Cyclofunctionalization of Olefinic Urethanes Using Benzeneselenenyl Chloride in the Presence of Silica Gel: A General Route to Nitrogen Heterocycles

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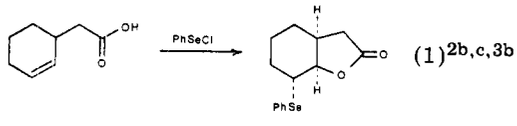
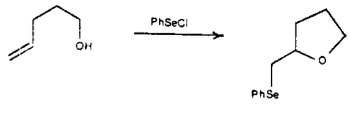
Ethyl urethanes derived from Δ^4 or Δ^5 olefinic amines undergo cyclofunctionalization to afford pyrrolidines and piperidines, respectively, when treated with benzeneselenenyl chloride. The reaction is an efficient one when carried out in the presence of silica gel, yields generally being above 80% for the examples studied.

We report here details of our work on the ring closure approach (see 1) to nitrogen heterocycles using benzeneselenenyl chloride. This reagent is known to effect a number of cyclizations[2-4] to give products carrying the synthetically useful[5] benzeneseleno group. We have named the process cyclofunctionalization,[2a] and typical examples involving heterocycles are shown in eq 1-3. Such reactions



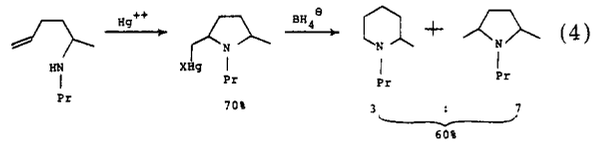
(1)[2b,c,3b]



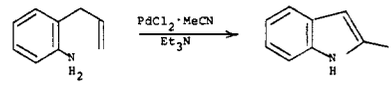
(2)[2d,3c]

(3)[2a]

usually proceed in good yield under mild conditions, and it was desirable to extend the method to unsaturated amines due to the general importance of alkaloid synthesis.[6a] The proposed strategy involves making a nitrogen-carbon bond, as in 1, to generate the heterocycle.[6b] Mercuric ion is a conventional reagent[7] for this approach, as shown by the example[7a] of eq 4, and a recent innovation



(4)



(5)

is a palladium-based methodology, which provides a good route to indoles[8] (eq 5). Before our own work[9] no amines, properly constituted for cyclofunctionalization, had been treated with arylselenenyl halides.[10] Simple anilines undergo electrophilic para substitution with such reagents, or the isolated products are those resulting from attack on nitrogen.[11] In the case of aliphatic amines, the few examples that had been examined[11,12] all reacted on nitrogen.

We treated 2-allylaniline and 4-pentenylamine with benzeneselenenyl chloride under the same conditions that had worked well for making oxygen heterocycles, but in no case did we observe a clean reaction. The presence of pyridine or prior conversion of the amine into its lithium salt was equally unpromising, and so these initial experiments indicated that primary amines are not appropriate substrates. We discovered that the derived urethanes, however, do undergo the desired transformation, as in eq 6,[9] and we have studied the ring closure in this form.

(6)

(1) (a) Izaak Walton Killam Scholar; H. H. Parlee Memorial Predoctoral Fellow (1978-1979). (b) Undergraduate research participant.

(2) (a) Clive, D. L. J.; Chittattu, G; Curtis, N. J.; Kiel, W. A.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1977**, 725. (b) Clive, D. L. J.; Chittattu, G. *Ibid.* **1977**, 484. (c) Clive, D. L. J.; Russell, C. G.; Chittattu, G.; Singh, A. *Tetrahedron*, in press. (d) Clive, D. L. J.; Chittattu, G.; Wong, C. K. *Can. J. Chem.* **1977**, *55*, 3894. (e) Clive, D. L. J.; Chittattu, G.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1978**, 441.

(3) (a) Nicolaou, K. C.; Lysenko, Z. *J. Am. Chem. Soc.* **1977**, *99*, 3185. (b) Nicolaou, K. C.; Seitz, S. P.; Sipio, W. J.; Blount, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 3884. (c) Nicolaou, K. C.; Lysenko, Z. *Tetrahedron Lett.* **1977**, 1257. (d) Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *J. Am. Chem. Soc.* **1978**, *100*, 2567.

(4) Cf. Corey, E. J.; Keck, G. E.; Szekely, I. *J. Am. Chem. Soc.* **1977**, *99*, 2006.

(5) (a) Clive, D. L. J. *Tetrahedron* **1978**, *34*, 1049. (b) Clive, D. L. J. *Aldrichimica Acta* **1978**, *11*, 43. (c) Reich, H. J. In "Oxidation in Organic Chemistry"; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; Part C, Chapter 1. (d) Sharpless, K. B.; Gordon, K. M.; Lauer, R. F.; Patrick, D. W.; Singer, S. P.; Young, M. W. *Chem. Scr.* **1975**, *8A*, 9.

(6) (a) See, for example "The Alkaloids"; Grundon, M. F.; Senior Reporter, Specialist Periodical Reports; The Chemical Society: London, 1976; Vol. 6. (b) 1 shows an exo closure.[20] We have not studied the endo mode, except as a competing process (see Table I, **4b**).

(7) (a) Perie, J. J.; Laval, J. P.; Roussel, J.; Lattes, A. *Tetrahedron* **1972**, 675. The pyrrolidine in eq 4 was a mixture of diastereoisomers. (b) Moriyama, Y.; Doan-Huynh, D.; Monneret, C.; Khuong-Huu, Q. *Tetrahedron Lett.* **1977**, 825.

(8) Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. L. *J. Am. Chem. Soc.* **1978**, *100*, 5800.

(9) Clive, D. L. J.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Chem. Soc., Chem. Commun.* **1978**, 379.

(10) For a recent example, see: Wilson, S. R.; Sawicki, R. A. *J. Org. Chem.* **1979**, *44*, 287.

(11) Klayman, D. L. In "Organic Selenium Compounds: Their Chemistry and Biology"; D. L. Klayman, D. L.; Günther, W. H. H., Eds.; Wiley-Interscience: New York, 1978; p 108.

(12) Reich, H. J.; Renga, J. M. *J. Org. Chem.* **1975**, *40*, 3313.

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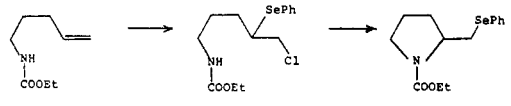
The required amines (cf. Table I) were generally known compounds, those of the aniline series being made by π-allyl nickel methodology[8] and the others by more classical procedures[13] (see Experimental Section). The derived urethanes were prepared by the standard Schotten–Baumann method in the yields indicated, but, in those cases (see Table I, compounds **6**, **7**, and **8**) where lithium aluminum hydride reduction of a primary amide was used to generate the amine, it was more convenient to derivatize the crude amine in situ without isolation. The structures of the urethanes were quite apparent from their spectroscopic properties.

In each of our initial experiments[9] on the cyclofunctionalization, a dichloromethane solution of benzeneselenenyl chloride was added to a solution of the urethane in the same solvent. The addition was carried out at −60 °C or at 0 °C, and the mixture was then allowed to warm to room temperature. In the case of urethanes **5** and **6** higher yields were obtained by adding the selenium reagent[14] to a solution of the urethane *and* a slight excess of silver trifluoroacetate.[15] By one or the other of these techniques, several olefinic urethanes (see Table I, compounds **2**, **3**, **5**, and **6**) were converted into the cyclofunctionalized products and further work was undertaken to improve the yields.

When we monitored some of these reactions by NMR it became clear that all the olefinic material disappeared rapidly but very little of the final product was formed, even though a substantial amount appeared to be present by TLC analysis. If the reaction mixture was worked up at such a stage, by evaporation and chromatography over silica gel, the required products were obtained in modest yield. These observations, taken together with the results of a mechanistic study of the cyclofunctionalization of olefinic acids,[2c] suggested that the selenium reagent adds rapidly to the double bond and that subsequent ring closure is facilitated by silica gel (eq 7).[16,17] Accordingly, we



(7)

examined the effect of having silica gel[18] present during the addition of benzeneselenenyl chloride. We found that the yield is increased substantially and the reactions were then routinely run in this fashion. As the tabulated data show, the modified procedure results in an average yield improvement of 21.5% over the earlier experiments. We have arbitrarily employed Merck silica gel 60 PF-254 (ca. 500 mg/mmol of urethane) which was oven-dried before use. In the case of urethane **3**, Merck aluminum oxide (PF-254, Type E) was also examined, but the effect was not significantly different from that of silica gel. Suitable reaction times are easily established for these reactions by periodic TLC analysis because the initial chloroselenide adducts show a characteristic tailing spot.

The case of urethane **4** revealed certain details which were not apparent from the other experiments. One of the byproducts of the cyclizations is hydrogen chloride, and it was necessary to inhibit hydrochlorination of the trisubstituted double bond by adding an acid trap. Propylene oxide was suitable.[19] Urethane **4** gave two products, **4a** and **4b**, arising formally by 5-exo and 6-endo closure,[20] respectively. When the reaction was done in the absence of silica gel and was worked up before completion, by rapid chromatography over silica, it was possible to obtain mixtures of **4a** and **4b** in which **4a** predominated. The relative composition of such mixtures was variable, but in one experiment almost pure **4a** was isolated (ca. 28% yield). Probably, the dihydroindole is the kinetic product. When present as mixtures, **4a** and **4b** could not be separated chromatographically, but the structures were confirmed by reduction with triphenyltin hydride[21] to **4c** and **4d** which were separable by VPC.

4c **4d**

In general, the structures of the cyclofunctionalized products could be deduced from ^{1}H NMR measurements. However, the spectra are very complicated, and they show temperature-dependent effects because the molecules possess a certain amount of conformational mobility. Additional support for structure and stereochemistry was sought as follows.

2a was synthesized by an independent route described in the Experimental Section. Each selenide was also treated in refluxing toluene with triphenyltin hydride[21] in order to replace the benzeneseleno group by hydrogen. In the case of **4a** and **4b** no significant change occurred in the ratio of the dihydroindole to tetrahydroquinoline species. All the reduction products[21] from **1a**–**8a** have comparatively simple NMR spectra which define the structures. **9a** and **10a**[22] have the cis stereochemistry shown for the substituents at the C-2 and C-6 positions of the piperidine ring. In both cases the reduction product is *cis*-*N*-carbethoxy-2-methyl-6-undecylpiperidine (**11**). Removal of the blocking group from the nitrogen gave **12**, whose properties (^{13}C NMR and melting point of the hydrochloride salt) were compared with reported data.[7b] Assignment of the stereochemistry shown for **9a** and **10a** requires that no isomerization (trans → cis) occurs in the triphenyltin hydride reduction, and **10a** was specifically tested for this possibility. It was found to be unchanged by heat (118 °C for 4 h) as judged by TLC and ^{13}C NMR, and so we view formation of **10a** as shown in **13**.[23]

(13) For methods based on the amino-Claisen rearrangement see: Jolidon, S.; Hansen, H-J. *Helv. Chim. Acta* **1977**, *60*, 978. Takamatsu, N.; Inoue, S.; Kishi, Y. *Tetrahedron Lett.* **1977**, 4661. For an alternative approach, see: Baldwin, J. E.; Tzodikov, N. R. *J. Org. Chem.* **1977**, *42*, 1978.

(14) PhSeBr was used for **5** and PhSeCl for **6**. The nature of the halide is probably immaterial.

(15) (a) Cf. Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1973**, 695. (b) Reich, H. J. *J. Org. Chem.* **1974**, *39*, 428.

(16) Equation 7 shows formation of the expected kinetic[17] product of addition to the double bond. We did not investigate isomerization to the thermodynamic adduct, but some of our NMR spectra suggested that such isomerization was occurring.

(17) Raucher, S. *J. Org. Chem.* **1977**, *42*, 2950.

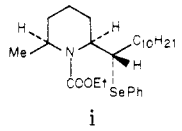
(18) Posner, G. H. *Angew. Chem.* **1978**, *90*, 527.

(19) In the absence of an acid trap, about 16% of the starting urethane reacted with HCl. Since NMR measurements show that all the starting *olefin* is quenched by PhSeCl, the formation of an HCl adduct indicates that the initial addition of PhSeCl is a reversible process.

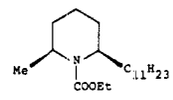
(20) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

(21) (a) Clive, D. L. J.; Chittattu, G.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1978**, 41. (b) Clive, D. L. J.; Chittattu, G.; Farina, V.; Kiel, W. A.; Menchen, S. M.; Russell, C. G.; Singh, A.; Wong, C. K.; Curtis, N. J. *J. Am. Chem. Soc.*, in press.

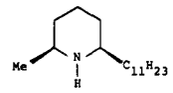
(22) On mechanistic grounds the stereochemistry in the undecyl side chain is expected to be as in **i**.



i



11



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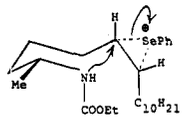


13

In the case of **5a** and **7a** the cis nature of the ring fusion was established chemically by comparing the triphenyltin hydride reduction products[21] with authentic samples of the respective urethanes.[24] The NMR spectra of **7a** and **8a** also define the stereochemistry at the carbon carrying the phenylseleno group. The signal due to H_a (see **7a**) is a doublet with J_{ab} = 7 Hz in the 200-MHz spectrum run in Me_2SO-d_6 at 70 °C. Each component has a width at half-height of 4 Hz, indicating $J_{ac} \leq 4$ Hz. Inspection of Dreiding models shows that if H_a and H_c were cis then J_{ac} should be about 8 Hz; for a trans arrangement J_{ac} is expected to be about 1.5 Hz.

The cyclizations described here proceed in high yield except for the urethane **10**. In that case *N*-phenylselenophthalimide[25] was also examined by using the reported procedure, but the yield of cyclized material[26] was raised only to 47%.

Apart from compound **10**, the selenium-based methodology is a reliable and efficient alternative to aminomercuration. It also complements palladium-induced cyclizations, which afford products at a different level of hydrogenation.

Experimental Section

Except where stated to the contrary the following particulars apply. Experiments were done under a slight static pressure of nitrogen, purified by passage through a column (3.5 × 42 cm) of R-311 catalyst[27] and then through a similar column of Drierite. Solvents were distilled before use for chromatography. Dry dichloromethane, benzene, and toluene were distilled from calcium hydride, dry acetone from anhydrous potassium carbonate, and dry THF and ether from sodium. During product isolation, solutions were evaporated under water-pump vacuum at room temperature. Where compounds were isolated simply by evaporation of their solutions the residues were kept under oil-pump vacuum and checked for constancy of weight. Isolated products were submitted directly for combustion analysis without need for additional purification. Plates for preparative layer chromatography (PLC) were 60 × 20 × 0.1 cm and were heated at 110 °C for 1 h before use. Silica gel for PLC was Merck type 60-PF-254. Silica gel for column chromatography was Merck type 60 (70–230 mesh). Silica gel for flash chromatography[28] was Merck type 60 (230–400 mesh). Commercial TLC plates were used; silica was Camag type DF-B or Merck 60F-254; alumina was Camag type DSF-B or Merck 60F-254. Mass spectra were run at an ionizing voltage of 70 eV. Boiling points quoted for products distilled in a Kugelrohr apparatus refer to the oven temperature. ^1H NMR spectra were run with a 100-MHz instrument. Silica gel used in cyclofunctionalizations was Merck type 60-PF-254. The material was dried overnight at 115 °C in an oven and then allowed to cool in a desiccator.

***N*-Carbethoxy-4-Pentenylamine (2).** 4-Pentenylamine[29] (1.45 g, 17.03 mmol) was dissolved in water (10 mL). Ethyl chloroformate (1.075 g, 9.91 mmol) was added and the mixture was shaken vigorously for about 5 min with intermittent cooling by immersion in a cold-water bath. A solution of sodium hydroxide (800 mg, 20 mmol) in water (5 mL) was added, followed immediately by more ethyl chloroformate (1.075 g, 9.91 mmol). The mixture was shaken vigorously for 15 min. It was then extracted with dichloromethane (2 × 30 mL) and the organic solution was dried (Na_2SO_4) and evaporated. Distillation of the residue gave 2.398 g (89%) of **2** as a colorless and homogeneous (VPC) oil: bp ~90 °C (2.3 mm); NMR ($CDCl_3$) δ 1.22 (t, J = 7 Hz, 3 H), 1.4–1.8 (m, 2 H), 1.88–2.32 (m, 2 H), 3.16 (q, J = 6.5 Hz, 2 H), 4.09 (q, J = 7 Hz, 2 H), 4.6–6.0 (m, 4 H); exact mass 157.1102 (calcd for $C_8H_{15}NO_2$, 157.1103). Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 61.10; H, 9.62; N, 8.94.

The following urethanes were prepared in an analogous fashion.

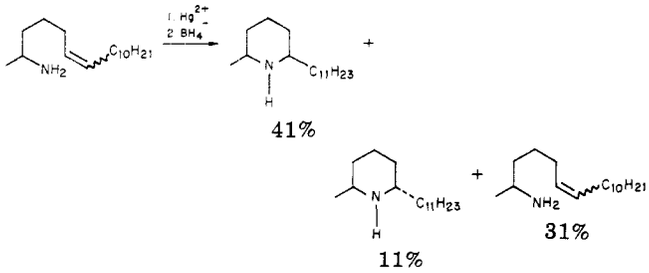
***N*-Carbethoxy-2-allylaniline (3)** was obtained from the corresponding aniline[8] in 84% yield: bp 120 °C (Kugelrohr) (0.1 mm); mp 45–46 °C; NMR ($CDCl_3$) δ 1.28 (t, J = 7.1 Hz, 3 H), 3.22–3.47 (m, 2 H), 4.16 (q, J = 7.1 Hz, 2 H), 4.9–5.27 (m, 2 H), 5.7–6.2 (m, 1 H), 6.54 (br s, 1 H), 6.9–7.35 (m, 3 H), 7.78 (br d, J = ca. 8 Hz, 1 H); exact mass 205.1101 (calcd for $C_{12}H_{15}NO_2$, 205.1099). Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.25; H, 7.31; N, 6.72.

***N*-Carbethoxy-2-(3-methyl-2-butenyl)aniline (4)** was obtained from the corresponding aniline[8] in 90% yield: bp 120 °C (Kugelrohr) (0.1 mm); NMR ($CDCl_3$) δ 1.28 (t, J = 7 Hz, 3 H), ca. 1.78 (br s, 6 H), 3.30 (br d, J = 7.2 Hz, 2 H), 4.20 (q, J = 7 Hz, 2 H), 5.20 (t of m, 1 H), 6.7 (br s, 1 H), 6.8–7.4 (m, 3 H), 7.77 (br d, J = 7.6, 1 H); exact mass 233.1419 (calcd for $C_{14}H_{19}NO_2$, 233.1416). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.03; H, 8.28; N, 5.86.

***N*-Carbethoxy-2-(2-cyclohexenyl)aniline (5)** was prepared from the corresponding aniline[8] in 86% yield: bp 175 °C (Kugelrohr) (0.8 mm); mp 38–39 °C; NMR ($CDCl_3$) δ 1.24 (t, J = 7 Hz, 3 H), 1.3–2.4 (m, 6 H), 3.5 (m, 1 H), 4.16 (q, J = 7 Hz, 2 H), 5.45–6.1 (m, 2 H), 6.6–7.3 (m, 4 H), 7.55–7.92 (m, 1 H); exact mass 245.1414 (calcd for $C_{15}H_{19}NO_2$, 245.1415). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.28; H, 7.66; N, 5.73.

***N*-Carbethoxy-2-allylbenzylamine (6).** 2-Allylbenzamide[30] (268.3 mg, 1.66 mmol) in ether (25 mL) was added dropwise to a magnetically stirred suspension of lithium aluminum hydride (212.6 mg, 5.60 mmol) in ether (5 mL). The mixture was refluxed for 48 h, cooled, and diluted successively with water (0.2 mL),

(23) This interpretation is not meant to exclude *kinetic* formation of a trans-2,6-disubstituted piperidine in a *reversible* process. Formation of **10a** represents a stereoselective process. Compare the following aminomercuration.[7b] The starting amine consists of $Z + E$ isomers in the ratio of about 6:1 (see preparation of the corresponding urethanes).



(24) For (4aα,9aα)-9-carbethoxy-1,2,3,4,4a,9a-hexahydrocarbazole see: Fletcher, M. A.; Lakin, M. W.; Plant, S. G. P. *J. Chem. Soc.* **1953**, 3898.

(25) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E., Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704.

(26) We did not prove that the material obtained in this way has the same relative stereochemistry at the carbon bearing the PhSe group as material formed with PhSeCl. Both products gave identical material on triphenyltin hydride reduction.

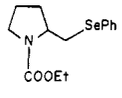
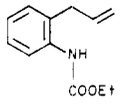
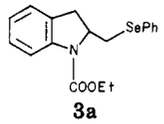
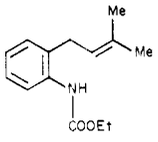
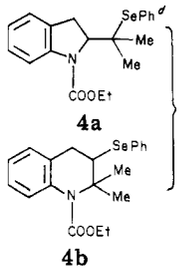
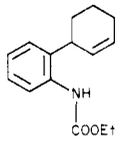
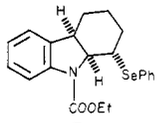
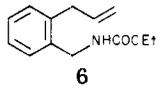
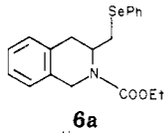
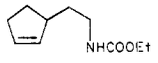
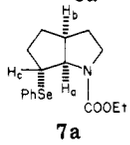
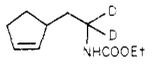
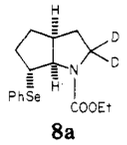
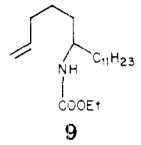
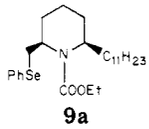
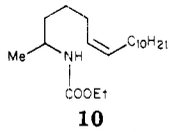
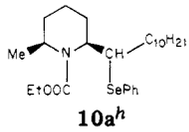
(27) An American supplier of this BASF catalyst is Chemical Dynamics Corp., South Plainfield, NJ 07080.

(28) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(29) Kjaer, A.; Jensen, R. B. *Acta Chem. Scand.* **1956**, *10*, 1365.

(30) Korte, D. E.; Hegedus, L. S.; Wirth, R. K. *J. Org. Chem.* **1977**, *42*, 1329.

Table I[a]

urethane	% yield[b]	product	time, h	% yield without silica[c]	% yield with silica
 2	89	 2a	~1.5	77	93
 3	84	 3a	24	73	85
 4	90	 4a, 4b	70		76
	86	 5a	24	59	82
 6	77[e]	 6a	16	52	87
 7	87[f]	 7a	ca. 16		94
 8	83[f]	 8a	ca. 16		83
 9	35[g]	 9a	40		84
 10	72	 10a[h]	15		35

[a] Yields refer to isolated material and times to the period at room temperature for reactions in the presence of silica gel. [b] The urethanes were prepared in the yield shown from the corresponding amines, except where noted. [c] See ref 9. [d] The products were formed in a ratio of ca. 1:1. [e] The parent amine was made from 2-allylbenzamide. [f] The parent amine was made from (2-cyclopentenyl)acetamide. [g] Prepared by Curtius rearrangement from 2-undecylhept-6-enoic acid. [h] See ref 22.

aqueous sodium hydroxide (15% w/v, 0.2 mL), and water (0.6 mL). The mixture was stirred with ice-bath cooling during the course of this workup and, after an additional 15 min, ethyl chloroformate (3 mL, 31.4 mmol) was added at a fast dropwise rate. Vigorous stirring was continued for 30 min and the mixture was filtered through a sintered disk. The insoluble material was washed liberally with ether and the combined filtrates were evaporated. Chromatography of the residue over silica gel (2 × 60 cm) with 1:4 ethyl acetate/heptane followed by Kugelrohr distillation (110 °C, 0.05 mm) gave 284 mg (77%) of 6 as a colorless and homogeneous (TLC, silica, 1:4 ethyl acetate/heptane) liquid: NMR ($CDCl_3$) δ 1.20 (t, J = 7 Hz, 3 H), 3.39 (t of d, J_1 = 6 Hz, J_2 = 1.5 Hz, 2 H), 4.11 (q, J = 7 Hz, 2 H), 4.32 (br d, J = 6 Hz, 2 H), 4.6–5.4 (m, 3 H), 5.65–6.15 (m, 1 H), 7.0–7.4 (m, 4 H); exact mass 219.1261 (calcd for $C_{13}H_{17}NO_2$, 219.1260). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.02; H, 7.82; N, 6.37.

(2-Cyclopentenyl)acetamide. A benzene solution of (2-cyclopentenyl)acetic acid chloride[31] was saturated with dry NH_3

(31) Cristol, S. J.; Freeman, P. K. *J. Am. Chem. Soc.* **1961**, *83*, 4427.

to afford (2-cyclopentenyl)acetamide (53%): mp 128–133 °C [lit.[32] mp 133 °C]; NMR ($CDCl_3$) δ 1.1–2.6 (m, 6 H), 2.8–3.3 (br t, J = ca. 7 Hz, 1 H), 5.70 (m, 2 H), ca. 5.0–7.0 [m (incorporating br NH signal), 2 H]. The amide was used directly for the preparation of **7** and **8**.

***N*-Carbethoxy-2-(2-cyclopentenyl)ethylamine (7).** (2-Cyclopentenyl)acetamide (1.030 g, 8.23 mmol) in dry THF (45 mL) was injected slowly into a vigorously stirred suspension of lithium aluminum hydride (2.00 g, 52.7 mmol) in THF (10 mL). The mixture was refluxed for 90 min and then cooled in ice. Successive portions of water (2 mL), aqueous sodium hydroxide (15% w/v, 2 mL), and water (6 mL) were added with stirring and, after a further 15 min, ethyl chloroformate (8 mL, 83.7 mmol) was injected dropwise. The cooling bath was removed and stirring was continued for 15 min. The resulting slurry was filtered through a sintered disk. The insoluble material was washed liberally with ether and the combined filtrates were evaporated. Chromatography of the residue over silica gel (5 × 65 cm) with 1:4 ethyl acetate/heptane and Kugelrohr distillation (118 °C, 0.18 mm) gave 1.313 g (87%) of **7** as a colorless, homogeneous (TLC, silica, 1:4 ethyl acetate/heptane) liquid: IR (film) 1698 cm^{-1}; NMR ($CDCl_3$) δ 1.0–2.5 [m (incorporating t, J = 7 Hz at δ 1.22), 6 H], 2.66 (br t, J = ca. 7.5 Hz, 1 H), 3–3.4 (m, 2 H), 4.10 (q, J = 7 Hz, 2 H), 4.80 (br s, 1 H), 5.6–5.85 (m, 2 H); exact mass 183.1258 (calcd for $C_{10}H_{17}NO_2$, 183.1267). Anal. Calcd for $C_{10}H_{17}NO_2$: C, 65.54; H, 9.35; N, 7.64. Found: C, 65.50; H, 9,28; N, 7.90.

***N*-Carbethoxy-2-(2-cyclopentenyl)ethyl-*1,1-d*$_2$-amine (8).** This compound was prepared (83%) by the same method used for **7** except that lithium aluminum deuteride was employed in the reduction step; NMR ($CDCl_3$) δ 1.0–1.8 [m (incorporating t, J = 7.2 Hz, at δ 1.28), 6 H], 1.8–2.5 (m, 3 H), 2.7 (br t, J = ca. 6 Hz, 1 H), 4.1 (q, J = 7.2 Hz, 2 H), 4.86 (br s, 1 H), 5.5–5.9 (m, 2 H); exact mass 185.1390 (calcd for $C_{10}H_{15}D_2NO_2$, 185.1385).

2-Undecylhept-6-enoic Acid.[33] Butyllithium (2.4 M, heptane solution, 20.9 mL, 50.16 mmol) was added dropwise, under nitrogen, to a magnetically stirred solution of dry diisopropylamine (4.90 g, 48.4 mmol) in THF (30 mL). The internal temperature of the reaction mixture was kept below −10 °C by using an acetone–dry ice cooling bath. Tridecanoic acid (4.715 g, 22.00 mmol) in THF (30 mL) was injected 10 min after the end of the addition at such a rate that the cooling bath was able to maintain the temperature below 0 °C. Hexamethylphosphoric triamide (4.5 mL, from a freshly opened bottle) was added in one lot, the cooling bath was removed, and the mixture was stirred for 30 min. 5-Bromopentene[34] (3.615 g, 24.26 mmol) in THF (20 mL) was then injected very rapidly, causing the temperature of the mixture to rise from −5 to +5 °C. Stirring at room temperature was continued overnight. At that stage the mixture was diluted with hydrochloric acid (10% w/v, 100 mL) and extracted with petroleum ether (400 mL; bp 30–60 °C). The organic solution was washed with hydrochloric acid (10% w/v, 3 × 100 mL) followed by brine and it was then dried (Na_2SO_4). Evaporation afforded 6.033 g (97%) of the product in a form sufficiently pure for the next stage: NMR ($CDCl_3$) δ 0.65–2.7 (m, 30 H), 4.8–5.2 (m, 2 H), 5.55–6.0 (m, 1 H), ca. 10 (br s, 1 H). Anal. Calcd for $C_{18}H_{34}O_2$: C, 76.53; H, 12.13. Found: C, 76.39; H, 12.29.

***N*-Carbethoxy-6-amino-1-heptadecene (9).**[35] Thionyl chloride (40 mL) was added to a solution of 2-undecylhept-6-enoic acid (6.03 g, 21.35 mmol) in dry toluene (40 mL) and the mixture was stirred, with protection from moisture, for 3.5 h. At this stage formation of the acid chloride was complete (IR control) and the solvent and excess of reagent were evaporated in vacuo at room temperature. The residual acid chloride was dissolved in dry acetone (30 mL) and added to an ice-cold solution of sodium azide (7.0 g, 107.7 mmol) in water (50 mL). The resulting suspension was stirred at room temperature for 1 h, diluted with water (100 mL), and extracted with toluene (200 mL). The organic layer was wahed with brine, dried (Na_2SO_4), and evaporated at room temperature. **Caution.**[36] The crude azide (IR (film) ν_{max} 2135 cm^{-1}) was dissolved in dry toluene (100 mL) and the mixture was protected from moisture by a calcium sulfate tube and heated at 95 °C for 3 h. At this stage all the azide had been converted into the corresponding isocyanate (IR (film) ν_{max} 2270 cm^{-1}). Absolute ethanol (20 mL) was added, a reflux condenser was fitted between the reaction flask and the calcium sulfate tube, and heating at 95 °C was continued for 40 h. During this period the isocyanate was converted into the ethyl urethane **9** (IR control). The mixture was evaporated and the residual solid was subjected to flash chromatograph[28] over silica gel[28] (5 × 16 cm) with 1:15 ethyl acetate/heptane to afford 2.718 g of **9** as a white, homogeneous (TLC, silica, 1:8 ethyl acetate/heptane) solid, mp 56–57 °C. (An impure fraction (702 mg) was also obtained but was not processed further.) Recrystallization from methanol gave 2.499 g (35%) of **9**: mp 61.5–63 °C; IR (solid) 1684 cm^{-1}; NMR ($CDCl_3$) δ 0.65–2.35 (m, 32 H), 3.55 (br s, 1 H), 3.85–4.55 [m (incorporating q, J = 7 Hz at δ 4.08), 3 H], 4.8–5.2 (m, 2 H), 5.55–6.0 (m, 1 H); exact mass 325.2977 (calcd for $C_{20}H_{39}NO_2$, 325.2981). Anal. Calcd for $C_{20}H_{39}NO_2$: C, 73.79; H, 12.08; N, 4.30. Found: C, 73.66; H, 12.18; N, 4.20.

***N*-Carbethoxy-2-aminoheptadec-6-ene (10) and *E* Isomer.** Ethyl chloroformate (1.085 g, 10 mmol) in ether (5 mL) was added to an ice-cold and magnetically-stirred mixture of (6-*EZ*)-2-aminoheptadec-6-ene[7b,37] (1.36 g, 5.37 mmol) in ether (15 mL) and sodium hydroxide (400 mg, 10 mmol) in water (5 mL). After 20 min no amine remained (TLC control) and the ether layer was dried (Na_2SO_4) and evaporated to afford a crude mixture (1.6785 g) of **10** and its *E* isomer. The material was chromatographed over neutral grade 3 alumina impregnated[38] with 5% w/w of silver nitrate (2 × 60 cm) by using 4:1 ethyl acetate/2,2,4-trimethylpentane as eluant. Appropriate fractions were evaporated to afford homogeneous (TLC, alumina impregnated with 5% w/w nitrate, 4:1 ethyl acetate/2,2,4-trimethylpentane) specimens of the *E* olefin (216.1 mg, 12.3%) and the *Z* isomer (**10**) (1.2713 g, 72.7%) as well as a mixture (141.9 mg) of both materials. *Z* isomer: IR (CCl_4) 1720 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.88 (t, J = 6.5 Hz, 3 H), 1–1.53 [m (incorporating d, J = 6.7 Hz at δ 1.13, 3 H), 26 H], 1.88–2.15 (m, 4 H), 3.67 (br s, 1 H), 4.07 (q, J = 7 Hz, 2 H), 4.4 (br s, 1 H), 5.34 (approximate octet, 2 H; irradiation of signal centered at δ ~2.0 caused the olefinic octet to collapse to an AB quartet, J = 11 Hz); ^{13}C NMR ($CDCl_3$) δ 14.11, 14.71, 21.42, 22.76, 26.17, 27.08, 27.33, 29.41, 29.71, 32.01, 36.94, 47.09, 60.61, 129.33, 130.61, 156.29; exact mass 325.2979 (calcd for $C_{20}H_{39}NO_2$, 325.2984). Anal. Calcd for $C_{20}H_{39}NO_2$: C, 73.92; H, 12.08; N, 4.30. Found: C, 73.77; H, 11.93; N, 4.24. *E* isomer: mp 44 °C; IR (CCl_4) 1725 cm^{-1}; NMR ($CDCl_3$, 200 MHz) δ 0.86 (t, J = 6.5 Hz, 3 H), 1.02–1.50 [m (incorporating d, J = 6.5 Hz, 3 H), 26 H], 1.82–2.10 (m, 4 H), 3.66 (br s, 1 H), 4.10 (q, J = 7 Hz, 2 H), 4.38 (br s, 1 H), 5.38 (almost symmetrical 10 line pattern, 2 H, irradiation of signal centered at δ 1.9 caused the olefinic multiplet to collapse to an AB quartet, J = 15.4 Hz); ^{13}C NMR ($CDCl_3$) δ 14.11, 14.71, 21.41, 22.75, 26.04, 29.28, 29.44, 29.74, 32.00, 32.48, 32.67, 36.82, 47.10, 60.61, 129.81, 131.15, 156.29, exact mass 325.2980 (calcd for $C_{20}H_{39}NO_2$, 325.2980). Anal. Calcd for $C_{20}H_{39}NO_2$: C, 73.92; H, 12.08; N, 4.30. Found: C, 73.99; H, 12.01; N, 4.17.

(±)-*N*-Carbethoxy-2-[(phenylseleno)methyl]pyrrolidine (2a). Tri-*n*-butylphosphine (413 mg, 2.04 mmol) was injected dropwise over about 3 min into a magnetically stirred solution of (±)-*N*-carbethoxy-2-(hydroxymethyl)pyrrolidine[39] (232 mg, 1.34 mmol) and phenyl selenocyanate (282 mg, 1.54 mmol) in THF (2.5 mL).[40] The red solution was stirred under nitrogen for 2

(32) Buu-Hoi, M. M.; Cagniant, P. *Bull. Soc. Chim. Fr.* **1945**, *12*, 978.
(33) Cf.: Pfeffer, P. E.; Silbert, L. S.; Chirinko, J. M., Jr. *J. Org. Chem.* **1972**, *37*, 451.
(34) Laforge, F. B.; Green, N.; Gersdorff, W. A. *J. Am. Chem. Soc.* **1948**, *70*, 3707.
(35) Cf.: Erhardt, P. W. *J. Org. Chem.* **1979**, *44*, 883.
(36) The evaporation and subsequent heating of the azide were done behind a safety shield. The apparatus was handled with large tongs and heavy asbestos gloves were worn.
(37) We thank Dr. Qui Khuong-Huu for providing us with details of the preparation.
(38) Neutral aluminum oxide (100 g) was added to a solution of silver nitrate (5 g) in distilled water (60 mL). The mixture was shaken for a few minutes, the water was evaporated under water-pump vacuum at 60 °C with protection from light, and the residue was dried for about 12 h in an oven at 120 °C.
(39) Wiegrebe, W.; Herrmann, E.-G.; Schlunegger, U. P.; Budzikiewicz, H. *Helv. Chim. Acta* **1974**, *57*, 301. Karrer, P.; Portmann, P.; Suter, M. *Helv. Chim. Acta* **1948**, *31*, 1617.
(40) Cf.: Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

h and then evaporated. Chromatography of the residue first over silica gel (1 × 50 cm) with 1:1 ethyl acetate/heptane and then over silica gel (1 × 50 cm) with 1:3 ethyl acetate/heptane followed by distillation in a Kugelrohr apparatus gave 87 mg (20%) of **2a** as a pale yellow, homogeneous (TLC, silica 1:3 ethyl acetate/heptane) oil: bp 130 °C (0.15 mm); IR (CCl_4) 1700 cm^{-1}; NMR ($CDCl_3$, 32 °C) δ 1.2 (t, J = 7 Hz, 3 H), 1.5–2.11 (m, 4 H), 2.44–3.06 (m, 1 H), 3.06–3.6 (m, 3 H), 3.74–4.3 [m (incorporating q, J = 7 Hz at δ 4.06), 3 H], 7.02–7.37 (m, 3 H), 7.37–7.70 (m, 2 H). Anal. Calcd for $C_{14}H_{19}NO_2Se$: C, 53.85; H, 6.13; N, 4.49; O, 10.25. Found: C, 53.61; H, 6.20; N, 4.58; O, 10.33.

General Procedure for Cyclofunctionalizations. (Reaction times are specified in Table I.)

***N*-Carbethoxy-2-[(phenylseleno)methyl]pyrrolidine (2a).** *N*-Carbethoxy-4-pentenylamine (378.5 mg, 2.41 mmol) and silica gel (735 mg) were weighed into a dry round-bottomed flask. A magnetic stirring bar was added and the flask was closed by a rubber septum carrying inlet and exit needles for nitrogen. Dry dichloromethane (10 mL) was injected and the resulting suspension was stirred and cooled by an acetone–dry ice bath at −78 °C. Phenylselenenyl chloride (514.4 mg, 2.69 mmol) in dichloromethane (8 mL) was added dropwise, the addition taking ca. 20 min. The red color of each drop was discharged instantaneously. More solvent (2 mL) was used to rinse all the reagent into the reaction vessel. The exit needle for nitrogen was removed and vigorous stirring was continued first for 10 min with the cooling bath in place and then for 75 min without the bath. During the latter period the reaction flask was wrapped with aluminum foil. The yellow suspension was filtered through a sintered disk and the insoluble material was washed with ethyl acetate. The combined filtrates were evaporated and the residue was chromatographed over silica gel (2 × 57 cm) with 1:4 ethyl acetate/heptane. When the diphenyl diselenide had been eluted, the solvent was changed to 1:1 ethyl acetate/heptane. Appropriate fractions were combined, evaporated, and distilled in a Kugelrohr apparatus (130 °C, 0.01 mm) to afford 706.2 mg (93%) of **2a** as a yellow, homogeneous (TLC, silica, 1:3 ethyl acetate/heptane) oil spectroscopically identical with material made from racemic proline. The present sample had the following spectral data: IR (film) 1700 cm^{-1}; NMR ($CDCl_3$, 0 °C) δ 1.04–1.4 (two overlapping t, J = 7.1 Hz, 3 H), 1.57–2.12 (m, 4 H), 2.49–3.0 (m, 1 H), 3.09–3.72 (m, 3 H), 3.72–4.36 [m (incorporating q, J = 7 Hz at δ 4.06), 3 H], 7.04–7.39 (m, 3 H), 7.39–7.75 (m, 2 H); exact mass 313.0581 (calcd for $C_{14}H_{19}NO_2{}^{80}Se$, 313.0581).

***N*-Carbethoxy-2,3-dihydro-2-[(phenylseleno)methyl]indole (3a).** The general method using *N*-carbethoxy-2-allylaniline (**3**) (76.7 mg, 0.374 mmol) and silica gel (85.0 mg) in dichloromethane (1 mL) together with phenylselenenyl chloride (74.8 mg, 0.391 mmol) in dichloromethane (1 mL plus 0.5 mL as a rinse) was followed. Isolation by PLC (one silica plate developed with 1:5 ethyl acetate/heptane), followed by distillation in a Kugelrohr apparatus (203 °C, 0.13 mm) gave 114.9 mg (85%) of **3a** as a homogeneous (TLC, silica, 1:4 ethyl acetate/heptane) oil: IR (film) 1703 cm^{-1}; NMR ($CDCl_3$, 32 °C) δ 1.3 (t, J = 7.1 Hz, 3 H), 2.64–3.52 (m, 4 H), 4.29 (q, J = 7.1 Hz, 2 H), 4.37–4.72 (m, 1 H), 6.73–7.90 (m, 9 H); exact mass 861.0607 (calcd for $C_{18}H_{19}NO_2{}^{80}Se$, 361.0581). Anal. Calcd for $C_{18}H_{19}NO_2Se$: C, 60.00; H, 5.31; N, 3.89; O, 8.88. Found: C, 60.22; H, 5.37; N, 3.83; O, 8.91.

***N*-Carbethoxy-2,3-dihydro[(1-methyl-1-phenylseleno)ethyl]indole (4a) and *N*-Carbethoxy-2,2-dimethyl-3-(phenylseleno)-1,2,3,4-tetrahydroquinoline (4b).** Apart from the presence of propylene oxide as an acid trap, the general method was followed. Phenylselenenyl chloride (191.1 mg, 0.99 mmol) in dichloromethane (2.5 mL plus 0.5 mL as a rinse) was added at −78 °C to a stirred mixture of *N*-carbethoxy-2-(3-methyl-2-butenyl)aniline (**4**) (214 mg, 0.92 mmol), propylene oxide (1 mL), and silica gel (572 mg) in dichloromethane (5 mL). A chromatographically homogeneous (TLC, silica, 3:1 benzene/heptane) product weighing 273.1 mg (76%) was isolated by PLC (2 silica plates, developed once with 3:1 benzene/heptane). The NMR spectrum showed the material to be a mixture of **4a** and **4b** in the ratio of ca. 51:49; NMR ($CDCl_3$, 30 °C) **4a**: δ 1.02 (s), 1.2 (t, J = 7.2 Hz), 1.42 (s), [signals at 1.02–1.42 represent 9 H],[41] 3.25–3.47 (br d, J = ca. 5.5 Hz, 2 H), 4.15 (q, J = 7.2 Hz, 2 H), 4.6 (d of d, J_1 = ca. 5 Hz, J_2 = 6.3 Hz, 1 H); **4b**: δ 1.25 (t, J = 7 Hz, 3 H), 1.68 (s, 3 H), 1.80 (s, 3 H), 2.89–3.28 (m, 2 H), 4.2 (q, J = 7 Hz, 2 H). The NMR spectrum of the mixture also showed a multiplet at δ 6.78–7.81 (9 H).[42] The material was characterized further by reduction with triphenyltin hydride.

***N*-Carbethoxy-2,3-dihydro-2-[1-methylethyl]indole (4c) and *N*-Carbethoxy-2,2-dimethyl-1,2,3,4-tetrahydroquinoline (4d).** Triphenyltin hydride (698 mg, 1.99 mmol) was added to a solution of **4a** and **4b** (235.9 mg combined weight, 0.61 mmol) in toluene (5 mL). The mixture was refluxed for 4.5 h (nitrogen atmosphere), cooled, filtered through a small pad of glass wool, and evaporated. The resulting grey slurry was distilled in a Kugelrohr apparatus (130 °C, 0.1 mm) to afford a colorless liquid which was chromatographed over silica gel (2 × 55 cm) with 1:15 ethyl acetate/heptane to give 116.3 mg (82%) of **4c** and **4d** as a chromatographically homogeneous (TLC, silica, 1:15 ethyl acetate/heptane) oil. The two components were separated by preparative VPC [40 ft × 0.25 in. o.d. Apiezon T 10% on Chromosorb W; column temperature 180 °C; injection temperature 250 °C]. **4d**: IR (film) 1700 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (t, J = 7 Hz, 3 H), 1.6 (s, 6 H), 1.65–1.86 (m, 2 H), 2.5–2.7 (m, 2 H), 4.22 (q, J = 7 Hz, 2 H), 6.9–7.35 (m, 4 H); exact mass 233.1415 (calcd for $C_{14}H_{19}NO_2$ 233.1419). **4c**: IR (film) 1706 cm^{-1}; NMR ($CDCl_3$) δ 0.8 (d, J = 7 Hz, 3 H), 0.9 (d, J = 7 Hz, 3 H), 1.34 (t, J = 7 Hz, 3 H), 2–2.5 (m, 1 H), 2.6–3.35 (m, 2 H), 3.95–4.55 [m (incorporating q, J = 7 Hz, at δ 4.3), 3 H], 6.65–7.4 (m, 3 H), 7.5–7.85 (m, 1 H); mass spectrum, m/e (relative intensity) 233 (13.9), 190 (47), 162 (3), 118 (100), 91 (15). The composition of the mixture before VPC separation was ca. 45% **4c** and 55% **4d** as judged by NMR.

9-Carbethoxy-1α-(phenylseleno)-1,2,3,4,4aα,9aα-hexahydrocarbazole (5a). The general method using *N*-carbethoxy-2-(2-cyclohexenyl)aniline (**5**) (265.0 mg, 1.08 mmol) and silica gel (1.020 g) in dichloromethane (5 mL) together with phenylselenenyl chloride (234.2 mg, 1.22 mmol) in dichloromethane (2 mL plus 1 mL as a rinse) was followed. Chromatography over silica gel (3 × 60 cm) with 1:9 ethyl acetate/heptane followed by crystallization from methanol gave 355.1 mg (82%) of **5a** as a white, homogeneous (TLC, silica, 1:4 ethyl acetate/heptane) solid: mp 99–100 °C; IR (solid) 1704 cm^{-1}; NMR ($CDCl_3$, 32 °C) δ 1.0–2.3 [m (incorporating t, J = 7 Hz, at δ 1.23), 9 H], 3.11 (t of d, br, J_1 = 10, J_2 = 4 Hz, 1 H), 3.54 (br t, J = 6 Hz, 1 H), 4.2 (q, J = 7 Hz, 2 H), 4.54 (d of d, J_1 = 7.5 Hz, J_2 = 9 Hz, 1 H), 6.8–7.8 (m, 9 H); exact mass 401.0902 (calcd for $C_{21}H_{23}NO_2{}^{80}Se$, 401.0894). Anal. Calcd for $C_{21}H_{23}NO_2Se$: C, 63.00; H, 5.79; N, 3.50; O, 7.99. Found: C, 62.95; H, 5.56; N, 3.35; O, 8.15.

2-Carbethoxy-3-[(phenylseleno)methyl]-1,2,3,4-tetrahydroisoquinoline (6a). The general method using *N*-carbethoxy-2-allylbenzylamine (**6**) (212.4 mg, 0.97 mmol) and silica gel (389 mg) in dichloromethane (3 mL) together with phenylselenenyl chloride (201.3 mg, 1.05 mmol) in dichloromethane (2 mL and 1 mL as a rinse) was followed. Chromatography over silica gel (3 × 50 cm) with 1:5 ethyl acetate/heptane followed by Kugelrohr distillation (200 °C, 0.1 mm) gave 315.6 mg (87%) of **6a** as a pale yellow, homogeneous (TLC, 1:5 ethyl acetate/heptane) oil: IR (film) 1701 cm^{-1}; NMR ($CDCl_3$, 31 °C) δ 1.23 (br t, J = 6.5 Hz, 3 H), 2.55–3.24 (m, 3 H), 3.95–4.9 (m, 5 H), 6.8–7.65 (m, 9 H); exact mass 375.0739 (calcd for $C_{19}H_{21}NO_2{}^{80}Se$, 375.0739). Anal. Calcd for $C_{19}H_{21}NO_2Se$: C, 60.96; H, 5.65; N, 3.74. Found: C, 60.93; H, 5.64; N, 3.59.

(3aα,6α,6aα)-1-Carbethoxy-6-(phenylseleno)octahydrocyclopenta[*b*]pyrrole (7a). The general method using *N*-carbethoxy-2-(2-cyclopentenyl)ethylamine (**7**) (320 mg, 1.75 mmol) and silica gel (290 mg) in dichloromethane (3 mL) together with phenylselenenyl chloride (367 mg, 1.92 mmol) in dichloromethane (4 mL plus 1 mL as a rinse) was followed. Chromatography over silica gel (2 × 60 cm) with 1:4 ethyl acetate/heptane followed by Kugelrohr distillation (180 °C, 0.1 mm) afforded 556.1 mg (94%) of **7a** as a yellow, homogeneous (TLC, silica, 1:4 ethyl acetate/heptane) oil: IR (film) 1699 cm^{-1}; NMR (Me_2SO-d_6, 200 MHz, 70 °C) δ 1.12 (t, J = 7 Hz, 3 H), 1.26–2.2 (m, 6 H), 2.74–2.98 (m, 1 H), 3.07–3.29 (m, 1 H), 3.54 (2 partially overlapping q, J_1 = 11.2

(41) The relative intensities are calculated on the basis of a 1:1 mixture.

(42) The relative intensity is based on setting the rest of the spectral integration at 14-H.

Hz, J_2 = 8.3 Hz, J_3 = 3.2 Hz), 3.89 (br s, $W_{1/2}$ = 11 Hz), 3.99 (q of d, J_1 = 8 Hz, J_2 = ca. 1 Hz), 4.12 (br d, J = 7 Hz), signals at 3.8–4.2 represent 4 H, 7.22–7.4 (m, 3 H), 7.5–7.66 (m, 2 H); exact mass 339.0734 (calcd for $C_{16}H_{21}NO_2{}^{80}Se$, 339.0738). Anal. Calcd for $C_{16}H_{21}NO_2Se$: C, 56.80; H, 6.26; N, 4.14; O, 9.46. Found: C, 56.62; H, 6.17; N, 3.94; O, 9.21.

(3aα,6α,6aα)-1-Carbethoxy-6-(phenylseleno)octahydrocyclopenta[*b*]pyrrole-*2,2-d*$_2$ (8a). *N*-Carbethoxy-2(2-cyclopentenyl)ethyl-*1,1-d*$_2$-amine was converted (83% yield), by the method used for the nondeuterated material, although on a smaller scale, into **8a**: NMR (Me_2SO-d_6, 400 MHz, 70 °C) δ 1.15 (t, J = 7 Hz, 3 H), 1.36–1.5 (m, 1 H), 1.59 (q, J_1 = 13 Hz, J_2 = 2 Hz, 1 H), 1.64–1.77 (m, 1 H), 1.88 (d of d, J_1 = 12 Hz, J_2 = 8 Hz, 1 H), 1.93–2.1 (m, 2 H), 2.8–2.96 (m, 1 H), 3.88 (br s, $W_{1/2}$ = 12.4 Hz, 1 H), 3.92–4.07 (m, 1 H), 4.12 (br d, J = 6.5 Hz, 1 H), 7.2–7.36 (m, 3 H), 7.52–7.66 (m, 2 H); exact mass 341.0864 (calcd for $C_{16}H_{19}D_2NO_2{}^{80}Se$, 341.0863).

***N*-Carbethoxy-*cis*-cyclopentano[*b*]pyrrolidine.** 2-Oxo-*cis*-cyclopentano[*b*]pyrrolidine[43] was converted (62%) into the urethane by the method used for compound **7**. The material was identical with a fully characterized sample made[21b] by reduction of **7a** with triphenyltin hydride.

***cis*-*N*-Carbethoxy-2-(phenylselenomethyl)-6-undecylpiperidine (9a).** The general method using *N*-carbethoxy-6-amino-1-heptadecene (**9**) (360.7 mg, 1.106 mmol) and silica gel (950 mg) in dichloromethane (12 mL) together with phenylselenenyl chloride (236.1 mg, 1.232 mmol) in dichloromethane (2.5 mL plus 0.5 mL as a rinse) was followed. Flash chromatography[28] over silica gel (3 × 18 cm) using first heptane (to elute diphenyl diselenide) and then 1:4 ethyl acetate/heptane afforded 449.9 mg (84%) of **28** as a homogeneous (TLC, silica or alumina, 1:9 ethyl acetate/heptane) oil: IR (film) 1693 cm^{-1}; NMR (Me_2SO-d_6, 70 °C, 200 MHz) δ 0.85 (t, J = 6.50, 3 H), 1.0–2.0 [m (incorporating t, J = 7 Hz, at δ 1.09],[44] 2.96–3.24 (m, 2 H), 3.88–4.13 [m (incorporating d of q, J_1 = 7.0 Hz, J_2 = 2.8 Hz, at δ 3.99), 3 H], 4.13–4.34 (m, 1 H), 7.2–7.4 (m, 3 H), 7.44–7.6 (m, 2 H); exact mass 481.2449 (calcd for $C_{26}H_{43}NO_2{}^{80}Se$, 481.2459). Anal. Calcd for $C_{26}H_{43}NO_2Se$: C, 64.98; H, 9.02; N, 2.91; O, 6.66. Found: C, 65.21; H, 9.18; N, 2.95; O, 6.51.

***cis*-*N*-Carbethoxy-2-methyl-6-undecylpiperidine (11).** *cis*-*N*-Carbethoxy-2-(phenylselenomethyl)-6-undecylpiperidine (**9a**) (631 mg, 1.313 mmol) was dissolved in toluene (12 mL). The mixture was stirred magnetically and refluxed by using an oil bath maintained at 120 °C. Portions of triphenyltin hydride were injected from a syringe as follows and all the material was rinsed from the syringe after each injection by a small amount (ca. 1 mL) of toluene: 409 mg (1.165 mmol) as soon as reflux started; 313 mg (0.892 mmol) after 0.5 h; 630 mg (1.795 mmol) after 2.5 h; and 400 mg (1.139 mmol) after 5 h. Refluxing was continued for a further 19 h by which stage no starting material was detectable (TLC). Evaporation of the solvent and flash chromatography[28] of the residue over silica gel[28] (5 × 15 cm) with 1:99 ethyl acetate/heptane gave 414 mg (96%) of **11** as a faintly yellow oil. Examination by TLC revealed traces of UV-active impurities, judged by NMR to amount to less than 2 mol % (assuming the impurity signals are due to triphenyltin groups). FT IR (film) 1695 cm^{-1}; NMR ($CDCl_3$) δ 0.72–2.0 (m, 35 H), 3.94–4.57 (br signal overlapping q, J = 7 Hz, at δ 4.13, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 14.7, 20.5, 22.7, 27.5, 27.6, 29.4, 29.7, 30.3, 31.9, 35.1, 45.9, 50.5, 60.8, 156.2; exact mass 310.2751 (calcd for $C_{19}H_{36}NO_2$ (M − CH_3), 310.2745). Anal. Calcd for $C_{20}H_{39}NO_2$: C, 73.80; H, 12.08; N, 4.30. Found: C, 74.03; H, 12.12; N, 4.30.

***cis*-2-Methyl-6-undecylpiperidine (12).** *cis*-*N*-Carbethoxy-2-methyl-6-undecylpiperidine (140.4 mg, 0.431 mmol) was stirred with 95% ethanol (7 mL) and concentrated hydrochloric acid (8 mL). The mixture was refluxed for 88 h, cooled, and evaporated. The residue was diluted with water, made strongly basic with sodium hydroxide, and extracted with ether. The extract was dried (Na_2SO_4) and evaporated. Flash chromatography[28] of the residue over silica gel[28] (2 × 17 cm) with 1:5 ethyl acetate/heptane gave 100.4 mg (71.5%) of starting material. Elution was continued with ethanol containing 2% (w/v) concentrated ammonia solution to afford 29.1 mg [26.6% (93.4% after correction for recovered starting material)] of **12** as a pale yellow, homogeneous (TLC, alumina, 1:7 ethyl acetate/heptane) oil: NMR ($CDCl_3$, 200 MHz) δ 0.81 (t, J = 6.4 Hz, 3 H), 0.94–1.86 (m, 29 H), 2.45–2.87 (m, 2 H), ca. 4.4 (br signal, 1 H); ^{13}C NMR δ 14.1, 22.7, 24.8, 26.0, 29.3, 29.6, 31.7, 31.9, 34.0, 36.9, 52.7, 57.3; exact mass 253.2755 (calcd for $C_{17}H_{35}N$, 253.2770), 238.2531 (calcd for $C_{16}H_{32}N$ (M − CH_3), 238.2535), 98.0966 (base peak, calcd for $C_6H_{12}N$ (M − $C_{11}H_{23}$), 98.0969). The amine was converted into its hydrochloride (by passing hydrogen chloride into an ethereal solution) which was recrystallized twice from ca. 1:10 ethanol/hexane, mp 153–155 °C [lit.[7b] 154–155 °C].

***cis*-*N*-Carbethoxy-2-methyl-6-[1-(phenylseleno)undecyl]piperidine (10a).** The general method using (*Z*)-*N*-carbethoxy-2-aminoheptadec-6-ene (**10**) (223.6 mg, 0.69 mmol) and silica gel (300 mg) in dichloromethane (10 mL) together with phenylselenenyl chloride (144.9 mg, 0.76 mmol) in dichloromethane (5 mL plus 5 mL as a rinse) was followed. After a reaction period of 15 h[45] chromatography over silica gel (1 × 59 cm) with 1:9 ethyl acetate/heptane gave 116.9 mg (35%) of **10a**. Examination by TLC (silica, 1:9 ethyl acetate/heptane) revealed trace impurities: NMR (200 MHz, $CDCl_3$, 30 °C) δ 0.82 (t, J = 6.6 Hz, 3 H), 0.96–2.0 (m, 30 H), 3.59–3.76 (m, 1 H), 4.0–4.23 (m, 2 H), 4.23–4.54 (m, 2 H), 7.30–7.47 (m, 3 H), 7.6–7.76 (m, 2 H); ^{13}C NMR δ 14.1, 14.7, 21.4, 22.7, 26.1, 27.0, 27.3, 29.4, 29.7, 32.0, 36.9, 47.0, 60.6, 128.9, 129.3, 130.6, 134.6, 156.2; exact mass 481.2459 (calcd for $C_{26}H_{43}NO_2Se$, 481.2459). The *E* isomer of **10** reacts less efficiently than **10**.

Reduction of **10a** (89.1 mg) with triphenyltin hydride (64 mg) in refluxing toluene (5 mL) gave, after a reaction period of 8 h, *cis*-*N*-carbethoxy-2-methyl-6-undecylpiperidine (**11**) in 74% yield. The material was identical with the sample made from **9a**.

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Registry No. 2, 67902-36-7; (±)-**2a**, 72844-92-9; **3**, 67902-35-6; **3a**, 67902-39-0; **4**, 72844-93-0; **4a**, 72844-94-1; **4b**, 72844-95-2; **4c**, 72844-96-3; **4d**, 72844-97-4; **5**, 67902-37-8; **5a**, 72844-98-5; **6**, 67902-38-9; **6a**, 67902-42-5; **7**, 72844-99-6; **7a**, 72845-00-2; **8**, 72845-01-3; **8a**, 72845-02-4; **9**, 72845-03-5; **9a**, 72845-04-6; **10**, 72845-05-7; **10** (*E* isomer), 72845-06-8; **10a**, 72845-07-9; **11**, 72845-08-0; **12**, 35285-24-6; 4-pentenylamine, 22537-07-1; ethyl chloroformate, 541-41-3; 2-allylaniline, 32704-22-6; 2-(3-methyl-2-butenyl)aniline, 27125-61-7; 2-(2-cyclohexenyl)aniline, 59816-86-3; 2-allylbenzamide, 61436-87-1; (2-cyclopentenyl)acetamide, 72845-09-1; (2-cyclopentenyl)acetic acid chloride, 933-03-9; 2-undecylhept-6-enoic acid, 72845-10-4; tridecanoic acid, 638-53-9; 5-bromopentene, 1119-51-3; (6*E*)-2-aminoheptadec-6-ene, 72845-11-5; (6*Z*)-2-aminoheptadec-6-ene, 72845-12-6; (±)-*N*-carbethoxy-2-(hydroxymethyl)pyrrolidine, 72881-26-6; phenyl selenocyanate, 2179-79-5; phenylselenenyl chloride, 5707-04-0; *N*-carbethoxy-*cis*-cyclopentano[*b*]pyrrolidine, 72845-13-7; 2-oxo-*cis*-cyclopentano[*b*]pyrrolidine, 72845-14-8.

(43) Booth, H.; King, F. E.; Mason, K. G.; Parrick, J.; Whitehead, R. L. St. D. *J. Chem. Soc.* **1959**, 1050.

(44) The integral for this region was too high.

(45) Longer reaction times did not improve the yield.