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STEREOSELECTIVE SYNTHESIS OF 4- OR 5-SUBSTITUTED 2-BENZYL- AND 2-BENZOYLPYRROLIDINES BY MEANS OF ANODIC OXIDATION OF δ-ALKENYLAMINES

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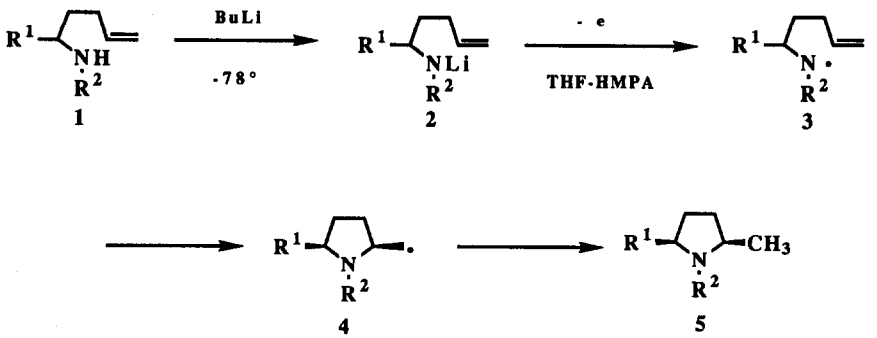
Abstract-The anodic oxidation of the lithium amides of δ-alkenylamines **6a**, **6b**, **6c**, **10a**, and **10b** gave stereoselectively *cis*-5-substituted 2-benzyl-1-methylpyrrolidines (**7a**, **7b**, **7c**) and 4-substituted 2-benzyl-1-methylpyrrolidines (**11a**, **11b**) in high yields. The anodic oxidation of *N*-methoxyl compounds of δ-alkenylamines (**12a**, **12b**) gave 5-substituted 2-benzoyl-1-methylpyrrolidines (**13a**, **13b**).

Apart from numerous studies on the synthesis of five-membered alicyclic compounds by intramolecular cyclization of carbon radicals,[1,2] a limited number of studies have been carried out on the synthesis of heterocycles by cyclization of hetero atom radicals. Especially, little attention has been paid to the synthesis of nitrogen heterocycles by means of the cyclization of neutral nitrogen-centered radicals (aminyl radicals),[3,4] although protonated aminyl radicals (aminium radicals) or aminyl radicals complexed with a metal ion are known to undergo facile cyclization.[3,5] The neutral aminyl radicals have been generated by either photolysis or thermolysis of *N*-chloroamines,[4] *N*-nitrosoamines,[6] 2-tetrazenes,[7] *N*-hydroxypyridine-2-thione carbamates,[8] or aminodiethoxyphosphines,[9] by an electron-transfer reaction of the amidate anion to tetracyanoethylene,[10] by anodic oxidation of dialkylamines,[11] or by anodic oxidation of metal dialkylamides.[11,12] We have already reported that neutral aminyl radicals (**3**) can be generated by anodic oxidation of lithium alkenylamides (**2**) and that these aminyl radicals undergo stereoselective cyclization to give *cis*-1-alkyl-2,5-disubstituted pyrrolidines (**5**) in 2-52% yields (Scheme 1).[13]

In this paper we report on the results of a further study in this area: the synthesis of 4- and 5-substituted 2-benzylpyrrolidines by the cyclization of several alkenylamines carrying a phenyl group at the terminal carbon of their double bonds and the synthesis of 5-substituted 2-benzoylpyrrolidines by the cyclization of *N*-methoxy-δ-alkenylamines.



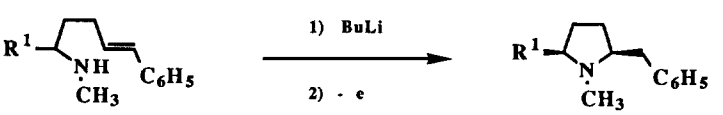
Scheme 1

RESULTS AND DISCUSSION

1-Substituted- (**6a-6c**) and 2-substituted *N*-methyl-5-phenylpent-4-enylamines (**10a, 10b**) were prepared according to the sequences outlined in Schemes 6 and 7.

Treatment of alkenylamines **6a**, **6b**, or **6c** with butyllithium at -78 °C followed by anodic oxidation of the resulting lithium amides of **6a-6c** at a constant current of 10 mA/cm^2 in a 30:1 mixture of THF and HMPA containing 0.25M lithium perchlorate at -10° C gave rise to 2-benzyl-1-methyl- (**7a**), 2-benzyl-1,5-dimethyl- (**7b**), or 2-benzyl-1-methyl-5-phenylpyrrolidines (**7c**) exclusively in 66-85% yields (Scheme 2). Electrolysis was carried out with a platinum anode and a platinum cathode using a divided cell. We passed an electricity of 1.2 Faradays per mol of **6a-6c**, and observed that the color of the catholyte turned dark-blue and that lithium metal was deposited on the surface of the cathode when the electrolysis was completed.

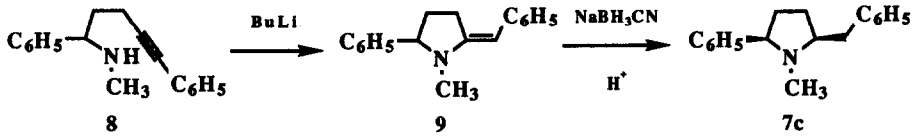
The structures of products **7a-7c** were confirmed by spectroscopy. The configurations of their 2,5-disubstituents were assigned to be *cis* on the basis of our previous results[13] as well as an independent chemical transformation. Thus, we recently found that an enamine pyrrolidine (**9**) having an exo double bond is formed in 85% yield when δ-alkynylamine **8** is treated with butyllithium.[14] The reduction of



6a $R^1 = H$
6b $R^1 = CH_3$
6c $R^1 = C_6H_5$

7a-7c

Scheme 2

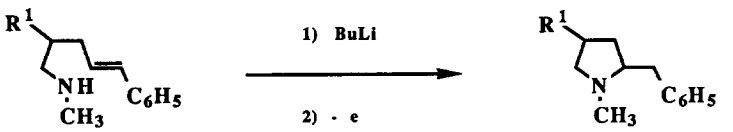


8 9 7c

Scheme 3

9 with sodium cyanoborohydride in the presence of acid gave *cis*-2-benzyl-1-methy-5-phenylpyrrolidine which was identical in all respects to the product **7c** obtained by aminyl radical cyclization of **6c**.

4-Substituted 2-benzyl-1-methylpyrrolidines **11a** or **11b** can be obtained analogously by cyclization of the aminyl radicals anodically generated from δ-alkenylamines **10a** and **10b** (Scheme 4). Thus, pyrrolidine **11a** was obtained as a 75:25 mixture of two stereoisomers from δ-alkenylamine **10a**, while a single stereoisomer of pyrrolidine **11b** was obtained from δ-alkenylamine **10b**. The configurations of the 2,4-disubstituents in **11a** and **11b** have not been determined, although the configurations of 2,4-disubstituents of the major product in **11a** and product **11b** are most probably *cis*, as in the case of the products from the aminyl radical cyclizations of **6a-6c**.



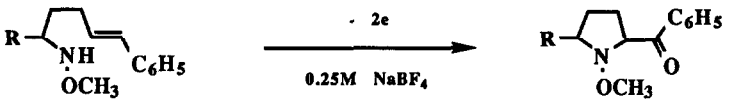
10a $R^1=CH_3$
10b $R^1=C_6H_5$

11a, 11b

Scheme 4

All of the cyclization of the above-mentioned δ-alkenylamines was achieved *via* aminyl radicals generated by anodic oxidation of lithium amides of the δ-alkenylamines. It has been reported that a direct anodic oxidation of dialkylamines may also generate aminyl radicals[3,11] or aminium radicals.[3] An attempted cyclization by direct anodic oxidation of δ-alkenylamines **6b** or **6c** under various electrolytic conditions failed to give any cyclization products. On the other hand, the direct anodic oxidation of *N*-methoxy derivatives (**12a**) or (**12b**) of δ-alkenylamines **6b** and **6c** according to a modified procedure of that used by Karady and colleagues[15] gave rise to a single stereoisomer of 5-substituted 2-benzoyl-1-methoxypyrrolidines (**13a**) or (**13b**) in each case (Scheme 5); the electrolysis was carried out at a constant current of 10 mA/cm^2 with a carbon felt anode and a stainless-steel cathode in a mixed solvent of THF, methanol, and water (10:1:1) containing 0.25 M sodium tetrafluoroborate.

Electricity passed was 2.4 Faradays per mol of **12a** or **12b**. The cyclization of **12a** or **12b** probably proceeds through a similar path as that proposed by Karaday.[15] 2-Benzoylpyrrolidine (**13a**) or (**13b**) is formed by either electrolytic or air oxidation of the initially generated 2-(1-hydroxybenzyl)-1-methoxypyrrolidines which are formed by the aminium radical cyclization, followed by a trapping of water by the resulting species.



12a R=CH_3

12b R=C_6H_5

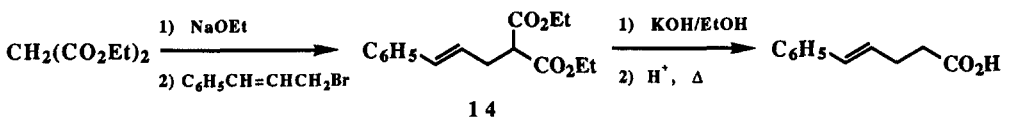
13a, 13b

Scheme 5

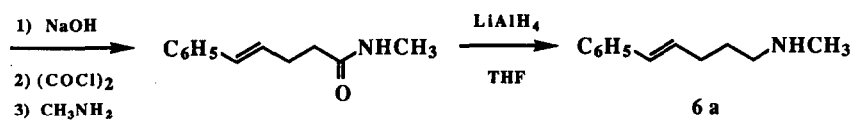
EXPERIMENTAL

Preparation of δ-alkenylamines. The starting δ-alkenylamines used in this study were prepared according to the procedures outlined in Schemes 6 and 7.

N-Methyl-5-phenylpent-4-enylamine (**6a**). Alkylation of diethyl malonate (0.32 mol) with cinnamyl bromide (0.32 mol) by a conventional method[16] gave 52.5 g of ethyl 2-(ethoxycarbonyl)-5-phenyl-4-pentenoate (**14**) (0.19 mol; 60%): bp 155-157 °C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, 6H), 2.79 (t, 2H), 3.48 (t, 1H), 4.20 (q, 4H), 5.8-6.6 (m, 2H), 7.2 (m, 5H). The hydrolysis of **14** (36 mmol) followed by decarboxylation gave an yellow solid, which was recrystallized from benzene-hexane to give 3.7 g of 5-phenyl-4-pentenoic acid (21 mmol; 58%): mp 90-91 °C; ^{1}H NMR ($CDCl_3$) δ 2.53 (m, 2H), 2.56 (m, 2H), 5.9-6.7 (m, 2H), 7.2 (m, 5H). 5-Phenyl-4-pentenoic acid (7.8 mmol) was converted to acid chloride by treatment with 10% sodium hydroxide and oxalyl



14

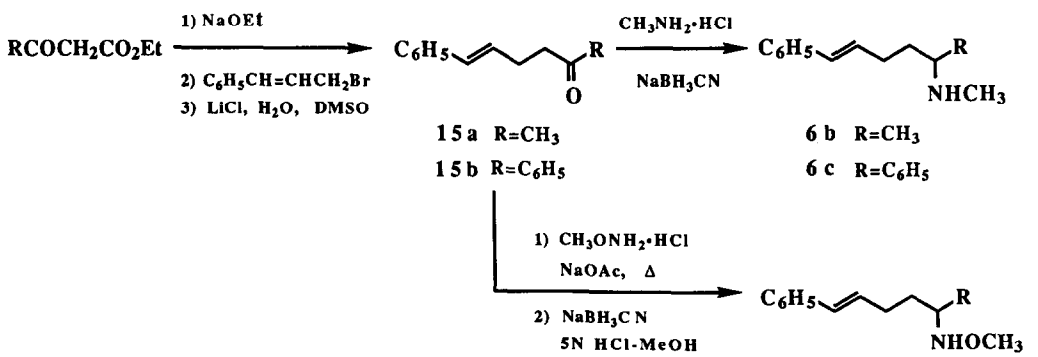


6a

Scheme 6

chloride. To a benzene solution of the acid chloride was added gaseous methylamine until the solution became basic. The usual work-up followed by column chromatography (silica gel; EtOAc) gave 1.03 g of *N*-methyl-5-phenyl-4-pentenamide (5.4 mmol; 69%): mp 72-74 °C; ^{1}H NMR ($CDCl_3$) δ 2.2-2.8 (m, 4H), 2.78 and 2.84 (each s, 3H), 5.5 (bs, 1H), 5.9-6.7 (m, 2H), 7.3 (m, 5H). The reduction of *N*-methyl-5-phenyl-4-pentenamide (3.1 mmol) with lithium aluminum hydride (6.2 mmol) in THF (60 °C, 1.5 h and room temperature, overnight) followed by bulb-to-bulb distillation gave 0.40 g of *N*-methyl-5-phenyl-pent-4-enylamine (**6a**) (2.3 mmol; 74%): bp 85-90 °C (0.3 mmHg); n_D^{20} 1.5366; IR (neat) 3290, 3080, 1651, 1599, 1495, 965, 742, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.7 (m, 2H), 1.65 (s, 1H), 2.25 (m, 2H), 2.43 (s, 3H), 2.62 (t, 2H), 6.12 (dt, 1H, *J*=6.0 and 16.0 Hz), 6.43 (d, 1H, *J*=16.0 Hz), 7.29 (m, 5H); mass spectrum *m/z* 175 (M^+, 9), 129 (11), 70 (28), 44 (100). Anal. Calcd for $C_{12}H_{17}N$: *m/z* 175.1360. Found: *m/z* 175.1360.

N-Methyl-1-methyl-5-phenylpent-4-enylamine (**6b**). This amine was prepared according to the procedure outlined in Scheme 7. Alkylation of ethyl acetoacetate (147 mmol) with cinnamyl bromide (98 mmol) in the presence of sodium ethoxide (108 mmol) gave 22.6 g of 4-(ethoxycarbonyl)-1-phenyl-1-hexen-5-one (94%). Decarbethoxylation of the alkylated acetoacetate ester (53 mmol) according to a published method[17] (LiCl 64 mmol, H_2O 27 ml, DMSO 270 ml; reflux, 10 h) gave 7.3 g of 1-phenyl-1-hexen-5-one (**15a**) (42 mmol; 79 %): bp 100-102 °C (0.6 mmHg); IR (neat) 3024, 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 3H), 2.48 (q, 2H), 2.61 (t, 2H), 6.19 (dt, 1H), 6.41 (d, 1H), 7.3 (m, 5H). Reductive amination[18] of **15a** (20 mmol) with methylamine (177 mmol) in the presence of sodium cyanoborohydride (11 mmol) and 9 ml of 5N hydrogen chloride in methanol (room temperature, 5 days) and the usual work-up followed by distillation gave 3.1 g of *N*-methyl-1-methyl-5-phenylpent-4-enylamine (**6b**) (16.3 mmol; 82%): bp 84-87 °C (0.3 mmHg); n_D^{20} 1.5369; IR (neat) 3280, 3080, 1651, 1599, 1496, 966, 742, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.07 (d, 3H, *J*=6.2 Hz), 1.30 (bs, 1H), 1.55 (m, 2H), 2.26 (m, 2H), 2.41 (s, 3H), 2.59 (m, 1H), 5.9-6.6



Scheme 7

(m, 2H), 7.29 (m, 5H); mass spectrum *m/z* 189 (M^+, 9), 117 (15), 91 (7), 84 (15), 58 (100). Anal. Calcd for $C_{13}H_{19}N$: *m/z* 189.1518. Found: *m/z* 189.1522.

N-Methyl-1,5-diphenylpent-4-enylamine (**6c**). This amine was prepared according to the procedure outlined in Scheme 7. Alkylation of ethyl benzoylacetate (72 mmol) with cinnamyl bromide (72 mmol) followed by decarbethoxylation[17] gave 12.9 g of 1.5-diphenyl-1-penten-5-one (**15b**) (55 mmol; 77 %): mp 58.0-59.3 °C; IR (neat) 3026, 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.67 (m, 2H), 3.16 (t, 2H), 6.2-6.5 (m, 2H), 7.3 (m, 5H), 7.52 (m, 3H), 7.98 (m, 2H). Reductive amination[18] of **15b** (11.4 mmol) with methylamine (57 mmol) and sodium cyanoborohydride (19 mmol) gave 2.19 g of *N*-methyl-1,5-diphenylpent-4-enylamine (**6c**) (8.7 mmol; 77 %): n_D^{20} 1.5787; IR (neat) 3334, 3080, 1650, 1599, 1493, 965, 747, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (s, 1H), 1.87 (m, 2H), 2.13 (m, 2H), 2.27 (s, 3H), 3.50 (t, 1H), 5.9-6.5 (m, 2H), 7.29 (m, 5H); mass spectrum *m/z* 251 (M^+, 9), 220 (19), 146 (19), 120 (100). Anal. Calcd for $C_{18}H_{21}N$: *m/z* 251.1673. Found: *m/z* 251.1665.

N-Methyl-2-methyl-5-phenylpent-4-enylamine (**10a**). This amine was prepared by a similar procedure as that for the preparation of **6a**. Alkylation of **14** with methyl iodide followed by hydrolysis and decarboxylation gave 2-methyl-5-phenyl-4-pentenoic acid: IR (neat) 1708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, 3H) 2.1-2.8 (m, 3H), 5.9-6.3 (m, 2H) 6.47 (d, 1H), 7.28 (m, 5H). Amidation of this acid with oxalyl chloride and methylamine gave *N*-methyl-2-methyl-5-phenyl-4-pentenamide (79%): IR (Nujol) 3306, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, 3H), 2.1-2.7 (m, 3H), 2.78 and 2.83 (each s, 3H), 5.4 (bs, 1H), 6.12 (dt, 1H), 6.45 (d, 1H), 7.28 (m, 5H). Reduction of *N*-methyl-2-methyl-5-phenyl-4-pentenamide (6.1 mmol) with lithium aluminum hydride (12.4 mmol) in THF gave 1.06 g of *N*-methyl-2-methyl-5-phenylpent-4-enylamine (**10a**) (5.6 mmol; 92%): bp 90-95 °C (1.0 mm Hg); IR (neat) 3298, 3026, 1653, 1602, 1498, 967, 746, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3H, *J*=6.4 Hz), 1.25 (s, 1H), 1.4-1.9 (m, 1H), 1.9-2.7 (m, 4H), 2.42 (s, 3H), 6.17 (dt, 1H, *J*=6.4 and 15.8 Hz), 6.42 (d, 1H, *J*=15.8 Hz), 7.28 (m, 5H); mass spectrum *m/z* 189 (M^+, 9), 129 (8), 91 (5), 84 (15), 44 (100). Anal. Calcd for $C_{13}H_{19}N$: *m/z* 189.1518. Found: *m/z* 189.1519.

N-Methyl-2,5-diphenylpent-4-enylamine (**10b**). This amine was prepared by a similar procedure as that for the preparation of **6a**. Alkylation of diethyl phenylmalonate with cinnamyl bromide followed by hydrolysis and decarboxylation gave 2,5-diphenyl-4-pentenoic acid: IR (Nujol) 1698 cm^{-1}, ^1H NMR ($CDCl_3$) δ 2.5-3.1 (m, 2H), 3.72 (t, 1H), 6.07 (dt, 1H), 6.45 (d, 1H), 7.28 (m, 10H). The reaction of sodium 2,5-diphenyl-4-pentenoate with oxalyl chloride and excess methylamine gave *N*-methyl-2,5-diphenyl-4-pentenamide (73%): mp 125-125.5 °C; IR (Nujol) 3356, 1651 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.72 and 2.77 (each s, 3H), 2.4-3.2 (m, 2H), 3.45 (t, 1H), 5.40 (bs, 1H), 6.07 (dt, 1H), 6.42 (d, 1H), 7.28 (m, 10H). The reduction of this amide (5.3 mmol) with lithium aluminum hydride (10.8 mmol) gave 1.33 g of *N*-methyl-2,5-diphenylpent-4-enylamine (**10b**) (5.3 mmol; 100 %): IR (neat) 3326, 3060, 1677, 1602, 1497, 968, 746, 702 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.36 (s, 3H), 2.53 (t, 2H), 2.87 (s, 1H), 2.6-3.1 (m, 3H), 6.05 (dt, 1H, *J*=6.2 and 15.8 Hz), 6.38 (d, 1H, *J*=15.8 Hz), 7.24 (m, 10H); mass

spectrum *m/z* 251 (M^+, 8), 91 (7), 44 (100). Anal. Calcd for $C_{18}H_{21}N$: *m/z* 251.1674. Found: *m/z* 251.1669.

N-Methoxy-1-methyl-5-phenylpent-4-enylamine (**12a**). This amine was prepared according to the procedure outlined in Scheme 7. The reaction of the ketone **15a** with an aqueous solution of sodium acetate and methoxyamine hydrochloride gave *N*-methoxy-1-phenyl-1-hexen-5-one oxime (100 %): IR (neat) 3026, 1735, 1638 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 and 1.88 (each s, 3H), 2.3-2.6 (m, 4H), 3.82 and 3.84 (each s, 3H), 6.19 and 6.20 (each dt, 1H), 6.42 (d, 1H), 7.31 (m, 5H). To a 10 ml of methanolic solution of this oxime (1.1 mmol) was added 5N HCl in absolute methanol (2 ml) and then sodium cyanoborohydride (2.2 mmol). The mixture was then stirred overnight at room temperature. The usual work-up and preparative TLC (silica gel, $CHCl_3$) gave 199 mg of *N*-methoxy-1-methyl-5-phenylpent-4-enylamine (**12a**) (0.97 mmol; 97%): IR (neat) 3244, 3024, 1649, 1599, 1495, 1053, 965, 741, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (d, 3H, *J*=6.2 Hz), 1.4-1.8 (m, 2H), 2.27 (m, 2H), 3.06 (m, 1H), 3.54 (s, 3H), 6.21 (dt, 1H, *J*=6.6 and 15.8 Hz), 6.41 (d, 1H, *J*=15.8 Hz), 7.32 (m, 5H); mass spectrum *m/z* 205 (M^+, 2), 190 (2), 174 (98), 129 (31), 117 (41), 91 (35), 74 (100), 44 (55). Anal. Calcd for $C_{13}H_{19}NO$: *m/z* 205.1466. Found: *m/z* 205.1471.

N-Methoxy-1,5-diphenylpent-4-enylamine (**12b**). This amine was prepared according to the procedure outlined in Scheme 7. The reaction of ketone **15b** with sodium acetate and an aqueous solution of methoxyamine hydrochloride gave *N*-methoxy-1,5-diphenyl-1-penten-5-one oxime (97%): IR (neat) 3024, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.47 (m, 2H), 2.88 (m, 2H), 3.99 (s, 3H), 6.18 (m, 1H), 6.43 (d, 1H), 7.27 (m, 5H), 7.37 (m, 3H), 7.62 (m, 2H). This oxime (0.97 mmol) was reduced with sodium cyanoborohydride (2.0 mmol) to give *N*-methoxy-1,5-diphenylpent-4-enylamine (**12b**) (0.66 mmol; 68%): IR (neat) 3446, 3246, 1652, 1600, 1495, 1063, 1029, 753, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59 (bs, 1H), 1.82 (m, 1H), 2.0 (m, 1H), 2.12 (m, 2H), 3.45 (s, 3H), 4.02 (dd, 1H, *J*=5.1 and 8.8 Hz), 6.16 (dt, 1H, *J*=6.6 and 15.8 Hz), 6.33 (d, 1H, *J*=15.8 Hz), 7.32 (m, 10H); mass spectrum *m/z* 267 (M^+, 2), 236 (50), 220 (22), 176 (58), 136 (45), 129 (40), 117 (100), 91 (44), 77 (24). Anal. Calcd for $C_{18}H_{21}NO$: *m/z* 267.1623. Found: *m/z* 267.1610.

Anodic oxidation of lithium amides of δ-alkenylamines (6a, 6b, 6c, 10a, and 10b). The electrochemical cell used in this study was an H-type cell in which the anode (33 mm o.d.x140 mm length) and the cathode compartment (23 mm o.d.x140 mm length) were separated by a fine fritted glass disc. Both compartments were equipped with stirring bars and inlets with serum caps for the addition of reagents and for the introduction of a nitrogen gas. Two platinum plate electrodes (20x20 mm^2) were used as the anode and cathode.

The typical procedure for anodic oxidation of lithium amide of *N*-methyl-1-methyl-5-phenylpent-4-enylamine (**6b**) was as follows. To a 12 ml of THF solution containing 378 mg of **6b** (2 mmol) was added dropwise butyllithium (2.4 mmol in hexane) at -78 °C under a nitrogen atmosphere, and the solution was first stirred at -78 °C for 30 min and then at -10 °C for 30 min. A THF solution of the lithium amide of **6b** was transferred to an anode chamber containing a solution of THF (18 ml; 30 ml as a total volume) and HMPA (1 ml) containing 0.25M lithium perchlorate as a

supporting electrolyte. The catholyte was the same solution of THF (19 ml) and HMPA (0.5 ml) containing lithium perchlorate. The mixture in the anode chamber was electrolyzed at a constant current of 10 mA/cm^2 at -10 °C under a nitrogen atmosphere. The electricity passed was 1.2 Faradays per mol of **6b**. During the electrolysis, a deposition of lithium metal on the cathode was observed. After the electrolysis, the anolyte was dissolved in 150 ml of diethyl ether. The solution was washed with water and saturated sodium chloride solution, and dried over magnesium sulfate. The usual work-up of the solution gave an almost pure product, which was subjected to a preparative TLC (silica gel; Et_2O-C_6H_6 5:2) to give 321 mg of *cis*-2-benzyl-1,5-dimethylpyrrolidine (**7b**) (85% yield). GLC analysis of a crude reaction mixture by the use of an internal standard method showed that **7b** was produced in 97% yield. Spectral data of **7b** as well as other cyclization products are given below.

2-Benzyl-1-methylpyrrolidine (**7a**) (70% yield). n_D^{20} 1.5207. IR (neat) 3026, 1605, 1496, 742, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.5-1.9 (m, 4H), 2.20 (m, 1H), 2.31 (m, 1H, *J*=4.2, 7.7, and 9.7 Hz), 2.40 (s, 3H), 2.45 (dd, 1H, *J*=9.7 and 12.8 Hz), 3.06 (dd, 1H, *J*=4.2 and 12.8 Hz), 3.11 (m, 1H), 7.23 (m, 5H); mass spectrum *m/z* 175 (M^+, 0.2), 91 (5), 84 (100), 42 (16). Anal. Calcd for $C_{12}H_{17}N$: *m/z* 175.1360. Found: *m/z* 175.1351.

cis-2-Benzyl-1,5-dimethylpyrrolidine (**7b**) (85% yield). n_D^{20} 1.5123; IR (neat) 3026, 1605, 1496, 1200, 1118, 741, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14 (d, 3H, *J*=6.2 Hz), 1.3-1.85 (m, 4H), 2.23 (m, 1H, *J*=6.2, 7.1 and 8.6 Hz), 2.34 (s, 3H), 2.3-2.45 (m, 1H), 2.46 (dd, 1H, *J*=9.7 and 12.1 Hz), 3.08 (dd, 1H, *J*=2.9 and 12.1 Hz), 7.23 (m, 5H); mass spectrum *m/z* 189 (M^+, 0.2), 117 (2), 98 (100), 42 (13). Anal. Calcd for $C_{13}H_{19}N$: *m/z* 189.1517. Found *m/z* 189.1507. In the ^{1}H NMR spectrum of **7b**, irradiation of the doublet at δ 1.14 caused the multiplet at δ 2.23 to collapse to a double-doublet (*J*=7.1 and 8.6 Hz).

cis-2-Benzyl-1-methyl-5-phenylpyrrolidine (**7c**) (66% yield). n_D^{20} 1.5687; IR (neat) 3026, 1603, 1492, 1030, 757, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.6-1.9 (m, 3H), 2.01 (m, 1H), 2.22 (s, 3H), 2.55-2.7 (m, 1H), 2.63 (dd, 1H, *J*=8.6 and 17.2 Hz), 3.09 (dd, 1H, *J*=8.1 and 17.2 Hz), 3.27 (t, 1H, *J*=7.7 Hz), 7.3 (m, 10H); mass spectrum *m/z* 251 (M^+, 0.1), 160 (100), 129 (11), 91 (10). Anal. Calcd for $C_{18}H_{21}N$: *m/z* 251.1674. Found: *m/z* 251.1666. An NOE enhancement (3.0 %) was observed between the signal due to the C-5 methine proton at δ 3.27 and that due to the C-2 methine proton at δ 2.55-2.7, indicating the *cis* relationship of the two substituents at the C-2 and C-5 positions.

2-Benzyl-1,4-dimethylpyrrolidine (**11a**) (57% yield). This pyrrolidine was obtained as a mixture of two stereoisomers in a ratio of 75:25. Spectral data of the major isomer are as follows: IR (neat) 3028, 1606, 1498, 1031, 745, 701 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.04 (d, 3H, *J*=6.6 Hz), 1.13 (m, 1H, *J*=7.0, 9.2 and 12.1 Hz), 1.93 (m, 1H, *J*=5.9, 8.4, and 12.1 Hz), 2.04 (m, 1H), 2.37 (s, 3H), 2.35-2.5 (m, 1H), 2.42 (dd, 1H, *J*=4.4 and 12.3 Hz), 2.46 (dd, 1H, *J*=5.5 and 9.5 Hz), 2.77 (dd, 1H, *J*=3.3 and 9.5 Hz), 3.06 (dd, 1H, *J*=3.1 and 12.3 Hz), 7.21 (m, 5H); mass spectrum *m/z* 189 (M^+, 0.2), 98 (100), 42 (15). Anal. Calcd for $C_{13}H_{19}N$: *m/z* 189.1534. Found: *m/z* 189.1526.

The ^{1}H NMR spectrum of the minor isomer exhibited a doublet ascribable to C-4

methyl protons at δ 0.93 and a singlet of *N*-methyl protons at δ 2.37.

2-Benzyl-1-methyl-4-phenylpyrrolidine (**11b**) (45% yield). IR (neat) 3026, 1605, 1496, 746, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.89 (m, 1H), 2.10 (m, 1H), 2.35 (m, 1H), 2.46 (s, 3H), 2.57 (dd, 1H, *J*=9.5 and 12.5 Hz), 2.69 (m, 1H), 3.10 (dd, 1H, *J*=4.3 and 12.5 Hz), 3.36 (m, 1H), 3.42 (dd, 1H, *J*=7.0 and 12.1 Hz), 7.23 (m, 10H); mass spectrum *m/z* 251 (M^+, 0.1), 160 (100), 91 (9), 42 (13). Anal. Calcd for $C_{18}H_{21}N$: *m/z* 251.1674. Found: *m/z* 251.1666.

Anodic oxidation of *N*-methoxy-δ-alkenylamines (12a, 12b). The electrochemical cell used in these electrolyses was the same as that used in the anodic oxidation of lithium amides of δ-alkenylamines. Carbon felt was used as the anode and stainless-steel as the cathode. Typically, 81 mg of *N*-methoxy-1-methyl-5-phenylpent-4-enylamine (**12a**) (0.4 mmol) in a solution of THF (25 ml), methanol (2.5 ml), and water (2.5 ml) containing 0.25M sodium tetrafluoroborate was transferred to an anode chamber. The mixture was then electrolyzed at a constant current of 10 mA/cm^2 at room temperature. Electricity of 2.4 Faradays per mol of **12a** was passed. After the electrolysis, the usual work-up of the product mixture followed by preparative TLC (silica gel; CH_2Cl_2/MeOH/aq. NH_3 20:1:0.1) gave 34 mg of 2-benzoyl-1-methoxy-5-methylpyrrolidine (**13a**) (0.17 mmol; 42%). Spectral data of the products (**13a**) and (**13b**) are recorded below.

2-Benzoyl-1-methoxy-5-methylpyrrolidine (**13a**) (42% yield). IR (neat) 3028, 1689, 1597, 1491, 1226, 1045, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (d, 3H, *J*=7.0 Hz), 1.57 (m, 1H), 2.0-2.3 (m, 4H), 3.43 (s, 3H), 4.85 (t, 1H, *J*=7.3 Hz), 7.4-7.6 (m, 3H), 8.08 (d, 2H); mass spectrum *m/z* 219 (M^+, 0.2), 204 (0.3), 114 (100), 105 (15), 77 (16). Anal. Calcd for $C_{13}H_{18}NO_2$ $(M+1)^+$: *m/z* 220.1338. Found: *m/z* 220.1352.

2-Benzoyl-1-methoxy-5-phenylpyrrolidine (**13b**) (38% yield). IR (neat) 3028, 1690, 1599, 1495, 1226, 1046, 910, 733, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0-2.3 (m, 2H), 2.3-2.45 (m, 2H), 3.17 (s, 3H), 4.52 (t, 1H, *J*=7.3 Hz), 5.00 (dd, 1H, *J*=5.5 and 7.7 Hz), 7.2-7.6 (m, 8H), 8.09 (d, 2H); mass spectrum *m/z* 281 (M^+, 0.2), 176 (100), 144 (26), 117 (29), 105 (22), 91 (32), 77 (33). Anal. Calcd for $C_{18}H_{20}NO_2$ $(M+1)^+$: *m/z* 282.1504. Found: *m/z* 282.1502.

Reduction of enamine pyrrolidine 9. (*E*)-2-Benzylidene-1-methyl-5-phenylpyrrolidine (**9**) (82 mg; 0.33 mmol) obtained by the anionic cyclization of δ-alkynylamine **8**[14] was treated with sodium cyanoborohydride (0.8 mmol) in the presence of 2 ml of 5N-HCl in methanol at room temperature for 3 days. The usual work-up and separation by TLC gave 59.0 mg of the 2,5-disubstituted pyrrolidine (72%), which was identical to the *cis*-2-benzyl-1-methyl-5-phenylpyrrolidine (**7c**) obtained by the anodic oxidation of lithium amide of **6c**.

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