Intramolecular Amidoselenation of N-Alkenylamides: Formation of Nitrogen Heterocycles

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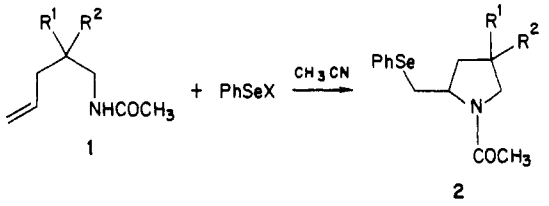
The reaction of N-alkenylamides with benzeneselenenyl halides affords pyrrolidine or piperidine derivatives through the cyclization by a nitrogen atom of the amide group induced by the addition of a phenylseleno group to the double bond. The introduction of substituents into the carbon atom between the double bond and amide moiety facilitates the cyclization reaction. The effect of a halide ion of the selenenylating reagent is also significant, bromide generally giving the best result. The method can be applied for the preparation of bicyclic nitrogen heterocycles such as pyrrolizidine derivatives and thienamycin skeleton.

Much attention has been paid to the methodology for the introduction of nitrogen functional groups to olefins accompanied by the addition of phenylseleno moiety, and many types of reactions have been reported in the literature.[1] This methodology has been utilized in the selective formation of allylic amides[1i,j] or conjugated nitroalkenes[1k,l,n] by oxidative elimination of the phenylseleno group.[2] On the other hand, the intramolecular version of this reaction has so far been limited to two types of reactions.[3,4] Reaction of organoselenium reagents with olefinic urethanes or 1-aza-4-cyclooctene affords pyrrolidine (or piperidine) derivatives[3a-d] or pyrrolizidine derivatives,[3e] respectively. We now report the reaction of benzeneselenenyl halides with N-alkenylamides to give nitrogen heterocycles in good yields. In our procedure, the substituent on nitrogen atom is an acyl group which can be utilized as carbon skeleton in the further elaboration of the ring. The application of our procedure for the synthesis of bicyclic β-lactams and pyrrolizidine derivatives is also reported.

Results and Discussion

By the reactions of N-(4-pentenyl)acetamide derivatives (1) with benzeneselenenyl halide, cyclization by the nitrogen atom proceeded to form nitrogen heterocycles bearing the (phenylseleno)methyl moiety (2) (Scheme I).

Scheme I



a, $R^1 = R^2 = H$
b, $R^1 = Me, R^2 = H$
c, $R^1 = Et, R^2 = H$
d, $R^1 = R^2 = Me$

Table I. Cyclization of 1c under Various Conditions[a]

entry	solvent (10 mL)	time, h	temp, °C	additive[b]	2c yield,[c] %
1	CH_3CN	2	20		58
2	CH_3CN	2	40		81
3	CH_3CN	2	20	SiO_2	68
4	CH_2Cl_2	2	20	SiO_2	68
5	benzene	2	20	SiO_2	53
6	THF	2	20	SiO_2	32
7	CH_3CN	24	20	SiO_2	94

[a] Carried out by using 1c (1 mmol), benzeneselenenyl chloride (1 mmol) in various solvent (10 mL). [b] The amount of silica gel (200 mesh) was 0.5 g. [c] Isolated yield by column chromatography.

Reaction conditions were briefly examined using **1c** as starting material, and the results are summarized in Table I. The yield of cyclization product was not satisfactory by the reaction of **1c** with benzeneselenenyl chloride in acetonitrile as solvent at 20 °C for 2 h (entry 1). After several trials (entries 2–6), we extended the reaction time to 24 h in the presence of silica gel[5] to obtain **2c** almost quantitatively (entry 7). It was found that the substituents on C_2 of the pentenyl group play an important role in this cyclization reaction. As summarized in Table II, the yields of a methyl-substituted **2b** were much better than those of unsubstituted **2a** (entries 1–5). By the introduction of ethyl or dimethyl substituents, the yields of cyclized products **2c,d** were further increased and nearly quantitative (entries 6–9).[6] Another important feature of Table

(1) (a) Reich, H. J.; Renga, J. M. *J. Org. Chem.* **1975**, *40*, 3313–3314. (b) Reich, H. J.; Renga, J. M.; Trend, J. E. *Tetrahedron Lett.* **1976**, 2217–2220. (c) Barton, D. H. R.; Britten-Kelly, M. R.; Ferreira, D. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1090–1110. (d) Denis, J. N.; Vicens, J.; Krief, A. *Tetrahedron Lett.* **1979**, 2697–2700. (e) Garratt, D. G.; Ryan, M. D.; Ujjainwalla, M. *Can. J. Chem.* **1979**, *57*, 2145–2153. (f) Garratt, D. G. *Ibid.* **1979**, *57*, 2180–2184. (g) Toshimitsu, A.; Aoai, T.; Uemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1980**, 1041–1042. (h) Bewick, A.; Coe, D. E.; Fuller, G. B.; Mellor, J. M. *Tetrahedron Lett.* **1980**, *21*, 3827–3828. (i) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1981**, 546–547. (j) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *J. Org. Chem.* **1981**, *46*, 4727–4733. (k) Hayama, T.; Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Chem. Lett.* **1982**, 1109–1112. (l) Hayama, T.; Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Tetrahedron Lett.* **1982**, *23*, 4733–4734. (m) Toshimitsu, A.; Uemura, S.; Okano, M.; Watanabe, N. *J. Org. Chem.* **1983**, *48*, 5246–5251. (n) Hayama, T.; Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Ibid.* **1984**, *49*, 3235–3236.

(2) Uemura, S.; Toshimitsu, A. *Bull. Inst. Chem. Res., Kyoto Univ.* **1984**, *62*, 105–123.

(3) (a) Clive, D. L. J.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Chem. Soc., Chem. Commun.* **1978**, 379–380. (b) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Sietz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704–3706. (c) Clive, D. L. J.; Farina, V.; Singh, A.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Org. Chem.* **1980**, *45*, 2120–2126. (d) Webb, R. R., II; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 1357–1360. (e) Wilson, S. R.; Sawicki, R. A. *J. Org. Chem.* **1979**, *44*, 287–291.

(4) (a) Quite recently, intramolecular amidoselenation of olefinic imidate to afford lactams has been reported: Toshimitsu, A.; Terao, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.*, in press. (b) After the preparation of this manuscript was almost completed, intramolecular aminoselenation of o-alkenylaniline derivatives was reported to be a useful tool for the synthesis of mytomycin congeners. Danishefsky, S.; Berman, E. M.; Ciufolini, M.; Etheredge, S. J.; Segmuller, B. E. *J. Am. Chem. Soc.* **1985**, *107*, 3891–3898.

(5) It has been reported that the addition of silica gel facilitates the cyclization of N-alkenylurethanes induced by benzeneselenenyl chloride (ref 3c).

(6) It has been well demonstrated that the substituents increase the population of conformation in which carbon–carbon or carbon–nitrogen bonds of N-pentenyl group are gauche to each other. As a result, nitrogen atom and episelenonium ion come nearer, and the yields of cyclization product are increased: Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701–704. Dale, J. *J. Chem. Soc.* **1963**, 93–111. Gschwend, H. W.; Lee, A. O. *J. Org. Chem.* **1973**, *38*, 2169–2175. Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033–1041.

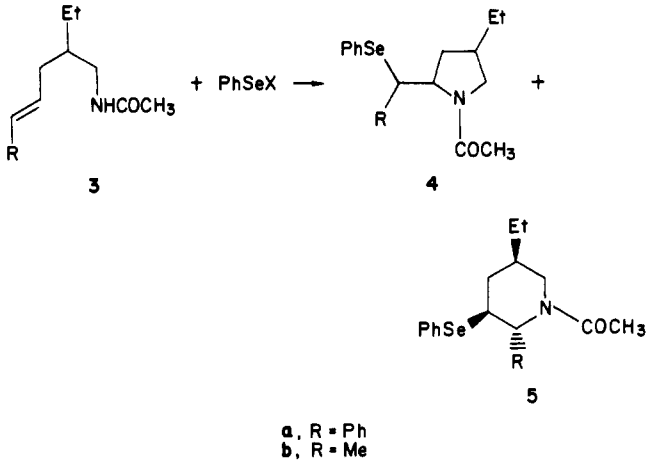
0022-3263/86/1951-1724$01.50/0

Table II. Cyclization of *N*-Pentenylacetamide Derivatives[a]

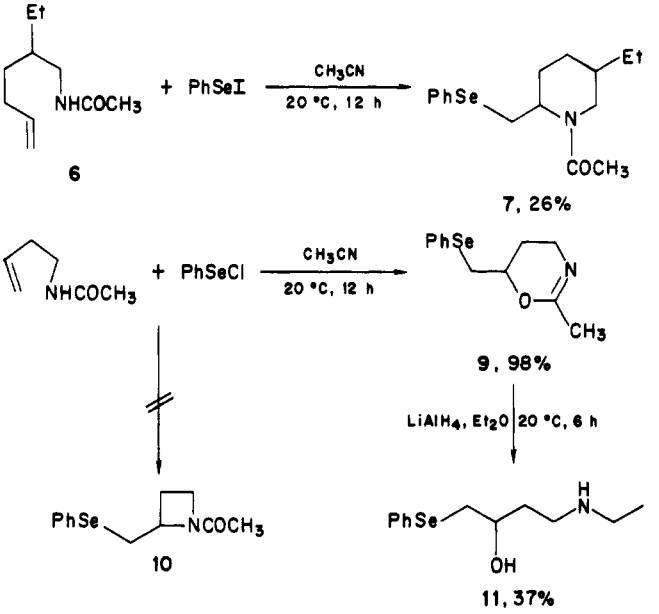
entry	substrate	X	time, h	additive[b]	product (ratio)	yield,[c] %
1	**1a**	Cl	24	SiO_2	**2a**	36
2	**1a**	Br	12		**2a**	66
3	**1a**	Br	12	SiO_2	**2a**	76
4	**1b**	Cl	24	SiO_2	**2b**	55
5	**1b**	Br	2		**2b**	83
6	**1c**	Cl	24	SiO_2	**2c**	94
7	**1c**	Br	20		**2c**	94
8	**1d**	Cl	24	SiO_2	**2d**	92
9	**1d**	Br	20		**2d**	98
10	**3a**	Cl	2		**5a**	79
11	**3a**	Br	6		**5a**	25
12	**3b**	Br	20		**4b** + **5b** (85:15)	76

[a] Carried out by the reaction of **1** or **3** (1 mmol) with benzeneselenenyl halide (1 mmol) in acetonitrile (10 mL) at 20 °C. [b] The amount of silica gel (200 mesh) was 0.5 g. [c] Isolated yield by column chromatography.

Scheme II



Scheme III



II is the effect of a gegen anion of the selenenylating reagent. The yields of **2a** and **2b** were insufficient when benzeneselenenyl chloride was used even in the presence of silica gel. By the use of benzeneselenenyl bromide, the yields were improved without the addition of silica gel and in much shorter reaction time (entries 1, 2, 4, and 5). In entries 6–9, where the yields of cyclization products were nearly quantitative, benzeneselenenyl bromide completed the reaction in a shorter time again without the addition of silica gel. These results clearly indicate that benzeneselenenyl bromide is a better reagent than the chloride in this cyclization reaction. As far as we know, this is the first example where benzeneselenenyl bromide gives better results than chloride in selenenylating reactions.[7] It was revealed by ^{13}C NMR spectra that **2b** and **2c** consisted of two isomers (ca. 60–70:40–30) which seem to be cis and trans with respect to two substituents on carbon atoms.

Neither the formation of a six-membered ring nor the cyclization by an oxygen atom was observed in a selenium-induced cyclization of **1**. However, the course of this cyclization reaction was changed by the introduction of a substituent on terminal olefinic carbon atom. Thus, by the reaction of a phenyl-substituted compound **3a** with benzeneselenenyl chloride, the six-membered nitrogen heterocycle **5a** was produced in 79% isolated yield (Scheme II). Formation of five-membered isomer (**4a**) was not observed. ^{13}C NMR of **5a** revealed that **5a** consists of one isomer, presumably three substituents on carbon atoms being on pseudoequatorial position. This observation agrees well with the results in the literature[3c,8] and may be ascribed to the thermodynamical stability of the cyclized products. Only in the case of **5a**, the yield was unsatisfactory (25%) when benzeneselenenyl bromide was used instead of chloride. This seems to be due to the presence of phenyl group which can stabilize the episelenonium ion intermediate, but the details are not yet clear. The ring size of cyclization product from **1** and **3a** can be rationalized in terms of regioselectivity of the addition which is a Markovnikov type.[9] In the case of methyl-substituted compound **3b**, regioselective addition can not be expected.[1e] By the reaction with benzeneselenenyl bromide, **3b** afforded a mixture of cyclization products in 76% total yield, five-membered **4b** being the major products (85% by liquid chromatography) (Scheme II). The compound **4b** was found to be a 1:1 mixture of stereoisomers which were separated by preparative TLC. The minor isomer (15%) seems to be **5b**; however, it could not be isolated and identified.

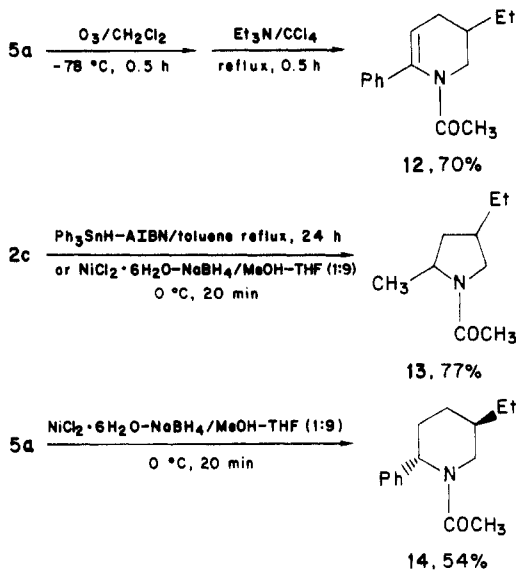
The length of alkenyl group in starting materials was changed to test the limitation of this cyclization reaction. When *N*-(2-ethylhex-5-enyl)acetamide (**6**) was used as starting material, the formation of nitrogen heterocycles was not observed when benzeneselenenyl chloride or

(7) We have already reported that benzeneselenenyl iodide shows a different reactivity from chloride or bromide: Toshimitsu, A.; Uemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1982**, 87–88.

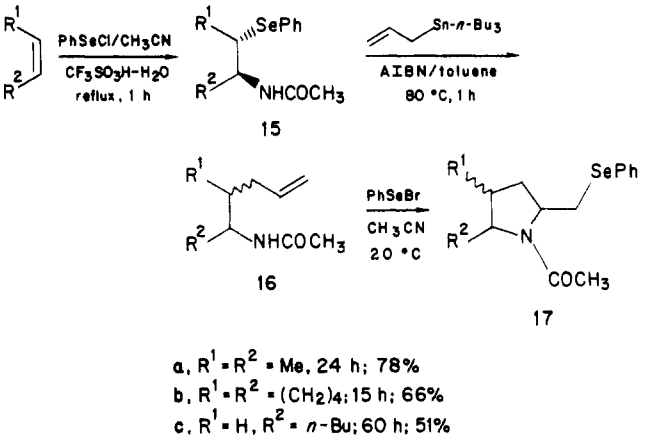
(8) Compare the following amidomercuration: Harding, K. E.; Marman, T. H. *J. Org. Chem.* **1984**, *49*, 2838–2840.

(9) Raucher, S. *J. Org. Chem.* **1977**, *42*, 2950–2951.

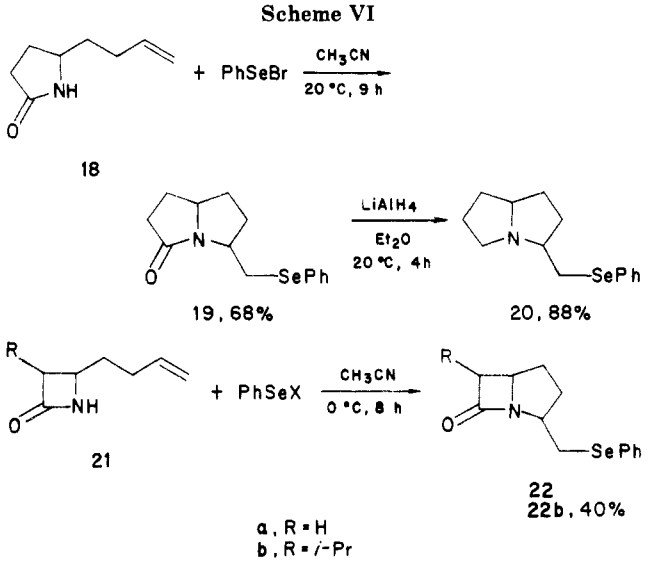
Scheme IV



Scheme V



Scheme VI



bromide was used as selenenylating reagent. By the reaction with benzeneselenenyl iodide[7] **6** afforded piperidine derivative **7**, although the yield was low (Scheme III). However, benzeneselenenyl iodide is not always a better reagent than chloride or bromide. For instance, in the case of **1c** where benzeneselenenyl bromide afforded the cyclization product **2c** in 94% yield, the yield of **2c** by benzeneselenenyl iodide was only 45%. In the case of *N*-3-butenylacetamide (**8**), cyclization did proceed by the reaction with benzeneselenenyl chloride. It should be noted that **8**, which possesses no substituents on carbon atoms between a double bond and a nitrogen atom, cyclized without the addition of silica gel. Moreover, the product was unstable to silica gel, and the isolated yield by alumina column chromatography was only 49%, although the ^1H NMR spectrum of the reaction mixture indicated the presence of a cyclized product in 97% yield. Lithium aluminum hydride reduction of the cyclized product afforded a linear secondary amine possessing a *vic*-hydroxy(phenylseleno)alkyl moiety (**11**) (Scheme III). This result clearly indicates that the cyclization by oxygen atom proceeded to afford a cyclic imidate derivative (**9**). Formation of the nitrogen heterocycle **10** was not observed.

We would like to describe here the results of our examination on oxidative and reductive elimination of the phenylseleno group from the nitrogen heterocycles thus prepared. By the ozonization[10] of piperidine derivative **5a**, an unsaturated compound (**12**) was produced in a good yield (Scheme IV). The double bond was found to be conjugated with the phenyl group providing the vinylic amide structure, and its regioisomer (allylic amide) was not detected in the products. We have previously reported that oxidative elimination of β-amidoalkyl phenyl selenides proceeded regioselectively "away" from the amide group to afford allylic amides.[1i,j] We now find that the amide group is less effective than phenyl group in determining the direction of selenoxide elimination.[11] Unworkable mixture of several products was produced by the oxidation of pyrrolidine derivative **2c** under similar conditions. As in the cases of β-amido selenides,[1j] the reductive removal of a phenylseleno group from pyrrolidine derivative **2c** was carried out by using triphenyltin hydride.[12] Recently reported nickel boride reduction[13] was also effective for the replacement of a phenylseleno group by a hydrogen atom to afford **13** in the same yield to that of triphenyltin hydride under much milder conditions (Scheme IV). The nickel boride reduction of **5a** afforded **14** as a single stereoisomer in moderate yield.

The intramolecular amidoselenation reaction described above was utilized in a three-step synthesis of pyrrolidine derivatives from olefins. As shown in Scheme V, olefins were converted to β-amidoalkyl phenyl selenides **15** by using our previously reported Ritter-type amidoselenation reaction.[1g,j] The phenylseleno group was substituted with an allyl group by a recently reported procedure[14] which used tributylallylstannane in the presence of azobisisobutyronitrile (AIBN). Intramolecular amidoselenation of *N*-alkenylamide **16** thus prepared would complete the transformation, and this was carried out by the reaction with benzeneselenenyl bromide in acetonitrile as solvent. The yields of the final step were listed in Scheme V for three representative substrates. Pyrrolidine derivatives

(10) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434–5447: Toshimitsu, A.; Owada, H.; Terao, K.; Uemura, S.; Okano, M. *J. Org. Chem.* **1984**, *49*, 3796–3800.

(11) It has been known that an amido group is less effective than a hydroxy group in determining the direction of selenoxide elimination: Liu, P. S.; Marquez, V. E.; Kelley, J. A.; Driscoll, J. S. *J. Org. Chem.* **1980**, *45*, 5225–5227.

(12) Clive, D. L. J.; Chittattu, G. J.; Farina, V.; Kiel, W. A.; Menchen, S. M.; Russell, C. G.; Singh, A.; Wong, C. K.; Curtis, N. J. *J. Am. Chem. Soc.* **1980**, *102*, 4438–4447.

(13) Back, T. G. *J. Chem. Soc., Chem. Commun.* **1984**, 1417–1418: See also ref 1c and: Barton, D. H. R.; Lusinchi, X.; Milliet, P. *Tetrahedron Lett.* **1982**, *23*, 4949–4952.

(14) Keck, G. E.; Yates, J. B. *J. Am. Chem. Soc.* **1982**, *104*, 5829–5831.

17 contained the carbon skeleton of olefinic compounds in their left half, but their configuration (R^1 and R^2) did not reflect the stereochemistry of the olefins. This is due to the second step of this transformation which was a radical reaction to afford a mixture of stereoisomers.

As another example of the utilization of the intramolecular amidoselenation reaction in organic synthesis, we tried the preparation of some bicyclic nitrogen heterocycles. The compound 5-(3-butenyl)pyrrolidin-2-one (**18**) is easily accessible by the combination of the recently reported "iodolactamization"[15] and the replacement of iodine by an allyl group using tributylallylstannane.[14] The reaction of **18** with benzeneselenenyl bromide led to the pyrrolizidine (**19**) in 68% yield (Scheme VI). The carbonyl group of **19** can be reduced to methylene by lithium aluminum hydride reduction. Thus, pyrrolizidine bearing a (phenylseleno)methyl substituent (**20**) was prepared in two steps starting from easily accessible compound by the use of intramolecular amidoselenation reaction. Another example is the construction of a bicyclic β-lactam having the carbapenem ring skeleton. The compound 4-(3-butenyl)azetidin-2-one (**21a**) was prepared by the literature method,[16] from the reaction of 1,5-hexadiene with chlorosulfonyl isocyanate followed by the reduction with sodium sulfite. The reaction of **21a** with benzeneselenenyl chloride, unfortunately, did not afford the expected bicyclic compound. Then, we introduced an isopropyl group into α-position of the carbonyl group of **21a** to obtain **21b**.[17] Intramolecular amidoselenation of **21b** proceeded by the reaction with benzeneselenenyl bromide in acetonitrile as solvent at 0 °C to afford a bicyclic β-lactam (**22b**) having thienamycin ring skeleton as shown in Scheme VI.

Experimental Section

IR spectra were recorded with a JASCO IR-810 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with JEOLCO JNM-FX-100 (100 MHz) and JEOLCO JNM-GX-400 (400 MHz) instruments on solutions in $CDCl_3$ with Me_4Si as an internal standard. Melting points were determined with a Shimadzu MM-2 micromelting point determination apparatus and were uncorrected. Liquid chromatographic analyses were carried out with a Waters HPLC system equipped with a 6000A solvent delivery system, a Model 44C absorbance detector (at 254 nm), and a Cosmosil 5SL packed column (4.6 mm × 100 mm). Mass spectra were measured on a JEOL JMS-DX mass spectrometer.

Benzeneselenenyl bromide and iodide were prepared by the reaction of diphenyl diselenide with 1 equiv of bromine and iodine, respectively, in dichloromethane as solvent. They were isolated by evaporation of solvent (in vacuo) and dried at 0.1 mmHg for ca. 15–60 min. Tetrahydrofuran (THF) was dried over benzophenone ketyl and was distilled just before use. A solution of *n*-butyllithium in hexane (1.5 M) was commercial product and used without purification. All other organic materials were commercial products and were purified before use by distillation. Aluminum trichloride was purified before use by sublimation. All other inorganic materials were commercial products and were used without purification.

N-4-Pentenylacetamide (**1a**) was prepared as follows. 4-Pentenonitrile was prepared from 1-bromo-4-butene and potassium cyanide (in ethylene glycol, 100 °C, 2 h) and then reduced with lithium aluminum hydride (in ether, 0 °C–room temperature, 3 h) and acetylated (with acetyl chloride in the presence of triethylamine, 0 °C–room temperature, 3 h). After the usual workup, column chromatography [silica gel (200 mesh), hexane–ethyl acetate (1:1) as eluant] afforded pure **1a**. **1a**: IR (film) 1650 cm^{-1}; ^1H NMR (100 MHz) δ 1.60 (quint, 2 H, J = 6.8 Hz), 1.98 (s, 3 H), 1.9–2.3 (m, 2 H), 3.26 (q, 2 H, J = 6.8 Hz), 4.99 (br d, 1 H, J = 10.0 Hz), 5.03 (br d, 1 H, J = 17.3 Hz), 5.81 (ddt, 1 H, J = 17.3, 10.0, 6.5 Hz), 5.6–6.0 (m, 1 H). Anal. Calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.96; H, 10.30; N, 11.06.

Substituted *N*-4-pentenylacetamide derivatives **1b–d** were prepared in the following method. The corresponding nitriles (R^1R^2CHCN) were deprotonated by lithium diisopropylamide (in THF, −78 to −65 °C, 2 h), and the produced carbanion was trapped with allyl bromide (−78 °C–room temperature, 12 h). Lithium aluminum hydride reduction and acetylation as described above afforded **1b–d**. Similarly, **3a**, **3b**, and **6** were prepared from butyronitrile by the use of cinnamyl bromide, crotyl bromide, and 4-bromo-1-butene, respectively.

***N*-(2-Methylpent-4-enyl)acetamide (1b)**: IR (film) 1650 cm^{-1}; ^1H NMR (100 MHz) δ 0.91 (d, 3 H, J = 6.8 Hz), 1.5–2.3 (m, 3 H), 1.98 (s, 3 H), 3.09 (dt, 1 H, J = 13.4, 6.4 Hz), 3.19 (dt, 1 H, J = 13.4, 6.4 Hz), 5.02 (br d, 1 H, J = 9.8 Hz), 5.21 (d, 1 H, J = 17.6 Hz), 5.4–5.8 (m, 1 H), 5.79 (ddd, 1 H, J = 17.6, 9.8, 6.8 Hz). Anal. Calcd for $C_8H_{15}NO$: C, 68.07; H, 10.71; N, 9.92. Found: C, 67.80; H, 10.57; N, 10.09.

***N*-(2-Ethylpent-4-enyl)acetamide (1c)**: IR (film) 1650 cm^{-1}; ^1H NMR (100 MHz) δ 0.91 (t, 3 H, J = 7.3 Hz), 1.2–1.7 (m, 3 H), 1.9–2.2 (m, 2 H), 1.98 (s, 3 H), 3.20 (t, 2 H, J = 6.1 Hz), 5.03 (d, 1 H, J = 9.3 Hz), 5.05 (d, 1 H, J = 17.6 Hz), 5.5–5.9 (m, 1 H), 5.80 (ddd, 1 H, J = 17.6, 9.3, 6.8 Hz). Anal. Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.30; H, 10.88; N, 8.93.

***N*-(2,2-Dimethylpent-4-enyl)acetamide (1d)**: IR (film) 1655 cm^{-1}; ^1H NMR (100 MHz) δ 0.89 (s, 6 H), 1.9–2.2 (m, 2 H), 2.00 (s, 3 H), 3.09 (d, 2 H, J = 6.8 Hz), 4.9–5.2 (m, 2 H), 5.6–6.1 (m, 2 H). Anal. Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.52; H, 11.06; N, 9.10.

***N*-(2-Ethyl-5-phenylpent-4-enyl)acetamide (3a)**: IR (film) 1650 cm^{-1}; ^1H NMR (100 MHz) δ 0.94 (t, 3 H, J = 6.8 Hz), 1.37 (quint, 2 H, J = 6.8 Hz), 1.57 (sept, 1 H, J = 6.6 Hz), 1.96 (s, 3 H), 2.22 (t, 2 H, J = 6.4 Hz), 3.24 (t, 2 H, J = 6.1 Hz), 5.55–5.85 (br s, 1 H), 6.19 (dt, 1 H, J = 15.6, 6.4 Hz), 6.41 (d, 1 H, J = 15.6 Hz), 7.0–7.4 (m, 5 H). Anal. (for parent amine) Calcd for $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.30; H, 10.05; N, 7.50.

***N*-(2-Ethylhex-4-enyl)acetamide (3b)**: IR (film) 1655 cm^{-1}; ^1H NMR (400 MHz) δ 0.89 (t, 3 H, J = 7.3 Hz), 1.31 (quint, 2 H, J = 7.3 Hz), 1.44–1.55 (m, 1 H), 1.66 (dd, 3 H, J = 5.9, 1.0 Hz), 1.97 (s, 3 H), 1.85–2.15 (m, 2 H), 3.16 (dt, 1 H, J = 13.7, 6.0 Hz), 3.20 (dt, 1 H, J = 13.7, 6.0 Hz), 5.38 (dtq, 1 H, J = 15.1, 6.8, 1.0 Hz), 5.46 (dq, 1 H, J = 15.1, 5.9 Hz), 5.7–5.85 (m, 1 H). Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.28. Found: C, 70.72; H, 11.38; N, 8.37.

***N*-(2-Ethylhex-5-enyl)acetamide (6)**: IR (film) 1650 cm^{-1}; ^1H NMR (100 MHz) δ 0.90 (t, 3 H, J = 6.8 Hz), 1.2–1.6 (m, 5 H), 1.8–2.2 (m, 2 H), 1.98 (s, 3 H), 3.20 (t, 2 H, J = 5.9 Hz), 4.96 (br d, 1 H, J = 9.8 Hz), 5.00 (br d, 1 H, J = 17.1 Hz), 5.4–5.9 (br s, 1 H), 5.81 (ddt, 1 H, J = 17.1, 9.8, 6.4 Hz). Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.28. Found: C, 70.88; H, 11.54; N, 8.45.

N-3-Butenylacetamide (**8**) was synthesized by the reduction of allyl cyanide by aluminum hydride (prepared in situ from aluminum chloride and 3 equiv of lithium aluminum hydride)[18] (in ether, room temperature, 3 h) followed by acetylation. **8**: IR (film) 1650 cm^{-1}; ^1H NMR (100 MHz) δ 1.97 (s, 3 H), 2.26 (q, 2 H, J = 6.7 Hz), 3.31 (q, 2 H, J = 6.5 Hz), 5.07 (br d, 1 H, J = 9.7 Hz), 5.09 (br d, 1 H, J = 17.5 Hz), 5.78 (ddt, 1 H, J = 17.5, 9.7, 6.6 Hz), 5.8–6.2 (br s, 1 H). Anal. Calcd for $C_6H_{11}NO$: C, 63.68; H, 9.80; N, 12.38. Found: C, 63.42; H, 9.79; N, 12.41.

Intramolecular Amidoselenation of 1c by the Reaction with Benzeneselenenyl Bromide. General Procedure. To a solution of **1c** (0.16 g, 1.0 mmol) in acetonitrile (5 mL) was added a solution of benzeneselenenyl bromide (0.24 g, 1.0 mmol) in the same solvent (5 mL), and the resulting solution was stirred at ambient temperature for 20 h. Saturated aqueous $NaHCO_3$ (20 mL) was added, and the products were extracted with CH_2Cl_2

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(17) Only one isomer (trans) was produced by this alkylation reaction: See, for example: Johnston, D. B.; Schmitt, S. M.; Bouffard, F. A.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 313–315. Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. G.; Bouffard, F. A. *Ibid.* **1980**, *102*, 6161–6163.

(18) Nystrom, R. F. *J. Am. Chem. Soc.* **1955**, *77*, 2544–2545.

(20 mL × 5). The organic layer was washed with brine, dried ($MgSO_4$), and evaporated to leave a yellow oil. Column chromatography [silica gel (200 mesh); hexane–ethyl acetate (1:1) as eluant] afforded diphenyl diselenide (0.09 g, 0.3 mmol, 6%) and *N*-acetyl-2-[(phenylseleno)methyl]-4-ethylpyrrolidine (**2c**) (0.29 g, 0.94 mmol, 94%) (a pale yellow oil, mixture of two isomers; ca. 60:40): IR (film) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 0.92 (t, 3 H, J = 7.3 Hz), 1.2–1.7 (m, 3 H), 1.86 (s, 3 H, major isomer), 1.96 (s, 3 H, minor isomer), 2.0–2.5 (m, 2 H), 2.7–3.7 (m, 4 H), 4.0–4.5 (m, 1 H), 7.1–7.4 (m, 3 H), 7.5–7.7 (m, 2 H); ^{13}C NMR δ (major isomer) 12.5 (q), 22.2 (q), 25.6 (t), 31.2 (t), 37.3 (t), 39.8 (d), 54.4 (t), 57.7 (d), 170.1 (s) [phenyl signals], (minor isomer) 12.5 (q), 22.2 (q), 26.2 (t), 29.2 (t), 35.3 (t), 38.7 (d), 53.8 (t), 57.7 (d), 170.1 (s) [phenyl signals]. Anal. Calcd for $C_{15}H_{21}NOSe$: C, 58.06; H, 6.82; N, 4.51. Found: C, 58.24; H, 6.76; N, 4.64.

Spectral data of other nitrogen heterocycles are as follows. All compounds are pale yellow oils.

***N*-Acetyl-2-[(phenylseleno)methyl]pyrrolidine (2a)**: IR (film) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 1.8–2.2 (m, 4 H), 1.95 (s, 3 H), 2.6–3.1 (m, 1 H), 3.3–3.6 (m, 3 H), 4.2–4.5 (m, 1 H), 7.1–7.4 (m, 3 H), 7.5–7.7 (m, 2 H). Anal. Calcd for $C_{13}H_{17}NOSe$: C, 55.32; H, 6.07; N, 4.96. Found: C, 55.13; H, 5.89; N, 5.13.

***N*-Acetyl-2-[(phenylseleno)methyl]-4-methylpyrrolidine (2b)** (mixture of two isomers; ca. 70:30): IR (film) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 1.03 (d, 3 H, J = 6.4 Hz, minor isomer), 1.05 (d, 3 H, J = 5.9 Hz, major isomer), 1.4–2.6 (m, 3 H), 1.85 (s, 3 H, major isomer), 1.94 (s, 3 H, minor isomer), 2.7–3.7 (m, 4 H), 4.1–4.5 (m, 1 H), 7.1–7.4 (m, 3 H), 7.5–7.7 (m, 2 H); ^{13}C NMR δ (major isomer) 16.7 (q), 22.8 (q), 31.3 (t), 32.8 (d), 39.6 (t), 55.7 (t), 57.4 (d), 169.0 (s) [phenyl signals], (minor isomer) 17.6 (q), 22.5 (q), 29.3 (t), 31.5 (d), 37.5 (t), 55.2 (t), 57.8 (d), 169.4 (s) [phenyl signals]. Anal. Calcd for $C_{14}H_{19}NOSe$: C, 56.76; H, 6.46; N, 4.73. Found: C, 56.67; H, 6.46; N, 4.88.

***N*-Acetyl-2-[(phenylseleno)methyl]-4,4-dimethylpyrrolidine (2d)**: IR (film) 1646 cm^{-1}; ^1H NMR (100 MHz) δ 0.97 (s, 3 H), 1.12 (s, 3 H), 1.5–2.2 (m, 2 H), 1.84 (s, 3 H), 3.0–3.6 (m, 4 H), 4.2–4.5 (m, 1 H), 7.1–7.4 (m, 3 H), 7.5–7.7 (m, 2 H); ^{13}C NMR δ 22.8 (q), 25.7 (q), 26.4 (q), 31.2 (t), 37.5 (s), 44.9 (t), 56.4 (d), 61.3 (t), 169.3 (s) [phenyl signals]. Anal. Calcd for $C_{15}H_{21}NOSe$: C, 58.06; H, 6.82; N, 4.51. Found: C, 57.70; H, 6.72; N, 4.75.

***N*-Acetyl-2-[1-(phenylseleno)ethyl]-4-ethylpyrrolidine (4b)**: one isomer of higher R_f value: IR (film) 1642 cm^{-1}; ^1H NMR (400 MHz) δ 0.92 (t, 3 H, J = 7.3 Hz), 1.32 (quint, 2 H, J = 7.3 Hz), 1.38 (d, 3 H, J = 7.3 Hz), 1.63 (s, 3 H), 2.11 (ddd, 1 H, J = 12.6, 7.3, 4.4 Hz), 2.2–2.5 (m, 1 H), 2.46 (ddd, 1 H, J = 12.6, 8.3, 6.8 Hz), 2.96 (dd, 1 H, J = 10.0, 7.3 Hz), 3.38 (dd, 1 H, J = 10.0, 7.3 Hz), 4.24 (ddd, 1 H, J = 8.3, 4.4, 3.9 Hz), 4.37 (dq, 1 H, J = 3.9, 7.3 Hz), 7.15–7.35 (m, 3 H), 7.5–7.65 (m, 2 H); ^{13}C NMR δ 12.4 (q), 19.4 (q), 22.7 (q), 27.1 (t), 32.8 (t), 39.5 (d), 42.6 (d), 53.8 (t), 61.7 (d), 169.9 (s) [phenyl signals]. Anal. Calcd for $C_{16}H_{23}NOSe$: C, 59.26; H, 7.15; N, 4.32. Found: C, 59.42; N, 7.05; N, 4.39. Another isomer of lower R_f value: IR (film) 1640 cm^{-1}; ^1H NMR (400 MHz) δ 0.96 (t, 3 H, J = 7.3 Hz), 1.36 (d, 3 H, J = 7.3 Hz), 1.49 (quint, 2 H, J = 7.3 Hz), 1.57 (s, 3 H), 1.61 (ddd, 1 H, J = 12.2, 11.7, 9.3 Hz), 1.95 (t of quint, 1 H, J = 11.7, 7.3 Hz), 2.17 (dt, 1 H, J = 12.2, 7.3 Hz), 2.96 (dd, 1 H, J = 11.7, 10.0 Hz), 3.46 (dd, 1 H, J = 10.0, 7.3 Hz), 4.18 (ddd, 1 H, J = 9.3, 7.3, 3.4 Hz), 4.58 (dq, 1 H, J = 3.4, 7.3 Hz), 7.15–7.3 (m, 3 H), 7.5–7.6 (m, 2 H); ^{13}C NMR δ 12.6 (q), 19.0 (q), 22.6 (q), 25.3 (t), 33.4 (t), 39.9 (d), 43.4 (d), 54.3 (t), 62.1 (d), 169.1 (s) [phenyl signals]. Anal. Calcd for $C_{16}H_{23}NOSe$: C, 59.26; H, 7.15; N, 4.32. Found: C, 58.86; H, 7.03; N, 4.35.

***N*-Acetyl-2-phenyl-3-(phenylseleno)-5-ethylpiperidine (5a)**: IR (film) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 0.91 (t, 3 H, J = 7.1 Hz), 1.2–1.9 (m, 4 H), 2.04 (s, 3 H), 2.0–2.4 (m, 1 H), 3.41 (dd, 1 H, J = 13.4, 4.9 Hz), 3.6–4.1 (m, 2 H), 5.1–5.3 (m, 1 H), 7.1–7.4 (m, 8 H), 7.4–7.6 (m, 2 H); ^{13}C NMR δ 11.8 (q), 21.6 (q), 27.4 (t), 32.4 (t), 35.2 (d), 43.3 (d), 43.6 (t), 60.3 (d), 170.8 (s) [phenyl signals]. Anal. Calcd for $C_{21}H_{25}NOSe$: C, 65.27; H, 6.52; N, 3.62. Found: C, 64.92; H, 6.59; N, 3.46.

***N*-Acetyl-2-[(phenylseleno)methyl]-5-ethylpiperidine (7)** (mixture of almost equal amount of two isomers): IR (film) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 0.8–1.1 (m, 3 H), 1.1–2.3 (m, 7 H), 1.86 and 2.07 (s, 3 H), 2.5–3.4 (m, 3 H), 3.4–4.1 (m, 1 H), 4.4–5.1 (m, 1 H), 7.1–7.4 (m, 3 H), 7.4–7.6 (m, 2 H); ^{13}C NMR δ (*two signals overlapping) 11.1* (q), 21.5 (q), 21.9 (q), 22.9 (t), 25.2 (t), 26.7 (t), 27.0* (t), 27.6 (t), 28.1 (t), 29.1 (t), 37.6 (d), 38.4 (d), 41.7 (t), 47.3 (t), 47.5 (d), 53.4 (d), 169.0* (s) [phenyl signals]. Anal. Calcd for $C_{16}H_{23}NOSe$: C, 59.25; H, 7.15; N, 4.32. Found: C, 59.58; H. 7.08; N, 4.52.

The Reaction of *N*-3-Butenylacetamide (8) with Benzeneselenenyl Chloride. To a solution of **8** (0.11 g, 1.0 mmol) in acetonitrile (5 mL) was added a solution of benzeneselenenyl chloride (0.20 g, 1.0 mmol) in acetonitrile (5 mL), and the resulting solution was stirred at ambient temperature for 12 h. Saturated aqueous $NaHCO_3$ (20 mL) was added, and the products were extracted with CH_2Cl_2 (20 mL × 5). The organic layer was washed with brine (20 mL), dried ($MgSO_4$), and evaporated in vacuo to leave a yellow oil (0.27 g, after complete removal of solvents). ^1H NMR measurement of this oil revealed that the ratio (in weight) of 2-methyl-6-[(phenylseleno)methyl]-1-oxa-3-azacyclohex-2-ene (**9**) to diphenyl diselenide is 97:3, indicating that the amount of **9** is 0.26 g (0.98 mmol, 98%). In one experiment, this oil was subjected to column chromatography [aluminum oxide, Woelm B (type W 200) activity grade V, hexane–ethyl acetate (1:1) as eluant] to afford pure **9** as a yellow oil (0.13 g, 0.49 mmol). **9**: IR (film) 1690 cm^{-1}; ^1H NMR (100 MHz) δ 1.3–2.2 (m, 2 H), 1.85 (s, 3 H), 2.97 (dd, 1 H, J = 12.7, 6.8 Hz), 3.15 (dd, 1 H, J = 12.7, 5.9 Hz), 3.2–3.4 (m, 2 H), 4.19 (dddd, 1 H, J = 9.3, 6.8, 5.9, 3.4 Hz), 7.1–7.3 (m, 3 H), 7.4–7.6 (m, 2 H); ^{13}C NMR δ 21.5 (q), 26.3 (t), 32.2 (t), 42.1 (t), 73.8 (d), 157.5 (s) [phenyl signals]. In another experiment, this oil was subjected to lithium aluminum hydride reduction. Thus, to a stirred suspension of lithium aluminum hydride (0.076 g, 2.0 mmol) in ether (5 mL) was added a solution of the oil in ether (5 mL) dropwise at 0 °C, and the resulting suspension was stirred at ambient temperature for 6 h. Then 5 N aqueous NaOH was added dropwise until the precipitate turned from gray to white and granular. The precipitates were filtrated and washed with ether, and the organic layer was washed with brine, dried ($MgSO_4$), and evaporated. Column chromatography of the residual oil [aluminum oxide, Woelm B (type W 200) activity grade V, hexane–ethyl acetate (2:1) as eluant] afforded [3-hydroxy-4-(phenylseleno)butyl]ethylamine (**11**) (0.10 g, 0.37 mmol, 38% from **9**): mp 65–66 °C [from hexane–CH_2Cl_2 (ca. 10:1)]: IR (KBr disk) 3420, 3260 cm^{-1}; ^1H NMR (100 MHz) δ 1.08 (t, 3 H, J = 7.1 Hz), 1.2–2.1 (m, 2 H), 2.3–3.4 (m, 8 H), 4.00 (ddt, 1 H, J = 9.0, 2.9, 6.1 Hz), 7.1–7.3 (m, 3 H), 7.4–7.6 (m, 2 H); ^{13}C NMR δ 15.0 (q), 34.2 (t), 35.5 (t), 43.8 (t), 48.1 (t), 72.5 (d) [phenyl signals]. Anal. Calcd for $C_{12}H_{19}NSe$: C, 52.94; H, 7.03; N, 5.14. Found: C, 53.05; H, 6.92; N, 5.16.

Oxidative Elimination of 5a to *N*-Acetyl-2-phenyl-5-ethyl-2,3-dehydropiperidine (12). Ozonization of **5a** (0.19 g, 0.5 mmol) was carried out in CH_2Cl_2 (10 mL) at −78 °C. The cold solution was then added to refluxing CCl_4 (25 mL) containing triethylamine (5 mmol) as reported in the literature.[10] After the evaporation of the solvents, column chromatography [silica gel, hexane–ethyl acetate (5:1) as eluant] afforded **12** (0.080 g, 0.35 mmol, 70%): IR (film) 1638, 1668 cm^{-1}; ^1H NMR (100 MHz) δ 0.98 (t, 3 H, J = 7.1 Hz), 1.2–1.5 (m, 2 H), 1.64 (br s, 3 H), 1.7–2.1 (m, 2 H), 2.40 (dt, 1 H, J = 3.7, 10.9 Hz), 2.94 (dd, 1 H, J = 12.0, 9.6 Hz), 4.48 (br d, 1 H, J = ca. 12 Hz), 5.53 (t, 1 H, J = 3.7 Hz), 7.32 (s, 5 H); ^{13}C NMR δ 11.4 (q), 24.9 (q), 26.9 (t), 30.7 (t), 36.7 (d), 47.9 (t), 118.6 (d), 125.5* (d), 127.7 (d), 128.7* (d), 139.5 (s), 140.4 (s), 171.2 (s); high-resolution mass spectrum, M^+ calcd for $C_{15}H_{19}NO$ 229.1466, found 229.1496.

Reductive Removal of Phenylseleno Group from 2c and 5a to *N*-Acetyl-2-methyl-4-ethylpyrrolidine (13) and *N*-Acetyl-2-phenyl-5-ethylpiperidine (14). The reactions of **2c** and **5a** with triphenyltin hydride[12] or nickel boride[13] were carried out in the reported procedure. The products were **13** and **14**, respectively. Their characterization is as follows. **13**:[19] IR (film) 1643 cm^{-1}; ^1H NMR (100 MHz) δ 0.8–1.1 (m, 3 H), 1.1–1.8 (m, 6 H), 1.99, 2.01, 2.03, 2.07 (s, 3 H), 1.9–2.6 (m, 1 H) 2.8–3.3 (m, 2 H), 3.5–3.8 (m, 1 H), 3.8–4.4 (m, 1 H); high-resolution mass spectrum, M^+ calcd for $C_9H_{17}NO$ 155.1310, found 155.1324. **14**: IR (film) 1642 cm^{-1}; ^1H NMR (100 MHz) (measured at 50 °C) δ 0.94 (t, 3 H, J = 6.8 Hz), 1.2–1.8 (m, 5 H), 1.9–2.2 (m, 2 H), 2.11

(19) Cottin, H. *Bull. Soc. Chim. Fr.* **1966**, 2729–2733.

(s, 3 H), 3.09 (dd, 1 H, J = 13.7, 2.4 Hz), 3.92 (br d, 1 H, J = 13.7 Hz), 5.42 (br s, 1 H), 7.1–7.5 (m, 5 H); ^{13}C NMR (measured at 50 °C) δ 12.1 (q), 21.4 (q), 23.9 (t), 24.3 (t), 26.1 (t), 35.6 (d), 43.6 (t), 54.1 (d), 126.2* (d), 126.8 (d), 128.7* (d), 140.2 (s), 170.5 (s); high-resolution mass spectrum, M^+ calcd for $C_{15}H_{21}NO$ 231.1623, found 231.1643.

Synthesis of *N*-Acetyl-2,3-dimethyl-5-[(phenylseleno)methyl]pyrrolidine (17a). Amidoselenation of *cis*- and *trans*-2-butene[1j] and the following replacement of the phenylseleno group by allyl group[14] were carried out in the reported procedures. As the olefinic amide **16a** thus prepared could not be separated from the remaining β-amido selenide **15a** by column chromatography, the mixture was subjected to the next intramolecular amidoselenation reaction. To a solution of a mixture of **15a** and **16a** (0.121 g) in acetonitrile (2 mL) was added a solution of benzeneselenenyl bromide (0.071 g, 0.3 mmol) in acetonitrile (3 mL), and the resulting solution was stirred at ambient temperature for 12 h. After the workup as described above, column chromatography [silica gel, hexane–ethyl acetate (2–1:1) as eluant] afforded pure **17a** (0.051 g, 0.16 mmol) and **15a** (0.088 g). This result indicates that the amount of **16a** was (at most) 0.033 g (0.21 mmol), and the yield of **17a** from **16a** was at least 78%. **17a** (mixture of four isomers): IR (film) 1638 cm^{-1}; ^{1}H NMR (100 MHz) δ 0.8–1.4 (m, 6 H), 1.4–2.1 (m, 3 H), 2.03, 2.05, 2.08 (s, 3 H), 2.1–3.1 (m, 2 H), 3.4–4.4 (m, 2 H), 7.1–7.4 (m, 3 H), 7.4–7.7 (m, 2 H). Anal. Calcd for $C_{15}H_{21}NOSe$: C, 58.06; H, 6.82; N, 4.51. Found: C, 58.40; H, 6.85; N, 4.66.

7-Acetyl-8-[(phenylseleno)methyl]-7-azabicyclo[4.3.0]nonane (17b) (mixture of two isomers, ca. 68:32): IR (film) 1635 cm^{-1}; ^{1}H NMR (100 MHz) δ 1.89 (s, 3 H, major isomer), 2.02 (s, 3 H, minor isomer); ^{13}C NMR δ (major isomer) 20.2 (q), 24.5 (t), 25.0 (t), 29.7 (t), 31.4 (t), 32.5 (t), 35.6 (t), 45.9 (d), 57.5 (d), 64.4 (d), 169.1 (s) [phenyl signals], (minor isomer) 22.5 (q), 23.8 (t), 25.7 (t), 28.6 (t), 29.1 (t), 30.6 (t), 35.2 (t), 45.9 (d), 56.6 (d), 59.3 (d), 171.6 (s) [phenyl signals]. Anal. Calcd for $C_{17}H_{23}NOSe$: C, 60.71; H, 6.89; N, 4.16. Found: C, 60.32; H, 7.16; N, 4.16.

***N*-Acetyl-2-butyl-5-[(phenylseleno)methyl]pyrrolidine (17c)** (mixture of two isomers, ca. 65:35): IR (film) 1623 cm^{-1}; ^{1}H NMR (100 MHz) δ 0.8–1.0 (m, 3 H), 1.1–1.6 (m, 6 H), 1.6–1.9 (m, 2 H), 2.01 (s, 3 H), 1.9–2.2 (m, 2 H), 2.6–3.9 (m, 1 H), 3.5–4.1 (m, 2 H), 4.1–4.4 (m, 1 H), 7.1–7.4 (m, 3 H), 7.5–7.7 (m, 2 H); ^{13}C NMR δ (major isomer) 14.0 (q), 22.5 (q), 22.6 (t), 27.0 (t), 27.8 (t), 28.4 (t), 29.0 (t), 34.8 (t), 57.3 (d), 59.8 (d), 169.4 (s) [phenyl signals], (minor isomer) 14.0 (q), 22.6 (t), 22.7 (q), 26.1 (t), 28.2 (t), 29.0 (t), 31.8 (t), 32.1 (t), 58.2 (d), 59.1 (d), 168.7 (s) [phenyl signals]. Anal. Calcd for $C_{17}H_{25}NOSe$: C, 60.35; H, 7.45; N, 4.14. Found: C, 60.49; H, 7.36; N, 4.18.

Synthesis of 2-[(Phenylseleno)methyl]-1-azabicyclo[3.3.0]octane (20). Iodolactamization of 4-pentenamide[15] and a subsequent replacement of iodine by allyl group[14] were carried out by the reported procedures to afford **18**. To a solution of **18** (0.055 g, 0.40 mmol) in acetonitrile (2 mL) was added a solution of benzeneselenenyl bromide (0.104 g, 0.44 mmol) in acetonitrile (3 mL) at 0 °C under nitrogen atmosphere, and the resulting solution was stirred at ambient temperature for 48 h. After the workup as described above, column chromatography [silica gel; hexane–ethyl acetate (1:1) as eluant] afforded 8-[(phenylseleno)methyl]-1-azabicyclo[3.3.0]octan-2-one (**19**) (0.080 g, 0.27 mmol, 68%). **19**: IR (film) 1680 cm^{-1}; ^{13}C NMR δ 28.2 (t), 28.5 (t), 29.4 (t), 34.4 (t), 37.4 (t), 53.1 (d), 64.4 (d), 126.7 (d), 129.1* (d), 129.8 (s), 131.9* (d), 172.2 (s). The reduction of **19** (0.055 g, 0.19 mmol) was carried out with lithium aluminum hydride (0.057 g, 1.5 mmol) as described above (in ether, room temperature, 4 h) to afford **20** (0.044 g, 0.16 mmol, 82%). **20**: ^{1}H NMR (400 MHz) δ 1.33–1.63 (m, 3 H), 1.75–1.97 (m, 4 H), 2.12 (ddt, 1 H, J = 12.2, 3.4, 7.8 Hz), 2.53 (dt, 1 H, J = 6.7, 9.4 Hz), 2.86 (ddd, 1 H, J = 8.8, 6.4, 2.4 Hz), 2.98 (dt, 1 H, J = 3.4, 10.6 Hz), 3.23–3.32 (m, 2 H), 3.52 (tt, 1 H, J = 7.7, 5.7 Hz), 7.19–7.28 (m, 3 H), 7.49–7.62 (m, 2 H); ^{13}C NMR δ 26.0 (t), 29.3 (t), 29.3 (t), 31.9 (t), 32.2 (t), 45.9 (t), 62.8 (d), 64.8 (d), 126.7 (d), 129.0* (d), 130.7 (s), 132.3* (d). Anal. Calcd for $C_{14}H_{19}NSe$: C, 60.00; H, 6.83; N, 5.00. Found: C, 59.94; H, 6.77; N, 5.12.

Synthesis of 2-[(Phenylseleno)methyl]-6-isopropyl-1-azabicyclo[3.2.0]heptan-7-one (22b). 4-(3-Butenyl)azetidin-2-one (**21a**), prepared by the reported procedure,[16] was lithiated by *n*-butyllithium[20] (in THF, 0 °C, 0.5 h) and then alkylated by isopropyl iodide (0 °C, 4 H) to afford 3-isopropyl-4-(3-butenyl)azetidin-2-one (**21b**) in 38% yield. **21b**: IR (film) 3250, 1750 cm^{-1}; ^{1}H NMR (100 MHz) δ 0.99 (d, 3 H, J = 6.4 Hz), 1.07 (d, 3 H, J = 6.4 Hz), 1.6–1.9 (m, 2 H), 1.9–2.3 (m, 3 H), 2.57 (ddd, 1 H, J = 7.8, 2.0, 1.5 Hz), 3.37 (dt, 1 H, J = 2.0, 6.4 Hz), 5.01 (br d, 1 H, J = 17.1 Hz), 5.05 (br d, 1 H, J = 10.3 Hz), 5.82 (ddt, 1 H, J = 17.1, 10.3, 6.4 Hz), 6.35 (br s, 1 H). Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37. Found: C, 71.42; H, 10.12; N, 8.27. To a solution of **21b** (0.084 g, 0.5 mmol) in acetonitrile (6 mL) was added a solution of benzeneselenenyl bromide (0.13 g, 0.55 mmol) in acetonitrile (4 mL) at 0° C, and the resulting solution was stirred at the same temperature for 8 h. After the workup as described above, column chromatography [silica gel; hexane–ethyl acetate (10:1) as eluant] afforded **22b** (0.065 g, 0.2 mmol, 40%). **22b**: IR (film) 1747 cm^{-1}; ^{1}H NMR δ 0.97 (d, 3 H, J = 7.3 Hz), 1.04 (d, 3 H, J = 7.3 Hz), 1.5–2.4 (m, 5 H), 2.64 (dd, 1 H, J = 7.8, 2.0 Hz), 3.02 (dd, 1 H, J = 12.2, 8.8 Hz), 3.3–3.6 (m, 2 H), 3.80 (dd, 1 H, J = 12.2, 4.9 Hz), 7.1–7.4 (m, 3 H), 7.4–7.6 (m, 2 H); ^{13}C NMR δ 20.0 (q), 20.4 (q), 28.0 (d), 28.6 (t), 29.1 (t), 36.7 (t), 56.8 (d), 61.5 (d), 63.5 (d), 127.1 (d), 129.1* (d), 130.0 (s), 132.7* (d), 176.6 (s). Anal. Calcd for $C_{16}H_{21}NOSe$: C, 59.62; H, 6.57; N, 4.35. Found: C, 59.41; H, 6.53; N, 4.30.

Registry No. **1a**, 54385-21-6; **1b**, 101347-52-8; **1c**, 101347-53-9; **1d**, 101347-54-0; **2a**, 101347-55-1; *cis*-**2b**, 101347-56-2; *trans*-**2b**, 101347-57-3; *cis*-**2c**, 101347-58-4; *trans*-**2c**, 101347-59-5; **2d**, 101347-60-8; **3a**, 101347-61-9; **3b**, 101347-62-0; **4b**, 101347-63-1; **5a**, 101347-64-2; **6**, 101347-65-3; *cis*-**7**, 101347-66-4; *trans*-**7**, 101347-67-5; **8**, 25420-64-8; **9**, 101347-68-6; **11**, 101347-69-7; **12**, 101347-70-0; *cis*-**13**, 101347-71-1; *trans*-**13**, 101347-72-2; **14**, 101347-73-3; (*R**,*S**)-**16a**, 101347-74-4; (*R**,*R**)-**16a**, 101347-75-5; *trans*-**16b**, 101347-76-6; *cis*-**16b**, 101347-77-7; **16c**, 101347-78-8; **17a** (isomer 1), 101347-79-9; **17a** (isomer 2), 101347-80-2; **17a** (isomer 3), 101347-81-3; **17a** (isomer 4), 101347-82-4; **17b**, 101347-83-5; *cis*-**17c**, 101347-84-6; *trans*-**17c**, 101347-85-7; **18**, 101347-86-8; **19**, 101347-87-9; **20**, 101347-88-0; **21a**, 74373-13-0; **21b**, 101347-89-1; **22b**, 101347-90-4; PhSeI, 81926-79-6; 2-ethyl-5-phenylpent-4-enylamine, 101347-91-5; 4-pentenonitrile, 592-51-8; 1-bromo-3-butene, 5162-44-7; propanenitrile, 107-12-0; butanenitrile, 109-74-0; 2-methylpropanenitrile, 78-82-0; allyl bromide, 106-95-6; cinnamyl bromide, 4392-24-9; crotyl bromide, 4784-77-4; allyl cyanide, 109-75-1; benzeneselenenyl bromide, 34837-55-3; benzeneselenenyl chloride, 5707-04-0; isopropyl iodide, 75-30-9.

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