Regio- and Stereoselective 5-*exo* Radical Cyclizations on a Chiral Perhydro-1,3-benzoxazine Moiety. An Access to Enantiopure 3-Alkylpyrrolidines

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Both enantiomers of chiral, nonracemic 3-alkyl-substituted pyrolidines are prepared by diastereoselective 5-*exo*-trig cyclization on (−)-8-aminomenthol-derived perhydro-1,3-benzoxazines used as chiral auxiliaries, followed by elimination of the menthol appendage. The diastereoselective radical cyclization is promoted by tributyltin hydride and occurs on a 3-aza-5-hexenyl-type radical, leading to five-membered rings in high yield. The stereocontrol of the cyclization is strongly influenced by 1,3-allylic strain so that an appropriate substitution pattern on the olefin-acceptor and the presence of a vicinal stereocenter are crucial for achieving good diastereoselectivity. The enantiopure pyrrolidines are obtained in three steps with concomitant recovering of the starting (+)-pulegone auxiliary.

Introduction

Radical cyclizations are considered a modern, powerful tool in the synthesis of carbocycles and heterocycles,[1] and aza radicals have been used in the preparation of four- to seven-membered nitrogen rings in several alkaloids and antibiotics.[2,3] The pyrrolidine nucleus is one of the most common target structures due to the widespread occurrence in numerous natural products,[4] and the main strategy to form this ring by radical cyclization is based on intramolecular addition of aza-5-hexenyl radicals previously generated by homolysis of sensitive carbon−heteroatom bonds present in the skeleton. The ring closure arises predominantly by addition to the inner olefinic position (C-5) to give a five-membered ring (5-*exo* attack), although the 6-*endo* addition is also possible, leading to piperidine derivatives. The position of nitrogen in the 5-hexenyl skeleton seems to determine the rate of cyclization, so that 3-aza-5-hexenyl radicals are known to be very useful and selective precursors.[5] On the other hand, the asymmetric synthesis of pyrrolidines using radical cyclizations is quite limited to date, and chiral auxiliaries play an attractive role in this kind of reaction, whose enantioselective version remains almost unexplored.[6] This fact encouraged us to perform a diastereoselective approach to pyrrolidine derivatives by cyclization of 3-aza-5-hexenyl radical structure attached to an N,O-acetalic chiral auxiliary[7] derived from (−)-8-aminomenthol (**1**).[8] In view of the structure of our system, two possibilities emerge for the starting perhydro-1,3-benzoxazines, which are positional isomers and differ in the attachment of the precursor of the radical site and the double bond (**A** and **B** in Figure 1). The choice of the starting compound is not trivial because aryl radicals derived from related positional isomers behave in a quite different way.[7d] If, as expected, both isomers participate in a 5-*exo* cyclization process, the pyrrolidine derivative will be formed, although the newly created stereocenters will appear in opposite configuration, thereby ensuring the synthesis of both enantiomers.

We report here on radical cyclizations of chiral positional isomeric *N*-alkylperhydro-1,3-benzoxazines **A** and **B**, using tributyltin hydride as promoter and the labile C−Se bond as a source of alkyl radicals.

Results

The cyclization study was started on the 2-vinyl-substituted perhydro-1,3-benzoxazines **4a**−**d** prepared from (−)-8-aminomenthol (**1**)[9] in three steps (Scheme 1). The condensation of **1** with phenylselenoacetaldehyde in dichloromethane afforded 2-(phenylseleno)methylperhydro-1,3-benzoxazine **2** as a single compound. The pres-

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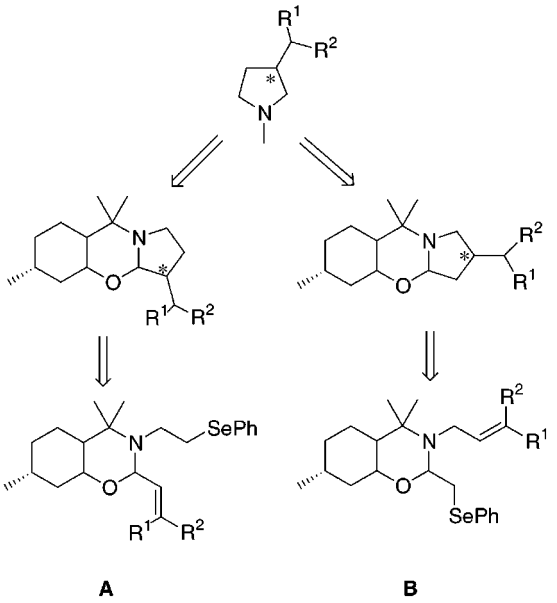
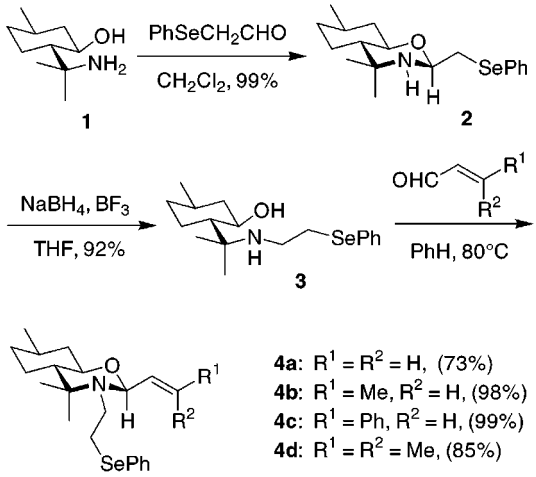


Figure 1.

Scheme 1



ence of the tautomeric hydroxyimine found in the preparation of related N-unsubstituted 1,3-oxazines[10] has not been detected. The experimental conditions for the reductive ring opening of **2** have been shown to be crucial. Thus, treatment of **2** with a mixture of sodium borohydride (1 equiv) and boron trifluoride-etherate (2.5 equiv) in THF at room temperature yielded the amino alcohol **3** in 92% yield, whereas the use of equimolar mixtures of $NaBH_4$ and $BF_3{\cdot}OEt_2$ highly decreased the yield, and the reduction with DIBALH produced significant amounts of diphenyldiselenide as byproduct.[11] Finally, condensation of **3** with acrolein, crotonaldehyde, cinnamaldehyde, and senecialdehyde in refluxing benzene led to perhydro-1,3-benzoxazines **4a**−**d** in good to excellent yields (73−99%). It is worthy to note that all the perhydro-1,3-benzoxazines **2** and **4a**−**d** have the same configuration at C-2, determined as *S* by NOE experiments. This implies that condensation of (−)-8-aminomenthol with aldehydes takes place in a completely stereoselective way, leading to an equatorial arrangement

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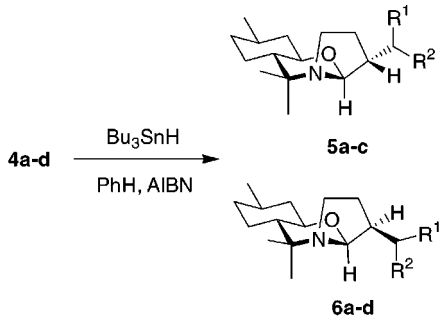
Table 1. Radical Cyclizations of Perhydro-1,3-benzoxazines 4a−d

entry no.	oxazine	R^1	R^2	yield (%)[a]	products ratio[b]
1	**4a**	H	H	82	**5a** (56), **6a** (44)
2	**4b**	Me	H	85	**5b** (61), **6b** (39)
3	**4c**	Ph	H	90	**5c** (53), **6c** (47)
4	**4d**	Me	Me	89	**6d** (100)[c]

[a] Combined chemical yield of pure isolated compounds. [b] Numbers in parentheses refer-to-diastereomeric ratio determined by integration of the signals of ^{1}H NMR spectra of reaction mixture. [c] A single diastereomer is observed in the reaction mixture by ^{1}H NMR.

Scheme 2



of the acetalic substituent on the tetrahydrooxazine chair.[12]

Radical cyclizations were accomplished by syringe pump addition (5−8 h) of 0.02 M solutions of tributyltin hydride and AIBN in benzene to 0.02 M solutions of **4a**−**c** in refluxing benzene. After a period of 24−48 h at reflux the conversion was completed, providing a mixture of two diastereoisomers, **5a**−**c** and **6a**−**c**, which could be isolated and purified by flash chromatography with some contamination of organotin derivatives (Table 1, Scheme 2). ^{1}H NMR analysis revealed that the compounds are the 5-*exo* ring closure diastereomers, and NOESY experiments led us to establish a 2,3-*cis* relationship between the acetalic hydrogen and that attached to the vicinal stereocenter for the major diastereomers **5a**−**c** and the *trans* stereochemistry for the minor ones, **6a**−**c**.

In general the facial discrimination in the cyclization of perhydro-1,3-benzoxazines **4a**−**c** is modest, although compound **4d** behaves in a different way. In the same reaction conditions cyclization of **4d** proceeds with a complete diastereoselection, yielding a single product, **6d**, whose stereochemistry was found to be 2,3-*trans* in the five-membered ring. On the other hand, NOESY studies showed an N-axial layout of the $-CH_2-N-$ group for each diastereomer **5** and **6**. This fact is consistent with a generalized anomeric effect exhibited by many tetrahydro-1,3-oxazines in which N-axial conformers dominate in the nitrogen inversion equilibrium.[13] Additionally, MO calculations performed on our system clearly confirmed this trend.[14] According to these observations, the slight preference toward 2,3-*cis* selectivity observed during the ring closure of precursors **4a**−**c** is in agreement with the

(12) This behavior clearly contrasts with that described for 1,3-oxazolidines. See for example: Higashiyama, H.; Inoue, H.; Yamauchi, T.; Takahashi, H. *J. Chem. Soc., Perkin Trans. 1* **1995**, 111.

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(14) Preliminary SCF-MO calculations indicate a preference toward the N-axial invertomer of about 1.9 kcal mol^{-1} (UHF/PM3) or 1.2 kcal mol^{-1} (UHF/6-31G*//UHF/3-21G*) in our benzoxazine radicals.

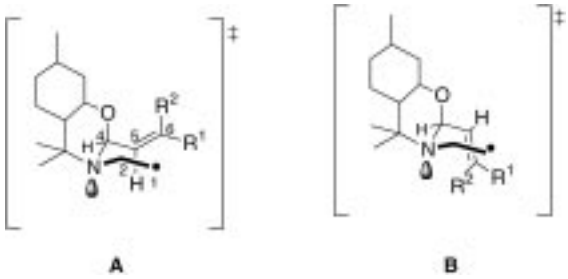
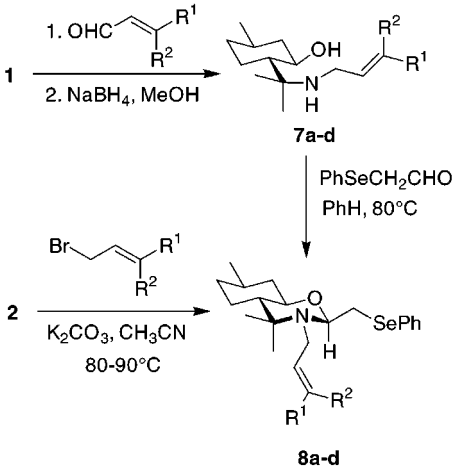


Figure 2. Transition structures for radical cyclization of **4a**−**d**.

Scheme 3



5-hexenyl radical cyclization model proposed by Beckwith and Houk.[15] The formation of the pyrrolidine derivatives could be interpreted taking into account the transition structures **A** and **B** (Figure 2). The chairlike structure **A** should be preferred on the basis of the Beckwith model, and therefore a 2,3-*cis* relationship will arise predominantly leading to the major diastereoisomers **5a**−**c**. On the contrary, the minor products **6a**−**c** would emerge from the less favored boatlike structures **B**. Obviously a different pathway should be followed when $R^2 \neq H$, because **4d** cyclized in a 2,3-*trans* fashion and a single diastereomer was obtained. This complete reversal of diastereoselection can be accounted for by an overwhelmingly preference for the boatlike transition structure **B**. The origin of this strong effect has been nicely investigated by Rajanbabu in some sugar-derived radicals, finding that a local allylic strain at the olefinic group plays a key role in the formation of *trans*-cyclic diastereomers.[16] By analogy we propose that the boatlike structures **B** compensate the normal stereoelectronic effects of standard 5-hexenyl radicals when $R^2 = Me$ because this arrangement contains the most favorable allylic conformation.[17] As a consequence, the *trans*-diastereomer **6d** is the single product observed.

The cyclization process on perhydrobenzoxazines bearing the radical acceptor on the nitrogen substituent was tested on compounds **8a**−**d**. The preparation of the starting compounds was carried out in two different ways (Scheme 3). Sequential reaction of (−)-8-aminomenthol (**1**) with α,β-unsaturated aldehydes and reduction of the intermediate N,O-acetals with sodium borohydride led to the *N*-allylic-8-aminomenthols **7a**−**d** that were condensed with phenylselenoacetaldehyde in refluxing benzene to yield 2-(phenylselenomethyl)perhydro-1,3-benzoxazines **8a**−**d**. Nevertheless, variable amounts (5−10%) of diphenyldiselenide (PhSeSePh) were formed during this condensation, and a careful chromatographic purification is needed to remove the excess of aldehyde and the formed PhSeSePh because of inhibition of the radical cyclization step in favor of a rapid intermolecular hydrogen abstraction.[18] A better approach, which avoids the formation of the organoselenium impurity, implies the N-alkylation of the perhydrobenzoxazine **2**. Treatment of **2** with allyl, crotyl, cinnamyl, and prenyl bromide and potassium carbonate in acetonitrile as solvent provides respectively **8a**−**d**, in very good yields.

Scheme 4

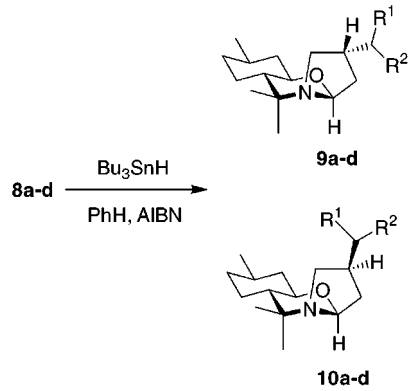


Table 2. Radical Cyclizations of Perhydro-1,3-benzoxazines 8a−d

entry no.	oxazine	R^1	R^2	yield (%)[a]	products ratio[b]
1	**8a**	H	H	84	**9a** (68), **10a** (32)
2	**8b**	Me	H	89	**9b** (65), **10b** (35)
3	**8c**	Ph	H	90	**9c** (58), **10c** (42)
4	**8d**	Me	Me	90	**9d** (66), **10d** (34)

[a] Combined chemical yield of pure isolated compounds. [b] Numbers in parentheses refer-to-diastereomeric ratio determined by integration of the signals of ^1H NMR spectra of reaction mixture.

The cyclization reaction was carried out by slow additions (5−7 h, syringe pump) of a 0.02 M solution of tributyltin hydride (1.25 equiv) and a catalytic amount (0.05 equiv) of AIBN in benzene to a 0.02 M solution of the crude perhydro-1,3-benzoxazine **8a**−**d** in refluxing benzene. After 1−2 h of additional heating a mixture of diastereomeric 5-*exo* cyclization products **9a**−**d** and **10a**−**d** was obtained in excellent yield (82−90%) but in modest de (Scheme 4, Table 2).

Diastereomers **9a**−**c** and **10a**−**c** were easily separated by flash chromatography,[19] but it was not possible to assign the absolute configuration at this stage. However, their transformation into the known substituted pyrrolidines allowed us to determine the configuration at the newly created stereocenter.

The stereoselection for the cyclization of *N*-allylperhydro-1,3-benzoxazines **8a**−**d** could be rationalized by taking into account the two possible chair−boat transition

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(16) Rajanbabu, T. V. *Acc. Chem. Res*. **1991**, *24*, 139.
(17) Hoffman, R. W. *Chem. Rev*. **1989**, *89*, 1841.
(18) Crich, D.; Jiao, X.-Y.; Harwood, J. S. *J. Org. Chem*. **1996**, *61*, 2368, and references therein.
(19) Cyclization products **9d** and **10d** could not be separated by chromatography. The other diastereomers were isolated by flash chromatography, although many attempts to remove the residual organotins were not successful in some cases.

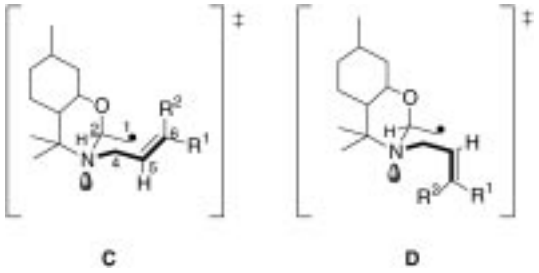
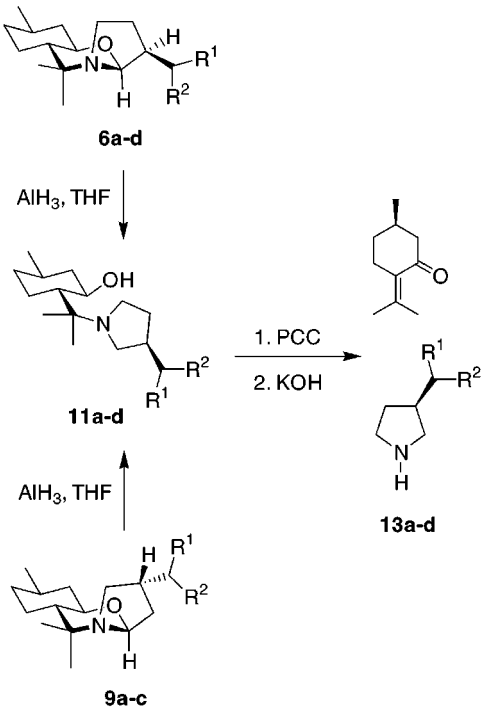


Figure 3. Transition structures for radical cyclization of **8a**−**d**.

Scheme 5



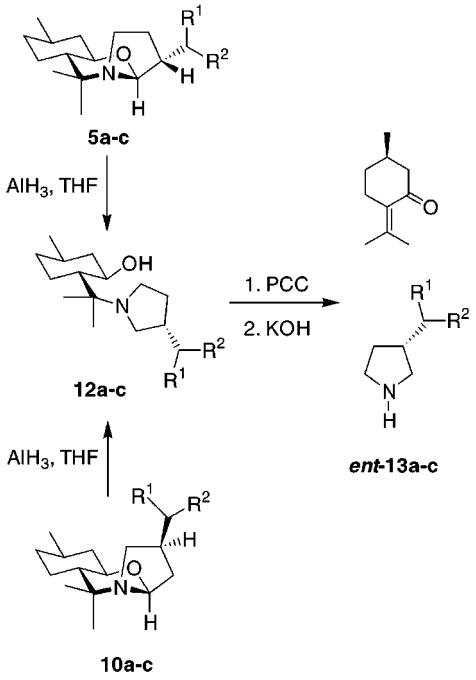
structures depicted in Figure 3. The favored chairlike radical **C** leads to the major stereoisomers **9a**−**d** with 2,4-*cis* relationship, whereas the boatlike **D** provides the minor compounds **10a**−**d** with 2,4-*trans* configuration. The low level of stereodifferentiation is in agreement with the absence of a strong local allylic strain even in the case in which R^2 = Me.

The transformation of the cyclization products into the final enantiopure 3-alkyl-substituted pyrrolidines was achieved with good chemical yields in two steps (Schemes 5 and 6). Reductive ring opening of the N,O-acetal moiety in **6a**−**d**, the minor stereoisomers obtained from the cyclization of **4a**−**d**, with LAH/$AlCl_3$ affords 8-pyrrolidinylmenthols **11a**−**d** in excellent yields (92−99%). In turn, compounds **11a**−**c** were also obtained by reduction of **9a**−**c**, the major cyclization stereoisomers obtained from **8a**−**c**. This fact allows us to assign the proposed stereochemistry for **9a**−**c**.

The epimeric 8-pyrrolidinylmenthols **12a**−**c** were obtained by reductive ring opening of the major diastereomers **5a**−**c** resulting from cyclization of **4a**−**c**, or instead by reduction of the minor ones **10a**−**c**, isolated from the cyclization of **8a**−**c**.

PCC oxidation of **11a**−**d** or **12a**−**c** yielded the corresponding 8-pyrrolidinylmenthones, which were submitted to β-elimination by treatment with an aqueous KOH

Scheme 6



solution in methanol−THF, leading to the enantiopure 3-substituted pyrrolidines **13a**−**d** or ***ent*-13a**−**c**, respectively, with the concomitant release of (+)-pulegone.

In summary, the above protocol constitutes a novel stereoselective approach to enantiopure 3-alkyl-substituted pyrrolidines based on a 5-*exo*-trig radical cyclization performed on a chiral perhydrobenzoxazine template. Both enantiomeric pyrrolidine derivatives can be obtained as major product by changing the substituents at C-2 and the nitrogen atom in the starting chiral perhydro-1,3-benzoxazine.The high level of diastereoselection disclosed under local minimum allylic strain is being investigated, and aplications will be reported in due course.

Experimental Section

General Methods. ^{1}H NMR spectra were registered at 300 MHz in $CDCl_3$ as solvent. ^{13}C NMR (75 MHz) spectra were obtained by the DEPT technique. Mass spectra were performed by electronic impact (EI) at 70 eV or chemical ionization (CI). Optical rotations were measured on a digital polarimeter. Melting points were measured on a capillary open tube and are uncorrected. Column chromatography was carried out on silica gel 60 using the flash technique.

(−)-8-Aminomenthol (1). A solution of (−)-8-benzylaminomenthol[9] (80 g, 0.31 mol) in ethanol (300 mL) containing 5 g of 10% Pd−C catalyst was stirred under hydrogen (10 atm) for 24 h. The mixture was filtered through a pad of Celite, the solution was concentrated under vacuum, and the residue was recrystallized from hexane, leading to (−)-8-aminomenthol (52 g, 99%) as a white solid, mp 68−69 °C (hexanes); $[\alpha]^{20}_D = -6.81$ (*c* 0.53, MeOH) (lit.[8] $[\alpha]^{20}_D = -7$; *c* 0.5, MeOH). ^{1}H NMR ($CDCl_3$) δ: 0.91 (d, 3H, J = 6.5 Hz); 0.91−1.10 (m, 4H); 1.11 (s, 3H); 1.17 (s, 3H); 1.30−1.50 (m, 1H); 1.60−1.70 (m, 2H); 1.85−2.05 (m, 1H); 3.35 (br s, 3H); 3.62 (dt, 1H, J = 10.2 Hz, J = 4.1 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.8; 22.0; 25.9; 30.7; 33.7; 34.6; 44.2; 52.0; 53.0; 72.1. IR (Nujol, cm^{-1}): 3320, 3260, 1600. CIMS (*m*/*z*, %): 172 (M + 1, 100), 155 (20), 137 (69).

Phenylselenoacetaldehyde.[20] To a vigorously stirred solution of diphenyldiselenide (PhSeSePh, 5.8 g, 18.6 mmol)

(20) See footnote 3 in: Kowalski, C. J.; Dung, J.-S. *J. Am. Chem. Soc.* **1980**, *102*, 7951.

in THF (60 mL) under argon atmosphere at 0 °C was added dropwise an equimolar amount of bromine (0.9 mL). After 15 min neat ethylvinyl ether (3.6 mL, 37.2 mmol) was added in one portion, and the purple color instantaneously changed to pale yellow. After stirring for 10 min, hydrochloric acid (2 N solution) was added, and the mixture was stirred for an additional 2 h at room temperature. Diethyl ether (50 mL) was added to the reaction mixture and, after separation, the aqueous layer was extracted with ether (2 × 50). The organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under vacuum to afford phenylselenoacetaldehyde (7.3 g, 36.7 mmol, 99%), yellow oil; bp 150−152 °C (4 Torr). ^{1}H NMR ($CDCl_3$) δ: 3.51 (d, 2H, J = 4.0 Hz); 7.25 (m, 3H); 7.50 (m, 2H); 9.48 (t, 1H, J = 4.0 Hz). IR (neat, cm^{-1}): 2820, 2720, 1570, 1470, 1430, 735, 690. EIMS (*m*/*z*, %): 200 (M, 8), 157 (21), 91 (100).

2-(Phenylseleno)methylperhydro-1,3-benzoxazine (2). A mixture of (−)-8-aminomenthol (**1**) (5.6 g, 33 mmol) and phenylselenoacetaldehyde (7.3 g, 37 mmol) in dichloromethane (100 mL) was stirred for 18 h at room temperature. The solvent was removed under vacuum, yielding the compound **2** (12.3 g, 99%) as a yellow oil, $[\alpha]^{20}_D$ = +17.8, (*c* 0.92, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.07 (m, 4H); 0.91 (d, 3H, J = 6.5 Hz); 1.07 (s, 3H); 1.08 (s, 3H); 1.40−1.52 (m, 1H); 1.60−1.85 (m, 3H); 1.90−2.00 (m, 1H); 3.01 (dd, 1H, J = 4.8 Hz, J = 7.1 Hz); 3.18 (dd, 1H, J = 4.8 Hz, J = 7.1 Hz); 3.42 (dt, 1H, J = 4.1 Hz, J = 10.4 Hz); 4.56 (t, 1H, J = 4.8 Hz); 7.20 (m, 3H); 7.55 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 20.3; 22.2; 25.0; 30.0; 31.4; 34.0; 35.2; 42.3; 50.9; 51.4; 74.8; 82.1; 126.4; 128.1; 131.3; 132.0. IR (neat, cm^{-1}) : 3270, 730, 685. EIMS (*m*/*z*, %): 352 (M, 0.23), 182 (100), 137 (33), 41 (21).

***N*-(Phenylseleno)ethyl-8-aminomenthol (3).** To a mixture of sodium borohydride (11.6 g, 116 mmol) and boron trifluoride−ether complex (94 mL, 290 mmol) in dry THF (300 mL) at 0 °C, under argon atmosphere, was added dropwise a solution of benzoxazine **2** (29.2 g, 83 mmol) in THF (100 mL), and the mixture was stirred at room temperature for 8 h. Then, the reaction mixture was quenched with methanol (120 mL), the solvent was evaporated under vacuum, and the residue was refluxed for 1 h with 20% NaOH aqueous solution (120 mL). The reaction mixture was extracted with chloroform (3 × 75 mL), and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum to give **3** (27 g, 92%) as a pale yellow oil, $[\alpha]^{20}_D$ = −13.3 (*c* 0.73, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.80−0.94 (m, 5H); 0.83 (d, 3H, J = 6.5 Hz); 0.94 (s, 3H); 1.01 (s, 3H); 1.10−1.25 (m, 1H); 1.30−1.42 (m, 1H); 1.50−1.65 (m, 2H); 1.80−1.90 (m, 1H); 2.68 (ddd, 1H, J = 5.0 Hz, J = 7.2 Hz, J = 12.7 Hz); 2.81−3.00 (m, 3H); 3.53 (dt, 1H, J = 4.1 Hz, J = 10.4 Hz); 7.20 (m, 3H); 7.45 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 21.6; 22.1; 25.7; 26.2; 28.8; 31.0; 34.9; 40.2; 44.3; 49.7; 56.6; 72.6; 127.2; 129.1; 129.1; 133.0. IR (neat, cm^{-1}): 3300, 1590, 1490, 740, 690. Anal. Calcd for $C_{18}H_{29}NOSe$: C, 61.00; H, 8.25; N, 3.95. Found: C, 61.29; H, 8.51; N, 3.76.

Condensation of Selenoaminomenthol 3 with Unsaturated Aldehydes. General Procedure. A mixture of selenoaminomenthol **3** (708 mg, 2.0 mmol) and the corresponding α,*β*-unsaturated aldehyde (3.1 mmol) was refluxed in benzene (50 mL) for 3 days. The solvent was removed under vacuum, and the residue was used without further purification. Flash chromatography on silica gel deactivated with triethylamine and ethyl acetate/hexanes as eluent yielded analytical samples.

***N*-(Phenylseleno)ethyl-4,4,7α-trimethyl-2α-vinyl-*trans*-octahydro-1,3-benzoxazine (4a).** Yield: 73%. ^{1}H NMR ($CDCl_3$) δ: 0.90 (d, 3H, J = 6.5 Hz); 1.07 (s, 3H); 1.08 (s, 3H); 1.15−1.50 (m, 4H); 1.53−1.78 (m, 3H); 1.89−1.98 (m, 1H); 2.55−2.75 (m, 1H); 2.75−3.00 (m, 3H); 3.42 (dt, 1H, J = 4.1 Hz, J = 10.5 Hz); 4.82 (d, 1H, J = 5.4 Hz), 5.14 (dt, 1H, J = 1.5 Hz, J = 10.4 Hz); 5.31 (dt, 1H, J = 1.5 Hz, J = 17.3 Hz); 5.76 (ddd, 1H, J = 5.4 Hz, J = 10.4, J = 17.3 Hz); 7.10−7.25 (m, 3H); 7.45−7.55 (m, 2H). Anal. Calcd for $C_{21}H_{31}NOSe$: C, 64.27; H, 7.96; N, 3.57. Found: C, 64.57; H, 8.01; N, 3.58.

***N*-(Phenylseleno)ethyl-2α-(2′-propenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (4b).** Yield: 98%. ^{1}H NMR ($CDCl_3$) δ: 0.89 (d, 3H, J = 6.4 Hz); 1.04 (s, 3H); 1.08 (s, 3H); 1.63 (dd, 3H, J = 1.5 Hz, J = 6.5 Hz); 2.50−3.00 (m, 4H); 3.40 (dt, 1H, J = 4.1 Hz, J = 10.5 Hz); 4.70 (d, 1H, J = 6.5 Hz), 5.42 (ddd, 1H, J = 1.5 Hz, J = 6.4 Hz, J = 15.4 Hz); 5.78 (ddq, 1H, J = 0.7 Hz, J = 6.5 Hz, J = 15.4 Hz); 7.10−7.40 (m, 5H). Anal. Calcd for $C_{22}H_{33}NOSe$: C, 65.01; H, 8.18; N, 3.45. Found: C, 64.89; H, 8.01; N, 3.72.

***N*-(Phenylseleno)ethyl-2α-stiryl-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (4c).** Yield: 99%. ^{1}H NMR ($CDCl_3$) δ: 0.89 (d, 3H, J = 6.6 Hz); 0.90−1.10 (m, 2H); 1.11 (s, 6H); 1.30−1.50 (m, 3H); 1.53−1.70 (m, 2H); 1.89−1.91 (m, 1H); 2.73−2.79 (m, 1H); 2.87−2.93 (m, 2H); 2.99−3.04 (m, 1H); 3.43 (dt, 1H, J = 4.1 Hz, J = 10.5 Hz); 5.03 (d, 1H, J = 5.1 Hz), 6.20 (dd, 1H, J = 5.1 Hz, J = 16.1 Hz); 6.63 (d, 1H, J = 16.1 Hz); 6.83 (t, 2H, J = 7.6 Hz); 6.97 (t, 1H, J = 7.2 Hz); 7.18−7.40 (m, 7H). ^{13}C NMR ($CDCl_3$): 18.2; 22.0; 24.7; 26.3; 29.2; 30.9; 34.5; 40.9; 45.1; 46.7; 56.9; 75.1; 86.8; 126.0; 126.3; 127.5; 128.1; 128.2; 128.5; 129.3; 131.5; 132.4; 136.0. IR (neat, cm^{-1}): 3080, 1680, 1600, 1480, 970, 740, 690. Anal. Calcd for $C_{27}H_{35}NOSe$: C, 69.21; H, 7.53; N, 2.99. Found: C, 69.56; H, 7.81; N, 2.85.

***N*-(Phenylseleno)ethyl-2α-(2′,2′-dimethylvinyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (4d).** Yield: 85%, pale yellow oil; $[\alpha]^{20}_D$ = −10.63 (*c* 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.05 (m, 3H); 0.90 (d, 3H, J = 6.5 Hz); 1.09 (s, 6H); 1.28 (m, 1H); 1.45 (m, 1H); 1.60−1.70 (m, 2H); 1.64 (s, 6H); 1.90 (m, 1H); 2.55−2.65 (m, 1H); 2.70−2.80 (m, 1H); 2.80−3.00 (m, 2H); 3.42 (dt, 1H, J = 4.1 Hz, J = 10.5 Hz); 5.05 (d, 1H, J = 7.0 Hz); 5.13 (d, 1H, J = 7.0 Hz); 7.20−7.28 (m, 3H); 7.45−7.51 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 17.7; 18.7; 22.2; 25.0; 25.7; 26.7; 30.2; 31.2; 34.8; 41.3; 45.4; 47.5; 56.8; 75.3; 84.0; 124.1; 126.6; 128.9; 129.8; 132.5; 136.8. IR (neat, cm^{-1}): 1680, 1580, 1480. Anal. Calcd for $C_{23}H_{35}NOSe$: C, 65.70; H, 8.39; N, 3.31. Found: C, 66.02; H, 8.28; N, 3.27.

Radical Cyclization of Perhydrobenzoxazines 4a−d. General Method. In a two-necked rounded flask equipped with a condenser and a septum, a solution of **4a**−**d** (1.0 mmol) in dry benzene (50 mL) was heated to reflux. Then, a previouly prepared solution of tributyltin hydride (0.35 mL, 1.25 mmol) and azobisisobutyronitrile (16 mg, 0.1 mmol) in the same solvent (12 mL) was added (syringe pump) over a period of 6−8 h. The reaction was monitored by TLC, and after completion (24−48 h) the solvent was removed and the residue analyzed by ^{1}H NMR. Flash chromatography yielded diastereomers **5a**−**c** and **6a**−**d** in 82−90% combined yield.

Compound 6a. Colorless oil; $[\alpha]^{20}_D$ = −57.7 (*c* 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.80−1.00 (m, 3H); 0.84 (d, 3H, J = 6.6 Hz); 0.97 (d, 3H, J = 6.8 Hz); 1.02 (s, 3H); 1.05 (s, 3H); 1.10−1.45 (m, 3H); 1.50−1.65 (m, 2H); 1.80 (m, 1H); 1.98 (m, 2H); 2.76 (dt, 1H, J = 3.0 Hz, J = 8.7 Hz); 1.95 (q, 1H, J = 8.0 Hz); 3.30 (dt, 1H, J = 4.2 Hz, J = 10.6 Hz); 4.21 (d, 1H, J = 1.8 Hz). ^{13}C NMR ($CDCl_3$) δ: 18.9; 19.6; 22.3; 24.8; 26.8; 29.5; 31.3; 34.9; 38.6; 41.5; 43.4; 44.8; 53.1; 74.8; 93.0. IR (neat, cm^{-1}): 1450, 1380, 1050, 1030. Anal. Calcd for $C_{15}H_{27}NO$: C, 75.88; H, 11.47; N, 5.90. Found: C, 75.52; H, 11.14; N, 5.42.

Compound 5a. Colorless oil; $[\alpha]^{20}_D$ = −43.2 (*c* 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.84 (d, 3H, J = 6.6 Hz); 0.85−1.05 (m, 3H); 0.91 (d, 3H, J = 6.9 Hz); 1.04 (s, 3H); 1.09 (s, 3H); 1.20−1.75 (m, 5H); 1.80 (m, 1H); 1.90 (m, 1H); 2.10 (m, 1H); 2.83 (dt, 1H, J = 4.7 Hz, J = 8.8 Hz); 3.00 (ddd, 1H, J = 5.5 Hz, J = 8.7 Hz, J = 10.6 Hz); 3.30 (dt, 1H, J = 4.1 Hz, J = 10.5 Hz); 4.51 (d, 1H, J = 4.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 14.1; 22.0; 22.3; 24.9; 26.5; 29.0; 31.3; 35.2; 37.4; 41.6; 42.8; 44.0; 53.1; 74.2; 87.8. IR (neat, cm^{-1}): 1460, 1370, 1050. Anal. Calcd for $C_{15}H_{27}NO$: C, 75.88; H, 11.47; N, 5.90. Found: C, 76.19; H, 11.71; N, 5.51.

Compound 6b. Colorless oil; $[\alpha]^{20}_D$ = −42.6 (*c* 1.02, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.88 (t, 3H, J = 7.4 Hz); 0.91 (d, 3H, J = 6.8 Hz); 1.09 (s, 3H); 1.11 (s, 3H); 1.20−1.75 (m, 7H); 1.85 (m, 2H); 2.00 (m, 1H); 2.80 (dt, 1H, J = 2.6 Hz, J = 8.4 Hz); 3.01 (q, 1H, J = 8.1 Hz); 3.36 (dt, 1H, J = 4.1 Hz, J = 10.5 Hz); 4.36 (d, 1H, J = 1.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.1; 19.5; 22.2; 25.2; 27.1; 27.2; 27.4; 31.5; 35.0; 41.6; 43.5; 44.5; 46.5; 53.2; 75.1; 91.5. IR (neat, cm^{-1}): 1460,

1380, 1200, 1030. Anal. Calcd for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57. Found: C, 76.69; H, 11.40; N, 5.81.

Compound 5b. Colorless oil, ^{1}H NMR ($CDCl_3$) δ: 0.85−1.05 (m, 3H); 0.88 (t, 3H, J = 7.4 Hz); 0.91 (d, 3H, J = 6.8 Hz); 1.10 (s, 3H); 1.17 (s, 3H); 1.20−1.75 (m, 7H); 1.85 (m, 1H); 2.00 (m, 2H); 2.90 (m, 1H); 3.07 (ddd, 1H, J = 4.8 Hz, J = 8.9 Hz, J = 10.7 Hz); 3.34 (dt, 1H, J = 4.2 Hz, J = 10.6 Hz); 4.66 (d, 1H, J = 3.6 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.7; 22.0; 22.2; 24.7; 26.3; 27.0; 29.6; 31.3; 35.1; 41.4; 42.7; 43.8; 45.0; 53.6; 74.2; 86.9. IR (neat, cm^{-1}): 1460, 1380, 1200, 1030. Anal. Calcd for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57. Found: C, 76.74; H, 11.75; N, 5.63.

Compound 6c. Colorless oil, ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.90 (d, 3H, J = 6.6 Hz); 1.13 (s, 6H); 1.25−1.50 (m, 3H); 1.55−1.75 (m, 2H); 1.85 (m, 1H); 1.95 (m, 1H); 2.35 (m, 1H); 2.51 (dd, 1H, J = 9.2 Hz, J = 13.6 Hz); 2.90 (m, 2H); 3.03 (q, 1H, J = 8.3 Hz); 3.35 (dt, 1H, J = 4.1 Hz, J = 10.4 Hz); 4.50 (d, 1H, J = 1.2 Hz); 7.13−7.28 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 20.3; 22.2; 24.8; 26.9; 27.4; 31.2; 35.0; 40.2; 41.5; 43.5; 43.9; 45.4; 53.0; 74.7; 90.9; 125.7; 128.1; 128.8; 140.8. IR (neat, cm^{-1}): 1460, 1380. Anal. Calcd for $C_{21}H_{31}NO$: C, 80.46; H, 9.97; N, 4.47. Found: C, 80.29; H, 10.30; N, 4.81.

Compound 5c. Colorless oil, $[\alpha]^{20}_D$ = −62.1 (c 1.48, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.05 (m, 3H); 0.90 (d, 3H, J = 6.5 Hz); 1.06 (s, 3H); 1.10 (s, 3H); 1.20−1.75 (m, 5H); 1.85−2.00 (m, 2H); 2.40−2.46 (m, 1H); 2.57 (dd, 1H, J = 7.2 Hz, J = 13.4 Hz); 2.87 (dd, 1H, J = 8.3 Hz, J = 13.4 Hz); 2.93 (dt, 1H, J = 4.5 Hz, J = 8.8 Hz); 3.11 (ddd, 1H, J = 5.6 Hz, J = 8.9 Hz, J = 10.5 Hz); 3.34 (dt, 1H, J = 4.1 Hz, 10.4 Hz); 4.55 (d, 1H, J = 3.9 Hz); 7.13−7.27 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 22.0; 22.1; 25.0; 26.5; 27.5; 31.5; 35.5; 35.7; 42.0; 43.0; 44.2; 45.2; 54.1; 74.5; 87.2; 125.5; 128.5; 129.0; 142.1. IR (neat, cm^{-1}): 3050, 1600, 1500, 1450, 750, 690. Anal. Calcd for $C_{21}H_{31}NO$: C, 80.46; H, 9.97; N, 4.47. Found: C, 80.31; H, 9.71; N, 4.63.

Compound 6d. Colorless oil; $[\alpha]^{20}_D$ = −52.6 (c 1.03, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85 (d, 3H, J = 6.5 Hz); 0.85−1.05 (m, 3H); 0.90 (d, 3H, J = 6.5 Hz); 0.93 (d, 3H, J = 6.5 Hz); 1.09 (s, 3H); 1.11 (s, 3H); 1.34−1.50 (m, 3H); 1.50−1.80 (m, 4H); 1.90 (m, 2H); 2.70 (dt, 1H, J = 2.6 Hz, J = 8.1 Hz); 3.00 (q, 1H, J = 8 Hz); 3.40 (dt, 1H, J = 4.2 Hz, J = 10.5 Hz); 4.50 (d, 1H, J = 2.1 Hz). ^{13}C NMR ($CDCl_3$) δ: 19.4; 19.9; 21.3; 22.2; 24.9; 25.7; 27.0; 31.0; 31.3; 35.0; 41.6; 43.7; 44.6; 51.8; 53.0; 74.7; 90.0. IR (neat, cm^{-1}): 1450, 1380. Anal. Calcd for $C_{17}H_{31}NO$: C, 76.92; H, 11.77; N, 5.28. Found: C, 77.12; H, 12.02; N, 5.19.

***N*-Allyl-8-aminomenthol (7a).** To a mixture of (−)-8-aminomenthol **1** (10 g, 58.5 mmol) and anhydrous potasium carbonate (8.9 g, 64 mmol) in dry acetonitrile (200 mL) under argon atmosphere, and cooled to 0 °C, was slowly added (4 h) allyl bromide (5.4 mL, 64 mmol). The mixture was stirred at room temperature for 2 days, and then, the solids were eliminated by filtration and the solution was concentrated in vacuo. The residue was recrystallized from hexanes, obtaining **7a** (9.0 g, 42.7 mmol, 73%) as white solid, mp 53−54 °C (hexanes); $[\alpha]^{20}_D$ = −27.9, (c 1.11, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.86 (d, 3H, J = 6.5 Hz); 0.90−1.07 (m, 5H); 1.08 (s, 3H); 1.09 (s, 3H); 1.30 (m, 1H); 1.45 (br. s, 1H); 1.56 (m, 2H); 1.92 (m, 1H); 3.16 (ddt, 1H, J = 1.3 Hz, J = 5.5 Hz, J = 13.3 Hz); 3.26 (ddt, 1H, J = 1.3 Hz, J = 5.5 Hz, J = 13.3 Hz); 3.58 (dt, 1H, J = 4.0 Hz, J = 10.2 Hz); 5.02 (dq, 1H, J = 1.3 Hz, J = 10.2 Hz); 5.12 (dq, 1H, J = 1.3 Hz, J = 17.9 Hz); 5.84 (ddt, 1H, J = 5.5 Hz, J = 10.2 Hz, J = 17.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.9; 22.1; 25.8; 26.3; 31.0; 35.0; 43.9; 44.4; 49.3; 56.6; 72.5; 115.8; 136.3. IR (Nujol, cm^{-1}): 3200, 1640. CIMS (m/z, %): 212 (M + 1, 100); 210 (3). Anal. Calcd for $C_{13}H_{25}NO$: C, 73.88; H, 11.92; N, 6.63. Found: C, 73.69; H, 11.66; N, 6.82.

***N*-Crotyl-8-aminomenthol (7b)**. A mixture of (−)-8-aminomenthol (**1**) (5 g, 29 mmol) and crotonaldehyde (2.7 mL, 32 mmol) in dichloromethane (50 mL) was stirred at room temperature for 24 h. The solvent was removed under vacuum, and the residue was redissolved in methanol (50 mL) and cooled to 0 °C. To this solution sodium borohydride (3.4 g, 90 mmol) was added in portions over 1 h and the mixture stirred at room temperature overnight. The reaction mixture was hydrolyzed by addition of 10% aqueous solution of HCl (50 mL) and extracted with ethyl acetate (3 × 75 mL). The organic layer was washed with brine and dried over $MgSO_4$. Evaporation of the solvent under vacuum afforded a residue (5.7 g, 25 mmol), which was further purified by recrystallization to yield **7b** (84%) as a white solid, mp 50−51 °C (hexanes); $[\alpha]^{20}_D$ = −29.0 (c 1.19, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.90−1.10 (m, 4H); 0.91 (d, 3H, J = 6.5 Hz); 1.11 (s, 6H,); 1.28 (m, 1H); 1.45 (br s, 1H); 1.60−1.70 (m, 5H); 1.95 (m, 1H); 3.10 (dd, 1H, J = 5.9 Hz, J = 12.4 Hz); 3.20 (dd, 1H, J = 5.1 Hz, J = 12.4 Hz); 3.61 (dt, 1H, J = 4.1 Hz, J = 10.2 Hz); 5.44−5.65 (m, 2H); 8.45 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ: 17.6; 21.7; 22.0; 25.6; 26.2; 30.9; 35.0; 43.0; 44.3; 49.2; 56.3; 72.4; 127.1; 128.9. IR (Nujol, cm^{-1}): 3240; 960; 840. CIMS (m/z, %): 226 (M + 1, 100); 137 (20); 112 (43). Anal. Calcd for $C_{14}H_{27}NO$: C, 74.61; H, 12.08; N, 6.61. Found: C, 74.43; H, 11.87; N, 6.39.

***N*-Cinnamyl-8-aminomenthol (7c).** Following the procedure described for **7b** this amino alcohol was obtained by condensation of **1** with cinnamaldehyde followed by reduction with $NaBH_4$ in a 98% total yield, white solid, mp 43−45 °C (hexanes); $[\alpha]^{20}_D$ = −46.4, (c 1.29, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.90−1.10 (m, 5H); 0.91 (d, 3H, J = 6.5 Hz); 1.14 (s, 6H); 1.32 (m, 1H); 1.43 (br s, 1H); 1.68 (m, 2H); 1.98 (m, 1H); 3.33 (ddd, 1H, J = 1.3 Hz, J = 6.3 Hz, J = 13.1 Hz); 3.44 (ddd, 1H, J = 1.3 Hz, J = 6.3 Hz, J = 13.1 Hz); 3.64 (dt, 1H, J = 4.0 Hz, J = 10.3 Hz); 6.24 (dt, 1H, J = 6.3 Hz, J = 15.9 Hz); 6.49 (dt, 1H, J = 1.3 Hz, J = 15.9 Hz); 7.20−7.38 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 21.9; 22.1; 25.7; 26.3; 30.9; 35.0; 43.5; 44.4; 49.1; 56.6; 72.5; 126.2; 127.4; 127.7; 128.4; 131.3; 136.8. IR (Nujol, cm^{-1}): 3050, 1590, 740, 690. EIMS (m/z, %): 287 (M, 1); 174 (46); 117 (100), 115 (25), 91 (13), 41 (16). Anal. Calcd for $C_{19}H_{29}NO$: C, 79.39; H, 10.17; N, 4.87. Found: C, 79.54; H, 9.91; N, 5.08.

***N*-Prenyl-8-aminomenthol (7d).** Yield: 96%, white solid, mp 55−57 °C (hexanes); $[\alpha]^{20}_D$ = −22.4, (c 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.90−1.10 (m, 4H); 0.91 (d, 3H, J = 6.4 Hz); 1.11 (s, 3H); 1.13 (s, 3H); 1.27 (m, 1H); 1.45 (br s, 1H); 1.60−1.75 (m, 3H); 1.64 (s, 3H); 1.68 (s, 3H); 1.93 (m, 1H); 3.14 (dd, 1H, J = 6.0 Hz, J = 7.0 Hz); 3.20 (dd, 1H, J = 6.0 Hz, J = 7.0 Hz); 3.61 (dt, 1H, J = 4.1 Hz, J = 10.2 Hz); 5.20 (t, 1H, J = 7.0 Hz).^{13}C NMR ($CDCl_3$) δ: 17.8; 21.5; 22.1; 25.6; 25.7; 26.2; 31.0; 35.1; 38.7; 44.5; 49.7; 56.5; 72.6; 122.2; 134.8. IR (Nujol, cm^{-1}): 3350, 3140, 1670. CIMS (m/z, %): 240 (M + 1, 100). Anal. Calcd for $C_{15}H_{29}NO$: C, 75.26; H, 12.21; N, 5.85. Found: C, 75.58; H, 12.42; N, 5.91.

Condensation of *N*-Allylic-8-aminomenthols with Phenylselenoacetaldehyde. General Procedure. A mixture of the corresponding amino alcohol **7a**−**d** (5.7 mmol) and phenylselenoacetaldehyde (1.7 g, 8.5 mmol) in anhydrous benzene (20 mL) was heated at reflux for 48 h. The solvent was removed and the residue was filtered through Celite, obtaining **8a**−**d** as dark yellow oils acompanied by variable amounts of PhSeSePh as impurity.

***N*-Alkylation of Benzoxazine 2 with Allylic Bromides. General Procedure.** A mixture of benzoxazine **2** (1.7 g, 5.8 mmol), potasium carbonate (1.7 g, 12.0 mmol), and the corresponding allylic bromide (7.0 mmol) in dry acetonitrile was heated in an oil bath at 80−90 °C for 48 h. The reaction mixture was diluted with ether, the solid was filtered off, and the solvent was concentrated under vacuum. The oily residue was used without further purification for the radical cyclization protocol. Analytical samples were obtained by flash chromatography on silica gel pretreated with triethylamine (5%) and EtOAc/hexane as eluent.

***N*-Allyl-2α-(phenylseleno)methyl-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (8a).** Pale yellow oil, 97% yield. ^{1}H NMR ($CDCl_3$) δ: 0.98−1.15 (m, 3H); 0.91 (d, 3H J = 6.5 Hz); 1.12 (s, 6H); 1.40 (m, 1H); 1.45−1.52 (m, 2H); 1.60−1.75 (m, 2H); 1.90 (m, 1H); 3.05 (d, 2H, J = 6.1 Hz); 3.20 (dd, 1H, J = 5.2 Hz, J = 17.9 Hz); 3.40−3.52 (m, 2H); 4.83 (t, 1H J = 6.0 Hz); 4.99 (dd, 1H, J = 1.8 Hz, J = 10.2 Hz); 5.21 (dd, 1H, J = 1.8 Hz, J = 17.1 Hz); 5.87−5.98 (m, 1H); 7.20−7.30 (m, 3H); 7.45−7.52 (m, 2H).^{13}C NMR ($CDCl_3$) δ: 20.3; 22.2; 25.0; 26.8; 31.3; 31.4; 34.9; 41.2; 45.3; 46.1; 57.4; 76.3; 87.2; 114.0; 126.8; 128.9; 131.3; 132.0; 140.8. IR (neat, cm^{-1}) : 3090, 1640,

1600, 740, 690. Anal. Calcd for $C_{21}H_{31}NOSe$: C, 64.27; H, 7.96; N, 3.57. Found: C, 64.61; H, 7.89; N, 3.49.

***N*-Crotyl-2α-(phenylseleno)methyl-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (8b).** Pale yellow oil, 98% yield. ^{1}H NMR ($CDCl_3$) δ: 0.90−1.15 (m, 3H); 0.99 (d, 3H, J = 6.5 Hz); 1.20 (s, 3H); 1.23 (s, 3H); 1.25−1.55 (m, 2H); 1.58−1.75 (m, 2H); 1.73 (s, 3H); 1.90 (m, 1H); 3.07 (d, 2H, J = 6.3 Hz); 3.13 (d, 1H, J = 15.6 Hz); 3.37 (d, 1H, J = 15.6 Hz); 3.43 (dt, 1H, J = 4.0 Hz, J = 10.4 Hz); 4.80 (t, 1H, J = 6 Hz); 5.50−5.54 (m, 2H); 7.20−7.30 (m, 3H); 7.45−7.55 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 17.8; 20.1; 22.6; 25.1; 27.0; 31.4; 31.7; 35.0; 41.3; 44.7; 46.3; 57.3; 76.3; 87.4; 124.8; 126.5; 128.9; 131.4; 132.1; 133.4. IR (neat, cm^{-1}): 3030, 1600, 760. Anal. Calcd for $C_{22}H_{33}NOSe$: C, 65.01; H, 8.18; N, 3.45. Found: C, 65.17; H, 8.03; N, 3.42.

***N*-Cinnamyl-2α-(phenylseleno)methyl-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (8c).** Pale yellow oil, 85% yield. ^{1}H NMR ($CDCl_3$) δ: 0.92 (d, 3H, J = 6.5 Hz); 0.95−1.20 (m, 3H); 1.16 (s, 3H); 1.18 (s, 3H); 1.40−1.55 (m, 2H); 1.62 (m, 1H); 1.70 (m, 1H); 1.92 (m, 1H); 3.11 (d, 2H, J = 6 Hz); 3.39 (dd, 1H, J = 5.5 Hz, J = 17.9 Hz); 3.48 (dt, 1H, J = 4.0 Hz, J = 10.5 Hz); 3.62 (dd, 1H, J = 5.6 Hz, J = 17.9 Hz); 4.85 (t, 1H, J = 6.0 Hz); 6.32 (dt, 1H, J = 5.3 Hz, J = 15.9 Hz); 6.52 (d, 1H, J = 15.9 Hz); 7.30−7.40 (m, 8H); 7.45−7.55 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 20.3; 22.2; 25.0; 26.9; 31.3; 31.5; 35.0; 41.3; 45.0; 46.4; 57.4; 76.4; 87.3; 126.1; 126.5; 127.0; 128.4; 128.9; 129.1; 131.5; 132.1; 132.7; 137.5. IR (neat, cm^{-1}): 3080, 1660, 1600, 740, 690. Anal. Calcd for $C_{27}H_{35}NOSe$: C, 69.21; H, 7.53; N, 2.99. Found: C, 69.39; H, 7.42; N, 3.02.

***N*-Prenyl-2α-(phenylseleno)methyl-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (8d).** Pale yellow oil, 85% yield. $[\alpha]^{20}_D$ = −9.64 (*c* 0.28, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.91 (d, 3H, J = 6.6 Hz); 0.95−1.10 (m, 3H); 1.11 (s, 3H); 1.13 (s, 3H); 1.25−1.50 (m, 3H); 1.58 (s, 3H); 1.60−1.80 (m, 1H); 1.66 (d, 3H, J = 1.3 Hz); 1.90 (m, 1H); 3.07 (d, 2H, J = 5.9 Hz); 3.07−3.16 (m, 1H); 3.35−3.54 (m, 2H); 4.78 (t, 1H, J = 5.9 Hz); 5.25−5.30 (m, 1H); 7.20−7.30 (m, 3H); 7.45−7.50 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 17.9; 19.8; 22.2; 25.0; 25.7; 27.0; 31.3; 31.6; 35.0; 41.1; 41.2; 46.4; 57.1; 77.0; 87.3; 126.4; 127.8; 128.8; 129.3; 131.4; 132.0. IR (neat, cm^{-1}): 1670, 1580, 1480. Anal. Calcd for $C_{23}H_{35}NOSe$: C, 65.70; H, 8.39; N, 3.31. Found: C, 65.98; H, 8.54; N, 3.38.

Radical Cyclization of Benzoxazines 8a−d. Following the general method described for **4a−d**, to a refluxing solution of the corresponding benzoxazine **8a−d** (1.0 mmol) in dry benzene (50 mL) was slowly added (syringe pump, 6 h) a solution of tributyltin hydride (0.35 mL, 1.25 mmol) and AIBN (8 mg, 0.05 mmol) in anhydrous benzene (10 mL). The reaction was completed after additional reflux of 1−2 h. The solvent was removed under vacuum, and the residue was chromatographed on silica gel (ethyl acetate/hexanes 1:15), affording diastereomers **9a−c** and **10a−c** in 84−90% combined yield. Compounds **9d** and **10d** could not be separated.

Compound 9a. Colorless oil; $[\alpha]^{20}_D$ = −36.7 (*c* 1.05, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 1.08 (d, 3H, J = 6.4 Hz); 1.12 (s, 3H); 1.15 (s, 3H); 1.20−1.50 (m, 3H); 1.50−1.75 (m, 2H); 1.85 (m, 1H); 2.20 (m, 2H); 2.66 (t, 1H, J = 8 Hz); 3.03 (t, 1H, J = 8 Hz); 3.39 (dt, 1H, J = 4.2 Hz, J = 10.5 Hz); 4.85 (dd, 1H, J = 1.2 Hz, J = 5.3 Hz). ^{13}C NMR ($CDCl_3$) δ: 20.6; 20.7; 22.2; 24.8; 27.1; 29.4; 31.2; 35.0; 40.1; 41.5; 43.3; 52.0; 53.2; 74.6; 87.8. Anal. Calcd for $C_{15}H_{27}NO$: C, 75.88; H, 11.47; N, 5.90. Found: C, 75.61; H, 11.79; N, 5.53.

Compound 10a. Colorless oil; $[\alpha]^{20}_D$ = −26.7 (*c* 1.06, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.91 (d, 3H, J = 6.5 Hz); 1.04 (d, 3H, J = 6.6 Hz), 1.11 (s, 3H); 1.12 (s, 3H); 1.20−1.45 (m, 3H); 1.45−1.70 (m, 2H); 1.80−2.00 (m, 2H); 2.40−2.45 (m, 2H); 3.24 (t, 1H, J = 10.2 Hz); 3.39 (dt, 1H, J = 4.2 Hz, J = 10.4 Hz); 4.75 (dd, 1H, J = 1.9 Hz, J = 4.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 19.6; 21.5; 22.2; 24.7; 26.7; 28.4; 31.3; 35.0; 40.3; 41.5; 43.9; 51.5; 53.1; 74.6; 87.5. Anal. Calcd for $C_{15}H_{27}NO$: C, 75.88; H, 11.47; N, 5.90. Found: C, 75.55; H, 11.72; N, 5.62.

Compound 9b. Colorless oil; $[\alpha]^{20}_D$ = −41.8 (*c* 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.13 (m, 3H); 0.87 (t, 3H, J = 4.7 Hz); 0.91 (d, 3H, J = 6.0 Hz); 1.13 (s, 3H); 1.15 (s, 3H); 1.20−1.70 (m, 7H); 1.80−1.90 (m, 1H); 1.90−2.15 (m, 1H); 2.15−2.25 (m, 1H); 2.69 (t, 1H, J = 8.2 Hz); 3.02 (t, 1H, J = 8.0 Hz); 3.39 (dt, 1H, J = 4.3 Hz, J = 10.5 Hz); 4.84 (dd, 1H, J = 1.2 Hz, J = 5.3 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.8; 20.7; 22.2; 24.8; 27.1; 28.8; 31.2; 35.0; 36.9; 38.2; 41.5; 43.3; 50.2; 53.1; 74.6; 86.6. IR (neat, cm^{-1}): 1460, 1380, 1100, 1080. Anal. Calcd for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57. Found: C, 76.23; H, 11.86; N, 5.72.

Compound 10b. Colorless oil; $[\alpha]^{20}_D$ = −31.2 (*c* 0.62, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.12 (m, 3H); 0.87 (t, 3H, J = 7.4 Hz); 0.91 (d, 3H, J = 6.4 Hz); 1.12 (s, 6H); 1.35−1.65 (m, 6H); 1.65−1.75 (m, 1H); 1.85−1.95 (m, 2H); 2.15−2.30 (m, 1H); 2.50 (dd, 1H, J = 5.1 Hz, J = 8.8 Hz); 3.20 (t, 1H, J = 8.8 Hz); 3.39 (dt, 1H, J = 4.2 Hz, J = 10.4 Hz); 4.75 (dd, 1H, J = 1.7 Hz, J = 4.7 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.7; 19.9; 22.3; 24.8; 26.8; 29.3; 31.3; 35.1; 36.0; 38.4; 41.6; 43.8; 49.8; 53.1; 74.7; 87.0. Anal. Calcd for $C_{16}H_{29}NO$: C, 76.44; H, 11.63; N, 5.57. Found: C, 76.56; H, 11.83; N, 5.61.

Compound 9c. Colorless oil; $[\alpha]^{20}_D$ = −33.6 (*c* 0.78, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.90−1.08 (m, 3H); 0.92 (d, 3H, J = 6.6 Hz); 1.08 (s, 3H); 1.12 (s, 3H); 1.40−1.50 (m, 3H); 1.50−1.60 (m, 1H); 1.65−1.75 (m, 1H); 1.80−1.90 (m, 1H); 2.18 (ddd, 1H, J = 5.2 Hz, J = 10.3 Hz, J = 13.6 Hz); 2.42−2.49 (m, 1H); 2.69−2.82 (m, 3H); 2.93 (t, 1H, J = 8 Hz); 3.41 (dt, 1H, J = 4.2 Hz, J = 10.5 Hz); 4.84 (dd, 1H, J = 1.2 Hz, J = 5.2 Hz); 7.13−7.28 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 20.6; 22.2; 24.8; 27.1; 31.2; 35.0; 36.5; 38.2; 41.5; 41.8; 43.4; 50.1; 53.1; 74.6; 86.5; 125.6; 128.1; 128.5; 141.3. Anal. Calcd for $C_{21}H_{31}NO$: C, 80.46; H, 9.97; N, 4.47. Found: C, 80.61; H, 10.10; N, 4.52.

Compound 10c. Colorless oil; $[\alpha]^{20}_D$ = −40.2 (*c* 2.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.90 (d, 3H, J = 6.5 Hz); 1.03 (s, 3H); 1.13 (s, 3H); 1.30−1.50 (m, 2H); 1.50−1.70 (m, 3H); 1.80−1.92 (m, 2H); 2.57−2.69 (m, 4H); 3.13 (dd, 1H, J = 3.8 Hz, J = 8.2 Hz); 3.39 (dt, 1H, J = 4.2 Hz, J = 10.5 Hz); 4.80 (dd, 1H, J = 1.4 Hz, J = 4.7 Hz); 7.13−7.28 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 20.5; 22.3; 24.8; 26.8; 31.3; 35.1; 35.6; 38.6; 41.6; 42.2; 43.4; 49.3; 53.1; 74.5; 86.9; 125.8; 128.2; 128.7; 141.3. Anal. Calcd for $C_{21}H_{31}NO$: C, 80.46; H, 9.97; N, 4.47. Found: C, 80.55; H, 10.13; N, 4.50.

Compounds 9d and 10d. As a mixture of diastereoisomers. ^{1}H NMR ($CDCl_3$) δ: 0.91 and 0.93 (d, 6H, J = 6.5 Hz and J = 7.5 Hz); 0.85−1.10 (m, 3H); 0.95 (d, 3H, J = 7.5 Hz); 1.16 and 1.17 (s, 3H); 1.17 and 1.18 (s, 3H); 1.35−1.65 (m, 5H); 1.65−1.90 (m, 3H); 1.90−2.05 and 2.05−2.20 (m, 1H); 2.87 (t, J = 8.0 Hz) and 2.63 (dd, 1H, J = 3.5 Hz, J = 8.5 Hz); 3.00 and 3.20 (t, 1H, J = 8.0 Hz and J = 8.5 Hz); 3.43 (dt, 1H, J = 4.0 Hz, J = 10.0 Hz,); 4.77 and 4.89 (dd, 1H, J = 1.3 Hz, J = 5.3 Hz and J = 1.7 Hz, J = 3.4 Hz).

Reductive Ring Opening of Compounds 5, 6, 9, and 10. General Procedure. A mixture of lithium aluminum hydride (39 mg, 2.0 mmol) and aluminum chloride (55 mg, 0.4 mmol) in dry THF (10 mL) was stirred under argon atmosphere in an ice−salt bath (ca. −10 °C). Then, a solution of compound **5, 6, 9, or 10** (0.4 mmol) in THF (10 mL) was slowly added and the reaction stirred for 10 min. The reaction mixture was quenched by careful addition of water. The solvents were removed under vacuum, and the residue was diluted with water and extracted with chloroform (3 × 25 mL). The organic layer was washed with brine and dried over anhydrous sodium sulfate. After evaporation of the solvent, the corresponding pyrrolidinylmenthols **11a−d** and **12a−c** were obtained as colorless oils in 95−99% yield.

(3′*R*)-8-(3′-Methylpyrrolidinyl)menthol (11a). Yield: 99%. Colorless oil; $[\alpha]^{20}_D$ = −14.7 (*c* 1.08, CH_2Cl_2). ^{1}H NMR (330 K, $CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.90 (d, 3H, J = 6.2 Hz); 1.05 (s, 3H); 1.10 (d, 3H, J = 7.3 Hz); 1.20−1.50 (m, 3H); 1.35 (s, 3H); 1.50−1.70 (m, 4H); 1.95−2.10 (m, 2H); 2.20 (m, 1H); 2.70−3.40 (broad, 3H); 3.77 (dt, 1H, J = 4.2 Hz, J = 10.5 Hz). ^{13}C NMR (330 K, $CDCl_3$) δ: 13.3; 17.6; 20.9; 21.7; 25.8; 26.6; 27.7; 31.0; 31.8; 32.2; 34.7; 44.3; 48.6; 53.4; 71.8. IR (neat, cm^{-1}): 3400, 1440. CIMS (*m*/*z*, %): 240(M + 1, 100), 126 (75). Anal. Calcd for $C_{15}H_{29}NO$: C, 75.24; H, 12.22; N, 5.85. Found: C, 74.96; H, 12.47; N, 6.04.

(3′*R*)-8-(3′-Ethylpyrrolidinyl)-menthol (11b). Yield: 97%, colorless oil; $[\alpha]^{20}_D = -14.5$ (*c* 1.02, CH_2Cl_2). ^{1}H NMR (330 K, $CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.88 (t, 3H, *J* = 7.5 Hz); 0.90 (d, 3H, *J* = 6.2 Hz); 0.91 (s, 3H); 1.16 (s, 3H); 1.20−1.75 (m, 8H); 1.85−2.10 (m, 3H); 2.35−3.20 (br, 3H); 3.62 (dt, 1H, *J* = 4.2 Hz, *J* = 10.5 Hz); 7.40−8.20 (br s, 1H). ^{13}C NMR (330 K, $CDCl_3$) δ: 12.0; 17.1; 21.5; 22.0; 25.5; 28.0; 29.6; 31.0; 34.8; 39.3; 43.8; 58.6; 58.9; 72.8. IR (neat, cm^{-1}): 3100, 1450. CIMS (*m*/*z*, %): 254 (M +1, 100), 238 (8), 140 (41), 113 (5). Anal. Calcd for $C_{16}H_{31}NO$: C, 75.83; H, 12.33; N, 5.53. Found: C, 75.76; H, 12.38; N, 5.50.

(3′*S*)-8-(3′-Benzylpyrrolidinyl)menthol (11c). Yield: 99%, colorless oil; $[\alpha]^{20}_D = +4.6$ (*c* 1.02, CH_2Cl_2). ^{1}H NMR (330 K, $CDCl_3$) δ: 0.95 (s, 3H); 0.90−1.15 (m, 3H); 0.97 (d, 3H, *J* = 6.6 Hz); 1.20 (s, 3H); 1.35−1.80 (m, 6H); 1.80−2.05 (m, 2H); 2.35−2.55 (m, 2H); 2.70 (d, 2H, *J* = 7.4 Hz); 2.75−3.00 (m, 3H); 3.70 (dt, 1H, *J* = 4.2 Hz, *J* = 10.5 Hz); 7.06−7.20 (m, 5H). ^{13}C NMR (330 K, $CDCl_3$) δ: 16.6; 21.6; 22.0; 25.6; 30.5; 31.0; 35.1; 38.8; 40.9; 44.5; 44.8; 48.6; 50.8; 58.9; 72.8; 125.7; 128.1; 128.6; 140.9. IR (neat, cm^{-1}): 3200, 3050, 1600, 740, 690. Anal. Calcd for $C_{21}H_{33}NO$: C, 79.95; H, 10.54; N, 4.44. Found: C, 80.12; H, 10.65; N, 4.38.

(3′*S*)-8-(3′-Isopropylpyrrolidinyl)menthol (11d). Yield: 98%, colorless oil; $[\alpha]^{20}_D = -12.9$ (*c* 1.04, CH_2Cl_2). ^{1}H NMR (acetone-d_6) δ: 0.85−1.10 (m, 3H); 0.88 (d, 6H, *J* = 7.0 Hz); 0.91 (d, 3H, *J* = 6.7 Hz); 1.03 (s, 3H); 1.23 (s, 3H); 1.25−2.15 (m, 10H); 2.40−3.20 (br, 3H); 3.59 (dt, 1H, *J* = 4.0 Hz, *J* = 10.5 Hz); 8.20 (br s, 1H). ^{13}C NMR (acetone-d_6) δ: 17.1; 21.3; 21.6; 21.7; 22.5; 26.8; 29.5; 31.7; 33.1; 35.7; 45.4; 45.9; 49.2; 50.8; 61.4; 72.7. IR (neat, cm^{-1}): 3200, 1380. Anal. Calcd for $C_{17}H_{33}NO$: C, 76.34; H, 12.44; N, 5.24. Found: C, 76.14; H, 12.67; N, 5.20.

(3′*S*)-8-(3′-Methylpyrrolidinyl)menthol (12a). Yield: 92%, colorless oil; $[\alpha]^{20}_D = -14.2$ (*c* 1.02, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.90 (d, 3H, *J* = 6.2 Hz); 0.91 (d, 3H, *J* = 3.1 Hz); 0.95 (s, 3H); 1.15 (s, 3H); 1.16 (s, 3H); 3.67 (dt, 1H, *J* = 4.2 Hz, *J* = 10.5 Hz); 8.8−9.0 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ: 17.1; 19.2; 21.3; 22.0; 25.5; 30.8; 31.1; 31.9; 35.4; 43.5; 45.0; 48.6; 53.4; 59.0; 62.3. IR (neat, cm^{-1}): 3120, 1440, 1025. CIMS (*m*/*z*, %): 240 (M +1, 100), 126 (50), 102 (66). Anal. Calcd for $C_{15}H_{29}NO$: C, 75.24; H, 12.22; N, 5.85. Found: C, 75.48; H, 12.51; N, 5.59.

(3′*S*)-8-(3′-Ethylpyrrolidinyl)menthol (12b). Yield: 98%, colorless oil; $[\alpha]^{20}_D = -14.5$ (*c* 1.03, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.10 (m, 3H); 0.87 (t, 3H, *J* = 7.3 Hz); 0.91 (d, 3H, *J* = 6.5 Hz); 0.91 (s, 3H); 1.15 (s, 3H); 1.25−1.50 (m, 5H); 1.50−1.75 (m, 3H); 1.95 (m, 3H); 2.20−3.20 (br, 3H); 3.61 (dt, 1H, *J* = 4.2 Hz, *J* = 10.5 Hz); 8.80 (br s, 1H). ^{13}C NMR ($CDCl_3$) δ: 12.6; 17.9; 21.2; 22.0; 25.3; 28.9; 30.8; 35.4; 38.3; 44.0; 48.2; 58.5; 73.5. IR (neat, cm^{-1}): 3200, 1440. CIMS (*m*/*z*, %): 254 (M +1, 100), 238 (8), 140 (82), 113 (38). Anal. Calcd for $C_{16}H_{31}NO$: C, 75.83; H, 12.33; N, 5.53. Found: C, 75.74; H, 12.48; N, 5.40.

(3′*R*)-8-(3′-Benzylpyrrolidinyl)menthol (12c). Yield: 99%, colorless oil; $[\alpha]^{20}_D = -26.4$ (*c* 1.00, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.85−1.05 (m, 3H); 0.90 (d, 3H, *J* = 6.5 Hz); 0.91 (s, 3H); 1.07 (s, 3H); 1.12 (s, 1H); 1.25−1.50 (m, 4H); 1.60 (m, 1H); 1.70−2.20 (m, 2H); 2.00−3.10 (m, 7H); 3.60 (dt, 1H, *J* = 4.2 Hz, *J* = 10.5 Hz); 7.10−7.30 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 17.0; 21.9; 22.1; 25.6; 30.1; 31.0; 35.0; 39.0; 41.5; 44.2; 44.3; 48.3; 51.0; 58.8; 72.8; 125.8; 128.3; 129.0; 141.5. IR (neat, cm^{-1}): 3200, 1600, 740, 690. Anal. Calcd for $C_{21}H_{33}NO$: C, 79.95; H, 10.54; N, 4.44. Found: C, 80.22; H, 10.75; N, 4.51.

Auxiliary Removal Procedure. Synthesis of 3-Alkyl Pyrrolidines. General Method. A mixture of pyrrolidylmenthol **11a**−**d** or **12a**−**c** (2.4 mmol), pyridinium chlorocromate (2.1 g, 9.7 mmol), and molecular sieves (4 Å) in dicloromethane (40 mL) was stirred for 2 h at room temperature. Then, the mixture was added to a 15% aqueous solution of NaOH (25 mL) and extracted with chloroform (4 × 30 mL). The organic layer was decanted, washed with H_2O, and concentrated in vacuo without heating. The residue was immediately treated with a 2.5 M solution (16 mL) of KOH in THF/MeOH/H_2O (2:1:1) for 2−3 h at room temperature. After completion of the reaction (TLC), the mixture was acidified by addition of a 2 N aqueous solution of HCl and concentrated in vacuo to remove the organic solvents. The remaining acidic solution was extracted with Et_2O (2 × 25 mL) to recover (+)-pulegone. The aqueous layer was alkalinized with concentrated NaOH solution and extracted with chloroform (4 × 25 mL). The organic layer was washed with brine and dried over anhydrous sodium sulfate. The pyrrolidines were isolated as hydrochlorides by bubbling dry HCl throughout the solution and removing the solvent. Chromatographic purification of this salt in alumina afforded analytical samples.

(*R*)-3-Methylpyrrolidine (13a). Hydrochloride: 61% yield; $[\alpha]^{20}_D = +6.9$ (*c* 1.67, MeOH). ^{1}H NMR ($CDCl_3$) δ: 1.15 (d, 3H, *J* = 7.1 Hz); 1.50−1.65 (m, 1H); 2.10−2.20 (m, 1H); 2.35−2.50 (m, 1H); 2.80 (dd, 1H, *J* = 9.0 Hz, *J* = 11.0 Hz); 3.25−3.35 (m, 1H); 3.40−3.50 (m, 2H); 9.40−10.1 (br. s, 2H). ^{13}C NMR ($CDCl_3$) δ: 17.0; 31.8; 33.0; 44.7; 51.3. EIMS (*m*/*z*, %): 85 (M-HCl, 16), 68 (3), 43 (100). *N*-Benzoyl derivative: white solid, mp 64−65 °C (hexanes); $[\alpha]^{20}_D = +70.2$ (*c* 1.03, CH_2Cl_2). ^{1}H NMR ($CDCl_3$), 1:1 mixture of rotamers δ: 1.01 (d, 3H, *J* = 6.6 Hz); 1.13 (d, 3H, *J* = 6.6 Hz); 1.40−1.60 (m, 2H); 1.90−2.15 (m, 2H); 2.15−2.40 (m, 2H); 3.01 (dd, 1H, *J* = 8.4 Hz, *J* = 10.2 Hz); 3.18 (dd, 1H, *J* = 8.4 Hz, *J* = 12.0 Hz); 3.40−3.60 (m, 3H); 3.63−3.72 (m, 1H); 3.73 (dd, 1H, *J* = 8.4 Hz, *J* = 3.5 Hz); 3.83 (dd, 1H, *J* = 7.4 Hz, *J* = 12 Hz); 7.30−7.60 (m, 10H). ^{13}C NMR ($CDCl_3$), mixture of rotamers, δ: 17.2 and 17.7; 32.3 and 34.1; 46.0 and 49.3; 53.1 and 56.5; 125.2; 127.0; 128.1; 129.0; 129.7; 137.0 and 137.8; 169.6. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.84; H, 8.12; N, 7.39.

(*S*)-3-Methylpyrrolidine (*ent*-13a). Hydrochloride: 65% yield; $[\alpha]^{20}_D = -6.0$ (*c* 1.0, MeOH). Spectral data are identical to those of **13a**.

(*R*)-3-Ethylpyrrolidine (13b). Hydrochloride: 54% yield; $[\alpha]^{20}_D = +6.9$ (*c* 1.25, MeOH). ^{1}H NMR ($CDCl_3$) δ: 0.96 (t, 3H, *J* = 7.4 Hz); 1.40−1.70 (m, 3H); 2.10−2.30 (m, 2H); 2.85 (dd, 1H, *J* = 9.2 Hz, *J* = 11.3 Hz); 3.25−3.35 (m, 1H); 3.40−3.50 (m, 2H); 9.30−9.70 (br. s, 2H). ^{13}C NMR ($CDCl_3$) δ: 13.0; 25.2; 30.1; 39.8; 44.9; 50.2. EIMS (*m*/*z*, %): 99 (M − HCl, 20), 68 (9), 43 (100). *N*-Benzoyl derivative: oil; $[\alpha]^{20}_D = +104$ (*c* 0.70, CH_2Cl_2). ^{1}H NMR ($CDCl_3$), mixture of rotamers δ: 0.88 (t, 3H, *J* = 7.4 Hz); 0.98 (t, 3H, *J* = 7.4 Hz); 1.30−1.65 (m, 6H); 1.90−2.20 (m, 4H); 3.05 (dd, 1H, *J* = 8.8 Hz, *J* = 10.3 Hz); 3.22 (dd, 1H, *J* = 8.8 Hz, *J* = 12 Hz); 3.40−3.70 (m, 4H); 3.74 (dd, 1H, *J* = 3.1 Hz, *J* = 8.8 Hz); 3.85 (dd, 1H, *J* = 7.6 Hz, *J* = 12 Hz); 7.40 (m, 6H); 7.55 (m, 4H). ^{13}C NMR ($CDCl_3$) mixture of rotamers, δ: 12.4 and 12.5; 25.6 and 26.2; 30.1 and 32.1; 39.5 and 41.4; 46.0 and 49.4; 51.6 and 54.9; 127.0; 128.1; 130.1; 137.2; 137.9; 170.0. IR (neat, cm^{-1}): 1620, 1570, 715, 700. $C_{13}H_{17}NO$. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.50; H, 8.10; N, 6.59.

(*S*)-3-Ethylpyrrolidine (*ent*-13b). Hydrochloride: 53% yield; $[\alpha]^{20}_D = -5.9$ (*c* 1.04, MeOH). Spectral data are identical to those of **13b**.

(*R*)-3-Benzylpyrrolidine (*ent*-13c). This pyrrolidine was isolated and characterized as *N*-benzoyl derivative: oil, 49% yield; $[\alpha]^{20}_D = -57.4$ (*c* 0.76, CH_2Cl_2). ^{1}H NMR ($CDCl_3$), mixture of rotamers, δ: 1.53−1.74 (m, 2H); 1.89−1.98 (m, 1H); 2.00−2.08 (m, 1H); 2.40 (quintuplet, 1H, *J* = 7.2 Hz); 2.52 (quintuplet, 1H, *J* = 7.2 Hz); 2.61−2.70 (m, 2H); 2.72−2.81 (m, 2H); 3.17 (dd, 1H, *J* = 8.0 Hz, *J* = 10.5 Hz); 3.32 (dd, 1H, *J* = 8.6 Hz, *J* = 12.1 Hz); 3.41 (dd, 1H, *J* = 2.9 Hz, *J* = 9.5 Hz); 3.45−3.54 (m, 2H); 3.58 (dd, 1H, *J* = 4.2 Hz, *J* = 8.1 Hz); 3.64−3.82 (m, 2H); 7.0−7.6 (m, 20H). ^{13}C NMR ($CDCl_3$) mixture of rotamers, δ: 29.9 and 31.9; 38.5 and 39.1; 39.4 and 41.1; 45.5 and 49.0; 51.3 and 54.2; 126.1; 126.9; 128.0; 128.3; 128.4; 128.5; 129.6; 138.0; 139.6; 139.8; 170.0. IR (neat, cm^{-1}): 3030, 3010, 1640, 1580, 1500. Anal. Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.84; H, 7.02; N, 5.32.

(*S*)-3-Benzylpyrrolidine (13c). This pyrrolidine was isolated and characterized as *N*-benzoyl derivative: oil, 52% yield; $[\alpha]^{20}_D = +56.2$ (*c* 0.64, CH_2Cl_2). Anal. Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.66; H, 7.49; N, 5.02. Spectral data coincide with those described for the benzoyl derivative of *ent*-13c.

(*S*)-3-Isopropylpyrrolidine (13d). *N*-Tosyl derivative: white solid, 63% yield, mp 69−70 °C (pentane); $[\alpha]^{20}_D = +22.17$ (*c* 0.46, CH_2Cl_2). ^{1}H NMR ($CDCl_3$) δ: 0.84 (d, 6H, $J = 6.6$ Hz); 1.26−1.39 (m, 2H); 1.70 (m, 1H); 1.90 (m, 1H); 2.44 (s, 3H); 2.78 (t, 1H, $J = 9.6$ Hz); 3.15 (dt, 1H, $J = 6.9$ Hz, $J = 9.9$ Hz); 3.37 (dt, 1H, $J = 2.3$ Hz, $J = 8.6$ Hz); 3.45 (dd, 1H, $J = 7.7$ Hz, $J = 9.6$ Hz); 7.35 (m, 3H); 7.72 (m, 2H). ^{13}C NMR ($CDCl_3$) δ: 20.9; 21.3; 21.5; 29.9; 31.7; 46.3; 48.1; 52.1; 127.4; 129.5; 133.7; 143.2. IR (Nujol, cm^{-1}): 1600, 1470, 1460, 1340. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 63.04; H, 7.72; N, 5.37.

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Supporting Information Available: Copies of ^{1}H NMR and ^{13}C DEPT spectra of compounds **2**, **3**, **4d**, **5a**−**c**, **6a**−**d**, **7a**−**d**, **8a**−**d**, **9a**−**c**, **10a**−**c**, **11a**−**d**, **12a**−**c**, **13a**−**c** (N−Bz), **13d** (N-Ts), and ***ent*-13a,b** (HCl); COSY and NOESY spectra of **5a**−**c**, **6a,b,d** and NOE difference spectra of **5c** and **6c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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