Intramolecular amidoselenation of N-alkenylamides: Formation of nitrogen heterocycles

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Intramolecular Amidoselenation of *N*-Alkenyl Imidates to *N*-Heterocycles

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The reactions of *N*-alkenyl imidates with benzeneselenenyl chloride and bromide in chloroform at ambient temperature afford pyrrolidine and piperidine derivatives having a phenylseleno moiety in good to excellent yields under neutral conditions. The key step of this new reaction consists of an intramolecular carbon–nitrogen bond formation and a simultaneous carbon–oxygen bond fission.

Organoselenium-induced cyclization of olefinic urethanes[1] or 1-azacyclo-oct-4-ene[2] has been reported to produce pyrrolidine or piperidine derivatives. We have also disclosed the reactions of *N*-alkenylacetamides[3] with organoselenium reagents which afford *N*-heterocycles. However, these cyclization reactions are carried out under acidic conditions owing to the formation of hydrogen halide as a side-product during the reaction; these conditions being undesirable in some cases[4] for organic synthesis. For example, when we tried the reaction of *N*-(2-trimethylsiloxymethylpent-4-enyl)acetamide **(1)** with
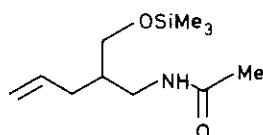
(1)

benzeneselenenyl bromide, a clean reaction was not observed.† In order to overcome this difficulty, we developed a new type of amidoselenation reaction which utilizes an imidate as the synthetic equivalent to an amide group,[5] a working hypothesis illustrated in Scheme 1.
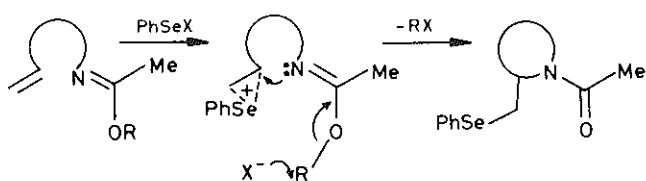
Scheme 1.

If it worked the reaction could then be carried out under neutral conditions since an alkyl halide is formed as the side-product in this case. In the event, we obtained satisfactory results, the details of which are reported here.

Results and Discussion

When benzeneselenenyl chloride was added to a solution of ethyl *N*-(2-ethylpent-4-enyl)acetimidate‡ **(2a)** in chloroform and the resulting solution was stirred at ambient temperature for 3 days, *N*-acetyl-4-ethyl-2-(phenylselenomethyl)pyrrolid-

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† When the reaction of compound (1) with benzeneselenyl bromide was complete, it was observed by ^{1}H n.m.r. spectroscopy that the trimethylsilyl group had disappeared, although the components of the reaction mixture could not be identified.

‡ *N*-alkenyl imidates are easily prepared by the condensation of olefinic amines with alkyl acetimidate hydrochlorides.[12]

Table 1. Amidoselenation of compounds **(2a)** or **(2b)** leading to **(3a)**[a]

Entry	Sub-strate	Selenium	Equiv.	Time[b] (h)	Temp. (°C)	Yield[c] (%)
1	(2a)	PhSeCl	1.0	72	20	41[d]
2	(2a)	PhSeCl	1.0	6	62	42
3	(2b)	PhSeCl	1.0	18	20	64
4	(2b)	PhSeBr	1.0	3	20	75
5	(2b)	PhSeI	1.0	5	20	13
6	(2b)	PhSeBr	1.1	12	20	88

[a] Carried out by using the imidate (1.0 mmol) in chloroform (100 ml). [b] Determined by t.l.c. [c] Isolated yield by column chromatography on SiO_2. [d] The effect of the solvent was examined under these conditions. The yields are as follows: 0% in acetonitrile, 19% in benzene, 12% in THF, and 24% in dichloromethane.

ine[3] **(3a)** was produced in 41% yield *via* the Markovnikov type addition of the phenylseleno moiety upon the carbon–carbon double bond (Scheme 2). The reaction was carried out at a concentration of 0.01M of the reactant, as the yield of **(3a)** was inferior at higher concentrations due to side-reactions. Typical results are summarized in Table 1 together with the various reaction conditions employed.

(2)a; R = Et
  b; R = Me

(3a)
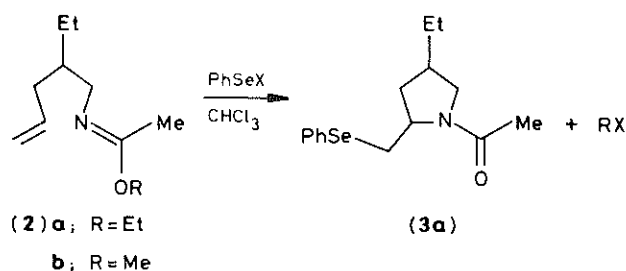
Scheme 2.

As shown in the Table, compound **(2b)** was revealed to be a better starting compound for **(3a)** and benzeneselenenyl bromide§ was most effective for this transformation.

In the cases of alkenyl amides,[3] we have already found that the introduction of an alkyl substituent on carbon atoms between the nitrogen atom and the double bond facilitates the cyclization. Thus, 66 and 94% yields of the cyclized product was obtained from compounds (**5a** and **b**), respectively. In view of this, we also investigated how the presence of a substituent on the alkyl chain of *N*-alkenyl imidates affects the yield. The results are shown in Table 2.

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§ Benzeneselenenyl bromide is known to be a superior reagent for effecting intramolecular amidoselenations of *N*-alkenylamides.[3]
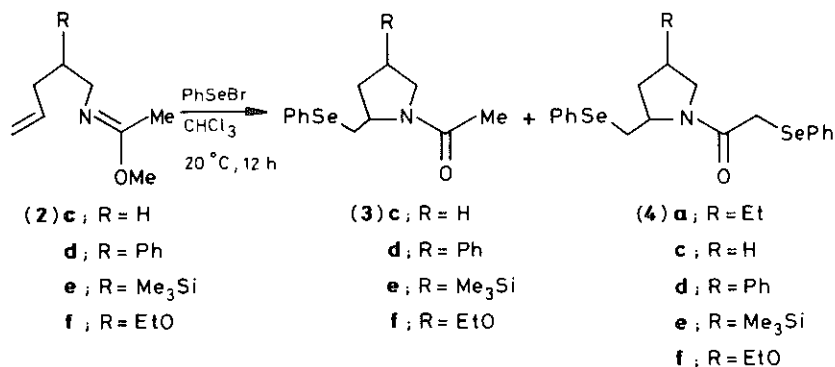
Table 2. Amidoseleniation of compounds (2b—f) leading to (3) and (4)[a]

Entry	Substrate (2)	Products and yield (%)[b]	
		(3)	(4)
1	(2b)	(3a) 88	(4a) Trace[c]
2	(2c)	(3c) 75	(4c) 11
3	(2d)	(3d) 66	(4d) 12
4	(2e)	(3e) 83	(4e) 0[c]
5	(2f)	(3f) 62	(4f) 14

[a] N-Alkenyl imidate (1.0 mmol), PhSeBr (1.1 mmol), and chloroform (100 ml) were used. [b] Isolated yield by column chromatography on SiO_2. [c] Determined by t.l.c.
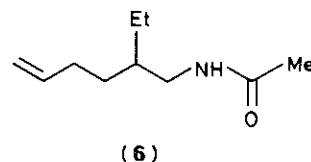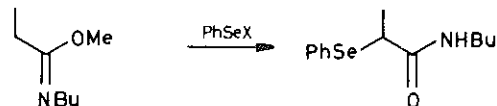

(5) a; R = H

b; R = Et
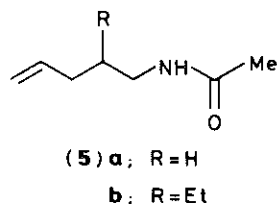
In the case of compound (2b) a very good yield of N-heterocyclic compound (3a) (88%) was obtained as expected, while even from (2c), which has no substituent on the alkyl chain, 75% of the expected compound (3c) was formed (Entries 1 and 2). This fact shows that the substituent effect upon the product yield is smaller in case of N-alkenyl imidate than that of N-alkenyl amide. Careful examination of the products from imidates (2b—f) revealed the presence of a small amount of compound (4a—f) which has a phenylseleno moiety on the α-carbon of the carbonyl group, besides the expected pyrrolidines (3a—f) (Entries 2, 3, and 5; Scheme 3). The detailed mechanism of the side-reaction for compound (4) is not clear.*
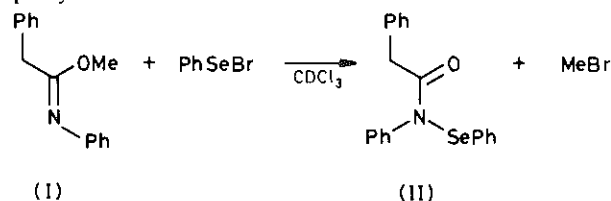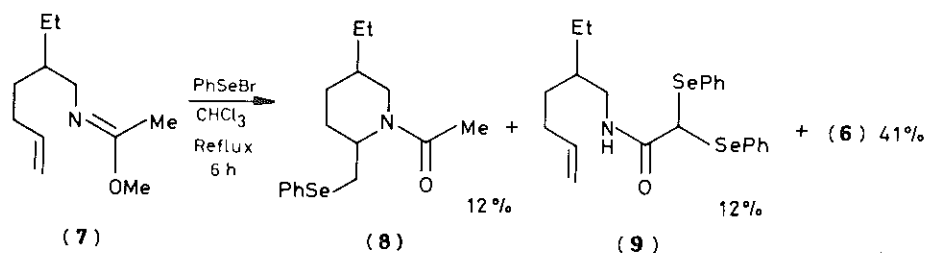

(6)

When the reaction was applied to an imidate possessing a cyclic alkene (10), two products were isolated in 33 and 37% yield by column chromatography. Each product was revealed to be a mixture of two compounds by ^{13}C n.m.r. spectroscopy. Lithium aluminium hydride reduction of each product, however, afforded a single product indicating that these two compounds are the conformers concerning the acetyl substituent on nitrogen atom. We, have tentatively assigned these products as compounds (11a and b) differing only in the configuration of the ethyl substituent, those being formed by the attack of the nitrogen of the imidate (10) upon the vinylic C-2. However, structure of (12), which may be formed by the attack on the vinylic C-3 cannot be completely excluded. The configuration of the phenylseleno group in (11a and b) was assumed as shown in Scheme 5, based on the *trans*-stereoselectivity of amidoseleniation reactions.[6]

In the case where an imidate possessing cinnamyl moiety (13a, b) was used as the starting compound, a piperidine derivative (14) was produced with a very high stereoselectivity in 30—40% yield † by the same Markovnikov type of reaction, as in the cases of imidates possessing a terminal alkene (Scheme 6). All efforts to improve the product yield were unsuccessful.
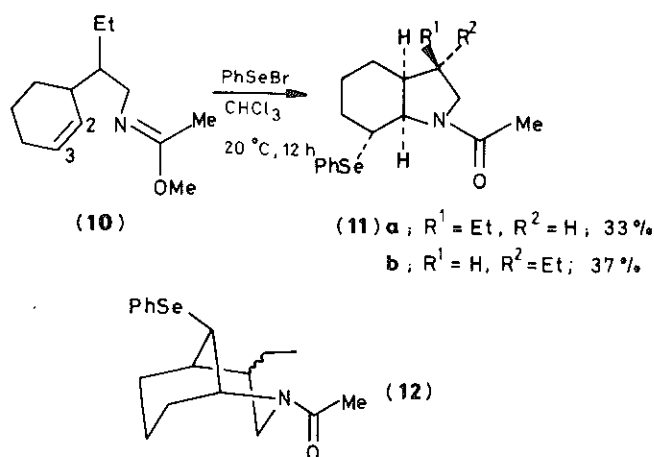
Intramolecular amidoseleniation procedures known so far have severe limitations owing to acidic reaction conditions, which are usually incompatible with a large number of important functional groups including protecting groups.[4] For example, it was found that the deprotection[7] of alcohols occurred easily when the trimethylsilyl ether (16) was

(2)c; R = H

d; R = Ph

e; R = Me$_3$Si

f; R = EtO

(3)c; R = H

d; R = Ph

e; R = Me$_3$Si

f; R = EtO

(4)a; R = Et

c; R = H

d; R = Ph

e; R = Me$_3$Si

f; R = EtO

Scheme 3.

It is known that the reaction of N-(2-ethylhex-5-enyl)acet-amide (6) with benzeneselenenyl bromide does not afford the expected N-acetyl-5-ethyl-2-(phenylselenomethyl)piperidine (8) at all. In sharp contrast to this, the desired product (8) was produced, albeit in low yield, from methyl N-(2-ethylhex-5-enyl)acetimidate (7) together with side-products (9) and (6) (Scheme 4).

† Diphenyl diselenide was recovered in 40—60% yield but the N-alkenyl imidate was not recovered. Products other than (14) were highly polar and could not be analysed by t.l.c. In another experiment we monitored the reaction of an N-alkenyl imidate (I) with benzene-selenenyl bromide by ^1H n.m.r. spectroscopy. The signals corresponding to (I) disappeared and new signals appeared assignable to (II) and methyl bromide. However, the attempted isolation of (II) as well as the reaction of (II) with certain alkenes resulted in the isolation of only disphenyl diselenide in both cases.

* We also noticed that the reaction of methyl N-butylpropionimidate with benzeneselenenyl halides affords N-butyl-(α-phenyl-seleno)propionamide. This work will be reported shortly.

(I)

(II)

Scheme 4.

(10)

(11) a ; R^1 = Et, R^2 = H ; 33%

b ; R^1 = H, R^2 = Et ; 37%

Scheme 5.

introduced into a solution of N-(2-ethylpent-4-enyl)acetamide (15) and benzeneselenenyl bromide (Scheme 7). On the contrary, when compound (16) was added to a solution containing compound (2b) and benzeneselenenyl bromide, 85% of (16) was recovered intact, with none of compound (17) being

(13) a; R = Et

b; R = Me

(14) a; R = Et, X = Cl; 39%

b; R = Me, X = Cl; 31%

c; R = Me, X = Br; 39%
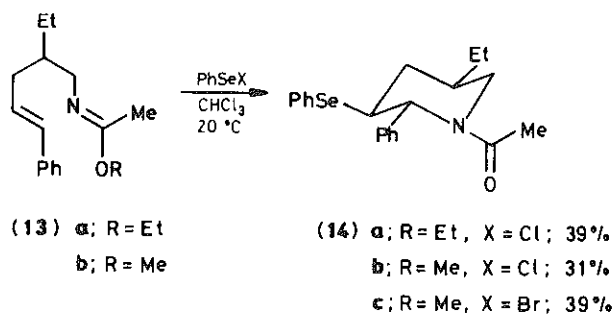
Scheme 6.

detected (Scheme 8). Furthermore, treatment of compound (18) possessing a trimethylsiloxy group with benzeneselenenyl bromide gave the expected pyrrolidine derivative (19) in a good yield together with a small amount of a side-product (20) (Scheme 9); the trimethylsiloxy groups were all completely

intact and no hydroxy compounds such as (21) were produced. Interestingly, the reaction of N-alkenyl amides containing a trimethylsiloxy group (1) with benzeneselenenyl bromide, did not afford either compounds (19) or (21). These results clearly demonstrate the wide scope and applicability of this new reaction.

We have already reported that the reductive deseleniation of compound (3a) containing a tertiary amide group to (22) was achieved by the use of nickel boride[8,6a] or tributyltin hydride.[9] When (3a) was treated with lithium aluminium hydride, it was reduced to the cyclic tertiary amine (23) in excellent yield (91%) which has a skeleton occurring in a number of useful alkaloids (Scheme 10).[10] During this reduction the phenylseleno group was not affected at all, in sharp contrast to the nickel boride reduction. From other pyrrolidines such as (3d, f), and (11a, b), the corresponding cyclic tertiary amines (24), (25), and (26a, b) were obtained in good to excellent yields, respectively. These results are listed in Table 3. The overall procedures, intramolecular amidoseleniation reaction followed by lithium aluminium hydride reduction, represent an intramolecular aminoseleniation reaction of olefinic secondary amines such as (27), a reaction which has otherwise been unsuccessful.[11]
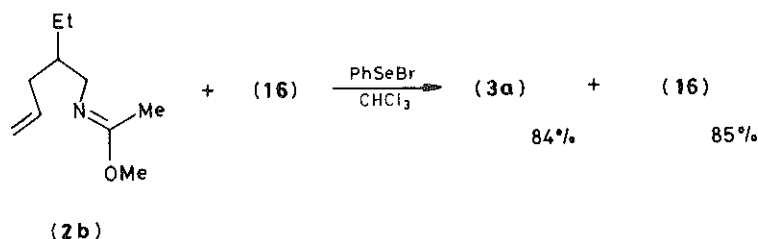
Experimental
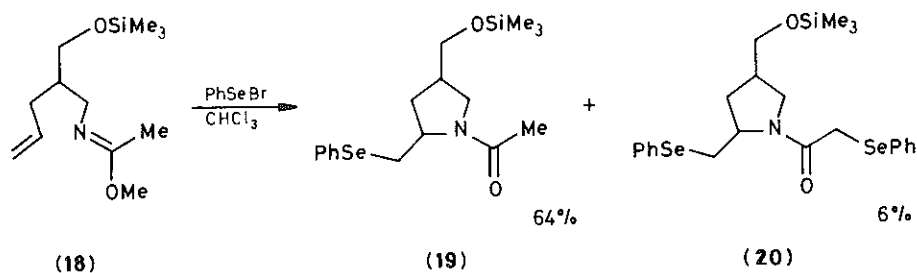
Preparation of Ethyl N-(2-Ethylpent-4-enyl)acetimidate (2a) without Purification of Intermediates: General Procedure.—To a

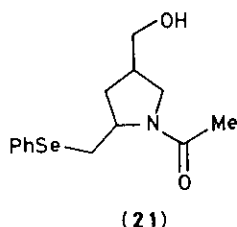(15)   (16)   (3a)   96%   (17)   97%
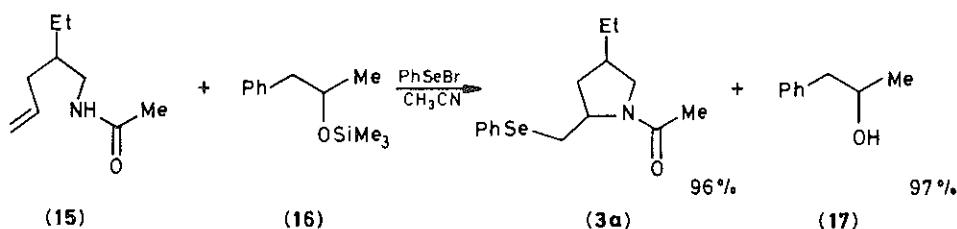
Scheme 7.

Scheme 8.

Scheme 9.

acetimidate hydrochloride (1.11 g, 9 mmol) in dichloromethane (40 ml) and the resulting solution was stirred at 0 °C for 6 h. The reaction mixture was poured into water (20 ml), and after the usual work-up, evaporation of the solvent left a pale yellow oil which was purified by column chromatography [alumina Woelm N activity grade V; hexane–ethyl acetate (10:1) as the eluant] to give *ethyl* N-(*2-ethylpent-4-enyl*)*acetimidate* (**2a**) as a colourless oil (**2a**) (1.3 g, 7.1 mmol, 79%) (Found: C, 72.35; H,
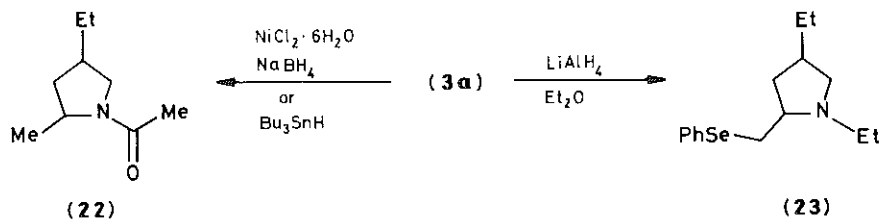
Scheme 10.

solution of lithium di-isopropyl amide (LDA) (40 mmol) in THF and hexane (40 ml + 26.8 ml) was added butyronitrile (3.66 ml, 42 mmol) at −78 °C by a syringe and the resulting solution was stirred at −78 to −60 °C for 2 h to complete the anion formation. Allyl bromide was then added dropwise to the solution at −78 °C, and the solution was allowed to warm to 20 °C during 12 h. After being quenched by the addition of 10% aqueous NH₄Cl (50 ml), the products were extracted with dichloromethane (3 × 50 ml) and the organic layer was washed with brine (15 ml) and dried (MgSO₄). Evaporation of the solvent left an oily residue, distillation (b.p. 162—163 °C) of which afforded 1-ethylbut-3-enyl cyanide (2.3 g, 21 mmol, 53%). The cyanide (991 mg, 9 mmol) in diethyl ether (9 ml) was injected dropwise over 5 min into a stirred suspension of LiAlH₄ (342 mg, 9 mmol) in diethyl ether (34 ml) at 0 °C and the resulting grey suspension was stirred at 0—20 °C for 6 h. 5M-Aqueous NaOH was then added dropwise until the suspension became white. The precipitates were filtered off and washed with ether, and the combined organic layers were separated and dried (MgSO₄). Evaporation of the solvent left crude 2-ethylpent-4-enylamine (1.02 g). A solution of the crude amine in dichloromethane (10 ml) was added slowly to a solution of ethyl

(24)

(25)

(26) a; R¹ = Et, R² = H

·b; R¹ = H, R² = Et
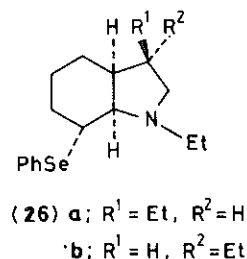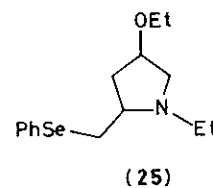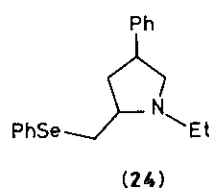
11.25; N, 7.35. $C_{11}H_{21}NO$ requires C, 72.08; H, 11.55; N, 7.64%); $v_{max.}$(film) 1 683 cm⁻¹; δ_H (100 MHz) 0.90 (3 H, t, *J* 7.3 Hz), 1.24 (3 H, t, *J* 7.1 Hz), 1.2—1.7 (3 H, m), 1.83 (3 H, s), 2.09 (2 H, t, *J* 6.8 Hz), 3.07 (2 H, d, *J* 5.9 Hz), 4.04 (2 H, q, *J* 7.1 Hz), 4.9—5.1 (2 H, m), and 5.81 (1 H, ddt, *J* 17.6, 9.3, 6.8 Hz).

Table 3. LiAlH$_4$ reduction of *N*-acetylpyrrolidines[a]

Entry	Substrate	Product	Yield[b] (%)
1	(3a)	(23)	91
2	(3d)	(24)	75
3	(3f)	(25)	61
4	(11a)[c]	(26a)	79
5	(11b)[c]	(26b)	75

[a] Carried out using pyrrolidine (1.0 mmol) and LiAlH$_4$ (2.0 mmol) in diethyl ether (10 ml) at ambient temperature for 2 h. [b] Isolated yield by column chromatography on SiO$_2$. [c] Assignment for compounds (11a) and (11b) may be reversed.
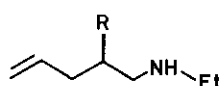
(27)

All acetimidates are new compounds and their spectral and combustion analytical data are as follows:

Methyl N-(2-*ethylpent-4-enyl*)*acetimidate* (2b): (Found *M*$^+$, 169.145 96 C$_{10}$H$_{19}$NO requires *M*, 169.146 64); ν$_{max.}$(film) 1 690 cm^{-1}; δ$_H$ (100 MHz) 0.90 (3 H, t, *J* 7.3 Hz), 1.2—1.7 (3 H, m), 1.84 (3 H, s), 2.10 (2 H, t, *J* 6.8 Hz), 3.09 (2 H, d, *J* 6.4 Hz), 3.60 (3 H, s), 4.9—5.1 (2 H, m), and 5.82 (1 H, ddt, *J* 17.6, 9.3, 6.8 Hz).

Methyl N-*pent-4-enylacetimidate* (2c): (Found: C, 67.8; H, 10.8; N, 9.85. C$_8$H$_{15}$NO requires C, 68.04; H, 10.71; N, 9.92%); ν$_{max.}$(film) 1 685 cm^{-1}; δ$_H$ (100 MHz) 1.63 (2 H, quint., *J* 6.8 Hz), 1.85 (3 H, s), 2.12 (2 H, dt, *J* 6.8, 6.3 Hz), 3.20 (2 H, t, *J* 6.8 Hz), 3.60 (3 H, s), 4.9—5.1 (2 H, m), and 5.85 (1 H, ddt, *J* 17.1, 10.3, 6.3 Hz).

Methyl N-(2-*phenylpent-4-enyl*)*acetimidate* (2d): (Found: C, 77.3; H, 8.7; N, 6.45. C$_{14}$H$_{19}$NO requires C, 77.38; H, 8.81; N, 6.45%); ν$_{max.}$(film) 1 688 cm^{-1}; δ$_H$ (100 MHz) 1.66 (3 H, s), 2.4—2.6 (2H, m), 2.91 (1 H, tt, *J* 8.3, 6.3 Hz), 3.38 (2 H, d, *J* 6.8 Hz), 3.58 (3 H, s), 4.9—5.1 (2 H, m), 5.74 (1 H, ddt, *J* 17.1, 10.3, 6.8 Hz), and 7.1—7.4 (5 H, m).

Methyl N-(2-*trimethylsilylpent-4-enyl*)*acetimidate* (2e): (Found: C, 61.9; H, 11.0; N, 6.65. C$_{11}$H$_{23}$NOSi requires C, 61.91; H, 10.86; N, 6.55%); ν$_{max.}$(film) 1 688 cm^{-1}; δ$_H$ (100 MHz) 0.03 (9 H, s), 0.95 (1 H, dq, *J* 7.8, 5.9 Hz), 1.82 (3 H, s), 2.1—2.4 (2 H, m), 3.25 (2 H, d, *J* 5.4 Hz), 3.59 (3 H, s), 4.9—5.1 (2 H, m), and 5.88 (1 H, ddt *J* 17.6, 9.3, 6.8 Hz).

Methyl N-(2-*ethylhex-5-enyl*)*acetimidate* (7): (Found *M*$^+$, 183.160 17 C$_{11}$H$_{21}$NO requires *M*, 183.162 28); ν$_{max.}$(film) 1 690 cm^{-1}; δ$_H$ (100 MHz) 0.89 (3 H, t, *J* 7.1 Hz), 1.2—2.1 (5 H, m), 1.85 (3 H, m), 2.0—2.2 (2 H, m), 3.10 (2 H, d, *J* 5.4 Hz), 3.60 (3 H, s), 4.9—5.1 (2 H, m), and 5.84 (1 H, ddt, *J* 17.1, 10.3, 6.4 Hz).

Methyl N-(2-*cyclohex-2-enylbutyl*)*acetimidate* (10): (Found: C, 74.45; H, 10.75; N, 6.8. C$_{13}$H$_{23}$NO requires C, 74.59; H, 11.07; N, 6.69%); ν$_{max.}$(film) 1 690 cm^{-1}; δ$_H$ (100 MHz) 0.92 (3 H, t, *J* 7.1) Hz), 1.2—2.1 (9 H, m), 1.85 (3 H, s), 2.2—2.5 (1 H, m) 3.13 (2 H, d, *J* 6.8 Hz), 3.60 (3 H, s), and 5.4—5.8 (2 H, m).

Ethyl N-(2-*ethyl-5-phenylpent-4-enyl*)*acetimidate* (13a): (Found: C, 78.8; H, 9.7; N, 5.3. C$_{17}$H$_{25}$NO requires C, 78.72; H, 9.71; N, 5.40%); ν$_{max.}$(film) 1 683 cm^{-1}; δ$_H$ (100 MHz) 0.93 (3 H, t, *J* 7.1 Hz), 1.24 (3 H, t, *J* 7.1 Hz), 1.1—1.8 (3 H, m), 1.83 (3 H, s), 2.25 (2 H, dd, *J* 6.4, 5.9 Hz), 3.11 (2 H, d, *J* 5.9 Hz), 4.05 (2 H, q, *J* 7.1 Hz), 6.25 (1 H, dt, *J* 15.6, 6.4 Hz), 6.34 (1 H, d, *J* 15.6 Hz), and 7.1—7.4 (5 H, m).

Methyl N-(2-*ethyl-5-phenylpent-4-enyl*)*acetimidate* (13b): (Found: C, 78.35; H, 9.65; N, 5.5. C$_{16}$H$_{23}$NO requires C, 78.32;

H, 9.45; N, 5.71%); ν$_{max.}$(film) 1 683 cm^{-1}; δ$_H$ (100 MHz) 0.93 (3 H, t, *J* 7.1 Hz), 1.3—1.9 (3 H, m), 1.83 (3 H, s), 2.26 (2 H, dd, *J* 6.4, 5.9 Hz), 3.13 (2 H, d, *J* 5.9 Hz), 3.62 (3 H, s), 6.25 (1 H, dt, *J* 15.6, 6.4 Hz), 6.34 (1 H, d, *J* 15.6 Hz), and 7.1—7.4 (5 H, m).

Preparation of Methyl N-(2-*Ethoxypent-4-enyl*)*acetimidate* (2f) *without Purification of Intermediates*.—To a mixture of vinylacetaldehyde diethyl acetal (4.46 g, 30.9 mmol) and trimethylsilyl cyanide (3.8 ml, 30 mmol) was added BF$_3$–Et$_2$O (0.3 ml, 2 mmol) at 25 °C and the mixture was stirred at ambient temperature for 3 h. After the usual work-up, 1-ethoxybut-3-enyl cyanide was isolated by distillation (bath temp. 70 °C, 50 mmHg), 3.4 g, 27.2 mmol, 91%. The cyanide was converted into imidate (2f) by reduction with LiAlH$_4$ followed by the reaction with methyl acetimidate hydrochloride in 12% overall yield (see above procedure), (Found: C, 64.7; H, 10.4; N, 7.3. C$_{10}$H$_{19}$NO$_2$ requires C, 64.83; H, 10.34; N, 7.56%); ν$_{max.}$(film) 1 690 cm^{-1}; δ$_H$ (100 MHz) 1.17 (3 H, t, *J* 6.8 Hz), 1.87 (3 H, s), 2.2—2.4 (2 H, m), 3.24 (2 H, d, *J* 6.4 Hz), 3.4—3.7 (1 H, m), 3.59 (2 H, q, *J* 6.8 Hz), 3.61 (3 H, s), 5.0—5.2 (2 H, m), and 5.90 (1 H, ddt, *J* 17.1, 10.3, 6.8 Hz).

Preparation of Methyl N-(2-*Trimethylsiloxymethylpent-4-enyl*)*acetimidate* (18).—Ethyl cyanoacetate (17 g, 0.15 mol) was injected dropwise over 15 min into a vigorously stirred suspension of NaH (2.4 g, 0.1 mol) in DMF (100 ml) at ambient temperature. The mixture was stirred until a clear solution is obtained, and then a solution of allyl bromide (6.9 ml, 80 mmol) in DMF (20 ml) was added all at once. The resulting solution was slowly heated to 100 °C over 3 h, during which time the colour of the solution turned dark-red and NaBr was precipitated out. The mixture was allowed to stand overnight at ambient temperature and then most of the solvent was evaporated. The residual semi-solid was mixed with water (150 ml) and extracted with diethyl ether (5 × 50 ml). Evaporation of the dried (MgSO$_4$) extract left a residual oil, column chromatography [SiO$_2$ 200 mesh; hexane–ethyl acetate (10:1)] of which afforded ethyl 2-cyanopent-4-enoate (4.3 g, 28 mmol, 35%). A solution of ethyl 2-cyanopent-4-enoate (2.5 g, 16.3 mmol) in diethyl ether (20 ml) was injected dropwise over 10 min into a stirred suspension of LiAlH$_4$ (1.24 g, 33 mmol) in diethyl ether (80 ml) at 0 °C and the resulting solution was stirred at ambient temperature for 13 h. After being quenched by the addition of 5M-aqueous NaOH, the white precipitate was filtered off and the filtrate was concentrated to afford crude 2-aminomethylpent-4-enol as an oil (1.1 g). To a solution of the crude amino alcohol (3.3 g) and Et$_3$N (24.1 mol, 0.17 mol) in THF (140 ml) was added trimethylsilyl chloride, and the solution was stirred at ambient temperature for 6 h. After the usual work-up, 2-trimethylsiloxymethylpent-4-enylamine was isolated by distillation (b.p. 75—80 °C/1 mmHg); (1.53 g, 8.2 mmol, 17% yield from ethyl 2-cyanopent-4-enoate). The siloxy amine was converted into the imidate (18) by condensation with methyl acetimidate hydrochloride (see above procedure). (Found: C, 59.15; H, 10.2; N, 5.75. C$_{12}$H$_{25}$NO$_2$Si requires C, 59.21; H, 10.35; N, 5.75%); ν$_{max.}$(film) 1 685 cm^{-1}; δ$_H$ (100 MHz) 0.09 (9 H, s), 1.6—1.9 (1 H, m), 1.84 (3 H, s), 2.12 (2 H, t, *J* 6.8 Hz), 3.15 (2 H, d, *J* 5.9 Hz), 3.54 (1 H, dd, *J* 11.2, 5.9 Hz), 3.55 (1 H, dd, *J* 11.2, 4.9 Hz), 3.59 (3 H, s), 4.9—5.1 (2 H, m), and 5.82 (1 H, ddt, *J* 18.1, 9.3, 6.8 Hz).

Conversion of Compound (2b) *into* N-*Acetyl-4-ethyl-2-*(phenylselenomethyl)pyrrolidine (3a): General Procedure.—To a solution of the imidate (2b) (169 mg, 1.0 mmol) in CHCl$_3$ (90 ml) was added a solution of benzeneselenenyl bromide (260 mg, 1.1 mmol) in CHCl$_3$ (5 ml). A further portion (5 ml) of CHCl$_3$ was used as a rinse for complete transfer of all benzeneselenenyl bromide. The resulting pale yellow solution was stirred at

ambient temperature for 12 h. The solvent was evaporated to leave a yellow oil, column chromatography [SiO$_2$ 200 mesh; hexane–ethyl acetate (1:1)] of which yielded compound (3a)[3] (273 mg, 0.88 mmol, 88%).

Spectral data of new *N*-heterocycles are as follows:

N-*Acetyl-4-phenyl-2-(phenylselenomethyl)pyrrolidine* (3d): [a mixture of two isomers (73:27)] $v_{max.}$(film) 1 645 cm^{-1}; δ_H (100 MHz) 1.84 (1 H, s, major isomer), 1.97 (1 H, s, minor isomer), 1.8—2.7 (2 H, m), 2.9—3.9 (5 H, m), 4.3—4.6 (1 H, m), 7.1—7.4 (8 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) major isomer: 22.9(q), 31.5(t), 38.7(t), 43.4(d), 55.3(t), 57.0(d), 169.4(s), and phenyl signals; minor isomer: 22.7(q), 29.3(t), 36.5(t), 42.1(d), 54.8(t), 57.4(d), 169.1(s), and phenyl signals.

N-*Acetyl-2-(phenylselenomethyl)-4-(trimethylsilyl)pyrrolidine* (3e): (an equimolar mixture of two isomers) $v_{max.}$(film) 1 645 cm^{-1}; δ_H (100 MHz) 0.00 (9 H, s, one isomer), 0.03 (9 H, s, other isomer), 1.1—2.4 (3 H, m), 1.86 (3 H, s, one isomer), 2.00 (3 H, s, other isomer), 2.6—3.7 (4 H, m), 4.1—4.5 (1 H, m), 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) −3.2(q),† −3.0(q),† 22.6(q), 23.0(q), 24.0(d), 26.3(d), 28.5(t), 31.0(t), 31.4(t), 33.9(t), 50.3(t), 51.1(t), 57.8(d), 58.1(d), 168.7(s), 169.0(s), and phenyl signals.

N-*Acetyl-4-ethoxy-2-(phenylselenomethyl)pyrrolidine* (3f): [a mixture of two isomers (64:36)]: $v_{max.}$(film) 1 640 cm^{-1}; δ_H (100 MHz) 1.17 (3 H, t, *J* 6.8 Hz, major isomer), 1.19 (3 H, t, *J* 6.8 Hz, minor isomer), 1.85 (3 H, s, major isomer), 2.00 (3 H, s, minor isomer), 2.0—2.4 (2 H, m), 2.8—3.8 (5 H, m), 3.8—4.3 (2 H, m), 4.3—4.6 (1 H, m), 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) major isomer: 15.3(q), 22.8(q), 30.8(t), 36.2(t), 53.8(t), 55.8(d), 64.4(t), 76.6(d), 169.7(s), and phenyl signals; minor isomer: 15.3(q), 22.8(q), 29.5(t), 34.0(t), 54.3(t), 56.9(d), 64.4(t), 77.9(d), 169.5(s), and phenyl signals.

7-*Acetyl-9-ethyl-5-(phenylseleno)-7-azabicyclo*[4.3.0]*nonane* (11): (*a*) (11a) [one isomer of higher R_F value, a mixture of two conformers; (64:36)] $v_{max.}$(film) 1 645 cm^{-1}; δ_H (100 MHz) 0.92 (3 H, t, *J* 7.3 Hz), 1.2—2.1 (6 H, m), 1.33 (2 H, q, *J* 7.3 Hz), 1.65 (3 H, s, minor conformer), 2.04 (3 H, s, major conformer), 2.3—2.7 (2 H, m), 3.22 (1 H, t, *J* 11.2 Hz), 3.52 (1 H, dd, *J* 11.2, and 7.8 Hz), 4.11 (1 H, br s), 5.10 (1 H, br s), 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) major conformer; 12.3(q), 21.9(q), 22.3(t), 24.3(t), 25.6(t), 32.4(t), 40.1(d), 43.8(d), 44.9(d), 52.4(t), 60.6(d), 170.0(s), and phenyl signals; minor conformer: 12.5(q), 21.9(q), 23.0(t), 24.2(t), 26.4(t), 33.6(t), 38.1(d), 46.0(d), 46.7(d), 49.7(t), 65.3(d), 169.5(s), and phenyl signals.

(*b*) (11b) [Another isomer of lower R_F value, a mixture of two conformers (76:24)]: $v_{max.}$(film) 1 650 cm^{-1}; δ_H (100 MHz) 0.93 (3 H, t, *J* 6.8 Hz), 1.1—2.3 (10 H, m), 2.01 (3 H, s, major conformer), 2.29 (3 H, s, minor conformer), 3.07 (1 H, dd, *J* 10.3, and 8.3 Hz), 3.47 (1 H, br d, *J* 7.8 Hz), 3.75 (1 H, dd, *J* 10.3, 7.8 Hz), 4.37 (1 H, dd, *J* 10.3, 5.9 Hz), 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) major conformer: 12.4(q), 20.2(t), 20.7(t), 21.8(t), 24.0(q), 26.7(t), 36.7(d), 40.9(d), 42.6(d), 52.9(t), 63.7(d), 171.6(s), and phenyl signals; minor conformer: 12.4(q), 19.9(t), 21.1(t), 21.5(t), 22.4(q), 25.7(t), 40.6(d), 43.6(d), 46.8(t), 61.8(d), 69.2(d), 170.1(s), and phenyl signals.

N-*Acetyl-2-(phenylselenomethyl)-4-(trimethylsiloxymethyl)-pyrrolidine* (19): [a mixture of two isomers (56:44)] (Found: C, 52.8; H, 7.35; N, 4.0. C$_{17}$H$_{27}$NO$_2$SeSi requires C, 53.11; H, 7.08; N, 3.64%); $v_{max.}$(film) 1 640 cm^{-1}; δ_H (100 MHz) 0.10 (9 H, s, major isomer), 0.12 (9 H, s, minor isomer), 1.88 (3 H, s, major isomer), 1.94 (3 H, s, minor isomer), 1.4—2.7 (3 H, m), 2.8—3.7 (6 H, m), 4.2—4.5 (1 H, m), 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) major isomer: −0.6(q),† 22..9(q), 31.2(t), 33.5(t), 40.5(d), 50.8(t), 56.8(d), 63.7(t), 169.5(s), and

phenyl signals; minor isomer: −0.6(q),† 22.6(q), 29.1(t), 32.0(t), 39.5(d), 52.0(t), 57.0(d), 63.7(t), 169.2(s), and phenyl signals.

N-[(*Phenylseleno*)acetyl]-2-(phenylselenomethyl)-4-(tri-methylsiloxymethyl)pyrrolidine* (20): [a mixture of two isomers (55:45)] (Found: C, 51.4; H, 5.9; N, 2.9. C$_{23}$H$_{31}$NO$_2$Se$_2$Si requires C, 51.20; H, 5.79; N, 2.60%); $v_{max.}$(film) 1 627 cm^{-1}; δ_H (100 MHz) 0.09 (9 H, s, major isomer), 0.11 (9 H, s, minor isomer), 1.2—2.6 (3 H, m), 3.45 (2 H, s, minor isomer), 3.51 (2 H, s, major isomer), 2.6—3.9 (6 H, m), 4.1—4.5 (1 H, m), 7.1—7.4 (6 H, m), and 7.4—7.7 (4 H, m); δ_C (25 MHz) major isomer: −0.6(q),† 29.4(t), 29.7(t), 31.8(t), 39.7(d), 50.5(t), 57.6(d), 63.6(t), 168.3(s), and phenyl signals; minor isomer: −0.6(q),† 29.4(t), 30.9(t), 33.3(t), 40.5(d), 51.7(t), 57.6(d), 63.6(t), 168.1(s), and phenyl signals.

N-[(*Phenylseleno*)acetyl]-2-(phenylselenomethyl)pyrrolidine* (4c): (Found: M^+, 438.995 33. C$_{19}$H$_{21}$NOSe$_2$ requires M, 438.995 22); $v_{max.}$(film) 1 627 cm^{-1}; δ_H (100 MHz) 1.7—2.1 (4 H, m), 2.83 (1 H, dd, *J* 12.2, 9.3 Hz), 3.3—3.8 (3 H, m), 3.51 (2 H, s), 4.2—4.4 (1 H, m), 7.1—7.4 (6 H, m), and 7.4—7.7 (4 H, m).

4-*Phenyl*-N-[(*phenylseleno*)acetyl]-2-(phenylselenomethyl)-pyrrolidine* (4d): (Found: M^+, 515.028 92. C$_{25}$H$_{25}$NOSe$_2$ requires M, 515.026 48); $v_{max.}$(film) 1 627 cm^{-1}; δ_H (100 MHz) 1.5—2.7 (2 H, m), 2.7—4.0 (7 H, m), 4.2—4.6 (1 H, m), 7.0—7.4 (11 H, m), and 7.4—7.7 (4 H, m).

4-*Ethoxy*-N-[(*phenylseleno*)acetyl]-2-(phenylselenomethyl)-pyrrolidine* (4d): (Found: M^+, 515.028 92. C$_{25}$H$_{25}$NOSe$_2$ requires M, 483.021 43); $v_{max.}$(film) 1 627 cm^{-1}; δ_H (100 MHz) 1.16 (3 H, t, *J* 6.8 Hz), 1.6—2.4 (2 H, m), 2.8—3.8 (6 H, m), 3.54 (2 H, s), 3.8—4.2 (1 H, m), 4.2—4.5 (1 H, m), 7.1—7.4 (6 H, m), and 7.4—7.7 (4 H, m).

LiAlH$_4$ *Reduction of* (3a) *to* N,4-*Diethyl-2-(phenyl-selenomethyl)pyrrolidine* (23): *General Procedure.*—To a stirred suspension of lithium aluminium hydride (76 mg, 2.0 mmol) in diethyl ether (5 ml) was added dropwise a solution of compound (3a) (310 mg, 1.0 mmol) in diethyl ether (5 ml) at 0 °C and the resulting grey suspension was stirred at ambient temperature for 2 h. Aqueous 5M-NaOH was then added dropwise until the suspension became white. The precipitate was filtered and washed with ether, and after work-up the combined organic layers were separated and dried (MgSO$_4$). The solvent was evaporated to leave a yellow oil, column chromatography [SiO$_2$ 200 mesh; hexane–ethyl acetate (1:1)] of which yielded compound (23) (270 mg, 0.91 mmol, 91%) as a mixture of two isomers (62:38) (Found: C, 61.0; H, 7.85; N, 4.65. C$_{15}$H$_{23}$NSe requires C, 60.80; H, 7.82; N, 4.73%); $v_{max.}$(film) 2 960, 2 930, 2 870, 2 790, 1 475, 735, and 690 cm^{-1}; δ_H (100 MHz) 0.86 (3 H, t, *J* 7.3 Hz), 1.05 (3 H, t, *J* 6.8 Hz), 1.2—1.6 (3 H, m), 1.6—2.6 (4 H, m), 2.6—3.4 (5 H, m), 7.1—7.3 (3 H, m), and 7.3—7.6 (2 H, m); δ_C (25 MHz) major isomer: 12.7(q), 13.6(q), 28.8(t), 32.5(t), 37.3(d), 38.6(t), 48.0(t), 58.8(t), 64.4(d), 126.3(d), 128.8(d),* 131.3(s), and 132.0(d);* minor isomer: 12.7(q), 13.7(q), 27.4(t), 33.5(t), 37.5(t), 37.9(d), 48.4(t), 60,3(t), 63.4(d), 126.3(d), 128.8(d),* 131.1(s), and 132.0(d).*

All cyclic tertiary amines prepared are new compounds and pale yellow oils, and the spectral and combustion data are as follows:

N-*Ethyl-4-phenyl-2-(phenylselenomethyl)pyrrolidine* (24): [a mixture of two isomers (68:32)] (Found: C, 66.5; H, 6.7; N, 4.15. C$_{19}$H$_{23}$NSe requires C, 66.27; H, 6.73; N, 4.07%); $v_{max.}$(film) 2 970, 2 940, 2 790, 1 475, 735, 700, and 690 cm^{-1}; δ_H (100 MHz) 1.08 (3 H, t, *J* 6.8 Hz), 1.7—2.6 (3 H, m), 3.11 (2 H, q, *J* 6.8 Hz), 2.6—3.4 (4 H, m), 3.4—3.6 (1 H, m), 7.1—7.4 (8 H, m), and 7.4—7.6 (2 H, m); δ_C (25 MHz) major isomer: 13.7(q), 32.4(t),

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† Three signals overlapping.

* Two signals overlapping.

41.2(d), 41.4(t), 48.1(t), 60.9(t), 64.6(d), and phenyl signals; minor isomer: 13.7(q), 33.8(t), 38.8(t), 41.9(d), 48.4(t), 61.7(t), 63.8(d), and phenyl signals.

4-*Ethoxy*-N-*ethyl*-2-(*phenylselenomethyl*)*pyrrolidine* (25): [a mixture of two isomers (58:42)] (Found: C, 57.8; H, 7.4; N, 4.5. $C_{15}H_{23}NOSe$ requires C, 57.69; H, 7.42;, N, 4.48%); $\nu_{max.}$(film) 2 975, 2 935, 1 475, 1 120, 735, and 690 cm^{-1}; δ_H (100 MHz) 1.06 (3 H, t, J 7.3 Hz), 1.18 (3 H, t, J 6.8 Hz), 1.6—2.5 (4 H, m), 2.5—3.2 (4 H, m), 3.40 (2 H, q, J 6.8 Hz), 3.2—3.6 (1 H, m), 3.8—4.1 (1 H, m), 7.1—7.4 (3 H, m), and 7.4—7.6 (2 H, m); δ_C (25 MHz) major isomer: 13.3(q), 15.4(q), 32.5(t), 38.3(t), 47.7(t), 59.4(t), 62.0(d), 64.5(t), 76.3(d), and phenyl signals; minor isomer: 13.3(q), 15.4(q), 32.2(t), 38.6(t), 48.0(t), 59.4(t), 63.5(d), 64.2(t), 76.6(d), and phenyl signals.

7,9-*Diethyl*-5-(*phenylseleno*)-7-*azabicyclo*[4.3.0]*nonane* (26): (*a*) (26a) obtained by the reduction of (11a) (Found: C, 64.45; H, 7.75; N, 4.3. $C_{18}H_{27}NSe$ requires C, 64.27; H, 8.07; N, 4.16%); $\nu_{max.}$(film) 2 960, 2 930, 2 850, 2 790, 1 475, 740, and 695 cm^{-1}; δ_H (100 MHz) 0.87 (3 H, t, J 7.3 Hz), 1.02 (3 H, t, J 7.3 Hz), 1.0—2.4 (12 H, m), 2.65 (1 H, t, J 5.4 Hz), 2.87 (1 H, ddt, J 11.7, 7.3, 7.3 Hz), 3.42 (1 H, dd, J 8.8, 6.4 Hz), 3.57 (1 H, br d, J 4.4 Hz), 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) 12.5(q), 13.2(q), 21.8(t), 27.7(t), 28.3(t), 28.4(t), 42.1(d), 43.5(d), 45.3(d), 49.2(t), 59.1(t), 66.9(d), 127.1(d), 128.8(d),* 130.3(s), and 134.2(d).*

(*b*) (26b) Obtained by the reduction of compound (11b) (Found: C, 64.45; H, 8.0; N, 4.3. $C_{18}H_{27}NSe$ requires C, 64.27; H, 8.07; N, 4.16%); $\nu_{max.}$(film) 2 960, 2 940, 2 860, 1 475, 735, and 690 cm^{-1}; δ_H (100 MHz) 0.86 (3 H, t, J 7.3 Hz), 0.97 (3 H, t, J 7.3 Hz), 1.1—2.4 (11 H, m), 2.4—2.9 (3 H, m), 2.91 (1 H, t, J 3.4 Hz), 3.66 (1 H, q, J 2.5 Hz) 7.1—7.4 (3 H, m), and 7.4—7.7 (2 H, m); δ_C (25 MHz) 12.8(q), 13.7(q), 21.1(t), 21.7(t), 22.2(t), 26.0(t), 38.1(d), 42.4(d), 44.6(d), 48.1(t), 56.9(t), 68.2(d), 126.8(d), 128.9(d),* 131.0(s), and 133.5(d).*

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* Two signals overlapping.

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