# A Short Diastereoselective Synthesis of Enantiopure Highly Substituted Tetrahydroepoxyisoindolines†

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*Received October 5, 1999*

Diastereoselective intramolecular Diels−Alder reaction on 3-allyl-2-furyl- or 3-furfuryl-2-vinyl-substituted chiral perhydro-1,3-benzoxazines derived from (−)-aminomenthol is described. The [4 + 2] cycloaddition is highly stereo- and regioselective leading to the thermodynamic adducts as major products. Reduction of the N,O-acetal, followed by elimination of the menthol appendage, allows both enantiomers of disubstituted epoxy tetrahydroisoindolines to be prepared. Nucleophilic ring opening of the N,O-moiety in the adducts by magnesium or aluminum derivatives, followed by elimination of the menthol, leads to the synthesis of enantiopure regioisomeric trisubstituted epoxy tetrahydroisoindolines with up to five stereocenters.

## Introduction

The application of the intramolecular Diels−Alder reaction to the construction of aza-bicyclic compounds has been practiced for more than 25 years,[1,2] and interest in this methodology has been reinforced during the past few years.[3] As such, syntheses of hydroquinolines,[4] hydroindoles,[5] hydroisoquinolines,[6] hydroisoindoles,[7] indolizidines,[8] and quinolizidines[9] have been carried out by the intramolecular [4 + 2] cycloaddition of different azatrienes.

The furan ring shows low reactivity toward unactivated dienophiles, and the competing retro-Diels−Alder reaction becomes a problem from a synthetic point of view,[10] but the placement of the furan ring and the dienophile into the same molecule can circumvent these problems because it has been demonstrated that the intramolecular reaction occurs at lower temperatures than its intermolecular counterpart.[11] In this respect, the intramolecular Diels−Alder reaction of furyl-substituted $\alpha,\beta$-unsaturated amides has been reported,[12] and even more significantly, unactivated $\pi$ bonds are often suitable dienophiles for the internal cycloadditions.[13]

On the other hand, we have recently reported the diastereoselective intramolecular [4 + 2] cycloaddition of 2-furyl substituted acrylamides derived from (−)-8-aminomenthol to oxatricyclic adducts that can be further elaborated to enantiomerically pure epoxy tetrahydroisoindolines in excellent chemical yields.[14] In conjunction with these studies, we now report on the application of this reaction, followed by nucleophilic ring opening of the N,O-acetal[15] in the perhydrobenzoxazine system, directed to the diastereoselective synthesis of enantiopure 1- or 3-substituted epoxy tetrahydroisoindolines with up to five stereocenters.

Retrosynthetic analysis (Figure 1) illustrates that both enantiomers of 3- or 4-substituted epoxy tetrahydroisoindolines (**8** or *ent*-**8**) can be synthesized from the regioisomeric (−)-8-aminomenthol-derived perhydrobenzoxazines **2** and **3**, which differ in the position of the furan, acting as diene, and the unactivated dienophile in the heterocycle. Thermally induced cycloaddition of **2** and **3**

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† Dedicated to Prof. Dr. Angel Alberola on occasion of his 70th birthday.

(1) (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Oppolzer, W. *Synthesis* **1978**, 793. (c) Oppolzer, W. *Heterocycles* **1980**, *14*, 1615. (d) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63.

(2) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187.

(3) See for instance: Kappe, C. O.; Murphree, S. S.; Padwa, A. *Tetrahedron* **1997**, *53*, 14179 and references therein.

(4) (a) Oppolzer, W.; Flaskamp, E. *J. Am. Chem. Soc.* **1977**, *60*, 204. (b) Stork, G. Morgan Jr., D. J. *J. Am. Chem. Soc.* **1979**, *101*, 7110. (c) Keck, G. E.; Boden, E.; Sonnewald, V. *Tetrahedron Lett.* **1981**, *22*, 2615. (d) Gallagher, T.; Magnus, P.; Huffman, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 1140.

(5) (a) Martin, S. F.; Desai, S. R.; Phillips, G. W.; Miller, A. C. *J. Am. Chem. Soc.* **1980**, *102*, 3294. (b) Martin, S. F.; Tu, C.; Kimura, M.; Simonsen, S. H. *J. Org. Chem.* **1982**, *47*, 3634. (c) Padwa, A.; Dimitroff, M.; Waterson, A. G.; Wu, T. *J. Org. Chem.* **1998**, *63*, 3986. (d) Padwa, A.; Brodney, M. A.; Dimitroff, M. *J. Org. Chem.* **1998**, *63*, 5304.

(6) (a) Oppolzer, W.; Francotte, E,; Bättig, K. *Helv. Chim. Acta* **1981**, *64*, 478. (b) Hudlicky, T.; Butora, G.; Fearnley, S. P.; Gum, A. G.; Persichini, P. J., III; Stabile, M. R.; Merola, J. S. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2393, and references therein. (c) Leonard, J.; Fearnley, S. P.; Hague, A. B.; Wong, G.; Jones, M. F. *Tetrahedron Lett.* **1997**, *38*, 3067.

(7) (a) Frater, G. *Tetrahedron Lett.* **1976**, 4517. (b) Parker, K. A.; Adamchuck, M. R. *Tetrahedron Lett.* **1978**, 1689. (c) Pyne, S. G.; Hensel, M. J.; Byrn, S. R.; McKenzie, A. T.; Fuchs, P. L. *J. Am. Chem. Soc.* **1980**, *102*, 5960. (d) Mukaiyama, T.; Iwasana, N. *Chem. Lett.* **1981**, 29. (e) Brettle, R.; Jafri, I. A. *J. Chem. Soc., Perkin Trans. 1* **1983**, 387. (f) Mellor, J. M.; Wagland, A. M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 997.

(8) Khatri, N. A.; Schmitthenner, H. F.; Shringarpure, J.; Weinreb, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 6387.

(9) Cheng, Y. S.; Fowler, F. W.; Lupo, A. T. *J. Am. Chem. Soc.* **1981**, *103*, 2090.

(10) Lipshuts, B.*Chem. Rev.* **1986**, *86*, 795.

(11) (a) Sternbach, D. D.; Rossana, D. M.; Onan, K. D. *J. Org. Chem.* **1984**, *49*, 3427. (b) Klein, L. L. *J. Org. Chem.* **1985**, *50*, 1770. (c) Jung, M. E.; Gervey, J. *J. Am. Chem. Soc.* **1989**, *111*, 5469.

(12) (a) Jung, M. E.; Street, L. J. *J. Am. Chem. Soc.* **1984**, *106*, 8327. (b) Prajapati, D.; Sandhu, J. S. *Heterocycles* **1985**, *23*, 17. (c) Prajapati, D.; Borthakur, D. R.; Sandhu, J. S. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1197. (d) Zylber, J.; Tubul, A.; Brun, P. *Tetrahedron: Asymmetry.* **1995**, *6*, 377.

(13) (a) Mance, A. D.; Sindler-Kulyk, M.; Jakopcic, K.; Hergold-Brundk, A.; Nagl, A. *J. Heterocycl. Chem.* **1997**, *34*, 1315. (b) Choony, N.; Badabhoy, A.; Sammes, J. *J. Chem. Soc., Chem. Commun.* **1997**, 513. (c). Choony, N.; Badabhoy, A.; Sammes, J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2017. (d) Andrés, C.; Nieto, J.; Pedrosa, R.; Vicente, M. *J. Org. Chem.* **1998**, *63*, 8570.

(14) Andrés, C.; Maestro, G.; Nieto, J.; Pedrosa, R.; García-Granda, S.; Pérez- Carreño, E. *Tetrahedron Lett.* **1997**, *38*, 1463.

(15) Andrés, C.; Nieto, J.; Pedrosa, R.; Villamañán, N. *J. Org. Chem.* **1996**, *61*, 4130.

10.1021/jo991544q CCC: $19.00 
Published on Web 01/14/2000

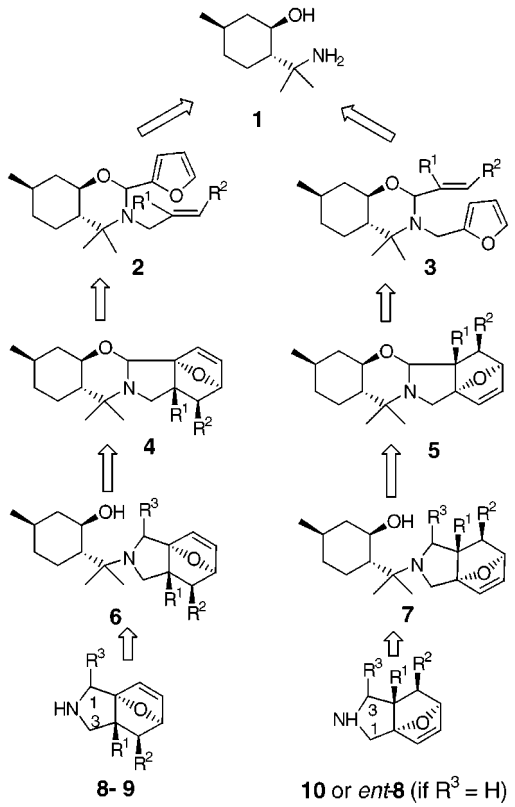



**Figure 1.**

was expected to give diastereomeric cycloadducts **4** and **5**, respectively, which, after reductive ring opening to **6** and **7**, followed by elimination of the menthol appendage will lead to **8** and *ent*-**8**. This switch in selectivity, which allows epoxytetrahydroisoindoline derivatives of opposite absolute configuration to be produced, is seen to be a consequence of changing the faces of both components that participate in the reaction. In addition, the ring opening of **4** and **5** by a nucleophile and elimination of the menthol allow regioisomeric 1- and 3-substituted epoxytetrahydroisoindoline derivatives **9** and **10** to be prepared.

## Results and Discussion

The preparation of 3-allyl-2-furyl-substituted perhydro-1,3-benzoxazines (**2a**−**d**) was achieved by condensation of (−)-8-allylaminomenthols **11a**−**d** with furfural. In turn, compounds **11a**−**d** were synthesized by alkylation of (−)-8-aminomenthol **1** with the corresponding allyl bromide, and **12** was prepared, in two steps, by condensation of **1** with furfural, followed by reduction of the N-unsubstituted 2-furyl perhydro-1,3-benzoxazine with sodium borohydride in methanol, at room temperature.

The condensation of **11a**−**d** with furfural did not occur under the standard conditions, even in the presence of Lewis acids.[15] Instead, the reactions took place after heating a mixture of **11a**−**d** and furfural (1.2 equiv) in toluene at reflux. Under these conditions, it was not possible to isolate perhydrobenzoxazine **2a** because it was totally transformed into a mixture of cycloadducts **4a** and **4′a** (97:3). On the contrary, Diels−Alder reaction of the isolated allylic perhydrobenzoxazines **2b**−**d**, with substituents at the dienophile, was not complete after heating for long periods of time (Table 1).

**Table 1. Diels-Alder Cycloaddition of Perhydro-1,3-benzoxazines 2a−d**

| oxazine | $R^1$ | $R^2$ | reaction time (h) | yield[a] (%) | products (ratio,%)[b] |
|---|---|---|---|---|---|
| **2a** | H | H | 120 | 93 | **4a** (97), **4′a** (3) |
| **2b** | Me | H | 240 | 60[c] | **4b** (97), **4′b** (3) |
| **2c** | H | Me | 160 | 80[d] | **4c** (97), **4′c** (3) |
| **2d** | H | Ph | 300 | 50[e] | **4d** (100) |

[a] Chemical yields of pure and isolated compounds. [b] Determined by integration of the signals of $^1$H NMR spectra of the reaction mixtures. [c] 35% of perhydrobenzoxazine **2b** was recovered. [d] 12% of perhydrobenzoxazine **2c** was recovered. [e] 37% of perhydrobenzoxazine **2d** was recovered.

The moderate chemical yield in intramolecular Diels−Alder reaction of the furan diene (IMDAF) and substituted dienophiles is a well-documented fact in both catalyzed[16] and uncatalyzed[17] processes and is a consequence of the reversible character of the reaction. By contrast, the reactions occurred with excellent, for compounds **2a**−**c**, or total, for compound **2d**, stereofacial discrimination. The absolute configuration of the cycloadducts was assigned by transformation into the epoxy isoindolines **8a**−**c** and *ent*-**8a**−**c** (vide infra).

The change of the substituents at the starting perhydro-1,3-benzoxazines would lead to obtain the enantiomeric tetrahydroepoxyisoindolines. To this end, the regioisomeric 2-vinyl-3-methylfurylperhydro-1,3-benzoxazines **3a**−**d** were prepared by condensation of 8-furfurylaminomenthol (**12**) with acrolein, methacrolein, crotonaldehyde, and cinnamaldehyde, respectively, in toluene at reflux (Scheme 1). As described for compounds **2a**−**d**, compounds **3a**,**b** were totally transformed into a mixture of cycloadducts **5a**,**b** and **5′a**,**b**, whereas **3c**,**d** give a mixture of cyclization products and unreacted perhydrobenzoxazines (Table 2).

It is interesting to note that the chemical yields for the cyclizations of **3a**−**d** were better than those of **2a**−**d**, but the diastereoselection decreased, varying from moderate, for **3c** or **3d**, to good, for **3a**,**b**. Nevertheless, the stereochemistry of cycloadducts **5a**−**c** and **5′a**−**c**, determined by correlation with *ent*-**8a**−**c** and **8a**−**c**, respectively, denoted that the IMDAF reaction followed the same trend as that for their regioisomeric **2a**−**d** counterpart. In this respect, only exo cyclization took place, leading to the thermodynamically more stable diastereoisomers **5a**−**d**.

After separation of the diastereoisomers by flash chromatography, they were converted into the enantiopure tetrahydroepoxyisoindolines **8** or *ent*-**8** in two steps (Scheme 2). Reductive ring opening of **4a**−**d** with a mixture of lithium aluminum hydride and aluminum trichloride in THF led to the menthol derivatives **6a**−**d** in excellent chemical yields, whereas the same treatment on **4′a**−**d** yielded diastereoisomers **6′a**−**d**. Cycloadduts **5a**−**d** or **5′a**−**d** were transformed into **6′a**−**d** or **6a**−**d**, respectively, by the same method. Elimination of the menthol appendage was carried out by oxidation of **6** and **6′** with PCC to the corresponding aminomenthone derivatives, which were not isolated, but immediately subjected to elimination by treatment with a solution of KOH in MeOH/ THF/ $H_2O$ to the known[18] tetrahydro-

(16) Hunt, I. R.; Rauk, A.; Keay, B. A. *J. Org. Chem.* **1996**, *61*, 751 and references therein.
(17) Gschwend, H. W.; Hillman, M. J.; Kiss, B.; Rodebaugh, R. K. *J. Org. Chem.* **1976**, *41*, 104.

**Scheme 1**

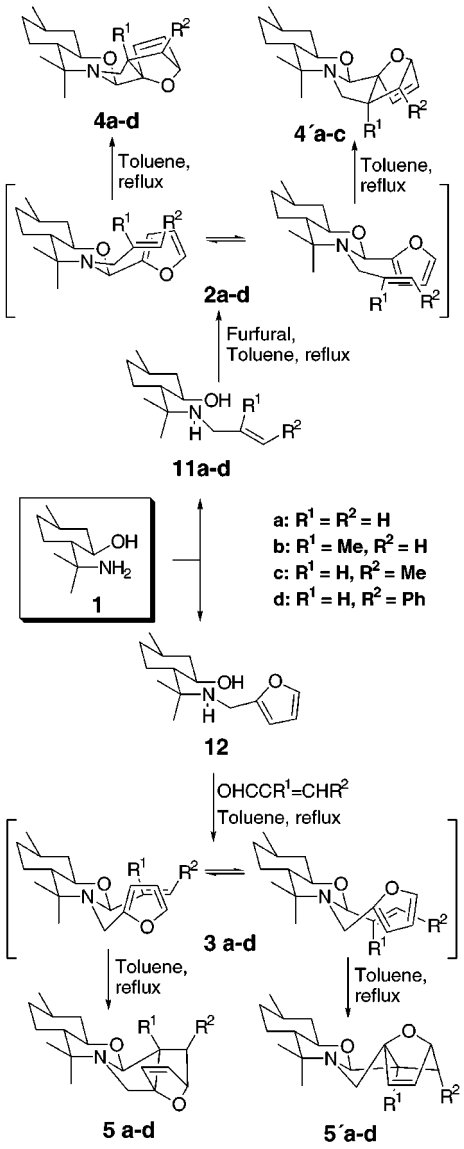



**Table 2. Diels–Alder Cycloaddition of Perhydro-1,3-benzoxazines 3a–d**

| oxazine | $R^1$ | $R^2$ | reaction time (h) | yield[a] (%) | products (ratio,%)[b] |
|---|---|---|---|---|---|
| **3a** | H | H | 80 | 96 | **5a** (90), **5′a** (10) |
| **3b** | Me | H | 240 | 85 | **5b** (91), **5′b** (9) |
| **3c** | H | Me | 100 | 80[c] | **5c** (77), **5′c** (23) |
| **3d** | H | Ph | 200 | 73[d] | **5d** (86), **5′d** (14) |

[a] Chemical yields of pure and isolated compounds. [b] Determined by integration of the signals of $^1$H NMR spectra of the reaction mixtures. [c] 13% of perhydrobenzoxazine **3c** was recovered. [d] 23% of perhydrobenzoxazine **3d** was recovered.

epoxyisoindolines **8a–c** and *ent*-**8a–c** and (+)-pulegone (Table 3).

It is noteworthy that all the aminomenthol derivatives **6** and **6′**, and tetrahydro isoindolines **8a–c**, and their enantiomers showed high thermal stability, but the isolation of both phenyl-substituted tetrahydroisoindolines **8d** or *ent*-**8d** was not possible because the oxidation–elimination protocol on **6d** and **6′d** was followed by

(18) Andrés, C.; García-Valverde, M.; Nieto, J.; Pedrosa, R. *J. Org. Chem.* **1999**, *64*, 5230.

**Scheme 2**

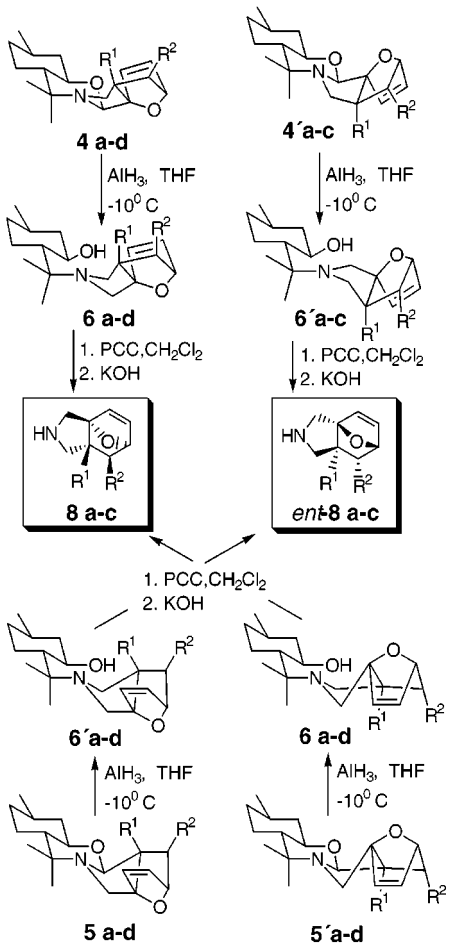
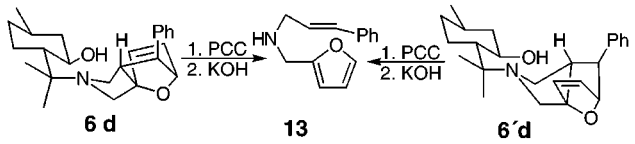



**Table 3. Reductive Ring Opening of Cycloadducts 4, 4′, 5, and 5′ and Elimination of the Menthol Appendage**

| entry | cycloaddut | aminomenthol (%) | tetrahydroepoxyisoindoline (%) |
|---|---|---|---|
| 1 | **4a** | **6a** (88) | **8a** (72) |
| 2 | **4b** | **6b** (90) | **8b** (73) |
| 3 | **4c** | **6c** (80) | **8c** (66) |
| 4 | **4d** | **6d** (77) | |
| 5 | **4′a** | **6′a** (83) | *ent*-**8a** (70) |
| 6 | **4′b** | **6′b** (80) | *ent*-**8b** (67) |
| 7 | **4′c** | **6′c** (91) | *ent*-**8c** (63) |
| 8 | **5a** | **6′a** (93) | *ent*-**8a** (65) |
| 9 | **5b** | **6′b** (88) | *ent*-**8b** (66) |
| 10 | **5c** | **6′c** (92) | *ent*-**8c** (70) |
| 11 | **5d** | **6′d** (90) | |
| 12 | **5′a** | **6a** (92) | **8a** (74) |
| 13 | **5′b** | **6b** (78) | **8b** (66) |
| 14 | **5′c** | **6c** (82) | **8c** (70) |
| 15 | **5′d** | **6d** (84) | |

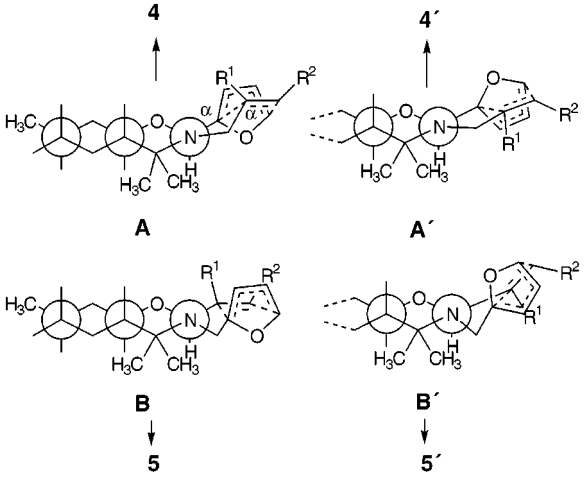
**Scheme 3**




a cycloreversion process[13b,c] leading to the cinnamyl furfurylamine **13** as the only product (Scheme 3).

The stereochemistry of **4d**, **5d**, and **5′d** was determined by COSY and NOESY experiments, and the enantiomeric relationship between the epoxyisoindolines obtained from **4a–c** and **4′a–c**, or from **5′a–c** or **5a–c**, allowed

**Scheme 4**




establishment of not only the stereochemistry of the cyclization products but also the stereochemical course of the reaction. As expected, the facial discrimination in the cycloadditions of **2a**−**d** and **3a**−**d** is imposed by the size of the tether between diene and dienophile,[19] the exo adducts being the only diastereoisomers formed. On the other hand, the formation of **4a**−**d** as single or major diastereoisomers from **2a**−**d** is the result of the interaction of the α-*Si* face of the dienophile toward the α-*Si* face of the diene, demonstrating that the less polar transition state **A** (Scheme 4) is favored over **A′**. Conversely, **5a**−**d**, the major diastereoisomers formed from **3a**−**d**, arise from the interaction of the α-*Re* face of the diene and α-*Re* face of the dienophile, also via the less polar transition state **B**. This facial discrimination, better than for the corresponding acrylamide derivatives, is a consequence of the thermodynamic control of the reaction, wich is dictated by the experimental conditions[14] (nonpolar solvent and high reaction temperature).

Taking into account the regiochemical relationship between cycloadducts **4** and **5** and the easy stereoselective ring opening of the N,O-acetals in perhydro-1,3-benzoxazine derivatives,[15] the synthesis of regioisomeric epoxytetrahydroisoindolines **9** and **10** was prepared by nucleophilic ring opening of cycloadducts with organometallics. To this end, **4a**−**d** were treated with excess of trimethylaluminum in toluene, at room temperature (Scheme 5). Under these conditions, reaction was completed after 15−20 min leading to methyl derivatives **14a**−**d**, in both excellent yields and diastereomeric excess (Table 4).

After purification by flash chromatography, compounds **14a**−**d** were transformed into the enantiopure 1-methylepoxytetrahydroisoindolines **9a**−**d** by oxidation−elimination in good yield except for compound **14d**. In this case, (*S*)-*N*-cinnamyl-1-furylethylamine (40%), resulting from the retro Diels−Alder reaction, was also isolated. Surprisingly, the reaction of **5a** with trimethylaluminum under the above conditions gave **7a** as a nearly equimolar mixture of epimers at the newly created stereocenter. Treatment of **5a**−**c** with 4 equiv of methylmagnesium iodide in diethyl ether, at room temperature, yielded in excellent yield a mixture of epimeric aminomenthol derivatives **7a**−**c** and **7′a**−**c**, in moderate de. The only exception was the reaction of **5b** (entry 7 in Table 4),

(19) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224.

**Scheme 5**

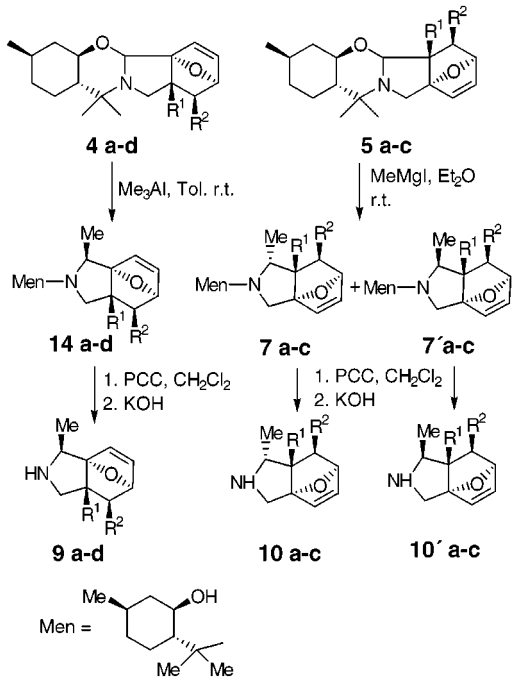



**Table 4. Ring Opening of Cycloadducts 4 and 5 by Organometallics and Elimination of the Menthol Appendage**

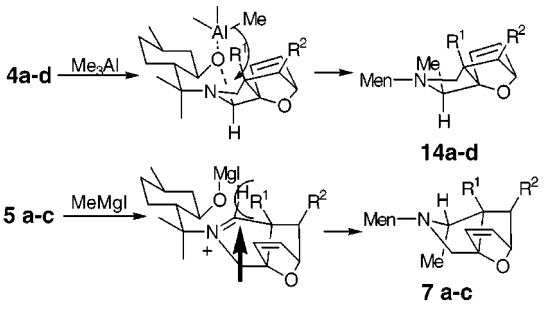
| | | | amino menthol | | |
|---|---|---|---|---|---|
| entry | cyclo-adduct | alkylmetal | yield[a] (%) | products[b] (dr) | epoxy-isoindoline[a] |
| 1 | **4a** | $Me_3Al$ | 97 | **14a** (100) | **9a** (80) |
| 2 | **4b** | $Me_3Al$ | 95 | **14b** (97) | **9b** (68) |
| | | | | **14′b** (3) | |
| 3 | **4c** | $Me_3Al$ | 93 | **14c** (97) | **9c** (72) |
| | | | | **14′c** (3) | |
| 4 | **4d** | $Me_3Al$ | 90 | **14d** (96) | **9d** (42) |
| | | | | **14′d** (4) | |
| 5 | **5a** | $Me_3Al$ | 94 | **7a** (49) | |
| | | | | **7′a** (51) | |
| 6 | **5a** | MeMgI | 90 | **7a** (68) | **10a** (76) |
| | | | | **7′a** (32) | **10′a** (70) |
| 7 | **5b** | MeMgI | 97 | **7b** (100) | **10b** (70) |
| 8 | **5c** | MeMgI | 92 | **7c** (75) | **10c** (72) |
| | | | | **7′c** (25) | **10′c** (68) |

[a] Chemical yields of pure and isolated compounds. [b] Determined by integration of the signals of $^1H$ NMR spectra of the reaction mixtures.

which gave **7b** with total stereoselection. After separation by flash chromatography, **7a**−**c** and **7′a**−**c** were individually transformed by the oxidation−elimination sequence into enantiopure 3-methylepoxytetrahydroisoindolines **10a**−**c** and **10′a**−**c**, respectively.

COSY and NOESY experiments allowed assignment of the configuration of the newly stereocenter (C-1) as *S* in compounds **9a**−**d**, whereas the configuration at C-3 in the major stereoisomers **10a**−**c** or minor ones **10′a**−**c**, arising from the opening of **5a**−**c** was assigned as *R* and *S*, respectively. These results indicated that the nucleophilic ring opening of **4a**−**d** with trimethylaluminum was highly stereoselective and that the reaction occurred from the oxygen face of the heterocycle with retention of the configuration. As expected, the opening of the heterocycle by Grignard derivatives occurred through the iminium ion,[15,20] from the less hindered face, leading to the inversion product as the major diastereo-

**Scheme 6**




isomer. The steric shielding of the α methyl group in the methacrolein derivative **7b** could explain the total stereoselection observed in this case (Scheme 6).

In summary, a short and efficient way to both enantiomers or regioisomers of enantiopure epoxyisoindolines, with four or five stereocenters has been achieved in five steps from (−)-8-aminomenthol. This methodology allows the introduction of a variety of substituents on the isoindoline nucleous and, combined with the transformations of the oxanorbornene moiety,[21] opens a way to the synthesis of complex structures.

## Experimental Section

**General Methods.** All reactions were carried out under argon atmosphere, in oven-dried glassware. $^1$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) were registered in $CDCl_3$ as solvent, and TMS as internal standard, and chemical shifts are given in ppm. Specific rotations were determined on a digital polarimeter using a Na lamp, and concentration is given in g per 100 mL. Melting points were obtained with open capillary tubes and are uncorrected. Solvents were dried by standard methods. 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 a Ce/Mo reagent. Flash column chromatography was carried out on silica gel 60 (230−240 mesh).

**Synthesis of 8-*N*-Methacrylaminomenthol (11b).** This compound was prepared as previously described[22] for **11a**, **11c**, and **11d** starting from a mixture of (−)-aminomenthol (1.71 g, 10 mmol), anhydrous $K_2CO_3$ (1.66 g, 1.2 mmol), and methacryl bromide (1.62 g, 1.2 mmol) in acetonitrile (70 mL). Colorless solid. Mp = 72−73 °C (from hexane). $[\alpha]^{25}_D = -17.6$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.82−1.03 (m, 3H), 0.85 (d, 3H, $J$ = 5.6 Hz), 1.08 (s, 3H), 1.09 (s, 3H), 1.24 (m, 1H), 1.39 (m, 1H), 1.56−1.64 (m, 2H), 1.71 (s, 3H), 1.88 (m, 1H), 3.04 (d, 1H, $J$ = 13.3 Hz), 3.16 (d, 1H, $J$ = 13.3 Hz), 3.57 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.3 Hz), 4.75 (s, 1H), 4.81 (s, 1H), 5.30−5.42 (broad s, 2H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 21.2, 21.5, 22.0, 25.7, 26.1, 30.9, 34.9, 44.4, 47.1, 49.7, 56.5, 72.4, 110.8, 143.5. IR (Nujol dispersion): $\nu$ = 3220, 1185 cm$^{-1}$. MS (chemical ionization): $m/z$ = 226 ($M^+ + 1$) (100). Anal. Calcd for $C_{14}H_{27}NO$: C, 74.61; H, 12.08; N, 6.21. Found: C, 74.40; H, 12.12; N, 6.02.

**Synthesis of 8-Furfurylaminomenthol (12).** A mixture of (−)-8-aminomenthol (8.55 g, 50 mmol), freshly distilled furfural (5.76 g, 60 mmol), and 4 Å molecular sieves (3 g) in anhydrous benzene (150 mL) was stirred at room temperature for 40h. The reaction mixture was filtered through Celite, and the solids were washed with benzene. The solvent was evaporated in vacuo, and the residue was recrystallized from pentane to give 2α-(2-furyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (11.95 g, 96%) as a colorless solid (mp 32−34 °C). To a solution of this compound (5 g, 20 mmol), in methanol (50 mL) was added in portions sodium borohydride (2.28 g, 60 mmol) for 1.5 h. The reaction mixture was stirred at room temperature for an additional 10 h and quenched by addition of a saturated aqueous solution of $NH_4Cl$ (50 mL) at 0 °C. After removal of the methanol in vacuo, the aqueous phase was extracted four times with EtOAc. The organic layer was washed with brine and dried over anhydrous $Na_2SO_4$. The solvent was evaporated, and the residue was recrystallized from hexane. Yield: 4.12 g, 82%. Colorless solid. Mp = 70−71 °C (from hexane). $[\alpha]^{25}_D = -26.6$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.87−1.08 (m, 3H), 0.91 (d, 3H, $J$ = 6.6 Hz), 1.16 (s, 3H), 1.17 (s, 3H), 1.34 (m, 1H), 1.42 (m, 1H), 1.60−1.71 (m, 2H), 1.95 (m,1H), 3.64 (dt, 1H, $J_1$ = 4.0 Hz, $J_2$ = 10.2 Hz), 3.75 (d, 1H, $J$ = 13.4 Hz), 3.84 (d, 1H, $J$ = 13.4 Hz), 6.18 (dd, 1H, $J_1$ = 0.7 Hz, $J_2$ = 3.1 Hz), 6.28 (dd, 1H, $J_1$ = 1.8 Hz, $J_2$ = 3.1 Hz), 7.33 (dd, 1H, $J_1$ = 0.7 Hz, $J_2$ = 1.8 Hz),8.12−8.46 (br s, 2H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 21.6, 22.1, 25.8, 26.2, 31.0, 35.0, 38.6, 44.4, 49.6, 56.8, 72.4, 106.6, 110.2, 141.8, 153.2. IR (Nujol dispersion): $\nu$ = 3240, 1590 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 251 ($M^+$) (1), 81 (100). Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.02; N, 5.57. Found: C, 71.42; H, 10.31; N, 5.82.

**Synthesis of Octahydro-1,3-benzoxazines 2a−d and Cycloaddition to 4a−d.** A solution of furfural (2.4 g, 25 mmol) and the corresponding 8-allylaminomenthol **11a**−**d** (10 mmol) in dry toluene (25 mL) was refluxed on a Dean−Stark trap for 48−72h. The solvent and the excess of furfural were eliminated in vacuo, and the residue was chromatographed on silica gel using hexanes−EtOAc (3:1 for **4a**−**c** and 8:1 for **4d**). Under these conditions, it was not possible to isolate **2a** because it was totally transformed into **4a**; the yields for the reactions are given in Table 1.

***N*-Methacryl-2α-(2-furyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2b).** Colorless oil. $[\alpha]^{25}_D = -24.9$ ($c$ = 2.8, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.80−0.91 (m, 2H), 0.84 (d, 3H, $J$ = 6.5 Hz), 1.02−1.16 (m, 1H), 1.03 (s, 3H), 1.14 (s, 3H), 1.35−1.52 (m, 2H), 1.42 (s, 3H), 1.53−1.63 (m, 2H), 1.87 (m, 1H), 2.87 (d, 1H, $J$ = 17.6 Hz), 3.17 (d, 1H, $J$ = 17.6 Hz), 3.49 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 4.48 (d, 1H, $J$ = 0.8 Hz), 4.72 (d, 1H, $J$ = 0.8 Hz), 5.50 (s, 1H), 6.14 (dd, 1H, $J_1$ = 1.7 Hz, $J_2$ = 3.3 Hz), 6.20 (dd, 1H, $J_1$ = 0.8 Hz, $J_2$ = 3.3 Hz), 7.18 (dd, 1H, $J_1$ = 0.8 Hz, $J_2$ = 1.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 19.0, 20.1, 22.1, 24.9, 26.4, 31.2, 34.8, 41.1, 46.1, 49.5, 56.7, 76.2, 83.7, 107.3, 109.2, 109.8, 141.1, 145.1, 152.7. IR (neat): $\nu$ = 3060, 1150 cm$^{-1}$. Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.51; H, 9.88; N, 4.45.

***N*-Crotyl-2α-(2-furyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2c).** Colorless oil. $[\alpha]^{25}_D = -14.3$ ($c$ = 3.4, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.84−0.95 (m, 2H), 0.85 (d, 3H, $J$ = 6.5 Hz), 1.04−1.19 (m, 1H), 1.12 (s, 3H), 1.14 (s, 3H), 1.34−1.53 (m, 2H), 1.42 (dd, 3H, $J_1$ = 1.3 Hz, $J_2$ = 6.3 Hz), 1.53−1.64 (m, 2H), 1.88 (m, 1H), 2.83 (dd, 1H, $J_1$ = 6.2 Hz, $J_2$ = 16.2 Hz), 3.16 (dd, 1H, $J_1$ = 6.2 Hz, $J_2$ = 16.2 Hz), 3.48 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 4.97 (dq, 1H, $J_1$ = 6.3 Hz, $J_2$ = 15.2 Hz), 5.12 (dtq, 1H, $J_1$ = 1.3 Hz, $J_2$ = 6.2 Hz, $J_3$ = 15.2 Hz), 5.45 (s, 1H), 6.21 (dd, 1H, $J_1$ = 1.8 Hz, $J_2$ = 3.2 Hz), 6.26 (dd, 1H, $J_1$ = 1.0 Hz, $J_2$ = 3.2 Hz), 7.25 (dd, 1H, $J_1$ = 1.0 Hz, $J_2$ = 1.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.5, 18.0, 22.0, 24.9, 26.8, 31.1, 34.8, 41.1, 46.1, 46.8, 56.9, 75.9, 83.3, 108.0, 109.8, 124.5, 131.5, 141.3, 152.2. IR (neat): $\nu$ = 3060, 1150 cm$^{-1}$. Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.47; H, 9.79; N, 4.80.

***N*-Cinnamyl-2α-(2-furyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (2d).** Colorless oil. $[\alpha]^{25}_D = -9.3$ ($c$ = 1.6, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.92−1.12 (m, 2H), 1.00 (d, 3H, $J$ = 6.5 Hz), 1.18−1.32 (m, 1H), 1.30 (s, 3H), 1.32 (s, 3H), 1.54 (m, 1H), 1.65 (m, 1H), 1.69−1.79 (m, 2H), 2.11 (m, 1H), 3.21 (dd, 1H, $J_1$ = 5.3 Hz, $J_2$ = 16.8 Hz), 3.53 (dd, 1H, $J_1$ = 4.9 Hz, $J_2$ = 16.8 Hz), 3.67 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 5.65 (s, 1H), 6.02−6.17 (m, 2H), 6.33 (dd, 1H, $J_1$ = 1.8 Hz, $J_2$ = 3.1 Hz), 6.45 (d, 1H, $J$ = 3.1 Hz), 7.18−7.34 (m, 6H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 18.1, 22.2, 25.0, 26.9, 31.2, 34.8, 41.3, 46.6, 47.1, 57.2, 76.2, 83.5, 108.3, 110.0, 126.0 (2C), 126.6, 128.2 (2C), 128.6, 131.2, 137.5, 141.8, 149.3. IR (neat): $\nu$ = 3015, 1150 cm$^{-1}$. Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 79.04; H, 8.81; N, 3.62.

(20) Wu, M. J.; Pridgen, L. N. *J. Org. Chem.* **1991**, *56*, 1340.
(21) Woo, S.; Keay, B. A. *Synthesis* **1996**, 669.
(22) Andrés, C.; Duque-Soladana, J. P.; Pedrosa, R. *J. Org. Chem.* **1999**, *64*, 4273.

**Cycloadduct (4a).** Colorless solid. Mp = 70−71 °C (from hexane). $[\alpha]^{25}_D = -69.9$ ($c = 1.0$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.88−1.14 (m, 3H), 0.93 (d, 3H, $J$ = 6.5 Hz), 1.15 (s, 3H), 1.19 (s, 3H), 1.42−1.63 (m, 4H), 1.74 (m, 2H), 1.93 (m, 1H), 2.20 (m, 1H), 2.71 (dd, 1H, $J_1$ = 5.8 Hz, $J_2$ = 9.3 Hz), 3.32 (t, 1H, $J$ = 9.3 Hz), 3.53 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 4.95 (s, 1H), 5.03 (dd, 1H, $J_1$ = 1.4 Hz, $J_2$ = 4.3 Hz), 6.24 (dd, 1H, $J_1$ = 1.4 Hz, $J_2$ = 5.8 Hz), 6.56 (d, 1H, $J$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 20.3, 22.3, 24.8, 26.1, 31.3, 32.5, 35.1, 40.0, 41.6, 44.7, 48.5, 53.2, 75.0, 79.3, 84.9, 96.7, 134.5, 134.6. IR (Nujol dispersion): $\nu$ = 1600, 1100 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 289 ($M^+$) (4), 41 (100). Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 75.01; H, 9.46; N, 4.71.

**Cycloadduct (4′a).** Yellow oil. $[\alpha]^{25}_D = +16.7$ ($c = 1.8$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.82−1.02 (m, 2H), 0.90 (d, 3H, $J$ = 6.6 Hz), 1.02−1.18 (m, 1H), 1.06 (s, 3H), 1.14 (s, 3H), 1.36−1.52 (m, 2H), 1.46 (dd, 1H, $J_1$ = 8.1 Hz, $J_2$ = 11.3 Hz), 1.64 (m, 2H), 1.77 (dt, 1H, $J_1$ = 4.4 Hz, $J_2$ = 11.3 Hz), 1.87−2.00 (m, 2H), 2.88 (dd, 1H, $J_1$ = 7.3 Hz, $J_2$ = 8.7 Hz), 3.08 (t, 1H, $J$ = 8.7 Hz), 3.48 (dt, 1H, $J_1$ = 4.2 Hz, $J_2$ = 10.5 Hz), 5.05 (s, 1H), 5.11 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.29 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.45 (d, 1H, $J$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 14.9, 22.1, 24.8, 26.5, 31.2, 31.4, 34.8, 40.6, 41.2, 47.2, 48.1, 54.2, 75.9, 79.8, 83.8, 95.1, 134.7,135.8. IR (neat): $\nu$ = 1600, 1105 cm$^{-1}$. Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.52; H, 9.59; N, 4.96.

**Cycloadduct (4b).** Colorless solid. Mp = 67−68 °C (from pentane). $[\alpha]^{25}_D = -22.3$ ($c = 1.1$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.83−1.08 (m, 3H), 0.93 (d, 3H, $J$ = 6.6 Hz), 1.08−1.21 (m, 1H), 1.09 (s, 3H), 1.14 (s, 3H), 1.20 (s, 3H), 1.44−1.57 (m, 2H), 1.62 (m, 1H), 1.72 (m, 1H), 1.93 (m, 1H), 2.14 (dd, 1H, $J_1$ = 4.6 Hz, $J_2$ = 11.2 Hz), 3.02 (d, 1H, $J$ = 9.3 Hz), 3.07 (d, 1H, $J$ = 9.3 Hz), 3.50 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.4 Hz), 4.96 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.6 Hz), 5.02 (s, 1H), 6.31 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.55 (d, 1H, $J$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 20.7, 22.3, 24.8, 25.9, 27.6, 31.2, 35.1, 41.9, 42.1, 44.7, 46.4, 52.8, 57.6, 74.4, 79.1, 85.0, 97.4, 133.1, 134.6. IR (Nujol dispersion): $\nu$ = 3080, 1100 cm$^{-1}$. MS (chemical ionization): $m/z$ = 304 ($M^+ + 1$) (74), 191 (100). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 74.96; H, 9.42; N, 4.78.

**Cycloadduct (4c).** Colorless solid. Mp = 80−81 °C (from pentane). $[\alpha]^{25}_D = -100.2$ ($c = 1.0$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.82−1.11 (m, 3H), 0.83 (d, 3H, $J$ = 7.0 Hz), 0.89 (d, 3H, $J$ = 6.5 Hz), 1.13 (s, 3H), 1.15 (s, 3H), 1.41−1.52 (m, 2H), 1.60 (m,1H), 1.71 (m, 2H), 1.94 (m, 1H), 2.12 (m, 1H), 2.73 (dd, 1H, $J_1$ = 5.5 Hz, $J_2$ = 9.2 Hz), 3.32 (t, 1H, $J$ = 9.2 Hz), 3.52 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 4.77 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 4.90 (s, 1H), 6.22 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.61 (d, 1H, $J$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.3, 20.5, 22.3, 24.8, 26.0, 31.3, 35.1, 41.1, 41.6, 44.4, 48.2, 48.5, 53.1, 74.9, 82.6, 85.1, 97.7, 132.6, 135.6. IR (Nujol dispersion): $\nu$ = 3060, 1110 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 303 ($M^+$) (3), 55 (100). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.49; H, 9.78; N, 4.81.

**Cycloadduct (4′c).** Yellow oil. $[\alpha]^{25}_D = +3.3$ ($c = 1.1$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.84−1.20 (m, 3H), 0.86 (d, 3H, $J$ = 7.1 Hz), 0.96 (d, 3H, $J$ = 6.6 Hz), 1.05 (s, 3H), 1.14 (s, 3H), 1.31−1.50 (m, 3H), 1.50−1.72 (m, 2H), 1.96 (m, 1H), 2.19 (m, 1H), 2.93 (dd, 1H, $J_1$ = 6.9 Hz, $J_2$ = 8.7 Hz), 3.11 (t, 1H, $J$ = 8.7 Hz), 3.46 (dt, 1H, $J_1$ = 4.2 Hz, $J_2$ = 10.5 Hz), 4.89 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 4.97 (s, 1H), 6.29 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.53 (d, 1H, $J$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 14.6, 17.1, 22.1, 24.8, 26.5, 31.3, 34.7, 39.6, 41.1, 46.7, 48.1, 49.0, 54.3, 75.9, 83.2, 83.9, 95.9, 133.7, 135.8. IR (neat): $\nu$ = 3040, 1110 cm$^{-1}$. Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.00; H, 9.85; N, 4.50.

**Cycloadduct (4d).** Yellowish oil. $[\alpha]^{25}_D = -165.1$ ($c = 1.3$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.77−1.10 (m, 3H), 0.88 (d, 3H, $J$ = 6.5 Hz), 1.10 (s, 3H), 1.16 (s, 3H), 1.38−1.45 (m, 2H), 1.56 (m, 1H), 1.66 (m, 1H), 1.89 (m, 1H), 2.41 (ddd, 1H, $J_1$ = 4.4 Hz, $J_2$ = 5.3 Hz, $J_3$ = 9.3 Hz), 2.85 (dd, 1H, $J_1$ = 5.3 Hz, $J_2$ = 9.3 Hz), 3.32 (t, 1H, $J$ = 4.4 Hz), 3.38 (t, 1H, $J$ = 9.3 Hz), 3.49 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 4.92 (s, 1H), 4.98 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.08 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.71 (d, 1H, $J$ = 5.8 Hz), 7.04−7.20 (m, 5H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 20.2, 22.2, 24.7, 25.9, 31.2, 34.9, 41.4, 44.4, 48.4, 48.6, 52.2, 53.2, 75.0, 83.1, 84.9, 98.3, 126.4, 127.8, (2C), 128.0 (2C), 132.8, 135.3, 140.2. IR (neat): $\nu$ = 3020, 1490 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 365 ($M^+$) (1), 117 (100). Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 78.61; H, 8.81; N, 4.01.

**Synthesis of Octahydro-1,3-benzoxazines 3a−d and Cycloaddition to 5a−d.** A solution of 8-furfurylaminomenthol **12** (2.11 g, 10 mmol) and acrolein, methacrolein, crotonaldehyde, or cinnamaldehyde (12 mmol) in anhydrous toluene was refluxed for 96 h on a Dean−Stark trap. The solvent was eliminated in vacuo, and the residue was subjected to flash chromatography on silica gel using hexanes−EtOAc (5:1 for **5a**, 5:1 for **5c**, or 8:1 for **5d**) or EtOAc−$CHCl_3$ 1:40 (for **5b**) as eluents. Under these conditions, compounds **3a** and **3b** cannot be isolated because they were totally transformed into the corresponding cycloadducts. The yields for the reactions are given in Table 2.

***N*-Furfuryl-2α-(1-propenyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (3c).** Colorless oil. $[\alpha]^{25}_D = -34.8$ ($c = 0.6$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.88−1.00 (m, 2H), 0.92 (d, 3H, $J$ = 6.5 Hz), 1.00−1.20 (m, 2H), 1.11 (s, 3H), 1.17 (s, 3H), 1.38−1.53 (m, 2H), 1.63−1.75 (m,1H), 1.65 (dd, 3H, $J_1$ = 1.5 Hz, $J_2$ = 6.5 Hz), 1.93 (m, 1H), 3.49 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.6 Hz), 3.61 (d, 1 H, $J$ = 17.1 Hz), 3.90 (d, 1H, $J$ = 17.1 Hz), 4.96 (dd, 1H, $J_1$ = 0.9 Hz, $J_2$ = 5.5 Hz), 5.46 (ddq, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.5 Hz, $J_3$ = 15.4 Hz), 5.83 (ddq, 1H, $J_1$ = 0.9 Hz, $J_2$ = 6.5 Hz, $J_3$ = 15.4 Hz), 6.03 (m, 1H), 6.27 (dd, 1H $J_1$ = 1.9 Hz, $J_2$ = 3.0 Hz), 7.29 (m, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.8, 18.0, 22.2, 25.1, 26.9, 31.3, 34.9, 41.0, 41.3, 47.1, 56.8, 75.4, 87.7, 106.1, 110.0, 129.3, 130.8, 140.7, 157.0. IR (neat): $\nu$ = 1600, 1380 cm$^{-1}$. Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.52; H, 9.84; N, 4.45.

***N*-Furfuryl-2α-(1-cinnamyl)-4,4,7α-trimethyl-*trans*-octahydro-1,3-benzoxazine (3d).** Yellow oil. $[\alpha]^{25}_D = -41.2$ ($c$ = 2.8, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.85−1.03 (m, 2H), 0.94 (d, 3H, $J$ = 6.5 Hz), 1.08−1.39 (m, 1H), 1.19 (s, 3H), 1.21 (s, 3H), 1.40−1.60 (m, 2H), 1.64−1.76 (m, 2H), 1.99 (m, 1H), 3.56 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 3.65 (d, 1H, $J$ = 16.9 Hz), 3.95 (d, 1H, $J$ = 16.9 Hz), 5.22 (dd, 1H, $J_1$ = 0.9 Hz, $J_2$ = 4.8 Hz), 6.02 (dd, 1H, $J_1$ = 0.6 Hz, $J_2$ = 3.1 Hz), 6.15 (dd, 1H, $J_1$ = 4.8 Hz, $J_2$ = 16.1 Hz), 6.23 (dd, 1H, $J_1$ = 1.8 Hz, $J_2$ = 3.1 Hz), 6.72 (dd, 1H, $J_1$ = 0.9 Hz, $J_2$ = 16.1 Hz), 7.14−7.30 (m, 6H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 18.9, 22.2, 25.0, 26.9, 31.3, 34.9, 41.0, 41.3, 46.6, 56.9, 75.6, 87.2, 106.3, 110.0, 126.6 (2C), 127.5, 128.3 (2C), 129.1, 132.0, 136.7, 140.9, 156.7. IR (neat): $\nu$ = 3020, 1595 cm$^{-1}$. Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 78.52; H, 8.72; N, 4.01.

**Cycloadduct 5a.** Colorless solid. Mp = 71−72 °C (from pentane). $[\alpha]^{25}_D = -26.7$ ($c = 1.0$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.89−1.07 (m, 2H), 0.93 (d, 3H, $J$ = 6.5 Hz), 0.95 (s, 3H), 1.10−1.17 (m, 1H), 1.16 (s, 3H), 1.26 (m,1H), 1.39−1.53 (m, 2H), 1.68−1.72 (m, 2H), 1.89−1.99 (m, 3H), 3.08 (d, 1H, $J$ = 11.2 Hz), 3.37 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.5 Hz), 3.67 (d, 1H, $J$ = 11.2 Hz), 4.14 (d, 1H, $J$ = 6.9 Hz), 5.01 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 6.31 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.7 Hz), 6.41 (d, 1H, $J$ = 5.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 11.3, 22.1, 24.7, 26.6, 28.6, 31.4, 34.7, 41.4, 45.7, 48.3, 50.1, 54.7, 76.4, 79.7, 91.6, 92.6, 136.1, 136.6. IR (neat): $\nu$ = 3070, 1560 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 289 ($M^+$) (2), 81 (100). Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.49; H, 9.65; N, 4.81.

**Cycloadduct 5′a.** Colorless solid. Mp = 104−105 °C (from hexane/EtOAc). $[\alpha]^{25}_D = -57.7$ ($c = 1.0$, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.89−1.03 (m, 2H), 0.91 (d, 3H, $J$ = 6.4 Hz), 1.07−1.27 (m, 2H), 1.17 (s, 3H), 1.20 (s, 3H), 1.40−1.51 (m, 2H), 1.58 (m, 1H), 1.69 (m, 1H), 1.84 (m, 1H), 1.98−2.09 (m, 2H), 3.31 (d, 1H, $J$ = 10.9 Hz), 3.39 (dt, 1H, $J_1$ = 4.2 Hz, $J_2$ = 10.3 Hz), 3.48 (d, 1H, $J$ = 10.9 Hz), 4.85 (d, 1H, $J$ = 4.4 Hz), 5.02 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.1 Hz), 6.22 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.7 Hz), 6.49 (d, 1H, $J$ = 5.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 21.9, 22.2, 24.3, 24.8, 26.5, 31.1, 35.0, 41.4, 43.0, 47.5, 49.2, 53.7, 74.5, 79.2, 84.1, 94.6, 135.4, 138.1. IR (Nujol dispersion): $\nu$ = 3090, 1330 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 289 ($M^+$)

(15), 81 (100). Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.91; H, 9.29; N, 4.62.

**Cycloadduct 5b.** Colorless solid. Mp = 95−96 °C (from hexane). $[\alpha]^{25}_D = -24.53$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.87−0.95 (m, 3H), 0.90 (m, 3H), 0.91 (s, 3H), 0.92 (d, 3H, $J$ = 6.6 Hz), 1.03−1.23 (m, 2H), 1.10 (s, 3H), 1.44 (m, 1H), 1.65−1.70 (m, 2H), 1.95 (m, 1H), 2.13 (dd, 1H, $J_1$ = 4.7 Hz, $J_2$ = 11.5 Hz), 3.04, d, 1H, $J$ = 11.4 Hz), 3.34 (dt, 1H, $J_1$ = 4.2 Hz, $J_2$ = 10.5 Hz), 3.52 (d, 1H, $J$ = 11.4 Hz), 4.22 (s, 1H), 4.92 (dd, 1H, $J_1$ = 1.2 Hz, $J_2$ = 4.7 Hz), 6.37 (d, 1H, $J$ = 5.8 Hz), 6.38 (d, 1H, $J$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 10.6, 17.3, 22.2, 24.7, 26.8, 31.4, 34.7, 37.2, 41.4, 44.5, 49.9, 50.6, 54.3, 76.1, 79.9, 93.4, 94.6, 134.6, 136.9. IR (Nujol dispersion): $\nu$ = 3060 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 303 ($M^+$,7), 81 (100). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.43; H, 9.89; N, 4.79.

**Cycloadduct 5′b.** Yellowish oil. $[\alpha]^{25}_D = -10.9$ ($c$ = 3.1, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.77−0.90 (m, 3H), 0.90 (d, 3H, $J$ = 6.5 Hz), 0.94 (s, 3H), 1.67 (m, 1H), 1.85 (m, 1H), 2.43 (dd, 1H, $J_1$ = 4.7 Hz, $J_2$ = 10.9 Hz), 3.30 (d, 1H, $J$ = 10.8 Hz), 3.37 (dt, 1H, $J_1$ = 4.2 Hz, $J_2$ = 10.4 Hz), 3.42 (d, 1H, $J$ = 10.8 Hz), 4.51 (s, 1H), 4.91 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.7 Hz), 6.34 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.6 Hz), 6.40 (d, 1H, $J$ = 5.6 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 21.6, 22.3, 24.3, 24.9, 26.4, 31.4, 33.9, 35.0, 41.5, 43.8, 47.2, 52.7, 53.3, 74.7, 79.2, 90.6, 96.2, 134.2 (2C). IR (neat): $\nu$ = 3080, 1190 cm$^{-1}$. Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.50; H, 9.40; N, 4.51.

**Cycloadduct 5c.** Colorless solid. Mp = 85−86 °C (from pentane). $[\alpha]^{25}_D = +8.8$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.85−1.01 (m, 2H), 0.88 (d, 3H, $J$ = 7.1 Hz), 0.93 (d, 3H, $J$ = 6.5 Hz), 0.96 (s, 3H), 1.02−1.14 (m, 1H), 1.14 (s, 3H), 1.28 (m, 1H), 1.44 (m, 1H), 1.51 (dd, 1H, $J_1$ = 3.4 Hz, $J_2$ = 6.6 Hz), 1.61−1.74 (m, 2H), 1.96 (m, 1H), 2.33 (m, 1H), 3.00 (d, 1H, $J$ = 11.1 Hz), 3.35 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.6 Hz), 3.61 (d, 1H, $J$ = 11.1 Hz), 4.22 (d, 1H, $J$ = 6.6 Hz), 4.80 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 6.29 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.7 Hz), 6.50 (d, 1H, $J$ = 5.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 11.9, 17.0, 22.1, 24.7, 26.6, 31.4, 34.7, 36.9, 41.5, 46.0, 49.7, 54.5, 56.9, 76.1, 83.2, 91.1, 93.4, 134.4, 137.2. IR (Nujol dispersion): $\nu$ = 3030 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 303 ($M^+$) (2), 81 (100). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.47; H, 9.69; N, 4.49.

**Cycloadduct 5′c.** Colorless oil. $[\alpha]^{25}_D = -70.3$ ($c$ = 0.6, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.82−1.01 (m, 2H), 0.85 (d, 3H, $J$ = 7.2 Hz), 0.91 (d, 3H, $J$ = 6.5 Hz), 1.05−1.28 (m, 2H), 1.16 (s, 3H), 1.20 (s, 3H), 1.44−1.53 (m, 2H), 1.58 (m, 1H), 1.71 (m, 1H), 1.85 (m, 1H), 2.47 (m, 1H), 3.24 (d, 1H, $J$ = 10.8 Hz), 3.40 (dt, 1H, $J_1$ = 4.3 Hz, $J_2$ = 10.4 Hz), 3.44 (d, 1H, $J$ = 10.8 Hz), 4.79 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 4.89 (d, 1H, $J$ = 4.7 Hz), 6.25 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 6.56 (d, 1H, $J$ = 5.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.0, 21.9, 22.2, 24.8, 26.5, 31.4, 31.9, 35.0, 41.4, 42.9, 47.8, 53.7, 57.5, 74.6, 82.8, 83.8, 95.5, 133.5, 138.9. IR (neat): $\nu$ = 3060, 1330 cm$^{-1}$. Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.52; H, 9.80; N, 4.78.

**Cycloadduct 5d.** Colorless solid. Mp = 118−119 °C (from hexane/EtOAc). $[\alpha]^{25}_D = +141.2$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.83−0.98 (m, 2H), 0.91 (d, 3H, $J$ = 6.5 Hz), 1.00−1.12 (m, 1H), 1.02 (s, 3H), 1.19 (s, 3H), 1.22−1.33 (m, 1H), 1.40 (m, 1H), 1.65−1.71 (m, 2H), 1.92 (m, 1H), 2.29 (dd, 1H, $J_1$ = 4.2 Hz, $J_2$ = 6.4 Hz), 3.12 (d, 1H, $J$ = 11.2 Hz), 3.37 (dt, 1H, $J_1$ = 4.2 Hz, $J_2$ = 10.5 Hz), 3.58 (t, 1H, $J$ = 4.2 Hz), 3.72 (d, 1H, $J$ = 11.2 Hz), 4.39 (d, 1H, $J$ = 6.4 Hz), 5.15 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.2 Hz), 6.16 (dd, 1H, $J_1$ = 1.6, $J_2$ = 5.7 Hz), 6.57 (d, 1H, $J$ = 5.7 Hz), 7.10−7.25 (m, 5H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 12.1, 22.1, 24.7, 26.6, 31.4, 34.7, 41.4, 46.0, 48.0, 49.6, 54.7, 56.4, 76.2, 83.4, 91.4, 93.9, 126.3, 128.0 (2C), 128.1 (2C), 135.0, 137.0, 140.2. IR (Nujol dispersion): $\nu$ = 3030, 1360 cm$^{-1}$. MS (EI, 70 eV): $m/z$ = 365 ($M^+$) (2), 81 (100). Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 79.08; H, 8.32; N, 3.61.

**Cycloaddut 5′d.** Colorless oil. $[\alpha]^{25}_D = -198.4$ ($c$ = 0.9, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.86−1.00 (m, 2H), 0.92 (d, 3H, $J$ = 6.5 Hz), 1.12−1.27 (m, 1H), 1.18 (s, 3H), 1.20 (s, 3H), 1.37−1.54 (m, 2H), 1.60 (m, 1H), 1.62−1.71 (m, 1H), 1.90 (m, 1H), 2.28 (dd, 1H, $J_1$ = 4.6 Hz, $J_2$ = 4.8 Hz), 3.34 (d, 1H, $J$ = 10.8 Hz), 3.40 (dt, 1H, $J_1$ = 4.1 Hz, $J_2$ = 10.3 Hz), 3.53 (d, 1H, $J$ = 10.8 Hz), 3.75 (dd, 1H, $J_1$ = 4.4 Hz, $J_2$ = 4.8 Hz), 4.93 (d, 1H, $J$ = 4.6 Hz), 5.05 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.14 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.6 Hz), 6.67 (d, 1H, $J$ = 5.6 Hz), 7.11−7.27 (m, 5H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 22.0, 22.2, 24.8, 26.5, 31.3, 35.0, 41.4, 42.9 (2C), 47.7, 53.7, 56.9, 74.6, 83.4, 83.7, 96.1, 126.3, 128.0 (2C), 128.1 (2C), 133.9, 138.6, 140.6. IR (neat): $\nu$ = 3040, 1330 cm$^{-1}$. Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 78.59; H, 8.41; N, 3.68.

**Reductive Ring Opening of 4a−d and 5a−d to 6a−d and 6′a−d.** Compounds **6a**−**d** and **6′a**−**d** were prepared by reduction with LAH−$AlCl_3$ in THF at −10 °C as previously described.[18] Compounds **6a**−**c** and **6′a**−**c** have been previously described.[18]

**(3a*S*,6*R*,7*R*,7a*S*)-*N*-(8-Mentholyl)-3a,6-epoxy-7-phenyl-3a,6,7,7a-tetrahydroisoindoline (6d).** Colorless solid. Mp = 104−105 °C (from hexane). $[\alpha]^{25}_D = +136.8$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.89−1.11 (m, 3H), 0.93 (d, 3H, $J$ = 6.5 Hz), 1.02 (s, 3H), 1.21 (s, 3H), 1.34−1.54 (m, 2H), 1.54−1.71 (m, 2H), 1.95 (m, 1H), 2.24 (m,1H), 2.55 (m, 1H), 3.04 (d, 1H, $J$ = 11.8 Hz), 3.33−3.39 (m, 2H), 3.66 (dt, 1H, $J_1$ = 3.9 Hz, $J_2$ = 10.3 Hz), 3.69 (m, 1H), 5.08 (dd, 1H, $J_1$ = 1.4 Hz, $J_2$ = 4.4 Hz), 6.13 (dd, 1H, $J_1$ = 1.4 Hz, $J_2$ = 5.7 Hz), 6.60 (d, 1H, $J$ = 5.7 Hz), 7.07 (m, 2H), 7.16−7.27 (m, 3H), 8.59 (s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.1, 21.9, 22.1, 25.5, 31.0, 35.0, 44.1, 47.4, 48.5, 48.9, 50.5, 51.2, 59.4, 73.0, 84.1, 96.6, 126.5, 127.9 (2C), 128.2 (2C), 134.6, 136.7, 139.7. IR (Nujol dispersion): $\nu$ = 3100, 1320 cm$^{-1}$. MS (chemical ionization): $m/z$ = 368 ($M^+$ + 1) (100), 254 (52). Anal. Calcd for $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.72; H, 8.91; N, 3.69.

**(3a*R*,6*S*,7*S*,7a*R*)-*N*-(8-Mentholyl)-3a,6-epoxy-7-phenyl-3a,6,7,7a-tetrahydroisoindoline (6′d)**. Colorless solid. Mp = 107−108 °C (from hexane). $[\alpha]^{25}_D = -167.8$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.79−1.08 (m, 3H), 0.89 (d, 3H, $J$ = 6.5 Hz), 1.00 (s, 3H), 1.20 (s, 3H), 1.42 (m, 1H), 1.50−1.68 (m, 3H), 1.90 (m, 1H), 2.22 (m, 1H), 2.42 (m, 1H), 2.99 (d, 1H, $J$ = 10.4 Hz), 3.32 (dd, 1H, $J_1$ = 4.0 Hz, $J_2$ = 4.4 Hz), 3.46−3.61 (m, 2H), 3.65 (dt, 1H, $J_1$ = 3.9 Hz, $J_2$ = 10.2 Hz), 5.04 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.4 Hz), 6.12 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.7 Hz), 6.55 (d, 1H, $J$ = 5.7 Hz), 7.04−7.28 (m, 5H), 8.29 (br s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.8, 21.2, 22.0, 25.7, 30.9, 35.0, 44.2, 47.7, 48.4 (2C), 50.3, 50.9, 59.2, 72.7, 84.0, 96.1, 126.4, 127.9 (2C), 128.0 (2C), 134.4, 136.7, 139.4. IR (Nujol dispersion): $\nu$ = 3140, 1600 cm$^{-1}$. MS (chemical ionization): $m/z$ = 368 ($M^+$ + 1) (100), 254 (85). Anal. Calcd for $C_{24}H_{33}NO_2$: C, 78.43; H, 9.05; N, 3.81. Found: C, 78.67; H, 9.26; N, 3.71.

**Reaction of 5a−c with Methylmagnesium Iodide. Synthesis of 7a−c.** To a solution of the corresponding adducts **5a**−**c** (2.5 mmol) in diethyl ether (20 mL), under argon, was slowly syringed a 0.5 M solution of methylmagnesium iodide (20 mL, 10 mmol). After the addition was completed, the reaction mixture was refluxed for 6 h and then cooled to 0 °C. The reaction was quenched by addition, at 0 °C, of a saturated $NH_4Cl$ solution (30 mL); the organic phase was decanted, and the aqueous layer was extracted five times with EtOAc. The organic extracts were washed with brine and dried over anhydrous $Na_2SO_4$. The solvents were evaporated in vacuo, and the residues were chromatographed on silica gel using hexanes−EtOAc (3:1) for **7c** or hexanes−EtOH (10:1) for **7a** and **7b** as eluents.

**(1*R*,3a*S*,6*S*,7a*S*)-*N*-(8-Mentholyl)-3a,6-epoxy-1-methyl-3a,6,7,7a-tetrahydroisoindoline (7a).** Colorless solid. Mp = 92−93 °C (from hexane/EtOAc). $[\alpha]^{25}_D = -4.7$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.88−1.49 (m, 14H), 0.91 (d, 3H, $J$ = 6.5 Hz), 1.50−1.90 (m, 4H), 1.92−2.04 (m, 2H), 3.04−3.18 broad, 1H), 3.21−3.45 (broad, 1H), 3.60−3.72 (m, 2H), 4.97 (dd, 1H, $J_1$ = 1.4 Hz, $J_2$ = 4.5 Hz), 6.31 (broad, 1H), 6.47 (broad, 1H), 8.70 (br s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 14.0, 19.2, 19.8, 22.1, 23.9, 25.6, 31.0, 35.1, 43.9, 44.6, 48.1, 54.6, 58.8, 61.3, 72.8, 79.4, 95.2, 136.1, 137.6. IR (Nujol dispersion): $\nu$ = 3110, 1050 cm$^{-1}$. MS (chemical ionization): $m/z$ = 306 ($M^+$ +

1) (100), 192 (38). Anal. Calcd for $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.96; H, 10.08; N, 4.38.

**(1*S*,3a*S*,6*S*,7a*S*)-*N*-(8-Mentholyl)-3a,6-epoxy-1-methyl-3a,6,7,7a-tetrahydroisoindoline (7′a).** Colorless solid. Mp = 98−99 °C (from pentane). $[\alpha]^{25}_D = -44.9$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.87−1.16 (m, 3H), 0.92 (d, 3H, $J$ = 6.5 Hz), 0.99 (s, 3H), 1.23 (s, 3H), 1.30 (d, 3H, $J$ = 5.9 Hz), 1.33−1.50 (m, 3H), 1.55−1.78 (m, 4H), 1.92−1.97 (m, 1H), 2.85 (dq, 1H, $J_1$ = 5.9 Hz, $J_2$ = 8.7 Hz), 3.42 (d, 1H, $J$ = 13.2 Hz), 3.66 (d, 1H, $J$ = 13.2 Hz), 3.70 (dt, $J_1$ = 4.0 Hz, $J_2$ = 10.3 Hz), 5.00 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.4 Hz), 6.30 (d, 1H, $J$ = 5.8 Hz), 6.34 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.8 Hz), 9.10 (br s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 19.0, 22.1, 22.4, 24.0, 25.4, 31.0, 31.9, 35.1, 44.3, 49.7, 50.1, 52.0, 60.1, 61.6, 72.9, 79.5, 93.5, 134.9, 136.7. IR (Nujol dispersion): $\nu$ = 3080, 1170 cm$^{-1}$. MS (chemical ionization): $m/z$ = 306 ($M^+$ + 1) (100), 192 (48). Anal. Calcd for $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.49; H, 10.42; N, 4.68.

**(1*R*,3a*S*,6*S*,7a*S*)-*N*-(8-Mentholyl)-3a,6-epoxy-1,7a-dimethyl-3a,6,7,7a-tetrahydroisoindoline (7b).** Colorless solid. Mp = 119−120 °C (from hexane). $[\alpha]^{25}_D = -41.2$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.87−1.23 (m, 7H), 0.91 (d, 3H, $J$ = 6.5 Hz), 1.09 (s, 3H), 1.29 (m, 6H), 1.32−1.50 (m, 1H), 1.58−1.70 (m, 3H), 1.93−2.04 (m, 1H), 2.30 (m, 1H), 3.00−3.50 (broad, 3H), 3.64 (dt, 1H, $J_1$ = 3.8 Hz, $J_2$ = 10.3 Hz), 4.87 (dd, 1H, $J_1$ = 1.3 Hz, $J_2$ = 4.9 Hz), 6.33 (broad, 1H), 6.41 (m, 1H), 7.78 (br s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 22.1 (4C), 26.1, 26.4, 31.1, 35.3 (2C), 37.4, 44.6, 48.3, 50.1, 60.1, 73.1, 79.0, 96.5, 134.3, 137.4, 137.5. IR (Nujol dispersion): $\nu$ = 3100, 1190 cm$^{-1}$. MS (chemical ionization): $m/z$ = 320 ($M^+$ + 1) (100), 318 (21). Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 74.90; H, 10.32; N, 4.17.

**(1*R*,3a*S*,6*S*,7*R*,7a*S*)-*N*-(8-Mentholyl)-3a,6-epoxy-1,7-dimethyl-3a,6,7,7a-tetrahydroisoindoline (7c).** Colorless solid. Mp = 109−110 °C (from hexane). $[\alpha]^{25}_D = +21.2$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.80 (d, 3H, $J$ = 7.0 Hz), 0.83−1.51 (m, 14H), 0.91 (d, 3H, $J$ = 6.5 Hz), 1.61 (m, 2H), 1.72 (m, 1H), 1.92 (m, 1H), 2.14 (broad, 1H), 2.96 (broad, 1H), 3.54−3.78 (m, 3H), 4.77 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.5 Hz), 6,28 (m, 1H), 6.55 (broad, 1H), 8.63 (br s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 14.4, 17.1, 19.9, 22.1, 23.8, 25.6, 31.0, 33.6, 35.2, 44.0, 44.6, 48.1, 54.1, 56.4, 58.7, 72.8, 83.1, 96.4, 133.7, 138.8. IR (Nujol dispersion): $\nu$ = 3090 cm$^{-1}$. MS (chemical ionization): $m/z$ = 320 ($M^+$ + 1) (100), 318 (22). Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.38; H, 10.50; N, 4.51.

**(1*S*,3a*S*,6*S*,7*R*,7a*S*)-*N*-(8-Mentholyl)-3a,6-epoxy-1,7-dimethyl-3a,6,7,7a-tetrahydroisoindoline (7′c).** Colorless solid. Mp = 137−138 °C (from hexane). $[\alpha]^{25}_D = -5.9$ ($c$ = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.85 (d, 3H, $J$ = 7.1 Hz), 0.91−1.07 (m, 3H), 0.92 (d, 3H, $J$ = 6.5 Hz), 0.98 (s, 3H), 1.17−1.27 (m, 1H), 1.22 (s, 3H), 1.32 (d, 3H, $J$ = 5.9 Hz), 1.43 (m, 2H), 1.55 (m, 1H), 1.66 (m, 1H), 1.94 (m, 1H), 2.20 (m, 1H), 2.93 (dq, 1H, $J_1$ = 5.9 Hz, $J_2$ = 8.5 Hz), 3.33 (d, 1H, $J$ = 13.3 Hz), 3.62 (d, 1H, $J$ = 13.3 Hz), 3.69 (dt, 1H, $J_1$ = 4.0 Hz, $J_2$ = 10.3 Hz), 4.82 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.31 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.39 (d, 1H, $J$ = 5.8 Hz), 9.05 (s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.1, 18.9, 22.1, 22.4, 24.8, 25.4, 31.0, 35.1, 40.8, 44.3, 50.1, 50.2, 60.1, 60.6, 61.5, 72.9, 83.3, 94.5, 134.6, 136.1. IR (Nujol dispersion): $\nu$ = 3080, 1070 cm$^{-1}$. MS (chemical ionization): $m/z$ = 320 ($M^+$ + 1) (100), 318 (23). Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 74.92; H, 10.29; N, 4.36.

**Reaction of 4a−d with Trimethylaluminum. Synthesis of 14a−d.** Compounds **4a−d** were reacted with $Me_3Al$ in toluene at room temperature as previously described.[15] The yields are collected in Table 4.

**(3*S*,3a*R*,6*R*,7a*R*)-*N*-(8-Mentholyl)-3a,6-epoxy-3-methyl-3a,6,7,7a-tetrahydroisoindoline (14a).** Colorless solid. Mp = 118−119 °C (from hexane). $[\alpha]^{25}_D = -10.6$ ($c$ = 1.1, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.85−1.08 (m, 3H), 0.91 (d, 3H, $J$ = 6.6 Hz), 1.00 (s, 3H), 1.27 (s, 3H), 1.32−1.46 (m, 2H), 1.37 (d, 3H, $J$ = 6.7 Hz), 1.47−1.64 (m,2H), 1.65−1.75 (m, 2H), 1.92 (m, 1H), 2.02 (m, 1H), 2.43 (dd, 1H, $J_1$ = 8.8 Hz, $J_2$ = 10.0 Hz), 3.40 (q, 1H, $J$ = 6.7 Hz), 3.52 (dd, 1H, $J_1$ = 7.8 Hz, $J_2$ = 8.8 Hz), 3.69 (dt, 1H $J_1$ = 3.9 Hz, $J_2$ = 10.1 Hz), 4.98 (dd, 1H, $J_1$ =1.6 Hz, $J_2$ = 4.5 Hz), 6.32 (d, 1H, $J$ = 5.8 Hz), 6.37 (dd, 1H, $J_1$ =1.6 Hz, $J_2$ = 5.8 Hz), 8.63 (s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 18.9, 21.9, 22.1, 23.0, 25.4, 30.8, 31.0, 34.9, 38.8, 43.9, 48.6, 52.6, 52.9, 60.1, 72.8, 79.1, 98.4, 133.4, 136.4. IR (Nujol dispersion): $\nu$ = 3100, 1560 cm$^{-1}$. MS (chemical ionization): $m/z$ = 306 ($M^+$ + 1) 100), 304 (22). Anal. Calcd for $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.48; H, 10.08; N, 4.41.

**(3*S*,3a*R*,6*R*,7a*R*)-*N*-(8-Mentholyl)-3a,6-epoxy-3,7a-dimethyl-3a,6,7,7a-tetrahydroisoindoline (14b).** Colorless solid. Mp = 134−135 °C (from hexane). $[\alpha]^{25}_D = +29.9$ ($c$ = 1.1, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.83−1.04 (m, 4H), 0.84 (d, 3H, $J$ = 6.5 Hz), 0.92 (s, 3H), 0.97 (s, 3H), 1.20 (s, 3H), 1.32−1.40 (m, 1H), 1.35 (d, 3H, $J$ = 6.9 Hz), 1.50 (m, 2H), 1.59 (m, 1H), 1.86 (m, 1H), 1.98 (dd, 1H, $J_1$ = 4.6 Hz, $J_2$ = 11.0 Hz), 2.64 (d, 1H, $J$ = 8.4 Hz), 3.19 (d, 1H, $J$ = 8.4 Hz), 3.29 (q, 1H, $J$ = 6.8 Hz), 3.63 (dt, 1H, $J_1$ = 3.9 Hz, $J_2$ = 10.3 Hz), 4.82 (d, 1H, $J$ = 4.6 Hz), 6.32 (s, 2H), 8.53 (s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 18.7, 21.8, 22.3, 22.4, 23.1, 25.4, 30.7, 34.8, 39.6, 44.0, 46.3, 48.6, 53.3, 58.7, 60.1, 72.8, 79.0, 99.4, 132.6, 135.6. IR (Nujol dispersion): $\nu$ = 3120, 1630 cm$^{-1}$. MS (chemical ionization): $m/z$ = 320 ($M^+$ + 1) (48), 206 (100). Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.42; H, 10.32; N, 4.26.

**(3*S*,3a*R*,6*S*,7*S*,7a*R*)-*N*-(8-Mentholyl)-3a,6-epoxy-3,7-dimethyl-3a,6,7,7a-tetrahydroisoindoline (14c).** Colorless solid. Mp = 114−115 °C (from pentane). $[\alpha]^{25}_D = -48.1$ ($c$ = 1.1, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.72−0.97 (m, 3H), 0.74 (d, 3H, $J$ = 7.1 Hz), 0.84 (d, 3H, $J$ = 6.6 Hz), 0.92 (s, 3H), 1.18 (s, 3H), 1.28 (d, 3H, $J$ = 6.7 Hz), 1.37 (m, 1H), 1.50 (m, 3H), 1.62 (m, 1H), 1.85 (m, 1H), 2.08 (m, 1H), 2.41 (dd, 1H $J_1$ = 8.8 Hz, $J_2$ = 9.9 Hz), 3.25 (q, 1H, $J$ = 6.7 Hz), 3.53 (dd, 1H, $J_1$ = 7.7 Hz, $J_2$ = 8.8 Hz), 3.62 (dt, 1H, $J_1$ = 3.9 Hz, $J_2$ = 10.3 Hz), 4.74 (dd, 1H, $J_1$ = 1.7 Hz, $J_2$ = 4.5 Hz), 6.28 (dd, 1H, $J_1$ = 1.7 Hz, $J_2$ = 5.9 Hz), 6.35 (d, 1H, $J$ = 5.9 Hz), 8.56 (s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 16.4, 19.0, 22.1, 22.3, 23.3, 25.6, 31.0, 25.1, 39.8, 44.1, 47.7, 48.9, 52.6, 53.5, 60.3, 73.0, 83.1, 99.7, 134.5, 134.8. IR (Nujol dispersion): $\nu$ = 3120, 1610 cm$^{-1}$. MS (chemical ionization): $m/z$ = 320 ($M^+$ + 1) (33), 166 (100). Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.37; H, 10.59; N, 4.49.

**(3*S*,3a*R*,6*S*,7*S*,7a*R*)-*N*-(8-Mentholyl)-3a,6-epoxy-3-methyl-7-phenyl-3a,6,7,7a-tetrahydroisoindoline (14d).** Colorless oil. $[\alpha]^{25}_D = -163.2$ ($c$ = 2.1, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.77−1.00 (m, 3H), 0.83 (d, 3H, $J$ = 6.5 Hz), 0.98 (s, 3H), 1.22 (s, 3H), 1.27−1.38 (m, 1H), 1.35 (d, 3H, $J$ = 6.7 Hz), 1.48−1.54 (m, 2H), 1.60 (m, 1H), 1.85 (m, 1H), 2.32 (m, 1H), 2.59 (dd, 1H, $J_1$ = 9.1 Hz, $J_2$ = 9.8 Hz), 3.32−3.38 (m, 2H), 3.59−3.69 (m, 2H), 5.05 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.07 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.42 (d, 1H, $J$ = 5.8 Hz), 6.96−7.20 (m, 5H), 8.45 (s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 19.1, 22.1, 22.4, 23.4, 25.7, 31.0, 35.1, 44.1, 47.2, 49.0, 51.1, 53.2, 53.5, 60.5, 73.1, 83.5, 100.2, 126.4, 127.9 (2C), 128.1 (2C), 134.6, 135.1, 139.5. IR (neat): $\nu$ = 3080, 1600 cm$^{-1}$. MS (chemical ionization): $m/z$ = 382 ($M^+$ + 1) (100), 268 (84). Anal. Calcd for $C_{25}H_{35}NO_2$: C, 78.70; H, 9.25; N, 3.67. Found: C, 78.99; H, 9.51; N, 3.58.

**Elimination of the Menthol Appendage. Synthesis of the Final Epoxytetrahydroisoindolines.** The elimination of the menthol appendage was carried out in two steps by oxidation−elimination as previously described.[22] The total yields for both steps are summarized in Tables 3 and 4. Compounds **8a−c** and *ent*-**8a−c** have been previously described.[18]

**(3*S*,3a*R*,6*R*,7a*R*)-3a,6-Epoxy-3-methyl-3a,6,7,7a-tetrahydroisoindoline (9a).** Colorless oil. $[\alpha]^{25}_D = -34.5$ ($c$ = 1.2, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 1.27 (d, 3H, $J$ = 6.9 Hz), 1.36 (dd, 1H, $J_1$ =7.7 Hz, $J_2$ = 11.5 Hz), 1.66 (ddd, 1H, $J_1$ = 3.0 Hz, $J_2$ = 4.4 Hz, $J_3$ = 11.5 Hz), 1.95 (ddt, 1H, $J_1$ =3.0 Hz, $J_2$ = 7.7 Hz, $J_3$ = 9.4 Hz), 2.57 (dd, 1H $J_1$ = 9.4 Hz, $J_2$ = 10.4 Hz), 3.25 (dd, 1H, $J_1$ = 7.7 Hz, $J_2$ = 10.4 Hz), 3.35 (s, 1H), 3.42 (q, 1H, $J$ = 6.9 Hz), 4.96 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.4 Hz), 6.30 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.9 Hz), 6.34 (d, 1H, $J$ = 5.9 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 19.2, 31.0, 43.2, 51.0, 53.5, 79.4, 100.6,

133.6, 136.5. IR (neat): $\nu$ = 3300, 1050 cm$^{-1}$. Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.78; H, 8.80; N, 9.17.

**(3*S*,3a*R*,6*R*,7a*R*)-3a,6-epoxy-3,7a-dimethyl-3a,6,7,7a-tetrahydro isoindoline (9b).** Colorless oil. $[\alpha]^{25}_D$ = +32.2 (*c* = 1.5, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.85 (s, 3H), 0.86 (d, 1H *J* = 11.3 Hz), 1.23 (d, 3H, *J* = 7.0 Hz), 1.91 (dd, 1H, $J_1$ = 4.7 Hz, $J_2$ = 11.3 Hz), 2.65 (s, 1H), 2.78 (d, 1H, *J* = 9.9 Hz), 2.83 (d, 1H, *J* = 9.9 Hz), 3.31 (q, 1H, *J* = 7.0 Hz), 4.82 (d, 1H, *J* = 4.7 Hz), 6.22−6.30 (m, 2H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 20.3, 22.5, 38.7, 49.3, 53.4, 58.2, 79.4, 101.1, 132.7, 135.7. IR (neat): $\nu$ = 3310, 1370 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.91; H, 8.96; N, 8.29.

**(3*S*,3a*R*,6*S*,7*S*,7a*R*)-3a,6-Epoxy-3,7-dimethyl-3a,6,7,7a-tetrahydro isoindoline (9c).** Colorless oil. $[\alpha]^{25}_D$ = −80.7 (*c* = 2.4, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.86 (d, 3H, *J* = 7.1 Hz), 1.29 (d, 3H, *J* = 6.9 Hz), 1.56 (ddd, 1H, $J_1$ = 3.2 Hz, $J_2$ = 7.8 Hz, $J_3$ = 8.8 Hz), 2.15 (m, 1H), 2.69 (dd, 1H, $J_1$ = 8.8 Hz, $J_2$ = 10.7 Hz), 3.13 (s, 1H), 3.35 (dd, 1H, $J_1$ = 7.8 Hz, $J_2$ = 10.7 Hz), 3.41 (q, 1H, *J* = 6.9 Hz), 4.83 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.36 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.9 Hz), 6.50 (d, 1H, *J* = 5.9 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 16.9, 19.0, 39.9, 50.6, 52.0, 54.1, 82.9, 101.8, 134.5, 134.9. IR (neat): $\nu$ = 3320, 1375 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.45; H, 9.36; N, 8.59.

**(3*S*,3a*R*,6*S*,7*S*,7a*R*)-3a,6-Epoxy-3-methyl-7-phenyl-3a,6,7,7a-tetrahydro isoindoline (9d).** Colorless oil. $[\alpha]^{25}_D$ = −200.3 (*c* = 1.2, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 1.26 (d, 3H, *J* = 6.9 Hz), 2.22 (ddd, 1H, $J_1$ = 3.9 Hz, $J_2$ = 7.8 Hz, $J_3$ = 8.6 Hz), 2.75 (dd, 1H, $J_1$ = 8.6 Hz, $J_2$ = 10.7 Hz), 2.92 (s, 1H), 3.27 (dd, 1H, $J_1$ = 3.9 Hz, $J_2$ = 4.4 Hz), 3.34 (dd, 1H, $J_1$ = 7.8 Hz, $J_2$ = 10.7 Hz), 3.40 (q, 1H, *J* = 6.9 Hz), 5.00 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.4 Hz), 6.12 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.9 Hz), 6.52 (d, 1H, *J* = 5.9 Hz), 7.01−7.19 (m, 5H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 18.9, 50.8, 51.0, 52.0, 53.8, 83.3, 102.3, 126.4, 127.8 (2C), 128.0 (2C), 134.6, 134.7, 139.9. IR (neat): $\nu$ = 3250, 1325 cm$^{-1}$. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.52; H, 7.51; N, 5.98.

**(1*R*,3a*S*,6*S*,7a*S*)-3a,6-Epoxy-1-methyl-3a,6,7,7a-tetrahydroisoindoline (10a).** Colorless oil. $[\alpha]^{25}_D$ = +17.0 (*c* = 0.7, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 1.20 (d, 3H, *J* = 7.0 Hz), 1.32 (dd, 1H, $J_1$ = 8.4 Hz, $J_2$ = 11.9 Hz), 1.85 (ddd, 1H, $J_1$ = 3.6 Hz, $J_2$ = 4.6 Hz, $J_3$ = 11.9 Hz), 2.18 (ddd, 1H, $J_1$ = 3.6 Hz, $J_2$ = 8.4 Hz, $J_3$ = 8.7 Hz), 3.40 (d, 1H, *J* = 13.5 Hz), 3.45 (d, 1H, *J* = 13.5 Hz), 3.71 (dq, 1H, $J_1$ = 7.0 Hz, $J_2$ = 8.7 Hz), 4.96 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.6 Hz), 6.05 (br s, 1H), 6.32 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.8 Hz), 6.38 (d, 1H, *J* = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.4, 27.9, 46.3 (2C), 54.0, 79.0, 97.2, 134.5, 137.1. IR (neat): $\nu$ = 3340, 1060 cm$^{-1}$. Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.21; H, 8.89; N, 9.02.

**(1*S*,3a*S*,6*S*,7a*S*)-3a,6-Epoxy-1-methyl-3a,6,7,7a-tetrahydroisoindoline (10′a).** Colorless oil. $[\alpha]^{25}_D$ = −23.7 (*c* = 1.0, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 1.19 (d, 3H, *J* = 6.5 Hz), 1.35 (dd, 1H, $J_1$ = 7.7 Hz, $J_2$ = 11.2 Hz, $J_3$ = 8.7 Hz), 1.46 (ddd, 1H, $J_1$ = 2.8 Hz, $J_2$ = 7.7 Hz, $J_3$ = 9.1 Hz), 1.69 (ddd, 1H, $J_1$ = 2.8 Hz, $J_2$ = 4.4 Hz, $J_3$ = 11.2 Hz), 2.45 (s, 1H), 2.91 (dq, 1H, $J_1$ = 6.5 Hz, $J_2$ = 9.1 Hz), 3.28 (d, 1H, *J* = 12.8 Hz), 3.53 (d, 1H, *J* = 12.8 Hz), 5.04 (dd, 1H, $J_1$ = 1.7 Hz, $J_2$ = 4.4 Hz), 6.32 (dd, 1H, $J_1$ = 1.7 Hz, $J_2$ = 5.7 Hz), 6.42 (d, 1H, *J* = 5.7 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 19.6, 29.3, 47.9, 52.1, 59.4, 80.2, 98.9, 136.0, 136.2. IR (neat): $\nu$ = 3300, 1070 cm$^{-1}$. Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.32; H, 8.46; N, 9.15.

**(1*R*,3a*S*,6*S*,7a*S*)-3a,6-Epoxy-1,7a-dimethyl-3a,6,7,7a-tetrahydroisoindoline (10b).** Colorless oil. $[\alpha]^{25}_D$ = −55.1 (*c* = 1.2, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.90 (s, 3H), 0.98 (d, 1H, *J* = 11.8 Hz), 1.17 (d, 3H, *J* = 6.7 Hz), 2.22 (dd, 1H, $J_1$ = 4.9 Hz, $J_2$ = 11.8 Hz), 3.07 (q, 1H, *J* = 6.7 Hz), 3.12 (d, 1H, *J* = 13.2 Hz), 3.19 (s, 1H), 3.28 (d, 1H, *J* = 13.2 Hz), 4.88 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.9 Hz), 6.40 (d, 1H, *J* = 5.8 Hz), 6.48 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 20.0, 27.3, 37.3, 46.5, 50.8, 61.8, 77.9, 99.7, 133.6, 137.4. IR (neat): $\nu$ = 3400, 1420 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}NO$: C, 72,69; H, 9.15; N, 8.48. Found: C, 72.88; H, 9.01; N, 8.31.

**(1*R*,3a*S*,6*S*,7*R*,7a*S*)-3a,6-Epoxy-1,7-dimethyl-3a,6,7,7a-tetrahydroisoindoline (10c).** Colorless oil. $[\alpha]^{25}_D$ = +66.9 (*c* = 0.5, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.80 (d, 3H, *J* = 7.0 Hz), 1.34 (d, 3H, *J* = 7.0 Hz), 1.76 (dd, 1H, $J_1$ = 3.9 Hz, $J_2$ = 8.6 Hz), 2.28 (m, 1H), 3.46 (d, 1H, *J* = 13.2 Hz), 3.52 (d, 1H, *J* = 13.2 Hz), 3.91 (dq, 1H, $J_1$ = 7.0 Hz, $J_2$ = 8.6 Hz), 4.80 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 4.5 Hz), 6.33 (dd, 1H, $J_1$ = 1.5 Hz, $J_2$ = 5.8 Hz), 6.46 (d, 1H, *J* = 5.8 Hz), 7.47 (br s, 1H). $^{13}$C NMR ($CDCl_3$): $\delta$ = 17.5, 18.5, 35.6, 48.4, 53.3, 55.7, 81.6, 99.9, 134.3, 136.1. IR (neat): $\nu$ = 3250, 1070 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.47; H, 9.36; N, 8.59.

**(1*S*,3a*S*,6*S*,7*R*,7a*S*)-3a,6-Epoxy-1,7-dimethyl-3a,6,7,7a-tetrahydro isoindoline (10′c).** Colorless oil. $[\alpha]^{25}_D$ = +23.9 (*c* = 0.7, $CH_2Cl_2$). $^1$H NMR ($CDCl_3$): $\delta$ = 0.85 (d, 3H, *J* = 7.1 Hz), 1.11 (dd, 1H, $J_1$ = 3.2 Hz, $J_2$ = 9.3 Hz), 1.28 (d, 3H, *J* = 6.3 Hz), 2.13 (m, 1H), 3.04 (dq, 1H, $J_1$ = 76.3 Hz, $J_2$ = 9.3 Hz), 3.24 (d, 1H, *J* = 12.9 Hz), 3.57 (d, 1H, *J* = 12.9 Hz), 4.07 (br s, 1H), 4.86 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 4.3 Hz), 6.32 (dd, 1H, $J_1$ = 1.6 Hz, $J_2$ = 5.8 Hz), 6.53 (d, 1H, *J* = 5.8 Hz). $^{13}$C NMR ($CDCl_3$): $\delta$ = 16.8, 19.3, 37.9, 47.8, 59.3, 60.3, 83.7, 99.4, 134.1, 136.8. IR (neat): $\nu$ = 3350, 1080 cm$^{-1}$. Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.41; H, 9.32; N, 8.69.

**Acknowledgment.** The authors thank the Spanish DGICYT (Project PB95-707) and Junta de Castilla y León (VA79/99) for financial support of this work. J.N. also thanks the Spanish MEC for a predoctoral fellowship (FPU).

**Supporting Information Available:** Copies of $^{13}$C NMR spectra for compounds **2b**−**d**, **3c**−**d**, **4a**−**d**, **4′a**−**c**, **5a**−**d**, **5′a**−**d**, **6d**, **6′d**, **7a**−**c**, **7′a**−**c**, **9a**−**d**, **10a**−**c**, **10′a**−**c**, **11b**, **12**, and **14a**−**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO991544Q