JOC Article

Synthesis of Enantiopure 3-Azabicyclo[3.2.0]heptanes by Diastereoselective Intramolecular [2+2] Photocycloaddition Reactions on Chiral Perhydro-1,3-benzoxazines

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[2+2] photocycloadditions involving chiral 3-acryloyl-2-vinylperhydro-1,3-benzoxazines derived from (−)-8-aminomenthol are highly diastereoselective reactions. The facial selectivity depends on the type of substitution at the vinyl double bond, and always leads to *cis*-fused bicyclic derivatives. The de is good for compounds with one substituent at the outer carbon of the double bond at C-2, but only one diastereomer is formed in cyclizations of compounds with two substituents at that position. The elimination of the menthol appendage gives enantiopure 3-azabicyclo[3.2.0]heptanes.

Introduction

Photochemical cycloaddition between two 2π-electron-containing entities giving rise to four-membered ring structures is one of the most successful contributions of photochemistry to organic synthesis.[1] Two new carbon−carbon bonds are formed, and a maximum of four new stereocenters are introduced in the process. Consequently, it has been extensively applied toward the synthesis of natural products and other complex molecules.[2]

The control of the regio- and/or stereoselectivity is an important problem of bimolecular photocycloadditions that limits its applications in organic synthesis; in the intramolecular variant of the reaction these problems are substantially reduced owing to geometrical constraints imposed on the reacting functional groups.[3] In general, the regioselectivity can be satisfactorily predicted by the "rule of five",[4] and the facial diastereoselectivity of the reaction can be controlled by a stereogenic center within the carbon chain. In contrast to the intermolecular asymmetric cycloaddition,[5] the intramolecular version using a removable chiral auxiliary[6] or chiral catalysis[7] has been less studied.

Some of these efforts have been directed to the stereoselective synthesis of azabicyclo[3.2.0]heptanes because of their interest as target intermediates in synthesis[8] and pharmacologically active agents.[9] In this way, such compounds have been prepared by photochemical cycloadditions on diallylamines,[10] diallyl carbamates,[11] and 3-allyl-4-vinyl-substituted oxazolidinones[12] derived from chiral glycine. Diastereoselective cyclizations promoted by metals lead to this class of bicyclic compounds,[13] and 3-azabicyclo[3.2.0]heptan-2-ones have also been obtained by thermally induced intramolecular [2+2] cycloaddition of keteniminium salts and olefinic bonds.[14]

In previous works we have shown that chiral perhydro-1,3-benzoxazines derived from (−)-8-aminomenthol[15] constitute useful chiral auxiliaries in different diastereoselective cycloaddition processes leading to nitrogen heterocyclic systems.[16]

We now report on the synthesis of enantiopure 3-azabyciclo[3.2.0]heptanes by intramolecular [2+2] photocycloaddition of α,β-unsaturated amides with alkenes, each

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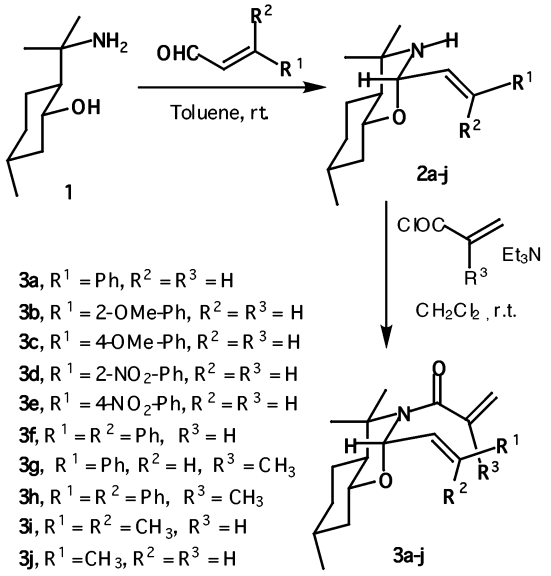
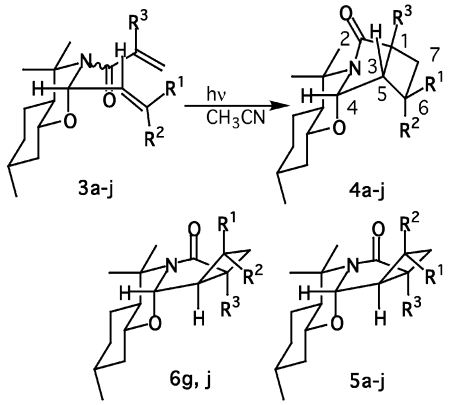
SCHEME 1



SCHEME 2



attached to a chiral perhydro-1,3-benzoxazine acting as a chiral template.

Results and Discussion

The chiral perhydro-1,3-benzoxazines **3a**−**j** used in the photocyclizations were synthesized in two steps[17] and excellent yields (83−91%) from (−)-8-aminomenthol (**1**) (Scheme 1). The condensation of **1** with α,*β*-unsaturated aldehydes in toluene at room temperature afforded a nearly quantitative yield of *N*-unsubstituted 2-alkenylperhydro-1,3-benzoxazines **2a**−**j**, which were acylated with acryloyl or methacryloyl chloride and triethylamine at 0 °C in CH_2Cl_2.

Intramolecular [2+2] photocycloadditions were carried out using a water-cooled Pyrex immersion well photoreactor equipped with a 125 W mercury medium-pressure lamp. The argon-purged solutions of **3a**−**j** in acetonitrile (0.07 M) were irradiated at room temperature until disappearance of the starting compound was observed. The progress of the reaction was monitored by TLC or ^{1}H NMR, and the results are summarized in Scheme 2 and Table 1.

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TABLE 1. Photochemical Cycloadditions of Amides 3a−j

entry	amide	R^1	R^2	R^3	time (h)	yield[a] (%)	products (ratio)[b]
1	**3a**	Ph	H	H	30	61	**4a** (71), **5a** (29)
2	**3b**	2-OMePh	H	H	15	54	**4b**(70), **5b** (30)
3	**3c**	4-OMePh	H	H	25	58	**4c** (78), **5c** (22)
4	**3d**	2-NO_2Ph	H	H	5		
5	**3e**	4-NO_2Ph	H	H	6	92	**4e** (88), **5e** (12)
6	**3f**	Ph	Ph	H	39	55	**5f** (100)
7	**3g**	Ph	H	Me	68	60	**4g** (16) **5g** (77), **6g** (7)
8	**3h**	Ph	Ph	Me	92	52	**5h** (100)
9	**3i**	Me	Me	H	80	24[c]	**5i** (100)
10	**3j**	Me	H	H	90	26[c]	**4j** (13), **5j** (55), **6j** (32)

[a] Yields refer to isolated compounds after column chromatography. [b] Determined by ^{1}H NMR of the reaction mixture. [c] Photodecomposition acryloyl amides of (−)-8-aminomenthol were the major products obtained in these cases.

The reactivity of styryl derivatives **3a**−**h** (R^1 and/or R^2 = Ar) substantially differs from that shown by 2-allyl-substituted perhydro-1,3-benzoxazines **3i**−**j** (R^1 and/or R^2 = Me). **3i** leads to **5i** as a single diastereomer after 80 h of irradiation in only 24%, and **3j**, after 90 h of irradiation, was also transformed (26%) into a mixture of diastereomeric cyclobutane derivatives **4j**, **5j**, and **6j**. In these reactions the major byproducts detected were the α,*β*-unsaturated amides of (−)-8-aminomenthol formed by decomposition of the starting compounds. Perhydrobenzoxazines with aryl substituents at the outer carbon of the vinyl moiety (**3a**−**h**) react easier than **3i**−**j**, leading to the cyclization products in moderate to very good yields. An exception to this general behavior was 2-nitrophenyl derivative **3d**, which does not provide the cyclization products after irradiation.

These results could be explained on the basis of the maximum absorption in the ultraviolet spectra of the starting amides, and the photocyclization was tested by changing the Pyrex by a quartz immersion well, but photodecomposition products were obtained as major compounds. Some other experimental conditions, such as the addition of Cu(I) salts[11] or irradiation in the presence of benzophenone as sensitizer,[10] were tested, but neither the chemical yields nor the ratio of diastereomers changed.

As expected for intramolecular [2+2] photocycloaddition in structures with a short tether connecting the unsaturated units, the reaction occurs with total regioselectivity, providing the fused adducts. The formation of the initial bond gives a 1,4-diradical bearing a five-membered ring, and bridgehead products were not observed.

Interestingly, the facial diastereoselectivity is dependent on the nature and number of substituents appended to the double bonds. In this way, acryloyl amides **3a**−**e** with only one aryl substituent at the outer carbon in the allyl group yield a mixture of two diastereomers (**4a**−**e** and **5a**−**e**) in moderate to good de. For these diastereomers, the ring junction between the cyclobutane and the *γ*-lactam ring is *cis* and the relative configuration of the substituent at C-6 (see the numbering in Scheme 2) is *exo*, but they differ in the relative configuration of the hydrogen at the *N*,*O*-ketal carbon (H at C-4 in Scheme 2) and the bicyclic junction, being *cis* for compounds **4a**−**e** and *trans* for **5a**−**e**.

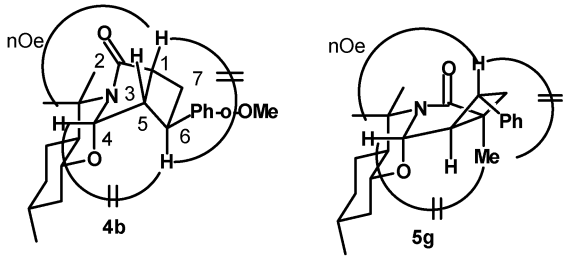

FIGURE 1. ^{1}H NOESY contacts recorded for compounds **4b** and **5g**.

The facial selectivity is complete for acryloyl (**3f** and **3i**) or methacryloyl (**3h**) amides with two substituents at the terminal carbon of the allyl group at the *N*,*O*-ketal carbon. In the same reaction conditions these compounds gave **5f**, **5h**, and **5i**, respectively, as single diastereomers.

Perhydro-1,3-benzoxazine **3g**, with a methyl group at the α-carbon of the α,*β*-unsaturated amide provides up to three photocycloadducts: two *exo* products (**4g** and **5g**), and one diastereomer (**6g**) which differs from **5g** only in the *endo* orientation of the substituents at C-6. An ^{1}H NMR study of the course of the reaction of **3g** shows that the [2+2] photocycloaddition process occurred at the same time as the *Z*−*E* isomerization[18] of the styryl unit. After 20 h of irradiation (ca. 25% conversion) the remaining (*E*)-styryl derivative **3g** was isomerized to a ca. 1:1 *Z*−*E* mixture. During the remainder of the reaction the (*Z*)-styryl derivative predominates, although the final cyclization product *endo*-**6g** was only obtained in 7% yield.

Amide **3j** also provides a mixture of three photocycloadducts (*exo*-**4j**, *exo*-**5j**, and *endo*-**6j**), although in this case, the photoisomerization of **3j** is not observed when the reaction is followed by ^{1}H NMR. Dienes do not equilibrate during the irradiation. The triplet 1,4-biradical initially formed in accord with the rule of five has a lifetime sufficiently long to allow rotation prior to ring closure, but does not revert to starting material.[19]

Photocycloadducts were isolated and purified by flash chromatography and their stereochemistries determined at this stage from their ^{1}H NMR spectra and NOESY experiments. For instance, the NOESY of compound **4b** shows one cross-peak between the signals for protons at C-1 and C-4, indicating their *cis* relationship, and the absence of this signal between protons at C-1 and C-6 and protons at C-4 and C-6 points to a relative *trans* disposition between them. On the contrary, NOESY experiments for **5g** show a cross-peak between the signals of protons at C-4 and C-6 (*cis* relationship), but there is no cross-signal between the proton at C-4 and the methyl group at C-1 or between the proton at C-6 and the methyl group at C-1, indicating relative *trans* disposition between these atoms (Figure 1).

Interestingly, ^{1}H NMR signals for H-4 in compounds **4** appear as doublets (J = 6.0−6.6 Hz) but as a singlet for diastereomers **5**, indicating that for the latter the dihedral angle between H-4 and H-5 is near 90°, and therefore, the amide substituents at the nitrogen atom are in an axial arrangement. This fact was confirmed by X-ray diffraction analysis of compounds **4a** and **5i**. The substituent at the nitrogen atom in **4a** occupies an equatorial position (*trans* fusion for the *N*,*O*-ketal and lactam cycles), but it is in an axial position in diastereomer **5i** (*cis* fusion for the same heterocycles).[20] On the other hand, H-1 for compounds **5** resonates downfield (ca. 0.23−0.30 ppm) of the same proton in diastereomer **4**, and the resonance for H-5 is shifted upfield (ca. 0.63−0.71 ppm) in adducts **5** with respect to the same proton in compounds **4**. This general trend allowed the assignation of the stereochemistry for all these compounds.

The stereochemistry of adducts **6g** and **6j** was also established on the basis of their ^{1}H and ^{13}C NMR spectra. Thus, H-4 appears as a doublet with a small coupling constant (J = 2.0 Hz) for **6g** and as a singlet for **6j**. The shielding ring current effect of the *endo*-aryl group in **6g** shifts the ^{13}C NMR signal of C-4 3.6 ppm upfield with respect to the same carbon in **5g**. On the other hand, the ^{13}C NMR signal for the methyl group at C-6 in *endo* adduct **6j** is shifted upfield ($\Delta\delta$ = 5 ppm) as compared with that of the *exo* isomer **5j**. This phenomenon has been previously observed in related 3-azabicyclo[3.2.0]heptane derivatives.[8]

The stereochemical course of these photocycloadditions can be interpreted on the basis of the generally accepted proposal for these reactions[21] taking into account the following facts: (i) The *cis* fusion of the cyclobutane and the *γ*-lactam in all the diastereomers indicates that the cyclization occurs by interaction of the *Re* face of one double bond (α-carbon) with the *Si* face of the other, and not by *Re*−*Re* or *Si*−*Si* interactions. (ii) The *trans* junction (substituent at the nitrogen atom in an equatorial position) between the lactam and the *N*,*O*-heterocycle for major stereoisomers **4a**−**e** obtained from **3a**−**e** or the *cis* stereochemistry (substituent at the nitrogen in an axial position) for compounds **5f**−**j** obtained as major or single isomers from **3f**−**j** point to both diastereomers being formed from different conformations of the starting perhydro-1,3-benzoxazines or their exciplexes.[22]

On the basis of these facts the formation of the final products can be proposed (Scheme 3) to occur from two different conformations (**A** and **B**) of the starting compounds, which undergo cyclization to form two different 1,4-biradicals that collapse to diastereomers **4** and **5**, respectively. Amides **3a**−**e** (R^2 = H) preferably react in conformation **A** where the acyl substituent at the nitrogen lies in an equatorial position, and the formation of the five-membered heterocyclic biradicals occurs by interaction of the *Re* face (α carbon) of the allylic double bond with the *Si* face of the double bond of the amide. In contrast, compounds **3f**, **3h**, and **3i** ($R^2 \neq$ H) cyclize from conformation **B** probably because of the $A^{1,3}$ strain in conformation **A**. The reaction in these cases occurs by interaction of the *Si* face of the allylic substituent and the *Re* face of the double bond of the α,*β*-unsaturated amide in axial disposition.

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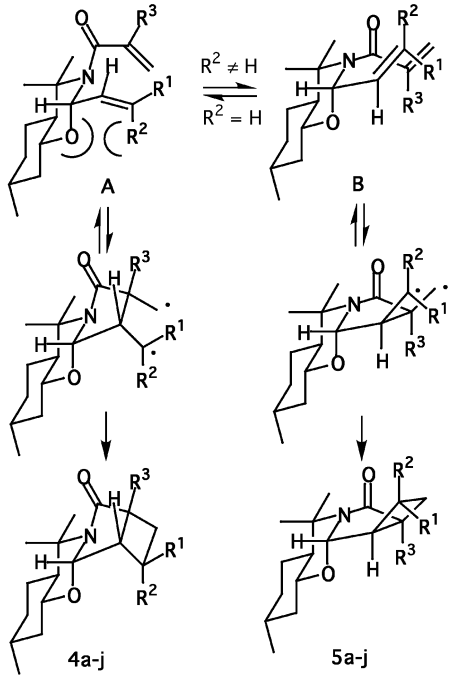
SCHEME 3



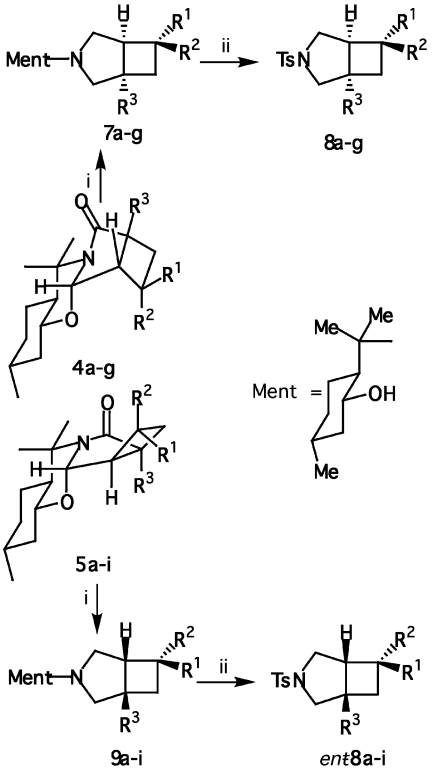
Amide **3g**, with a methyl substituent at the α-carbon of the α,*β*-unsaturated amide, also reacts from conformer **B** due to steric interactions between the methyl group and the axial hydrogen at the *N*,*O*-ketal carbon. Due to the methyl substitution, the rate of cyclization of **3g** is retarded, the exciplex decays back to the ground state, and *Z*−*E* isomerization occurs. This trend is very similar to the steric effect observed in the cyclization of 5-substituted 5-hexenyl radicals. Alternatively, *endo* photoadducts **6g** and **6j** can be generated by free rotation in the cyclized 1,4-biradical prior to ring closure.

The transformation of the photocycloadducts into the final enantiopure 3-azabicyclo[3.2.0]heptanes was achieved with good chemical yields in two steps (Scheme 4). Reductive ring opening of the *N*,*O*-acetal moiety and concomitant reduction of the amide group with alane in THF at −10 °C leads to the menthol derivatives in excellent yields. After isolation, these menthol derivatives were subjected to oxidation with PCC in CH_2Cl_2 at room temperature, affording the menthone derivatives, which without isolation, were treated with an aqueous solution (2.5 N) of KOH in THF−MeOH, leading to the enantiopure 3-azabicyclo[3.2.0]heptanes. These compounds were isolated and characterized as *N*-tosyl derivatives by treatment with tosyl chloride and diisopropylethylamine in ethyl acetate.

The final 3-azabicyclo[3.2.0]heptanes obtained from *exo* adducts **4a**−**c**, **4e**, and **4g** were enantiomers of those obtained from **5a**−**c**, **5e**, and **5g**, respectively. The absolute stereochemistry of the 3-azabicyclo derivative *ent*-**8g** was established by X-ray diffraction analysis,[20] corroborating the absolute configuration of the photocycloadduct **5g**.

In conclusion, [2+2] photocycloadditions on these perhydro-1,3-benzoxazines derived from (−)-8-aminomenthol, used as a chiral template, occur with moderate to good yields and good to excellent de. The described methodology constitutes a facile entry to enantiopure 3-azabicyclo[3.2.0] heptanes.

SCHEME 4[a]



[a] Reagents and conditions: (i) AlH_3, THF, −10 °C, 30 min; (ii) (a) PCC, 3 Å molecular sieves, CH_2Cl_2, rt; (b) 2.5 M KOH, H_2O, MeOH, THF (1:1:2), rt, 12 h, then TsCl, DIPEA, EtOAc, rt, (47−75%).

Experimental Section

General Methods. All reactions were carried out under an argon atmosphere in oven-dried glassware. Solvents were dried by standard methods: acetonitrile was distilled from P_2O_5, CH_2Cl_2 from CaH_2 and THF, and toluene from sodium. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were registered in $CDCl_3$ as solvent, and chemical shifts are reported relative to tetramethylsilane as internal reference. Specific rotations were determined on a digital polarimeter using a Na lamp, and concentration is given in grams per 100 mL. Melting points were determined in open capillary tubes and are uncorrected. TLC was performed on glass-backed plates coated with silica gel 60 with an F_{254} indicator; the chromatograms were visualized under UV light and/or by staining with I_2 or phosphomolybdic acid. Flash chromatography was carried out on silica gel 60 (230−240 mesh).

General Procedure for [2+2] Photocycloaddition Reactions. A 0.07 M solution of the appropiate amide (10.5 mmol) in acetonitrile (150 mL) was poured into a water-cooled Pyrex immersion well photoreactor, degassed by bubbling argon through the solution for 15 min, and then irradiated under an argon atmosphere with a medium-pressure mercury lamp (125 W) until disappearance of the starting amide was evident. The solvent was evaporated and the residue purified by flash chromatography on silica gel using hexanes−EtOAc as eluent.

(2*R*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aR*)-2-Phenyl-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (4a). Colorless solid. Mp: 129−130 °C (from hexane). $[\alpha]^{25}_D = -163.8$ ($c = 1.0$, $CHCl_3$). ^1H NMR (δ): 0.88−

1.17 (m, 3H); 0.95 (d, 3H, J = 6.5 Hz); 1.22 (s, 3H); 1.33 (m, 1H); 1.52 (m, 1H); 1.71−1.78 (m, 2H); 1.80 (s, 3H); 2.01 (m, 1H); 2.42−2.63 (m, 2H); 2.77 (m, 1H); 2.97 (ddd, 1H, J_1 = 6.2 Hz, J_2 = 6.6 Hz, J_3 = 6.9 Hz); 3.46 (td, 1H, J_1 = 4.2 Hz, J_2 = 10.6 Hz); 4.02 (q, 1H, J = 6.9 Hz); 5.07 (d, 1H, J = 6.2 Hz); 7.14−7.32 (m, 5H). ^{13}C NMR (δ): 18.2; 21.9; 23.8; 25.2; 29.3; 31.0; 34.4; 36.6; 36.9; 40.9; 42.2; 49.6; 56.7; 75.9; 85.6; 125.7; 126.3 (2C); 128.1 (2C); 144.4; 175.1. IR (Nujol): 3050, 1675, 760, 730, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.63; H, 8.80; N, 4.36.

(2*S*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2-Phenyl-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (5a). Colorless oil. $[\alpha]^{25}_D$ = +37.47 (c = 0.86, $CHCl_3$). ^{1}H NMR (δ): 0.86−1.11 (m, 3H); 0.93 (d, 3H, J = 6.5 Hz); 1.33 (s, 3H); 1.38−1.46 (m, 2H); 1.73−1.77 (m, 2H); 1.81 (s, 3H); 1.92 (m, 1H); 2.41−2.58 (m, 2H); 2.82 (dd, 1H, J_1 = 6.9 Hz, J_2 = 7.3 Hz); 3.06 (m, 1H); 3.31 (dt, 1H, J_1 = 7.3 Hz, J_2 = 8.4 Hz); 3.52 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 5.02 (s, 1H); 7.22−7.26 (m, 3H); 7.30−7.35 (m, 2H). ^{13}C NMR (δ): 20.9; 22.0; 24.3; 25.1; 31.2 (2C); 34.4; 37.8; 41.0; 41.7; 42.7; 50.9; 57.8; 76.6; 90.4; 126.3 (2C); 126.4; 128.5 (2C); 143.5; 176.2. IR (film): 3060, 1680, 760, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.98; H, 8.86; N, 4.05.

(2*R*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aR*)-2-(2′-Methoxyphenyl)-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]-benzoxazin-10-one (4b). Colorless solid. Mp: 123−124 °C (from hexanes−EtOAc). $[\alpha]^{25}_D$ = −178.6 (c = 1.0, $CHCl_3$). ^{1}H NMR (δ): 0.86−1.09 (m, 3H); 0.90 (d, 3H, J = 6.8 Hz); 1.21 (s, 3H); 1.31 (m, 1H); 1.45 (m, 1H); 1.73−1.80 (m, 2H); 1.81 (s, 3H); 1.90 (m, 1H); 2.37−2.56 (m, 2H); 2.77 (m, 1H); 3.27 (dt, 1H, J_1 = 6.6 Hz, J_2 = 6.9 Hz); 3.40 (td, 1H, J_1 = 4.2 Hz, J_2 = 10.6 Hz); 3.79 (s, 3H); 4.07 (ddd, 1H, J_1 = 6.9 Hz, J_2 = 9.1 Hz, J_3 = 9.8 Hz); 5.08 (d, 1H, J = 6.6 Hz); 6.81 (d, 1H, J = 8.0 Hz); 6.90 (t, 1H, J = 7.5 Hz); 7.17 (dd, 1H, J_1 = 7.5 Hz, J_2 = 8.0 Hz); 7.18 (d, 1H, J = 7.5 Hz). ^{13}C NMR (δ): 18.1; 21.9; 23.8; 25.2; 31.0; 31.4; 33.4; 34.4; 37.1; 38.8; 40.9; 49.5; 55.1; 56.6; 75.9; 85.9; 110.4; 120.2; 127.1; 127.5; 132.3; 157.3; 175.6. IR (Nujol): 3060, 1680, 770, 730 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.52; H, 8.67; N, 3.91.

(2*S*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2-(2′-Methoxyphenyl)-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]-benzoxazin-10-one (5b). Colorless oil. $[\alpha]^{25}_D$ = +28.49 (c = 1.5, $CHCl_3$). ^{1}H NMR (δ): 0.89−1.11 (m, 3H); 0.93 (d, 3H, J = 6.4 Hz); 1.33 (s, 3H); 1.36−1.54 (m, 2H); 1.72−1.76 (m, 2H); 1.81 (s, 3H); 1.93 (m, 1H); 2.39−2.59 (m, 2H); 2.74 (t, 1H, J = 7.8 Hz); 3.00 (m, 1H); 3.44 (dt, 1H, J_1 = 7.8 Hz, J_2 = 8.7 Hz); 3.52 (td, 1H, J_1 = 3.9 Hz, J_2 = 10.6 Hz); 3.80 (s, 3H); 5.10 (s, 1H); 6.82 (d, 1H, J = 8.1 Hz); 6.92 (t, 1H, J = 7.4 Hz); 7.16−7.22 (m, 2H). ^{13}C NMR (δ): 20.6; 21.8; 24.1; 24.9; 28.5; 31.0; 34.2; 37.3; 37.9; 40.9; 41.8; 50.8; 54.9; 57.5; 76.4; 90.5; 109.9; 120.1; 126.3; 127.2; 130.8; 156.8; 176.1. IR (film): 3040, 1670, 780, 750, 730, 700 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.59; H, 8.31; N, 3.93.

(2*R*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aR*)-2-(4′-Methoxyphenyl)-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]-benzoxazin-10-one (4c). Colorless oil. $[\alpha]^{25}_D$ = −145.12 (c = 1.1, $CHCl_3$). ^{1}H NMR (δ): 0.87−1.16 (m, 3H); 0.95 (d, 3H, J = 6.5 Hz); 1.21 (s, 3H); 1.29 (m, 1H); 1.47 (m, 1H); 1.71−1.76 (m, 2H); 1.79 (s, 3H); 2.02 (m, 1H); 2.38−2.57 (m, 2H); 2.74 (m, 1H); 2.89 (dt, 1H, J_1 = 6.3 Hz, J_2 = 6.7 Hz); 3.43 (td, 1H, J_1 = 4.2 Hz, J_2 = 10.6 Hz); 3.75 (s, 3H); 3.95 (ddd, 1H, J_1 = 6.7 Hz, J_2 = 8.7 Hz, J_3 = 9.0 Hz); 5.04 (d, 1H, J = 6.3 Hz); 6.83 (d, 2H, J = 8.6 Hz); 7.15 (d, 2H, J = 8.6 Hz). ^{13}C NMR (δ): 18.1; 21.8; 23.7; 25.1; 29.3; 30.9; 34.3; 35.9; 36.6; 40.8; 42.3; 49.5; 54.9; 56.5; 75.8; 85.5; 113.4 (2C); 127.2 (2C); 136.3; 157.5; 175.0. IR (film): 3060, 3040, 1680, 1610, 1580, 1510, 830, 730, 680 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.52; H, 8.22; N, 3.90.

(2*S*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2-(4′-Methoxyphenyl)-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1, 3]benzoxazin-10-one (5c). Colorless oil. $[\alpha]^{25}_D$ = +46.76 (c = 0.99, $CHCl_3$). ^{1}H NMR (δ): 0.89−1.10 (m, 3H); 0.92 (d, 3H, J = 6.5 Hz); 1.32 (s, 3H); 1.37−1.55 (m, 2H); 1.73−1.77 (m, 2H); 1.80 (s, 3H); 1.90 (m, 1H); 2.39−2.54 (m, 2H); 2.76 (t, 1H, J = 7.1 Hz); 3.04 (m, 1H); 3.25 (dt, 1H, J_1 = 7.1 Hz, J_2 = 8.4 Hz); 3.51 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 3.78 (s, 3H); 5.00 (s, 1H); 6.85 (d, 2H, J = 8.6 Hz); 7.14 (d, 2H, J = 8.6 Hz). ^{13}C NMR (δ): 20.8; 21.9; 24.2; 25.0; 31.1; 31.3; 34.3; 37.6; 40.9; 41.0; 42.9; 50.8; 55.1; 57.7; 76.4; 90.2; 113.7 (2C); 127.2 (2C); 135.5; 158.0; 176.0. IR (film): 3060, 3040, 1680, 1610, 1580, 1510, 820, 790, 730, 700, 670 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.57; H, 8.62; N, 3.56.

(2*S*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aR*)-2-(4′-Nitrophenyl)-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (4e). Pale yellow oil. $[\alpha]^{25}_D$ = −182.90 (c = 1.0, $CHCl_3$). ^{1}H NMR (δ): 0.90−1.18 (m, 3H); 0.97 (d, 3H, J = 6.5 Hz); 1.25 (s, 3H); 1.35 (m, 1H); 1.51 (m, 1H); 1.71−1.80 (m, 2H); 1.81 (s, 3H); 2.03 (m, 1H); 2.50−2.67 (m, 2H); 2.82 (m, 1H); 3.02 (dt, 1H, J_1 = 6.3 Hz, J_2 = 7.1 Hz); 3.51 (td, 1H, J_1 = 4.2 Hz, J_2 = 10.6 Hz); 4.12 (ddd, 1H, J_1 = 7.1 Hz, J_2 = 8.7 Hz, J_3 = 9.0 Hz); 5.12 (d, 1H, J = 6.3 Hz); 7.40 (d, 2H, J = 8.7 Hz); 8.16 (d, 2H, J = 8.7 Hz). ^{13}C NMR (δ): 18.3; 21.9; 23.8; 25.2; 28.9; 31.1; 34.4; 36.9 (2C); 40.9; 42.5; 49.7; 56.9; 76.1; 85.3; 123.5 (2C); 127.3 (2C); 146.1; 152.0; 174.5. IR (film): 3065, 1688, 1597, 851, 742, 719, 698 cm^{-1}. Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.51; H, 7.52; N, 7.38.

(2*S*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2-(4′-Nitrophenyl)-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (5e). Pale yellow oil. $[\alpha]^{25}_D$ = +70.12 (c = 1.0, $CHCl_3$). ^{1}H NMR (δ): 0.91−1.12 (m, 3H); 0.94 (d, 3H, J = 6.5 Hz); 1.34 (s, 3H); 1.40−1.51 (m, 2H); 1.72−1.79 (m, 2H); 1.81 (s, 3H); 1.92 (m, 1H); 2.44−2.65 (m, 2H); 2.84 (t, 1H, J = 7.2 Hz); 3.10 (m, 1H); 3.43 (ddd, 1H, J_1 = 7.2 Hz, J_2 = 8.4 Hz, J_3 = 8.7 Hz); 3.55 (td, 1H, J_1 = 4.01 Hz, J_2 = 10.7 Hz); 5.06 (s, 1H); 7.39 (d, 2H, J = 8.7 Hz); 8.19 (d, 2H, J = 8.7 Hz). ^{13}C NMR (δ): 20.9; 22.0; 24.3; 25.1; 30.9; 31.2; 34.4; 37.7; 40.9; 41.3; 42.6; 50.8; 58.0; 76.7; 90.0; 123.8 (2C); 127.2 (2C); 146.5; 151.1; 175.5). IR (film): 3110, 3077, 1691, 1598, 1519, 849, 752, 737, 686 cm^{-1}. Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.81; H, 7.52; N, 7.12.

(2a*S*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2,2-Diphenyl-5,8,8-trimethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (5f). Colorless solid. Mp: 154−155 °C (from hexanes−EtOAc). $[\alpha]^{25}_D$ = +172.07 (c = 1.0, $CHCl_3$). ^{1}H NMR (δ): 0.74 (s, 3H); 0.78−0.86 (m, 2H); 0.92 (d, 3H, J = 6.5 Hz); 1.04 (m, 1H); 1.27 (m, 1H); 1.45 (m, 1H); 1.61−1.65 (m, 2H); 1.66 (s, 3H); 1.95 (m, 1H); 2.94 (m, 1H); 3.06 (d, 1H, J = 9.3 Hz); 3.07 (m, 1H); 3.21 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 3.40 (m, 1H); 4.61 (s, 1H); 7.13−7.20 (m, 4H); 7.25−7.34 (m, 6H). ^{13}C NMR (δ): 18,7; 21.9; 24.0; 25.0; 31.1; 34.4; 36.1; 36.4; 41.0; 45.1; 50.3; 50.9; 57.4; 76.4; 87.5; 126.0; 126.1; 126.4 (2C); 127.2 (2C); 128.2 (2C); 128.4 (2C); 143.5; 148.5; 174.9. IR (Nujol): 3020, 1670, 755, 700 cm^{-1}. Anal. Calcd for $C_{28}H_{33}NO_2$: C, 80.93; H, 8.00; N, 3.37. Found: C, 81.08; H, 8.21; N, 3.52.

(2*R*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aR*)-2-Phenyl-10a,5,8,8-tetramethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]-benzoxazin-10-one (4g). Colorless oil. $[\alpha]^{25}_D$ = −115.53 (c = 0.53, $CHCl_3$). ^{1}H NMR (δ): 0.91−1.17(m, 3H); 0.95 (d, 3H, J = 6.5 Hz); 1.21 (s, 3H); 1.24 (s, 3H); 1.34 (m, 1H); 1.49 (m, 1H); 1.71−1.78 (m, 2H); 1.80 (s, 3H); 2.02 (m, 1H); 2.15 (dd, 1H, J_1 = 9.7 Hz, J_2 = 11.8 Hz); 2.60 (dd, 1H, J_1 = 8.8 Hz, J_2 = 11.8 Hz); 2.68 (dd, 1H, J_1 = 6.0 Hz, J_2 = 6.3 Hz); 3.45 (td, 1H, J_1 = 4.3 Hz, J_2 = 10.6 Hz); 3.81 (ddd, 1H, J_1 = 6.3 Hz, J_2 = 8.8 Hz, J_3 = 9.7 Hz); 5.08 (d, 1H, J = 6.0 Hz); 7.15−7.33 (m, 5H). ^{13}C NMR (δ): 18.3; 21.2; 22.0; 23.9; 25.2; 31.1; 33.5; 34.4; 36.3; 40.9; 41.6; 48.4; 49.7; 56.6; 75.9; 84.5; 125.7; 126.5 (2C); 128.1 (2C); 144.7; 177.4. IR (film): 3020, 1685, 750, 730, 700 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.29; H, 8.99; N, 4.08.

(2*S*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2-Phenyl-10a,5,8,8-tetramethylperhydrocyclobuta[3,4]pyrrolo[2, 1-b]-[1,3]-benzoxazin-10-one (5g). Colorless oil. $[\alpha]^{25}_D = +37.00$ (c = 1.3, $CHCl_3$). ^{1}H NMR (δ): 0.89−1.11 (m, 3H); 0.92 (d, 3H, J = 6.5 Hz); 1.32 (s, 3H); 1.36 (s, 3H); 1.41−1.50 (m, 2H); 1.67−1.78 (m, 2H); 1.80 (s, 3H); 1.91 (m, 1H); 2.02 (dd, 1H, J_1 = 8.8 Hz, J_2 = 11.9 Hz); 2.54 (d, 1H, J = 6.8 Hz); 2.64 (dd, 1H, J_1 = 11.9 Hz, J_2 = 9.1 Hz); 3.09 (ddd, 1H, J_1 = 6.8 Hz, J_2 = 8.8 Hz, J_3 = 9.1 Hz); 3.51 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 4.98 (s, 1H); 7.18−7.26 (m, 3H); 7.30−7.34 (m, 2H). ^{13}C NMR (δ): 21.0; 21.9; 22.4; 24.3; 25.1; 31.2; 34.4; 37.8; 38.2; 41.1; 42.7; 48.3; 51.0; 57.7; 76.4; 88.9; 126.3; 126.4 (2C); 128.4 (2C); 143.7; 178.6. IR (film): 3040, 1680, 755, 730, 695 cm^{-1}. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.32; H, 8.67; N, 4.11.

(2*R*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2-Phenyl-10a,5,8,8-tetramethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]-benzoxazin-10-one (6g). Colorless oil. $[\alpha]^{25}_D = +35.02$ (c = 1.3, $CHCl_3$). ^{1}H NMR (δ): 0.75−1.06 (m, 3H); 0.89 (d, 3H, J = 6.5 Hz); 0.94 (s, 3H); 1.22−1.38 (m, 2H); 1.45 (s, 3H); 1.63−1.67 (m, 2H); 1.71 (s, 3H); 1.87 (m, 1H); 2.31 (ddd, 1H, J_1 = 2.0 Hz, J_2 = 9.8 Hz, J_3 = 12.5 Hz); 2.43 (dd, 1H, J_1 = 8.5 Hz, J_2 = 12.5 Hz); 2.58 (dt, 1H, J_1 = 2.0 Hz, J_2 = 9.2 Hz); 3.18 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 3.95 (ddd, 1H, J_1 = 8.5 Hz, J_2 = 9.2 Hz, J_3 = 9.8 Hz); 4.49 (d, 1H, J = 2.0 Hz); 7.13−7.35 (m, 5H). ^{13}C NMR (δ): 19.1; 20.9; 21.9; 24.0; 25.2; 31.1; 34.4; 34.6; 34.7; 41.0; 42.6; 45.2; 50.3; 57.4; 76.6; 85.3; 126.3; 127.4 (2C); 128.3 (2C); 139.7; 177.5. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.37; H, 8.91; N, 4.15.

(2a*S*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2,2-Diphenyl-10a,5,8,8-tetramethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]-benzoxazin-10-one (5h). Colorless oil. $[\alpha]^{25}_D = +186.33$ (c = 1.0, $CHCl_3$). ^{1}H NMR (δ): 0.66 (s, 3H); 0.73−0.86 (m, 2H); 0.92 (d, 3H, J = 6.5 Hz); 1.05 (m, 1H); 1.26 (m, 1H); 1.27 (s, 3H); 1.42 (m, 1H); 1.60−1.70 (m, 2H); 1.65 (s, 3H); 1.96 (m, 1H); 2.52 (d, 1H, J = 12.7 Hz); 3.18 (s, 1H); 3.22 (m, 1H); 3.24 (d, 1H, J = 12.7 Hz); 4.53 (s, 1H); 7.10−7.36 (m, 10H). ^{13}C NMR (δ): 18.6; 21.9 (2C); 23.9; 24.9; 31.0; 34.2; 41.0; 41.3; 42.1; 48.0; 49.5; 50.4; 57.2; 76.6; 86.4; 125.6; 125.8; 126.4 (2C); 127.2 (2C); 128.0 (2C); 128.2 (2); 143.4; 149.2; 177.3. IR (film): 3060, 3020, 1695, 750, 700 cm^{-1}. Anal. Calcd for $C_{29}H_{35}NO_2$: C, 81.08; H, 8.21; N, 3.26. Found: C, 81.26; H, 8.42; N, 3.05.

(2a*S*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2,2,5,8,8-Pentamethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (5i). Colorless solid. Mp: 115−116 °C (from hexane). $[\alpha]^{25}_D = -24.90$ (c = 1.0, $CHCl_3$). ^{1}H NMR (δ): 0.85−1.11 (m, 3H); 0.93 (d, 3H, J = 6.6 Hz); 1.07 (s, 3H); 1.22 (s, 3H); 1.29 (s, 3H); 1.36 (m, 1H); 1.46 (m, 1H); 1.69−1.80 (m, 3H); 1.76 (s, 3H); 1.93 (m, 1H); 2.11 (dd, 1H, J_1 = 9.9 Hz, J_2 = 12.4 Hz); 2.23 (d, 1H, J = 8.2 Hz); 2.94 (ddd, 1H, J_1 = 4.4 Hz, J_2 = 8.2 Hz, J_3 = 12.4 Hz); 3.51 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 5.07 (s, 1H). ^{13}C NMR (δ): 20.2; 22.0; 24.2; 24.3; 25.1; 31.2 (2C); 34.4; 34.6; 35.2; 37.4; 41.1; 44.2; 50.6; 57.7; 76.8; 86.9; 176.9. IR (Nujol): 3020, 1670, 800, 710 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 74.02; H, 10.21; N, 4.62.

(2*R*,2*aS*,2*bS*,3*aR*,5*R*,7*aS*,10*aR*)-2,5,8,8-Tetramethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (4j). Colorless solid. Mp: 135−137 °C (from hexane). ^{1}H NMR (δ): 0.87−1.15 (m, 3H); 0.95 (d, 3H, J = 6.5 Hz); 1.10 (d, 3H, J = 7.0 Hz); 1.18 (s, 3H); 1.27 (m, 1H); 1.45 (m, 1H); 1.60−1.73 (m, 2H); 1.75 (s, 3H); 1.88 (m, 1H); 1.98 (m, 1H); 2.17 (ddd, 1H, J_1 = 2.5 Hz, J_2 = 8.4 Hz, J_3 = 11.4 Hz); 2.48 (dt, 1H, J_1 = 6.3 Hz, J_2 = 7.4 Hz); 2.68 (ddd, 1H, J_1 = 2.5 Hz, J_2 = 7.4 Hz, J_3 = 9.6 Hz); 2.80 (m, 1H); 3.40 (td, 1H, J_1 = 4.3 Hz, J_2 = 10.6 Hz); 4.98 (d, 1H, J = 6.3 Hz). ^{13}C NMR (δ): 18.2; 21.8; 22.0; 23.9; 25.3; 27.5; 31.2; 31.6; 34.5; 36.7; 41.0 (2C); 49.6; 56.6; 76.0; 86.2; 175.9. IR (Nujol): 1670, 710, 680 cm^{-1}. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.40; H, 9.65; N, 4.92.

(2*S*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2,5,8,8-Tetramethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (5j). Colorless oil. $[\alpha]^{25}_D = -3.68$ (c = 1.2, $CHCl_3$). ^{1}H NMR (δ): 0.86−1.13 (m, 3H); 0.93 (d, 3H, J = 6.5 Hz); 1.16 (d, 3H, J = 6.2 Hz); 1.27 (s, 3H); 1.37 (m, 1H); 1.50 (m, 1H); 1.70−1.75 (m, 2H); 1.76 (s, 3H); 1.89−1.98 (m, 2H); 2.13−2.23 (m, 3H); 2.95 (m, 1H); 3.49 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.7 Hz); 4.88 (s, 1H). ^{13}C NMR (δ): 20.5; 21.3; 21.9; 24.2; 25.1; 31.2; 31.3; 32.3; 34.4; 37.5; 41.0; 42.5; 50.7; 57.5; 76.5; 90.6; 176.5. IR (film): 1680, 740, 670 cm^{-1}. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.81; H, 9.64; N, 5.22.

(2*R*,2*aR*,2*bS*,3*aR*,5*R*,7*aS*,10*aS*)-2,5,8,8-Tetramethylperhydrocyclobuta[3,4]pyrrolo[2,1-b]-[1,3]benzoxazin-10-one (6j). Colorless solid. Mp: 100−101 °C (from hexane). ^{1}H NMR (δ): 0.86−1.11 (m, 3H); 0.94 (d, 3H, J = 6.5 Hz); 1.07 (d, 3H, J = 7.2 Hz); 1.30 (s, 3H); 1.31 (m, 1H); 1.50 (m, 1H); 1.58 (m, 1H); 1.70−1.75 (m, 2H); 1.76 (s, 3H); 1.93 (m, 1H); 2.53−2.64 (m, 2H); 2.76 (m, 1H); 2.96 (m, 1H); 3.52 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.6 Hz); 5.13 (s, 1H). ^{13}C NMR (δ): 16.6; 20.0; 22.0; 24.2; 25.1; 27.8; 31.2; 31.3; 34.4; 37.7; 38.2; 41.0; 50.5; 57.7; 76.8; 86.2; 176.8. IR (Nujol): 1670, 790, 750, 670 cm^{-1}. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.59; H, 10.00; N, 5.23.

Synthesis of Amino Alcohols 7a−g and 9a−i. General Method. To a suspension of $LiAlH_4$ (0.82 g, 21.6 mmol) in anhydrous THF (40 mL) cooled to −10 °C and under an argon atmosphere was added, in portions, dry $AlCl_3$ (0.95 g, 7.13 mmol). The mixture was stirred for 15 min, and a solution of the corresponding photocycloadduct (2.16 mmol) in dry THF (30 mL) was slowly added. The reaction mixture was stirred for 10 min at −10 °C and quenched by addition of a 10% aqueous solution of NaOH (4 mL). The resulting mixture was filtered, the solid was washed with EtOAc, and the organic layer was dried over anhydrous $MgSO_4$. The solvent was eliminated under reduced pressure, and the residue was chromatographed on silica gel using hexane/EtOAc (3:1) as eluent.

(1*R*,5*S*,6*R*)-N-(8-Mentholyl)-6-phenyl-3-azabicyclo[3.2.0]-heptane (7a). Yield: 98%. Colorless solid. Mp: 71−72 °C (from pentane). $[\alpha]^{25}_D = -109.29$ (c = 1.0, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.83−1.13 (m, 3H); 0.90 (s, 3H); 0.91 (d, 3H, J = 6.6 Hz); 1.23 (s, 3H); 1.45 (m, 1H); 1.57−1.68 (m, 3H); 1.98 (m, 1H); 2.15−2.32 (m, 2H); 2.38−2.46 (m, 2H); 2.71−2.78 (m, 2H); 2.91 (d, 1H, J = 9.5 Hz); 3.08 (d, 1H, J = 9.6 Hz); 3.15 (m, 1H); 3.72 (td, 1H, J_1 = 3.8 Hz, J_2 = 10.2 Hz); 7.13 (m, 1H); 7.19−7.24 (m, 4H); 8.24 (br s, 1H). ^{13}C NMR (333 K) (δ): 16.3; 21.4; 21.8; 25.2; 30.3; 31.1; 32.3; 34.6; 42.0; 43.5; 44.0; 48.2; 50.4; 51.6; 58.2; 72.3; 124.9; 125.6 (2C); 127.5 (2C); 146.0. IR (Nujol): 3180 (br), 3020, 1600, 750, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{33}NO$: C, 80.68; H, 10.16; N, 4.28. Found: C, 80.89; H, 9.98; N, 4.46.

(1*R*,5*S*,6*R*)-N-(8-Mentholyl)-6-(o-methoxyphenyl)-3-azabicyclo[3.2.0]heptane (7b). Yield: 95%. Colorless solid. Mp: 75−76 °C (from hexane). $[\alpha]^{25}_D = -69.12$ (c = 1.0, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.88−1.13 (m, 3H); 0.91 (s, 3H); 0.92 (d, 3H, J = 6.4 Hz); 1.26 (s, 3H); 1.43 (m, 1H); 1.57−1.69 (m, 3H); 1.98 (m, 1H); 2.17 (m, 1H); 2.33 (m, 1H); 2.42 (m, 1H); 2.48 (m, 1H); 2.73 (m, 2H); 3.00 (d, 1H, J = 9.4 Hz); 3.09 (d, 1H, J = 9.4 Hz); 3.36 (m, 1H); 3.72 (m, 1H); 3.73 (s, 3H); 6.76 (d, 1H, J = 8.1 Hz); 6.86 (t, 1H, J = 7.5 Hz); 7.09 (dd, 1H, J_1 = 8.1 Hz, J_2 = 7.5 Hz); 7.17 (d, 1H, J = 7.5 Hz); 8.52 (br s, 1H). ^{13}C NMR (333 K) (δ): 16.6; 21.8; 22.1; 25.6; 28.9; 30.8; 32.8; 35.0; 37.8; 43.5; 44.4; 48.6; 50.9; 52.1; 54.9; 58.6; 72.7; 110.1; 120.0; 126.3 (2C); 133.9; 157.1. IR (Nujol): 3100 (br), 3060, 1600, 1585, 750 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_2$: C, 77.27; H, 9.87; N, 3.92. Found: C, 77.46; H, 9.61; N, 4.11.

(1*R*,5*S*,6*R*)-N-(8-Mentholyl)-6-(p-methoxyphenyl)-3-azabicyclo[3.2.0]heptane (7c). Yield: 92%. Colorless solid. Mp: 82−83 °C (from hexane). $[\alpha]^{25}_D = -111.88$ (c = 1.0, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.85−1.13 (m, 3H); 0.93 (d, 3H, J = 6.3 Hz); 0.94 (s, 3H); 1.27 (s, 3H); 1.45 (m, 1H); 1.59−1.71 (m, 3H); 1.98 (m, 1H); 2.16−2.28 (m, 2H); 2.43 (m, 1H); 2.47 (m, 1H); 2.76−2.81 (m, 2H); 2.94 (d, 1H, J = 9.5 Hz); 3.11 (m, 1H); 3.12 (d, 1H, J = 9.4 Hz); 3.74 (m, 1H); 3.75 (s, 3H); 6.81 (d, 2H, J = 8.6 Hz); 7.12 (d, 2H, J = 8.6 Hz); 8.52 (br s, 1H).

^{13}C NMR (333 K) (δ): 17.0; 22.0; 22.4; 25.8; 31.0; 32.1; 32.9; 35.2; 42.0; 44.4; 44.6; 48.9; 51.1; 52.3; 55.2; 58.9; 73.0; 113.8 (2C); 127.2 (2C); 139.0; 157.8. IR (Nujol): 3120 (br), 3020, 1610, 1575, 820, 705 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_2$: C, 77.27; H, 9.87; N, 3.92. Found: C, 77.08; H, 9.92; N, 3.71.

(1*R*,5*S*,6*R*)-N-(8-Mentholyl)-6-(p-nitrophenyl)-3-azabicyclo[3.2.0]heptane (7e). Yield: 94%. Colorless oil. $[\alpha]^{25}_D = -131.16$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.86−1.14 (m, 3H); 0.93 (d, 3H, $J = 6.5$ Hz); 0.96 (s, 3H); 1.29 (s, 3H); 1.49 (m, 1H); 1.61−1.72 (m, 3H); 1.98 (m, 1H); 2.20−2.41 (m, 2H); 2.48 (dd, 1H, $J_1 = 5.9$ Hz, $J_2 = 9.6$ Hz); 2.58 (dd, 1H, $J_1 = 5.2$ Hz, $J_2 = 9.7$ Hz); 2.80−2.88 (m, 2H); 2.99 (d, 1H, $J = 9.7$ Hz); 3.16 (d, 1H, $J = 9.6$ Hz); 3.28 (m, 1H); 3.74 (td, 1H, $J_1 = 4.1$ Hz, $J_2 = 10.3$ Hz); 7.36 (d, 2H, $J = 8.7$ Hz); 8.11 (d, 2H, $J = 8.7$ Hz); 8.47 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.0; 21.9; 22.3; 25.7; 30.9; 31.4; 32.8; 35.1; 42.4; 43.9; 44.5; 48.8; 50.8; 52.1; 58.9; 72.9; 123.4 (2C); 127.0 (2C); 146.2; 154.2. IR (film): 3100 (broad), 3040, 1595, 850, 750, 695 cm^{-1}. Anal. Calcd for $C_{22}H_{32}N_2O_3$: C, 70.94; H, 8.66; N, 7.52. Found: C, 71.16; H, 8.78; N, 7.33.

(1*R*,5*S*,6*R*)-N-(8-Mentholyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane (7g). Yield: 93%. Colorless oil. $[\alpha]^{25}_D = -84.36$ ($c = 0.78$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.76−1.05 (m, 3H); 0.85 (d, 3H, $J = 6.5$ Hz); 0.88 (s, 3H); 1.18 (2s, 6H); 1.35 (m, 1H); 1.52−1.65 (m, 3H); 1.83−1.95 (m, 2H); 2.12 (d, 1H, $J = 9.3$ Hz); 2.29 (dd, 1H, $J_1 = 5.2$ Hz, $J_2 = 6.0$ Hz); 2.46 (dd, 1H, $J_1 = 9.9$ Hz, $J_2 = 12.4$ Hz); 2.59 (dd, 1H, $J_1 = 6.0$ Hz, $J_2 = 9.4$ Hz); 2.86 (d, 1H, $J = 9.4$ Hz); 2.95−3.02 (ddd, 1H, $J_1 = 5.2$ Hz, $J_2 = 7.2$ Hz, $J_3 = 9.9$ Hz); 3.05 (d, 1H, $J = 9.3$ Hz); 3.65 (td, 1H, $J_1 = 4.1$ Hz, $J_2 = 10.4$ Hz); 7.05 (m, 1H); 7.13−7.21 (m, 4H); 8.50 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.0; 22.0; 22.2; 25.1; 25.9; 31.1; 35.3; 38.6; 39.4; 39.6; 44.7; 48.8; 49.8; 52.4; 58.1; 59.0; 73.1; 125.6; 126.6 (2C); 128.3 (2C); 146.6. IR (film): 3160 (br), 3020, 1590, 760, 730, 700 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO$: C, 80.88; H, 10.33; N, 4.10. Found: C, 80.69; H, 10.22; N, 3.91.

(1*S*,5*R*,6*S*)-N-(8-Mentholyl)-6-phenyl-3-azabicyclo[3.2.0]-heptane (9a). Yield: 88%. Colorless solid. Mp: 150−151 °C (from hexane). $[\alpha]^{25}_D = +44.53$ ($c = 0.78$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.78−1.13 (m, 3H); 0.85 (d, 3H, $J = 6.5$ Hz); 0.88 (s, 3H); 1.20 (s, 3H); 1.38 (m, 1H); 1.53−1.64 (m, 3H); 1.92 (m, 1H); 2.11−2.22 (m, 2H); 2.42 (m, 1H); 2.51 (m, 1H); 2.73−2.76 (m, 2H); 2.83 (d, 1H, $J = 9.5$ Hz); 3.11 (d, 1H, $J = 9.6$ Hz); 3.20 (ddd, 1H, $J_1 = 3.8$ Hz, $J_2 = 6.7$ Hz, $J_3 = 9.9$ Hz); 3.66 (td, 1H, $J_1 = 4.1$ Hz, $J_2 = 10.6$ Hz); 7.06 (m, 1H); 7.16−7.23 (m, 4H); 8.55 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.2; 22.0; 22.3; 25.9; 31.1; 32.2; 32.8; 35.3; 41.8; 44.7; 44.8; 48.9; 51.5; 52.2; 59.1; 73,1; 125.6; 126.4 (2C); 128.2 (2C); 147.0. IR (Nujol): 3120 (br), 3020, 1600, 750, 740, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{33}$-NO: C, 80.68; H, 10.16; N, 4.28. Found: C, 80.43; H, 10.29; N, 4.12.

(1*S*,5*R*,6*S*)-N-(8-Mentholyl)-6-(o-methoxyphenyl)-3-azabicyclo[3.2.0]heptane (9b). Yield: 96%. Colorless oil. $[\alpha]^{25}_D = +38.24$ ($c = 1.2$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.86−1.13 (m, 3H); 0.92 (d, 3H, $J = 6.7$ Hz); 0.93 (s, 3H); 1.25 (s, 3H); 1.46 (m, 1H); 1.56−1.70 (m, 3H); 1.97 (m, 1H); 2.06 (m, 1H); 2.37 (m, 1H); 2.47 (m, 1H); 2.61 (m, 1H); 2.67−2.80 (m, 2H); 2.85 (d, 1H, $J = 9.2$ Hz); 3.18 (d, 1H, $J = 9.5$ Hz); 3.46 (m, 1H); 3.71 (td, 1H, $J_1 = 4.1$ Hz, $J_2 = 10.2$ Hz); 3.76 (s, 3H); 6.78 (d, 1H, $J = 8.2$ Hz); 6.87 (t, 1H, $J = 7.5$ Hz); 7.10 (dd, 1H, $J_1 = 7.5$ Hz, $J_2 = 8.2$ Hz); 7.18 (d, 1H, $J = 7.5$ Hz); 8.55 (br s, 1H). ^{13}C NMR (333 K) (δ): 16.9; 21.9; 22.1; 25.6; 29.4; 30.8; 32.5; 35.1; 37.3; 43.9; 44.5; 48.6; 51.3; 52.0; 55.1; 58.6; 72.8; 110.4; 120.0; 126.3; 126.4; 134.0; 157.3. IR (film): 3100 (br), 3060, 1590, 1580, 750 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_2$: C, 77.27; H, 9.87; N, 3.92. Found: C, 77.06; H, 9.99; N, 4.07.

(1*S*,5*R*,6*S*)-N-(8-Mentholyl)-6-(p-methoxyphenyl)-3-azabicyclo[3.2.0]heptane (9c). Yield: 97%. Colorless solid. Mp: 124−126 °C (from hexane). $[\alpha]^{25}_D = +53.05$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.85−1.13 (m, 3H); 0.92 (d, 3H, $J = 5.8$ Hz); 0.93 (s, 3H); 1.26 (s, 3H); 1.45 (m, 1H); 1.59−1.70 (m, 3H); 1.98 (m, 1H); 2.11−2.21 (m, 2H); 2.45 (m, 1H); 2.55 (m, 1H); 2.72−2.81 (m, 2H); 2.87 (d, 1H, $J = 9.4$ Hz); 3.16 (d, 1H, $J = 9.8$ Hz); 3.21 (m, 1H); 3.72 (td, 1H, $J_1 = 4.0$ Hz, $J_2 = 10.4$ Hz); 3.76 (s, 3H); 6.82 (d, 2H, $J = 8.6$ Hz); 7.15 (d, 2H, $J = 8.6$ Hz); 8.51 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.0; 22.0; 22.3; 25.8; 31.0; 32.4; 32.6; 35.2; 41.0; 44.7; 45.0; 48.9; 51.4; 52.1; 55.2; 58.9; 73.0; 113.8 (2C); 127.3 (2C); 139.2; 157.8. IR (Nujol): 3120 (br), 3020, 1610, 1570, 820, 740, 720, 680 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO_2$: C, 77.27; H, 9.87; N, 3.92. Found: C, 77.08; H, 10.03; N, 3.76.

(1*S*,5*R*,6*S*)-N-(8-Mentholyl)-6-(p-nitrophenyl)-3-azabicyclo[3.2.0]heptane (9e). Yield: 97%. Colorless solid. Mp: 147−148 °C (from hexane). $[\alpha]^{25}_D = +76.10$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.93 (d, 3H, $J = 6.5$ Hz); 0.96 (s, 3H); 1.02−1.14 (m, 3H); 1.29 (s, 3H); 1.46 (m, 1H); 1.61−1.72 (m, 3H); 1.99 (m, 1H); 2.24−2.27 (m, 2H); 2.50 (m, 1H); 2.59 (m, 1H); 2.84 (m, 2H); 2.93 (d, 1H, $J = 9.6$ Hz); 3.22 (d, 1H, $J = 9.8$ Hz); 3.40 (m, 1H); 3.75 (m, 1H); 7.38 (d, 2H, $J = 8.7$ Hz); 8.12 (d, 2H, $J = 8.7$ Hz); 8.45 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.1; 22.0; 22.3; 25.8; 31.0; 31.9; 32.7; 35.2; 41.6; 44.6 (2C); 48.9; 51.2; 52.0; 59.0; 73.1; 123.5 (2C); 127.2 (2C); 146.3; 154.5. IR (Nujol): 3160 (br), 3060, 1600, 850, 750, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{32}N_2O_3$: C, 70.94; H, 8.66; N, 7.52. Found: C, 70.77; H, 8.49; N, 7.66.

(1*S*,5*R*)-N-(8-Mentholyl)-6,6-diphenyl-3-azabicyclo[3.2.0]-heptane (9f). Yield: 95%. Colorless solid. Mp: 129−130 °C (from hexane). $[\alpha]^{25}_D = +127.41$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.71−0.89 (m, 3H); 0.84 (s, 3H); 0.85 (d, 3H, $J = 6.7$ Hz); 1.12 (s, 3H); 1.29−1.46 (m, 2H); 1.49 (m, 1H); 1.59 (m, 1H); 1.78 (m, 1H); 2.59 (m, 1H); 2.67−2.74 (m, 3H); 2.86−2.88 (m, 3H); 3.45−3.51 (m, 2H); 7.06−7.09 (m, 4H); 7.19−7.26 (m, 4H); 7.32−7.35 (m, 2H); 7.78 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.2; 22.0; 22.1; 25.7; 31.0; 32.0; 35.1; 38.6; 44.4; 47.1; 48.0; 48.4; 49.8; 51.4; 58.7; 72.7; 125.3; 125.4; 126.3 (2C); 127.0 (2C); 128.0 (2C); 128.2 (2C); 146.5; 149.9. IR (Nujol): 3160 (br), 3020, 1590, 750, 730, 700 cm^{-1}. Anal. Calcd for $C_{28}H_{37}NO$: C, 83.33; H, 9.24; N, 3.47. Found: C, 83.20; H, 9.41; N, 3.65.

(1*S*,5*R*,6*S*)-N-(8-Mentholyl)-1-methyl-6-phenyl-3-azabicyclo[3.2.0]heptane (9g). Yield: 98%. Colorless solid. Mp: 81−82 °C (from hexane). $[\alpha]^{25}_D = +41.52$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.89−1.12 (m, 3H); 0.92 (d, 3H, $J = 6.5$ Hz); 0.95 (s, 3H); 1.24 (s, 6H); 1.43 (m, 1H); 1.59−1.71 (m, 3H); 1.98 (m, 1H); 1.97 (dd, 1H, $J_1 = 6.3$ Hz, $J_2 = 12.4$ Hz); 2.29 (d, 1H, $J = 9.2$ Hz); 2.36−2.44 (m, 2H); 2.57 (dd, 1H, $J_1 = 6.2$ Hz, $J_2 = 9.6$ Hz); 2.88 (d, 1H, $J = 9.2$ Hz); 3.14 (d, 1H, $J = 9.6$ Hz); 3.19 (m, 1H); 3.71 (td, 1H, $J_1 = 4.0$ Hz, $J_2 = 10.4$ Hz); 7.14 (m, 1H); 7.22−7.29 (m, 4H); 8.50 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.0; 22.0; 22.2; 24.7; 25.8; 31.0; 35.2; 38.4; 38.6; 39.0; 44.6; 48.5; 50.0; 51.5; 58.9; 59.0; 73.0; 125.4; 126.5 (2C); 128.1 (2C); 146.6. IR (Nujol): 3150 (br), 3020, 1600, 750, 730, 690 cm^{-1}. Anal. Calcd for $C_{23}H_{35}NO$: C, 80.88; H, 10.33; N, 4.10. Found: C, 80.71; H, 10.54; N, 3.92.

(1*S*,5*R*)-N-(8-Mentholyl)-1-methyl-6,6-diphenyl-3-azabicyclo[3.2.0]heptane (9h). Yield: 95%. Colorless solid. Mp: 159−160 °C (from hexane). $[\alpha]^{25}_D = +142.23$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.57−0.64 (m, 3H); 0.76 (s, 3H); 0.79 (d, 3H, $J = 6.4$ Hz); 1.02 (s, 3H); 1.06 (s, 3H); 1.12−1.27 (m, 2H); 1.42 (m, 1H); 1.53 (m, 1H); 1.68 (m, 1H); 2.44−2.52 (m, 2H); 2.58 (d, 1H, $J = 9.0$ Hz); 2.78−2.85 (m, 2H); 2.91 (d, 1H, $J = 11.9$ Hz); 3.18 (m, 1H); 3.38 (m, 1H); 6.95−7.37 (m, 10H); 7.50 (br s, 1H). ^{13}C NMR (333 K) (δ): 17.2; 22.0; 22.1; 24.1; 25.8; 31.0; 35.2; 39.0; 43.7; 44.5; 47.6; 48.2; 48.8; 51.0; 58.7; 59.2; 72.6; 125.1; 125.2; 126.5 (2C); 126.9 (2C); 128.1 (2C); 128.2 (2C); 146.6; 150.6. IR (Nujol): 3140 (br), 3080, 3060, 3020, 1595, 1580, 740, 690 cm^{-1}. Anal. Calcd for $C_{29}H_{39}NO$: C, 83.40; H, 9.41; N, 3.35. Found: C, 83.68; H, 9.22; N, 3.34.

(1*S*,5*R*)-N-(8-Mentholyl)-6,6-dimethyl-3-azabicyclo[3.2.0]-heptane (9i). Yield: 82%. Colorless solid. Mp: 80−81 °C (from pentane). $[\alpha]^{25}_D = +9.28$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (333 K) (δ): 0.88−1.09 (m, 3H); 0.91 (d, 3H, $J = 6.4$ Hz); 0.92 (s, 3H); 0.98 (s, 3H); 1.14 (s, 3H); 1.20 (s, 3H); 1.45 (m, 1H); 1.50 (dd, 1H, $J_1 = 7.0$ Hz, $J_2 = 11.8$ Hz); 1.58−1.76 (m, 4H); 1.96 (m, 1H); 2.25 (m, 1H); 2.37−2.46 (m, 2H); 2.63−2.78 (m, 2H); 3.12

(d, 1H, J = 10.3 Hz); 3.62 (td, 1H, J_1 = 4.1 Hz, J_2 = 10.4 Hz); 8.10 (br s, 1H). ^{13}C NMR (333 K) (δ): 16.8; 21.8; 22.2; 23.2; 25.6; 30.6; 30.8; 31.7; 32.6; 35.1; 37.7; 44.6; 45.9; 46.9; 48.5; 50.8; 58.8; 72.6. IR (Nujol): 3120 (br), 830, 750 cm^{-1}. Anal. Calcd for $C_{18}H_{33}NO$: C, 77.36; H, 11.90; N, 5.01. Found: C, 77.20; H, 11.69; N, 5.14.

Elimination of the Menthol Appendage. General Method. A solution of the aminomenthol derivative (1.48 mmol) and PCC (2.56 g, 11.90 mmol) in anhydrous CH_2Cl_2 (35 mL) and 3 Å molecular sieves (1.5 g) was stirred under an argon atmosphere until the oxidation was finished (TLC, 5−6 h). The solvent was removed under reduced pressure, the residue was dissolved in a 10% aqueous solution of NaOH to pH 12, and the resulting solution was extracted with $CHCl_3$ (5 × 25 mL). The organic phase was washed with brine and dried over anhydrous $MgSO_4$. The solvents were removed under vacuum, the residue was taken up in a 2.5 M solution of KOH in THF/MeOH/H_2O (2:1:1), and the solution was stirred at room temperature for 24−48 h (TLC). After elimination of the solvents under reduced pressure the residue was acidified with a 1 N solution of HCl to pH 2 and extracted with Et_2O (3 × 20 mL). The aqueous solution was neutralized to pH 12 with a 10% aqueous solution of NaOH and extracted with $CHCl_3$ (5 × 20 mL). The organic layers were washed with H_2O and dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum. The 3-azabicyclo[3.2.0]heptane derivatives were characterized as *N*-tosyl derivatives.

(1*R*,5*S*,6*R*)-N-Tosyl-6-phenyl-3-azabicyclo[3.2.0]-heptane (8a). Yield: 56%. Colorless solid. Mp: 135−137 °C (from hexanes−EtOAc). $[\alpha]^{25}_D$ = +1.45 (c = 0.60, $CHCl_3$). ^{1}H NMR (δ): 2.28−2.35 (m, 2H); 2.44 (s, 3H); 2.64 (dd, 1H, J_1 = 5.4 Hz, J_2 = 9.7 Hz); 2.72 (dd, 1H, J_1 = 6.5 Hz, J_2 = 9.7 Hz); 2.80−2.91 (m, 2H); 3.36−3.43 (m, 1H); 3.54 (d, 1H, J = 9.7 Hz); 3.59 (d, 1H, J = 9.7 Hz); 7.16−7.26 (m, 3H); 7.29−7.36 (m, 4H); 7.71−7.75 (m, 2H). ^{13}C NMR (δ): 21.5; 31.7; 34.0; 41.8; 45.6; 54.3; 54.4; 126.1; 126.3 (2C); 128.0 (2C); 128.4 (2C); 129.5 (2C); 131.7; 143.6; 145.3. IR (Nujol): 3040, 1600, 810, 770, 740, 700, 670 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.46; N, 4.28. Found: C, 69.47; H, 6.38; N, 4.35.

(1*S*,5*R*,6*S*)-N-Tosyl-6-phenyl-3-azabicyclo[3.2.0]-heptane (ent-8a). Yield: 55%. Colorless solid. $[\alpha]^{25}_D$ = −2.14 (c = 0.28, $CHCl_3$). Melting point, ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **8a**.

(1*R*,5*S*,6*R*)-N-Tosyl-6-(o-methoxyphenyl)-3-azabicyclo-[3.2.0]heptane (8b). Yield: 60%. Colorless solid. Mp: 124−125 °C (from hexanes−EtOAc). $[\alpha]^{25}_D$ = +20.34 (c = 1.0, EtOAc). ^{1}H NMR (δ): 2.13−2.21 (m, 1H); 2.43 (s, 3H); 2.43−2.51 (m, 1H); 2.66 (dd, 1H, J_1=5.5 Hz, J_2=9.5 Hz); 2.74−2.80 (m, 3H); 3.52 (d, 1H, J = 8.5 Hz); 3.59 (m, 1H); 3.68 (d, 1H, J = 9.5 Hz); 3.79 (s, 3H); 6.83 (d, 1H, J = 8.1 Hz); 6.92 (t, 1H, J = 7.4 Hz); 7.15−7.25 (m, 2H); 7.33 (d, 2H, J = 8.0 Hz); 7.74 (d, 2H, J = 8.0 Hz). ^{13}C NMR (δ): 21.4; 28.9; 33.9; 37.1; 44.9; 54.5; 54.6; 55.0; 110.0; 120.1; 126.2; 127.0; 128.0 (2C); 129.4 (2C); 131.8; 132.5; 143.4; 157.1. IR (Nujol): 3020, 1590, 810, 750, 700, 660 cm^{-1}. Anal. Calcd for $C_{20}H_{23}NO_3S$: C, 67.20; H, 6.49; N, 3.92. Found: C, 67.31; H, 6.60; N, 4.08.

(1*S*,5*R*,6*S*)-N-Tosyl-6-(o-methoxyphenyl)-3-azabicyclo-[3.2.0]heptane (ent-8b). Yield: 52%. Colorless solid. $[\alpha]_D$ = −18.34 (c = 0.92, EtOAc). Melting point, ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **8b**.

(1*R*,5*S*,6*R*)-N-Tosyl-6-(p-methoxyphenyl)-3-azabicyclo-[3.2.0]heptane (8c). Yield: 51%. Colorless solid. Mp: 116−117 °C (from hexane/EtOAc). $[\alpha]^{25}_D$ = +4.99 (c = 1.0, EtOAc). ^{1}H NMR (δ): 2.25−2.30 (m, 2H); 2.44 (s, 3H); 2.63 (dd, 1H, J_1 = 5.1 Hz, J_2 = 9.6 Hz); 2.72 (dd, 1H, J_1 = 6.4 Hz, J_2 = 9.6 Hz); 2.78−2.86 (m, 2H); 3.33 (m, 1H); 3.53 (d, 1H, J = 9.6 Hz); 3.58 (d, 1H, J = 9.6 Hz); 3.78 (s, 3H); 6.85 (d, 2H, J = 8.6 Hz); 7.13 (d, 2H, J = 8.6 Hz); 7.34 (d, 2H, J = 8.1 Hz); 7.72 (d, 2H, J = 8.1 Hz). ^{13}C NMR (δ): 21.5; 32.0; 33.8; 41.1; 45.8; 54.3; 54.4; 55.2; 113.8 (2C); 127.3 (2C); 128.0 (2C); 129.5 (2C); 131.6; 137.4; 143.6; 157.8. IR (Nujol): 3100, 3040, 1610, 1600, 1580, 710, 700, 670 cm^{-1}. Anal. Calcd for $C_{20}H_{23}NO_3S$: C, 67.20; H, 6.49; N, 3.92. Found: C, 67.36; H, 6.32; N, 4.06.

(1*S*,5*R*,6*S*)-N-Tosyl-6-(p-methoxyphenyl)-3-azabicyclo-[3.2.0]heptane (ent-8c). Yield: 47%. Colorless solid. $[\alpha]^{25}_D$ = −3.60 (c = 0.94, AcOEt). Melting point, ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **8c**.

(1*R*,5*S*,6*R*)-N-Tosyl-6-(p-nitrophenyl)-3-azabicyclo[3.2.0]-heptane (8e). Yield: 58%. Colorless solid. Mp: 146−147 °C (from hexane/EtOAc). $[\alpha]^{25}_D$ = +1.40 (c = 1.0, EtOAc). ^{1}H NMR (δ): 2.33−2.38 (m, 2H); 2.43 (s, 3H); 2.64 (dd, 1H, J_1 = 5.1 Hz, J_2 = 9.8 Hz); 2.71 (dd, 1H, J_1 = 6.4 Hz, J_2 = 9.7 Hz); 2.87−2.90 (m, 2H); 3.52 (m, 1H); 3.55 (d, 1H, J = 9.7 Hz); 3.62 (d, 1H, J = 9.8 Hz); 7.34 (m, 4H); 7.70 (d, 2H, J = 8.2 Hz); 8.14 (d, 2H, J = 8.7 Hz). ^{13}C NMR (δ): 21.5; 31.4; 33.9; 41.6; 45.2; 54.1; 54.2; 123.7 (2C); 127.1 (2C); 128.0 (2C); 129.5 (2C); 131.4; 143.8; 146.2; 152.8. IR (Nujol): 3040, 1595, 810, 745, 695, 660 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2O_4S$: C, 61.27; H, 5.41; N, 7.52. Found: C, 61.14; H, 5.29; N, 7.38.

(1*S*,5*R*,6*S*)-N-Tosyl-6-(p-nitrophenyl)-3-azabicyclo[3.2.0]-heptane (*ent*-8e). Yield: 56%. Colorless solid. $[\alpha]^{25}_D$ = −1.78 (c = 0.56, EtOAt). Melting point, ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **8e**.

(1*S*,5*R*)-N-Tosyl-6,6-diphenyl-3-azabicyclo[3.2.0]-heptane (*ent*-8f). Yield: 58%. Colorless oil. $[\alpha]^{25}_D$ = +86.00 (c = 0.79, EtOAc). ^{1}H NMR (δ): 2.42 (s, 3H); 2.62 (ddd, 1H, J_1 = 3.4 Hz, J_2 = 8.1 Hz, J_3 = 11.5 Hz); 2.78−2.89 (m, 2H); 2.91 (m, 1H); 2.94 (dd, 1H, J_1 = 8.4 Hz, J_2 = 10.8 Hz); 3.28 (dd, 1H, J_1 = 2.3 Hz, J_2 = 10.8 Hz); 3.39 (d, 1H, J = 9.6 Hz); 3.60 (m, 1H); 7.02−7.05 (m, 2H); 7.11−7.16 (m, 2H); 7.23−7.32 (m, 8H); 7.58 (d, 2H, J = 8.2 Hz). ^{13}C NMR (δ): 21.5; 33.1; 36.6; 47.3; 49.5; 50.0; 53.4; 125.8; 125.9; 126.4 (2C); 127.0 (2C); 127.8 (3C); 128.3 (3C); 129.4 (2C); 132.6; 143.3; 144.7; 149.1. IR (film): 3050, 3020, 1590, 810, 750, 700, 660 cm^{-1}. Anal. Calcd for $C_{25}H_{25}NO_2S$: C, 74.41; H, 6.24; N, 3.47. Found: C, 74.36; H, 6.11; N, 3.49.

(1*R*,5*S*,6*R*)-N-Tosyl-1-methyl-6-phenyl-3-azabicyclo-[3.2.0]heptane (8g). Yield: 48%. Colorless solid. Mp: 144−145 °C (from hexanes−EtOAc). $[\alpha]^{25}_D$ = −6.54 (c = 0.26, EtOAc). ^{1}H NMR (δ): 1.18 (s, 3H); 2.03 (dd, 1H, J_1 = 7.8 Hz, J_2 = 12.3 Hz); 2.39−2.44 (m, 2H); 2.44 (s, 3H); 2.52 (dd, 1H, J_1 = 10.2 Hz, J_2 = 12.3 Hz); 2.74 (dd, 1H, J_1 = 5.6 Hz, J_2 = 9.8 Hz); 3.26 (ddd, 1H, J_1 = 5.7 Hz, J_2 = 7.8 Hz, J_3 = 10.2 Hz); 3.57 (d, 1H, J = 9.8 Hz); 3.56 (d, 1H, J = 10.8 Hz); 7.16−7.28 (m, 3H); 7.31−7.36 (m, 4H); 7.71−7.74 (m, 2H). ^{13}C NMR (δ): 21.5; 24.4; 38.5; 38.7; 41.1; 51.0; 54.4; 60.2; 126.0; 126.5 (2C); 128.0 (2C); 128.4 (2C); 129.5 (2C); 131.8; 143.6; 145.2. IR (Nujol): 3020, 1600, 810, 760, 700, 670 cm^{-1}. Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10. Found: C, 70.47; H, 6.91; N, 3.96.

(1*S*,5*R*,6S)-N-Tosyl-1-methyl-6-phenyl-3-azabicyclo[3.2.0]-heptane (*ent*-8g). Yield: 65%. Colorless solid. $[\alpha]^{25}_D$ = +5.96 (c = 1.0, EtOAc). Melting point, ^{1}H NMR, ^{13}C NMR, and IR data are coincident with those reported for **8g**.

(1*S*,5*R*)-N-Tosyl-1-methyl-6,6-diphenyl-3-azabicyclo-[3.2.0]heptane (*ent*-8h). Yield: 46%. Colorless solid. Mp: 141−142 °C (from hexanes−EtOAc). $[\alpha]^{25}_D$ = +112.97 (c = 0.74, EtOAc). ^{1}H NMR (δ): 1.02 (s, 3H); 2.38 (s, 3H); 2.39 (d, 1H, J = 9.3 Hz); 2.44 (dd, 1H, J_1 = 3.0 Hz, J_2 = 12.0 Hz); 2.88 (dd, 1H, J_1 = 8.0 Hz, J_2 = 10.7 Hz); 3.16 (d, 1H, J = 12.0 Hz); 3.25 (m, 2H); 3.34 (d, 1H, J = 9.3 Hz); 7.05−7.34 (m, 12H); 7.55 (d, 2H, J = 8.3 Hz). ^{13}C NMR (δ): 21.4; 22.3; 40.5; 42.2; 47.0; 50.4; 50.8; 59.4; 125.4; 125.6; 126.6 (2C); 127.0 (2C); 127.8 (2C); 128.3(2C); 128.2 (2C); 129.3 (2C); 132.3; 143.2; 144.5; 149.6. IR (Nujol): 3040, 1590, 830, 810, 760, 700, 660 cm^{-1}. Anal. Calcd for $C_{26}H_{27}NO_2S$: C, 74.79; H, 6.52; N, 3.35. Found: C, 74.88; H, 6.65; N, 3.27.

(1*S*,5*R*)-N-Tosyl-6,6-dimethyl-3-azabicyclo[3.2.0]-heptane (*ent*-8i). Yield: 75%. Colorless solid. Mp: 115−117 °C (from hexane). $[\alpha]^{25}_D$ = −12.65 (c = 1.0, EtOAc). ^{1}H NMR (δ): 1.02 (s, 3H); 1.12 (s, 3H); 1.64 (dd, 1H, J_1 = 6.3 Hz, J_2 = 12.0 Hz); 1.87 (ddd, 1H, J_1 = 1.9 Hz, J_2 = 8.7 Hz, J_3 = 12.0 Hz); 2.28 (m, 1H); 2.43 (s, 3H); 2.46 (dd, 1H, J_1 = 7.2 Hz, J_2 =

10.2 Hz); 2.47 (dd, 1H, $J_1 = 5.8$ Hz, $J_2 = 9.3$ Hz); 2.75 (m, 1H); 3.32 (d, 1H, $J = 9.3$ Hz); 3.59 (d, 1H, $J = 10.2$ Hz); 7.32 (d, 2H, $J = 8.1$ Hz); 7.70 (d, 2H, $J = 8.1$ Hz). ^{13}C NMR (δ): 21.5; 23.1; 31.2; 31.4; 32.7; 38.2; 46.8; 49.5; 53.6; 128.1 (2C); 129.4 (2C); 131.7; 143.4. IR (Nujol): 3020, 1600, 810, 755, 710, 670 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.48; H, 7.58; N, 5.01. Found: C, 64.59; H, 7.71; N, 4.88.

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Supporting Information Available: Synthesis and spectral and physical data for perhydro-1,3-benzoxazines **2a**−**j** and **3a**−**j**, ORTEP representation of X-ray structures of **4a**, **5i**, and *ent*-**8g**, ^{1}H NMR spectra for compounds **4a**−**j** and **5a**−**j**, and NOESY experiments for **4b** and **5g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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