)" and "$H_{7a\beta}$ - Me($C_{2\beta}$)". These results indicated that the C_1-phenyl group, C_2-methyl group, C_5-methyl group, and C_{7a}-H all had a *cis* configuration. On the other hand, correlations between "Me($C_{5\beta}$) - $H_{6\beta}$ - $H_{7a\beta}$ - Phenyl($C_{1\beta}$) - $H_{2\beta}$" were observed in **9**, as outlined in Figure 1, indicating that the C_1-phenyl group, C_5-methyl group, and C_{7a}-H had a *cis* configuration, and the C_2-methyl group and others had a *trans* configuration. These results suggested that the first cyclization of the aminyl radical took place stereoselectively to form a *trans*-2,5-disubstituted pyrrolidine ring as a single configuration.

Aminyl radical cyclization of the cyclohexylamine derivative **4a** was also carried out. A toluene solution of *N*-chloroamine **13**, generated *in situ* from amine **4a** and NCS, was heated under reflux in the presence of Bu_3SnH and AIBN to afford pyrroloindole derivatives **14** and **15** in 18% and 36% yields, respectively, together with a starting amine **4a** (14%) (Scheme 3). Stereochemical assignments were determined in a similar manner to that mentioned above. In ^1H NOESY of **14**, correlations of NOE were observed between "$H_{1\alpha}$ - $H_{2\alpha}$ - $H_{3\alpha}$",

"Ph($C_{1\beta}$) - Me($C_{2\beta}$) - $H_{9a\beta}$", and "Ph($C_{1\beta}$) - $H_{3\beta}$" (Figure 2). On the other hand, correlations between "Ph($C_{1\beta}$) - $H_{2\beta}$ - $H_{9a\beta}$", and "Me($C_{2\alpha}$) - $H_{4a\alpha}$" were observed in that of **15**.

Table 1. Results of ^1H and ^{13}C NMR Spectra of Compounds **8** and **9** in $CDCl_3$

	δ_H (270 MHz)		δ_C (67.5 MHz)	
	8	**9**	**8**	**9**
C1	2.99	2.27	55.55	60.79
C2	2.60	2.56-2.71	38.47	44.69
C3	2.81 (α), 2.92 (β)	2.29 (α), 3.47 (β)	60.06	62.43
C5	2.75-2.85	2.75-2.84	63.70	63.65
C6	1.4-1.7 (β), 1.9-2.1 (α)	1.5-1.7 (β), 1.95-2.1 (α)	35.76	35.99
C7	1.4-1.7 (α), 2.1-2.2 (β)	1.5-1.7 (α), 1.85-1.95 (β)	31.95	30.59
C7a	4.02	3.70	68.88	73.73
C2-Me	0.71	0.91	14.56	15.69
C5-Me	1.18	1.12	20.69	20.52
C1-Ph	7.15-7.35	7.15-7.35	126.00	126.42
			128.05	127.66
			128.67	128.43
			140.68	141.01

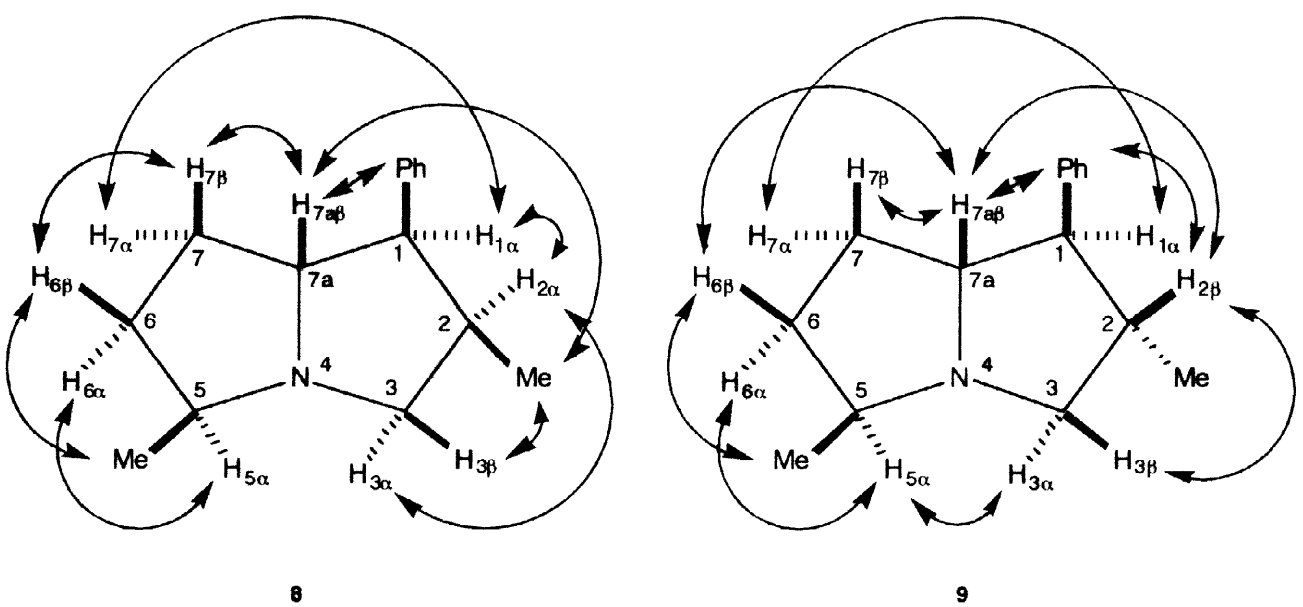
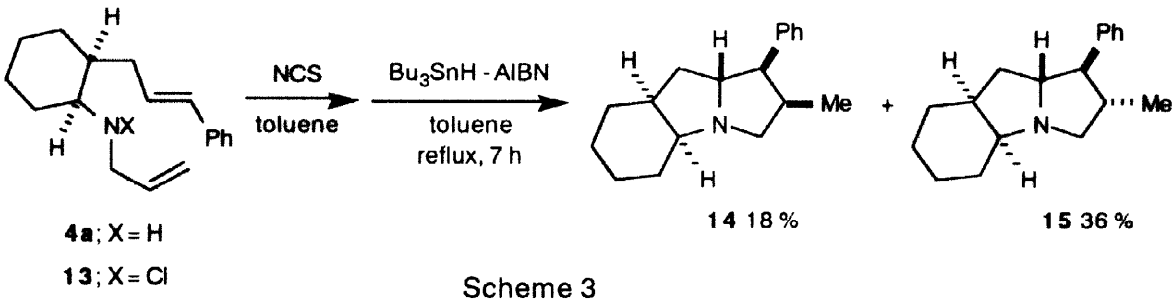


Figure 1

Probable reaction pathways are shown in Scheme 4. Starting *N*-allylalk-4-enylamine (**A**) is converted into the corresponding *N*-chloroamine **B** by treatment with NCS in toluene. Chlorine atom abstraction from *N*-

chloroamine **B** by $Bu_3Sn^•$ generates the corresponding neutral aminyl radical **C**, which cyclizes stereoselectively to form the carbon radical intermediate having a *trans*-2,5-disubstituted pyrrolidine ring **D**. Successive 5-*exo* cyclization of the resulting carbon radical to the C=C double bond of the *N*-allyl group takes place rapidly to give intermediate **E** having a pyrrolizidine ring. Hydrogen abstraction of E from Bu_3SnH gives a final cyclization product **F**.



Scheme 3

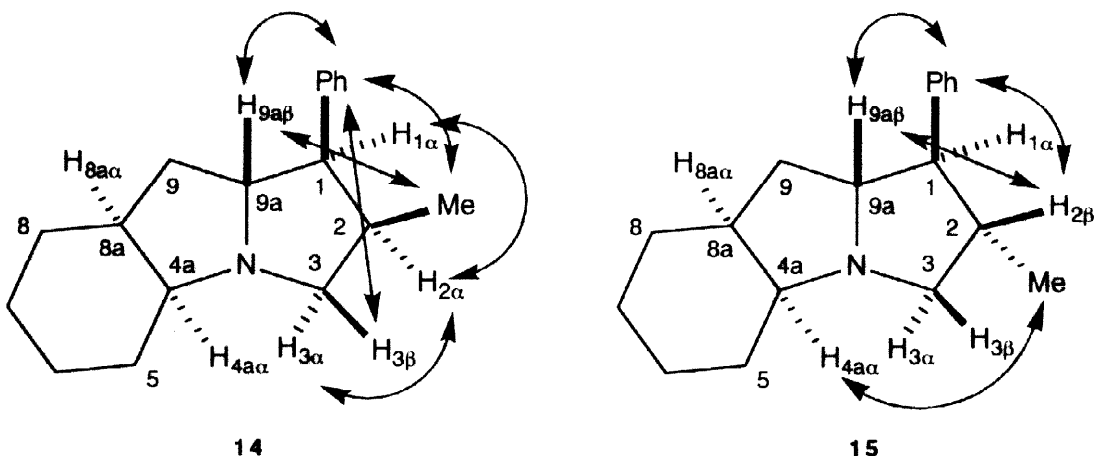
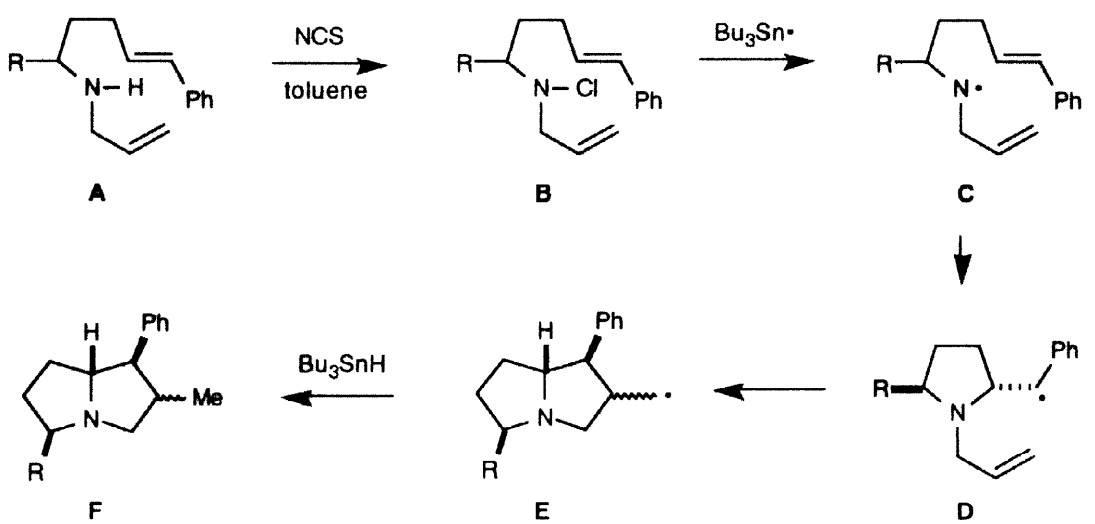
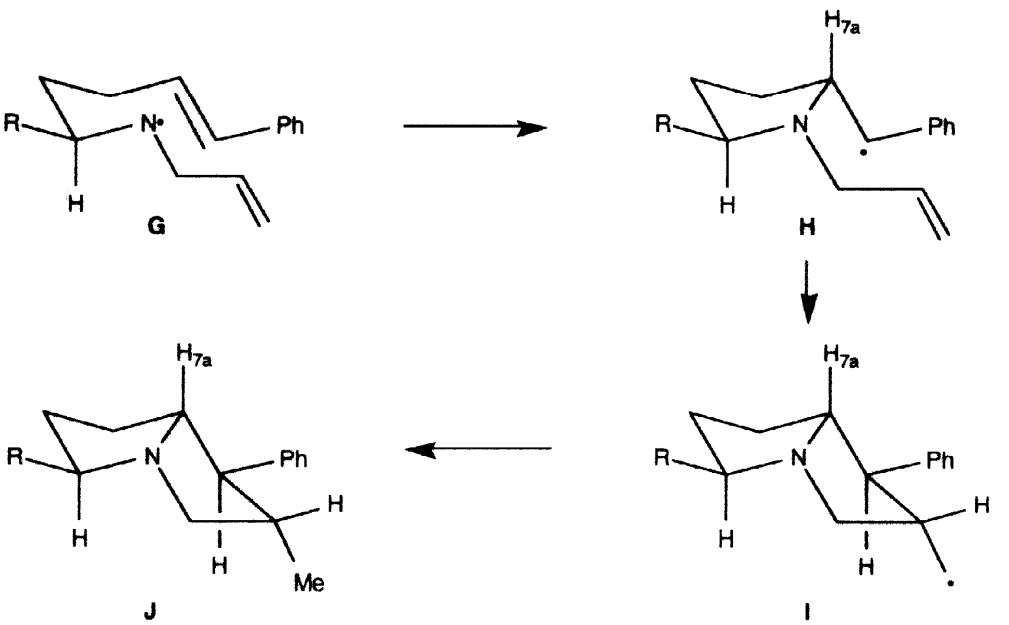


Figure 2



Scheme 4

A possible explanation for the stereochemical outcome is shown in Scheme 5. Aminyl radical **C**, generated from amine **A** in Scheme 4, probably has the transition structure of **G**, in which a substituent of R is located in a pseudoequatrial position. Cyclization could take place *via* this stable 5-*exo*-chair-like transition structure **G** to give a carbon radical intermediate **H**, having a *trans*-2,5-disubstituted pyrrolidine ring, stereoselectively. Successive radical cyclization with an *N*-allyl group could occur to form a pyrrolizidine skeleton, in which the relationship between the phenyl group and H_{7a} is a *cis* configuration. Very rapid cyclization of **H** would result in fixing the *cis* configuration between a phenyl group and H_{7a}. These explanations are in good accordance with theoretical calculation of the cyclization of a 5-hexenyl radical.[14]



Scheme 5

EXPERIMENTAL

IR spectra were determined in a neat form with a JASCO IR-810 infrared spectrophotometer. The ^1H and ^{13}C NMR spectra were determined in $CDCl_3$ ($SiMe_4$ as an internal reference) with a JEOL JNM EX-270 high-resolution spectrometer, and ^1H NOESY spectra were determined with a JEOL JMN EX-400 high-resolution spectrometer. The *J*-values are in Hz. MS spectra were recorded using a JEOL JMS DX-303 or JMS AX-500 spectrometer (70 eV). Elemental analyses were performed by the staff of the analytical laboratory of the Faculty of Pharmaceutical Science. Preparative TLC was carried out with Merck aluminum oxide $60F_{254}$ (Type E).

2-Cinnamylcyclohexanone (**3**) was prepared by alkylation of cyclohexanone *via* its silyl enol ether. Thus, a transformation of cyclohexanone into silyl enol ether by the reported procedure[15] and successive formation of its lithium enolate with methyl lithium followed by treatment with cinnamyl bromide in THF gave **3** in 59% overall yield from cyclohexanone.

Preparation of N-Allylalk-4-enylamines.

i) *N*-Allyl-1-methyl-5-phenylpent-4-enylamine (2) - Reductive amination of the corresponding ketone was carried out by the reported procedure.[11] Thus, a 1,2-dichloroethane solution (20 ml) of 6-phenylhex-5-en-2-one[10] (**1**) (1.0 g, 5.75 mmol) was stirred with acetic acid (0.33 ml, 5.75 mmol), sodium triacetoxyborohydride (1.71 g, 8.05 mmol) and allylamine (0.43 ml, 5.75 mmol) at rt under an argon atmosphere until the starting ketone had disappeared (confirmed by TLC). To the reaction mixture was added 1N NaOH, and then the mixture was extracted with ether. The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave almost pure **2** (1.05 g, 85%): δ_H 1.09 (3H, d, J = 6.3), 1.4-1.6 (1H, m), 1.6-1.8 (1H, m), 2.2-2.3 (2H, m), 2.73 (1H, sixt, J = 6.3), 5.07 (1H, ddd, J = 1.3, 3.0, and 10.2), 5.17 (1H, ddd, J = 1.7, 3.3, and 17.2), 5.92 (1H, ddt, J = 6.0, 10.2, and 17.2), 6.22 (1H, dt, J = 6.6 and 15.8), 6.40 (1H, d, J = 15.8), 7.1-7.4 (5H, m); IR 3330, 1644, 1600, 1495, 1448, 1374, 965, 916, 741, 693 cm^{-1}; MS *m/z* 215 (M^+, 3), 214 (4), 200 (3), 158 (2), 143 (5), 129 (16), 117 (17), 110 (10), 84 (100), 41 (28); Anal. Found C: 71.35, H: 8.77, N: 5.47, Cl: 14.19. Calcd for $C_{15}H_{21}N$•HCl C: 71.55, H: 8.81, N: 5.47, Cl: 14.08.

ii) *cis*-*N*-Allyl-2-cinnamylcyclohexylamine (4a) - In the same way as mentioned above, reductive amination of 2-cinnamylcyclohexanone (**3**) (129 mg, 0.60 mmol) with allylamine gave cyclohexylamine **4a** (115 mg, 75%) and *trans*-isomer **4b** (9 mg, 6%) by TLC separation (Hexane : AcOEt / 10 : 1). **4a**: mobile fraction; δ_H 1.16 (1H, br s), 1.2-1.7 (8H, m), 1.80 (1H, m), 2.16 (1H, m), 2.34 (1H, m), 2.74 (1H, m), 3.19 (1H, ddt, J = 1.3, 6.3, and 13.9), 3.30 (1H, ddt, J = 1.3, 5.9, 13.9), 5.07, (1H, ddd, J = 1.3, 3.3, and 10.2), 5.18 (1H, ddd, J = 1.3, 3.3, and 17.2), 5.93, (1H, dddd, J = 5.9, 6.3, 10.2, and 17.3), 6.21 (1H, ddd, J = 6.3, 7.6, and 15.8), 6.40 (1H, J = 15.8), 7.17 (1H, m), 7.28 (4H, m); δ_C 22.57, 23.18, 27.41, 28.66, 32.69, 39.64, 49.89, 56.43, 115.45, 125.82, 126.69, 128.37, 130.08, 130.69, 137.50, 137.81; IR 3334, 3022, 1644, 1600, 1496, 1450, 966, 916, 741, 693; MS *m/z* 255 (M^+, 19), 254 (23), 212 (28), 198 (14), 164 (34), 160 (26), 150 (22), 136 (27), 124 (83), 96 (100), 91 (27), 41 (23); Anal. Found C: 74.03, H: 8.91, N: 4.71, Cl: 12.27. Calcd for $C_{18}H_{25}N$•HCl C: 74.07, H: 8.98, N: 4.80, Cl: 12.15. **4b**: polar fraction; δ_H 1.0-1.5 (5H, m), 1.5-1.9 (4H, m), 1.9-2.2 (2H, m), 2.23 (1H, dt, J = 4.0 and 9.9), 2.59 (1H, dddd, J = 1.3, 4.0, 6.3, and 14.2), 3.16 (1H, ddt, J = 1.3, 6.3, and 13.9), 3.37 (1H, ddt, J = 1.3, 5.6, and 13.9), 5.06 (1H, ddd, J = 1.3, 3.0, and 10.2), 5.17 (1H, ddd, J = 1.3, 3.0, and 17.2), 5.92 (1H, m), 6.22 (1H, ddd, J = 6.6, 7.9, and 15.8), 6.39 (1H, d, J = 15.8), 7.19 (1H, m), 7.31 (4H, m); δ_C 25.27, 25.75, 31.18, 32.38, 36.57, 43.13, 49.65, 59.84, 115.47, 125.93, 126.81, 128.48, 129.34, 131.19, 137.63, 137.82; IR 3326, 3024, 1644, 1599, 1496, 1448, 966, 742, 693 cm^{-1}; MS *m/z* 255 (M^+, 15), 254 (13), 212 (22), 198 (24), 164 (28), 160 (26), 150 (37), 117 (56), 96 (100), 91 (57), 71 (53), 56 (53), 41 (94); HRMS Found *m/z* 255.1991. Calcd for $C_{18}H_{25}N$ *m/z* 255.1987.

iii) *N*-Allyl-1,5-diphenylpent-4-enylamine (6) - This amine was prepared by the reduction of the corresponding imine, prepared from 1,5-diphenylpent-4-en-1-one[10] (**5**) by the reported procedure.[12] Thus, to a benzene solution (21 ml) of 1,5-diphenylpent-4-en-1-one (**5**) (1.0 g, 4.24 mmol) and allylamine (3.2 ml, 42.4

mmol) was slowly added a benzene solution (4 ml) of $TiCl_4$ (0.28 ml, 2.54 mmol) at 0 - 5 °C, and the reaction mixture was stirred at rt for 2 days. After the usual work-up, the crude product was dissolved in EtOH (20 ml) and then treated with $NaBH_4$ until the starting imine had disappeared (confirmed by TLC). The usual work-up gave almost pure **6** (1.09 g, 93%). δ_H 1.44 (1H, br.s), 1.8-2.0 (2H, m), 2.1-2.2 (2H, m), 3.0-3.2 (2H, m), 3.67 (1H, dd, J = 5.9 and 7.2), 5.05 (1H, ddd, J = 1.3, 3.0, and 10.2), 5.11 (1H, ddd, J = 1.7, 3.3, and 17.2), 5.87 (1H, ddt, J = 6.3, 10.2, and 17.2), 6.16 (1H, dt, J = 6.6 and 15.8), 6.33 (1H, d, J = 15.8), 7.2-7.4 (10H, m); IR 3320, 1644, 1600, 1494, 1452, 965, 918, 745, 701 cm^{-1}; MS *m/z* 277 (M^+, 4), 276 (6), 220 (13), 172 (9), 146 (100), 129 (17), 117 (11), 91 (8); HRMS Found *m/z* 277.1812. Calcd for $C_{20}H_{23}N$ *m/z* 277.1830.

Tandem Cyclization of Aminyl Radicals.

i) 2,5-Dimethyl-1-phenylpyrrolizidines (8) and (9) - To a toluene solution (8.9 ml) of alk-4-enylamine **2** (165 mg, 0.77 mmol) was added *N*-chlorosuccinimide (NCS, 102 mg, 0.77 mmol) under an atmosphere of nitrogen at rt. After stirring for 30 min, Bu_3SnH (0.21 ml, 0.77 mmol) and AIBN (25 mg) were added and the solution was heated under reflux for 7 h. The reaction mixture was extracted with 2N HCl, and the acidic aqueous layer was made basic with 2N NaOH. The resulting basic aqueous solution was extracted several times with ether. The combined ethereal solution was washed with water and saturated brine successively, and it was then dried over anhydrous $MgSO_4$. Evaporation of the solvent gave crude products, which were separated by TLC (Hexane : AcOEt / 4 : 1) to give two fractions. The mobile fraction was **8** (50 mg, 30%): δ_H 0.71 (3H, d, J = 6.9), 1.18 (3H, d, J = 6.0), 1.4-1.7 (2H, m), 1.9-2.1 (1H, m), 2.1-2.2 (1H, m), 2.60 (1H, sept, J = 6.9), 2.75-2.85 (1H, m), 2.81 (1H, dd, J = 6.9 and 10.9), 2.92 (1H, dd, J = 5.9 and 10.9), 2.99 (1H, t, J = 6.9), 4.02 (1H, dd, J = 6.9 and 14.2), 7.15-7.35 (5H, m); δ_C 14.56, 20.69, 31.95, 35.76, 38.47, 55.55, 60.06, 63.70, 68.88, 126.00, 128.05, 128.67, 140.68; MS *m/z* 215 (M^+, 13), 200 (10), 186 (2), 172 (2), 158 (3), 145 (5), 130 (13), 117 (26), 115 (27), 97 (100), 91 (42), 82 (30), 55 (48), 41 (27); HRMS Found *m/z* 215.1641. Calcd for $C_{15}H_{21}N$ *m/z* 215.1674. The polar fraction was **9** (86 mg, 52%): δ_H 0.91 (3H, d, J = 6.3), 1.12 (3H, d, J = 6.3), 1.5-1.7 (2H, m), 1.85-1.95 (1H, m), 1.95-2.1 (1H, m), 2.27 (1H, dd, J = 9.6 and 11.2), 2.29 (1H, dd, J = 9.2 and 10.9), 2.55-2.7 (1H, m), 3.47 (1H, dd, J = 6.3 and 9.2), 3.70 (1H, dt, J = 6.9 and 9.6), 7.15-7.35 (5H, m); δ_C 15.69, 20.52, 30.59, 35.99, 44.69, 60.79, 62.43, 63.65, 73.73, 126.42, 127.66, 128.43, 141.01; MS *m/z* 215 (M^+, 18), 200 (7), 158 (4), 144 (5), 130 (13), 117 (44), 115 (36), 97 (100), 91 (58), 82 (32), 55 (56), 41 (37); HRMS Found *m/z* 215.1689. Calcd for $C_{15}H_{21}N$ *m/z* 215.1674.

ii) 2-Methyl-1,5-diphenylpyrrolizidines (11) and (12) - A similar treatment of **5** (180 mg, 0.65 mmol) with NCS (87 mg, 0.65 mmol) in toluene (7.5 ml) gave the corresponding *N*-chloroamine **10**. Successive heating of this toluene solution with Bu_3SnH (0.175 ml, 0.65 mmol) and AIBN (21 mg) under an atmosphere of nitrogen for 7 h followed by the usual work-up gave crude products. Separation by TLC (Hexane : Acetone / 30 : 1) afforded two fractions. The mobile fraction (42 mg, 23%) was pyrrolizidine **11**: δ_H 0.73 (3H, d, J = 6.9), 1.5-1.7 (1H, m), 1.75-1.95 (1H, m), 2.1-2.4 (2H, m), 2.64 (1H, sept, J = 6.9), 2.75-2.95 (2H, m), 3.09 (1H, t, J = 6.6), 3.85 (1H, dd, J = 5.6 and 10.2), 4.06 (1H, dd, J = 6.6 and 14.2), 7.15-7.5 (10H, m); δ_H 14.50, 32.51, 37.85, 38.46, 55.47, 60.63, 69.06, 71.95, 126.00, 126.54, 126.74, 128.09, 128.18, 128.64, 141.02, 145.07; MS *m/z* 277 (M^+, 50), 159 (100), 117 (29), 104 (82), 91 (25), 55 (30); HRMS Found *m/z* 277.1810. Calcd for $C_{20}H_{23}N$ *m/z* 277.1830. The polar fraction (65 mg, 36%) was pyrrolizidine **12**: δ_H 0.92 (3H, d, J = 6.3), 1.6-1.8 (1H, m), 1.85-2.05 (2H, m), 2.25-2.45 (2H, m), 2.6-2.75 (1H, m), 3.39 (1H, dd, J = 6.3 and 9.2), 3.8-

3.95 (2H, m), 7.2-7.5 (10H, m); δ_C 15.80, 30.95, 37.86, 44.80, 60.95, 62.77, 72.29, 74.00, 126.49, 126.70, 127.73, 128.25, 128.50, 141.00, 144.29; Ms *m/z* 277 (M^+, 18), 159 (100), 117 (16), 104 (37), 91 (13), 55 (15); HRMS *m/z* Found 277.1808. Calcd for $C_{20}H_{23}N$ *m/z* 277.1830.

iii) Perhydro-2-methyl-1-phenylpyrrolo[1,2-*a*]indoles (14) and (15) - A similar treatment of *N*-allylcyclohexylamine **4a** (175 mg, 0.69 mmol) with NCS (92 mg, 0.69 mmol) in toluene (8 ml) gave a toluene solution of **13**. This solution was heated under reflux with Bu_3SnH (0.19 ml, 0.69 mmol) and AIBN (23 mg) under a nitrogen atmosphere for 7 h. After the usual work-up, crude products were separated by TLC (Hexane : AcOEt / 10 : 1) to give three fractions. The most mobile fraction (31 mg, 18%) was pyrroloindole **14**: δ_H 0.71 (3H, d, *J* = 6.9), 1.15-1.4 (2H, m), 1.4-1.7 (7H, m), 1.86 (1H, ddd, *J* = 3.3, 7.3, and 12.2), 2.13 (1H, m), 2.56 (1H, sept, *J* = 6.9), 2.75 (1H, dd, *J* = 5.9 and 10.6), 2.80 (1H, q, *J* = 4.3), 2.89 (1H, dd, *J* = 5.3 and 10.6), 2.96 (1H, t, *J* = 6.9), 7.2-7.3 (5H, m); δ_C 14.61, 21.06, 24.53, 27.89, 28.99, 37.97, 38.35, 39.71, 55.74, 60.61, 66.24, 66.78, 125.89, 128.01, 128.68, 141.28; MS *m/z* 255 (M^+, 17), 205 (7), 137 (100), 95 (24), 94 (29), 91 (13), 55 (20), 41 (16); HRMS Found *m/z* 255.1988. Calcd for $C_{18}H_{25}N$ *m/z* 255.1987. The second mobile fraction (25 mg, 14%) was starting amine **4a**. The polar fraction (63 mg, 36%) was pyrroloindole **15**: δ_H 0.89 (3H, d, *J* = 6.3), 1.1-1.4 (2H, m), 1.4-1.8 (8H, m), 2.15-2.35 (2H, m), 2.5-2.7 (1H, m), 2.80 (1H, q, *J* = 4.6), 3.45 (1H, dd, *J* = 6.3 and 8.9), 3.72 (1H, m), 7.15-7.4 (5H, m); δ_C 15.53, 21.80, 23.58, 27.51, 28.29, 35.73, 39.01, 43.54, 61.19, 62.89, 66.58, 126.43, 127.76, 128.45, 141.22; MS *m/z* 255 (M^+, 21), 212 (5), 137 (100), 95 (23), 94 (26), 91 (15), 55 (12), 44 (8); HRMS Found *m/z* 255.1942. Calcd for $C_{18}H_{25}N$ *m/z* 255.1987.

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